Polytrauma patient management: Processes and performance in the Netherlands and beyond

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ISBN: 978-94-6361-465-8

Cover Design: Erwin Timmerman
Lay-out and print: Optima Grafische Communicatie, Rotterdam, The Netherlands

Financial support for the publication of this thesis was kindly provided by Trauma Centrum West, ABN Amro Nederland and Chipsoft.

Polytrauma patient management:

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Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof. mr. C.J.J.M. Stolker,
volgens besluit van het College voor Promoties
te verdedigen op donderdag 29 oktober 2020
klokke 16.15 uur

door

Suzan Dijkink
geboren te Hengelo (Ov.) op 25 juli 1992

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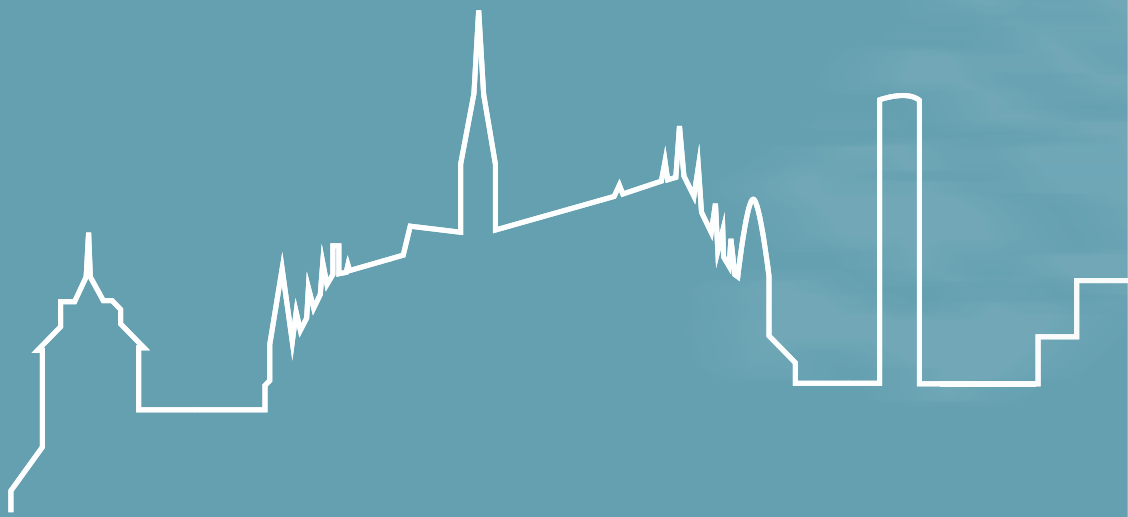


1

General introduction, aim and outline of the thesis

On average, every six seconds someone dies as a consequence of accidental or intentional trauma, resulting in more than 5 million deaths per year around the globe.[1] Trauma is one of the leading causes of death in people under 45 years of age. It is estimated that injuries are responsible for 16% of the total disease burden and 9% of total mortality worldwide.[1] Data from the World Health Organization (WHO) estimate that the number of deceased caused by violence and injuries to be nearly twice as high as the combined number of deaths from HIV / AIDS, tuberculosis, and malaria worldwide. [Figure 1]

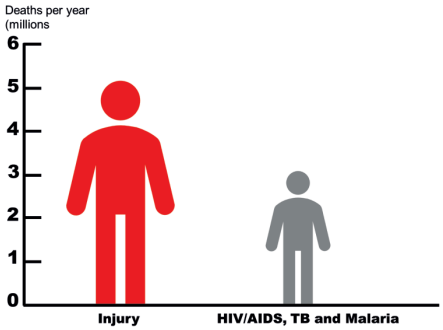


Figure 1. Number of deaths (in millions per year) as a consequence of traumatic injuries and HIV/AIDS, tuberculosis and malaria[1]

Even so, the millions of deaths that occur each year due to injuries are only the tip of the iceberg of the entire burden of trauma-related disease, as shown in Figure 2. For every death there are many more who survive their injuries but are left with permanent disability. Injuries are estimated to be responsible for up to 6% of all years lived with disability.[1] Therefore, despite trauma being recognized as a major public health problem for over 50 years, it still remains "the neglected disease of modern society".[2]

Besides leading to physical, emotional, and economic losses for the victims and their families, the financial burden of trauma affects nations as a whole, primarily in relation to the young and working population, as they are being precluded from production.[3] For example, it has been estimated that the consequences of road traffic crashes consume approximately 2% of the gross domestic product (GDP) of high-income countries and around 5% of the GDP of low- and middle-income countries.[1] Costs are expected to increase even further in the future. The WHO indicates that the number of injury-related deaths will rise dramatically, partly due to a projected 65% increase in road traffic deaths and injuries worldwide.[4, 5]

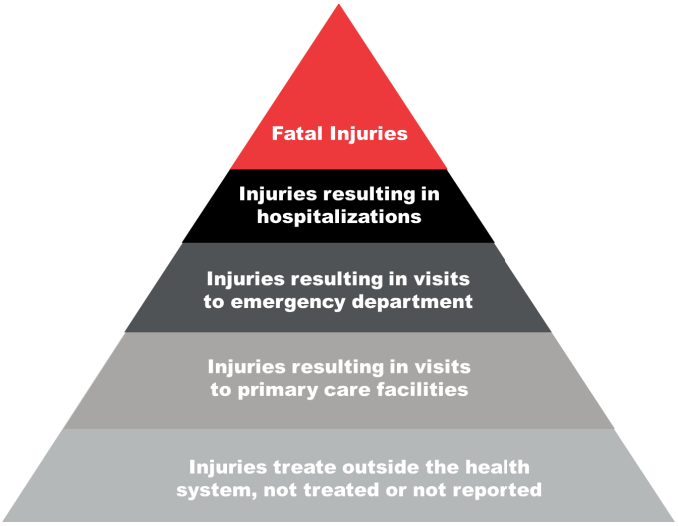


Figure 2. Pyramid of injuries reported in the health care system.[1]

DEVELOPMENT OF TRAUMA CARE SYSTEMS

Up until the second half of the 20th century trauma was managed in an unstructured and unpredictable way, without any organized approach or system. The patient was usually transferred directly to the closest hospital and trauma care was provided by the on-call general surgeon, regardless of interest or expertise in trauma. Thus, the quality of care the injured patient received was more or less dependent upon chance. This became painfully obvious after the tragic airplane crash of Dr. Styner and his family.[2] The care that he and his family received in rural Nebraska was considered below the standards of customary clinical care. This event and the finding that a large proportion of the trauma deaths were "*preventable deaths*" further motivated improvements in trauma care.[6, 7] Among multiple processes and interventions, it led to the introduction of the Advanced Trauma Life Support (ATLS) and the extensive document of the American College of Surgeons (ACS) that describes the guidelines on optimizing hospital resources for the injured patient.[8, 9]

Following the establishment of the ATLS course and the dissemination of the ACS guidelines, the *first trauma systems* were developed and implemented. In these systems the care of the severely injured patients was centralized to designated trauma centers. If the patient was instead transferred to a non-trauma center, stabilization was ensued and transport to a trauma center followed according to pre-established protocols. Often, transport times were long, and delays plagued transport to the places of definitive care. Although this *exclusive* trauma system worked well in urban areas with a sufficient number of acute care facilities and relatively short transport times, it produced suboptimal

results in rural areas. Therefore, an *inclusive* trauma system was proposed. In this system, trauma care is regionalized and coordinated throughout the entire chain of trauma care. All hospitals in a certain region participate in trauma care to the extent that their resources allow.[10, 11] In 1999 the American College of Surgeons - Committee on Trauma (ACS-COT) proposed criteria for the *inclusive* trauma system by categorizing hospitals according to their available resources.[12]

Based on these criteria, hospitals providing trauma care were categorized into five different levels; a level I trauma center provides comprehensive trauma care and is required to have around-the-clock immediate availability of a trauma team with high level facilities; level II and III hospitals have the ability to provide prompt assessment, perform emergent operations, maintain intensive care facilities, and function as a supplement to the level I facilities; level IV and V centers, often located in remote areas, have the capacity to stabilize polytrauma patients according to ATLS principles before transferring the patient to a center with a higher level of care.[13] After the introduction of this trauma system in the United States, other countries, such as Canada, Hong Kong, Australia, the United Kingdom, Israel, the Netherlands, and Germany implemented an inclusive trauma system based on the ACS-COT guidelines adapted to their local needs and policies.[14-24]

The implementation of inclusive trauma systems has since proven its positive effect on outcomes, resulting in lower overall mortality rates in numerous countries, especially for the severely injured.[25-29] However, despite the obvious and evidence-based advantages of a trauma system, international differences in the organization of trauma care remain. There is neither consensus about the ideal organization of trauma systems worldwide nor is a trauma system implemented in every country.[30, 31]

TRAUMA SYSTEMS IN THE NETHERLANDS

Similar to the rest of the world, injuries present a public health problem in the Netherlands, affecting all ages and strata of society. Currently, more than one-third of the approximately 2,000,000 annual Emergency Department (ED) visits are injury-related. In 150,000 cases, hospital admission is required, of which more than 5,000 patients are admitted with serious or multiple injuries.[32]

Annually, an average of 8,000 people die as a result of an accident or violence in the Netherlands.[33] An even greater number of patients suffer disabilities.[34] Approximately 6% of the victims of injuries have a permanent handicap.[32] It has been estimated that the total economic burden due to injuries in the Netherlands is approximately €3.5 billion annually, of which €2.0 billion is attributable to direct health care costs and €1.5 billion to loss of productivity.[35, 36]

In the early 1980s, Dutch surgeons first expressed their concern about the absence of trauma care standardization, collaboration, organization, and the suboptimal quality of both prehospital and in-hospital care provided to injured patients.[16, 37] Following this concern and the subsequent increase in political and societal awareness, the Dutch Association for Trauma Surgery was founded in 1982. Directly thereafter the association joined the discussion about the organization of trauma care in the Netherlands. The first mission and vision report was published in 1985 and described an initial set of criteria that hospitals receiving trauma should meet.[38-40] However, despite good intentions, none of the Dutch hospitals met those criteria and a formal system for transferring patients between hospitals continued to be non-existent.[38]

A horrifying airplane crash in Amsterdam (The Bijlmer Disaster, 1992) and a compelling report by the Public Health Inspectorate were needed to make trauma care a matter of political and public priority. This report showed that a formal prehospital and in-hospital trauma system was lacking in both daily practice and during a disaster.[39, 41]. In 1998, almost 20 years after these first concerns about the organization of trauma care, the Dutch Government appointed ten (later 11) trauma centers in the Netherlands [Figure 3].

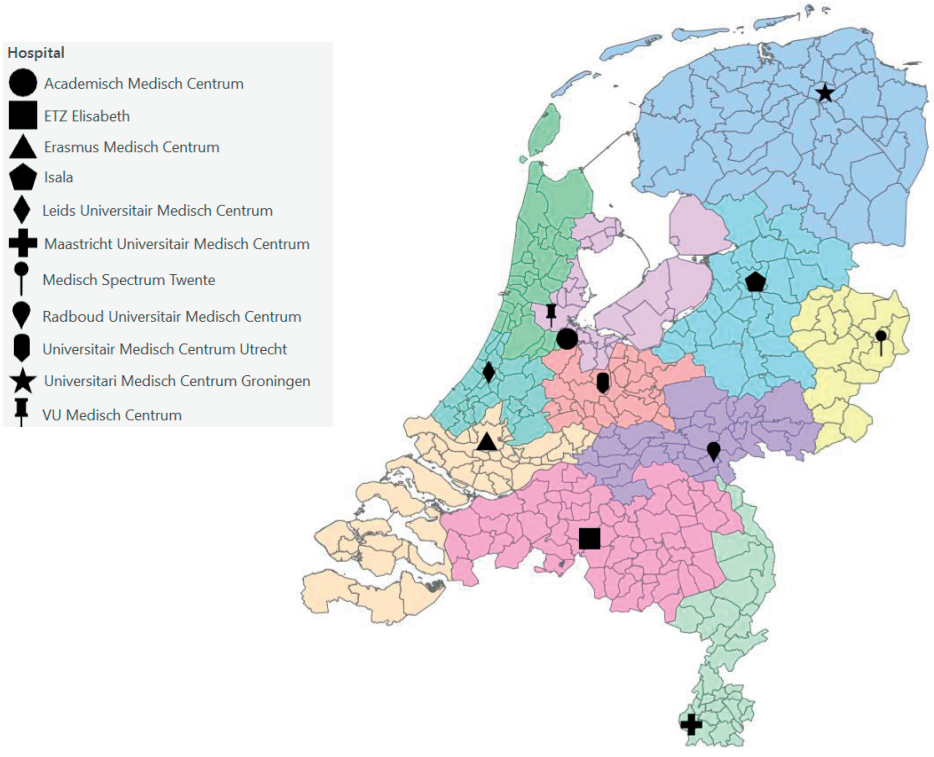


Figure 3. Eleven trauma centers and their trauma regions in the Netherlands

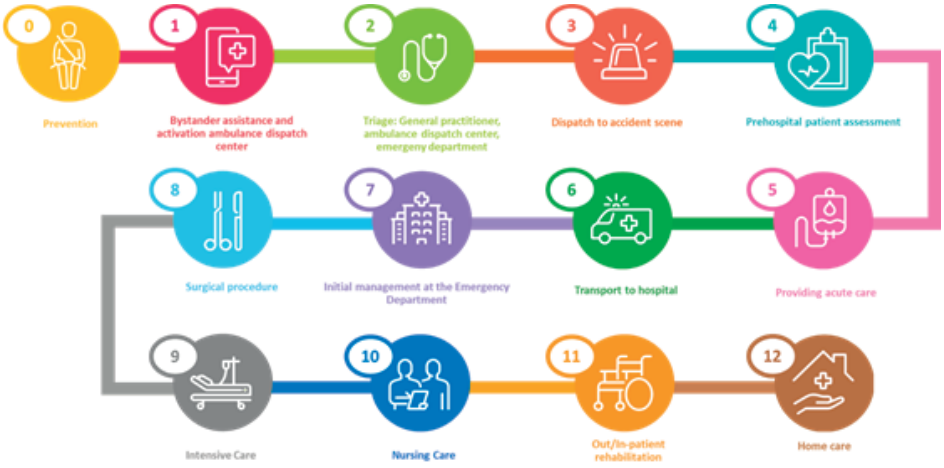


Figure 4. Chain of trauma care in the Netherlands

The aim of the trauma center appointment was to optimize Dutch trauma care through regionalization of care with one coordinating center per trauma region. Consequently, the entire chain of trauma care, from prevention to recovery was to be improved [Figure 4].[42, 43] Quality measures were installed to guarantee quality of care and its ongoing improvement: trauma hospital level criteria were defined for level 1, 2 and 3 centers, a national trauma registry became mandatory for all hospitals, and the certification for specialist (orthopedic) trauma surgeons was established. Since then, the outcomes for the injured patients have improved significantly with a mortality rate reduction of 16% in all injured patients and a striking 21% mortality rate reduction in the most severely injured patients.[28, 29, 44]

CHALLENGES IN OPTIMIZING TRAUMA CARE

Significant improvements in outcomes were seen after the implementation of all-inclusive trauma systems. Nevertheless, it is still a challenge to define the most efficient way to provide structured and optimal care. Considerable variation in the organization of trauma care remains between and even within countries, despite internationally accepted standards for trauma care. However, not all of these standards are evidence-based. Many factors that influence trauma system functionality and their relationship to clinically important outcomes remain unclear.

Although the American and Dutch trauma systems share many similarities, there are also considerable differences. Amongst others, the incidence and nature of the trauma mechanisms, patient volumes, trauma training, prehospital care, clinical experience and

rehabilitation differ between the two countries. These differences in demographics and healthcare processes could potentially affect outcomes. Clarifying the differences and the resulting effects by comparing trauma system characteristics and demographics internationally might help us identify modifiable factors that could improve outcomes.

Since the first introduction of the concept of trauma systems, the trade-off between centralization of care and accessibility of trauma centers has been controversial. On the one hand, centralization of care resulting in higher hospital volumes will increase the expertise of the trauma teams and pose organizational and process of care advantages. On the other hand, trauma center accessibility and population coverage could be better achieved by multiple, and consequently smaller-volume trauma centers. Given that the advantages and disadvantages of these differing organizational approaches have not been rigorously studied, the ideal trauma center configuration is still unknown. There is a need for a generally applicable model that could be modified to a trauma region's needs, based on local injury data, capacity, and demographical data. Identifying factors that influence trauma center accessibility, such as traffic flow, in combination with -for example- population coverage, is essential in order to determine the optimal geographic location of trauma centers in a certain region.

As important as it is to seek structural improvement in broad organizational aspects, the care of the individual patient and the improvements we can create on a case-by-case base are equally important. One of the areas in which progress is direly needed relates to the nutrition therapy of trauma patients, particularly during the acute phase of care. About 20-40% of all hospitalized patients are affected by malnutrition, a percentage that is even higher in critically ill patients.[45-48] Malnutrition is considered a risk factor for poor clinical outcomes, such as higher morbidity and mortality, in hospitalized patients.[45, 49-51] However, little is known about the influence of malnutrition in trauma patients during hospitalization. More insight into malnutrition, how to recognize it and eventually prevent it, is necessary. Therefore, the Department of Trauma Surgery of the Leiden University Medical Center, initiated in collaboration with its American research partners a multi-center prospective study to investigate the occurrence and effect of malnutrition in trauma patients admitted to the Intensive Care Unit.

AIM AND OUTLINE OF THIS THESIS

Differences in trauma care between countries result in inconsistent care and present an opportunity to identify areas of improvement. The primary aim of this thesis is to analyze the presence and structure of trauma systems and evaluate specific care-delivery processes and their parameters. The second aim is to evaluate one of these parameters, the role of the nutritional status in the outcome of polytrauma patients.

Chapter 2 gives an overview of the current state of trauma systems globally. **Chapter 3** aims to compare the demographics, injury characteristics, and outcomes of patients with blunt polytrauma treated in two comparable, urban, academic, Level I Trauma Centers, one in the United States and the other one in the Netherlands. **Chapter 4** discusses the characteristics and outcomes of patients with penetrating injuries treated at multiple urban level-1 trauma centers in the United States and the Netherlands. **Chapter 5** introduces a new model for the quantification of the effects of trauma center distribution on transportation time. In **chapter 6** we aim to evaluate the impact of structured trauma care on the concentration of severely injured patients over time. **Chapter 7** provides an overview of the current knowledge about the pathophysiology, prevalence, and effects of malnutrition in severely injured patients. **Chapter 8** shows the proportion of total caloric and protein deficit that is attributable to the RAMP-UP protocol (i.e. initiating enteral nutrition (EN) at a low rate and slowly increasing the rate) in patients admitted to the Surgical Intensive Care Unit. **Chapter 9** discusses the study protocol of the international multicenter prospective Malnutrition in Polytrauma Patients [MaPP] study, which aims to describe the effect and consequences of malnutrition in polytrauma patients admitted to the Intensive Care Unit. In **chapter 10** a discussion on the topics described above is presented, as are the future perspectives and potential implications of the findings in this thesis.

REFERENCES

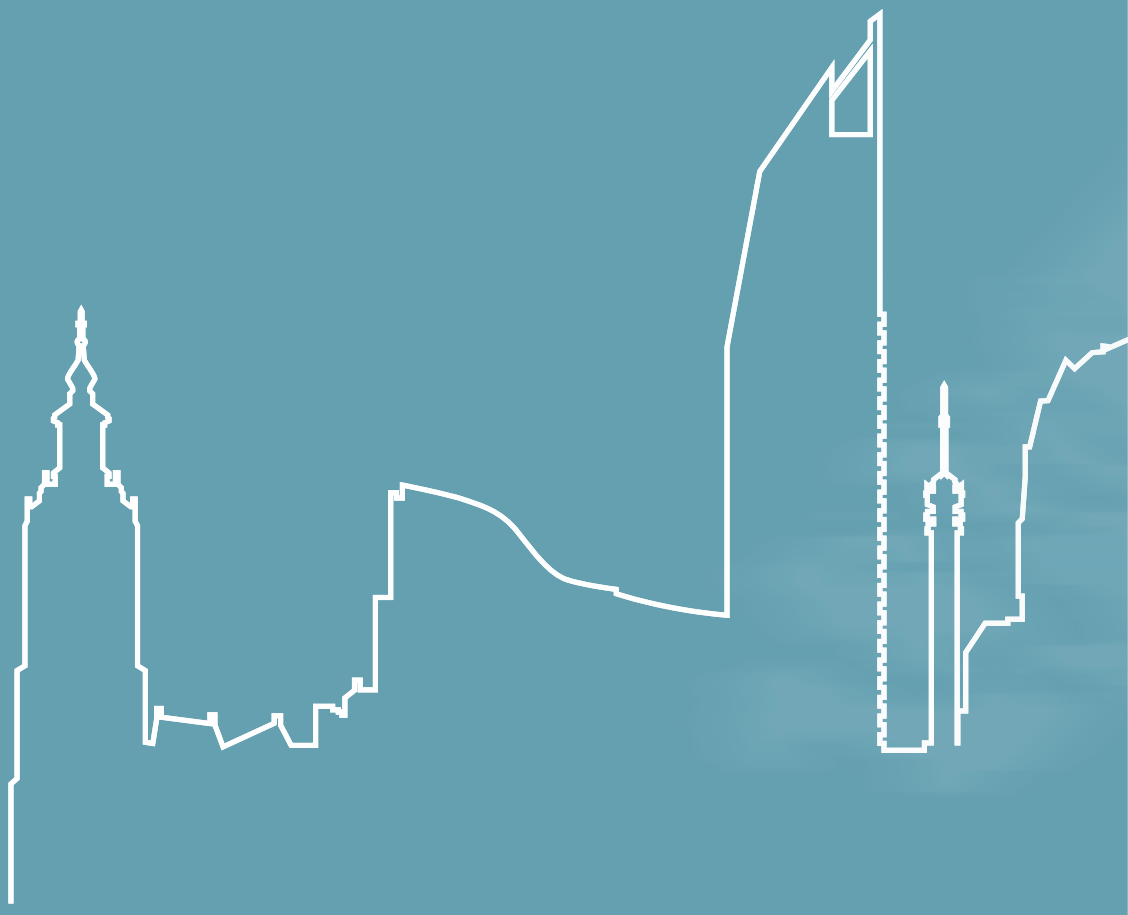
1. World Health Organization. Injuries and violence: the facts 2014. Geneva; 2014.
2. National Academy of Sciences, National Research Council Committee on Trauma,. Accidental Death and Disability: The Neglected Disease of Modern Society. Washington (DC): National Academies Press (US) Copyright (c) National Academy of Sciences.; 1966.
3. Patton GC, Coffey C, Sawyer SM, Viner RM, Haller DM, Bose K, Vos T, Ferguson J, Mathers CD. Global patterns of mortality in young people: a systematic analysis of population health data. Lancet. 2009;374(9693):881-92.
4. World Health Organization. Saving millions of lives: decade of action for road safety 2011-2020. Geneva; 2011.
5. Peden M, Scurfield R, Sleet D, Hyder AA, Mathers C, Jarawan E, Hyder A, Mohan D, Jarawan E. World report on road traffic injury prevention: World Health Organization; 2004.
6. Van Wagoner FH. A three year study of deaths following trauma. Journal of Trauma and Acute Care Surgery. 1961;1(4):401-8.
7. Cales RH, Trunkey DD. Preventable Trauma Deaths: A Review of Trauma Care Systems Development. JAMA. 1985;254(8):1059-63.
8. Carmont MR. The Advanced Trauma Life Support course: a history of its development and review of related literature. Postgraduate Medical Journal. 2005;81(952):87-91.
9. Hospital resources for optimal care of the injured patient. Prepared by a Task force of the Committee on Trauma of the American College of Surgeons. Bull Am Coll Surg. 1979;64(8):43-8.
10. Nathens AB, Brunet FP, Maier RV. Development of trauma systems and effect on outcomes after injury. The Lancet. 2004;363(9423):1794-801.
11. Narad RA, Becker JL, Frecceri C. A decentralized trauma system design for a rural area. Prehospital and disaster medicine. 1996;11(2):134-40.
12. American College of Surgeons - Committee on Trauma. Resources for optimal care of the injured patient 1999. Chicago: American College of Surgeons; 1999.
13. Nathens AB, Brunet FP, Maier RV. Development of trauma systems and effect on outcomes after injury. Lancet. 2004;363(9423):1794-801.
14. Sturm JA, Pape HC, Dienstknecht T. Trauma care in Germany: an inclusive system. Clin Orthop Relat Res. 2013;471(9):2912-23.
15. Oestern H-J, Garg B, Kotwal P. Trauma Care in India and Germany. Clinical Orthopaedics and Related Research®. 2013;471(9):2869-77.
16. ten Duis HJ, van der Werken C. Trauma care systems in The Netherlands. Injury. 2003;34(9):722-7.
17. Zakrison T, Ball CG, Kirkpatrick AW. Trauma in Canada: a spirit of equity & collaboration. World J Surg. 2013;37(9):2086-93.
18. Kortbeek JB, Buckley R. Trauma-care systems in Canada. Injury. 2003;34(9):658-63.
19. Blackwell T, Kellam JF, Thomason M. Trauma care systems in the United States. Injury. 2003;34(9):735-9.
20. Westhoff J, Hildebrand F, Grotz M, Richter M, Pape HC, Krettek C. Trauma care in Germany. Injury. 2003;34(9):674-83.
21. Albert J, Phillips H. Trauma care systems in the United Kingdom. Injury. 2003;34(9):728-34.
22. DeKeyser F, Avitzour M, Watts DD, Trask AL, Muggia-Sullam M. International trauma care: a comparison between Jerusalem, Israel, and Fairfax County, Virginia, USA. Isr Med Assoc J. 2002;4(2):103-8.

23. Cheng CH, Graham CA, Gabbe BJ, Yeung JH, Kossmann T, Judson RT, Rainer TH, Cameron PA. Trauma care systems: a comparison of trauma care in Victoria, Australia, and Hong Kong, China. Ann Surg. 2008;247(2):335-42.
24. Delprado AM. Trauma systems in Australia. J Trauma Nurs. 2007;14(2):93-7.
25. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, Salkever DS, Scharfstein DO. A national evaluation of the effect of trauma-center care on mortality. N Engl J Med. 2006;354(4):366-78.
26. Lansink KW, Leenen LP. Do designated trauma systems improve outcome? Curr Opin Crit Care. 2007;13(6):686-90.
27. Celso B, Tepas J, Langland-Orban B, Pracht E, Papa L, Lottenberg L, Flint L. A systematic review and meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems. J Trauma. 2006;60(2):371-8; discussion 8.
28. Spijkers AT, Meylaerts SA, Leenen LP. Mortality decreases by implementing a level I trauma center in a Dutch hospital. J Trauma. 2010;69(5):1138-42.
29. Twijnstra MJ, Moons KG, Simmermacher RK, Leenen LP. Regional trauma system reduces mortality and changes admission rates: a before and after study. Ann Surg. 2010;251(2):339-43.
30. ROBERT J. WINCHELL RMS, MICHELLE PRICE. Committee on Trauma introduces needs assessment tool aimed at resolving trauma center debat. 2016.
31. Dijkink S, Nederpelt CJ, Krijnen P, Velmahos GC, Schipper IB. Trauma systems around the world: a systematic overview. Journal of trauma and acute care surgery. 2017;83(5):917-25.
32. RIVM. SEH bezoeken cijfers en context Bilthoven2017 [cited 2019 September 12]. Available from: https://www.volksgezondheidenzorg.info/onderwerp/letsels/cijfers-context/seh-bezoeken.
33. Statistics Netherlands (CBS). CBS Doodsoorzakenstatistiek [Available from: https://www.volksgezondheidenzorg.info/onderwerp/letsels/cijfers-context/sterfte#node-sterfte-door-letsels.
34. Christine Stam BB. Letsels 2017. Kerncijfers LIS. Amsterdam; 2017.
35. Polinder S, Haagsma J, Panneman M, Scholten A, Brugmans M, Van Beeck E. The economic burden of injury: Health care and productivity costs of injuries in the Netherlands. Accident Analysis & Prevention. 2016;93:92-100.
36. RIVM. Kosten letsels door ongeval 2016 [cited 2019 September 12]. Available from:https://www.volksgezondheidenzorg.info/onderwerp/letsels/kosten/kosten.
37. Goris RJA DJ. De zorg voor detrauma-patiënt: meer en beter onderzoek nodig. . Medisch Contact 1984;39:301-2.
38. Goris R. De acute zorg voor ernstig gewonde patienten. Ned Tijdschr Geneeskd. 1990;134:1439-42.
39. Goris R. Honderd jaar Nederlandse Vereniging voor Heelkunde. v. Traumatologie. Ned Tijdschr Geneeskd. 2002;146(24):1144-7.
40. Nederlandse Vereniging voorTraumatologie. Organisatietraumatologie in Nederlandse algemene ziekenhuizen. Utrecht; 1985
41. Inspectie voor Volksgezondheid. De keten rammelt. 1995.
42. Ministerie van Volksgezondheid Welzijn en Sport. Met Zorg Verbonden. 1997.
43. Nederlandse Vereniging voor Traumatologie. Traumazorg; onze zorg1997.
44. Lansink KW, Gunning AC, Spijkers AT, Leenen LP. Evaluation of trauma care in a mature level I trauma center in the Netherlands: outcomes in a Dutch mature level Itrauma center. World J Surg. 2013;37(10):2353-9.
45. Mogensen KM, Robinson MK, Casey JD, Gunasekera NS, Moromizato T, Rawn JD, Christopher KB. Nutritional Status and Mortality in the Critically Ill. Crit Care Med. 2015;43(12):2605-15.

46. Barker LA, Gout BS, Crowe TC. Hospital malnutrition: prevalence, identification and impact on patients and the healthcare system. Int J Environ Res Public Health. 2011;8(2):514-27.
47. Pirlich M, Schütz T, Norman K, Gastell S, Lübke HJ, Bischoff SC, Bolder U, Frieling T, Güldenzoph H, Hahn K, et al. The German hospital malnutrition study. Clinical Nutrition. 2006;25(4):563-72.
48. Edington J, Boorman J, Durrant ER, Perkins A, Giffin CV, James R, Thomson JM, Oldroyd JC, Smith JC, Torrance AD, et al. Prevalence of malnutrition on admission to four hospitals in England. The Malnutrition Prevalence Group. Clin Nutr. 2000;19(3):191-5.
49. Correia MI, Waitzberg DL. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. Clin Nutr. 2003;22(3):235-9.
50. Keel M, Trentz O. Pathophysiology of polytrauma. Injury. 2005;36(6):691-709.
51. Kruizenga H, van Keeken S, Weijs P, Bastiaanse L, Beijer S, Huisman-de Waal G, Jager-Wittenaar H, Jonkers-Schuitema C, Klos M, Remijnse-Meester W, et al. Undernutrition screening survey in 564,063 patients: patients with a positive undernutrition screening score stay in hospital 1.4 d longer. Am J Clin Nutr. 2016;103(4):1026-32.

PART I

EVALUATION OF TRAUMA CARE SYSTEMS



2

Trauma systems around the world: A systematic overview

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I.B. Schipper

Journal of Trauma and Acute Care Surgery. 2017 Nov;83(5):917-925.

ABSTRACT

Background

Implementation of trauma care systems has resulted in improved patient outcomes, but international differences obviously remain. Improvement of care can only be established if we recognize and clarify these differences. The aim of the current review is to provide an overview of the recent literature on the state of trauma systems globally.

Methods

The literature review over the period 2000 to 2016 was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. Prehospital care, acute hospital care and quality assurance were classified using the World Health Organization Trauma System Maturity Index in four levels from I (least mature) to IV (most mature).

Results

The search yielded 93 articles about trauma systems in 32 countries: 23 high-income (HI), 8 middle-income (MI) countries and 1 low-income (LI) country. Trauma-related mortality was highest in the MI and LI countries. Level IV prehospital care with Advanced Life Support was established in 19 HI countries, in contrast to the MI and LI countries where this was only reported in Brazil, China, and Turkey. In 18 HI countries, a Level III/IV hospital-based trauma system was implemented, whereas in nine LI- and MI countries Level I/II trauma systems were seen, mostly lacking dedicated trauma centers and teams. A national trauma registry was implemented in 10 HI countries.

Conclusion

Despite the presence of seemingly sufficient resources and the evidence-based benefits of trauma systems, only nine of the 23 HI countries in our review have a well-defined and documented national trauma system. Although 90% of all lethal traumatic injuries occur in middle and LI countries, according to literature which our study is limited to, only few of these countries a hold formal trauma system or trauma registry. Much can be gained concerning trauma systems in these countries, but unfortunately, the economic situation of many countries may render trauma systems not at their top priority list.

INTRODUCTION

Trauma is a major health problem worldwide and the leading cause of death in people younger than 45 years.[1] Each year about 5 million people die as a result of traumatic injuries, of which 90% occur in low-income (LI) and middle-income (MI) countries.[2] A study by Mock et al.[3] showed that mortality due to trauma is inversely related to the economic level of a country. According to their results, an injured patient in Ghana is almost twice as likely to die as a patient with the same injuries in the United States. These differences are even more dramatic for multiple injuries patients (Injury Severity Score ≥ 16), for whom the mortality rate is six times higher in LI countries compared with high-income (HI) countries.[4]

In HI countries, the implementation of trauma care systems has led to a significant decrease in mortality and disability. It is estimated that improvements in trauma care systems worldwide may prevent about one third of injury-related deaths.[1] However, these improvements come at a cost, and the economic situation of many countries may render trauma systems not at their top priority list. The World Health Organization (WHO) published guidelines for essential trauma care and for trauma quality improvement programs to reduce the trauma-related mortality differences between the HI and LI countries.[2] Still, the management of trauma requires personnel for a preferably multidisciplinary approach, not only within the hospital, but also for prehospital care. The American College of Surgeons-Committee on Trauma (ACS-COT) identified several aspects as crucial for optimal trauma care.[5] Education, adequate resources, and an organized system need to be in place. The presence or absence of all of these individual parts of the chain of trauma care determines the potential for existence of a trauma system. The goal of this review is to give an overview of the similarities and differences of trauma systems around the world, based on the available literature. In this review, we focused on prehospital care, acute hospital care, and quality assurance.

MATERIALS AND METHODS

The review was conducted according to the preferred reporting items for systematic reviews and meta-analyses statement.[6]

Search Strategy and Article Selection

An extensive literature search in PubMed was performed with the help of an experienced medical librarian in June 2016. We used the following search terms: "Traumatology/organization and administration,""trauma management,""trauma system,""emergency medical services," "emergency medical service," "trauma care system," "trauma care,"" prehospital

care," "trauma registry," "national," "nationwide," "global," "worldwide." The exact search strategy is provided in the Appendix. Title and abstract of identified articles were screened for relevancy. Articles from 2000 until June 2016 were included. The full text of selected articles was retrieved. Articles providing descriptive national data on trauma epidemiology, prehospital care, acute hospital care, and quality assurance were included in the definite selection. To provide a comprehensive overview, we aimed to include at least one article from a country in every continent. Articles that primarily focused on pediatric trauma systems were excluded. Also, when an article provided information about just one parameter (prehospital care, acute hospital care, or quality assurance), this article was excluded from the review. Furthermore, only articles in English, German, and Dutch were included. The reference lists of the included articles were screened for additional relevant articles. Also, official websites mentioned in the publications (ACS, WHO, German Trauma Register, Canadian Institute for Health Information) were accessed to obtain recent and valid data.

Classification of Trauma Systems

The level of prehospital care, acute hospital care, and quality assurance in each country was scored according to the Trauma System Maturity Index. This index was developed by the WHO to assess and determine the maturity of trauma systems within countries, according to a classification in four levels ranging from Level I maturity (least mature) to Level IV maturity (most mature) (Table 1).[7] It is of interest to note that this classification is the opposite of the classification of trauma centers by the ACS-COT, in which the Level I trauma centers provide the highest level of trauma care. If there were differences noted in trauma system implementation within countries, such as in the United States, we generalized the information based on the available literature to be able to classify the country within one level.

Prehospital Care

The level of prehospital trauma care and the level of education and training of emergency medical services (EMS) personnel are both important factors for the outcome of patients.[8] Level of prehospital care was scored according to the Trauma System Maturity Index (Table 1). Levels I and II of the prehospital care maturity index reflect "unorganized prehospital care." In these levels, no formal Emergency Medical Service (EMS) system is implemented, and patients are transported to the hospitals mostly by private or public vehicles.[9] Levels III and IV of the prehospital care maturity index reflect well- established and organized prehospital care systems with the difference that in Level IV systems, a formal lead agency and legislative system is established.

Two types of EMS systems and prehospital care training were distinguished, based on an article by Roudsari et al.[9] In Basic Life Support (BLS) EMS systems, noninvasive care is given by emergency medical technicians, whereas in Advanced Life Support (ALS) EMS

systems, more sophisticated and invasive therapy is given by either medical technicians or physicians (Doc-ALS). For countries where prehospital care is not provided by personnel with a training, the type of EMS system was scored as "no formal training."

Acute Hospital Care

The level of facility-based trauma care was scored according to the WHO Trauma System Maturity Index (Table 1). In contrast to the ACS-COT criteria, the Level I and II maturity categories of the WHO Trauma System Maturity Index concerns acute hospital care for which no formal hospital-based trauma system is implemented. Also, resources are not always available, and the methods of referring patients are not always clear. Level III hospital-based care provides comprehensive trauma care but without a formal network, with a lead agency but no formal accreditation and verification by the (federal) government in place. In Level IV hospital-based trauma care verification and accreditation by the government is in place, and a lead agency is established with mandate to supervise trauma care. Also, the presence of dedicated Level I trauma centers according to the ACS-COT guidelines and of dedicated trauma teams were scored.

Education and Training

Besides the level of the facility-based trauma care, the level of education and training of hospital personnel according to the WHO Trauma System Maturity Index (Table 1) and the implementation of Advanced Trauma Life Support (ATLS) or equivalent courses were scored for each country.

Quality Assurance

The level of quality assurance was scored according to the WHO Maturity Index (Table 1). Also, the presence or absence of a trauma registry was recorded, since this is considered to be a key element of a mature trauma care system and to form the basis of quality assurance programs.[10]

Data Extraction

Two independent readers (S.D. and C.N.) classified the trauma systems according to the parameters described above. They classified data from the included papers and other mentioned sources using a predesigned data extraction form. Disagreement on scores was resolved by consensus discussion, if needed with involvement of the senior authors.

The trauma-related mortality rate in each country was derived from data of the WHO.[11]

The development of trauma systems comes at a cost, and the economic welfare is possibly related to the development of trauma systems. Therefore, the economic income level of the countries described in the selected articles was classified according to data of the World Bank.[12]

Table 1. WHO Maturity Index Trauma System[7]

	Level I	Level II	Level III	Level IV
Prehospital Trauma Care	• No mapping of prehospital resources • No formal EMS, unavailability or duplication of prehospital services • No defined communication system	• Prehospital resources are identifiable • No coordination between public and private providers of prehospital care • No universal access number, weak links of communication	• Formal EMS present • Universal Access Number available • Coordination seen between various agencies for prehospital care delivery • Well defined communication	• Formal EMS controlled by a lead agency • National universal access number • Legislative mechanism in place to govern EMS and allow universal coverage
Education and Training	• No identified health personnel to offer primary trauma care in community	• Identified health personnel in the community for emergency trauma care • No definite training requirement for health workers or ambulance personnel	• Health professionals and paramedics are trained in provision of emergency trauma care • Training courses are available for trauma education	• Educational standards and training for emergency trauma care providers laid down • Licensing and renewal norms for different levels of paramedics are in place
Facility based Trauma care	• Role of secondary and tertiary facilities unclear • Health facilities lack human and physical resources • No clear referral linkages	• Roles of various health care facilities are clear • Referral linkages are present • No documentation or needs assessment of facilities in line with EsTC guidelines • No lead agency in the system	• Health facilities in the systems are assessed in line with EsTC guidelines • Guidelines and documented human and physical resources are available and ensured round the clock • Lead agency present	• Mechanism of hospital verification and accreditation is in place through Ministry of Health or professional bodies • Lead agency established with mandate to supervise trauma care
Quality Assurance	• No injury surveillance or registry mechanism in place to get comprehensive data	• Injury data available but no formal attempts to document and analyze the data • No initiative for Quality Assurance program	• Basic Quality Assurance programs in line with EsTC guidelines • Guidelines are in place	• Formal Quality Assurance programs are in place and are mandated in prehospital and facility based services

EsTC, Essential Trauma Care Project.

RESULTS

Selection of Articles

The search identified 2,728 articles. After removal of duplicates and screening the titles and abstracts for relevance, 231 full-text articles were screened for eligibility. After application of the exclusion criteria, 63 articles on trauma systems in 32 countries were included (Fig. 1). Additionally, 30 references were identified through the other sources. Articles with data from countries in all continents were included. All 14 included European countries as well as two North-American countries and two countries in Oceania were classified as HI. Of the included countries in Africa, one was classified as HI, one as LI, and two as MI countries. Four countries in Asia were classified as HI, and five as MI (Table 2). The trauma-related mortality rates are summarized also by sex in Table 2.

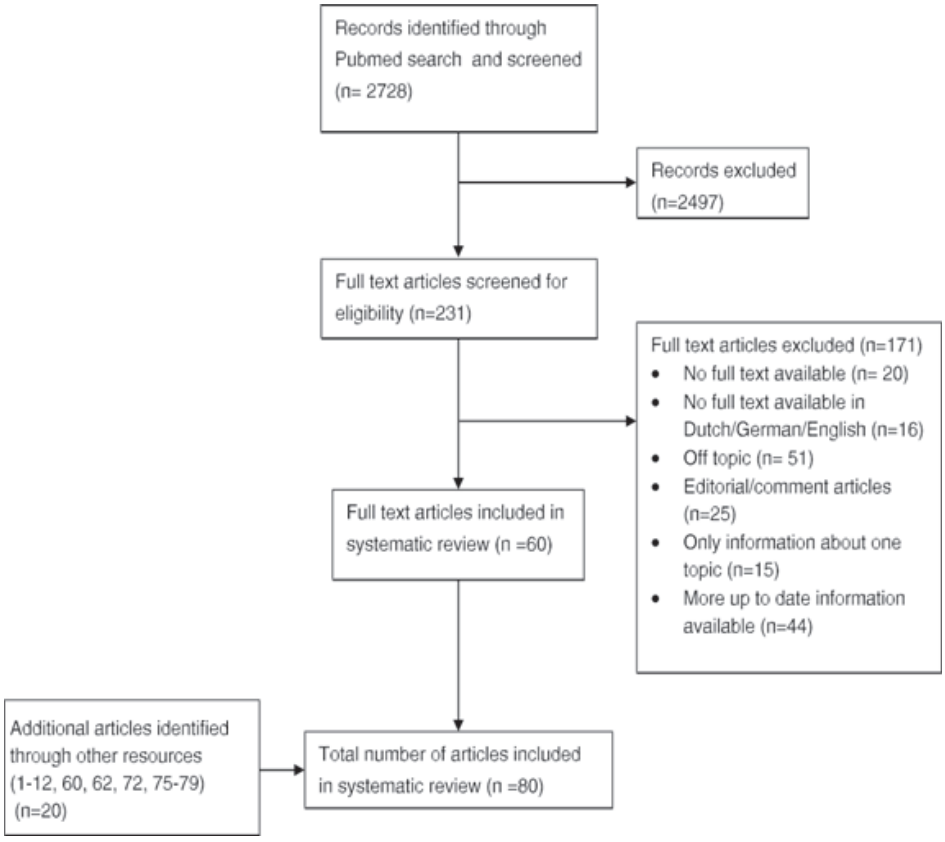

Figure 1. Flowchart search strategy

Prehospital Care

In all low and middle economic income level countries described in this review, a well-organized prehospital care system is absent or still in its early stages, and a substantial part of the injured patients is not transported to hospital by specialized EMS vehicles (Table 2).[13,16,36] In most of these countries, the persons involved in the transport of injured patients had not followed any form of certified training.[19,25,36] Differences in access to prehospital care between the cities and rural areas were reported for some countries.[19,27] The Seychelles Islands formed an exception in this group being an HI country lacking a prehospital system.[15]

Levels III and IV of the prehospital care were typically found in HI countries and upcoming upper MI countries, such as Brazil, China, and Turkey (Table 2). In China and Turkey, an educational system for paramedics was implemented, and in Brazil, the government was prioritizing education programs on emergency medicine.[20,37,68] In these EMS systems, certified EMS personnel provided BLS or ALS. In many countries with formally trained EMS personnel, such as New Zealand, Croatia, and Saudi Arabia, the organization of prehospital care, and type and skills of EMS personnel was dependent on the national geography, with a lower level of life support available in the more rural areas.[33,40,72] Although the prehospital care trauma systems in HI countries were well established and organized, they were not entirely similar. Differences existed not only with regard to EMS personnel training skills but also in the organization of prehospital care. In many European countries, ambulances were staffed with both highly trained paramedics and physicians, depending on the severity of the injuries[29,38,41,45,50,54,57,59,60,63,] whereas in, for example, the United States, Hong Kong, and Japan, the EMS system was entirely run by paramedics.[23,31,65] In most countries, ground ambulances formed the core of the EMS system. Differences were noticed in the number of helicopters and dispatch criteria for helicopter EMS. Mostly, helicopters were used to enable rapid transportation of severely injured patients to the trauma center.[63,65] The use of helicopters was not only dependent on the earlier mentioned criteria but also on the geographical differences between countries. Helicopters were used less frequently in the smaller and more densely populated countries, whereas countries, such as Canada, Australia, and the Scandinavian countries with less densely populated areas relied more on air transport.[8,41,45,46,51,60,63,70]

Acute Hospital Care

Facility-Based Trauma Care

Levels I and II hospital-based trauma care based on the WHO Trauma System Maturity Index was mostly found in LI and MI countries with maturing trauma systems, such as India, Iran, Saudi Arabia, Brazil, Thailand, Ghana, and China (Table 2). In many countries, a formal hospital trauma care pathway was lacking and surgical residents or general

surgeons were responsible for the initial care of the injured patients. Their availability, however, was far less than 24/7 in many hospitals. [14,19,21,36] Differences between hospitals in the urban and rural areas were seen within countries, well-trained personnel and advanced facilities were available in large hospitals located in more urban areas, resembling level III facility based care, but were not available in rural regions of, for example, Saudi-Arabia, India, and Iran.[26,28,34]

In most HI countries, some form of hospital trauma care pathway was documented. In WHO Trauma System Maturity Index Level III hospital-based care, severely injured patients were often attended to by a physician trained in emergency medicine or by a general surgeon. Several differences between countries were found. For example, a trauma team was implemented in 88% of the hospitals that receive trauma patients in Norway, but only in 20% of those hospitals in Finland.[41,42,53] The care in the majority of trauma receiving hospitals is organized ad hoc, mostly without having legislation and protocols for transfer, triage and management in place.[37,38,40,44,50,51,58,72,73] A different situation is found in South Africa, which had seven specialized trauma centers spread over the country with an experienced general surgeon and immediately available surgical facilities, however, without a formal network.[17]

Level IV hospital-based care according to the WHO Trauma System Maturity Index was primarily seen in the HI countries with dedicated trauma centers and trauma teams. Many countries based their trauma system and the distribution of trauma centers on the criteria set by the American College of Surgeons-Committee on Trauma (ACS-COT) published in 1999.[5] As a consequence of the implementation of these guide- lines, trauma care became increasingly regionalized first in the United States, and subsequently in many other countries, such as Canada, Hong Kong, Australia, The United Kingdom, Israel, the Netherlands, and Germany.[24,45,46,54,61,63,66,70] However, other organizational models are seen, for instance, in Japan, where a three-tiered trauma care system has been implemented.[32] Despite the well-implemented trauma systems in these countries, there are still differences in organization of trauma care and the distribution of trauma centers due to local policies, population density, and geographical differences.[46,63] At a facility base level, it was seen that what all these countries have in common is that they implemented a system with dedicated trauma centers and dedicated trauma teams (Table 2). Various studies in numerous countries have shown that inclusive trauma systems result in an overall lower mortality risk for severely injured patients.[55,56,74]

Education and Training

ATLS courses are given in 28 of the 32 countries included in this review[75], although this training has not been implemented nationwide in many LI and MI countries. However, efforts for improvement are undertaken, for instance, in India which participated in the Essential Trauma Care Project since 2003 and in Saudi Arabia where a trauma system

Table 2. Trauma System Characteristics

Continent/ Country	Economic income level [12]	Trauma-related mortality per 100,000 Population[11]	Prehospital care		Acute Hospital Care	
			WHO level of Prehospital Trauma Care[7]	Education and training of EMS Personnel[9]	WHO level of Facility Based Trauma Care [7]	Dedicated level-1 trauma centers
Africa						
Ghana[13,14]	Lower Middle	♂ 100.1 ♀ 41.1	I	No formal training	I/II	No
Seychelles[15]	High	♂ 81.7 ♀ 17.2	I/II	No formal training	I/II	No
South Africa[16–18]	Upper Middle	♂ 93.9 ♀ 34.7	II/III	No formal training	II/III	Yes
Zimbabwe[19]	Low	♂ 86.8 ♀ 26.9	II	No formal training	I	No
Asia						
China[20–22]	Upper Middle	♂ 86.3 ♀ 53.1	III	ALS/BLS	I/II	No
Hongkong[23,24]	High	♂ n/a ♀ n/a	IV	ALS	IV	Yes
India[25,26]	Lower Middle	♂ 103.0 ♀ 26.6	I/II	No formal training	I/II	No
Iran[27,28]	Lower Middle	♂ 108.4 ♀ 43.2	I/II	No formal training	I/II	No
Israel[29,30]	High	♂ 37.8 ♀ 17.4	IV	ALS/BLS	IV	Yes
Japan[31,32]	High	♂ 76.1 ♀ 46.4	IV	ALS	IV	Yes
Saudi Arabia[33–35]	High	♂ 89.9 ♀ 26.9	II	BLS	I/II	No
Thailand[36]	Upper Middle	♂ 169.9 ♀ 46.3	I/II	No formal training	II	No
Turkey[37]	Upper Middle	♂ 42.8 ♀ 13.6	IV	ALS	II/III	No
Europe						
Belgium[38,39]	High	♂ 72.7 ♀ 44.6	IV	ALS	III	No
Croatia[39,40]	High	♂ 92.1 ♀ 45.1	III	ALS/BLS	III	Yes
Finland[41–43]	High	♂ 114.7 ♀ 45.6	IV	ALS	III	No
France[44]	High	♂ 74.1 ♀44.5	IV	ALS	III	No
Germany[45–47]	High	♂ 48.6 ♀ 29.3	IV	ALS		Yes

			Quality assurance	
Trauma team	**WHO level of Education and Training[7]**	**ATLS or equivalent course [60]**	**WHO level of Quality Assurance [7]**	**Trauma registry**
			I/II	No national trauma registry
No	II	Yes (Mass Casualty Incident Responder Course)		
No	II/III	Yes	II	Hospital-based registries
	II			
			II	Initiatives for, Chinese National Injury Surveillance System
Yes	IV	Yes	III	Trauma registries in trauma centres, no central system
No	II	Yes	II	Hospital based registries
No	II	Yes	I	No trauma registry established.
Yes	IV	Yes	IV	Israel National Trauma Registry
No	IV	Yes (and JATEC)	IV	Japan Trauma Data Bank
	I/II	Yes	II	Currently building a nationwide surveillance system for injury
No	II	Yes		
No	III	No (Turkish Association for Trauma and Emergency)		
No	IV	Yes (European trauma course)		
No	II/III	No	III	Joining EuroTARN
Yes (20% trauma team)	III	Yes	III	Hospital based registries, some hospitals join TARN
No	III	Yes	III	Regional and hospital based Registries
Yes	IV	Yes	IV	TraumaRegister DGU

Table 2. Trauma System Characteristics (continued)

Continent/ Country	Economic income level [12]	Trauma-related mortality per 100,000 Population[11]	Prehospital care		Acute Hospital Care	
			WHO level of Prehospital Trauma Care[7]	Education and training of EMS Personnel[9]	WHO level of Facility Based Trauma Care [7]	Dedicated level-1 trauma centers
Greece[48,49]	High	♂ 54.0 ♀ 14.3	III	ALS		No
Italy[39,50]	High	♂ 49.7 ♀ 32.6	IV	ALS		No
Ireland[51,52]	High	♂ 52.6 ♀ 21.7	III	ALS/BLS		No
Norway[41,43,53]	High	♂ 62.3 ♀ 39.3	IV	ALS/BLS		No
the Netherlands[54–56]	High	♂ 36.8 ♀ 28.2	IV	ALS		Yes
Scotland[57,58]	High	♂ 43.2 (= UK numbers) ♀ 26.8	III	ALS		No
Spain[59]	High	♂ 45.6 ♀ 26.4	IV	ALS		No
Sweden[41,43]	High	♂ 64.1 ♀ 37.6	IV	ALS		No
United Kingdom[60–62]	High	♂ 43.2 ♀ 26.8	IV	ALS		Yes
North America						
Canada[63,64]	High	♂ 52.7 ♀ 29.9	IV	ALS		Yes
USA[65–67]	High	♂ 83.3 ♀ 38.0	IV	ALS		Yes
South America						
Brazil[68,69]	Upper Middle	♂ 125.7 ♀ 27.5	II/III	BLS		No
Oceania						
Australia[24,67,70,71]	High	♂ 50.0 ♀ 24.8	IV	ALS		Yes.
New Zealand[71–73]	High	♂ 56.8 ♀ 28.2	III	ALS/BLS		Yes

JATEC, Japan advanced trauma evaluation and care course;
NTRC, National Trauma Registry Consortium; STAG, Scotland Trauma Audit Group;
TARN, Trauma Audit & Research Network.

			Quality assurance	
Trauma team	**WHO level of Education and Training[7]**	**ATLS or equivalent course [60]**	**WHO level of Quality Assurance [7]**	**Trauma registry**
No	II/III	Yes	II	Hospital and multiregional registries
	IV	Yes	III	Hospital based registries, initiatives to implement national trauma registry, EuroTARN
		Yes	IV	Collaborating with the TARN, implementing Major Trauma Audit
Yes	IV	Yes	III	Individual or hospital based registries, working toward national registry (Kvalitetsregister i traumasjukvården (Kvittra)
Yes	IV	Yes	IV	National Trauma Registry
No	III	Yes	IV	STAG
No	III	Yes	II	No nationwide trauma registry, initiatives in autonomous regions
	IV	Yes	III	Individual or hospital based registries, initiatives for national registry
Yes	IV CNIII	Yes	IV	TARN
Yes	III	Yes	III	Canadian National Trauma Registry (1997–2014), currently regional trauma registries
Yes	IV	Yes	IV	National Trauma Data Bank
		Yes	I/II	No National Trauma Data Bank
Yes	IV	Yes (and Emergency Management of Severe Trauma course)	IV	NTRC
No	III	Yes (and Emergency Management of Severe Trauma course	IV	NTRC

with internationally accepted trauma courses was being implemented since 2010.[26,34] Although, in South Africa, a similar situation is seen, where not every surgeon is being trained according to ATLS course, this seems to be compensated for by the high exposure and experience with trauma.[17]

In the HI countries, differences regarding the implementation of trauma courses were noticed as well. Some countries, such as Turkey, have implemented their own course or combined the ATLS course with another course. Examples of such courses included the Emergency Management of Severe Trauma in Australia and New Zealand, the Japan Advanced Trauma Evaluation and Care course in Japan and the European Trauma Course in Belgium.[37,38,72,73] The availability of a training program in a country did not necessarily mean that all trauma care doctors in a hospital were trained accordingly.[40,41,45,48,54]

Quality Assurance

Despite the major trauma burden, in LI and MI countries, trauma registries are generally not part of the trauma care system (Table 2).[76] Apart from local and private initiatives in some of these countries, there was no nationwide trauma registry in India, South Africa, Iran, Brazil, Saudi Arabia, Spain, Ghana, and China at the dates of publication of these articles.[14,18,20,22,26,28,69] In many countries, the need for a trauma registry is acknowledged, for example, in 2015, Saudi Arabia initiated plans for a nationwide trauma registry.[35]

Mainly, the HI countries had nationally implemented trauma registries based on strict criteria, which subsequently would be classified as a Level IV trauma registry.[24,30,45,58,67] Several international collaborations in the field of trauma registries were seen. Some contribute to the German Trauma Register-DGU, United Kingdom and Ireland are collaborating within the Trauma Audit & Research Network, Australia and New Zealand established the binational National Trauma Registry Consortium, and the Scandinavian countries are collaborating in the Scandinavian Trauma Registry.[43,47,51,62,67,71] Some European countries that were classified as having Level III quality assurance, such as Croatia and Italy, did not have a national trauma registry but worked together since 2007 in creating a European database, the EuroTARN.[39] In other countries without a nationwide trauma registry, local initiatives were present, for example, in Greece, only 40% of the health care facilities contributed to the trauma registry, and in 2009, some autonomous regions in Spain had shown initiatives to implement a registry.[49,59] In contrast, the Canadian National Trauma Registry, which was established in 1997, was closed in 2014 for diverse reasons, such as availability of data elsewhere and changing priorities.[64]

DISCUSSION

The goal of this article is to give an international overview of the trauma systems worldwide, based on the available literature over the past 16 years. Despite internationally accepted standards and several initiatives by the WHO, it is apparent that there are still important differences between the organization and maturity of trauma care systems worldwide. Mature trauma systems are implemented in all included HI countries, whereas these are absent in most of the LI and MI countries, despite their high trauma burden. It seems that improvements in trauma care are, at least in part, related to a country's level of economic welfare. Mock et al.[3] suggested that increased economic welfare most likely first led to a reduction of prehospital trauma deaths due to improvements in prehospital care. This assumption is supported by historic data from the United States, where a decrease in prehospital deaths was seen over time.[77] On the other hand, a global rise in motor vehicle ownership in countries with increasing welfare is expected to lead to an increase in deaths due to road traffic crashes from 1.3 million deaths currently to 1.9 million deaths worldwide in 2020.[78] Although this is not a part of the trauma system, also preventive measures including legislation and improvement of infrastructure are needed to decrease trauma-related mortality in upcoming economies.[78] Research has shown that measures aimed at prevention, prehospital care, and in-hospital care are cost-effective in decreasing mortality of injured patients.[3]

Several initiatives, such as the Essential Trauma Care Project, have been initiated by the WHO to improve trauma care worldwide with affordable and reasonable minimum standards of care. Basic innovations have had a major effect on trauma care which offers leads for further development of trauma systems in several countries. For example, the collaboration between the government of Ghana and the Essential Trauma Care Project has led to initiatives to implement a National Ambulance.[79] A systematic review by La-Grone et al.[80] concerning the implementation of the guidelines of the Essential Trauma Care project showed that 40% of all LI countries and 30% MI countries documented some form of implementation of the Essential Trauma Care Project Guidelines. However, in only 14% of the countries, this implementation led to the formulation of policy. This trend is also seen in the implementation of trauma registries. It has been acknowledged worldwide that trauma registries are important for assessing and evaluating the development and improvement of global trauma care and quality assurance programs.[10] However, this review showed that a nationwide trauma registry is absent in most countries, especially in MI and LI countries (Table 2). The implementation of a trauma registry not only requires a central organization but also a digital infrastructure and trained staff. Subsequently maintaining an implemented trauma registry is costly.[10] However, the lack of any form of trauma registry has a negative impact on the development of a mature trauma system and the implementation of rules and regulations concerning trauma

care.[26] The development and worldwide implementation of an internationally accepted minimum set of data on trauma patients could facilitate and improve future trauma care improvement projects.

Limitations

This review has some limitations. First, we used the most commonly used instrument for classifying trauma systems, the WHO trauma system maturity index.[7] We had difficulty, however, to apply the level criteria of the index for some countries information. Especially if specific criteria were not mentioned and some of the criteria within one level were not met. If we hesitated between two levels, we chose to assign the higher level. A classification system with less composite levels and clearer criteria would help to classify trauma systems in a less ambiguous manner. For countries in which trauma care is organized on a federal or regional level, such as the United States, possible differences in the levels of care between the federal or regional trauma systems could not be identified due to a lack of data. Second, the literature on which we based the review was published over a period of 16 years. Although we did our best to retrieve the most up-to-date information available and did not include articles published before to the year 2000, some countries will have improved their trauma systems since the publication of the selected articles in this review. Improvements that had not been published and of which we were not aware could thus not be addressed in this review. Similarly, some countries may not have published about their trauma system at all. Finally, the methodological quality of the selected articles could not be assessed, because we are not aware of an instrument that can be used to evaluate the quality of this type of descriptive literature.

CONCLUSION

Despite the presence of seemingly sufficient resources and the evidence-based benefits of trauma systems, only nine of the 23 HI countries in our review have a well-defined and documented national trauma system. In most MI and LI countries, a formal trauma system is absent despite the high trauma burden in these countries. Much can be gained by improving trauma systems in these countries, but unfortunately, it also is apparent that trauma system development depends, at least in part, on the economic welfare.

REFERENCES

1. Mock C, Joshipura M, Arreola-Risa C, Quansah R. An estimate of the number of lives that could be saved through improvements in trauma care glob- ally. *World J Surg*. 2012;36(5):959–963.
2. Mock C, Brundage S, Goosen J, Joshipura M. Guidelines for trauma quality improvement programmes. *World Health Organization; Geneva*. 2009.
3. Mock CN, Jurkovich GJ, nii-Amon-Kotei D, Arreola-Risa C, Maier RV. Trauma mortality patterns in three nations at different economic levels: implications for global trauma system development. *J Trauma*. 1998;44(5): 804–812. discussion 12–4.
4. Mock CN, Adzotor KE, Conklin E, Denno DM, Jurkovich GJ. Trauma out- comes in the rural developing world: comparison with an urban level I trauma center. *J Trauma*. 1993;35(4):518–523.
5. *Resources for Optimal Care of the Injured Patients*. Chicago: American College of Surgeons' Committee on Trauma; 1999.
6. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097.
7. World Health Organization. Trauma system maturity index. http://apps.who. int/violence_injury_prevention/services/traumacare/maturity_index/en/index.html. Accessed May 15, 2016.
8. Harmsen AM, Giannakopoulos GF, Moerbeek PR, Jansma EP, Bonjer HJ, Bloemers FW. The influence of prehospital time on trauma patients outcome: a systematic review. *Injury*. 2015;46(4):602–609.
9. Roudsari BS, Nathens AB, Cameron P, Civil I, Gruen RL, Koepsell TD, Lecky FE, Lefering RL, Liberman M, Mock CN, et al. International comparison of prehospital trauma care systems. *Injury*. 2007;38(9):993–1000.
10. O'Reilly GM, Gabbe B, Moore L, Cameron PA. Classifying, measuring and improving the quality of data in trauma registries: a review of the literature. *Injury*. 2016;47(3):559–567.
11. World Health Organization Organization. Disease and injury country estimates. In: Global_burden_disease_death_estimates_sex_2008, editor. Excel. Switzerland 2008.
12. The World Bank Group. http://data.worldbank.org/. Accessed July 17 2016.
13. Mock CN, Tiska M, Adu-Ampofo M, Boakye G. Improvements in prehospital trauma care in an African country with no formal emergency medical services. *J Trauma*. 2002;53(1):90–97.
14. Quansah R. Essential trauma care in Ghana: adaptation and implementation on the political tough road. *World J Surg*. 2006;30(6):934–939.
15. Savitsky E, Rehnborg GB, Ibarra K. Emergency medical services development in the Seychelles Islands. *Am J Emerg Med*. 2000;18(3):332–335.
16. MacFarlane C, van Loggerenberg C, Kloeck W. International EMS systems in South Africa–past, present, and future. *Resuscitation*. 2005; 64(2):145–148.
17. Goosen J, Veller M. Trauma and emergency surgery: South African model. *World J Surg*. 2008;32(8):1622–1625.
18. Laing GL, Bruce JL, Aldous C, Clarke DL. The design, construction and implementation of a computerised trauma registry in a developing South African metropolitan trauma service. *Injury*. 2014;45(1):3–8.
19. Thomson N. Emergency medical services in Zimbabwe. *Resuscitation*. 2005;65(1):15–19.
20. Zong ZW, Li N, Cheng TM, Ran XZ, Shen Y, Zhao YF, Guo QS, Zhang LY. Current state and future perspectives of trauma care system in mainland China. *Injury*. 2011;42(9):874–878.
21. Kong G, Yin X, Wang T, Body R, Chen YW, Wang J, Cao L, Wu S, Gao J, Wang G, et al. Current state of trauma care in China, tools to predict death and ICU admission after arrival to hospital. *Injury*. 2015;46(9):1784–1789.

22. Fitzharris M, Zhong W, Myburgh J, Xuezhong Y, Yu J, Hammond N, Finfer SR, Taylor C, Wu Y. The status of trauma registry systems in Chinese hospitals. *Inj Prev*. 2011;17(6):419–421.
23. Lo CB, Lai KK, Mak KP. Prehospital care in Hong Kong. *Hong Kong Med J*. 2000;6(3):283–287.
24. Cheng CH, Graham CA, Gabbe BJ, Yeung JH, Kossmann T, Judson RT, Rainer TH, Cameron PA. Trauma care systems: a comparison of trauma care in Victoria, Australia, and Hong Kong, China. *Ann Surg*. 2008;247(2): 335–342.
25. Garg RH. Who killed Rambhor?: the state of emergency medical services in India. *J Emerg Trauma Shock*. 2012;5(1):49–54.
26. Joshipura MK. Trauma care in India: current scenario. *World J Surg*. 2008; 32(8):1613–1617.
27. Khashayar P, Amoli HA, Tavakoli H, Panahi F. Efficacy of pre-hospital care in trauma patients in Iran. *Emerg Med J*. 2010;27(6):430–432.
28. Zargar M, Kalantar Motamedi SM, Karbakhsh M, Ghodsi SM, Rahimi- Movaghar V, Panahi F, Saadat S, Khaji A, Davachi SM, Ganji S, et al. Trauma care system in Iran. *Chin J Traumatol*. 2011;14(3):131–136.
29. Soffer D, Klausner JM. Trauma system configurations in other countries: the Israeli model. *Surg Clin North Am*. 2012;92(4):1025–1040, x.
30. Aharonson-Daniel L, Avitzour M, Giveon A, Peleg K. A decade to the Israel National Trauma Registry. *Isr Med Assoc J*. 2007;9(5):347–351.
31. Tanigawa K, Tanaka K. Emergency medical service systems in Japan: past, present, and future. *Resuscitation*. 2006;69(3):365–370.
32. Mashiko K. Trauma systems in Japan: history, present status and future perspectives. *J Nippon Med Sch*. 2005;72(4):194–202.
33. Al-Ghamdi AS. Emergency medical service rescue times in Riyadh. *Accid Anal Prev*. 2002;34(4):499–505.
34. Al-Naami MY, Arafah MA, Al-Ibrahim FS. Trauma care systems in Saudi Arabia: an agenda for action. *Ann Saudi Med*. 2010;30(1):50–58.
35. Alanazi F, Hussain SA, Mandil A, Alamro N. Towards an electronic national injury surveillance system in Saudi Arabia. *East Mediterr Health J*. 2015;21(2): 140–146.
36. Bavonratanavech S. Trauma care systems in Thailand. *Injury*. 2003;34(9): 720–721.
37. Taviloğlu K, Ertekin C. Current status and future options for trauma and emergency surgery in Turkey. *Ulus Travma Acil Cerrahi Derg*. 2008;14(1): 10–13.
38. Nijs SJ, Broos PL. Trauma care systems in Belgium. *Injury*. 2003;34(9): 652–657.
39. Edwards A, Di Bartolomeo S, Chieregato A, Coats T, Della Corte F, Giannoudis P, Gomes E, Groenborg H, Lefering R, Leppaniemi A, et al. A comparison of European Trauma Registries. The first report from the EuroTARN Group. *Resuscitation*. 2007;75(2):286–297.
40. Antoljak T, Dobric I, Bakota B, Zigman T, Rajacic D, Ehrenfreund T.A plea for Croatian trauma system. *Injury*. 2013;44(Suppl 3):S3–S6.
41. Kristiansen T, Søreide K, Ringdal KG, Rehn M, Krüger AJ, Reite A, Meling T, Naess PA, Lossius HM. Trauma systems and early management of severe injuries in Scandinavia: review of the current state. *Injury*. 2010; 41(5):444–452.
42. Handolin L, Leppaniemi A, Vihtonen K, Lakovaara M, Lindahl J. Finnish Trauma Audit 2004: current state of trauma management in Finnish hospitals. *Injury*. 2006;37(7):622–625.
43. Ringdal KG, Lossius HM. Feasibility of comparing core data from existing trauma registries in scandinavia. Reaching for a Scandinavian major trauma outcome study (MTOS). *Scand J Surg*. 2007;96(4):325–331.

44. Masmejean EH, Faye A, Alnot JY, Mignon AF. Trauma care systems in France. *Injury*. 2003;34(9):669–673.
45. Sturm JA, Pape HC, Dienstknecht T. Trauma care in Germany: an inclusive system. *Clin Orthop Relat Res*. 2013;471(9):2912–2923.
46. Oestern HJ, Garg B, Kotwal P. Trauma Care in India and Germany. *Clin Orthop Relat Res*. 2013;471(9):2869–2877.
47. DGU Trauma Register. Teilnehmende Länder 2016. http://www. traumaregister-dgu.de/de/startseite_tr.html. Accessed June 6, 2016.
48. Theodorou D, Toutouzas K, Drimousis P, Larentzakis A, Kleidi E, Georgiou G, Gymnopoulos D, Kandylakis S, Theodoraki ME, Katsaragakis S. Emergency room management of trauma patients in Greece: preliminary report of a national study. *Resuscitation*. 2009;80(3):350–353.
49. Katsaragakis S, Theodoraki ME, Toutouzas K, Drimousis PG, Larentzakis A, Stergiopoulos S, Aggelakis C, Lapidakis G, Massalis I, Theodorou D. The implementation of a national trauma registry in Greece. Methodology and preliminary results. *J Trauma*. 2009;67(6):1421–1425.
50. Pace A. Trauma care systems in Italy. *Injury*. 2003;34(9):693–698.
51. Balasubramanian I, Mohan HM, Whelan RJ, McDermott F, Winter DC. Restructuring an evolving Irish trauma system: what can we learn from Europe and Australia? *Surgeon*. 2016;14(1):44–51.
52. Deasy C, Cronin M, Cahill F, Geary U, Houlihan P, Woodford M, Lecky F, Mealy K, Crowley P. Implementing major trauma audit in Ireland. *Injury*. 2016;47(1):166–172.
53. Dehli T, Gaarder T, Christensen BJ, Vinjevoll OP, Wisborg T. Implementation of a trauma system in Norway: a national survey. *Acta Anaesthesiol Scand*. 2015;59(3):384–391.
54. ten Duis HJ, van der Werken C. Trauma care systems in The Netherlands.*Injury*. 2003;34(9):722–727.
55. Spijkers AT, Meylaerts SA, Leenen LP. Mortality decreases by implementing a level I trauma center in a Dutch hospital. *J Trauma*. 2010;69(5): 1138–1142.
56. Twijnstra MJ, Moons KG, Simmermacher RK, Leenen LP. Regional trauma system reduces mortality and changes admission rates: a before and after study. *Ann Surg*. 2010;251(2):339–343.
57. Newton AI, Adams JR, Simpson KE, Egan G, Gowens PA, Donald MJ. Capability of Scottish emergency departments to provide physician-based prehospital critical care teams: a national survey. *Eur J Emerg Med*. 2013; 20(6):387–390.
58. Morrissey BE, Delaney RA, Johnstone AJ, Petrovick L, Smith RM. Do trauma systems work? A comparison of major trauma outcomes between Aberdeen Royal Infirmary and Massachusetts General Hospital. *Injury*. 2015;46(1):150–155.
59. Queipo de Llano E, Mantero Ruiz A, Sanchez Vicioso P, Bosca Crespo A, Carpintero Avellaneda JL, de la Torre Prado MV. Trauma care systems in Spain. *Injury*. 2003;34(9):709–719.
60. Black JJ, Davies GD. International EMS systems: United Kingdom. *Resuscitation*. 2005;64(1):21–29.
61. Metcalfe D, Perry DC, Bouamra O, Salim A, Woodford M, Edwards A, Lecky FE, Costa ML. Regionalisation of trauma care in England. *Bone Joint J*. 2016;98-B(9):1253–1261.
62. Racy M, Al-Nammari S, Hing CB. A survey of trauma database utilisation in England. *Injury*. 2014;45(3):624–628.
63. Zakrison T, Ball CG, Kirkpatrick AW. Trauma in Canada: a spirit of equity & collaboration. *World J Surg*. 2013;37(9):2086–2093.
64. Canadian Insitute for Health Information, 2014. http://www.cihi.ca/CIHI-ext- portal/internet/EN/TabbedContent/types+of+care/specialized+services/trauma +and+injuries/cihi010639. Accessed June 29 2016.
65. Pozner CN, Zane R, Nelson SJ, Levine M. International EMS systems: the United States: past, present, and future. *Resuscitation*. 2004;60(3):239–244.

66. Blackwell T, Kellam JF, Thomason M. Trauma care systems in the United States. *Injury*. 2003;34(9):735–739.
67. Zeckey C, Hildebrand F, Probst C, Krettek C. Trauma care systems in Germany, USA and Australia. An international comparison. *Unfallchirurg*. 2010;113(9):771–774. 6–7.
68. Timerman S, Gonzalez MM, Zaroni AC, Ramires JA. Emergency medical services: Brazil. *Resuscitation*. 2006;70(3):356–359.
69. Masella CA, Pinho VF, Costa Passos AD, Spencer Netto FA, Rizoli S, Scarpelini S. Temporal distribution of trauma deaths: quality of trauma care in a developing country. *J Trauma*. 2008;65(3):653–658.
70. Delprado AM. Trauma systems in Australia. *J Trauma Nurs*. 2007;14(2): 93–97.
71. Palmer CS, Davey TM, Mok MT, McClure RJ, Farrow NC, Gruen RL, Pollard CW. Standardising trauma monitoring: the development of a mini- mum dataset for trauma registries in Australia and New Zealand. *Injury*. 2013;44(6):834–841.
72. Christey GR. Trauma care in New Zealand: it's time to move ahead. *World J Surg*. 2008;32(8):1618–1621.
73. Paice R. An overview of New Zealand's trauma system. *J Trauma Nurs*. 2007;14(4):211–213.
74. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, Salkever DS, Scharfstein DO. A national evaluation of the effect of trauma- center care on mortality. *N Engl J Med*. 2006;354(4):366–378.
75. American College of Surgeons. https://www.facs.org/quality%20programs/ trauma/atls. Accessed October 20 2016.
76. O'Reilly GM, Cameron PA, Joshipura M. Global trauma registry mapping: a scoping review. *Injury*. 2012;43(7):1148–1153.
77. Evans JA, van Wessem KJ, McDougall D, Lee KA, Lyons T, Balogh ZJ. Epidemiology of traumatic deaths: comprehensive population-based assessment. *World J Surg*. 2010;34(1):158–163.
78. World Health Organization. Decade of Action for Road Safety 2011–2020 *Saving millions of lives*. 2011.
79. Charles Mock CJ. Manjul Joshipura, Jacques Goosen. *Strengthening Care for the Injured: Success Stories and Lessons Learned From Around the World*. Vienna: World Health Organization; 2010.
80. LaGrone L, Riggle K, Joshipura M, Quansah R, Reynolds T, Sherr K, Mock C. Uptake of the World Health Organization's trauma care guidelines: a systematic review. *Bull World Health Organ*. 2016;94(8):585–598c.

APPENDIX I: SEARCH STRATEGY

Years: 2000-2016

("trauma management"[ti] OR "Traumatology/organization and administration"[Mesh] OR "trauma system"[ti] OR "trauma systems"[ti] OR "polytrauma"[ti] OR "polytraumas"[ti] OR "poly trauma"[ti] OR "poly traumas"[ti] OR "trauma care systems"[ti] OR "trauma care system"[ti] OR " trauma care" [ti] OR "emergency medical services" [ti] OR "emergency medical service" [ti] OR " prehospital care" [ti] OR "pre-hospital care" [ti] OR "trauma registry" [ti] OR " trauma registries" [ti]) AND ("Geographic Locations"[Mesh] OR "national"[tw] OR "nationwide"[tw] OR "global"[tw] OR "worldwide"[tw])

3

Polytrauma patients in the Netherlands and the USA: A bi-institutional comparison of processes and outcomes of care

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Injury. 2018 Jan; 49(1):104-109.

ABSTRACT

Background

Modern trauma systems differ worldwide, possibly leading to disparities in outcomes. We aim to compare characteristics and outcomes of blunt polytrauma patients admitted to two Level 1 Trauma Centers in the US (USTC) and the Netherlands (NTC).

Methods

For this retrospective study the records of 1367 adult blunt trauma patients with an Injury Severity Score (ISS) ≤ 16 admitted between July 1, 2011 and December 31, 2013 (640 from NTC, 727 from USTC) were analyzed.

Results

The USTC group had a higher Charlson Comorbidity Index (mean [standard deviation] 1.15 [2.2] vs. 1.73 [2.8], $p < 0.0001$) and Injury Severity Score (median [interquartile range, IQR] 25 [17 - 29] vs. 21 [17 - 26], $p < 0.0001$). The in-hospital mortality was similar in both centers (11% in USTC vs. 10% NTC), also after correction for baseline differences in patient population in a multivariable analysis (adjusted odds ratio 0.95, 95% confidence interval 0.61–1.48, $p = 0.83$). USTC patients had a longer Intensive Care Unit stay (median [IQR] 4 [2 - 11] vs. 2 [2 - 7] days, $p = 0.006$) but had a shorter hospital stay (median [IQR] 6 [3 - 13] vs. 8 [4 - 16] days, $p < 0.0001$). USTC patients were discharged more often to a rehabilitation center (47% vs 10%) and less often to home (46% vs. 66%, $p < 0.0001$), and had a higher readmission rate (8% vs. 4%, $p = 0.01$).

Conclusion

Although several outcome parameters differ in two urban area trauma centers in the USA and the Netherlands, the quality of care for trauma patients, measured as survival, is equal. Other outcomes varied between both trauma centers, suggesting that differences in local policies and processes do influence the care system, but not so much the quality of care as reflected by survival.

INTRODUCTION

Despite several internationally accepted standards for trauma care, there is still significant variation among countries according to unique national demands and regulations. In the United States of America (U.S.), trauma care is organized according to the recommendations set by the American College of Surgeons Committee on Trauma (ACS-COT).[1] With five levels for Trauma Center designation and strict criteria for the resources required at each level, trauma care in the U.S. has been regionalized and the outcomes have improved after the implementation of the trauma system.[2–4]

The Dutch trauma system is comparable to the U.S. model in many ways. In 1999, the Dutch government designated 10 hospitals as trauma centers in an effort to regionalize prehospital patient triage of severely injured patients.[5] All hospitals were categorized into level 1, 2, or 3 trauma centers, based on nationally adopted trauma level criteria set by the Dutch Society for Trauma Surgery and closely resembling the ACS-COT criteria. Currently, the Dutch system is organized in eleven trauma regions, with a coordinating level 1 trauma center commanding a catchment area of minimally 1.2 million inhabitants in every region.[6] In The Netherlands, the implementation of trauma centers has reduced the overall mortality risk by 16%, and by 21% in polytrauma patients.[7,8]

Despite the similarities between the U.S. and the Dutch trauma systems, differences do exist, for instance regarding trauma training, patient volumes, type of injuries, prehospital care, distances travelled, and access to rehabilitation, possibly leading to differences in outcomes of care. The purpose of this study was to compare two urban Level-1 Trauma Centers, one in the U.S. and the other in the Netherlands, regarding demographics, injury characteristics, and outcomes of severely injured patients after blunt trauma.

MATERIAL AND METHODS

Trauma centers

This retrospective cohort study was performed at the Level 1 Trauma Center of the Massachusetts General Hospital in Boston, USA (USTC) and two Level 1 locations of Trauma Center West Netherlands (NTC), the Haaglanden Medical Center Westeinde and Leiden University Medical Center. The same trauma protocols apply for both Dutch trauma center locations and a previous study demonstrated that the characteristics of the polytrauma patients were similar. No differences were found in in-hospital mortality adjusted for clinical predictors between both Dutch trauma center locations (unpublished data).

The basic characteristics of trauma organization and management of USTC and NTC are summarized in Table 1. Differences were noted in the catchment area, the number of patients admitted annually, and the composition of the trauma team.

Table 1. Characteristics of trauma systems

	NTC	USTC
Level trauma center	1	1
Number of locations	2	1
Hospital catchment area	Urban area 2 million inhabitants	Urban area 6.0 million inhabitants
Total number of trauma patients/year	2270	2500
Polytrauma patients/ year	400	600
ATLS training	Yes	Yes
Protocol 'Management of polytrauma'	Yes	No
Specific criteria for activation of the trauma team	Yes	Yes
24/7 in house coverage	Yes (junior surgical resident, under close supervision of an attending surgeon)	Yes (attending surgeon)
CT-scan available at ED	In 1 of 2 locations	Yes
X-ray/ultrasound available at ED	Yes	Yes
Operating room available 24/7	Yes	Yes
OR-team available 24/7	Yes, on call	Yes
ICU bed available	Yes	Yes
Trauma team members	Attending surgeon, surgical resident, emergency physician, an anesthesiologist, intensive care doctor, radiologist, ICU-nurse, two emergency department nurses and an OR-nurse	Attending surgeon, fellow in trauma surgery (junior attending), senior resident, intern, ED senior resident, ED junior resident, nurse practitioner
Other specialties available for consultation	Yes	Yes

The Institutional Review Boards of both trauma centers granted permission for this study.

Patients and data collection

All trauma patients admitted to the NTC or USTC following a blunt trauma between July 1, 2011 and December 31, 2013, older than 16 years of age, and with an Injury Severity Score (ISS) of 16 or higher, were included for analysis. Patients who died before arrival or in the emergency department were excluded from the analysis. Also, patients who were first managed in another hospital before arriving at the NTC or USTC were excluded.

Patients were identified in the trauma registries of the two trauma centers. [9,10] Data obtained from the trauma registries were supplemented in identical databases in each TC by information acquired from the electronic medical records.

Data

Demographic data, type and severity of injuries classified according to the Abbreviated Injury Scale (AIS update 1998)[11], Injury Severity Score (ISS)[12], and vital signs and Revised Trauma Score (RTS) on admission were obtained from the trauma registries.[13] Missing data for the RTS were determined based on vital signs documented in the hospital records in 16.3% of all the cases in both trauma centers. Injuries with AIS code >2 were considered serious injuries. Data on comorbidity, intubation, and complications was collected from the medical charts. To describe the pre-trauma condition of the patients, the age-adjusted Charlson Comorbidity Index (CCI) was calculated by using a Microsoft Excel Macro. [14,15]The APACHE II score was used to assess the severity of illness of the patients admitted to the Intensive Care Unit (ICU).[16]

The primary outcome was in-hospital mortality. Secondary outcomes included length of stay in the hospital (HOS-LOS) and the ICU (ICU–LOS), ventilator-free days, complications (surgical complications including superficial and deep surgical site infections and rebleeding, pneumonia, urinary tract infections (UTI), deep venous thrombosis (DVT) and pulmonary embolism), readmission, and discharge disposition.

Statistical analysis

After data collection, the two TC databases were merged for statistical analysis. The demographic and clinical characteristics of the (NTC and USTC populations were compared by univariable analysis. Normally distributed continuous variables were summarized as mean and standard deviation (SD) and compared using unpaired t-tests. Skewed continuous data were summarized as median and interquartile range (IQR), and compared using Wilcoxon rank sum tests. Categorical variables were summarized as number (%), and compared using the Chi-squared test with continuity correction. The odds ratios with 95% confidence interval (CI) for in-hospital mortality, ICU-admission, complications and (unplanned) readmission after polytrauma in the NTC compared to the USTC were calculated using multivariable logistic regression analysis. Multiple linear regression analysis was used to calculate the mean difference (with 95% CI) in HOS-LOS and ICU-LOS between the NTC and USTC. In all multivariable analyses, available relevant clinical characteristics (age, gender, CCI, ISS and RTS) were included as independent variables to adjust for differences in case mix between the USTC and NTC. In the multivariable analysis for unplanned readmission, discharge disposition was also added as an independent variable. In the multiple linear regression analysis used to analyze ICU-LOS the APACHE-score was also added. For this observational study, no hypothesis was prespecified, and therefore no formal sample size was calculated.

Two-sided p-values <0.05 were considered statistically significant. The statistical analyses were performed using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA).

RESULTS

Comparison of trauma populations

Over the study period, 853 blunt polytrauma patients in the NTC and 1520 patients in the USTC met the inclusion criteria. Application of the exclusion criteria resulted in 640 NTC patients and 727 USTC patients eligible for analysis (Fig. 1).

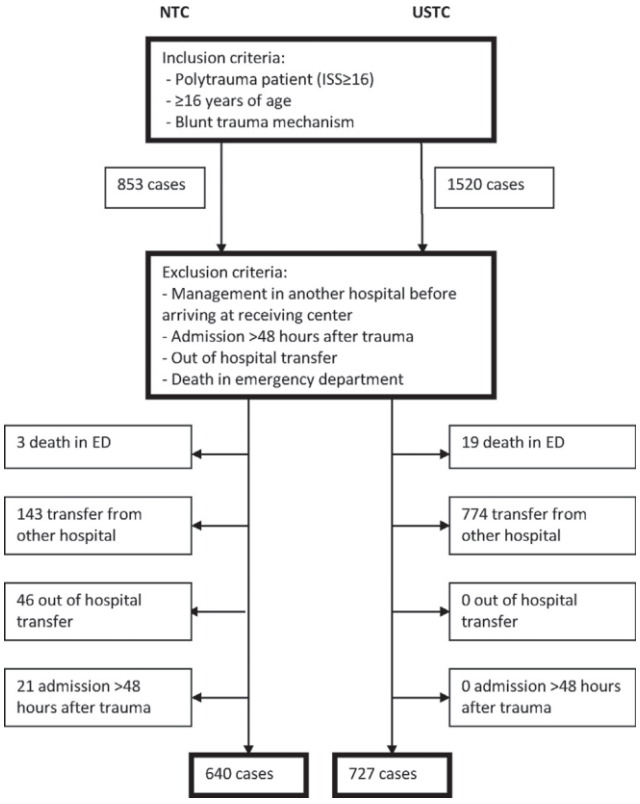

Figure 1. Flowchart of patient selection

Table 2 presents the characteristics of the patients in both trauma centers. USTC patients were more frequently male and had higher CCI and ISS compared to NTC patients. Fig. 2 shows that USTC patients had more often serious injuries in the chest (43.6% vs. 37.8%, $p = 0.02$) and extremities (29.6% vs. 19.5%, $p < 0.0001$), as well as injuries in more than one body region (47.5% vs. 34.7%, $p < 0.0001$).

Table 2. Patient characteristics

	NTC (N = 640)	USTC (N = 727)	P
Age, mean (SD)	56.5 (21.0)	55.0 (23.0)	0.19
Male, n (%)	398 (62.2)	493 (67.8)	0.03
CCI, median (IQR)	0 (0–2)	0 (0–4)	<0.0001
Mean (SD)	1.2 (2.3)	1.8 (2.8)	
Trauma mechanism, n (%)			0.03
Road traffic accident	242 (38.4)	280 (38.5)	
Fall from height	353 (55.9)	375 (51.6)	
Assault	16 (2.5)	34 (4.7)	
Other	20 (3.2)	38 (5.2)	
ISS, median (IQR)	21 (17–26)	25 (17–29)	<0.0001
RTS, n (%)			0.13
RTS 12	447 (69.8)	522 (72.4)	
RTS 11	71 (11.1)	57 (7.9)	
RTS ≤10	122 (19.1)	142 (19.7)	
Initial vital signs at ED			
SBP, mean (SD)	145.0 (30.9)	143.7 (32.6)	0.46
HR, mean (SD)	85.0 (20.7)	89.1 (22.6)	0.001
GCS, n (%)			
Mild TBI; GCS 13–15	464 (73.2)	542 (75.0)	0.08
Moderate TBI; GCS 9–12	60 (9.5)	45 (6.2)	
Severe TBI; GCS 3–8	110 (17.4)	136 (18.8)	
APACHE-score[a], median (IQR)	14 (9–24)	20 (15–25)	<0.0001

NTC: Trauma Center West Netherlands; USTC: Massachusetts General Hospital; SD: standard deviation; CCI: Charlson Comorbidity Index; ISS: Injury Severity Score; IQR: interquartile range; RTS: Revised Trauma Score; SBP: systolic blood pressure in mmHg; HR: heart rate in beats/min; GCS: Glasgow Coma Scale; APACHE: Acute Physiology and Chronic Health Evaluation. a In patients admitted to the Intensive Care Unit (n = 303 in NTC and n = 373 in USTC).

In-hospital mortality

The crude in-hospital mortality rate was 10.0% at the NTC and 10.9% at the USTC (p = 0.60) (Table 3) with an unadjusted odds ratio for mortality at the NTC compared to the USTC of 0.91 (95% CI 0.64- 1.29). After correction for differences in patient populations at baseline, the adjusted odds ratio for in-hospital mortality in the NTC compared to the USTC was 0.95 (95% CI 0.61-1.48; p = 0.83) (Table 4). Higher age, ISS, and RTS < 12 were statistically significant predictors of in-hospital mortality in the model.

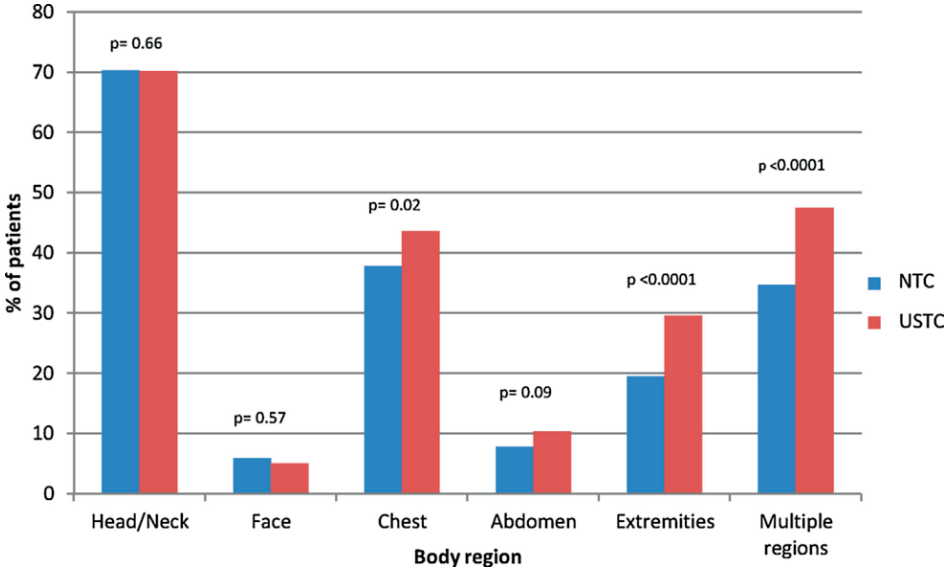

Figure 2. Distribution of injured body regions (AIS >2) by trauma center

Secondary outcome measures

HOS-LOS was longer for NTC patients compared to USTC patients (Table 3). Admission rates for the ICU were similar for both trauma centers but, when admitted, ICU-LOS was longer at the USTC. (Table 3) These results were unchanged after correction for differences in clinically relevant variables between the patient populations in the multivariable analyses (data not shown). In ICU- admitted patients, the number of ventilator-free days was also comparable between the two hospitals (Table 3).

DVT occurred more frequently in the USTC patients compared to the NTC patients (2.2% vs. 0.3%, $p = 0.002$). The incidence of other complications was comparable between the centers.

There was a statistically significant difference in discharge destination between the trauma centers ($p < 0.0001$); more NTC patients were sent home compared to USTC patients (66.3% vs. 46.1%), whereas more USTC patients were sent to a rehabilitation center (46.8% vs. 9.7%). The unadjusted unplanned readmission rate after the primary admission was higher in the USTC (7.6% vs. 4.2%, $p = 0.01$) (Table 3). This association was no longer statistically significant after correction for clinically relevant differences in the case mix of the patient populations (odds ratio 0.63, 95% CI 0.35-1.15, $p = 0.13$). Discharge to any other location than home was predictive for readmission in the multivariable model (data not shown).

Table 3. Outcomes

	NTC (N = 640)	USTC (N = 727)	P
In-hospital mortality, n (%)	64 (10.0)	79 (10.9)	0.66
HOS-LOS in days, median (IQR)	8 (4-16)	6 (3-13)	<0.0001
ICU admission, n (%)	303 (47.3)	373 (51.7)	0.12
ICU-LOS in days[a], median (IQR)	2 (2-7)	4 (2-11)	0.0006
Ventilator-free days[a], median (IQR)	26 (17-28)	26 (14-28)	0.47
Complications			
Surgical complications[b], n (%)	18 (2.5)	11 (1.7)	0.44
Pneumonia, n (%)	68 (10.6)	91 (12.5)	0.31
Urinary tract infection, n (%)	47 (7.3)	45 (6.2)	0.46
Deep venous thrombosis, n (%)	2 (0.3)	16 (2.2)	0.005
Pulmonary embolism, n (%)	7 (1.1)	11 (1.5)	0.66
Discharge locations[c], n (%)			<0.0001
Home	382 (66.3)	299 (46.1)	
Rehabilitation center	56 (9.7)	303 (46.8)	
Nursing facility	104 (18.1)	25 (3.9)	
Other institution	34 (5.9)	21 (3.2)	
Readmission (unplanned)[c], n (%)	24 (4.2)	49 (7.6)	0.01

Table 4. Multivariable logistic regression analysis of in-hospital mortality by center, adjusted for differences in patient populations at baseline

Factor	OR (95% CI)	P
Center		
USTC	1	
NTC	0.95 (0.61–1.48)	0.83
Age	1.05 (1.03–1.06)	<0.0001
Gender		
Female	1	
Male	1.14 (0.72–1.81)	0.58
CCI	1.05 (0.96–1.14)	0.31
ISS	1.04 (1.02–1.06)	0.001
RTS		
RTS 12	1	
RTS 11	3.44 (1.74–6.82)	<0.0001
RTS ≤ 10	16.42 (9.72–27.73)	<0.0001

USTC: Massachusetts General Hospital; NTC: Trauma Center West Netherlands; OR: odds ratio; CI: confidence interval; CCI: Charlson Comorbidity Index, ISS: Injury Severity Score, RTS: Revised Trauma Score.

DISCUSSION

In an overseas collaboration between two trauma centers in the Netherlands and the United States we compared the demographic disposition existed with the majority of USTC patients being discharged to a rehabilitation center and the majority of NTC patients being discharged home.

The study populations of polytrauma patients in the USTC and NLTC were not entirely similar. For instance, the patients from the USTC had higher injury severity scores than the patients from the NTC which may be explained by the fact that the patients from the USTC had severe injuries in more body areas than the patients from the NTC (Fig. 2). At the same time the RTS scores on admittance were comparable. In general, we do know that the RTS only moderately correlates with the AIS scores. For instance, elderly patients often have the combination of a hip fracture and 3 rib fractures. This results in an ISS of 18 for a stable patient that does have a normal RTS and generally no indication for ICU admittance. Despite the fact that the USTC patients had higher ISS scores, the ICU-admission rate was similar in both centers (47% vs. 51%).

The CCI scores were low in both study groups, which reflects the fact that the CCI was not developed to assess comorbidities in trauma patients, who are generally young and healthy. [17,18] Nevertheless, there was a small but statistically significant difference between the study groups regarding the age-adjusted Charlson Comorbidity Index, which was higher CCI in USTC. We cannot rule out that this difference might be explained by differences in history taking in the participating trauma centers. However, we think it is more likely that the slightly higher CCI in the US population can be explained by the fact that the prevalence of various chronic diseases, such as diabetes, hypertension, obesity and heart disease are more prevalent in the US population than in the general population in Western European countries including the Netherlands. [19–21]

In-hospital mortality was 10% in both trauma centers, which is similar to or lower than the percentage found in other studies.[2,7,8,22–25] Although some differences between the patient populations were statistically significant, the clinical relevance of these differences should not be overestimated. Correction for the potentially confounding effect of patient characteristics (age, gender, comorbidity, ISS and RTS) in the multivariable analysis of in-hospital mortality, did not lead to a notable change in the odds ratio of in-hospital mortality (unadjusted OR 0.91, adjusted OR 0.95).

Nearly every other outcome measure in the study differed between both centers. For example, the ICU stay was longer in the USTC. This may be explained by the higher injury severity of the USTC patients admitted to the ICU in comparison to the NTC patients (median ISS [IQR] of 26 [21 - 34] vs 25 [17 - 29], $p < 0.0001$) and their consequently higher APACHEII-scores (median [IQR] of 20 [15 - 25] vs. 14 [9 - 24], $p < 0.0001$).[19,20] However, beside the generally sicker ICU population in the USTC, their ICU stay may also be pro-

longed due to the unavailability of floor beds. The USTC operates constantly at a 100% capacity, which may result in delays in ICU discharge when a floor bed is not empty. Another possible explanation is the use of a Medium Care Unit (MC-unit) in TCWN in which patients can be closely monitored but cannot receive advanced respiratory support. This unit makes it possible to transfer patients out of the ICU if they are weaned from the ventilator even if they still need close monitoring. Despite the differences in ICU-LOS, these numbers are in agreement with those found in other North American and Dutch studies.[22,26]

The average total hospital length of stay of NTC patients was statistically and relevantly longer compared to USTC patients, but comparable or even shorter than that reported in other studies from the Netherlands.[7,22] The shorter length of stay for USTC patients might be explained by the fact that more patients were discharged to rehabilitation centers, suggesting a difference in discharge disposition policy. There are indeed differences between both countries in the organization of care after discharge from the hospital. In the Netherlands home support after discharge is very common and well organized. Most hospitals have a specialized nurse who is responsible for discharge disposition. Based on the advice of the doctor, nurses, and often a physical therapist, the best discharged location is determined. If home is the decided discharge location, home support will be organized. Home support is given by well-trained community health nurses who help patients with their personal care but are also able to provide more advanced medical care such as wound care. The USTC in this study has a close collaboration with an extensive regional rehabilitation network, a consortium of advanced rehabilitation centers. In these institutes patients not only receive intensive rehabilitative therapy but also medical care, thus allowing for earlier discharge from the hospital. It has been suggested that the establishment of trauma centers influenced discharge policies with an increasing number of patients being discharged to a rehabilitation center in the US.[27] A study by Brotemarkle et al. in the elderly trauma population showed that many factors, beside demographic and clinical characteristics, such a personal circumstances (e.g., family support, type of housing), financial (e.g. insurance) and political factors (e.g., organization health care), play a role in the discharge disposition.[28] In this study, data on these types of personal, financial and political factors were not available and could not be compared.

Although the readmission rates in both centers fell within the range of rates reported in literature (4.3–14.6%)[29–31], these rates differed between the centers. In our multivariable analysis, the increased risk of readmission in the USTC was no longer statistically significant after correction for differences in case mix, which was (at least in part) due to a lack of statistical power (unadjusted OR 1.8, $p = 0.02$; adjusted OR 1.5, $p = 0.13$). The higher readmission rate in the USTC might be influenced by the varying discharge dispositions between the centers. A study by Copertino et al. identified discharge dispo-

sition to a rehabilitation center or nursing facility as predictors for readmission. Also in our study, discharge to any other location than home was as well identified as a statistically significant predictor for readmission. Other established predictors for readmission in the literature, comorbidities (CCI) and ISS, were not found to be statistically significant predictors in our study.[32]

Last to be mentioned are the higher deep venous thrombosis rates seen in USTC. DVT is a common complication in admitted trauma patients, with rates ranging from 5–58% in the literature depending on the populations and diagnostic methods used.[33] In both centers in this study diagnostic approaches, such as an ultrasound, were used to diagnose DVT and all patients with clinical signs of DVT received prophylactic treatment such a low molecular weight heparin. Risk factors for the development of a DVT are longer ICU stay, 3 ventilator days, age 40, venous injury and lower extremity fracture with AIS 3.[34,35] Our study showed that USTC patients had more risk factors, such as longer ICU stay and more lower extremity injuries, which might the explain the higher incidence of DVT in the USTC. It has been suggested that pulmonary embolism is a better quality indicator for outcome of care due less variability in diagnostic approaches and aggressiveness. However, we think it is important to report the incidence of DVT as well as of pulmonary embolism, as both complications are considered clinically relevant. In addition, increasing evidence suggests that a different pathophysiology causes pulmonary embolism in trauma patients which might make DVT and PE two potential different and unrelated complications in this population. [3]

Strengths and limitations

A strength of our study is the detailed collection of data in comparison to previous publications on this topic. Data from the trauma registry was complemented by data collected from electronic medical records. Although our study is limited by its retrospective design the amount of missing data was minimal and all data was collected in a uniform manner by one researcher (SD). This was in contrast to other studies that used trauma registries established in two different countries without collecting more detailed data.[37] We excluded patients who were managed in another hospital before being admitted to one of the participating centers. Although the literature shows that there is no difference in mortality between transferred and non-transferred patients, it has been shown that there are differences in complications and time between injury and definitive care.[38,39] Exclusion of transferred patients from our analyses may have caused a biased interpretation of the patient population at the USTC, because about 50% of the polytrauma patient population was managed at another (typically small) hospital first. Since it was not feasible to collect the primary data of these transferred patients, we felt compelled to exclude them from our study group. Lastly, although we feel that the NTC and USTC are representative for Level 1 trauma centers in the US and

the Netherlands, they may not offer an complete representation of the trauma systems in these two countries.

CONCLUSION

The in-hospital mortality for polytrauma patients of two Level 1 trauma centers in two Western countries was similar, but there were notable differences in several other outcomes. Possible differences in critical care delivery, discharge disposition policies, and availability of rehabilitation centers may have contributed to these differences. As we move to integrated and standardized systems of trauma care around the world, it may be important to continue comparing trauma systems worldwide in order to uncover differences in outcomes. Such differences may point to best practices, which when applied, could improve care worldwide.

REFERENCES

1. American College of Surgeons – Committee on Trauma. Resources for optimal care of the injured patients. Chicago: American College of Surgeons; 1999.
2. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al. A national evaluation of the effect of trauma-center care on mortality. N Engl J Med 2006;354:366–78.
3. Nathens AB, Brunet FP, Maier RV. Development of trauma systems and effect on outcomes after injury. Lancet 2004;363:1794–801.
4. Celso B, Tepas J, Langland-Orban B, Pracht E, Papa L, Lottenberg L, et al. A systematic review and meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems. J Trauma 2006;60:371–8 discussion 8.
5. ten Duis HJ, van der Werken C. Trauma care systems in The Netherlands. Injury 2003;34:722–7.
6. Ministry of Health, Welfare and Sport. Beleidsvisie Traumazorg 2006–2010. Den Haag: Dutch Government; 2006.
7. Spijkers AT, Meylaerts SA, Leenen LP. Mortality decreases by implementing a level I trauma center in a Dutch hospital. J Trauma 2010;69:1138–42.
8. MJ, Moons KG, Simmermacher RK, Leenen LP. Regional trauma system reduces mortality and changes admission rates: a before and after study. Ann Surg 2010;251:339–43.
9. Sturms LM, Hoogeveen JM, Le Cessie S, Schenck PE, Pahlplatz PV, Hogervorst M, et al. Prehospital triage and survival of major trauma patients in a Dutch regional trauma system: relevance of trauma registry. Langenbecks Arch Surg 2006;391:343–9.
10. Ewing M, Funk GA, Warren AM, Rapier N, Reynolds M, Bennett M, et al. Improving National Trauma Data Bank(R) coding data reliability for traumatic injury using a prospective systems approach. Health Informatics J 2016; 22:1076–82.
11. Association for the Advancement of Automatic Medicine. The Abbreviated Injury Scale, 1990 Revision, Update 98. Barrington, USA.
12. Baker SP, O'Neill B, Haddon Jr. W, Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma 1974;14:187–96.
13. Champion HR SW, Copes WS, Gann DS, Gennarelli TA, Flanagan ME. A revision of the trauma score. J Trauma Acute Care Surg 1989;29:623–9.
14. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
15. Hall WH, Ramachandran R, Narayan S, Jani AB, Vijayakumar S. An electronic application for rapidly calculating Charlson comorbidity score. BMC Cancer 2004;4:94.
16. Zimmerman JE, Wagner DP, Draper EA, Wright L, Alzola C, Knaus WA. Evaluation of acute physiology and chronic health evaluation III predictions of hospital mortality in an independent database. Crit Care Med 1998;26: 1317–26.
17. St-Louis E, Iqbal S, Feldman LS, Sudarshan M, Deckelbaum DL, Razek TS, et al. Using the age-adjusted Charlson comorbidity index to predict outcomes in emergency general surgery. J Trauma Acute Care Surg 2015;78:318–23.
18. Gabbe BJ, Magtengaard K, Hannaford AP, Cameron PA. Is the Charlson Comorbidity Index useful for predicting trauma outcomes? Acad Emerg Med 2005;12:318–21.
19. Michaud PC, Goldman D, Lakdawalla D, Gailey A, Zheng Y. Differences in health between americans and western europeans: effects on longevity and public finance. Soc Sci Med 2011;73:254–63.
20. Banks J, Marmot M, Oldfield Z, Smith JP. Disease and disadvantage in the United States and in England. JAMA 2006;295:2037–45.

21. OECD. Health at a Glance. OECD Publishing; 2015.
22. Gunning AC, Lansink KW, van Wessem KJ, Balogh ZJ, Rivara FP, Maier RV, et al. Demographic patterns and outcomes of patients in level I trauma centers in three international trauma systems. World J Surg 2015;39:2677–84.
23. Lansink KW, Gunning AC, Spijkers AT, Leenen LP. Evaluation of trauma care in a mature level I trauma center in the Netherlands: outcomes in a Dutch mature level I trauma center. World J Surg 2013;37:2353–9.
24. Nathens AB, Jurkovich GJ, Maier RV, Grossman DC, MacKenzie EJ, Moore M, et al. Relationship between trauma center volume and outcomes. JAMA 2001;285:1164–71.
25. Templeton J, Oakley PA, MacKenzie G, Cook AL, Brand D, Mullins RJ, et al. A comparison of patient characteristics and survival in two trauma centres located in different countries. Injury 2000;31:493–501.
26. Brinkman S, Bakhshi-Raiez F, Abu-Hanna A, de Jonge E, de Keizer NF. Determinants of mortality after hospital discharge in ICU patients: literature review and Dutch cohort study. Crit Care Med 2013;41:1237–51.
27. Kelly ML, Roach MJ, Banerjee A, Steinmetz MP, Claridge JA. Functional and long-term outcomes in severe traumatic brain injury following regionalization of a trauma system. J Trauma Acute Care Surg 2015;79:372–7.
28. Brotemarkle RA, Resnick B, Michaels K, Morton P, Wells C. Length of hospital stay and discharge disposition in older trauma patients. Geriatr Nurs 2015;36: S3–9.
29. Moore L, Stelfox HT, Turgeon AF, Nathens AB, Le Sage N, Emond M, et al. Rates, patterns, and determinants of unplanned readmission after traumatic injury: a multicenter cohort study. Ann Surg 2014;259:374–80.
30. Morris DS, Rohrbach J, Sundaram LM, Sonnad S, Sarani B, Pascual J, et al. Early hospital readmission in the trauma population: are the risk factors different? Injury 2014;45:56–60.
31. Laupland KB, Svenson LW, Grant V, Ball CG, Mercado M, Kirkpatrick AW. Long- term mortality outcome of victims of major trauma. Injury 2010;41:69–72.
32. Copertino LM, McCormack JE, Rutigliano DN, Huang EC, Shapiro MJ, Vosswinkel JA, et al. Early unplanned hospital readmission after acute traumatic injury: the experience at a state-designated level-I trauma center. Am J Surg 2015;209:268–73.
33. Rogers FB, Cipolle MD, Velmahos G, Rozycki G, Luchette FA. Practice management guidelines for the prevention of venous thromboembolism in trauma patients: the EAST practice management guidelines work group. J Trauma 2002;53:142–64.
34. Michetti CP, Franco E, Coleman J, Bradford A, Trickey AW. Deep vein thrombosis screening and risk factors in a high-risk trauma population. J Surg Res 2015;199:545–51.
35. Knudson MM, Ikossi DG, Khaw L, Morabito D, Speetzen LS. Thromboembolism after trauma: an analysisof 1602 episodes from the american college of surgeons national trauma data bank. Ann Surg 2004;240:490–6 discussion 6–8.
36. Van Gent JM, Zander AL, Olson EJ, Shackford SR, Dunne CE, Sise CB, et al. Pulmonary embolism without deep venous thrombosis: de novo or missed deep venous thrombosis? J Trauma Acute Care Surg 2014;76:1270–4.
37. Jurkovich GJ, Mock C. Systematic review of trauma system effectiveness based on registry comparisons. J Trauma 1999;47:S46–55.
38. Pickering A, Cooper K, Harnan S, Sutton A, Mason S, Nicholl J. Impact of prehospital transfer strategies in major trauma and head injury: systematic review, meta-analysis, and recommendations for study design. J Trauma Acute Care Surg 2015;78:164–77.

39. Hill AD, Fowler RA, Nathens AB. Impact of interhospital transfer on outcomes for trauma patients: a systematic review. J Trauma 2011;71:1885–900 discussion 901.

4

Differences in characteristics and outcome of patients with penetrating injuries in the USA and the Netherlands: A multi-institutional comparison

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World Journal of Surgery. 2018 nov;42(11):3608-3615.

ABSTRACT

Introduction

The incidence and nature of penetrating injuries differ between countries. The aim of this study was to analyze characteristics and clinical outcomes of patients with penetrating injuries treated at urban Level-1 trauma centers in the USA (USTC) and the Netherlands (NLTC).

Methods

In this retrospective cohort study, 1331 adult patients (470 from five NLTC and 861 from three USTC) with truncal penetrating injuries admitted between July 2011 and December 2014 were included. In-hospital mortality was the primary outcome. Outcome comparisons were adjusted for differences in population characteristics in multi- variable analyses.

Results

In USTC, gunshot wound injuries (36.1 vs. 17.4%, p = 0.001) and assaults were more frequent (91.2 vs. 77.7%, p = 0.001). ISS was higher in USTC, but the Revised Trauma Score (RTS) was comparable. In-hospital mortality was similar (5.0 vs. 3.6% in NLTC, p = 0.25). The adjusted odds ratio for mortality in USTC compared to NLTC was 0.95 (95% confidence interval 0.35–2.54). Hospital stay length of stay was shorter in USTC (difference 0.17 days, 95% CI -0.29 to -0.05, p = 0.005), ICU admission rate was comparable (OR 0.96, 95% CI 0.71–1.31, p = 0.80), and ICU length of stay was longer in USTC (difference of 0.39 days, 95% CI 0.18–0.60, p = 0.0001). More USTC patients were discharged to home (86.9 vs. 80.6%, p = 0.001). Readmission rates were similar (5.6 vs. 3.8%, p = 0.17).

Conclusion

Despite the higher incidence of penetrating trauma, particularly firearm-related injuries, and higher hospital volumes in the USTC compared to the NLTC, the in-hospital mortality was similar. In this study, outcome of care was not significantly influenced by differences in incidence of firearm-related injuries.

INTRODUCTION

Worldwide, traumatic injuries are an important cause of death and disability, especially under 45 years of age.[1] In most developed countries, blunt trauma is responsible for the majority of the trauma burden, while roughly 15% of all injuries are caused by penetrating trauma.[2] Despite the lower incidence, penetrating trauma is a considerable health burden leading to premature mortality, permanent disability and psychological problems.[3, 4]

The incidence and nature of penetrating injuries differ between countries. In the USA and South Africa, urban epidemics of penetrating injuries are seen, with penetrating injuries being responsible for 20–45% and up to 60–80% of all injuries, respectively.[2, 5] In European countries, the incidence of penetrating trauma is low; for instance, 3–4% of all injuries in the Netherlands are penetrating, and in Switzerland, only 0.2% of all emergency department visits are penetrating injuries.[3, 6, 7] However, in the Netherlands, 70% of the fatal violent incidents penetrating injuries were seen.[3] Besides the varying incidence, differences in penetrating trauma mechanism are also reported. In European countries, stab wounds represent the majority of penetrating injury, whereas in the USA a considerable proportion of penetrating trauma are gunshot wounds. The overall firearm-related mortality rate is roughly six times higher in the USA compared to European countries.[3, 7–13]

Both the primary assessment and treatment of patients with penetrating injuries are often highly complex and require a multidisciplinary team. Similar to the American situation, regionalized inclusive trauma systems are implemented in the Netherlands with dedicated Level-1 trauma centers providing 24/7 comprehensive trauma care.[14, 15] However, differences in clinical routine and experience with penetrating injuries may exist between these countries due to the low incidence of penetrating trauma in the Netherlands, potentially affecting the clinical outcome.

The goal of this study was to compare the demographics, trauma mechanism, injury characteristics and outcomes of patients with truncal penetrating injuries treated in urban Level-1 trauma centers in the USA and the Netherlands. We aimed to gain insight into differences in care to identify factors that may influence patient outcome.

MATERIALS AND METHODS

Trauma centers

This multi-institutional retrospective cohort study was performed at five Level-1 trauma centers in the Netherlands (Netherlands trauma center (NLTC): Academic Medical Center, Erasmus Medical Center, Vrije Universiteit Medical Center, Haaglanden Medical Center

and Leiden University Medical Center) and three Level-1 trauma centers in Boston, USA (US trauma center (USTC): Boston Medical Center, Brigham and Women's Hospital, and Massachusetts General Hospital). These NLTC and USTC are all located in urban areas with comparable population densities (4200/km2 in Boston versus 5000/km2 in the Amsterdam–Leiden–Rotterdam region)[16, 17] and comparable violent crime rates (390 and 360/100.000 in Massachusetts and the Dutch region, respectively).[18, 19]

Patients and data collection

Eligible patients were identified in the trauma registries of the participating centers. All patients over 15 years of age who had been admitted to the NLTC or USTC with truncal penetrating injuries, i.e., penetrating injuries to the neck, thorax, abdomen, back or inguinal area, between July 1, 2011, and December 31, 2014, were included. Patients with isolated penetrating injuries to the head or the extremities (i.e., without truncal penetrating injuries) were excluded. Patients who were managed at another hospital before arriving at the participating hospital or were transferred to another hospital after initial treatment in participating hospital were excluded. Also, patients who died before arrival or arrived more than 48 h after trauma at the emergency department were excluded. Institutional review board permission was obtained from all participating centers.

Data

Demographic data and injury data, defined according to the Abbreviated Injury Score (AIS, updated 1998)[20], Injury Severity Score (ISS)[21], vital signs and Revised Trauma Score (RTS)[22] on admission were extracted from the trauma registries. Data on comorbidity, scored using the age-adjusted Charlson comorbidity index[23, 24], and complications were collected from the medical records.

The primary outcome was in-hospital mortality. Secondary outcomes included hospital length of stay (HOS- LOS), intensive care unit admission and length of stay (ICU-LOS) ventilator-free days[25], readmission rates, complications (pneumonia, urinary tract infection (UTI), deep venous thrombosis (DVT), sepsis and wound infection) and discharge disposition.

Statistical analysis

Demographic and clinical characteristics were compared by univariable analysis. Continuous variables were com- pared by the Pearson's t test or Wilcoxon rank sum test, depending on data distribution. Categorical variables were compared by the Chi-squared test or Fisher's exact test.

For in-hospital mortality, ICU admission, complications and (unplanned) readmission in NLTC compared to USTC, the odds ratio (OR) with 95% confidence interval (CI) were calculated using multivariable logistic regression analysis. Multiple linear regression

analysis was used to calculate the mean difference (with 95% CI) in HOS-LOS and ICU- LOS between NLTC and USTC. Based on the literature and biological plausibility, potential clinically relevant confounders were analyzed. Age, gender, penetrating trauma mechanism, ISS and RTS were identified as clinically potential important confounders in the univariate analysis and adjusted for in all multivariable analyses. For this observational study, no hypothesis was prespecified, and therefore, no formal sample size was calculated.

Statistical testing was two-sided, and p values <0.05 were considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY, USA).

RESULTS

Comparison of trauma populations

During the study period, 470 patients with truncal penetrating injuries were admitted in the NLTC and 861 in the USTC. The number of included patients per trauma center in each country is presented in Fig. 1. In general, more patients with penetrating trauma per trauma center were admitted in the USTC compared to the NLTC.

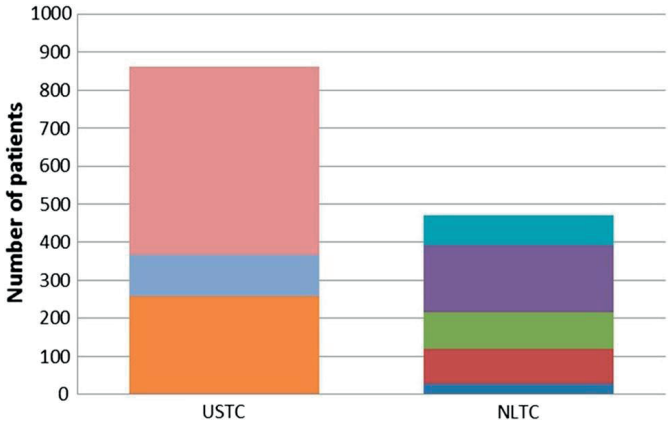

Figure 1. Number of patients with penetrating trauma, by trauma center location (USTC: 3 trauma centers in the USA; NLTC: 5 trauma centers in The Netherlands)

Table 1 summarizes the demographics and clinical characteristics in both centers. USTC patients were younger, slightly more often male and had a somewhat higher ISS than NLTC patients (median ISS 9 in both groups, p = 0.01), but no difference in RTS was seen. In USTC, significantly more patients with gunshot wounds were admitted (36.1 vs. 17.4%, p = 0.0001), which were more often the result of assault compared to NLTC.

Table 1. Characteristics of patients with truncal penetrating injuries

	NLTC (*n* = 470)	**USTC (*n* = 861)**	***P***
Age [median (IQR)]	31.0 (24.0–34.5)	27.0 (22.0–37.0)	<0.0001
Male gender [*n* (%)]	410 (87.2)	783 (90.9)	0.03
Comorbidity [*n* (%)]	42 (9.2%)	88 (10.2)	0.30
Penetrating mechanism [*n* (%)]			
Stab wound	388 (82.6)	550 (63.9)	<0.0001
Gunshot wound	82 (17.4)	311 (36.1)	
Mechanism of injury [*n* (%)]			
Assault	365 (77.7)	785 (91.2)	<0.0001
Self-inflicted	82 (17.4)	52 (6.0)	
Other/unknown	23 (4.9)	24 (2.8)	
ISS, median (IQR)	9 (2–14)	9 (3–16)	0.01
RTS [*n* (%)]			
12	373 (86.3)	702 (86.1)	0.30
11	35 (8.1)	53 (6.5)	
≤10	24 (5.6)	60 (7.4)	
GCS on admission [*n* (%)]			
GCS < 9	19 (4.4)	58 (6.8)	0.21
GCS 9–12	11 (2.6)	25 (2.9)	
GCS >12	401 (93.0)	768 (90.1)	
SBP on admission [mean (SD)]	130.1 (27.6)	134.1 (31.3)	0.02
RR on admission [mean (SD)]	20.2 (11.2)	19.2 (5.0)	0.03
HR on admission [mean (SD)]	93.2 (22.3)	95.6 (26.1)	0.09

NLTC Netherlands trauma center, *USTC* US trauma center, *SD* standard deviation, *CCI* Charlson comorbidity index, *ISS* Injury Severity Score, *IQR* interquartile range, *RTS* Revised Trauma Score, *GCS* Glasgow Coma Scale, *SBP* systolic blood pressure in mmHg, *RR* respiratory rate per minute, *HR* heart rate in beats/min

In both centers, the ISS of gunshot wound patients (NLTC median ISS 16 [interquartile range IQR 7.5 - 25] vs. USTC median ISS 16 [IQR 9 - 20], p = 0.82) was significantly higher compared to the ISS of patients with stab wounds (NLTC median ISS 9 [IQR 2 - 11] vs. USTC median ISS 6 [IQR 2 - 11], p = 0.64).

Figure 2 shows the distribution of severe penetrating injuries (AIS [2) per body region in both centers. NLTC patients had more often severe injuries to the spine (2.3 vs. 0.1%, p = 0.0001), while in USTC patients more penetrating injuries to the abdomen (24.2 vs. 18.9%, p = 0.03), extremities (9.4 vs. 4.9%, p = 0.0003) and multiple body regions (30.2 vs. 18.4%, p = 0.001) were seen.

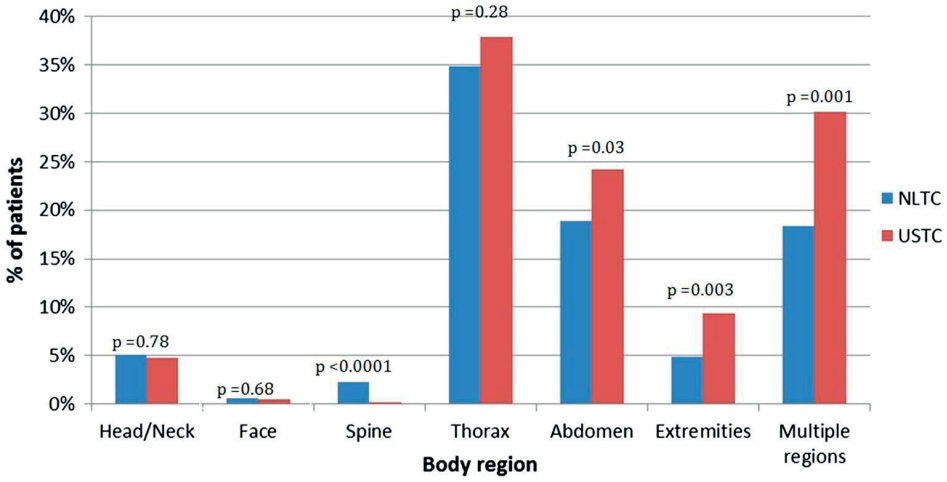

Figure 2. Percentage of patients with severe penetrating injury (AIS [2), per body region by trauma center location

In-hospital mortality

The in-hospital mortality rate in NLTC was 3.6% (17/470) compared to 5.0% (43/861) in USTC (p = 0.25) (Table 2). The unadjusted OR for mortality in the USTC compared to the NLTC was 1.40 (95% CI 0.75–2.49, p = 0.25). After correction for clinically relevant confounders, the adjusted OR for in-hospital mortality in the USTC compared to the NLTC was 0.95 (95% CI 0.35–2.54, p = 0.91). Higher ISS, RTS < 10 and gunshot wounds were statistically significant predictors of in-hospital mortality (Table 3). There was no difference in mortality in patients with gunshot wounds (NLTC 11.3% vs. USTC 11.0%, p = 0.48) and patients with stab wounds (NLTC 2.1% vs. USTC 1.5%, p = 0.94).

Secondary outcome measures

HOS-LOS was similar in both centers (Table 2). After correction for differences in case mix, USTC HOS-LOS was on average 0.17 days shorter than in NLTC (95% CI -0.29 to -0.05, p = 0.005). A higher age,gunshot wounds, higher ISS and low RTS were statistically significant predictors of a longer LOS. The ICU admission rate in USTC appeared higher compared to NLTC (33.8 vs. 28.6%, p = 0.05), but this association was not statistically significant after adjustment for differences in case mix (OR 0.96, 95% CI 0.71–1.31, p = 0.80). ICU-LOS was significantly longer in USTC compared to NLTC (median 2 [IQR 1 - 5] days vs. 1 [IQR 1 - 2] days, p = 0.0001). This association remained statistically significant after correction for differences in case mix (difference of 0.39 days, 95% CI 0.18–0.60, p = 0.0001). A higher ISS and gunshot wounds were statistically significant predictors of a longer ICU- LOS. More ICU admitted USTC patients received mechanical ventilation than NLTC patients (47.1 vs. 58.1%, p = 0.04), after correction for clinically relevant parameters

Table 2. Outcomes for patients with truncal penetrating injuries

	NLTC (*n* = 470)	USTC (*n* = 861)	P
In-hospital mortality [*n* (%)]	17 (3.6)	43 (5.0)	0.25
HLOS [median (IQR)]	3 (1–6)	2 (1–6)	0.11
ICU admission [*n* (%)]	134 (28.6)	291 (33.8)	0.05
ICU-LOS [median (IQR)]	1 (1–2)	2 (1–5)	\0.0001
Ventilator-free days[a] [median (IQR)]	27 (26–28)	27 (25–28)	0.02
Mechanical ventilation[a] [*n* (%)]	56 (47.1)	168 (58.1)	0.04
Complication [*n* (%)]			
Pneumonia	12 (2.6)	24 (2.8)	0.83
Urinary tract infection	4 (0.9)	15 (1.7)	0.20
Deep venous thrombosis	1 (0.2)	14 (1.6)	0.02
Sepsis	4 (0.9)	9 (1.0)	0.74
Wound infection	18 (3.9)	44 (5.1)	0.30
Discharge disposition [*n* (%)]			
Home	365 (80.6)	625 (86.9)	\0.0001
Mental health facility	42 (9.3)	40 (5.6)	
Rehabilitation	5 (1.1)	36 (5.0)	
Nursing home	11 (2.4)	5 (0.7)	
Other/unknown	30 (6.6)	13 (1.8)	
Readmission[b] [*n* (%)]	17 (3.8)	46 (5.6)	0.15

NLTC Netherlands trauma center, *USTC* US trauma center, *HLOS* hospital length of stay in days, *IQR* interquartile range, *ICU* intensive care unit, *ICU-LOS* intensive care unit length of stay in days [a]Of patients admitted to ICU [b]Of patients surviving hospital admission

this difference was no longer statistically significant (OR 1.59, 95% CI 0.99–2.57, p = 0.06). DVT was more often diagnosed in USTC, and the incidence of other complications was similar in both countries (Table 2). This difference in DVT incidence ceased to exist after adjustment for differences in case mix (OR 3.0, 95% CI 0.36–35.1, p = 0.31).

A statistically significant difference in discharge disposition was seen (p = 0.0001), with more USTC patients being discharged to a rehabilitation center (5.0 vs. 1.1%), while more NLTC patients were discharged to a mental health facility (9.3 vs. 5.6%) or nursing home (2.4 vs. 0.7%). Readmission rates were similar, even after correction for differences in case mix (OR 1.4, 95% CI 0.75–2.71, p = 0.28) (Table 2).

DISCUSSION

In this binational collaboration between five Level-1 trauma centers in the Netherlands and three Level-1 trauma centers in the USA, we found that patient volumes, especially

Table 3. Risk factors for in-hospital mortality in patients with truncal penetrating injuries

Risk factor	Odds ratio (95% CI)	P
Location		
NLTC	1 (reference)	
USTC	0.95 (0.35–2.54)	0.91
Gender		
Female	1 (reference)	
Male	0.60 (0.14–2.62)	0.49
Age	1.02 (0.99–1.06)	0.23
ISS	1.08 (1.04–1.13)	<0.0001
RTS		
12	1 (reference)	
11	4.28 (0.95–19.16)	0.06
≤10	59.26 (20.62–170)	<0.0001
Type of trauma		
Stab wound	1 (reference)	
Shot wound	3.85 (1.37–10.81)	0.01

of gunshot victims, were significantly higher in the USTC compared to NLTC. Apart from patient volumes and trauma mechanism, the patient populations were fairly comparable with similar ISS and RTS. The in-hospital mortality was similar (4–5%) and comparable with or lower than rates reported in other studies.[3, 26, 27]

Although the studied geographical areas in both countries had comparable urbanization and violent crime rates, the proportion of admitted patients with gunshot wounds was almost twice as high in the USTC. This is most likely due to differences in legislation concerning firearm use and ownership. Dutch citizens can only obtain a firearm permit under very strict conditions[28, 29], whereas guns can easily be obtained in the USA. Research has shown that a major determinant of firearm-related deaths is the availability of guns and that the implementation of restrictive laws in firearm purchase or access led to a reduction in firearm-related deaths in several countries, such as Australia, New Zealand, South Africa and Canada.[30–32]

In our study, no difference in in-hospital mortality was found between both centers, despite that the penetrating trauma patient volumes in USTC were generally higher than in NLTC. Although it has been suggested that higher trauma patient volumes are associated with better outcomes, this relationship remains inconclusive due to heterogeneity of studies.[33, 34] Nevertheless, there is evidence that regionalization of trauma care may lead to reduced mortality rates.[35] Implementation of comprehensive trauma systems by regionalizing and standardizing complex trauma care in Level-1 facilities is likely to be more effective for improving outcomes after trauma than case volume itself.[34, 36]

In both USTC and NLTC, all-inclusive trauma systems have been implemented that provide 24/7 acute trauma care and have similar facilities such as immediate availability of CT scanning, ICU beds and an in-house surgical team with an operating room available at all times. Surgeons and surgical residents in both systems receive similar surgical training, and management of penetrating trauma is broadly similar both following ATLS protocol.[37] Despite these similarities, some differences in clinical outcomes and processes were observed. Firstly, higher DVT rates were seen in USTC, although these differences ceased to exist after correction for differences in case mix. In both USTC and NLTC, patients received prophylactic treatment, mainly low molecular weight heparin, but inferior vena cava (IVC) filters were not routinely placed. Diagnostic approaches such as ultrasound were used if there were clinical signs indicating a potential DVT. Higher DVT rates might be explained by differences in clinical management; however, more likely it is explained by USTC patients experiencing more in the literature identified risk factors for DVT such as a younger age, and more thoracic and abdominal injuries.[38, 39]

Secondly, although the ICU admission rates were similar, the ICU-LOS in USTC was somewhat longer. Although this might be explained by the larger numbers of patients with gunshot wounds with a higher ISS and of patients needing mechanical ventilation, the longer ICU- LOS in USTC is most likely due to the unavailability of floor beds which may delay ICU discharge, as the USTC operates at a constantly 100% capacity. Another likely explanation is the availability of medium care units in most of the NLTC, to which patients can be discharged when they are weaned from the ventilator but still need close monitoring. However, although statistically significant, the differences for both ICU- and HOS-LOS less than 1 day were too small to be considered clinically relevant.

Lastly, although the majority of patients in both groups were discharged home, there were noticeable differences in discharge protocol. Significantly more NLTC patients were discharged to a mental health facility possibly explained by the higher incidence of self-inflicted wounds in this population. More USTC patients were discharged to a rehabilitation center, possibly explained by the extensive network of rehabilitation centers in the USTC region with which they work closely. Despite these differences in hospital discharge policy, the readmission rates were similar.

Strengths and limitations

The detailed data collection and the large cohort are strengths of our study. Data collected from the trauma registries were complemented by data from electronic medical records collected by one researcher (AH), limiting the amount of missing data. A limitation of our study was that no information on morbidity and mortality was available after hospital discharge. A second limitation is that we excluded specific patient groups from the study such as patients with isolated penetrating injuries to the brain and extremities. They are considered a different group, and the involvement of trauma surgery is often

limited after the initial resuscitation phase. Additionally, all patients who were first managed in another hospital before being admitted to one of the participating centers were excluded. Although studies have shown that mortality is similar between transferred and non-transferred patients, differences in complication rates do exist.[40] By excluding these patients, we may have caused a selection bias in the study groups, since transfer rates were higher in USTC. However, it was not feasible to collect primary data for these patients, so we felt compelled to exclude them. A third limitation is that the study was performed in a limited number of trauma centers in both countries. Although we feel that the participating USTC and NLTC are representative for the Level-1 trauma centers in the densely populated urban areas in the USA and Netherlands, the results of this study may not allow for a comparison of care for patients with penetrating injuries in the two countries as a whole.

CONCLUSION

Despite the higher incidence of penetrating trauma, particularly firearm-related injuries, and higher hospital volumes in the USTC compared to the NLTC in this study, the in-hospital mortality was similar in these centers. We also did not see clinically important differences in other outcomes between the centers in both countries. Despite variations in trauma system organization and clinical routine, implementation of all-inclusive trauma systems in both countries seems to have led to a comparable standard of care. More in-depth research is needed to uncover other potential factors that might contribute to differences in outcomes for specific patient subgroups, to further improve the care for penetrating trauma patients.

REFERENCES

1. Krug EG, Sharma GK, Lozano R (2000) The global burden of injuries. Am J Public Health 90:523–526
2. Soreide K (2009) Epidemiology of major trauma. Br J Surg 96:697–698
3. Boot F, Hoencamp R, van der Wilden GM et al (2016) Perforerend letsel in een binnenstadziekenhuis. Nederlands Tijdschrift voor Traumachirurgie 24:6–12
4. Holbrook TL, Hoyt DB (2004) The impact of major trauma: quality-of-life outcomes are worse in women than in men, inde- pendent of mechanism and injury severity. J Trauma 56:284–290
5. Exadaktylos A, Stettbacher A, Edul S et al (2003) Successful management of abdominal stab wounds with clinical evaluation: experiences of an South-African trauma unit with 496 consecutive patients. Unfallchirurg 106:215–219
6. Schreyer N, Carron PN, Demartines N et al (2010) Stab wounds in a Swiss emergency department: a series of 80 consecutive cases. Swiss Med Wkly 140:w13058
7. Spijkers AT, Meylaerts SA, Leenen LP (2010) Mortality decreases by implementing a level I trauma center in a Dutch hospital. J Trauma 69:1138–1142
8. Shepherd J, Brennan I (2008) Tackling knife violence. BMJ 337:a849
9. Bieler D, Franke AF, Hentsch S et al (2014) Gunshot and stab wounds in Germany—epidemiology and outcome: analysis from the TraumaRegister DGU(R). Unfallchirurg 117:995–1004
10. Crewdson K, Lockey D, Weaver A et al (2009) Is the prevalence of deliberate penetrating trauma increasing in London? experi- ences of an urban pre-hospital trauma service. Injury 40:560–563
11. Christensen MC, Nielsen TG, Ridley S et al (2008) Outcomes and costs of penetrating trauma injury in England and Wales. Injury 39:1013–1025
12. Krug EG, Powell KE, Dahlberg LL (1998) Firearm-related deaths in the United States and 35 other high-and upper-middle-income countries. Int J Epidemiol 27:214–221
13. Richardson EG, Hemenway D (2011) Homicide, suicide, and unintentional firearm fatality: comparing the United States with other high-income countries, 2003. J Trauma 70:238–243
14. American College of Surgeons—Committee on Trauma (1999) Resources for optimal care of the injured patients. American College of Surgeons, Chicago
15. Ministry of Health Welfare and Sport (2006) Beleidsvisie Traumazorg 2006–2010. Dutch Government, Den Haag
16. US Census Bureau. Major Urban Areas. (2013) http://www.city population.de/USA-UA.html?cityid=6088. Accessed 12 Nov 2016
17. Statistic Netherlands (2016) City population: Amsterdam. http:// www.citypopulation.de/php/netherlands-admin.php?adm2id= 0363. Accessed 12 Nov 2016
18. Federal Bureau of Investigation Criminal Justice Information Services Division (2015). Crime in the United States by Region, Geographic Division, and State, 2014–2015 https://ucr.fbi.gov/crime-in-the-u.s/2015/crime-in-the-u.s.-2015/tables/table-4. Accessed 08 Aug 2017
19. Centraal Bureau voor de Statistiek (2016) Registered crime: violent crime West Netherlands 2016. http://statline.cbs.nl/Stat web/publication/?DM=SLNL&PA=83648NED&D1=2&D2=42- 44,57&D3=3,21,25-26,30,34-35,45,53,60,66,72,79,84,92,96, 101,105,112,144,147,151-152,156,169,184,186,191,204,207, 211-213,219,222,225-227,235,248,261,266,273,278,283, 287-288,292,309,311-312,315,318,329,331,333,338,345, 349,357,365,373,378,389,405,409,411,416,418,427,429,449, 455-456,458,462&D4=4-6&VW=T. Accessed 08 Aug 2017
20. Association for the Advancement of Automatic Medicine (2001) The Abbreviated Injury Scale, 1990 revision, update 98. Asso- ciation for the Advancement of Automatic Medicine, Barrington

21. Baker SP, O'Neill B, Haddon W et al (1974) The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma 14:187–196
22. Champion HR, Copes WS, Gann DS et al (1989) A revision of the trauma score. J Trauma Acute Care Surg 29:623–629
23. Charlson M, Szatrowski TP, Peterson J et al (1994) Validation of a combined comorbidity index. J Clin Epidemiol 47:1245–1251
24. Hall WH, Ramachandran R, Narayan S et al (2004) An electronic application for rapidly calculating Charlson comorbidity score. BMC Cancer 4:94
25. Schoenfeld DA, Bernard GR (2002) Statistical evaluation of ventilator-free days as an efficacy measure in clinical trials of treatments for acute respiratory distress syndrome. Crit Care Med 30:1772–1777
26. Stormann P, Gartner K, Wyen H et al (2016) Epidemiology and outcome of penetrating injuries in a Western European urban region. Eur J Trauma Emerg Surg 42:663–669
27. Spence RT, Scott JW, Haider A et al (2017) Comparative assessment of in-hospital trauma mortality at a South African trauma center and matched patients treated in the United States. Surgery 162:620–627
28. Massachusetts Court System (2017) Massachusetts law about gun and other weapons. http://www.mass.gov/courts/case-legal-res/ law-lib/laws-by-subj/about/weapons.html. Accessed 28 Feb 2017
29. Sorgdrager W (1997) Wet wapens en munitie. In: Government D (ed) The Hague, 10-07-1997. http://wetten.overheid.nl/ BWBR0008804/2018-03-01. Accessed 28 Feb 2017
30. Santaella-Tenorio J, Cerda M, Villaveces A et al (2016) What do we know about the association between firearm legislation and firearm-related injuries? Epidemiol Rev 38:140–157
31. Lee LK, Fleegler EW, Farrell C et al (2017) Firearm laws and firearm homicides: a systematic review. JAMA Int Med 177:106–119
32. Shepherd JP (2001) Criminal deterrence as a public health strategy. Lancet 358:1717–1722
33. Caputo LM, Salottolo KM, Slone DS et al (2014) The relationship between patient volume and mortality in American trauma centres: a systematic review of the evidence. Injury 45:478–486
34. Calland JF, Stukenborg GJ (2016) Trauma centre patient volume and inpatient mortality risk reconsidered. Injury 47:1072–1077
35. Brown JB, Rosengart MR, Kahn JM et al (2017) Impact of volume change over time on trauma mortality in the United States. Ann Surg 266:173–178
36. Sakran JV, Jehan F, Joseph B (2018) Trauma systems: standardization and regionalization of care improve quality of care. Curr Trauma Rep 4:39–47
37. Dijkink S, van der Wilden GM, Krijnen P et al (2017) Polytrauma patients in the Netherlands and the USA: a bi-institutional com- parison of processes and outcomes of care. Injury 49:104
38. Frank B, Maher Z, Hazelton JP et al (2017) Venous thromboembolism after major venous injuries: competing priorities. J Trauma Acute Care Surg 83:1095–1101
39. Karcutskie CA, Meizoso JP, Ray JJ et al (2017) Association of mechanism of injury with risk for venous thromboembolism after trauma. JAMA Surg 152:35–40
40. Hill AD, Fowler RA, Nathens AB (2011) Impact of interhospital transfer on outcomes for trauma patients: a systematic review. J Trauma 71:1885–1900

5

Quantification of trauma center access using Geographical Information System-based technology

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Value in Health. 2020; 23(8):1020–1026

ABSTRACT

Background

There is no generally accepted methodology to assess trauma system access. The goal of this study is to determine the influence of the number and geographical distribution of trauma centers(TCs) on transport times(TT) using Geographical-Information-System(GIS)-technology.

Methods

Using ArcGIS-PRO, we calculated differences in TT and population coverage in seven scenarios with 1, 2, or 3 TCs during rush[R]- and low traffic[L] hours in a densely-populated region with 3TCs in the Netherlands.

Results

In all seven scenarios, the population that could reach the nearest TC within (<) 45minutes, varied between 96-99%. In the three-TC-scenario, roughly 57% of the population could reach the nearest TC <15minutes both during [R] and [L]. The hypothetical geographically well-spread two-TC-scenario showed similar results as the three-TC-scenario. In the one-TC-scenarios, the population reaching the nearest TC <15minutes decreased to between 19-32% in [R] and [L].

In the three-TC-scenario the average TT increased by about 1.5minutes to almost 21minutes during [R] and 19minutes during [L]. Similar results were seen in the scenarios with two geographically well-spread TCs. In the one-TC-scenarios and the less well-spread two-TC-scenario the average TT increased by 5-8minutes [L] and 7-9minutes [R] in comparison to the three-TC-scenario.

Conclusion

This study shows that a GIS-based model offers a quantifiable and objective method to evaluate trauma system access under different potential trauma system configurations. Transport time from accident to trauma center would remain acceptable, around 20 minutes,if the current three trauma center situation would be changed to a geographically well-spread two center scenario.

BACKGROUND

Although the implementation of trauma systems has proven to be effective in reducing mortality rates for injured patients, there are still controversies regarding trauma center (TC) access, and more specifically regarding the optimal number and geographical distribution of TCs.[1-4] According to the principles of the American College of Surgeons Committee on Trauma, TC designation and distribution should be based on the needs of the population served.

The trauma system in The Netherlands resembles the American trauma system and was initially based on the criteria set by the American College of Surgeons Committee on Trauma. Over time, the Dutch Trauma Society has adapted the criteria to the national needs.[5,6] Currently, the Dutch system is organized in 11 trauma regions, each with a coordinating TC, and a catchment area of a minimal 1.2 million inhabitants. All other hospitals within these trauma regions are classified as non-TCs.[7] Trauma centers have multidisciplinary trauma teams available 24/7 that are equipped to manage severely injured patients, including specialties such as neurosurgery and cardiothoracic surgery. The non-TCs are well-equipped trauma hospitals but lack the 24/7 presence of multidisciplinary trauma teams, including neurosurgeons and cardiothoracic surgeons.

Transport times are short in this small and densely populated country with 18 million inhabitants that measures only 300 km from north to south and 200 km from east to west. In the present situation, the numbers of severely injured (polytrauma) patients per TC are relatively low (140-420 per year). Per January 1, 2020, the minimum annual volume requirement was raised from 100 to 240 polytrauma patients per TC.[8] Without further concentration of polytrauma care, only 5 of 11 level-1 TCs fulfill the minimum volume requirements.[7]

In the most densely populated mid-western trauma region of The Netherlands, the TC is organized in a different way than in the other trauma regions. In this trauma region, 3 hospitals act as separate TC locations, together forming 1 TC. The increased volume requirement urges further regional concentration of polytrauma care in 1 or 2 of these 3 hospitals. It is unknown, however, how the quality of trauma care might be affected by further centralization, taking into account the prerequisite that all severely injured patients should be able to reach the nearest TC within 45 minutes after the call for ambulance assistance, with a maximum transport time of 20 minutes in case of high urgency.[6, 9]

To solve the ongoing debate about TC accessibility, not only in The Netherlands but also worldwide, there is a need for an objective, generally accepted methodology to assess trauma system access and optimal geographical TC distribution. Geographic information system (GIS)–based technology can facilitate decision making on trauma systems by combining local data from different sources. Geographic information sys-

tem–based technology was previously used for evaluation of different aspects of trauma systems in various countries, such as the relationship between TC access and outcome, quantification of trauma load, and the relationship between patient volume and TC location.[10-16] To our knowledge, this technology has not been deployed for the Dutch situation.

The goal of this study was to determine the effect of a reduced number of TCs in the mid-western trauma region in The Netherlands, in combination with traffic flow variation, on transport time from accident scene to the closest TC in different scenarios, using GIS-based technology.

MATERIAL AND METHODS

Setting

Trauma Center West Netherlands (TCWN) is located in the midwestern trauma region of The Netherlands. This TC has 3 locations: Leiden University Medical Center in Leiden and Haaglanden Medical Center Westeinde and Haga Hospital, both in The Hague (Fig. 1).[7]

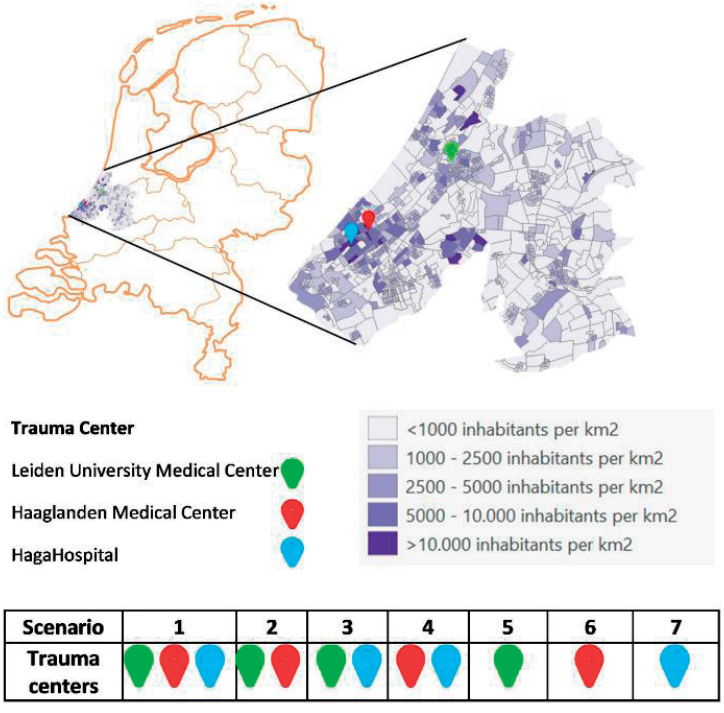


Figure 1. The region of Trauma Center West Netherlands with its population density and the location of the three trauma centers. The 7 scenarios for trauma center distribution are presented at the bottom.

These TCs are located in one of the most densely populated areas in The Netherlands, with roughly 1.86 million inhabitants in an area of 3403 km^2. According to the national guidelines, severely injured patients (defined as having an injury severity score ≥ 16) should be transported to a TC. Each year, approximately 500 severely injured patients are transported by the ambulance services in the TCWN region. According to national guidelines, which state that at least 90% of the severely injured patients primarily should be brought to a TC, patients classified as severely injured should be directly transported to the nearest TC in the region.[9]

Although Helicopter Emergency Medical Services are available 24/7 throughout in The Netherlands, only 3% of the polytrauma patients are transported by helicopter.[7] Most patients in the TCWN are brought to the TC by 2 regional ambulance services (RAS). RAS Mid-Netherlands mainly covers the area around the Leiden University Medical Center, whereas RAS Haaglanden mainly covers The Hague.

The high population density and mobility in the TCWN region are cause for constant traffic jams during rush hour. Also, ambulances are only allowed to go 40 km/h faster than the actual traffic, so they often cannot drive full speed. The high traffic flow and the speed limit could potentially contribute to longer transport times to the closest TC during rush hour.

Study Design

We assessed average high-urgency ambulance ride transport times to the nearest TC in 7 scenarios (Fig. 1); 1 scenario reflected the current situation with 3 trauma centers (3-TC scenario, 1), 3 hypothetical scenarios with 2 trauma centers (2-TC scenarios, 2-4), and 3 hypothetical scenarios with 1 trauma center (1-TC scenarios, 5-7). Each scenario was evaluated for situations with low and high traffic flow. Based on information of the Dutch Traffic Information Service, the traffic situation on an average Tuesday morning at 8 AM was used as proxy for rush hour, and on an average Saturday morning at noon was used as a proxy for low traffic hours to calculate average transport times to the nearest TC.[17] Ambulance rides are classified as high-urgency if the emergency medical dispatch center classifies the patient›s situation as potentially life-threatening or as associated with a high risk of immediate deterioration. In these cases, the ambulance is authorized to drive at high speed with lights and sirens.

GIS-based model and data sources

The ambulance transport times in the 7 scenarios were assessed using a geospatial approach. Over the past decade, the GIS-based technology has been increasingly used in population health and has become a distinct research area.[18,19] In our GIS-based model, different layers of information from independent sources were combined.

The first layer of information about the Dutch road network and traffic flow was obtained via Esri Netherlands Content.[20] This map is continuously updated to give the most up-to-date information about the road network and average traffic flow in The Netherlands, taking the average speed, speed limits, and traffic volume into account. The second layer of population density data was obtained from The Netherlands Statistics. A total of 27 municipalities within the trauma region were included, with 1023 neighborhoods and 1 866 160 inhabitants.[21] The third layer included the GPS locations of the TCs in the Trauma Center West Region. The fourth layer consists of assumed accident scene locations, being the accident location zip codes.

Analysis

All GIS-based analyses were performed using ArcGIS Pro 2.3 (Esri, Redlands, CA). All descriptive analyses were performed using IBM Statistics for Windows, version 23 (IBM Corp., Armonk, NY).

First, we validated the GIS-based model. The patient location GPS codes of the high-urgency rides provided by RAS Hollands Midden were uploaded in ArcGIS-Pro. These included all high-urgency rides with an indication to go to one of the TCs in the region, including but not limited to trauma patients. The transport times generated by the GIS-based model (calculated) were compared with factual transport times obtained from the RAS Hollands Midden (observed). The observed data were divided in 2 groups: (1) ambulance rides during rush hour (between 6:00AM and 9:00AM and 4:00PM and 7:00PM during weekdays), and (2) ambulance rides during low traffic (12:00AM 6:00AM, 9:00AM 4:00PM, 7:00PM 12:00AM on weekdays and on the weekend).[17]

The fastest transport time from the accident scene to hospital was calculated using the "Network Analyst Find Closest Facility" function in the ArcGIS-Pro system. Data about accident scene location and actual transport time from accident scene to the TC for high-urgency rides were obtained from the Regional Ambulance Service Mid-Netherlands and were imported in the model. Observed and calculated transport times were reported as median and interquartile range (IQR). To evaluate the agreement between the observed (factual) and calculated (model) transport times, the median difference between observed and expected transport times with IQR during low-traffic hours and during rush hours was reported and tested using a related-samples Wilcoxon signed rank test. Also, the intraclass correlation coefficient (ICC) between the observed and calculated transport times during low-traffic hours and during rush hours was calculated with the corresponding 95% confidence interval (CI).

To assess the effect of TC distribution in the 7 scenarios (Fig. 1), central data points ("centroids") in the 1023 neighborhoods in the TCWN region were created and used as accident scenes in the "network analyst" function in ArcGIS-Pro to assess transport times to the nearest TC in each scenario in rush hour as well as in low-traffic hours. Population

coverage was calculated by combining the centroids layer with the drive time layer by summing the population from all the centroids within the transport time bands, 0 to 15, 15 to 30, 30 to 45, and 45 to 60 minutes.

RESULTS

Validation of GIS-based transport time model

Between January 1, 2018 and December 31, 2018, a total of 28 556 patients were transported by ambulance. In total, 4963 patients, including but not limited to trauma patients, were transported by RAS Mid-Netherlands with high urgency to the emergency department of 1 of the 3 regional TCs. After excluding ambulance rides with missing zip code of the patient location or recorded transport time, 4487 were included in the analysis (n = 3689 during low-traffic hours and n = 798 during rush hour).

The median observed and expected transport times during low-traffic hours were, respectively, 11.4 minutes (IQR 7.8 - 16.3) and 11.1 minutes (IQR 7.9 - 16.0). The median difference between the observed transport and calculated transport times from patient location to the nearest TC in low-traffic hours was 0.3 minutes (IQR -1.8 - 2.1, Wilcoxon signed rank test $P<.0001$). The median observed and expected transport times during rush hour were, respectively, 12.1 minutes (IQR 8.5 - 17.5) and 12.0 (IQR 8.4 - 17.0). The median difference between the observed transport and calculated transport times from patient location to the nearest TC in rush hour was 0.1 minutes (IQR -2.4 - 2.4, Wilcoxon signed rank test $P=.20$). The ICC for the transport times in low-traffic hours was 0.82 (95% CI 0.81 - 0.83) and for transport times in rush hour was 0.77 (95% CI 0.74 - 0.80).

Effect of number of trauma centers and geographical distribution during rush hour and low traffic

In the 7 scenarios, the population that could reach the nearest TC location within 45 minutes varied from 97% to 99% among all models during low traffic, and 96% to 98% during rush hour (Figs. 2 and 3).

In scenario 1, roughly 57% of the population reached the nearest TC within 15 minutes in both rush hour and low-traffic hours (Fig. 3). The hypothetical scenarios with 2 geographically well-spread TC locations (2 and 3) showed similar results as the current 3-TC location scenario, with a population coverage within 15 minutes of about 53% in scenario 2 and 51% in scenario 3 in both traffic circumstances (Fig. 3).

This decrease in population coverage < 15 minutes was the largest in the 1-TC scenarios (5-7). In scenario 5, 19% of the population could reach the nearest TC within 15 minutes in both rush and low-traffic hours, and 31% to 34% of the population was able to reach the nearest TC within 15 minutes in scenario 6 and 7 in both rush hour and

low-traffic circumstances. Scenario 4 showed a decrease to 36% of the population that could reach the nearest TC within <15 minutes (Fig. 3).

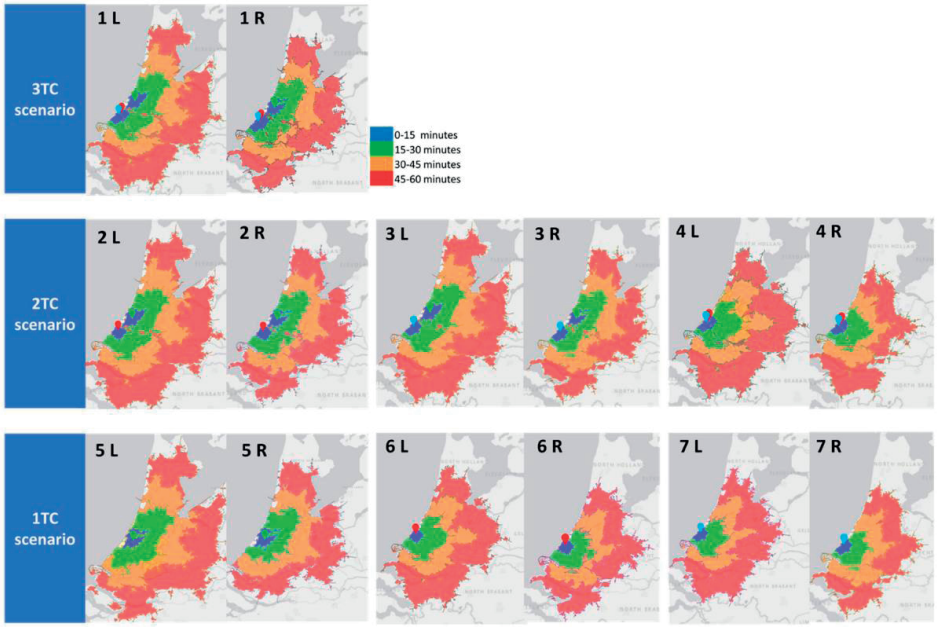


Figure 2. Seven scenarios in which the geographic coverage within 15, 30 , 45 and 60 minutes of closest trauma center for all models in rush hour (R) and low traffic hours (L) is shown

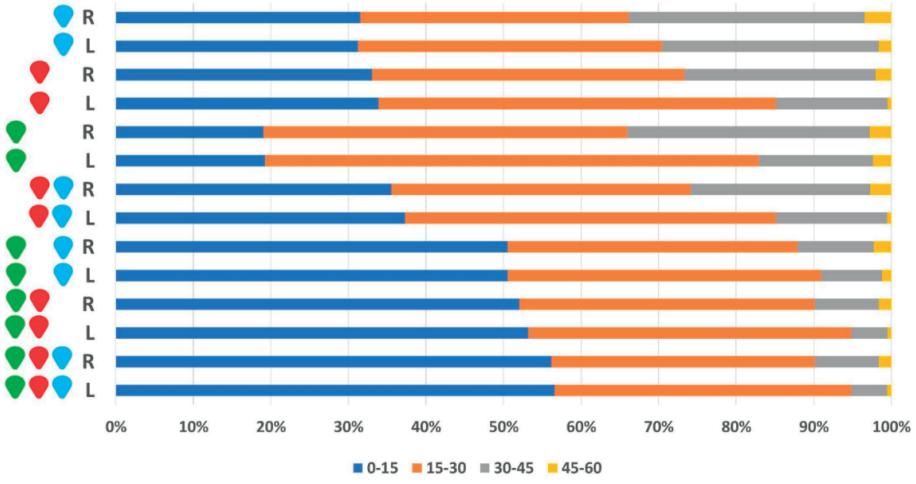


Figure 3. Percentage of TCWN population that can be brought to the closest trauma center in the seven scenarios during rush hour (R) and low traffic hours (L) within 15, 30, 45 and 60 minutes.

In scenario 1, the current situation (1), the average transport time of 19 minutes during low-traffic hours increased by about 1.5 minutes to almost 21 minutes in rush hour (Fig. 4). Transport times in both scenarios 2 and 3 were comparable to scenario 1 with a transport time of 20 minutes in low traffic and 22 minutes during rush hour. The 1-TC-location scenarios (5-7) and the geographically less well-spread 2-TC scenario (4) showed an increase of 5 to 8 minutes to the average transport time during low traffic, and an increase of 7 to 9 minutes during rush hours compared to the current 3-TC scenario (1) (Fig. 4).

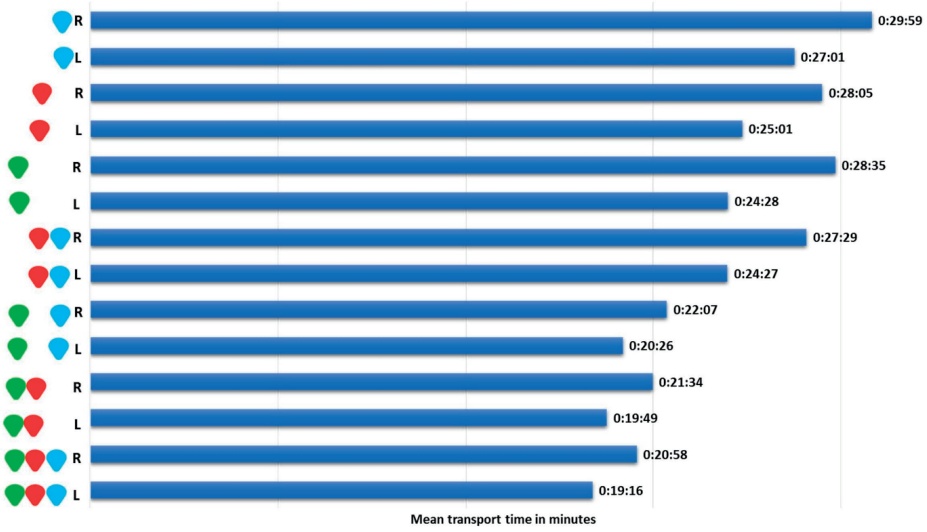


Figure 4. Mean transport times to closest trauma center in different models during rush hour (R) and low traffic hours (L)

DISCUSSION

This model allows for the assessment of different potential changes in the number and location of TCs in the midwest trauma region in The Netherlands, and predicts that a suboptimal approach to centralization of trauma care (scenario 4-7) could result in increased transport times to the closest TC, especially during rush hour. The influence of high traffic density on transport times was substantial in the 1-TC scenarios (5-7) and in the 2-TC scenario with 2 TCs that are geographically near to each other (scenario 4), compared with the current situation with 3 TCs in the region (scenario 1) and the situation with 2 geographically well-spread TCs (scenarios 2 and 3). As mentioned before, the Dutch government set a time limit of approximately 20 minutes for transporting severely injured patients to the nearest TC. This study showed that the transport time in

the geographically less well spread 2-TC scenario (scenario 4) and in the 1-TC scenarios (scenario 5-7) exceeds the maximum time with 4 to 10 minutes. Although in all scenarios roughly 98% of the population could reach the hospital within 45 minutes in both rush hour and low traffic, the transport time for the population living in the regions periphery did increase substantially. The transport times for these patients would, in fact, be shorter if they were to be brought to the nearest TC in an adjacent region.

Although the GIS-based approach has been used earlier to evaluate geographical TC distribution in other countries,[10,12,16,22-24] this study is, to our knowledge, the first that used the GIS-based technology to assess access to TCs in The Netherlands and validated the model. There was only a 0.3-minute difference between observed and expected transport times during low-traffic hours and 0.1-minute difference during rush hour. Although the difference in transport time was statistically significant owing to the large number of ambulance rides, this was not deemed clinically relevant. In combination with the good agreement between the calculated transport times and the observed transport times (ICC > 0.75),[25] this model can be considered a valid tool for evaluating the access to TCs in different geographic settings.

The GIS-based results may be useful to help guide policy decisions regarding trauma system organization. Although the importance of well-developed trauma systems is internationally recognized, there is still no consensus about their optimal organization. In almost all cases, trauma systems have developed organically, with TCs arising in existing hospitals based on historical practice patterns, instead of strategically locating the TCs geographically in the most efficient way, taking access and population coverage into account.[23]

The trade-off between centralization of care with sufficient hospital volumes on the one hand and better TC access in transport times and population coverage achieved by a distributed system of smaller centers on the other hand is a difficult one. Several studies have shown that reduced TC access led to differences in outcomes, such as higher mortality rates.[26-29] Nevertheless, providing 24/7 highly specialized trauma care comes at a cost. Year-round TC readiness costs around $2.7 million per TC annually in the Unites States.[30] Efficient planning of distribution of TCs could therefore not only lead to better outcomes in patients, but also to more efficient distribution of resources and potentially lower healthcare costs.

Although concentration of complex trauma care in fewer TCs could potentially increase the expertise of the trauma teams in the resulting higher-volume centers, and also may have organizational and process advantages, it would also have consequences for system access. Our results suggest that hospital volume is not the only objective aspect of trauma care that can be modeled and taken into account in trauma system planning. Research has shown that especially time is of the essence for the hemodynamically unstable trauma patients and that rapid transport to a TC can improve outcomes.[31,32] The

GIS-based model offers an objective way to evaluate the effects of proposed changes in trauma systems for specific regions or countries with their specific geography and demography.[10,12,16,22-24]

Strengths and Limitations

A major strength of this study is that the outcomes of the model were validated, using factual data of a large number of high-urgency cases, largely publicly available data, and commercially available GIS-based technology. There are also some limitations. Although we validated the model, we must emphasize that the results are based on a mathematical model, which is of course a simplification of the real world. For example, instead of using the exact geographic coordinates of the accident scenes, the zip codes were used as a proxy. In our opinion, these 4-digit, 2-letter zip codes are an acceptable proxy because these codes cover areas of a few streets at most, meaning that the actual accident scene is in close proximity. Another limitation is that the data used to validate the model outcomes may have contained erroneous transport times that could not be corrected, which is illustrated by some extremely short or very long transport times in the database provided by the RAS. Because it is not possible to determine which of the extreme data points were errors and which were actual outliers, we included all available data in the validation to not manipulate the data. Unfortunately, owing to strict privacy regulations, we were unable to include patient characteristics in this study. This prevented us from a more detailed investigating of the types and severity of the injuries of the included patients.

Third, as mentioned before, ambulances in The Netherlands are allowed to drive 40 km/h faster than the speed of the surrounding traffic for high-urgency transports. Unfortunately, we were not able to correct for the effect of the increased speed of the ambulance in the model. Nevertheless, the GIS-model transport times did not differ significantly from the actual RAS Hollands Midden data, despite the assumed speed differences.

Last, only a specific part of the trauma system (ie, transport time from accident scene to TC) was evaluated in this study. Other components that influence TC access, such as shifts in volumes as a consequence of changes in TC distribution, were not analyzed. Although we do feel that maximum capacity and shifts in patient volume should be an important part of strategic TC planning, this could not be analyzed using the currently available data. We therefore want to emphasize that decisions about the organization of trauma care, both prehospital and in-hospital, should be based on more factors than only transport times. Nevertheless, despite this limitation, we do think that this type of objective data can help to guide policy decisions such as those involving potential centralization of trauma care resources.

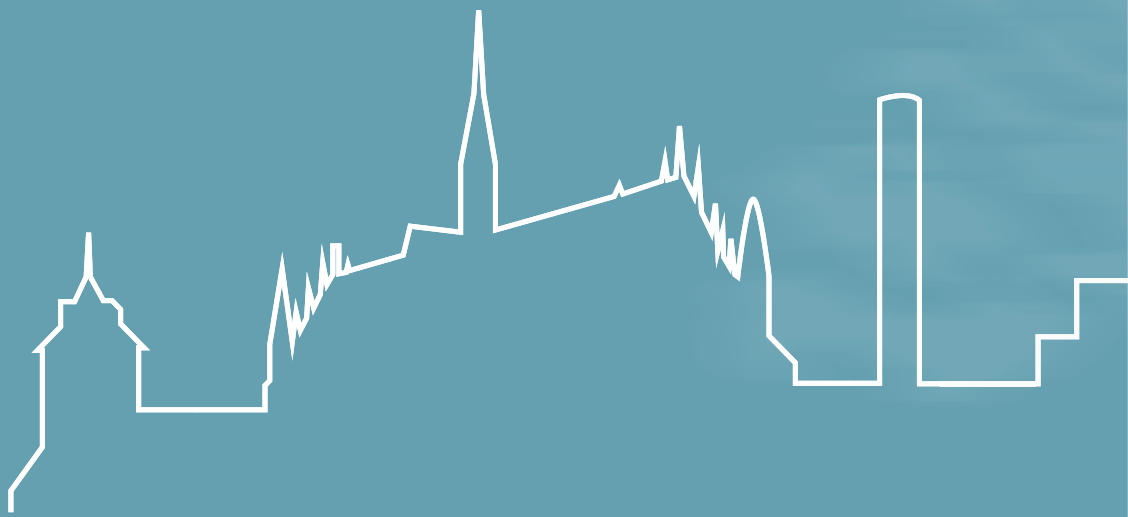
CONCLUSION

This study shows that a GIS-based model offers a quantifiable and objective method to evaluate trauma system access under different potential trauma system configurations. Applying this technology to one of the most densely populated areas in The Netherlands shows that the transport time from accident to TC would remain acceptable if the current situation with 3 TCs were changed to a scenario with 2 geographically well-spread centers; it also shows that a single-center configuration, or one with 2 poorly located centers, could have an adverse effect on patient access to care. This type of objective data can support strategical and political decisions, such as those involving potential centralization of resources.

REFERENCES

1. MacKenzie EJ, Rivara FP, Jurkovich GJ, et al. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med.* 2006;354(4):366-378.
2. Lansink KW, Leenen LP. Do designated trauma systems improve outcome? *Curr Opin Crit Care.* 2007;13(6):686-690.
3. Celso B., Tepas J., Langland-Orban B., et al. A systematic review and meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems. J Trauma. 2006;60(2):371–378. discussion 378.
4. Statement on trauma center designation based upon system need. Bull Am Coll Surg. 2015;100(1):51–52.
5. Committee on Trauma. Resources for Optimal Care of the Injured Patients. Chicago, IL: American College of Surgeons; 1999.
6. Ministry of Health Welfare and Sport. Beleidsvisie Traumazorg 2006–2010. Den Haag: Dutch Government; 2006.
7. Landelijk Netwerk Acute Zorg. Traumazorg in Beeld -Landelijke Traumaregistratie 2013 - 2017 - Rapportage Nederland. Utrecht; 2018.
8. Nederlandse Vereniging voor Traumachirurgie. Visiedocument 2016-2020. Utrecht; 2016.
9. Bos N., Hendriks M., de Booys M., Wets M. Spoed Moet Goed: Indicatoren en Normen Voor zes Spoedzorgindicaties. Diemen: Zorginstituut Nederland; 2015.
10. Tansley G., Schuurman N., Amram O., Yanchar N. Spatial access to emergency services in low-and middle-income countries: a GIS-based analysis. PLoS One. 2015;10(11):e0141113.
11. Gomez D., Larsen K., Burns B.J., Dinh M., Hsu J. Optimizing access and configuration of trauma centre care in New South Wales. Injury. 2019;50(5):1105–1110.
12. Winchell R.J., Xu P., Mount L.E., Huegerich R. Development of a geospatial approach for the quantitative analysis of trauma center access. J Trauma Acute Care Surg. 2019;86(3):397–405.
13. Lawson F.L., Schuurman N., Oliver L., Nathens A.B. Evaluating potential spatial access to trauma center care by severely injured patients. Health Place. 2013;19:131–137.
14. Hardcastle T.C., Samuels C., Muckart D.J. An assessment of the hospital disease burden and the facilities for the in-hospital care of trauma in KwaZulu-Natal, South Africa. World J Surg. 2013;37(7):1550–1561.
15. Hu W., Dong Q., Dong C., Yang J., Huang B. Access to trauma centers for road crashes in the United States. J Safety Res. 2018;65:21–27.
16. Tansley G., Schuurman N., Erdogan M., et al. Development of a model to quantify the accessibility of a Canadian trauma system. CJEM. 2017;19(4):285–292.
17. Ministry of Infrastructure and Water Management. Publieksrapportage Rijkswegennet. Den Haag: Rijkswaterstaat Water Verkeer en Leefomgeving; 2016.
18. Rushton G. Public health, GIS, and spatial analytic tools. Annu Rev Public Health. 2003;24:43– 56.
19. Bell N., Schuurman N. GIS and injury prevention and control: history, challenges, and opportunities. Int J Environ Res Public Health. 2010;7(3):1002–1017.
20. ESRI. Stratenkaart Nederland. https://services.arcgisonline.nl/arcgis/rest/services/Basiskaarten/Strat enkaart/MapServer. Accessed August 6th, 2019.
21. Centraal Bureau voor de Statistiek. Kerncijfers wijken en buurten 2017. https://opendata.cbs.nl/statline/#/CBS/nl/data set/83765ned/table?fromstatweb. Accessed August 6th, 2019.

22. Horst M.A., Gross B.W., Cook A.D., Osler T.M., Bradburn E.H., Rogers F.B. A novel approach to optimal placement of new trauma centers within an existing trauma system using geospatial mapping. J Trauma Acute Care Surg. 2017;83(4):705–710.
23. Jansen J.O., Moore E.E., Wang H., et al. Maximizing geographical efficiency: an analysis of the configuration of Colorado's trauma system. J Trauma Acute Care Surg. 2018;84(5):762–770.
24. Jansen J.O., Campbell M.K. The GEOS study: designing a geospatially optimised trauma system for Scotland. Surgeon. 2014;12(2):61–63.
25. Koo T.K., Li M.Y. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. 2016;15(2):155–163.
26. Brown J.B., Rosengart M.R., Billiar T.R., Peitzman A.B., Sperry J.L. Geographic distribution of trauma centers and injury-related mortality in the United States. J Trauma Acute Care Surg. 2016;80(1):42–49. discussion 49-50.
27. Hsia R.Y., Srebotnjak T., Maselli J., Crandall M., McCulloch C., Kellermann A.L. The association of trauma center closures with increased inpatient mortality for injured patients. J Trauma Acute Care Surg. 2014;76(4):1048–1054.
28. Sampalis J.S., Denis R., Lavoie A., et al. Trauma care regionalization: a process-outcome evaluation. J Trauma Acute Care Surg. 1999;46(4):565–581.
29. Branas C.C., MacKenzie E.J., Williams J.C., et al. Access to trauma centers in the United States. JAMA. 2005;293(21):2626–2633.
30. Taheri P.A., Butz D.A., Lottenberg L., Clawson A., Flint L.M. The cost of trauma center readiness. Am J Surg. 2004;187(1):7–13.
31. Harmsen A.M.K., Giannakopoulos G.F., Moerbeek P.R., Jansma E.P., Bonjer H.J., Bloemers F.W. The influence of prehospital time on trauma patients outcome: a systematic review. Injury. 2015;46(4):602–609.
32. Mills E.H.A., Aasbjerg K., Hansen S.M., et al. Prehospital time and mortality in patients requiring a highest priority emergency medical response: a Danish registry-based cohort study. BMJ Open. 2019;9(11):e023049.



6

The impact of regionalized trauma care on the distribution of severely injured patients in the Netherlands

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ABSTRACT

Background

Twenty years ago an inclusive trauma system was implemented in the Netherlands. The goal of this study was to evaluate the impact of structured trauma care on the concentration of severely injured patients over time.

Methods

All severely injured patients (Injury Severity Score [ISS] ≥16) documented in the Dutch Trauma Registry (DTR) in the calendar period 2008-2018 were included for analysis. We compared severely injured patients, with and without severe neurotrauma, directly brought to trauma centers (TC) and non-trauma centers (NTC). The proportion of patients being directly transported to a trauma center was determined, as was the total Abbreviated Injury Score (AIS), and ISS.

Results

The documented number of severely injured patients increased from 2350 in 2008 to 4694 in 2018. During this period on average 70% of these patients was directly admitted to a TC (range 63-74%). Patients without severe neurotrauma had a lower chance of being brought to a TC compared to those with severe neurotrauma. Patients directly presented to a TC were more severely injured, reflected by a higher total AIS and ISS, than those directly transported to a NTC.

Conclusion

Since the introduction of a well-organized trauma system in the Netherlands, trauma care has become progressively centralized, with more severely injured patients being directly presented to a TC. However, still 30% of these patients is initially brought to a NTC. Future research should focus on improving pre-hospital triage, to facilitate swift transfer of the right patient to the right hospital.

BACKGROUND

Following concerns about the organization of both pre-hospital and in-hospital trauma care and the increased public awareness about the importance of well-organized acute care [1,2], the Dutch government appointed ten trauma centers (TC) in 1998. [3,4] Currently, the Dutch trauma care is organized in eleven trauma regions and resembles the American trauma system based on the criteria set by the American College of Surgeons- Committee on Trauma.[5] Each region has a catchment area of at least 1.2 million inhabitants with one coordinating TC and several non-trauma centers (NTC) in every region. Since the introduction of the regionalized trauma care, several quality measures were deployed such as a mandatory participation in the Dutch Trauma Registry [DTR] (2008) which led to 100% participation by all emergency departments in the registry in 2015. Also, level criteria for trauma- and non-trauma centers (2013), and certification for trauma surgeons were implemented. In 2010, ten years after the introduction of well-organized trauma systems, the overall mortality risk after trauma was found to be reduced by 16%.[6] In the past decade further development of trauma care in the Netherlands concerned, amongst others, the regionalization of the ambulance care including an update of the national guideline for emergency medical service providers (2011), 24/7 availability of helicopter emergency services (HEMS) for acute trauma (2011), yearly quality reports by the Dutch Trauma Registry (2012) and the introduction of trauma related quality indicators by the Dutch government (2015) (Figure 1).

Twenty years after the introduction of trauma systems in the Netherlands knowledge about parameters that may influence the distribution of trauma patients is relevant, per se and as a prelude to the analysis of the clinical effects of this concentration of care over time. The objective of this study is to describe the impact of structured trauma care on the distribution of severely injured patients between trauma centers (TC) and non- trauma centers (NTC).

MATERIAL AND METHODS

Patients and data

Patients admitted to either one of the appointed regional trauma centers (TCs) or to a non-trauma center (NTCs) are registered in the Dutch Trauma Registry (DTR). This retrospective cohort study included all severely injured patients (Injury Severity Score [ISS] ≥16) who were registered in the DTR during the calendar period 2008-2018. Up to 2015, injury coding and calculation of the ISS[7] in the DTR was based on the Abbreviated Injury Scale (AIS) version 1998[8] and after 2015 on the AIS version 2008 [9]. To enable a comparison of patients' injury severity over time, a tool developed by Palmer et al. was used to reclassify all AIS1998 injury codes to AIS2008 injury codes. [10]

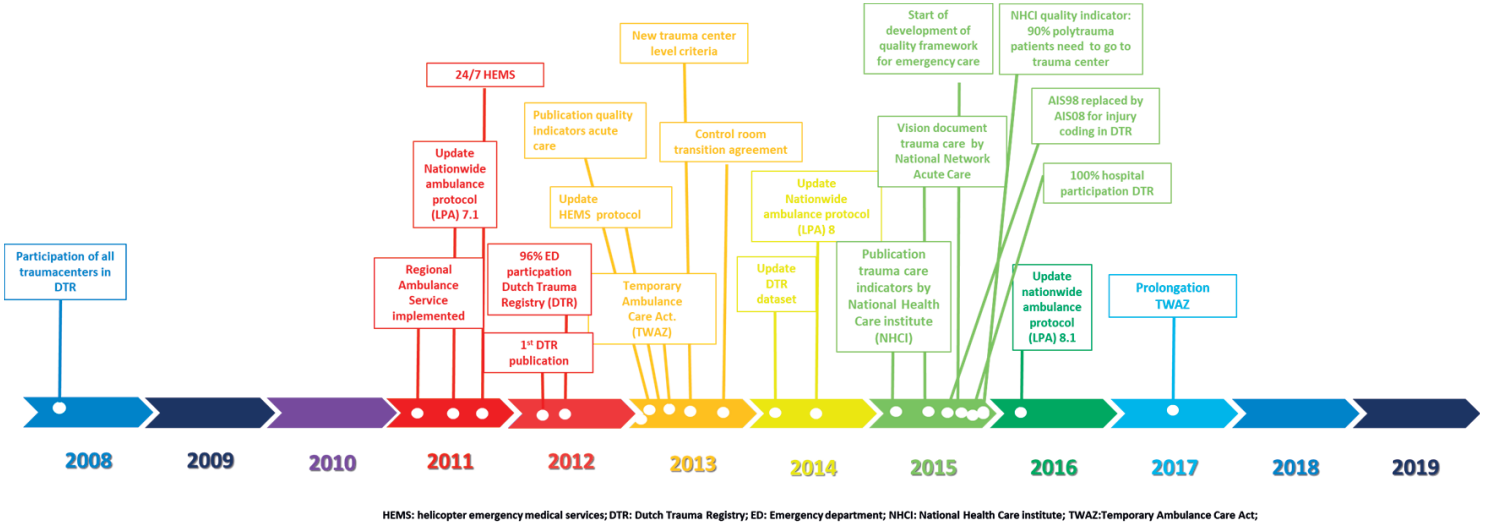


Figure 1. Changes in organization of trauma care in the Netherlands

Since 2008, all eleven coordinating TCs contribute data of their admitted trauma patients to the DTR. During the study period (2008-2018), the participation of NTCs in the DTR increased from 62% in 2008 to (near) 100% in 2018 (Table 1). From 2014 on, all Dutch hospitals participate in the DTR.

The distinction between TCs and NTCs is based on the set of trauma center- criteria established by the Dutch Society for Trauma Surgery. TCs (level-I centers) in the Netherlands need to have 24/7 multidisciplinary trauma team availability and are equipped for multidisciplinary management of severely injured patients, including the presence of facilities such as 24/7 angio-interventions, intensive care and specialties like neurosurgery and cardiothoracic surgery. The NTCs are well equipped trauma-hospitals but lack the 24/7 presence of multidisciplinary trauma teams, and are not appointed primarily to provide care to severely injured patients.

Table 1. Number of trauma centers (TCs) and non-trauma centers (NTCs) participating in the Dutch Trauma Registry, by calendar year.

	2008	**2009**	**2010**	**2011**
Total number of NTCs with ED	105	104	102	102
Number (%) of NTCs participating in the registry	76 (72)	79 (76)	85 (83)	89 (87)
Total number (%) of TCs participating in the registry	11 (100)	11 (100)	11 (100)	11 (100)
Total number of severely injured patients (ISS≥16) in the registry	2350	2450	2479	2968
Number (%) of patients with ISS≥16 and severe neurotrauma	1483 (63)	1515 (62)	1655 (67)	1950 (66)
Number (%) of patients with ISS≥16 without severe neurotrauma	867 (37)	935 (38)	824 (33)	1018 (34)

	2012	**2013**	**2014**	**2015**
Total number of NTCs with ED	101	101	99	96
Number (%) of NTCs participating in the registry	97 (96)	100 (99)	98 (99)	96 (100)
Total number (%) of TCs participating in the registry	11 (100)	11 (100)	11 (100)	11 (100)
Total number of severely injured patients (ISS≥16) in the registry	3394	3578	4006	4205
Number (%) of patients with ISS≥16 and severe neurotrauma	2211 (65)	2416 (68)	2783 (69)	2413 (57)
Number (%) of patients with ISS≥16 without severe neurotrauma	1183 (35)	1162 (32)	1223 (31)	1792 (43)

	2016	**2017**	**2018**
Total number of NTCs with ED	95	95	91
Number (%) of NTCs participating in the registry	95 (100)	95 (100)	89 (98)
Total number (%) of TCs participating in the registry	11 (100)	11 (100)	11 (100)
Total number of severely injured patients (ISS≥16) in the registry	4422	4450	4694
Number (%) of patients with ISS≥16 and severe neurotrauma	2410 (55)	2403 (54)	2545 (54)
Number (%) of patients with ISS≥16 without severe neurotrauma	2012 (45)	2047 (46)	2149 (45)

Statistical analysis

The statistical analyses were performed in R [11] for three types of patients:

A) all severely injured patients (ISS≥16),
B) patients with ISS≥16 and severe (head-AIS≥3) neurotrauma, and
C) patients with ISS≥16 without neurotrauma or with only mild to moderate (AIS≤2) neurotrauma.

Separate analysis of the subgroups with and without severe neurotrauma was considered relevant, since a large part of the patients with ISS≥16 have severe neurotrauma.

First, the distribution of severely injured patients who were directly brought to a TC and those who were directly brought to a NTC was described over time (Figure 2).

To assess a potential trend in the proportion of severely injured patients directly brought to a TC over time, the proportion per year was modelled with adjustment for case mix variables (Figure 3). For this purpose, the PSNL15 case mix model was used, which was developed by the National Network Acute Care (Landelijk Netwerk Acute Zorg, LNAZ), based on the TRISS-model[13] and adjusted to the Dutch population.[14] The PSNL15 case mix model includes factors associated with the survival of trauma patients, such as trauma mechanism, vital signs on admission, age and ISS.[14] The proportion of patients that were directly brought to a TC was also corrected for the centers that did not participate in the DTR from the start in 2007. Multiple imputation was used to estimate the number of (severely) injured patients in NTCs for the calendar years in which these centers did not report to the DTR. The multiple imputation for the not reported years was based on the number of and trend in the observed numbers of patients these centers had reported in later years.

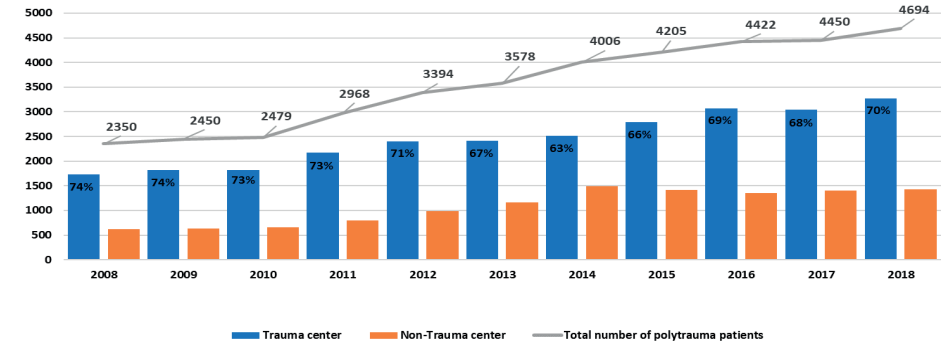
Second, the median ISS (Figure 4) and median total AIS (calculated as the sum of all separate AIS severity codes per patient) (Figure 5) of patients brought to the TCs and NTCs were described over time. The median total AIS was analyzed as several studies have shown that the low inter observer reliability of the ISS limits its use for benchmarking trauma system performance.[15,16] Total AIS might be a useful marker of injury severity because it includes all injuries (i.e. multiple injuries in one body region).[17]

RESULTS

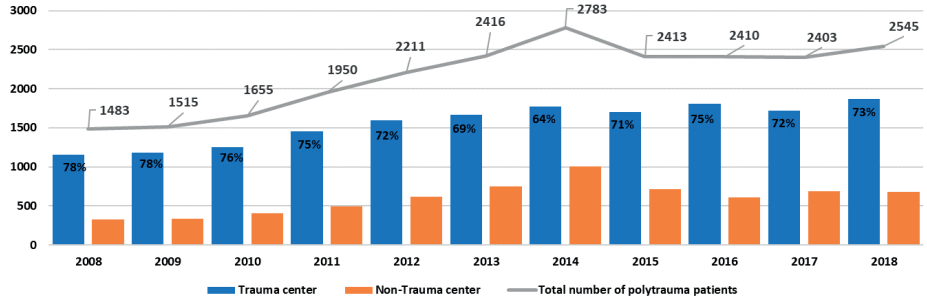
Distribution of severely injured patients

The number of severely injured patients registered in the Dutch Trauma Registry increased from 2350 patients in 2008 to 4694 in 2018 [Figure 2A]. At the same time the number of participating NTCs varied from 76 to 100 (72-100%; Table 1.) In the years 2008-2014, on average 66% of all documented severely injured patients had severe

a. All patients



b. Patients with severe neurotrauma (AIS≥3)



c. Patients without severe neurotrauma (no neurotrauma or only mild-moderate [AIS≤2] neurotrauma)

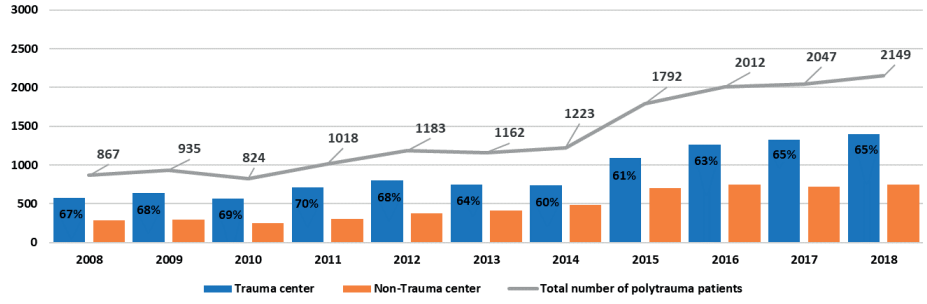


Figure 2. Distribution of severely injured patients (ISS≥16) registered in the Dutch Trauma Registry, directly brought to a level I trauma center or to a non-trauma center over time for (A) all patients, and separately for patients (B) with and (C) without severe neurotrauma, by calendar year.

neurotrauma, while this was 55% over the years 2015-2018 (Table 1). Both the numbers of registered patients with severe neurotrauma (Figure 2B) and without severe neurotrauma (Figure 2C) increased over the 10-year period. The unadjusted proportion of all severely injured patients that were directly brought to a TC was 70% on average. This proportion decreased from 74% to 63% between 2008 and 2014, when the number of NTCs participating in the DTR still increased, and then increased to 70% in 2018 (Figure

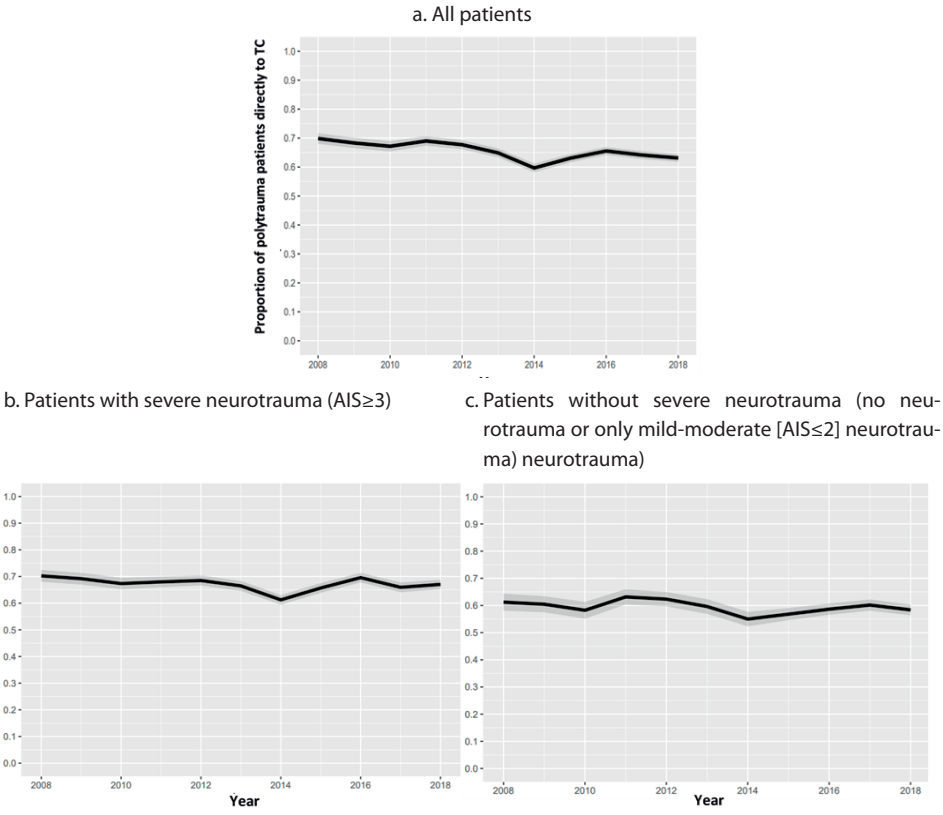


Figure 3. Proportion of severely injured patients (ISS≥16) directly brought to a trauma center, after correction for difference in case mix and for non-participation in the Dutch Trauma Registry, for all patients(A), and separately for patients with(B) and without(C) severe neurotrauma, per calendar year.

2A). A similar trend was seen in both the subgroup of patients with severe neurotrauma (Figure 2B) and the subgroup of patients without neurotrauma or with only mild/moderate neurotrauma (Figure 2C).

A similar trend in the proportion of severely injured patients that were directly brought to a TC was seen after adjustment for variation in case mix and for non-participation of NTCs (Figure 3). After a decreasing trend between 2008 and 2014, the adjusted proportion increased over the years 2014-2016 and remained stable thereafter. On average over the past decade 73% of the patients with severe neurotrauma and 66% of patients without severe neurotrauma were directly transported to a TC.

Injury severity

During the entire study period, the patients directly brought to a TC were more severely injured, reflected by a higher median ISS (22, interquartile range [IQR] 17 - 27) and higher

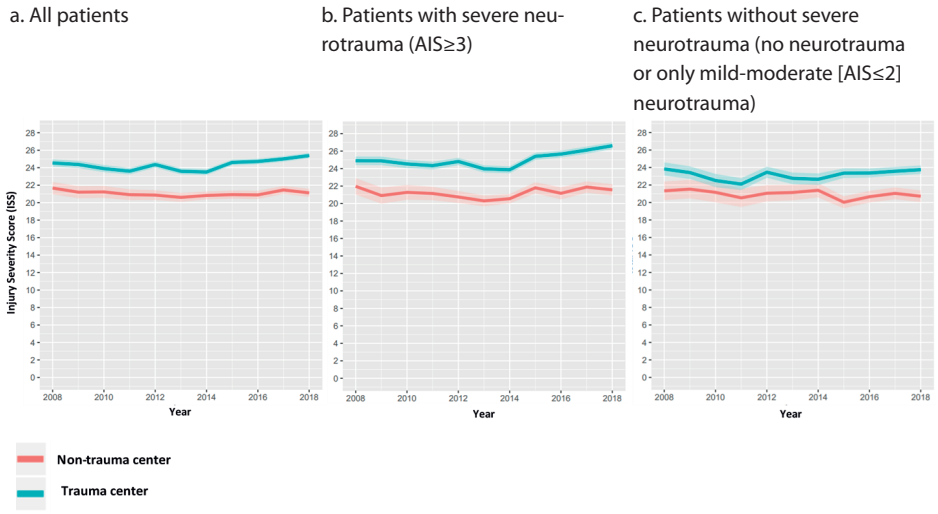


Figure 4. Median Injury Severity Score (ISS) for severely injured patients (ISS≥16) directly brought to a trauma center or a non-trauma center, for (A) all patients, and separately for patients (B) with and (C) without severe neurotrauma, by calendar year.

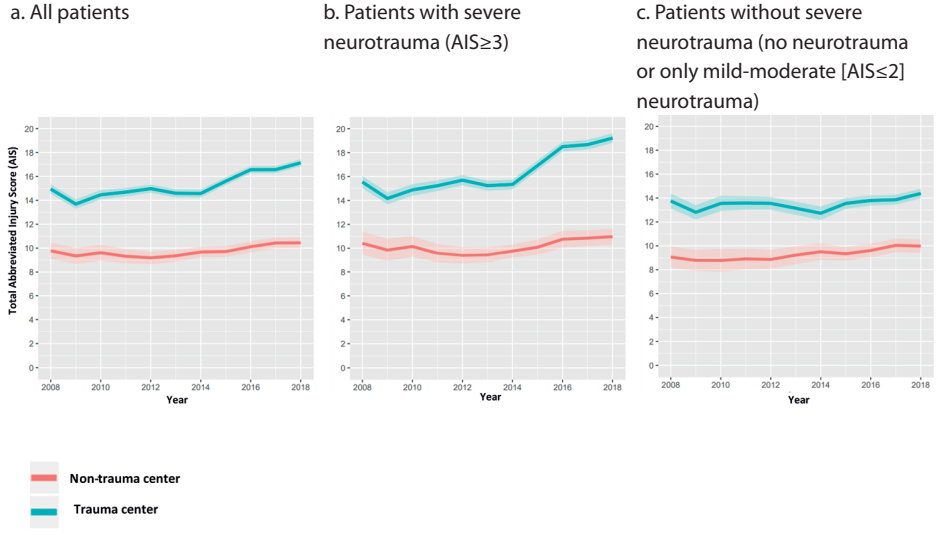


Figure 5. Median total Abbreviated Injury Score (AIS) for severely injured patients (ISS≥16) directly brought to a trauma center or a non-trauma center, for (A) all patients, and separately for patients (B) with and (C) without severe neurotrauma, by calendar year.

median total AIS (13, IQR 9 - 20), than the patients that were directly brought to a NTC (ISS 18, IQR 17 - 25 and total AIS 8, IQR 6 - 12) (Figures 4 and 5). For all severely injured patients and for the subgroup of patients with severe neurotrauma, the total AIS and ISS in the patients directly brought to a TC (median ISS 24, IQR17 - 29 and total AIS 14, IQR 9

- 21) increased from 2014 onward (ISS 2014 22, IQR 17 - 27 vs ISS 2018 25, IQR 19- 29 and total AIS 2014 13, IQR 9 - 20 vs total AIS 2018 17, IQR 12 - 24), while it remained steady over the years for the patients that were brought to a NTC (ISS 19, IQR 17 - 25 and total AIS 9, IQR 6 - 12) (Figures 4A-B and 5A-B). For the subgroup of severely injured patients without severe neurotrauma, the median ISS and total AIS remained similar over time, for both the patients that were directly brought to a TC (ISS 20, IQR 17 - 25 and total AIS 12, IQR 7 - 17) and for those directly brought to a NTC (ISS 18, IQR 17 - 22 and total AIS 8, IQR 5 - 12) (Figures 4C and 5C).

DISCUSSION

Over the period 2008-2018 the centralization of trauma care in the Netherlands continued. The total number of registered severely injured patients has increased to annually about 4500. This increase is at least partly attributable to increased participation of NTCs in the DTR and to a more accurate registration. As of 2014, all TCs and NTCs with an ED participated in the registry and from then on representative data was available. The proportion of the severely injured patients that were directly brought to a TC slightly increased, and stabilized at 70% in the most recent years. This proportion was somewhat higher for the severely injured patients with severe neurotrauma than for those without neurotrauma or only mild or moderate neurotrauma. The injury severity within the group of severely injured patients that were directly brought to a TC has increased since 2014, especially in the subgroup of patients with severe neurotrauma.

Despite many improvements, challenges remain to be faced. As a consequence of the introduction of a trauma system, severely injured patients are more likely to be admitted to a TC than in the 1990s.[6] However, about 30% of these patients are still transported to NTCs in the Netherlands. Similar percentages are seen in other countries such as Norway and the United States.[18-22] According to the American College of Surgeons- Committee on Trauma an under-triage rate above 5% is unacceptable, as under-triage increases the risk of mortality and morbidity due to patients not being managed in the best equipped hospital.[23] In addition, MacKenzie et al. showed in their study that, especially for the younger, more severely injured patients, treatment at a TC is not only more effective but also cost-effective, which underlines the importance of bringing the severely injured to a TC.[24] Studies show that especially the most severely injured patients, with ISS≥25, hemodynamically instable and patients with severe traumatic brain injury (AIS≥3), benefit the most from proper hospital triage, demonstrating lower mortality rates for these patients when brought to a TC.[25-28] Reducing under-triage should therefore be given priority. This does however, remain a major challenge even in mature trauma systems.[23,29] Van Rein et al. showed in their systematic review that almost all prehospital triage protocols had a

low sensitivity and therefore failed to identify all severely injured patients who needed treatment in a TC.[30] Especially identifying serious neurotrauma by EMS providers has proven to be difficult; 32% of all neurotrauma and 21% of the severe neurotrauma is not recognized at the accident scene.[12]Particularly for these patients, the hospital triage may be further optimized by advanced triage tools. In trauma patients, the effects of drugs and alcohol often obscure the real trauma related neurological symptoms so that symptoms often do not correspond with findings on the CT-scans once the patients have arrived at the ED.[12]

The current lack of field triage criteria able to adequately predict if a patient will be classified as severely injured contributes to the challenge to fulfill the Dutch Healthcare Institute's prerequisite of 90% severely injured patients being brought directly to a dedicated TC. In practice, emergency service providers guide their decision whether or not to go to a TC based on their clinical experience, and clinical signs of severe injury at the accident scene in addition to what the ambulance protocols prescribe.[31] Future research should focus on developing tools for scientifically substantiated assistance in this decision making and improve the quality of pre-hospital triage in severely injured patients.[32,33]

Strengths and limitations

A strength of this study is that it includes data of all documented severely injured patients over a period of 10 years in one country. There are also some limitations that need to be addressed. We observed an increasing number of (severely) injured patients in the study period. Although we tried to correct for the fact that some NTC's did not participate at the beginning of the DTR, the increase in patient numbers may still, at least partly, be explained by the increasing NTC participation over the years. The increase in trauma patient numbers might also be caused by more accurate registration. Another potential bias was posed by the AIS conversion in 2015, when the way of injury coding in the DTR was changed from the 1998 version of the Abbreviated Injury Scale to the 2005/2008 update version. It is well known that the AIS08 version substantially differs from the AIS98 version with regard to the classification of injury severity and accuracy. Specifically, the AIS08 classification results in less patients being classified as severely injured patients (ISS≥16) and less patients with severe (AIS≥3) neurotrauma. This probably also explains the increase in numbers of patients with minor TBI and the reduction in numbers of severely injured patients with severe neurotrauma, which was on average 66% over the years 2008-2014 and 55% over the years 2015-2018. This assumption is confirmed by Pal et al. who showed an increase in head AIS1 and AIS2 classifications and a decrease in AIS>3 or higher classifications after using the AIS2008 classification.[34] So, despite our best efforts in reclassifying the AIS98 to AIS08 codes according to Palmer's model[10], it remains challenging to combine the data of both classifications.[10,34,35]

CONCLUSION

Since the introduction of a well-organized trauma system in the Netherlands, trauma care has become progressively centralized, with more severely injured patients being brought directly to a TC. The injury severity within the group of severely injured patients that are directly transported to a TC has increased slightly in the most recent years, especially in the subgroup of patients with severe neurotrauma. However, still 30% of all severely injured patients is initially brought to a NTC. Future research should focus on improving pre-hospital triage, to facilitate swift transfer of the right patient to the right hospital.

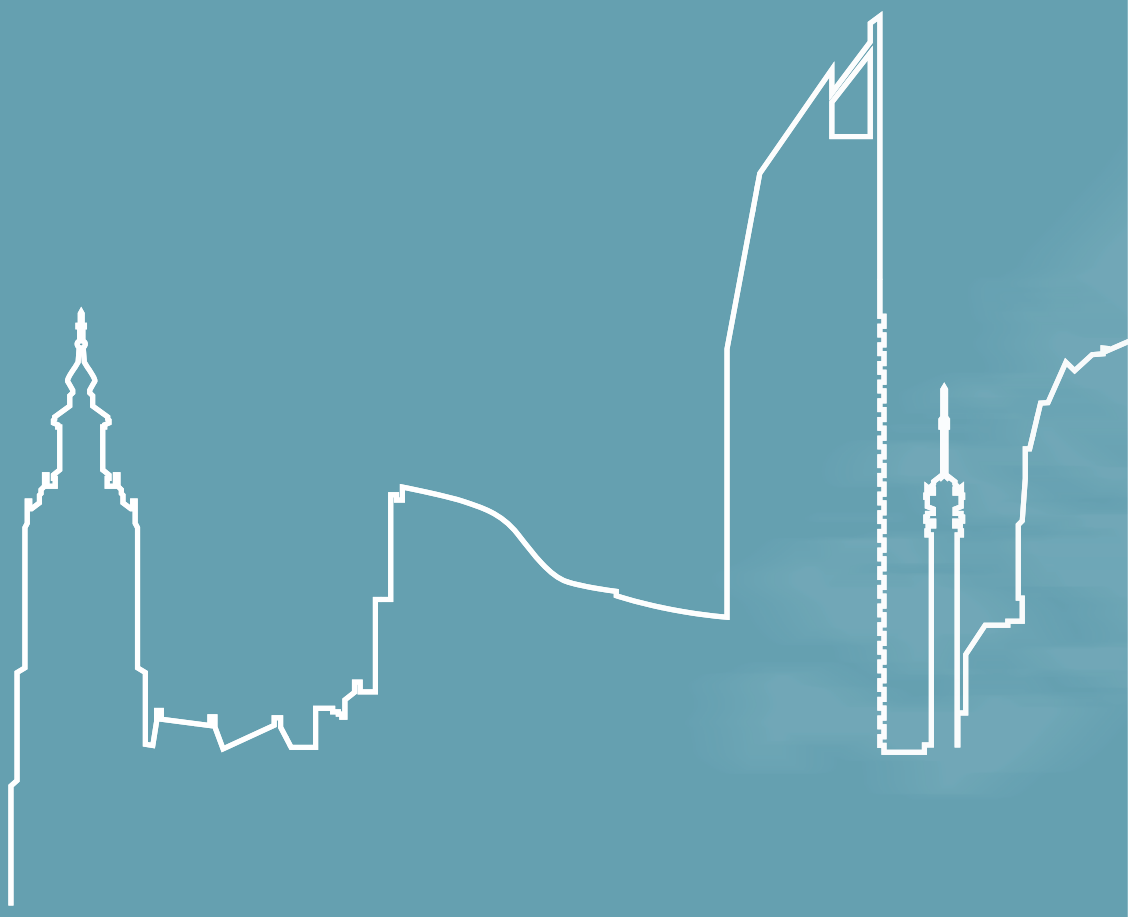
REFERENCES

1. ten Duis HJ, van der Werken C. Trauma care systems in The Netherlands. *Injury.* 2003;34(9):722-727.
2. Goris RJA DJ. De zorg voor detrauma-patiënt: meer en beter onderzoek nodig. . *Medisch Contact* 1984;39:301-302.
3. Ministerie van Volksgezondheid Welzijn en Sport. Met Zorg Verbonden. 1997.
4. Nederlandse Vereniging voor Traumatologie. *Traumazorg; onze zorg.* 1997.
5. American College of Surgeons - Committee on Traumao. Resources for optimal care of the injured patients. American College of Surgeons,; 1999; Chicago, 1998.
6. Twijnstra MJ, Moons KG, Simmermacher RK, Leenen LP. Regional trauma system reduces mortality and changes admission rates: a before and after study. *Annals of surgery.* 2010;251(2):339-343.
7. BAKER SP, O'NEILL B. THE INJURY SEVERITY SCORE: AN UPDATE. *Journal of Trauma and Acute Care Surgery.* 1976;16(11):882-885.
8. Barrington I. The Abbreviated Injury Scale 1990 revision–update 98. *Adv Automot Med.* 1998.
9. Gennarelli TA, Wodzin E. The abbreviated injury scale 2005. *Update.* 2008;20082008.
10. Palmer CS, Franklyn M, Read-Allsopp C, McLellan S, Niggemeyer LE. Development and validation of a complementary map to enhance the existing 1998 to 2008 Abbreviated Injury Scale map. *Scand J Trauma Resusc Emerg Med.* 2011;19:29.
11. Team RC. R development core team. *RA Lang Environ Stat Comput.* 2013.
12. van Rein EAJ, Jochems D, Lokerman RD, et al. Diagnostic value of emergency medical services provider judgement in the identification of head injuries among trauma patients. *European journal of neurology.* 2019;26(2):274-280.
13. Boyd CR, Tolson MA, Copes WS. Evaluating trauma care: the TRISS method. Trauma Score and the Injury Severity Score. *J Trauma.* 1987;27(4):370-378.
14. Sturms L. The Dutch Trauma Registry Facts and figures 2015. https://www.lnaz.nl/cms/files/symposium2016/6._Sturms_2_nov_2016_LNAZ_symposium.pdf. Published 2015. Accessed may 5th 2020.
15. Ringdal KG, Skaga NO, Hestnes M, et al. Abbreviated Injury Scale: not a reliable basis for summation of injury severity in trauma facilities? *Injury.* 2013;44(5):691-699.
16. Maduz R, Kugelmeier P, Meili S, Doring R, Meier C, Wahl P. Major influence of interobserver reliability on polytrauma identification with the Injury Severity Score (ISS): Time for a centralised coding in trauma registries? *Injury.* 2017;48(4):885-889.
17. Mimasaka S, Ohtsu Y, Tsunenari S, Funayama M. Postmortem cytokine levels and severity of traumatic injuries. *International Journal of Legal Medicine.* 2006;120(5):265-270.
18. Landelijk Netwerk Acute Zorg. *Landelijke Traumaregistratie 2012-2016. Rapportage Nederland.* Utrecht2017.
19. Jeppesen E, Cuevas-Østrem M, Gram-Knutsen C, Uleberg O. Undertriage in trauma: an ignored quality indicator? *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine.* 2020;28(1):34.
20. Uleberg O, Vinjevoll O, Eriksson U, Aadahl P, Skogvoll E. Overtriage in trauma–what are the causes? *Acta Anaesthesiologica Scandinavica.* 2007;51(9):1178-1183.
21. Newgard CD, Fu R, Zive D, et al. Prospective Validation of the National Field Triage Guidelines for Identifying Seriously Injured Persons. *J Am Coll Surg.* 2016;222(2):146-158.e142.
22. Xiang H, Wheeler KK, Groner JI, Shi J, Haley KJ. Undertriage of major trauma patients in the US emergency departments. *The American Journal of Emergency Medicine.* 2014;32(9):997-1004.

23. MacKenzie EJ, Rivara FP, Jurkovich GJ, et al. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med.* 2006;354(4):366-378.
24. MacKenzie EJ, Weir S, Rivara FP, et al. The value of trauma center care. *J Trauma.* 2010;69(1):1-10.
25. Vickers BP, Shi J, Lu B, et al. Comparative study of ED mortality risk of US trauma patients treated at level I and level II vs nontrauma centers. *Am J Emerg Med.* 2015;33(9):1158-1165.
26. Harmsen AMK, Giannakopoulos GF, Moerbeek PR, Jansma EP, Bonjer HJ, Bloemers FW. The influence of prehospital time on trauma patients outcome: A systematic review. *Injury.* 2015;46(4):602-609.
27. Mills EHA, Aasbjerg K, Hansen SM, et al. Prehospital time and mortality in patients requiring a highest priority emergency medical response: a Danish registry-based cohort study. *BMJ Open.* 2019;9(11):e023049.
28. Härtl R, Gerber LM, Iacono L, Ni Q, Lyons K, Ghajar J. Direct transport within an organized state trauma system reduces mortality in patients with severe traumatic brain injury. *Journal of Trauma and Acute Care Surgery.* 2006;60(6):1250-1256.
29. Newgard CD, Uribe-Leitz T, Haider AH. Undertriage Remains a Vexing Problem for Even the Most Highly Developed Trauma Systems: The Need for Innovations in Field Triage. *JAMA surgery.* 2018;153(4):328-328.
30. van Rein EAJ, Houwert RM, Gunning AC, Lichtveld RA, Leenen LPH, van Heijl M. Accuracy of prehospital triage protocols in selecting severely injured patients: A systematic review. *Journal of Trauma and Acute Care Surgery.* 2017;83(2):328-339.
31. Newgard CD, Nelson MJ, Kampp M, et al. Out-of-hospital decision making and factors influencing the regional distribution of injured patients in a trauma system. *The Journal of trauma.* 2011;70(6):1345-1353.
32. Voskens FJ, van Rein EAJ, van der Sluijs R, et al. Accuracy of Prehospital Triage in Selecting Severely Injured Trauma Patients. *JAMA surgery.* 2018;153(4):322-327.
33. van Rein EAJ, van der Sluijs R, Houwert RM, et al. Effectiveness of prehospital trauma triage systems in selecting severely injured patients: Is comparative analysis possible? *The American journal of emergency medicine.* 2018.
34. Pal C, Hirayama S, Sangolla N, et al. Effect of Abbrevieted Injury Scale (AIS) Change on Injury Severity Prediction for Advanced Automatic Crash Notification (AACN). *International Journal of Automotive Engineering.* 2017;8(2):71-78.
35. Palmer CS, Franklyn M. Assessment of the effects and limitations of the 1998 to 2008 Abbreviated Injury Scale map using a large population-based dataset. *Scand J Trauma Resusc Emerg Med.* 2011;19(1):1.

PART II

EVALUATION OF INDIVIDUALIZED TRAUMA CARE: MALNUTRITION IN POLYTRAUMA PATIENTS



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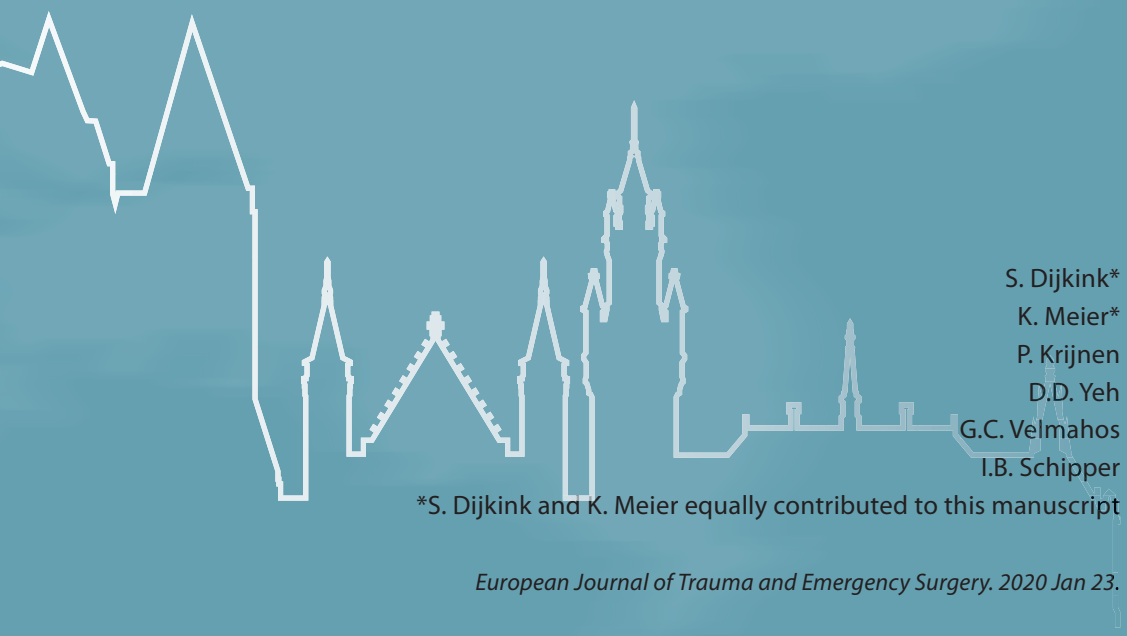
Malnutrition and its effects in severely injured trauma patients



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European Journal of Trauma and Emergency Surgery. 2020 Jan 23.

ABSTRACT

Background

In hospitalized patients, malnutrition is associated with adverse outcomes. However, the consequences of malnutrition in trauma patients are still poorly understood. This study aims to review the current knowledge about the pathophysiology, prevalence, and effects of malnutrition in severely injured patients.

Methods

A systematic literature review in PubMed and Embase was conducted according to PRISMA-guidelines.

Results

Nine review articles discussed the hypermetabolic state in severely injured patients in relation to malnutrition. In these patients, malnutrition negatively influenced the metabolic response, and vice versa, thereby rendering them susceptible to adverse outcomes and further deterioration of nutritional status. Thirteen cohort studies reported on prevalence of malnutrition in severely injured patients; ten reported clinical outcomes. In severely injured patients, the prevalence of malnutrition ranged from 7 to 76%, depending upon setting, population, and nutritional assessment tool used. In the geriatric trauma population, 7–62.5% were malnourished at admission and 35.6–60% were at risk for malnutrition. Malnutrition was an independent risk factor for complications, mortality, prolonged hospital length of stay, and declined quality of life.

Conclusions

Despite widespread belief about the importance of nutrition in severely injured patients, the quantity and quality of available evidence is surprisingly sparse, frequently of low-quality, and outdated. Based on the malnutrition-associated adverse outcomes, the nutritional status of trauma patients should be routinely and carefully monitored. Trials are required to better define the optimal nutritional treatment of trauma patients, but a standardized data dictionary and reasonable outcome measures are required for meaningful interpretation and application of results.

INTRODUCTION

Malnutrition is an underestimated problem in the general hospitalized population. Estimations up to a 50% prevalence of this condition have been reported, with probably even higher numbers in the critically ill.[1-4] Malnutrition in hospitalized patients is an important factor to consider, because it is associated with adverse outcomes such as prolonged hospital length of stay, increased complications, in- hospital mortality, and healthcare costs.[1,5,6] . Although most physicians are aware of the risk of malnutrition, half of all malnourished patients are not identified during their hospital stay.[7]

In severely injured patients, the relationship between nutritional status and clinical outcome is complicated by the systemic pathophysiological responses to trauma, which may affect, as well as may be affected by, the patient's nutritional status.[8-11] The impact of nutrition on metabolic changes and clinical outcomes in severely injured trauma patients is therefore unique and complex but remains poorly understood. More insight into these mechanisms may increase awareness of nutritional status in severely injured patients so that both, as classified by the American Society of Parenteral and Enteral Nutrition (A.S.P.E.N), acute disease or injury- related malnutrition and its consequences may be prevented.[12] The purpose of this systematic review is to summarize and evaluate the available literature on: (1) the metabolic effects of malnutrition in severely injured trauma patients, and (2) the incidence/prevalence of malnutrition, the risk of developing malnutrition, and clinical outcomes of malnutrition in severely injured patients.

MATERIAL AND METHODS

Search strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta- Analyses (PRISMA) statement.[13] A systematic literature search was performed in PubMed and Embase with help of an experienced medical librarian in May 2019. The search strategy, provided in Appendix 1, included related terms and synonyms for nutritional status, malnutrition, undernutrition, and adult polytrauma patients.

Eligibility criteria and article selection

Articles about the pathophysiology and metabolic effects of malnutrition in severely injured trauma patients were considered eligible for inclusion, as well as clinical studies in which the prevalence and/or outcomes of malnutrition in severely injured trauma patients were reported. We did not use a specific definition of malnutrition and severely injured patients because different criteria and assessments tools for both malnutrition

and severely injured patients were used in the literature. We selected publications in Dutch, English, French, and German without restriction on publication year. Identified articles were first screened for relevance based on title and abstract. Articles without full-text were not included; the majority (56%) of these were outdated (> 20 years old). The full-text of potentially eligible articles were read before inclusion in the review. The reference lists of the included articles were screened for additional literature. Expert opinions, conference papers and letters to the editor were excluded. Selected articles were grouped by topic: (1) articles describing the metabolic response of mal- nutrition in severely injured trauma patients, and (2) clinical cohort studies describing the prevalence of malnutrition and its association with clinical outcomes in severely injured trauma patients during hospital admission.

Data extraction and risk of bias assessment

Metabolic effects; reviews

All selected articles about the pathophysiology and metabolic effects of malnutrition in severely injured trauma patients were review articles. Data on pathophysiology and metabolic effects of malnutrition in these articles were summarized and combined in a model. The methodological quality of the included review articles could not be assessed according to the AMSTAR tool or equivalent as suggested by the PRISMA-guidelines. [14,15], because none of these articles were systematic reviews.

Incidence/prevalence and outcomes of malnutrition; cohort studies

Patients' age and gender, reported prevalence of malnutrition, type of nutritional assessment tool, and reported clinical outcomes were extracted from the selected cohort studies. Authors were contacted for more detailed information on the severely injured and geriatric patients groups in their studies, however none of the contacted authors responded to our query. Due to the inconsistent and different assessment tools and reported outcomes, the extracted data of these studies could not be pooled.

The risk of different types of bias of the included cohort studies was assessed using the 'Methodological index for non-randomized studies' (MINORS criteria) on a 3-point scale ranging from 2 (reported and adequate) to 0 (not reported).[16]

Article selection, data extraction and assessment of methodological quality were performed independently by the first two authors. Disagreement was resolved by discussion.

RESULTS

Selection of articles

The search yielded 3689 articles. After removing 418 duplicates, 3271 articles were screened for eligibility. Seventy- three articles were excluded because no full-text was avail- able. Twenty articles fulfilled the inclusion criteria and were included in this review. Two more studies were included based on hand search of the reference lists (Fig. 1).

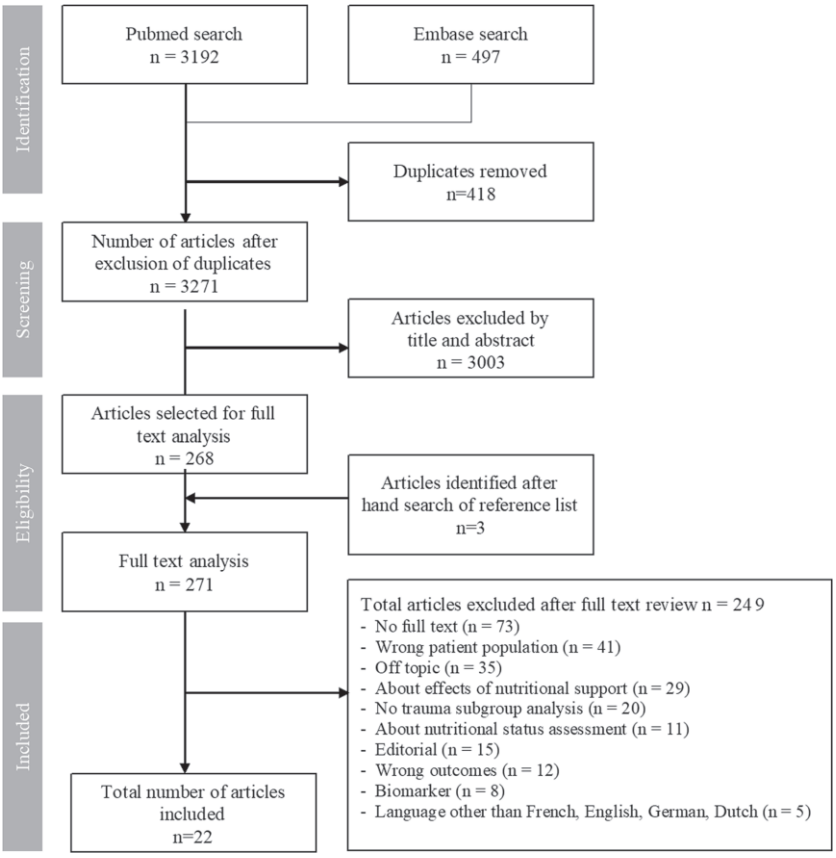

Figure 1. Studies resulting from literature search with reasons for in-/exclusion

Metabolic effects

Nine articles, published between 1968 and 2011, were non-systematic reviews about the altered metabolic state of severely injured trauma patients.[11, 17-24] All these articles discussed a specific part of the metabolic response in relationship to malnutrition.

Table 1. Included cohort studies about prevalence of malnutrition and its effects on outcomes in trauma patients in this review (n = 10)

Authors	Year	Country	Design	n	Male (%)	Age in years	Nutritional assessment tool
Wilson et al. [36]	2019	United States	Prospective cohort study	377	50.9	73.70[m] ± SD 12.73	Visceral proteins
Wilson et al. [34]	2019	United States	Retrospective cohort study	5,673	43.8	46.69 [m] ± SD 13.62	Visceral proteins
Wintermeyer et al. [35]	2019	Germany	Prospective cohort study	1,642	-	57.8[m] ± SD 16.6	NRS
Ihle et al. [33]	2017	Germany	Prospective cohort study	521	56.2	53.9[m] ± SD 18.1	NRS
Müller et al. [26]	2017	Switzerland	Non-comparative prospective cohort study	169	42.6	79.7[m] ± SD 6.5	MNA
Goisser et al. [27]	2015	Germany	Non-comparative retrospective cohort study	97	20.6	84.0[m] ± SD 5.0	MNA (long form)
Chakravarty et al.[28]	2013	India	Non-comparative prospective cohort study	61	78.7	-	SGA
Banks et al. [29]	2010	Ireland	Non-comparative prospective cohort study	30	37.0	78.5[med] IQR 68-85	MNA
Dhandapani et al. [25]	2007	India	Non-comparative prospective cohort study	61	92.0	35.4[m] ± SD not reported	Anthropometric measurements

Prevalence MN on admission (unless indicated otherwise) (%)	ARM (%)	Mortality	Length of stay in days	Complications
Hypoalbuminaemia: 17.5 Low TLC: 62.3	-	Hypoalbuminaemia: OR2.22 95% CI 1.26-3.92 TLC: n/a	Hypoalbuminaemia: r=-0.14, p=0.024 TLC:n/a	≥1 adverse event associated with MN, p < 0.001
Hypoalbuminaemia: 29.6		WN: 0.4%, MN: 3.2%, RR 4.86, 95% CI 2.66-8.87	WN: 3.57 (± SD 5.0) MN: 7.5 (± SD 10.45) p < 0.001	≥1 adverse event RR 1.46 95% CI 1.30-1.64; Sepsis RR 1.99 95% CI 1.03-3.86; Unplanned intubation RR 2.95 95% CI 1.49-5.84; Reoperation RR 1.52 95% CI 1.11-2.07; Readmission RR 2.0 95% CI 1.55-2.57
-	Overall: 18.3 Geriatric trauma: 35.6	-	-	≥1 adverse event associated with ARM, p < 0.01; quality of life negatively associated with ARM, p < 0.01
-	19.2	-	NRS ≥3 (ARM): 16 ± SD 12 NRS <3 (WN): 11 ± SD 10	≥1 adverse event associated with ARM, p < 0.001
7.1	49.1	-	-	-
17.0	38.0	WN:13%, ARM: 21%, MN: 0%, p = 0.120	WN:11^{med} IQR 10-16, ARM:12^{med} IQR 9-17, MN:10^{med} IQR 7-15, p = 0.388	WN: 86%, ARM: 97%, MN: 100%, p = 0.095
15.0	-	-	-	-
-	60.0	-	-	-
Clinical features of pedal edema, cheilosis, skeletal prominence, xerosis, gum bleed: Week 1: 45.0 Week 3: 76.0		-	-	-

Table 1. Included cohort studies about prevalence of malnutrition and its effects on outcomes in trauma patients in this review (n = 10) (continued)

Authors	Year	Country	Design	n	Male (%)	Age in years	Nutritional assessment tool
Goiburu et al. [10]	2006	Paraguay	Non-comparative prospective cohort study	161	94.0	27.0[med] IQR 14-92	SGA
Compan et al. [30]	1999	France	Non-comparative prospective cohort study	299	33.0	82.9[m] ± SD 7.0	MNA
McClave et al.[31]	1992	United States	Non-comparative prospective cohort study	-	-	-	Visceral proteins Anthropometric measurements
Kaufman et al. [32]	1987	United States	Non-comparative prospective cohort study	76	-	-	Visceral proteins Anthropometric measurements

* n refers to the number of trauma patients in the study
[m] mean [med] median
MN: Malnourished, ARM: At risk for malnutrition, WN: Well-nourished, NRS: Nutritional Risk Screening, MNA: Mini Nutritional Assessment, SGA: Subjective Global Assessment scale, TLC: Total lymphocyte count, SD: Standard deviation, IQR: Interquartile range, RR: relative risk, CI: confidence interval, OR: adjusted odds ratio

Incidence/prevalence and outcomes of malnutrition

Thirteen cohort studies about the prevalence of malnutrition in severely injured trauma patients were found, published between 1987 and 2019 (Table 1).[10, 25–33] Outcomes were reported in ten articles, of which six described the general trauma population with severe injuries[10, 25, 31, 33–35], four described the geriatric trauma population.[26, 27, 30, 34] The risk of bias in the included cohort studies was generally low (Table 2).

Malnutrition and the metabolic response in severely injured patients

The pathophysiological processes and metabolic effects of malnutrition in severely injured patients described in the nine review articles are summarized in Fig. 2. Essentially, the reviews describe the combination of a prolonged and/or disturbed metabolic response following traumatic injury and the negative influence of malnutrition upon this response that leads to a vicious circle of further deterioration of the nutritional- and health status and the metabolic response. [20, 21, 24]

After severe trauma, burns, or infection, a universal acute phase response is seen, characterized by a predominantly hypermetabolic catabolic state.[11, 17–20, 23, 24] Although this acute phase response seems to be essential for recovery, a maladaptive prolonged and/or disturbed metabolic response is associated with complications, morbidity and mortality.[24]

Prevalence MN on admission (unless indicated otherwise) (%)	ARM (%)	Mortality	Length of stay in days	Complications
40.0	-	RR 4; 95% CI 1-15	>14 days RR 2.3; 95% CI 1.2-4.7	RR 2.9; 95% CI 1.4-5.8
24.7	-	-	Longer stay associated with MN, p not reported	Death during hospitalization associated with MN, p <0.0001
Low visceral proteins (albumin, transferrin, TLC): 17.6%, Underweight: 20.6%, Mix: 15.6%		OR 4.04; p <0.05	OR 1.29; p <0.05	Sepsis: OR 2.64; p <.05; Nosocomial infections: OR 2.26; p <0.05
Albumin, transferrin, TLC, and others: not defined	-	-	-	-

The initial post-injury state in severely injured patients, caused by tissue damage, is characterized by an acute phase response and increased energy expenditure. Released cytokines (e.g., interleukins and tumor necrosis factor-α) together with post-injury released hormones (including epinephrine, cortisol, and glucagon), act as catabolic stimulants.[11, 17, 18, 23] Depending upon the severity of injury, energy expenditure increases by 20–50% in trauma patients compared to patients after elective surgery (Fig. 2).

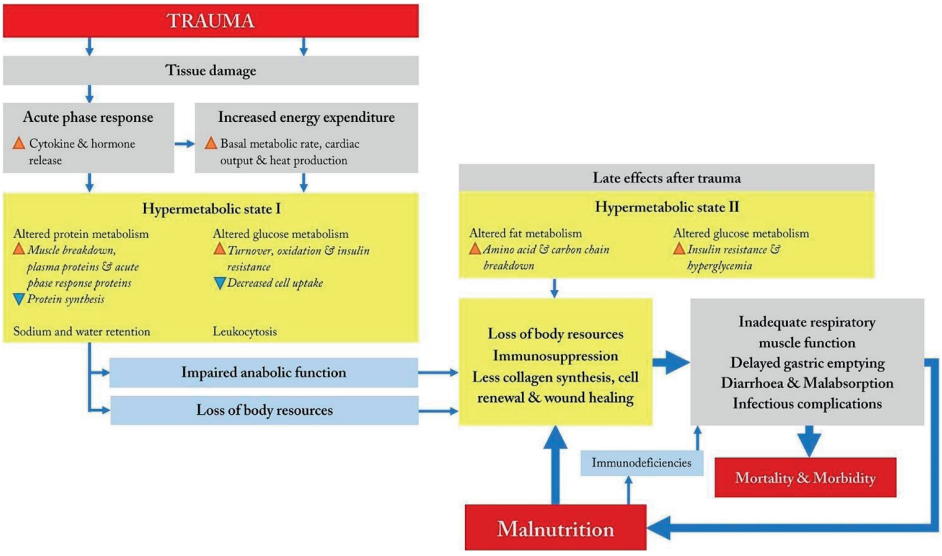

Figure 2. Model of effects of the hypermetabolic state and malnutrition in severely injured patients

Table 2. Risk of Bias in the included cohort studies according to Methodological Index for Non-Randomized Studies (MINORS) criteria. [16]

	Wilson et al.[36]	Wilson et al.[34]	Wintermeyer et al.[35]	Ihle et al.[33]	Müller et al.[26]	Goisser et al.[27]	Chakravarty et al.[28]	Banks et al.[29]	Dhandapani et al.[25]	Goiburu et al.[10]	Compan et al.[30]	McClave et al.[31]	Kaufman et al.[32]
1. Clearly stated aim	2	2	2	2	2	2	2	2	2	2	2	1	2
2. Inclusion of consecutive patients	2	2	2	2	2	2	2	2	2	2	2	0	0
3. Prospective collection of data	2	2	2	2	2	2	0	2	2	2	2	2	0
4. Endpoints appropriate to aim of study	2	2	2	2	2	2	2	2	2	2	2	0	2
5. Unbiased assessment of study endpoints	2	2	2	0	2	0	0	2	2	0	1	0	0
6. Follow-up period appropriate to aim of study	2	2	2	2	2	2	2	2	2	2	2	2	2
7. < 5% lost to follow-up	2	1	2	2	0	2	2	1	1	1	0	2	1
8. Prospective calculation of study size	0	0	0	0	2	2	2	1	1	1	1	0	0
Total	**14**	**13**	**14**	**12**	**14**	**14**	**12**	**14**	**14**	**12**	**12**	**7**	**7**

Criteria were scored 2 (reported and adequate), 1 (reported but inadequate) or 0 (not reported), with a maximum total score of 16

The combination of this acute phase response and increased energy expenditure after trauma leads to a hypermetabolic state (Fig. 2; "Hypermetabolic state I"). This hypermetabolic state alters protein metabolism, leading to increased muscle protein mobilization for energy, and decreased protein synthesis leading to catabolism.[19, 22] In addition, leukocytosis, changes in the glucose metabolism, and retention of sodium and water are seen.[18] These biochemical adaptations are distinctive for severely injured patients, and increase the susceptibility of the trauma patient for developing malnutrition.

Recovery of the trauma patient is threatened by the combination of increased loss of body resources and the prolonged and/or disturbed hypermetabolic state. This state is characterized by impaired anabolic function characterized by continued muscle protein breakdown and ongoing elevated energy expenditure remains high (Fig. 2).[18, 20, 23] Additionally, between three to seven days post-injury, severely injured trauma patients developed increased lipid metabolism, insulin resistance, and hyperglycemia (Fig. 2; "Hypermetabolic state II").[23] Due to this insulin resistance, patients develop a glucose deficit, causing the body to oxidize branched carbon chains from amino acids for energy production.[17, 18, 22, 23] This altered fat metabolism further contributes to significant breakdown in amino acids and body protein stores, reflected by a negative nitrogen balance.[24] It has been suggested that 10–15% of the weight loss in trauma patients is a consequence of depleting normal protein stores.[22] However, severely malnourished

patients are unable to increase their protein turnover, which has been associated with a higher risk of mortality, with inefficient wound healing, and less cell renewal.[24]

One clinically relevant consequence of muscle breakdown is seen in respiratory muscle inadequacy and the associated prolonged ventilator dependency, pneumonia, and subsequent risk of mortality.[17-22] Immunosuppression and the cytokine cascade can lead to a functionally impaired gastrointestinal tract, contributing to delayed gastric emptying, diarrhea, and malabsorption.[17,.24] These consequences of the distinctive metabolic response following traumatic injuries not only increase mortality and morbidity rates, but also potentiate deterioration of the nutritional status.[17, 22, 24] Once malnutrition has developed, the circle is complete, as it negatively influences the metabolic response, leading to relative immunodeficiency, such as an impaired white blood cell function, decreased T-cell function and anti-body and complex formation.[17, 22, 24] This again makes the patient particularly susceptible to infectious complications and further loss of body resources.[18, 20, 22, 24]

Prevalence of malnutrition and its association with patient outcomes

Thirteen cohort studies reported on the prevalence of malnutrition in severely injured trauma patients (Table 1). The prevalence of malnutrition ranged from 7 to 76% in trauma patients in general.[10, 25–32, 34–36]

Six studies specifically reported the prevalence of malnutrition on geriatric patients admitted with traumatic injuries. On admission, 7–62.6% of the geriatric trauma patients were malnourished and 35.6–60% were at risk for malnutrition according to the Mini Nutritional Assessment (MNA) tool, Nutritional Risk Screening (NRS 2002) tool and serum biomarkers (visceral proteins).[26, 27, 29, 30, 35, 36] Dhandapani et al. also examined the development of malnutrition during hospital stay and showed an increase in prevalence from 45% in the first week of hospital admission to 76% in the third week.[25]

Ten studies reported on clinical outcomes, such as mortality, hospital length of stay, quality of life, and complications associated with malnutrition, six in the general trauma population[10, 25, 31, 33–35] and four in the geriatric trauma population specifically (Table 1).[26, 27, 30, 36] Malnutrition was associated with higher morbidity, delayed mobilization both after conservative and operative treatment, higher in-hospital mortality, prolonged hospital length of stay, reoperation and readmissions.[10, 31, 33–35] In malnourished patients with traumatic brain injuries, neurological outcome after 6 months was less favorable, classified as death, persistent vegetative state or severe disability according to the Glasgow Outcome Scale (adjusted odds ratio 12.5; 95% confidence interval 2.6–61.0) compared to well-nourished patients.[25]

Geriatric patients at risk for malnutrition or suffering from malnutrition had more often cognitive impairments, infectious complications, depressive symptoms, comorbidity, less amelioration of their nutritional status, a higher prevalence of frailty and

suspected sarcopenia than well- nourished patients.[26, 27, 29, 36] Two studies observed no differences in length of stay, readmission rates and mortality rates[27, 30], while one cohort study observed a negative associations between malnutrition and these aforementioned outcomes.[36] Malnutrition seemed to have an influence on health-related quality of life, as malnourished geriatric trauma patients suffered more often than well-nourished geriatric trauma patients from irreversible loss of independency and worse physical, mental, and cognitive health after trauma.[27]

DISCUSSION

It is universally recognized that baseline "malnutrition" is a risk factor for worse clinical outcomes and that nutritional adequacy is important in component of the complex multidisciplinary care of severely injured patients. Yet, our comprehensive review of the published literature reveals that the evidence-base for these commonly held tenets is surprisingly sparse, outdated, and frequently of low-quality. The practice of critical care is rapidly changing, and many of the "landmark" studies in metabolism have been performed prior to recent treatment paradigm shifts in blood transfusion, fluid administration, sedation interruption, and ventilator management, to name but a few. Very few actual scientific studies have been conducted in the modern era of critical care and the literature is marked by heterogeneity in assessment tools, assessment times, interventions, and outcomes. It is thus impossible to quantitatively synthesize the literature. As such, we attempt to qualitatively synthesize the literature and offer suggestions to improve future studies in the field of nutrition in polytrauma patients.

The metabolic changes after trauma are distinctive and complex and make trauma patients more susceptible for developing malnutrition. Second, in these patients a vicious circle is set in motion by malnutrition, leading to further deterioration of the nutritional- and health status. The results of the review also underline the importance of early malnutrition recognition and intervention to prevent further deterioration.

The prevalence of malnutrition varied widely in the selected studies and depends upon the way in which malnutrition was defined and measured. Malnutrition has been defined in various ways[37, 38], due to the lack of a gold standard for diagnosing malnutrition. Sánchez-Rodriquez et al. compared two different tools in the same patient population and demonstrated little agreement on the presence of malnutrition.[39] To uniformly diagnose malnutrition and determine its prevalence, a generally accepted standard definition and validated assessment tool is required. According to the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) clinical guidelines there are currently 11 screening tools for assessing the risk of malnutrition, and two validated tools for diagnosing malnutrition.[40] We therefore conclude that there is a need for a simple, valid,

and generally accepted method for the assessment of nutritional status in hospitalized patients, which facilitates early identification and treatment of malnutrition but also determination of the prevalence of malnutrition in this patient population. At present, the best candidate for this assessment tool is the Nutrition Risk in the Critically Ill (NUTRIC) score.[41–44] The NUTRIC-score was specifically developed to identify critically ill patients who would benefit from nutritional support.[45] and has been well-validated for several important outcomes, such as ICU length of stay, ventilator-free days, and mortality. The NUTRIC-score is currently recommended by the Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) 2016 guidelines to assess the nutritional status.[42, 44, 46]

The detection of malnutrition in an early phase provides the clinician with the opportunity to intervene and attempt to prevent further deterioration of the nutritional status. The literature suggests that only a fraction of malnourished hospitalized patients receive timely nutritional support to prevent nutritional status decline.[47] Kondrup et al. suggested that hospitalized patients often receive less than the optimal amount of nutrition due to lack of awareness and suboptimal education of the medical staff.[48] This is supported by Dupertuis et al. who showed that if patients' nutritional requirements were not met, this was often due to other reasons than illness or treatment, such as inadequate meal services.[49] Improved training of medical staff in recognizing and treating malnutrition is needed to create more awareness for the underestimated problem of malnutrition. Although it seems intuitively obvious that the problem can be easily solved by providing the patients with the appropriate amount of calories and proteins, there is no strong evidence that increasing nutrient delivery improves clinical outcomes.[46, 50]. Recent high-profile trials even suggest that intensive medical nutrition therapy, (receiving > 75% of estimated daily energy and protein requirements) is associated with higher mortality and that permissive underfeeding does not worsen clinical outcomes in patients.[51–53] However, it is important to note that the majority of subjects enrolled in these trials were not malnourished at baseline. Large observational trials have demonstrated that only patients with a BMI < 25 or > 35 seem to benefit from increased nutrition elivery.[54, 55] Additionally, in both the EDEN- and PermiT-trials, the "full" nutrition group did not achieve currently recommended doses of calories nor protein. In all those studies, severely injured trauma patients only comprised a very small percentage of enrolled subjects. The potential benefit for early enteral nutrition in trauma patients is still debatable. Included studies are often of low-quality, heterogenous and included a small study population, and still leaves questions unanswered, such as composition of the enteral nutrition used, nutritional goal, use of supple- mental parenteral nutrition and adding supplements to the formula.[56] Thus, our current understanding about the role of malnutrition in trauma patients is built upon a thin evidence-base and most of current practice is extrapolated from studies in non-surgical and -trauma patients.

Limitations

A limitation of our systematic review on pathophysiological processes and metabolic changes after severe trauma is that this part was based on reviews (some published more than two decades ago) and mostly not performed according to the currently applied systematic review guidelines. We do consider this knowledge to be important, although we do acknowledge that there are currently new insights being developed. The clinical studies on prevalence and outcomes of malnutrition were small cohort studies, with ill-defined patient populations and great variation in outcomes. Other limitations are that our review was incomplete as the full-texts of 73 identified articles could not be retrieved, and that we imposed language restrictions.

Recommendations for future research

Based on the overall findings uncovered by this systematic review, we believe that future research on nutrition- related research in severely injured trauma patients should incorporate the following: First, as already mentioned, we recommend the widespread use of a uniform, simple, and validated risk stratification score for which we would recommend the NUTRIC-score. Second, recognizing that traditional biomarkers for monitoring nutritional status (i.e., albumin and prealbumin) are strongly influenced by the acute phase response, we recommend that a C-reactive protein be measured concomitantly to give information about the inflammation status to show that albumin and prealbumin are more related to the acute phase response than nutritional status.[57, 58] In addition, future research should focus on finding new biomarkers that are less affected by the acute phase response and pre-existent comorbidities.[57] Third, we recommend that future studies should carefully consider baseline nutritional status when defining inclusion/exclusion criteria and consider stratifying interventions according to malnourishment. Fourth, we recommend that clinical outcomes be carefully chosen to be reasonably affected by nutritional interventions, clinically relevant, and that time points be standardized across research studies.[59]

CONCLUSION

Despite widespread belief about the importance of nutrition in severely injured patients, the quantity and quality of available evidence is surprisingly sparse, low-quality, and outdated. Nutritional assessment and ongoing monitoring is hampered by low prioritization and heterogeneous, unvalidated tools. However, based on the malnutrition- associated adverse outcomes, the nutritional status of severely injured trauma patients should be routinely and carefully monitored. This review shows that the combination of a prolonged and/or disturbed metabolic response following severe traumatic

injuries that negatively influences the nutritional status and the negative influence of malnutrition upon this response, leads to a vicious circle of further deterioration of the nutritional- and health status. Additional trials are required to better define the optimal nutritional treatment of severely injured patients, but a standardized data dictionary and reasonable outcome measures are required for meaningful interpretation and application of results.

REFERENCES

1. Mogensen KM, Robinson MK, Casey JD, Gunasekera NS, Mor- omizato T, Rawn JD, et al. Nutritional status and mortality in the critically Ill. Crit Care Med. 2015;43(12):2605–15.
2. Barker LA, Gout BS, Crowe TC. Hospital malnutrition: preva- lence, identification and impact on patients and the healthcare system. Int J Environ Res Public Health. 2011;8(2):514–27.
3. Kruizenga HM, Van Tulder MW, Seidell JC, Thijs A, Ader HJ, Van Bokhorst-de van der Schueren MA. Effectiveness and cost- effectiveness of early screening and treatment of malnourished patients. Am J Clin Nutr. 2005;82(5):1082–9.
4. Thomas JM, Isenring E, Kellett E. Nutritional status and length of stay in patients admitted to an Acute Assessment Unit. J Hum Nutr Diet. 2007;20(4):320–8.
5. Correia MI, Waitzberg DL. The impact of malnutrition on morbid- ity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. Clin Nutr (Edinburgh, Scotland). 2003;22(3):235–9.
6. Amaral TF, Matos LC, Tavares MM, Subtil A, Martins R, Naz- are M, et al. The economic impact of disease-related malnutri- tion at hospital admission. Clin Nutr (Edinburgh, Scotland). 2007;26(6):778–84.
7. Kruizenga HM, Wierdsma NJ, van Bokhorst MA, de van der S, Haollander HJ, Jonkers-Schuitema CF, et al. Screening of nutritional status in The Netherlands. Clin Nutr (Edinburgh, Scotland). 2003;22(2):147–52.
8. Clendenen N, Nunns GR, Moore EE, Reisz JA, Gonzalez E, Peltz E, et al. Hemorrhagic shock and tis- sue injury drive distinct plasma metabolome derangements in swine. J Trauma Acute Care Surg. 2017;83(4):635.
9. Trunkey DD. Trauma. Sci Am Lancet. 1983;249:25–35.
10. Goiburu ME, Goiburu MM, Bianco H, Diaz JR, Alderete F, Palacios MC, et al. The impact of mal- nutrition on morbidity, mortality and length of hospital stay in trauma patients. Nutr Hosp. 2006;21(5):604–10.
11. Rogobete AF, Sandesc D, Papurica M, Stoicescu ER, Popovici SE, Bratu LM, et al. The influence of metabolic imbalances and oxidative stress on the outcome of critically ill polytrauma patients: a review. Burns Trauma. 2017;5:8.
12. Jensen GL, Mirtallo J, Compher C, Dhaliwal R, Forbes A, Grijalba RF, et al. Adult starvation and disease-related malnu- trition: a proposal for etiology-based diagnosis in the clinical practice setting from the International Consensus Guideline Committee. JPEN J Parenter Enteral Nutr. 2010;34(2):156–9.
13. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.
14. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol. 2007;7:10.
15. Shea BJ, Hamel C, Wells GA, Bouter LM, Kristjansson E, Grimshaw J, et al. AMSTAR is a reliable and valid measure- ment tool to assess the methodological quality of systematic reviews. J Clin Epidemiol. 2009;62(10):1013–20.
16. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non- randomized studies (minors): development and validation of a new instrument. ANZ J Surg. 2003;73(9):712–6.

17. Burns HJ. The metabolic and nutritional effects of injury and sepsis. Bailliere's Clin Gastroenterol. 1988;2(4):849–67.
18. Chiolero R, Revelly JP, Tappy L. Energy metabolism in sepsis and injury. Nutrition (Burbank, Los Angeles County, Calif). 1997;13(9 Suppl):45s–51s.
19. Cuthbertson DP, Tilstone WJ. Nutrition of the Injured. Am J Clin Nutr. 1968;21(9):911–22.
20. Gusberg RJ. The multiple trauma victim: a nutritional cripple. Yale J Biol Med. 1986;59(4):403–7.
21. Hoffmann M, Rueger JM. Nutritional status influences trauma outcome. Der Unfallchirurg. 2011;114(11):968–72.
22. Kinney JM, Elwyn DH. Protein metabolism and injury. Annu Rev Nutr. 1983;3:433–66.
23. Ryan NT. Metabolic adaptations for energy production during trauma and sepsis. Surg Clin North Am. 1976;56(5):1073–90.
24. Soeters PB, Grimble RF. Dangers, and benefits of the cytokine mediated response to injury and infection. Clin Nutr (Edin- burgh, Scotland). 2009;28(6):583–96.
25. Dhandapani SS, Manju D, Sharma BS, Mahapatra AK. Clini- cal malnutrition in severe traumatic brain injury: factors associated and outcome at 6 months. Indian J Neurotrauma. 2007;4(1):35–9.
26. Muller FS, Meyer OW, Chocano-Bedoya P, Schietzel S, Gagesch M, Freystaetter G, et al. Impaired nutritional status in geriatric trauma patients. Eur J Clin Nutr. 2017;71(5):602–6.
27. Goisser S, Schrader E, Singler K, Bertsch T, Gefeller O, Biber R, et al. Malnutrition according to mini nutritional assessment is associated with severe functional impairment in geriatric patients before and up to 6 months after hip fracture. J Am Med Dir Assoc. 2015;16(8):661–7.
28. Chakravarty C, Hazarika B, Goswami L, Ramasubban S. Preva- lence of malnutrition in a tertiary care hospital in India. Indian J Crit Care Med. 2013;17(3):170–3.
29. Banks LN, Byrne N, Henari S, Morris S, McElwain JP. Nutritional status of elderly trauma patients presenting to a South Dublin Teaching Hospital. Eur Geriatr Med. 2010;1(6):325–9.
30. Compan B, di Castri A, Plaze JM, Arnaud-Battandier F. Epide- miological study of malnutrition in elderly patients in acute, sub- acute and long-term care using the MNA. J Nutr Health Aging. 1999;3(3):146–51.
31. McClave SA, Mitoraj TE, Thielmeier KA, Greenburg RA. Dif- ferentiating subtypes (hypoalbuminemic vs marasmic) of pro- tein-calorie malnutrition: incidence and clinical significance in a university hospital setting. JPEN J Parenter Enteral Nutr. 1992;16(4):337–42.
32. Kaufman HH, Bretaudiere JP, Rowlands BJ, Stein DK, Bernstein DP, Wagner KA, et al. General metabolism in head injury. Neu- rosurgery. 1987;20(2):254–65.
33. Ihle C, Freude T, Bahrs C, Zehendner E, Braunsberger J, Biesalski HK, et al. Malnutrition—An underestimated factor in the inpatient treatment of traumatology and orthopedic patients: a prospective evaluation of 1055 patients. Injury. 2017;48(3):628–36.
34. Wilson J, Lunati M, Grabel Z, Staley C, Schwartz AM, Schenker M. Hypoalbuminemia is an independent risk factor for 30-day mortality, postoperative complications, readmission, and reopera- tion in the operative lower extremity orthopedic trauma patient. J Orthop Trauma. 2019;33:284–91.
35. Wintermeyer E, Ihle C, Ehnert S, Schreiner AJ, Stollhof L, Stockle U, et al. Assessment of the influence of diabetes mellitus and malnutrition on the postoperative complication rate and quality of life of patients in a clinic focused on trauma surgery. Zeitschrift fur Orthopadie und Unfallchirurgie. 2019;157(2):173–82.
36. Wilson JM, Boissonneault AR, Schwartz AM, Staley CA, Schen- ker ML. Frailty and malnutrition are associated with inpatient postoperative complications and mortality in hip fracture patients. J Orthop Trauma. 2019;33(3):143–8.

37. Kinosian B, Jeejeebhoy KN. What is malnutrition? Does it mat- ter? Nutrition (Burbank, Los Angeles County, Calif). 1995;11(2 Suppl):196–7.
38. Lochs H, Allison SP, Meier R, Pirlich M, Kondrup J, Schnei- der S, et al. Introductory to the ESPEN guidelines on enteral nutrition: terminology, definitions and general topics. Clin Nutr. 2006;25(2):180–6.
39. Sanchez-Rodriguez D, Marco E, Ronquillo-Moreno N, Maciel- Bravo L, Gonzales-Carhuancho A, Duran X, et al. ASPEN-AND- ESPEN: a postacute-care comparison of the basic definition of malnutrition from the American Society of Parenteral and Enteral Nutrition and Academy of Nutrition and Dietetics with the Euro- pean Society for Clinical Nutrition and metabolism definition. Clin Nutr (Edinburgh, Scotland). 2018;38:297–302.
40. Mueller C, Compher C, Ellen DM. A.S.P.E.N. clinical guidelines: nutrition screening, assessment, and intervention in adults. JPEN J Parenter Enter Nutr. 2011;35(1):16–24.
41. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying criti- cally ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. Crit Care (London, England). 2011;15(6):R268.
42. Mukhopadhyay A, Henry J, Ong V, Leong CS, Teh AL, van Dam RM, et al. Association of modified NUTRIC score with 28-day mortality in critically ill patients. Clin Nutr (Edinburgh, Scotland). 2017;36(4):1143–8.
43. Mendes R, Policarpo S, Fortuna P, Alves M, Virella D, Heyland DK. Nutritional risk assessment and cultural validation of the modified NUTRIC score in critically ill patients—-A multicenter prospective cohort study. J Crit Care. 2017;37:45–9.
44. de Vries MC, Koekkoek WK, Opdam MH, van Blokland D, van Zanten AR. Nutritional assessment of critically ill patients: validation of the modified NUTRIC score. Eur J Clin Nutr. 2018;72(3):428–35.
45. Coltman A, Peterson S, Roehl K, Roosevelt H, Sowa D. Use of 3 tools to assess nutrition risk in the intensive care unit. JPEN J Parenter Enter Nutr. 2015;39(1):28–33.
46. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically Ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enter Nutr. 2016;40(2):159–21111.
47. Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. Clin Nutr (Edinburgh, Scotland). 2008;27(1):5–15.
48. Kondrup J, Johansen N, Plum LM, Bak L, Larsen IH, Martinsen A, et al. Incidence of nutritional risk and causes of inadequate nutritional care in hospitals. Clin Nutr (Edinburgh, Scotland). 2002;21(6):461–8.
49. Dupertuis YM, Kossovsky MP, Kyle UG, Raguso CA, Genton L, Pichard C. Food intake in 1707 hospitalised patients: a prospective comprehensive hospital survey. Clin Nutr (Edinburgh, Scotland). 2003;22(2):115–23.
50. Wischmeyer PE. Tailoring nutrition therapy to illness and recovery. Crit Care (London, England). 2017;21(Suppl 3):316.
51. Rice TW, Wheeler AP, Thompson BT, Steingrub J, Hite RD, Moss M, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. JAMA. 2012;307(8):795–803.
52. Braunschweig CA, Sheean PM, Peterson SJ, Gomez Perez S, Freels S, Lateef O, et al. Intensive nutrition in acute lung injury: a clinical trial (INTACT). JPEN J Parenter Enter Nutr. 2015;39(1):13–20.
53. Arabi YM, Aldawood AS, Haddad SH, Al-Dorzi HM, Tamim HM, Jones G, et al. Permissive underfeeding or standard enteral feeding in critically Ill adults. N Engl J Med. 2015;372(25):2398–408.

54. Alberda C, Gramlich L, Jones N, Jeejeebhoy K, Day AG, Dhali- wal R, et al. The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an inter- national multi-center observational study. Intensiv Care Med. 2009;35(10):1728–37.
55. Wischmeyer PE, Hasselmann M, Kummerlen C, Kozar R, Kutso- giannis DJ, Karvellas CJ, et al. A randomized trial of supplemen- tal parenteral nutrition in underweight and overweight critically ill patients: the TOP-UP pilot trial. Crit Care (London, England). 2017;21(1):142.
56. Fuentes Padilla P, Martínez G, Vernooij RW, Urrútia G, Roqué I Figuls M, Bonfill Cosp X. Early enteral nutrition (within 48 hours) versus delayed enteral nutrition (after 48 hours) with or without supplemental parenteral nutrition in critically ill adults. Cochrane Database Syst Rev. 2019. https://doi.org/10.1002/14651 858.CD012340.pub2.
57. Yeh DD, Johnson E, Harrison T, Kaafarani HMA, Lee J, Fagen- holz P, et al. Serum levels of albumin and prealbumin do not correlate with nutrient delivery in surgical intensive care unit patients. Nutr Clin Pract. 2018;33(3):419–25.
58. Davis CJ, Sowa D, Keim KS, Kinnare K, Peterson S. The use of prealbumin and C-reactive protein for monitoring nutrition sup- port in adult patients receiving enteral nutrition in an urban medi- cal center. JPEN J Parenter Enter Nutr. 2012;36(2):197–204.
59. Bear DE, Griffith D, Puthucheary ZA. Emerging outcome meas- ures for nutrition trials in the critically ill. Curr Opin Clin Nutr Metab Care. 2018;21(6):417–22.

8

Nutrition in the surgical intensive care unit: The cost of starting low and ramping up rates

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Nutrition in Clinical Practice. 2016 Feb;31(1):86-90.

ABSTRACT

Background

Calorie/protein deficit in the surgical intensive care unit (SICU) is associated with worse clinical outcomes. It is customary to initiate enteral nutrition (EN) at a low rate and increase to goal (RAMP-UP). Increasing evidence suggests that RAMP-UP may contribute to iatrogenic malnutrition. We sought to determine what proportion of total SICU calorie/protein deficit is attributable to RAMP-UP.

Methods

This is a retrospective study of a prospectively collected registry of adult patients (N = 109) receiving at least 72 hours of EN in the SICU according to the RAMP-UP protocol (July 2012–June 2014). Subjects receiving only trophic feeds or with interrupted EN during RAMP-UP were excluded. Deficits were defined as the amount of prescribed calories/protein minus the actual amount received. RAMP-UP deficit was defined as the deficit between EN initiation and arrival at goal rate. Data included demographics, nutritional prescription/delivery, and outcomes.

Results

EN was started at a median of 34.0 hours (interquartile range [IQR], 16.5 - 53.5) after ICU admission, with a mean duration of 8.7 ± 4.3 days. The median total caloric deficit was 2185 kcal (249–4730), with 900 kcal (551–1562) attributable to RAMP-UP (41%). The protein deficit was 98.5 g (27.5–250.4), with 51.9 g (20.6–83.3) caused by RAMP-UP (53%).

Conclusion

In SICU patients initiating EN, the RAMP-UP period accounted for 41% and 53% of the overall caloric and protein deficits, respectively. Starting EN immediately at goal rate may eliminate a significant proportion of macronutrient deficit in the SICU.

INTRODUCTION

Malnutrition is prevalent in the intensive care unit (ICU), affecting as many as 40% of critically ill patients.[1] These patients are often incapable of maintaining adequate intake to meet metabolic demands, and artificial nutritional support is therefore an essential component of therapy. While the optimal amount of calorie and protein prescription is controversial[2] and likely depends on multiple factors (baseline nutritional status, degree of inflammation, severity of critical illness, etc), one fact is indisputable: once a target amount of calories/protein is decided for a patient, our ability to reliably deliver that amount is poor. Worldwide, cross-sectional studies demonstrate that, on average, ICU patients receive only about 50%–65% of prescribed nutrition, with surgical patients receiving less compared with their medical counterparts.[3,4] This gap between prescribed and actual received nutrition contributes to caloric and protein deficits, which are in turn associated with worse patient outcomes,[5-8] such as prolonged ventilator dependence, impaired immunologic function, and increased risk for infections.[9-1]

Caloric deficit can be partially attributable to interruptions in enteral nutrition (EN), commonly for intubation/extubation, bedside procedures involving the airway or gastrointestinal tract, and imaging studies.[13,14] However, the caloric and protein deficits that occur in the early phase of EN initiation have received little attention. In many ICUs, it is customary practice, when initiating EN, to begin at a low rate and gradually increase to the final goal rate (RAMP-UP).[15] The RAMP-UP practice was presumably introduced because EN initiation is sometimes poorly tolerated, and complications such as regurgitation and vomiting are believed to be associated with an increased risk of aspiration pneumonia. This RAMP-UP strategy is thus classically recommended as a prudent approach but may not be appropriate in all patients. Several recent studies have demonstrated that starting immediately at goal rate is usually well tolerated and does not increase complications.[16,17]

At present, it remains unclear to what extent the RAMP-UP period contributes to overall caloric deficit in the critically ill patient. The aim of this study was to determine what proportion of total cumulative calorie/protein deficit in surgical ICU (SICU) patients receiving EN is caused by the RAMP-UP practice. We hypothesized that the RAMP-UP period was a major contributor to overall cumulative macronutrient deficit.

SUBJECTS AND METHODS

This is a retrospective analysis of a prospectively collected registry. From July 2012 to June 2014, we enrolled adult SICU patients initiating EN and who received at least 72 hours of EN in the SICU. EN was delivered according to the local standards of care,

starting at 10 mL/h and increasing by 10 mL/h every 2 hours as tolerated (RAMP-UP) to the goal rate. Subjects who were kept deliberately at low rates ("trophic feeds") or who had extended interruptions (>24 hours) after EN initiation during the RAMP-UP period were excluded. Caloric/protein deficit was defined as the difference between the amount of prescribed calories and the actual amount of calories received. Cumulative caloric/protein deficit was calculated as the sum of all daily deficits, starting from EN initiation until progression to oral intake, ICU discharge, or death. The RAMP-UP deficit was defined as the caloric deficit accrued from EN initiation until arrival at goal rate. Subsequent interruptions (after at least 24 hours at goal rate) were not included in the RAMP-UP deficit. If the EN rate was decreased and again gradually increased to goal, only the initial RAMP-UP period was included in the RAMP-UP deficit. Data collected included age, sex, APACHE II (Acute Physiology and Chronic Health Evaluation II) score, Deyo-Charlson Comorbidity Index, Injury Severity Score, weight, body mass index, ICU admission diagnosis, presence/absence of gastro- intestinal surgery, nutrition prescription and delivery, ICU length of stay, 28-day ventilator-free days, hospital length of stay, and in-hospital mortality. Institutional Review Board approval was obtained, and the requirement for informed consent was waived.

Statistical Analysis

Data analysis was performed with SPSS 22.0 (SPSS Inc, Chicago, IL). Normally distributed data were expressed as mean ± SD, and nonnormally distributed data were expressed as median (interquartile range).

RESULTS

A total of 109 patients met inclusion criteria. The mean age was 60.1 ± 18.4 years, and 71.6% of the patients were men. Average body mass index was 27.8 ± 7.0, and the median Deyo-Charlson Comorbidity Index was 2.0 (0–4). The median APACHE II score was 14.0 (9.0–20.0), and the median Injury Severity Score was 26.0 (19.0–35.0) in injured patients (Table 1).

The median time of start of EN was 34.0 hours (16.5–53.5 hours) after ICU admission; 68.8% of the patients were started on EN within 48 hours after ICU admission. The mean duration of EN was 8.7 ± 4.3 days. The median total cumulative caloric deficit per patient was 2185 kcal (1248.8–4729.5), of which 900 kcal (550.6–1561.7) accumulated during the RAMP-UP period (41%). Figure 1 is a histogram displaying the distribution of subjects and the number of days elapsing from EN initiation until achievement of goal rate. During the ICU stay, the overall protein deficit was 98.5 g (27.5–250.4), of which 51.9 g (20.6–83.3) accumulated during the RAMP-UP period (53%). ICU and hospital length

of stay, 28-day ventilator-free days, 30-day readmission (in survivors), and mortality are summarized in Table 2.

Table 1. Baseline Demographics of Patients Admitted to the SICU.[a]

Characteristic	Patients (N = 109)
Age, y	60.1 ± 18.4
Male	78 (71.6)
APACHE II score	14.0 (9.0–20.0)
Deyo-Charlson Comorbidity Index	2.0 (0.0–4.0)
Injury Severity Score	26.0 (19.0–35.0)
Weight, kg	70.7 ± 14.0
Body mass index	27.8 ± 7.0
Reason for SICU admission	
Trauma	35 (32.1)
Emergency surgery	16 (14.7)
Elective surgery	23 (21.1)
Nonoperative	35 (32.1)
Gastrointestinal surgery	10 (9.1)

APACHE, Acute Physiology and Chronic Health Evaluation; SICU, surgical intensive care unit.
[a]Values presented as mean ± SD, No. (%), or median (interquartile range).

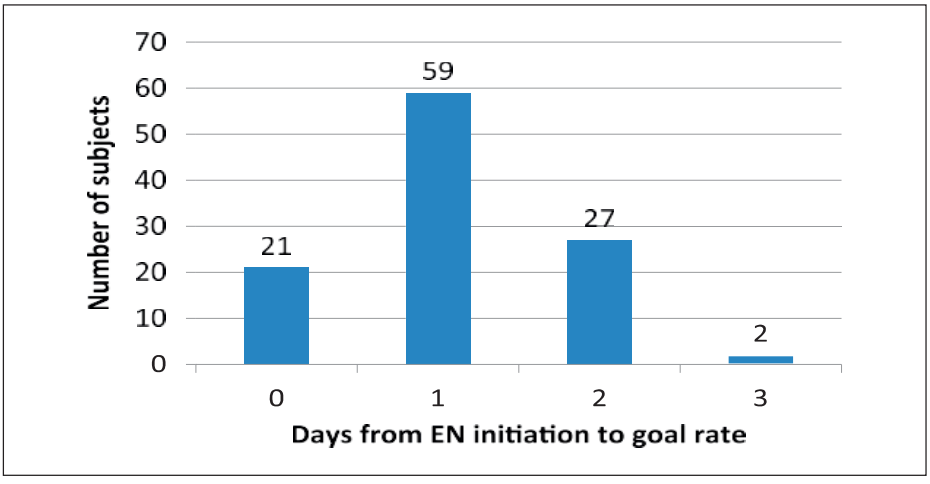

Figure 1. Histogram showing number of days from enteral nutrition (EN) initiation until achievement of goal rate.

Table 2. Nutrition and Clinical Outcomes of Patients Receiving EN in the Surgical ICU.[a]

Outcomes	Patients (n = 109)
Hours from ICU admission to EN initiation	34.0 (16.5–53.5
EN started, h	
<48	75 (68.8)
48–72	17 (15.6)
72–96	4 (3.7)
>96	13 (11.9)
Days on EN	8.7 ± 4.3
Parenteral nutrition	6 (5.5)
Total cumulative deficit	
Caloric, kcal	2185.4 (1248.8–4729.5)
Protein, g	98.5(27.5–250.4)
RAMP-UP deficit	
Caloric, kcal	900.0 (550.6–1561.7)
Protein, g	51.9 (20.6–83.3)
Length of stay, d	
ICU	11.0 (7.0–21.0)
Hospital	22.0 (15.0–33.0)
28-d ventilator-free days	20.0 (14.0–25.0)
30-d readmissions in survivors	17 (17.7)
Mortality	18 (16.5)

EN, enteral nutrition; ICU, intensive care unit; RAMP-UP, initiate EN at a low rate and gradually increase to goal.

[a]Values presented as mean ± SD, No. (%), or median (interquartile range).

DISCUSSION

In this study, we demonstrate that caloric and protein deficits occurring during the initial RAMP-UP period accounted for 41% of the overall cumulative caloric deficit and 53% of the cumulative protein deficit of the ICU patient. As such, they represent a major contributor to overall deficits and are an excellent potential target area for quality improvement.

The optimal amount and starting rate of EN for ICU patients are controversial, and there are some who question the need to provide any nutrition early in the course of illness.[18] Indeed, some observational studies have concluded that near-target nutrient delivery may be associated with worse clinical outcomes.[19,20] However, these conclusions may be confounded by the statistical methods used and the patient inclusion criteria. For example, healthy patients with lower severity of critical illness may have short ICU stays (<3 days) and generally do and proteins needs) as compared with patients who

received standard nutrition support care who were diagnosed with acute lung injury. These findings are concerning and need to be replicated in additional multicenter trials.

Several investigators have demonstrated the safety of higher, faster EN advancement or starting EN immediately at goal rate. In a comparison of 5 ICUs in the United Kingdom, Adamet al. did not report any difference in gastrointestinal intolerance despite varying RAMP-UPpractices.[23] In a randomized study involving brain-injured trauma patients, Taylor et al. usedan enhanced EN protocol (which included starting immediately at goal rate) to increase the amount of calories delivered to the intervention group. There was no increase in the incidence of aspiration. In that trial, the enhanced EN protocol also appeared to reduce the risk of major infectious complications and postinjury inflammatory responses.[17] Interestingly, the same EDEN trial that concluded no difference between initial trophic versus "full" EN also demonstrated the safety of a very short RAMP-UP period (<18 hours). There was no difference in the incidence of diarrhea, aspiration, or abdominal distention or cramping. While there was increased regurgitation, vomiting, and elevated gastric residual volumes, there was no difference in clinically important outcomes, such as pneumonia, ventilator-free days, and mortality.[22,24,25] Heyland et al. proposed an even more aggressive feeding protocol, the "Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol (PEP uP protocol)." This protocol is based on 4 pillars: (1) EN is initiated at goal rate; (2) a 24-hour volume goal is used (as opposed to hourly rate goal), and nurses are empowered to provide compensatory nutrition in case of EN interruption; (3) protein supplements are prescribed separately from tube feedings to prevent protein deficit; and (4) motility agents are prescribed prophylactically.[16] Implementation of the PEP-uP protocol has been shown to improve the delivery of EN.[26] However, full compliance with all components of the bundle may be difficult to achieve. As with any bundle, it may be difficult to determine the relative contributions of the bundle elements in case of successful implementation and improved clinical outcomes. Our study is an attempt to quantify the contribution to nutrient delivery of 1 element of the PEP-uP protocol: starting immediately at goal rate.

There are a few limitations to our study. This was a single- center study at an urban academic hospital with a relatively small sample size. Our collection of nutrition data ended once the patient progressed from artificially delivered EN (tube feeds) to oral intake, and we did not attempt to quantify the percentage of oral intake. As such, it is possible that the true caloric deficit is larger than what we have calculated and our RAMP-UP deficit may be proportionally smaller. Another fac- tor to consider is that we did not begin counting calorie or protein deficits until the patient actually started receiving EN, a median of 34 hours after ICU admission. We acknowledge that the patient begins accumulating macronutrient deficits from the moment of ICU admission. However, initiation of tube feeds is often deferred for reasons of hemodynamic instability requiring ongoing resuscitation or impending intubation/extubation. It is our belief that

aggressively feeding EN is not within the standard of care in these situations and may, in fact, be harmful overall to patient outcome.

Therefore, we did not count macronutrient deficits accumulating prior to the decision to initiate EN, because short of starting every patient routinely on parenteral nutrition, there is little that can be done to eliminate calorie/protein deficit in this very early stage. Second, we did not include patients who had extended (>24 hours) interruptions in their EN during the RAMP-UP period. These cases are infrequent, and it is possible that such extended interruptions have a clinically justified reason (eg, a newly discovered anastomotic leak or massive upper gastrointestinal bleeding requiring endoscopy) and, therefore, nothing can be done to eliminate the calorie/protein deficit. Given our study design (retrospective analysis of a registry), we were unable to deter- mine the clinical rationale and, as such, felt it best to exclude those patients. Furthermore, the main focus of our study was to quantify the deficits that accumulate when EN is being delivered and the intention (presumably) is to provide adequate nutrition. It is possible that shorter-duration interruptions occurred, which we were not able to discern on the daily caloric deficits. The fact that some patients took longer to achieve their goal rates suggests that either interruptions did occur or rate increase was performed even slower than our stated proto- col. Because this is a retrospective analysis of prospective data, we cannot determine a cause-and-effect relationship. However, the primary aim of this study was not to draw associations or establish causality but rather to provide descriptive characteristics of a practice (RAMP-UP) that we believe is unsupported by existing literature. Despite these limitations, we feel our study is informative because it provides quantitative evidence that the RAMP-UP practice contributes to a significant percentage of overall ICU macronutrient deficit. Objective reexamination of the benefits and potential harms of this practice is warranted.

CONCLUSION

The initial period (RAMP-UP) accounted for 41% of the overall caloric deficit and 53% of the overall protein deficit in SICU patients. Starting EN immediately at goal rate may eliminate a significant proportion of macronutrient deficit in the SICU.

REFERENCES

1. Giner M, Laviano A, Meguid MM, Gleason JR. In 1995 a correlation between malnutrition and poor outcome in critically ill patients still exists. Nutrition. 1996;12(1):23-29.
2. Stapleton RD, Jones N, Heyland DK. Feeding critically ill patients: what is the optimal amount of energy? Crit Care Med. 2007;35(9):S535-S540.
3. Drover JW, Cahill NE, Kutsogiannis J, et al. Nutrition therapy for the crit- ically ill surgical patient: we need to do better! JPEN J Parenter Enteral Nutr. 2010;34(6):644-652.
4. Hise ME, Halterman K, Gajewski BJ, Parkhurst M, Moncure M, Brown JC. Feeding practices of severely ill intensive care unit patients: an evaluation of energy sources and clinical outcomes. J Am Diet Assoc. 2007;107(3):458-465.
5. Dvir D, Cohen J, Singer P. Computerized energy balance and com- plications in critically ill patients: an observational study. Clin Nutr. 2006;25(1):37-44.
6. Elke G, Wang M, Weiler N, Day AG, Heyland DK. Close to recom- mended caloric and protein intake by enteral nutrition is associated with better clinical outcome of critically ill septic patients: secondary analysis of a large international nutrition database. Crit Care. 2014;18(1):R29.
7. Tsai JR, Chang WT, Sheu CC, et al. Inadequate energy delivery during early critical illness correlates with increased risk of mortality in patients who sur- vive at least seven days: a retrospective study. Clin Nutr. 2011;30(2):209-214.
8. Weijs PJ, Stapel SN, de Groot SD, et al. Optimal protein and energy nutri- tion decreases mortality in mechanically ventilated, critically ill patients: a prospective observational cohort study. JPEN J Parenter Enteral Nutr. 2012;36(1):60-68.
9. Faisy C, Lerolle N, Dachraoui F, et al. Impact of energy deficit calculated by a predictive method on outcome in medical patients requiring pro- longed acute mechanical ventilation. Br J Nutr. 2009;101(7):1079-1087.
10. Faisy C, Candela Llerena M, Savalle M, Mainardi JL, Fagon JY. Early ICU energy deficit is a risk factor for Staphylococcus aureus ventilator- associated pneumonia. Chest. 2011;140(5):1254-1260.
11. Rubinson L, Diette GB, Song X, Brower RG, Krishnan JA. Low caloric intake is associated with nosocomial bloodstream infections in patients in the medical intensive care unit. Crit Care Med. 2004;32(2):350-357.
12. Heyland DK, Stephens KE, Day AG, McClave SA. The success of enteral nutrition and ICU-acquired infections: a multicenter observational study. Clin Nutr. 2011;30(2):148-155.
13. McClave SA, Sexton LK, Spain DA, et al. Enteral tube feeding in the intensive care unit: factors impeding adequate delivery. Crit Care Med. 1999;27:1252-1256.
14. Peev MP, Yeh DD, Quraishi SA, et al. Causes and consequences of inter- rupted enteral nutrition: a prospective observational study in critically ill surgical patients. JPEN J Parenter Enteral Nutr. 2015;39(1):21-27.
15. Miller KR, Kiraly LN, Lowen CC, Martindale RG, McClave SA. "CAN WE FEED?" A mnemonic to merge nutrition and intensive care assessment of the critically ill patient. JPEN J Parenter Enteral Nutr. 2011;35(5):643-659.
16. Heyland DK, Cahill NE, Dhaliwal R, et al. Enhanced protein-energy pro- vision via the enteral route in critically ill patients: a single center feasibil- ity trial of the PEP uP protocol. Crit Care. 2010;14(2):R78.
17. Taylor SJ, Fettes SB, Jewkes C, Nelson RJ. Prospective, randomized, con- trolled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. Crit Care Med. 1999;27(11):2525-2531.

18. Koretz RL, Avenell A, Lipman TO, Braunschweig CL, Milne AC. Does enteral nutrition affect clinical outcome? A systematic review of the ran- domized trials. Am J Gastroenterol. 2007;102(2):412-429.
19. Krishnan JA, Parce PB, Martinez A, Diette GB, Brower RG. Caloric intake in medical ICU patients: consistency of care with guidelines and relationship to clinical outcomes. Chest. 2003;124(1):297-305.
20. Arabi YM, Haddad SH, Tamim HM, et al. Near-target caloric intake in critically ill medical-surgical patients is associated with adverse outcomes. JPEN J Parenter Enteral Nutr. 2010;34(3):280-288.
21. Heyland DK, Cahill N, Day AG. Optimal amount of calories for criti- cally ill patients: depends on how you slice the cake! Crit Care Med. 2011;39(12):2619-2626.
22. Rice TW, Wheeler AP, Thompson BT, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. JAMA. 2012;307(8):795-803.
23. Adam S, Batson S. A study of problems associated with the delivery of enteral feed in critically ill patients in five ICUs in the UK. Intensive Care Med. 1997;23(3):261-266.
24. Needham DM, Dinglas VD, Bienvenu OJ, et al. One year outcomes in patients with acute lung injury randomised to initial trophic or full enteral feeding: prospective follow-up of EDEN randomised trial. BMJ. 2013;346:f1532.
25. Rice TW, Mogan S, Hays MA, Bernard GR, Jensen GL, Wheeler AP. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. Crit Care Med. 2011;39(5):967-974.
26. Heyland DK, Murch L, Cahill N, et al. Enhanced protein-energy provi- sion via the enteral route feeding protocol in critically ill patients: results of a cluster randomized trial. Crit Care Med. 2013;41(12):2743-2753.

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The malnutrition in polytrauma patients (MaPP) study: Research protocol

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Nutrition and Health. 2019 Dec;25(4):291-301.

ABSTRACT

Background

Polytrauma patients are at risk of considerable harm from malnutrition due to the metabolic response to trauma. However, there is little knowledge of (the risk of) malnutrition and its consequences in these patients. Recognition of suboptimally nourished polytrauma patients and their nutritional needs is crucial to prevent complications and optimize their clinical outcomes.

Aim

The primary objective is to investigate whether polytrauma patients admitted to the Intensive Care Unit (ICU) who have or develop malnutrition have a higher complication rate than patients who are and remain well nourished. Secondary objectives are to determine the prevalence of pre-existent and in-hospital acquired malnutrition in these patients, to assess the association between malnutrition and long-term outcomes, and to determine the association between serum biomarkers (albumin and pre-albumin) and malnutrition.

Methods

This international observational prospective cohort study will be performed at three Level-1 trauma centers in the United States and two Level-1 centers in the Netherlands. Adult polytrauma patients (Injury Severity Score 16) admitted to the ICU of one of the participating centers directly from the Emergency Department are eligible for inclusion. Nutritional status and risk of malnutrition will be assessed using the Subjective Global Assessment (SGA) scale and Nutritional Risk in Critically Ill (NUTRIC) score, respectively. Nutritional intake, biomarkers and complications will be collected daily. Patients will be followed up to one year after discharge for long-term outcomes.

Conclusion

This international prospective cohort study aims to gain more insight into the effect and consequences of malnutrition in polytrauma patients admitted to the ICU.

INTRODUCTION

Malnutrition is widespread among hospitalized patients, with 20-40% of patients affected by malnutrition depending on the population, setting, and criteria used. This percentage is estimated to be even higher in the critically ill population.[1-4] Although there is still debate about the exact definition, malnutrition is currently defined as an imbalance in nutrition due to inadequate nutrient intake, or the inability to use or absorb ingested nutrients, resulting in an altered body composition (decreased fat-free mass and a decreased body cell mass) and diminished body function (e.g. muscular performance, organ function, body composition, and functional capacity).[5-7]

Malnutrition in hospitalized patients is a risk factor for increased morbidity and mortality.[1, 8-10] Patients with malnutrition suffer from decreased functional capabilities and impaired quality of life during their hospital stay.[11] Because of its negative effect on patient recovery and outcome, malnutrition is also associated with increased hospital costs: Annual costs of disease-associated malnutrition in the United States was estimated to be $156.7 billion.[12]

In a Dutch study, roughly 6% of admitted trauma patients were at risk for malnutrition.[10] Severely injured patients ('polytrauma patients') are at even greater risk for harm from malnutrition due to a trauma-related inflammatory ('stress') response. Because of the stress response following traumatic injuries, polytrauma patients often endure an altered metabolic state in order to preserve energy for vital tissues.[13-16] This state is associated with catabolic processes, tissue breakdown, muscle wasting and anorexia. [17] The more severe the injuries, the more severe the stress response. This renders polytrauma patients susceptible to complications such as infections, gastrointestinal dysfunction, acute kidney injury and multiple organ dysfunction syndrome. [9] However, there is little factual up-to-date knowledge about the consequences of malnutrition in the polytrauma patient population.

Currently, the diagnosis of malnutrition is often based on clinical questionnaires and measurement of body parameters ('anthropomorphic measurements'); however, both methods have proven to be challenging in polytrauma patients. The use of anthropomorphic measurements is limited due to edema and/or history taking is not possible in sedated or mechanically ventilated patients. There is increasing interest in the use of biomarkers to assess nutrition status, but their predictive value in polytrauma patients remains questionable.[18]

The overall aim of this study is to obtain insight into the prevalence, incidence and impact of malnutrition in polytrauma patients in the Intensive Care Unit (ICU). The primary objective is to investigate whether polytrauma patients (Injury Severity Score [ISS] ≥ 16) admitted to the ICU, who have or develop malnutrition during hospital admission, have a higher complication rate than polytrauma patients, who are and remain well-nourished

during hospital admission. Our primary hypothesis is that polytrauma patients who are and remain well-nourished have less complications compared to patients that are malnourished, and to patients that have a decline in nutritional status.

Secondary objectives are to determine the prevalence of patients with (a risk of) malnutrition on admission, and the incidence of patients that develop malnutrition on the ICU or during their stay in the hospital. Furthermore, we aim to assess whether calorie/protein deficiencies during ICU and hospital stay are associated with malnutrition and subsequently with worse clinical outcomes, and to assess the predictive value of biomarkers in the development of malnutrition during ICU admission and hospital admission. Also, we intend to determine the relationship between malnutrition and long-term outcomes, if any.

METHODS

For this prospective study a template for clinical research provided by the Dutch Central Committee on Research Involving Human Subjects Committee (CCMO) was used. This template incorporates all the checkpoints provided by the SPIRIT guidelines. [19]

Design and setting

This observational prospective cohort study will be performed at three Level-1 trauma centers in the United States (Massachusetts General Hospital and Brigham and Women's Hospital in Boston, and Ryder Trauma Center in Miami) and two Level-1 trauma centers in the Netherlands (Leiden University Medical Center in. Leiden and Haaglanden Medical Center Westeinde in The Hague).

Study Population

Inclusion criteria

Adult (≥18 years) polytrauma patients (Injury Severity Score [ISS] ≥ 16), with a blunt trauma mechanism, admitted to the ICU of one of the enrolling Level-1 trauma centers within 6 hours after trauma and for a period longer than 48 hours, are eligible for inclusion. Patients will be excluded if they are transferred from another hospital to the participating center. Patients with burn wounds or penetrating traumatic injuries will be excluded.

Sample size calculation

In the study by Goiburu et al. [20], 40% of the ICU trauma patient population was found to have malnutrition according to the Subjective Global Assessment [SGA] -tool. The complication rate in the well-nourished group was 50%, and 71% in the malnutrition

group. To determine such a difference in complication rate in our study with alpha of 0.05 and power of 0.80 (beta = 0.20), 195 patients are needed (117 in the well-nourished group and 78 in the malnutrition group). Our goal is to include 140 patients in both countries, thereby meeting our threshold to answer our primary aim.

Recruitment

Newly ICU-admitted trauma patients will be screened on inclusion criteria upon admission by the investigators in the participating hospitals. In case of uncertainty about presence of polytrauma (ISS ≥ 16), the attending trauma surgeon is consulted.

Eligible patients will be asked to provide written informed consent (IC) for study participation. If the patient is unable to do so (e.g. due to unconsciousness), a legal representative will be asked IC. When a legal representative has provided IC and the patient is able to give the IC him- or herself during the study, the patient will be asked to confirm the consent. If the patient does not have a legal representative data will be collected prospectively and the patient will be asked for IC when he is able to do so. If the patient does not want to participate in the study his or her data will be deleted from the electronic database. The patient and his/her legal representative can withdraw consent and leave the study at any time.

Study parameters

Demographic data and vital signs

The following study parameters will be acquired from the electronic patient files: age, sex, medical history, usual body weight (kg), height, actual body weight (ABW), body mass index (BMI), recent weight loss and the mechanism of injury on admission. Vital signs that are collected on admission are systolic blood pressure (SBP), heart rate (HR) and respiratory rate (RR).

Severity of disease classifications

Abbreviated Injury Scale (AIS) and Injury Severity Score (ISS)

The AIS (update 2008) score is a consensus-derived scoring system, that classifies injury severity on a 6-point scale and according to the anatomical body regions. [21] The overall severity of (multiple) injuries is expressed by the ISS. [22] The ISS is calculated as the sum of squares of highest AIS codes in the three most severely injured body regions. The ISS is an internationally recognized scoring system in trauma patients and correlates with mortality and morbidity. [22]

Acute Physiology and Chronic Health Evaluation II (APACHE II) score

The APACHE II score estimates ICU mortality based on the worst laboratory values and clinical parameters in the first 24 hours of ICU admission. The higher the APACHE II score

the higher the mortality risk. [23] The APACHE II score has been validated in different patient populations including the critically injured patient in whom it has shown accurate predictive value with a specificity and sensitivity of 94.6 and 79.2% respectively. [24, 25] The APACHE II score will be calculated within 24 hours of ICU admission. The full APACHE II score is shown in Appendix I[26].

Sequential Organ Failure Assessment (SOFA) score

The SOFA score is a tool used to track a patient's clinical status during ICU admission. Based on the score for each of the six variables (respiratory, hepatic, coagulation, renal, cardiovascular and neurological) the SOFA score is calculated. Both the mean SOFA score and the total maximum SOFA score on the ICU are predictors of outcome. [27] The SOFA score has been validated for the critically ill injured patient and a higher score is associated with a longer ICU LOS. [28] The SOFA score will be calculated daily during ICU admission (Appendix II)[29].

Nutritional status parameters

Malnutrition: Subjective Global Assessment (SGA) and Patient Generated Subjective Global Assessment (PG-SGA)

The SGA score is recommended as assessment tool of nutritional status in the critically ill. [5, 30-33] The SGA is validated for the acute hospital setting, surgical patients and patients admitted to the ICU requiring mechanical ventilation. [34-36] The PG-SGA was originally developed to assess the nutritional status of oncology patients, however it has been validated for diverse groups of patients, including surgical patients, since then and it has been translated into many languages. [37-39]

The SGA and PG-SGA scores are based on weight change (past 6 months and 2 weeks), adequate dietary intake change, gastrointestinal symptoms (less appetite, nausea, vomiting, diarrhea) and functional capacity (dysfunction, bedridden, difficulty with normal activities). Both scales include a physical examination on subcutaneous fat loss (eyes, triceps, biceps) and muscle wasting (e.g. clavicle, knee, shoulder and quadriceps). [34]

The SGA and PG-SGA scale range from 1 to 7. Patients are classified as A: well-nourished (scores 6-7), B: mild/moderate malnutrition (scores 3-5) and C: severe malnutrition (scores 1-2). Following general consensus, patients will be divided into two categories: Well-nourished (A, scores 6-7) and malnutrition (B and C, scores 1-5).

After inclusion in the study, the SGA scale will be scored within 24 hours after ICU admission by a trained dietician, nurse or member of the research team to determine pre-existing malnutrition. The SGA will be assessed every 5 days at the ICU and on the day of discharge from the ICU to determine in-ICU developed malnutrition. At the hospital ward the nutritional status will be assessed every 7 days to determine in-hospital developed malnutrition. The nutritional status will be assessed using the PG-SGA on

the hospital discharge day, and 3, 6, 9, 12 months after hospital discharge. The full SGA questionnaire is displayed in Appendix III[40]. The PG-SGA can be found on the website of the PG-SGA/Pt-Global Platform.[41]

Risk of malnutrition on admission: Nutrition Risk in the Critically Ill Score (NUTRIC score).

The NUTRIC is designed and recommended for nutritional risk assessment in critically ill adult patients. [42, 43] The NUTRIC score consists of six items collected from the electronic patient file: age, APACHE II score, number of comorbidities, Sequential Organ Failure Assessment (SOFA) score, days in-hospital prior to ICU admission and interleukin-6 (IL-6). The APACHE II score [26] is an item of the NUTRIC score, and is computed based on the following parameters: age, temperature, acute renal failure, history of severe organ failure (or immune-compromised), mean arterial pressure, pH, heart rate, respiratory rate, creatinine, hematocrit, potassium, sodium, and white blood cell count. The SOFA score [27] is computed based on the parameters PaO_2, FiO_2, bilirubin, creatinine, platelet count, hypotension level and GCS.

The NUTRIC scale ranges from 1 to 10, and a score ≥ 6 (if IL-6 is available) is regarded as high risk for malnutrition. (The items of) the NUTRIC score are all strongly correlated with mortality rate, mechanical ventilation duration and LOS. [42, 44] In this study, the NUTRIC score will be determined without IL-6. The NUTRIC scale without IL-6 available is as reliable (≥ 5 indicates high risk). [42]

After inclusion, the Nutrition Risk in the Critically Ill (NUTRIC) scale will be assessed within 24 hours after ICU admission by a dietitian, trained to score the questionnaire. The NUTRIC-score questionnaire is displayed in Appendix IV[42], the criteria for the SOFA-score in Appendix II and the criteria for the APACHE II score in Appendix I.

Nutritional needs and support

Resting energy expenditure

The energy expenditure is the amount of energy used for the basal metabolic processes, the thermic effect of food, e.g. the energy required to digest and absorb food, and the energy used for physical activity. Indirect calorimetry, which is considered clinical golden standard to measure resting energy expenditure [45], is not available in all participating hospitals. Therefore, the Harris-Benedict equation will be used to measure resting energy expenditure, which is a well-validated alternative, although it is known that it overestimates resting energy expenditure. [46-48] The following equation is used for women: 447,593 + (9,247 X weight) + (3,098 X height) - (4,33 X age). The equation for men is: *88,362 + (13,397 X weight) + (4,799 X height) - (5,677 X age)*. The resting energy expenditure will be assessed daily during hospital stay.

Nutritional support

During stay at the ICU, a careful record of caloric and protein prescription and intake is recorded in the electronic patient file of the patients staying at the ICU in the participating centers. In addition, the amount of propofol given is collected daily in the electronic patient file in the ICU. Propofol is a lipid-soluble emulsion often used in the ICU to provide sedation for patients on mechanical ventilation. This propofol lipid emulsion contains 1.1 kcal/ml. Although, on average the total contribution of propofol to the total calories received will not be clinically significant, if the continuous infusion rate is above 20ml/hour it has significant caloric value and can even contribute to overfeeding. [49] Calorie and protein deficiency will be computed as the calories and proteins delivered minus the calories and proteins prescribed. Both deficiencies are calculated daily from day 0 to ICU discharge. During hospital admission, type of nutritional support will also be registered as enteral nutrition, parenteral nutrition or oral diet.

Biomarkers of nutritional status

Albumin

Albumin is the most abundant plasma protein and is vital for maintaining the colloidal oncotic pressure within the vasculature. In clinical practice albumin is often considered an important factor in the nutritional status assessment. [50] However, the long half-life of roughly 20 days and the influence of systemic inflammation and acute phase proteins on albumin levels, makes the use of albumin as nutritional status marker in polytrauma patients possibly inaccurate. [18, 51] Our goal is to assess the relationship between albumin and nutritional status in polytrauma patients, therefore it will be assessed daily in the ICU and weekly in the ward.

Pre-albumin (PAB)

PAB is suitable as a malnutrition marker due to its shorter half-life of 2 days and its small total body pool. [52, 53] Research suggests that PAB levels increase during the course of adequate nutrition support. [53-57] In postoperative patients, PAB showed to be a better indicator of nutrition status than albumin. [54] Serial PAB measurements will be taken daily in ICU patients to assess the relationship with malnutrition and weekly in the ward. [53] An additional 5ml blood will be collected during standard blood draws (to minimize risks and additional discomfort) in a separate blood collection container to measure pre-albumin.

C-reactive protein (CRP)

CRP is a typical inflammation marker and is inversely related to pre-albumin. [53, 58] In traumatic brain injury patients, a shorter hospital LOS and a more aggressive enteral nutrition therapy are both associated with low CRP (in proportion to albumin). [59] This

inflammation marker can be used to determine if the changes in malnutrition (albumin and prealbumin) is caused by a change in inflammation response, or by a change in nutritional status. [52] CRP will be measured daily in the ICU and weekly at the ward.

White blood cell (WBC) count and differential count

WBC are a heterogeneous group of cells that play an important role in phagocytosis and immunity. The WBC count and differential count are used to assess the body's reaction to certain conditions such as inflammation, infection, but also to traumatic injuries. [60] In addition to CRP the WBC and differential count can be used to assess if the change in pre-albumin and albumin are due to changes in nutritional status or inflammatory status. This marker will be measured daily.

Primary outcome

Data will be collected prospectively from the electronic patient files and with questionnaires (see Table 1 and Table 2 for measurement moments). The primary outcome is the complication rate, calculated as the proportion of patients with one or more of the following complications which will be recorded from the electronic patient files during hospital stay and through surveys during one year after hospital discharge. Complications will be recorded from the electronic patient files:

- Systemic complications, such as sepsis (i.e. life-threatening organ dysfunction induced by a dysregulated response to infection [61]), multiple organ failure (MOF; i.e. potentially reversible and progressive physiologic dysfunction involving two or more organ systems, induced by various acute insults [62]), and acute respiratory distress syndrome (ARDS; acute, diffuse, bilateral inflammatory lung injury, not fully explained by fluid overload or cardiac failure [63])
- Surgery-related complications, such as anastomotic leak, abscess, (re)bleeding, and wound infection (i.e. deep, superficial, or organ/space surgical site infection within 30 days postoperatively [64])
- Acute kidney injury for which continuous renal replacement therapy is needed (AKI-CRRT). [65]
- Pneumonia
- Urinary tract infection
- Venous thromboembolisms, such as deep venous thrombosis and pulmonary embolism
- Fracture-related complications, such as compartment syndrome, thromboembolic disease, fat embolism syndrome, reoperation (other than due to non-union or malunion)
- In-hospital mortality

Table 1. Overview of study measurements during admission in the ICU department.

	< 24h after ICU admission	Daily at ICU	Every 5 days at the ICU	ICU discharge day
Baseline characteristics*	X			
Vital signs on admission				
SBP, HR, RR	**X**			
Weight	X			
NUTRIC score▸				
APACHE II				
SOFA	X			
Number of comorbidities				
Days in hospital before ICU admission				
APACHE II score				
A-a Gradient or PaO_2				
Potassium				
Sodium				
Creatinine				
Hematocrit	X			
WBC count				
GCS				
HR				
Mean arterial pressure				
Temperature				
RR				
SOFA score				
PaO_2				
FiO_2				
Bilirubin	X	X		X
Coagulation platelets				
Creatinine				
GCS				
Level of hypotension				
SGA scale▸				
Weight (change)				
Dietary intake				
Gastrointestinal symptoms				
Functional capacity	X		X	X
Comorbidities				
Subcutaneous fat loss				
Muscle wasting				
Edema				
Biomarkers				
Albumin				
Pre-albumin▸	X	X		X
CRP				
WBC count				
Differential count				
Resting energy expenditure▸	X	X		X
Harris-benedict calculation				

Table 1. Overview of study measurements during admission in the ICU department. (continued)

	< 24h after ICU admission	Daily at ICU	Every 5 days at the ICU	ICU discharge day
Energy intake and deficiency				
Calories prescribed (kcal/kg) *Calories received (kcal/kg)* *Protein prescribed (g/kg)* *Protein received (g/kg)* *Dose propofol received (ml)*	X	X		X
Type nutritional support				
Parenteral nutrition *Enteral nutrition* *Oral diet*	X	X		X
Complications**	X	X		X
Other study parameters***				X

▸ Parameters collected not part of standard clinical practice

* Age, sex, medical history, weight, height, ABW, BMI, weight loss, mechanism of injury on admission, AIS codes, ISS score, GCS, RTS, CCI

** Systemic complications (Sepsis, MOF, ARDS), surgery related complications (surgical site infection deep and superficial, abscess, (re)bleeding), wound infection, pneumonia, urinary tract infection deep venous thrombosis, pulmonary embolism, fracture-related complications (compartment syndrome, thromboembolic disease, fat embolism syndrome, reoperation rates due to non-union or mal-union), In-hospital mortality

*** ICU LOS, readiness for ICU discharge, hospital- LOS, readiness for hospital discharge, ventilator-free days, surgery, reoperation rates due to other reasons than non-union or mal-union, discharge disposition, readmission rates, 30-day mortality

Secondary outcomes

Secondary outcome parameters include ICU LOS until ready for discharge (i.e. judged clinical ready for discharge, but remains on the ICU beyond the ready for ICU discharge date), ICU LOS, hospital LOS until fit for hospital discharge (i.e. judged clinical ready for discharge, but remains on the ward beyond the ready for hospital discharge date), hospital LOS, ventilator-free days [66], surgery (if yes, the number of surgical procedures, elective or emergency procedure, and type of operation) and discharge disposition. Furthermore, ICU mortality, hospital mortality and 1-year mortality will be collected.

Long-term outcomes

Glasgow outcome scale extended (GOSE)

The GOSE is a global scale used to measure general functional outcome, ranging from death to good outcomes. [67, 68] Based on a structured interview the patient is classified in a specific category. It has been validated in patients with traumatic brain injury and has been shown to correlate well with the Glasgow Coma Scale. [69] The GOSE will be measured at discharge from the hospital and then 3 monthly until 1 year. The GOSE structured interview is shown in Appendix V.[70]

Table 2. Overview of study measurements after ICU discharge.

	Daily after ICU discharge during hospital stay	Weekly after ICU discharge during hospital stay	Hospital discharge	Every three months after hospital discharge up to one year after hospital admission (Survey)
SGA▸				
Weight (change)				
Dietary intake				
Gastrointestinal symptoms				
Functional capacity		X	X	
Comorbidities				
Subcutaneous fat loss				
Muscle wasting				
Fluid status				
PG-SGA▸			X	X
See SGA items				
Weight	X			
Biomarkers				
Albumin				
Pre-albumin▸		X		
CRP				
WBC count				
Differential count				
Resting energy expenditure▸	X			
Harris-benedict calculation				
Protein/caloric deficiency				
Calories prescribed (kcal/kg)				
Calories received (kcal/kg)	X			
Protein prescribed (g/kg)				
Protein received (g/kg)				
Type nutritional support				
Parenteral nutrition	X			
Enteral nutrition				
Oral diet				
Complications*	X		X	X
Other study parameters**	X		X	
Functional outcome and health related quality of life▸			X	X
GOSE				
EQ-5D				

▸ Parameters collected not part of standard clinical practice

*Systemic complications (Sepsis, SIRS, MOF, ARDS), surgery related complications (surgical site infection deep and superficial, abscess, (re)bleeding), wound infection, pneumonia, urinary tract infection deep venous thrombosis, pulmonary embolism, fracture-related complications (compartment syndrome, thromboembolic disease, fat embolism syndrome, reoperation rates due to non-union or mal-union), In-hospital mortality

** ICU LOS, readiness for ICU discharger, hospital- LOS, readiness for hospital discharge, ventilator-free days, surgery, reoperation rates due to other reasons than non-union or mal-union, discharge disposition, readmission rates, 30-day mortality

EQ-5D

The EQ-5D is a standardized tool to measure the health-related quality of life. The tool consists of five questions on different health dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) that together describe the respondent's health status and a visual analogue scale for rating the respondent's perceived health-related quality of life. The EQ-5D has been validated in many languages and in a wide variety of patient groups, including patients admitted to the ICU. [71]

Data handling and statistical analysis

After finishing the study and analysing the data, all patient data will be de-identified, and the key to decode the data will be held on a location separate from patient data. The database will be password-protected. Any paper forms such as signed consent forms will be locked in a file cabinet. Data and blood samples will be stored for 15 years with permission of the patient.

Statistical analyses are carried out using IBM SPSS Statistics. Before analysis, data will be checked for sphericity and homogeneity of variance. P-values < 0.05 are considered statistically significant. Normally distributed variables will be displayed as mean (± standard deviation) and compared using independent-samples t-test. Non-normally distributed variables are displayed as medians (± interquartile range) and compared with Wilcoxon-rank-sum-test. Categorical variables will be presented as percentage (%) and compared using Chi-squared test or Fisher's exact test. The proportion of patients with pre-existing malnutrition (according to SGA score < 24 hours after admission), patients that developed malnutrition (decline in SGA score from category well-nourished to malnutrition between admission at ICU and at hospital discharge), and patients at risk for malnutrition (according to NUTRIC score ≥ 6 on ICU admission) will be calculated. A chi-square test will be used to compare complication rate (yes/no) and long-term outcomes between the group that has or develops malnutrition and the group that remains well-nourished. Multivariate logistic regression analysis will be performed with complication rate (yes/no) as outcome, including potential confounders (e.g. age, gender, APACHE-II scores and ISS).

The difference between resting energy expenditure and calories and proteins prescribed by the clinicians will be calculated. An independent sample T-test is performed to test this difference between patients with and without in-ICU developed malnutrition, and between patients with and without in-hospital developed malnutrition. The association between caloric and protein deficiencies (i.e. calories and proteins delivered minus the calories and proteins prescribed) and in-ICU or in-hospital developed malnutrition is unknown. This will be explored graphically by visually inspecting the course of the deficiencies during ICU admission between patients with and without in-ICU developed malnutrition, and during hospital stay between patients with and without in-hospital

developed malnutrition. Multiple regression analysis or mixed models including potential confounders (e.g. age, gender, APACHE-II scores and ISS) will be used if there seems to be a trend over time.

The added value of the NUTRIC score for the identification of developing malnutrition in the ICU will be evaluated by constructing a Receiver Operating Characteristic (ROC) curve, and by calculating the area under the ROC curve (Area Under the Curve- AUC). The added value of the change in biomarkers over time (CRP, albumin, pre-albumin and white blood cell count) to the SGA score will be assessed using a multivariable logistic regression model. ROC analysis will be performed and a c-statistic (AUC) will be calculated for the SGA model and the SGA with the change in biomarkers model. Lastly, sensitivity and specificity for different cut-off points in the change of biomarkers will be calculated.

SUMMARY

Severely injured patients (polytrauma patients) are at risk of considerable harm from malnutrition, due to disease-related malnutrition with inflammation. Even though this is acknowledged, there is little knowledge of (the risk of) malnutrition and its consequences in the polytrauma patient population. The primary objective is to investigate whether polytrauma patients (Injury Severity Score [ISS] ≥ 16) admitted to the ICU who have or develop malnutrition have a higher complication rate than patients who are and remain well-nourished. Secondary objectives of the study are to investigate the prevalence of both pre-existent and in-hospital developed malnutrition in polytrauma patients admitted to the intensive care unit (ICU), to assess the association between malnutrition and complications, to determine the association between caloric and protein deficiencies and malnutrition and to assess the relationship between malnutrition and long-term outcomes. Lastly, we would like to assess the predictive value of biomarkers in malnutrition.

This international multicenter observational prospective cohort study will be performed at three Level-1 trauma centers in the United States and two Level-1 trauma centers in the Netherlands, including adult (age ≥18 years) polytrauma patients (ISS ≥ 16) admitted from January 2018 to January 2019, to the ICU within six hours after trauma. Patients are excluded if they are transferred from other hospitals to one of the participating trauma centers and if they stay less than 48 hours on the ICU.

Results of this study may help identify patients at risk and thus help optimize care for the vulnerable polytrauma patient. Trials like these, with standardized data dictionaries and clinically relevant outcomes are essential to further improve the nutritional status of polytrauma patients.

REFERENCES

1. Mogensen KM, Robinson MK, Casey JD, et al. Nutritional Status and Mortality in the Critically Ill. *Critical care medicine.* 2015;43:2605-2615.
2. Barker LA, Gout BS, Crowe TC. Hospital malnutrition: prevalence, identification and impact on patients and the healthcare system. *International journal of environmental research and public health.* 2011;8:514-527.
3. Pirlich M, Schütz T, Norman K, et al. The German hospital malnutrition study. *Clinical Nutrition.* 2006;25:563-572.
4. Edington J, Boorman J, Durrant ER, et al. Prevalence of malnutrition on admission to four hospitals in England. The Malnutrition Prevalence Group. *Clinical nutrition (Edinburgh, Scotland).* 2000;19:191-195.
5. Lochs H, Allison SP, Meier R, et al. Introductory to the ESPEN Guidelines on Enteral Nutrition: Terminology, definitions and general topics. *Clinical nutrition (Edinburgh, Scotland).* 2006;25:180-186.
6. Hoffer LJ. Clinical nutrition: 1. Protein–energy malnutrition in the inpatient. *CMAJ: Canadian Medical Association Journal.* 2001;165:1345-1349.
7. Jeejeebhoy KN. Nutritional assessment. *Nutrition (Burbank, Los Angeles County, Calif.).* 2000;16:585-590.
8. Correia MI, Waitzberg DL. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. *Clinical nutrition (Edinburgh, Scotland).* 2003;22:235-239.
9. Keel M, Trentz O. Pathophysiology of polytrauma. *Injury.* 2005;36:691-709.
10. Kruizenga H, van Keeken S, Weijs P, et al. Undernutrition screening survey in 564,063 patients: patients with a positive undernutrition screening score stay in hospital 1.4 d longer. *The American journal of clinical nutrition.* 2016;103:1026-1032.
11. Norman K, Kirchner H, Lochs H, Pirlich M. Malnutrition affects quality of life in gastroenterology patients. *World Journal of Gastroenterology : WJG.* 2006;12:3380-3385.
12. Snider JT, Linthicum MT, Wu Y, et al. Economic burden of community-based disease-associated malnutrition in the United States. *JPEN. Journal of parenteral and enteral nutrition.* 2014;38:77s-85s.
13. Rogobete AF, Sandesc D, Papurica M, et al. The influence of metabolic imbalances and oxidative stress on the outcome of critically ill polytrauma patients: a review. *Burns & Trauma.* 2017;5:8.
14. Cuesta JM, Singer M. The stress response and critical illness: a review. *Critical care medicine.* 2012;40:3283-3289.
15. Preiser JC, Ichai C, Orban JC, Groeneveld AB. Metabolic response to the stress of critical illness. *British journal of anaesthesia.* 2014;113:945-954.
16. Dijkink S, Meier K, Krijnen P, Yeh DD, Velmahos GC, B. SI. The pathophysiology and effects of malnutrition in severely injured trauma patients: a systematic review. *Forthcoming 2019.*
17. Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clinical nutrition (Edinburgh, Scotland).* 2017;36:49-64.
18. Yeh DD, Johnson E, Harrison T, et al. Serum Levels of Albumin and Prealbumin Do Not Correlate With Nutrient Delivery in Surgical Intensive Care Unit Patients. *Nutr Clin Pract.* 2018;33:419-425.
19. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Annals of internal medicine.* 2013;158:200-207.

20. Goiburu ME, Goiburu MM, Bianco H, et al. The impact of malnutrition on morbidity, mortality and length of hospital stay in trauma patients. *Nutricion hospitalaria.* 2006;21:604-610.
21. Gennarelli TA, Wodzin E, Association for the Advancement of Automotive M. *Abbreviated injury scale 2005 : update 2008*. Barrington, Ill.: Association for the Advancement of Automative Medicine; 2008.
22. Baker JP, Detsky AS, Wesson DE, et al. Nutritional assessment: a comparison of clinical judgement and objective measurements. *The New England journal of medicine.* 1982;306:969-972.
23. Zimmerman JE, Wagner DP, Draper EA, Wright L, Alzola C, Knaus WA. Evaluation of acute physiology and chronic health evaluation III predictions of hospital mortality in an independent database. *Critical care medicine.* 1998;26:1317-1326.
24. Rutledge R, Fakhry S, Rutherford E, Muakkassa F, Meyer A. Comparison of APACHE II, Trauma Score, and Injury Severity Score as predictors of outcome in critically injured trauma patients. *American journal of surgery.* 1993;166:244-247.
25. Aslar AK, Kuzu MA, Elhan AH, Tanik A, Hengirmen S. Admission lactate level and the APACHE II score are the most useful predictors of prognosis following torso trauma. *Injury.* 2004;35:746-752.
26. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Critical care medicine.* 1985;13:818-829.
27. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive care medicine.* 1996;22:707-710.
28. Antonelli M, Moreno R, Vincent JL, et al. Application of SOFA score to trauma patients. Sequential Organ Failure Assessment. *Intensive care medicine.* 1999;25:389-394.
29. Ferreira FL, Bota DP, Bross A, Mélot C, Vincent J-L. Serial Evaluation of the SOFA Score to Predict Outcome in Critically Ill Patients. *JAMA.* 2001;286:1754-1758.
30. Benbow M. Assessment, prevention and management of skin tears. *Nursing older people.* 2017;29:31-39.
31. Charney P. Nutrition screening vs nutrition assessment: how do they differ? *Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition.* 2008;23:366-372.
32. Correia M. Nutrition Screening vs Nutrition Assessment: What's the Difference? *Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition.* 2017:884533617719669.
33. van Bokhorst-de van der Schueren MA, Guaitoli PR, Jansma EP, de Vet HC. Nutrition screening tools: does one size fit all? A systematic review of screening tools for the hospital setting. *Clinical nutrition (Edinburgh, Scotland).* 2014;33:39-58.
34. Detsky AS, McLaughlin JR, Baker JP, et al. What is subjective global assessment of nutritional status? *JPEN. Journal of parenteral and enteral nutrition.* 1987;11:8-13.
35. Sheean PM, Peterson SJ, Gurka DP, Braunschweig CA. Nutrition assessment: the reproducibility of Subjective Global Assessment in patients requiring mechanical ventilation. *European journal of clinical nutrition.* 2010;64:1358-1364.
36. Bector S, Vagianos K, Suh M, Duerksen DR. Does the Subjective Global Assessment Predict Outcome in Critically Ill Medical Patients? *Journal of intensive care medicine.* 2016;31:485-489.
37. Ottery FD. Definition of standardized nutritional assessment and interventional pathways in oncology. *Nutrition (Burbank, Los Angeles County, Calif.).* 1996;12:S15-19.
38. Sealy MJ, Hass U, Ottery FD, van der Schans CP, Roodenburg JLN, Jager-Wittenaar H. Translation and Cultural Adaptation of the Scored Patient-Generated Subjective Global Assessment: An

Interdisciplinary Nutritional Instrument Appropriate for Dutch Cancer Patients. *Cancer nursing.* 2017.
39. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. *Eur J Clin Nutr.* 2002;56:779-785.
40. Steiber AL, Kalantar-Zadeh K, Secker D, McCarthy M, Sehgal A, McCann L. Subjective Global Assessment in chronic kidney disease: A review. *Journal of Renal Nutrition.* 2004;14:191-200.
41. Platform P-SP-G. Patient-Generated Subjective Global Assessment2015.
42. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Critical care (London, England).* 2011;15:R268.
43. Taylor BE, McClave SA, Martindale RG, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *Critical care medicine.* 2016;44:390-438.
44. Mendes R, Policarpo S, Fortuna P, Alves M, Virella D, Heyland DK. Nutritional risk assessment and cultural validation of the modified NUTRIC score in critically ill patients-A multicenter prospective cohort study. *Journal of critical care.* 2017;37:45-49.
45. Oshima T, Berger MM, De Waele E, et al. Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group. *Clinical nutrition (Edinburgh, Scotland).* 2017;36:651-662.
46. Harris JA, Benedict FG. A Biometric Study of Human Basal Metabolism. *Proceedings of the National Academy of Sciences of the United States of America.* 1918;4:370-373.
47. Roza AM, Shizgal HM. The Harris Benedict equation reevaluated: resting energy requirements and the body cell mass. *The American journal of clinical nutrition.* 1984;40:168-182.
48. Tignanelli CJ, Andrews AG, Sieloff KM, et al. Are Predictive Energy Expenditure Equations in Ventilated Surgery Patients Accurate? *Journal of intensive care medicine.* 2017:885066617702077.
49. DeChicco R, Matarese L, C. Hummell A, Speerhas R, Seidner D, Steiger Md E. *Contribution of Calories from Propofol to Total Energy Intake*1995.
50. Smith SH. Using albumin and prealbumin to assess nutritional status. *Nursing.* 2017;47:65-66.
51. Parent B, Seaton M, O'Keefe GE. Biochemical Markers of Nutrition Support in Critically Ill Trauma Victims. *JPEN J Parenter Enteral Nutr.* 2016.
52. Bharadwaj S, Ginoya S, Tandon P, et al. Malnutrition: laboratory markers vs nutritional assessment. *Gastroenterology Report.* 2016;4:272-280.
53. Raguso CA, Dupertuis YM, Pichard C. The role of visceral proteins in the nutritional assessment of intensive care unit patients. *Current opinion in clinical nutrition and metabolic care.* 2003;6:211-216.
54. Erstad BL, Campbell DJ, Rollins CJ, Rappaport WD. Albumin and prealbumin concentrations in patients receiving postoperative parenteral nutrition. *Pharmacotherapy.* 1994;14:458-462.
55. Nataloni S, Gentili P, Marini B, et al. Nutritional assessment in head injured patients through the study of rapid turnover visceral proteins. *Clinical nutrition (Edinburgh, Scotland).* 1999;18:247-251.
56. Sergi G, Coin A, Enzi G, et al. Role of visceral proteins in detecting malnutrition in the elderly. *Eur J Clin Nutr.* 2005;60:203-209.
57. Tuten MB, Wogt S, Dasse F, Leider Z. Utilization of prealbumin as a nutritional parameter. *JPEN. Journal of parenteral and enteral nutrition.* 1985;9:709-711.
58. Ingenbleek Y, Young V. Transthyretin (prealbumin) in health and disease: nutritional implications. *Annual review of nutrition.* 1994;14:495-533.

59. Taylor SJ, Fettes SB, Jewkes C, Nelson RJ. Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. *Critical care medicine.* 1999;27:2525-2531.
60. Hershkovitz Y, Naveh S, Kessel B, Shapira Z, Halevy A, Jeroukhimov I. Elevated white blood cell count, decreased hematocrit and presence of macrohematuria correlate with abdominal organ injury in pediatric blunt trauma patients: a retrospective study. *World journal of emergency surgery : WJES.* 2015;10:41.
61. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315:801-810.
62. C Bone R. *Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/ Society of Critical Care Medicine*1992.
63. Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin Definition. *Jama.* 2012;307:2526-2533.
64. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol.* 1992;13:606-608.
65. Alvarez G, Chrusch C, Hulme T, Posadas-Calleja JG. Renal replacement therapy: a practical update. *Canadian journal of anaesthesia = Journal canadien d'anesthesie.* 2019.
66. Schoenfeld DA, Bernard GR. Statistical evaluation of ventilator-free days as an efficacy measure in clinical trials of treatments for acute respiratory distress syndrome. *Critical care medicine.* 2002;30:1772-1777.
67. Teasdale GM, Pettigrew LE, Wilson JT, Murray G, Jennett B. Analyzing outcome of treatment of severe head injury: a review and update on advancing the use of the Glasgow Outcome Scale. *Journal of neurotrauma.* 1998;15:587-597.
68. Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet (London, England).* 1975;1:480-484.
69. Corral L, Ventura JL, Herrero JI, et al. Improvement in GOS and GOSE scores 6 and 12 months after severe traumatic brain injury. *Brain injury.* 2007;21:1225-1231.
70. TBI IMfPaAoCTi. Glasgow Outcome Scale 2011.
71. García Lizana F, Peres Bota D, De Cubber M, Vincent J-L. Long-term outcome in ICU patients. *Intensive care medicine.* 2003;29:1286-1293.

APPENDIX I APACHE II SCORE[26]

	High Abnormal Range					Low Abnormal Range			
Physiologic Variable	**+4**	**+3**	**+2**	**+1**	**0**	**+1**	**+2**	**+3**	**+4**
Temperature - rectal (°C)	≥41°	39 - 40.9°		38.5 - 38.9°	36 - 38.4°	34 - 35.9°	32 - 33.9°	30 - 31.9°	≤29.9°
Mean Arterial Pressure - mmHg	≥160	130 - 159	110 - 129		70 - 109		50 - 69		≤49
Heart Rate (ventricular response)	≥180	140 - 179	110 - 139		70 - 109		55 - 69	40 - 54	≤39
Respiratory Rate (non-ventilated or ventilated)	≥50	35 - 49		25 - 34	12 - 24	10 - 11	6 - 9		<5
Oxygenation: A-aDO_2 orPaO_2 (mm Hg) a. FIO_2 ≥0.5 record A-aDO2 b. FIO_2 <0.5 record PaO2	≥500	350 - 499	200 - 349		<200 PO2 >70	PO2 61 - 70		PO2 55 - 60	PO2 <55
Arterial pH (preferred)	≥7.7	7.6 - 7.69		7.5 - 7.59	7.33 - 7.49		7.25 - 7.32	7.15 - 7.24	<7.15
Serum HCO3 (venous mEq/l)		41 - 51.9		32 - 40.9	22 - 31.9		18 - 21.9	15 - 17.9	
(not preferred, but may use if no ABGs)	≥52								<15
Serum Sodium (mEq/l)	≥180	160 - 179	155 - 159	150 - 154	130 - 149		120 - 129	111 - 119	≤110
Serum Potassium (mEq/l)	≥7	6 - 6.9		5.5 - 5.9	3.5 - 5.4	3 - 3.4	2.5 - 2.9		<2.5
Serum Creatinine (mg/dl) Double point score for acute renal failure	≥3.5	2 - 3.4	1.5 - 1.9		0.6 - 1.4		<0.6		
Hematocrit (%)	≥60		50 - 59.9	46 - 49.9	30 - 45.9		20 - 29.9		<20
White Blood Count (total/ mm3) (in 1000s)	≥40		20 - 39.9	15 - 19.9	3 - 14.9		1 - 2.9		<1
Glasgow Coma Score (GCS) Score = 15 minus actual GCS									

A. Total Acute Physiology Score (sum of 12 above points)

B. Age points (years) ≤44=0; 45 to 54=2; 55 to 64=3; 65 to 74=5; ≥75=6

C. Chronic Health Points*

Total APACHE II score (add together the points from A+B+C)

*Chronic Health Points: If the patient has a history of severe organ system insufficiency or is immunocompromised as defined below, assign points as follows:

5 points for nonoperative or emergency postoperative patients

2 points for elective postoperative patients

APPENDIX II SOFA SCORE[29]

Variables	SOFA score				
	0	1	2	3	4
Respiratory PaO_2/FiO_2, mmHg	>400	≤400	≤300	≤200	≤100
Coagulation platelets $\times 10^3/\mu L$	>150	≤150	≤100	≤50	≤20
Liver bilirubin, mg/dl	<1.2	1.2~1.9	2.0~5.9	6.0~11.9	>12.0
Cardiovascular hypotension*	No hypotension	MAP <70 mmHg	Dop ≤5 or Dob (any dose)	Dop >5, Epi or Norepi ≤0.1	Dop >15, Epi >0.1, Norepi >0.1
Central nervous system Glasgow Coma Scale	15	13~14	10~12	6~9	<6
Renal creatinine, mg/dl or urine output, ml/dl	<1.2	1.2~1.9	2.0~3.4	3.4~4.9 or <500	> 5.0 or <200

APPENDIX III SGA[40]

Subjective Global Assessment (SGA) is a widely used and validated method for identifying and classifying malnutrition

SUBJECTIVE GLOBAL ASSESSMENT RATING FORM	
Patient Name: **ID #:** **Date:**	
HISTORY	
WEIGHT/WEIGHT CHANGE: ***(Included in K/DOQI SGA)***	**Rate 1-7**
1. Baseline Wt: _____(Dry weight from 6 months ago)	
Current Wt: _____(Dry weight today)	
Actual Wt loss/past 6 mo: _____ **% loss:**_____(actual loss from baseline or last SGA)	
2. Weight change over past two weeks: _____No change _____Increase _____Decrease	
DIETARY INTAKE No Change_____(Adequate) No Change_____(Inadequate)	
1. Change: Sub optimal Intake: _____ Protein _____ Kcal _____ Duration_____	
Full Liquid: _____ Hypocaloric Liquid _____ Starvation _____	
GASTROINTESTINAL SYMPTOMS ***(Included in K/DOQI SGA-anorexia or causes of anorexia)***	
Symptom: **Frequency:*** **Duration:+**	
_____ None _____ _____	
_____ Anorexia _____ _____	
_____ Nausea _____ _____	
_____ Vomiting _____ _____	
_____ Diarrhea _____ _____	
Never, daily, 2-3 times/wk, 1-2 times/wk > 2 weeks, < 2 weeks	
FUNCTIONAL CAPACITY	b
Description **Duration:**	
_____ No Dysfunction _____	
_____ Change in function _____	
_____ Difficulty with ambulation _____	
_____ Difficulty with activity (Patient specific "normal") _____	
_____ Light activity _____	
_____ Bed/chair ridden with little or no activity _____	
_____ Improvement in function _____	
DISEASE STATE/COMORBIDITIES AS RELATED TO NUTRITIONAL NEEDS	
Primary Diagnosis_____Comorbidities_____	
Normal requirements ____Increased requirements____ Decreased requirements _____	
Acute Metabolic Stress: _____None _____Low _____Moderate _____High	
PHYSICAL EXAM	
_____ Loss of subcutaneous fat (Below eye, triceps, biceps, chest) ***(Included in K/DOQI SGA)*** ____Some areas _____All areas	
_____ Muscle wasting (Temple, clavicle, scapula, ribs, quadriceps, calf, knee, interosseous ***(Included in K/DOQI SGA)*** ____Some areas _____All areas	
_____ Edema (Related to undernutrition/use to evaluate weight change)	
OVERALL SGA RATING	
Very mild risk to well-nourished=6 or 7 most categories or significant, continued improvement.	
Mild-moderate = 3, 4, or 5 ratings. No clear sign of normal status or severe malnutrition.	
Severely Malnourished = 1 or 2 ratings in most categories/significant physical signs of malnutrition.	

APPENDIX IV NUTRIC SCORE[42]

Critical Care Nutrition

NUTRIC Score[1]

The NUTRIC Score is designed to quantify the risk of critically ill patients developing adverse events that may be modified by aggressive nutrition therapy. The score, of 1-10, is based on 6 variables that are explained below. The scoring system is shown in Tables 1 and 2.

Table 1: NUTRIC Score variables

Variable	Range	Points
Age	<50	0
	50 - <75	1
	≥75	2
APACHE II	<15	0
	15 - <20	1
	20-28	2
	≥28	3
SOFA	<6	0
	6 - <10	1
	≥10	2
Number of Co-morbidities	0-1	0
	≥2	1
Days from hospital to ICU admission	0 - <1	0
	≥1	1
IL-6	0 - <400	0
	≥ 400	1

Table 2: NUTRIC Score scoring system: if IL-6 available

Sum of points	Category	Explanation
6-10	High Score	➢ Associated with worse clinical outcomes (mortality, ventilation). ➢ These patients are the most likely to benefit from aggressive nutrition therapy.
0-5	Low Score	➢ These patients have a low malnutrition risk.

Table 3. NUTRIC Score scoring system: If no IL-6 available*

Sum of points	Category	Explanation
5-9	High Score	➢ Associated with worse clinical outcomes (mortality, ventilation). ➢ These patients are the most likely to benefit from aggressive nutrition therapy.
0-4	Low Score	➢ These patients have a low malnutrition risk.

*It is acceptable to not include IL-6 data when it is not routinely available; it was shown to contribute very little to the overall prediction of the NUTRIC score.

[1] Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. Critical Care. 2011;15(6):R268.

March 19th 2013

APPENDIX V GLASGOW OUTCOME SCALE EXTENDED (GOSE)[70]

Key for scoring 8-point Extended Scale

The GOSE is a global scale for functional outcome that rates a patient status into one of five categories: Dead, Vegetative State, Severe Disability, Moderate Disability or Good Recovery. The GOSE provides more detailed categorization into eight categories by subdividing the categories into lower and upper categories.

Category	GOSE descriptor		Key features
1	Dead	0	
2	Vegetative state	VS	• *unable to obey commands or say words*
3	Severe disability - Lower	SD-	• *needs frequent help or someone to be around most of the time*
4	Severe disability - Upper	SD+	• *does not need frequent help, able to be alone at home for up to 8 hrs.* • *not able to shop without assistance* • *not able to travel locally without assistance*
5	Moderate disability - Lower	MD-	• *not able to work, or, only in a sheltered or non-competitive position* • *unable to participate (or, rarely if ever) in regular social and leisure activities outside home* • *constant and intolerable (daily) disruption of family relationships or friendships due to psychological problems*
6	Moderate disability - Upper	MD+	• *able to work or study but at a reduced capacity* • *participates much less (less than half as often) in regular social and leisure activities outside home* • *frequent but tolerable (once per week) disruption of family relationships or friendships due to psychological problems*
7	Good recovery – Lower	GR-	• *participates at least half as often as before in regular social and leisure activities outside home* • *occasional disruption of family relationships or friendships due to psychological problems* • *other problems relating to the injury (headache, fizziness, tiredness, sensory sensitivity, slowness, memory failures, concentration problems) affect daily life*
8	Good recovery - Upper	GR+	• *able to work to previous capacity* • *able to resume regular social and leisure activities outside home* • *no psychological problems resulting in ongoing family disruption or disruption to friendships*

10

General discussion

"*When I can provide better care in the field with limited resources than my children and I received at the primary facility, there is something wrong with the system and the system has to be changed.*"

Since Dr. Styner said those famous words, there have been many improvements in the field of trauma care, such as the introduction of the Advanced Trauma Life Support (ATLS) course and the implementation of all-inclusive trauma systems. Still, 5 million people die each year due to their injuries and 90% of these deaths occur in low- and middle-income countries.[1] The primary aim of this thesis is to analyze the trauma systems regarding their presence and organization in two high-income countries, their processes of care and their influence on clinical outcome of trauma patients. Although the low- and middle income countries carry the brunt of the trauma mortality burden, trauma continues to claim lives even in high-income countries. Given that high-income countries may serve as examples in developing trauma systems and establishing value-based care, we chose to focus on two countries, characterized by robust economies but also subject to different cultural, organizational, economic, and administrative principles. The second aim is directed towards individualized trauma care, specifically the evaluation of the role of nutritional status in polytrauma patients. To further improve trauma care both *globally* as a system and for the individual patient per se, many more questions need to be answered and challenges must be overcome. Several of these will be discussed below.

TRAUMA SYSTEMS

Injury prevention, pre-hospital care, facility-based care, and post-hospital care are all considered essential components of a mature trauma system [Figure 1].[2,3] The crucial part of a well-functioning trauma care system is that each of those four elements (Levels 1 through 4 trauma centers) work together to assure a seamless transition of patient care from each phase to the next; this is believed to result in improved outcomes and optimal utilization of resources. In addition, quality assurance by means of clinical training and registries, is considered an essential element of mature trauma systems.

Injury prevention

Injury prevention represents one of the great opportunities to: 1) further reduce mortality, 2) prevent long-term morbidity, and 3) lower the trauma burden and related costs. Many strategies for preventing injuries (such as improving road safety, installing smoke detectors, improving safety around the house, and firearm restrictions) have already shown to be both effective and cost-effective.[4,5] For example, in this thesis it was demonstrated that the proportion of patients admitted due to gun violence was almost

Figure 1. Components of a trauma system

twice as high in the USA compared to the Netherlands, despite both countries having comparable urbanization (population density 4200/km^2 in Boston versus 5000/km^2 in the Randstad region) and violent crime rates (respectively 390 and 360/100.000 population in Massachusetts and the Dutch region, respectively). **(Chapter 4)** However, despite having similar violent crime rates there is an enormous difference in firearm-related injuries; for example, there are many more mass shooting events in the USA.[6] The high numbers of firearm-related deaths could possibly be explained by the relatively lax laws on gun ownership in the USA, with more availability of firearms directly correlated to more firearm-related deaths.[7,8] The implementation of laws restricting firearm purchase or access, as a preventive measure have led in many countries, such as South Africa, New Zealand, Australia, and Canada, to a reduction in firearm-related deaths in those countries.[9-11]

The shift in paradigm in the recent era to an increase focus on injury prevention has resulted in many new initiatives. Examples are the "Stop the Bleed" initiative in the USA and new restrictive laws for telephone use while operating a bicycle or automobile in the Netherlands.[12,13] Other effective preventive strategies include programs aimed at preventing falls and fall-related injuries in the elderly. Each year, 25% of elderly (age > 65 years) fall and in 10-25% of the cases this results in injury, hospital admission, or

even death.[14,15] Randomized controlled trials have consistently shown that strength and balance training for the elderly can reduce falls by 15-50%.[16]

Gaining insight into epidemiological patterns of injury is essential to target preventive measures and evaluate the effectiveness of those interventions. Focusing more on prevention has the greatest potential in reducing injury-related deaths.[17,18]

Prehospital care

Unfortunately, not all injuries can be prevented despite extensive preventive measures and legislation. Therefore, it is essential that all other parts of the trauma system function optimally. This thesis has shown global variation in prehospital care, varying from non-existent, to fully developed paramedic- and physician-staffed emergency medical service (EMS) systems. (**Chapter 2**) With the majority of trauma-related deaths occurring in the prehospital setting (especially in the low-and middle-income countries) there is great opportunity for improvement.[19,20] Several studies have shown that relatively low-cost interventions, such as the introduction of Prehospital Trauma Life Support (PHTLS) training and increased numbers of ambulance dispatch centers, have resulted in lower numbers of prehospital deaths.[19,21,22]

Although education and training of EMS personnel improve outcomes, the level of advanced expertise needed at the trauma scene is controversial, with studies both refuting[23,24] and supporting physician-staffed EMS.[25-30] It seems that the advantage is mainly for the severely injured and severely ill patients (cardiac arrest, myocardial infarction and respiratory distress).[25-31]The presence of physician-assisted EMS is associated with increased on-scene time and more interventions; however, this association may be confounded by the severity of the injuries of the patients rather than being related to the presence of the physician.[31-33]Other factors likely also play a role in the number of interventions performed by medics and paramedics, with a longer transport time being associated with longer on-scene time and more interventions being performed.[34] This suggests that the difference between "scoop and run" vs "stay and play" may not be as clear as suggested, and that prehospital care is a more nuanced process.

A second ongoing debate is the tradeoff between optimizing trauma center accessibility with shorter transport times and more hospitals able to provide around-the-clock care of the severely injured on one hand versus having fewer, but high-volume hospitals and longer transport times. Currently there are eleven trauma centers in the Netherlands that are geographically close (in comparison to other countries) and care for relatively low volumes of severely injured patients.[35] This raises the question if there are too many trauma centers in the Netherlands and if outcomes of patients might be improved even more by further centralizing care for the severely injured. However, centralizing the trauma care into fewer high-volume centers inherently means longer transport times. In this thesis, the geographical distribution and number of trauma centers were shown to

influence the transport times, with longer transport times in scenarios with geographically suboptimal located centers especially during rush hour. (**Chapter 5**) Literature suggests that reduced trauma center access is associated with differences in outcomes such as higher mortality rates.[36-39] However, the threshold beyond which outcomes are affected is unknown. Although a transport that lasts two hours is intuitively more risk-prone than a transfer that lasts 10 minutes, it is not known whether outcomes are affected by a transfer of 10 vs. 20 minutes. In the Netherlands, even if trauma care would be further centralized, it is unlikely that the transfer times will be prohibitively long. However, the contrary scenario, whereby each trauma center can barely treat a critical mass of severely injured patients to ensure physician expertise, may ultimately lead to less optimal outcomes.[40] On the other hand, if a hospital is overburdened beyond its optimum trauma patient capacity, adding new accredited trauma centers in the region may improve outcome by reducing the burden.[41,42] Unfortunately, despite years of research, there is still no universal standard for trauma system planning and the optimal trade-off between transport times and hospital volumes remains unclear. The annual cost for having a fully staffed around-the-clock trauma center, including physician stipends, verification, outreach and prevention costs, has been estimated to be around 2.7 million dollars per trauma center in the USA.[43]

There is a need for an internationally applicable tool to evaluate the best geographical organization of trauma care (i.e., optimal combination of trauma center access, population coverage, and hospital trauma volume). The Geographical Information System (GIS)-based model offers an objective way to evaluate the effects of different scenarios with varying numbers of trauma centers and their geographical distribution in specific regions or countries taking the local geographical and demographical characteristics into account. (**Chapter 5**) Strategic planning of geographical trauma center distribution will lead to better patient care through efficient distribution of patient volumes and resources.

The efficient distribution of trauma patients, meaning getting the right patient to the right hospital remains a challenge. 20 years after the introduction of an inclusive trauma system in the Netherlands still 30% of the severely injured patients is primarily brought to a non-trauma center **(Chapter 6).** However, studies have shown that it is hard to predict which patient will be classified as a polytrauma patient (ISS≥16) and which are not, for example, 32% of the traumatic brain injuries (TBI) and 21% of the severe traumatic brain injuries are not recognized at the accident scene.[44] EMS providers often base their decision, despite many protocols, to go to trauma or non-trauma center on their own experience, the mechanism of injury, and early visual cues of severe injury at the accident scene.[45] Future research should focus on developing tools to improve the quality of pre-hospital triage in severely injured patients, such as the TraumaTriageApp.[46-48,49]

Facility-based care

Since the introduction of formalized trauma systems, the volume-outcome relationship in trauma care has been an ongoing debate, with the literature showing both supporting and opposing evidence.[50-58] Although in many surgical specialties, the volume-outcome relationship has been ascertained, even with clear cut off points, this has not been the case for trauma surgery.[59-61] However, Chowdhury et al. showed in their review that not only hospital volume, but also specialization and high surgeon volume, are associated with improved outcomes.[62] Also in trauma care, it seems that other factors, such as the experience of the trauma surgeon[63,64], implementation of accreditation and verification measures [65,66], standardization of complex care[2,67], and the implementation of a dedicated trauma team[68,69] may potentially influence outcome independently of hospital patient volume. This is consistent with results shown in this thesis, in which it was demonstrated that mature trauma systems have similar outcomes (measured as in-hospital mortality) despite differences in volume of both blunt polytrauma and truncal penetrating trauma patients. **(Chapters 3 and 4)**.

Despite the inconclusive evidence, minimum volume requirements are still in place in many countries, including the Netherlands. The Dutch Trauma Society, in collaboration with the Dutch National Health Care Institute, raised the minimal annual volume requirement from 100 to 240 polytrauma patients per trauma center.[70] Currently, only five out of eleven level I trauma centers fulfill the minimum volume requirements [Figure 2].[35] The currently available evidence suggests that, if we want to improve outcomes for severely injured patients in the Netherlands, we should focus on improving processes of care within the hospital, rather than simply focus on volume. [2,63-67]

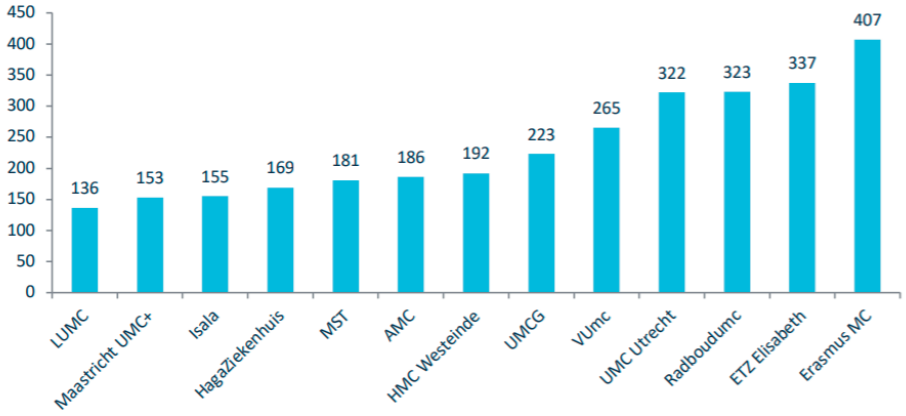


Figure 2. Polytrauma patient volumes per level-1 traumacenter in 2017 the Netherlands*[33]
*Landelijk Netwerk Acute Zorg. Traumazorg in beeld - landelijke traumaregistratie 2013-2017- rapportage Nederland. Utrecht 2018.

Post-hospital care

With an increasing number of patients surviving their injuries, focusing on mortality as the sole outcome does not seem appropriate anymore in the evaluation of the quality of trauma care. This raises two major questions: 1) which outcomes to monitor, and 2) how to improve outcomes for patients surviving their injuries?

For many studies, including the studies in this thesis **(Chapters 3 and 4),** parameters such as in-hospital mortality, hospital length of stay, and ICU length of stay are considered the primary outcomes to measure quality of care. Several studies have shown that although severely injured patients may have good functional outcomes, they have a significantly lower quality of life compared to the general population, and often do not regain preinjury functional status.[71-73] A significant proportion of these patients (about 20-25%) cannot return to their preinjury employment.[72-78] Focusing on outcomes relevant for trauma patients instead of only focusing on mortality rates could further improve quality of life. Comprehensive rehabilitation programs have been proven effective in improving outcomes in patients with severe brain injury.[79] A recently published study by Wiertsema et al. concluded that a rehabilitation program specifically for trauma patients, in which trauma surgeons work in close collaboration with hospital-based and primary care physical therapists, improved disease-specific health-related quality of life, reduced pain, and improved functional status in comparison to regular care. [80,81] It seems that further establishing cooperation between rehabilitation and trauma care for the severely injured is both effective and cost-effective. [82,83]

Quality Improvement

Improvements in mature trauma systems have been driven by evaluation of data on outcomes and processes of care in regional and national trauma registries. [84,85] However, this thesis has shown that, despite having the largest trauma burden, the majority of low-and middle-income countries lack a formal trauma registry. **(Chapter 2)**. It seems that implementation of a trauma system including a formal national trauma registry is inversely related to a country's economic status.[20]

The development of a global standardized data set with clearly defined inclusion/exclusion criteria to evaluate trauma care would not only facilitate national improvements in trauma care but also allow international comparisons. With higher survival rates, the shift towards a greater focus on patient-centered long-term outcomes is justified and much needed.[86,87] Several studies have shown that currently used parameters, such as the Glasgow Outcome Score, EQ-5D, and Functional Independence Measure were not predictive of long-term outcomes in severely injured patients.[88,89] Patient Reported Outcome Measures (PROMs), specifically developed for severely injured patients, offer new options to measure long-term outcomes.[90] Unfortunately, although some of these newer tools, such as the Trauma Quality of Life Measure (TQLM) and Trauma Outcome

Profile (TOP), they were only used in 4% of studies published.[90-92] In the future we should focus on using standardized PROM's, such as TQLM and TOP, better reflecting the patients' perspectives on outcome and quality of life, in clinic and research to provide more insight in trauma outcomes beside mortality and to improve trauma care in the long run.[93]

Training residents, surgeons, and other healthcare providers is essential to maintain good quality of care in a mature trauma system. **(Chapter 2)** Due to stricter duty-hour restrictions in both Europe and the US and the rise in non-operative and endovascular treatment, the experience in trauma care and more specifically certain operative skills are becoming more difficult to maintain for both residents and attending surgeons. [94-96] Trauma skills courses such as the Advanced Trauma Life Support (ATLS), Definitive Surgical Trauma Care (DSTC), Advanced Trauma Operative Management (ATOM) and many more have been developed to improve the residents' and surgeons' skills with regards to trauma management. Mackenzie et al. identified 21 trauma courses given all across the globe, many with overlapping parts and focal points. Although most courses demonstrated benefits for the patient when compared to no training, it is still unclear what is the most efficient and effective trauma training, mostly due to lack of standardization, different levels of trainees, and disparities in training conditions.[96] To further improve trauma training, future research should focus on standardized evaluation of both technical and non-technical skills before and after trauma courses and long-term skills in order to identify the most efficient and effective way of training (future) trauma surgeons.

MALNUTRITION IN TRAUMA PATIENTS

In this thesis, malnutrition was shown to be an underestimated and underrecognized problem in trauma patients. The review in **chapter 7** has shown that trauma patients are particularly susceptible to deterioration of their nutritional status and associated complications due to the unique metabolic response following injury. Early recognition of malnutrition and targeted interventions could prevent malnutrition-related complications. Unfortunately, malnutrition is not easy to prevent and treat. Many challenges lie ahead and questions need to be answered before we can move forward in nutritional support management.

The study in **chapter 8** showed that slowly increasing the enteral nutrition delivery rate contributes to a protein and calorie deficit. Intuitively, malnutrition could be prevented by giving the patient the needed nutritional support, e.g. sufficient energy and protein. However, the evidence supporting the stance that improved nutritional support leads to better outcomes is not robust.[97,98] Some trials have even suggested that receiving more than 75% of the daily energy and protein requirements is associated with *higher* mortal-

ity in patients with acute lung injury.[99,100] Permissive underfeeding, receiving 40-60% of the estimated needed requirements, did not improve clinical outcomes in critically ill patients.[101] However, large observational studies have demonstrated that critically ill patients with a BMI<25 kg/m^2 or >35 kg/m^2 do seem to benefit from increased energy delivery.[102,103] Unfortunately, the proportion of severely injured trauma patients enrolled in these studies was very low. Thus, the current knowledge about the best nutritional support for the severely injured patient is based upon sparse evidence, heterogeneous data, and is mostly extrapolated from studies in which trauma patients were not enrolled or only comprised a very small proportion.

Recognizing the need for more insight into the prevalence and effects of malnutrition in polytrauma patients, the Malnutrition in Polytrauma Patients (MaPP) study was initiated. (**Chapter 9**) Designing this multicenter prospective observational study, we experienced the hardships of conducting malnutrition-related research. The main problem in all malnutrition-related research is the absence of a gold standard for diagnosing malnutrition and assessing its severity.[104] Although BMI is still considered an important element of diagnosing malnutrition[104], it is actually a poor surrogate.[105,106] Nutritional deficiencies are often present in obese patients, despite their high BMI.[107-110] Higher mortality and morbidity rates have been shown in obese patients [111,112]; however, Robinson et al. advocate that it is actually malnutrition, not obesity, that causes worse outcomes.[105] This is probably also the case in so-called "sarcopenic obese elderly". These elderly patients appear to be well-nourished because of their normal or elevated BMI, but actually suffer from relative muscle loss e.g. sarcopenia.[113-115] Several studies have shown an association between worse outcomes and sarcopenic obesity. [116-118] Current definitions do not assess malnutrition in these patients. Developing a definition for malnutrition without relying on BMI is essential.

In an effort to promote consistency and agreement on malnutrition, the Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) proposed their combined consensus guidelines for documenting and diagnosing malnutrition in 2012.[119] The adult malnutrition consensus (AMC) characteristics consists of five components: weight loss, energy intake, body fat, muscle mass, fluid accumulation, and hand grip strength. Malnutrition, classified from well-nourished to moderate and severe malnutrition, is divided in three categories: acute illness and injury-related malnutrition; chronic disease-related malnutrition; and social and environmental related-malnutrition.[120] Although these diagnostic criteria have shown some promising results in feasibility and reliability, big validation studies have not been published yet and are much needed. [121]

In addition to the need for a generally applicable definition of malnutrition, there is a need for objective diagnostic tools to identify malnutrition. As mentioned in the AMC, hand grip strength is an accurate marker of malnutrition and can be used to as-

sess malnutrition as well as evaluate nutritional support interventions.[122-124] Bioelectric impedance analysis (BIA) also offers potential as a noninvasive, low-cost, diagnostic tool that can be used to assess the body composition, in particular fat and muscle mass. [125] Some studies suggest that malnutrition is related to changes in tissue electrical properties, which can be detected by BIA.[126] However, before implementation in clinical practice, clear cutoff points for defining malnutrition in different patient groups need to be identified for all diagnostic tools.[127]

In the current practice, albumin and transthyretin (i.e., prealbumin) are often considered valuable markers of a patient's nutritional status. However, increasing evidence suggests that these biomarkers are more reflective of the acute phase response after trauma rather than the nutritional status.[128,129] The developing fields of proteomics and metabolomics may be suitable to characterize and anticipate acute changes in trauma patients' metabolism and energy needs, as it reflects the response to nutrition deficiencies and the effects of nutrition administration in trauma (i.e. oxidative stress metabolites, muscle catabolism metabolites, and nucleotide synthesis metabolites).[128,130-134] So far, several metabolites have been found to be associated with nutritional status in critically ill patients: purine, tathione, kynurenine, tryptophan pathways.[135] Fatty acid patterns are highly correlated with nutrition and the particular catabolic state in trauma patients.[130] There are several limitations to the studies that presented, including the small study sample sizes, low metabolite numbers, and the small number of measured time points. New studies designed to overcome the previously mentioned limitations are needed to further evaluate the value of metabolomics for diagnosing malnutrition in severely injured patients.

To improve nutritional support and allow for comparison between studies, we recommend a standardized data set of clinically relevant outcomes and time points affected by nutritional support for future studies.[127, 136] At the moment, the best potential for a validated standardized nutritional risk assessment tool is the Nutrition Risk in the Critically Ill (NUTRIC) score, which is also supported by the Society of Critical Care Medicine (SCCM) and A.S.P.E.N. [97,137-139].

FINAL CONSIDERATION

Although it may seem that malnutrition and trauma systems are not directly connected, this thesis has shown that both elements are essential in the management of the care for the injured patient. Trauma care improved greatly in the past 40 years; however global differences remain. There is no "one-size-fits-all" model for the optimal care for the injured, though there are certain elements essential for all trauma systems, independent of location, population, and regulation: *dedicated trauma teams*, *strategically*

planned trauma center distribution, *quality control measures* and *individualized care*. Many decennia ago it has been recognized that trauma care is built on disciplines working together; team-work is the corner stone of trauma care. In the future, we need to further focus on the continuum of trauma care, recognizing that strengthening each element of the trauma care chain improves outcomes for the severely injured patient. Further well designed studies, that take the four essential trauma system elements into account will help to take the next step in trauma care, locally, regionally and eventually globally.

REFERENCES

1. Gosselin RA, Spiegel DA, Coughlin R, Zirkle LG. Injuries: the neglected burden in developing countries. *Bulletin of the World Health Organization.* 2009;87:246-246a.
2. Sakran JV, Jehan F, Joseph B. Trauma systems: standardization and regionalization of care improve quality of care. *Current Trauma Reports.* 2018;4(1):39-47.
3. Dunn J. Trauma Systems. The Trauma System: By Design Web site. http://www.aast.org/trauma-systems. Published 2012. Accessed October 14, 2019.
4. Organization WH. Preventing injuries and violence: a guide for ministries of health. 2007.
5. Mock C, Quansah R, Krishnan R, Arreola-Risa C, Rivara F. Strengthening the prevention and care of injuries worldwide. *The Lancet.* 2004;363(9427):2172-2179.
6. Lankford A. Are America's public mass shooters unique? A comparative analysis of offenders in the United States and other countries. *International journal of comparative and applied criminal justice.* 2016;40(2):171-183.
7. Miller M, Azrael D, Hemenway D. Firearm availability and unintentional firearm deaths. *Accident Analysis & Prevention.* 2001;33(4):477-484.
8. Hepburn LM, Hemenway D. Firearm availability and homicide: A review of the literature. *Aggression and Violent Behavior.* 2004;9(4):417-440.
9. Santaella-Tenorio J, Cerdá M, Villaveces A, Galea S. What do we know about the association between firearm legislation and firearm-related injuries? *Epidemiologic reviews.* 2016;38(1):140-157.
10. Lee LK, Fleegler EW, Farrell C, et al. Firearm laws and firearm homicides: a systematic review. *JAMA internal medicine.* 2017;177(1):106-119.
11. Shepherd JP. Criminal deterrence as a public health strategy. *The Lancet.* 2001;358(9294):1717-1722.
12. Fisher AD, Carius BM, Lacroix J, et al. National Stop the Bleed Day: The impact of a social media campaign on the Stop the Bleed program. *J Trauma Acute Care Surg.* 2019;87(1S Suppl 1):S40-s43.
13. Ministry of Infrastructure and Water Management. Reglement verkeersregels en verkeerstekens 1990 (RVV 1990). In: Ministry of Infrastructure and Water Management, ed. The Hague 2019.
14. Bolding DJ, Corman E. Falls in the Geriatric Patient. *Clinics in Geriatric Medicine.* 2019;35(1):115-126.
15. Rubenstein LZ. Falls in older people: epidemiology, risk factors and strategies for prevention. *Age and Ageing.* 2006;35(suppl_2):ii37-ii41.
16. Kannus P, Sievänen H, Palvanen M, Järvinen T, Parkkari J. Prevention of falls and consequent injuries in elderly people. *The Lancet.* 2005;366(9500):1885-1893.
17. Mulder S, Meerding WJ, van Beeck EF. Setting priorities in injury prevention: the application of an incidence based cost model. *Injury Prevention.* 2002;8(1):74-78.
18. Mulder S, Blankendaal F, Vriend I, Schoots W, Bouter L. Epidemiological data and ranking home and leisure accidents for priority-setting. *Accid Anal Prev.* 2002;34(5):695-702.
19. Arreola-Risa C, Mock CN, Lojero-Wheatly L, et al. Low-Cost Improvements in Prehospital Trauma Care in a Latin American City. *Journal of Trauma and Acute Care Surgery.* 2000;48(1):119.
20. Mock CN, Jurkovich GJ, nii-Amon-Kotei D, Arreola-Risa C, Maier RV. Trauma mortality patterns in three nations at different economic levels: implications for global trauma system development. *J Trauma.* 1998;44(5):804-812; discussion 812-804.
21. Mock C. Improving prehospital trauma care in rural areas of low-income countries. In: LWW; 2003.

22. Husum H, Gilbert M, Wisborg T, Van Heng Y, Murad M. Rural prehospital trauma systems improve trauma outcome in low-income countries: a prospective study from North Iraq and Cambodia. *J Trauma.* 2003;54(6):1188-1196.
23. Liberman M, Mulder D, Sampalis J. Advanced or basic life support for trauma: meta-analysis and critical review of the literature. *Journal of Trauma and Acute Care Surgery.* 2000;49(4):584-599.
24. Lirola TT, Laaksonen MI, Vahlberg TJ, Pälve HK. Effect of physician-staffed helicopter emergency medical service on blunt trauma patient survival and prehospital care. *European Journal of Emergency Medicine.* 2006;13(6):335-339.
25. Garner AA. The role of physician staffing of helicopter emergency medical services in prehospital trauma response. *Emergency Medicine.* 2004;16(4):318-323.
26. Garner A, Rashford S, Lee A, Bartolacci R. Addition of physicians to paramedic helicopter services decreases blunt trauma mortality. *Australian and New Zealand journal of surgery.* 1999;69(10):697-701.
27. Bøtker MT, Bakke SA, Christensen EF. A systematic review of controlled studies: do physicians increase survival with prehospital treatment? *Scandinavian journal of trauma, resuscitation and emergency medicine.* 2009;17(1):12.
28. Osterwalder JJ. Mortality of blunt polytrauma: a comparison between emergency physicians and emergency medical technicians—prospective cohort study at a level I hospital in eastern Switzerland. *Journal of Trauma and Acute Care Surgery.* 2003;55(2):355-361.
29. Pakkanen T, Virkkunen I, Kämäräinen A, et al. Pre-hospital severe traumatic brain injury – comparison of outcome in paramedic versus physician staffed emergency medical services. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine.* 2016;24(1):62.
30. Fevang E, Lockey D, Thompson J, Lossius HM, Collaboration TTR. The top five research priorities in physician-provided pre-hospital critical care: a consensus report from a European research collaboration. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine.* 2011;19(1):57.
31. van der Velden MWA, Ringburg AN, Bergs EA, Steyerberg EW, Patka P, Schipper IB. Prehospital interventions: time wasted or time saved? An observational cohort study of management in initial trauma care. *Emergency Medicine Journal.* 2008;25(7):444-449.
32. Carr BG, Caplan JM, Pryor JP, Branas CC. A meta-analysis of prehospital care times for trauma. *Prehospital Emergency Care.* 2006;10(2):198-206.
33. Sampalis JS, Lavoie A, Salas M, Nikolis A, Williams JI. Determinants of on-scene time in injured patients treated by physicians at the site. *Prehospital and Disaster Medicine.* 1994;9(3):178-188.
34. Hedges JR, Feero S, Moore B, Shultz B, Haver DW. Factors contributing to paramedic onscene time during evaluation and management of blunt trauma. *The American journal of emergency medicine.* 1988;6(5):443-448.
35. Landelijk Netwerk Acute Zorg. *Traumazorg in beeld - landelijke traumaregistratie 2013-2017- rapportage Nederland.* Utrecht 2018.
36. Brown JB, Rosengart MR, Billiar TR, Peitzman AB, Sperry JL. Geographic distribution of trauma centers and injury-related mortality in the United States. *J Trauma Acute Care Surg.* 2016;80(1):42-49; discussion 49-50.
37. Hsia RY, Srebotnjak T, Maselli J, Crandall M, McCulloch C, Kellermann AL. The association of trauma center closures with increased inpatient mortality for injured patients. *The journal of trauma and acute care surgery.* 2014;76(4):1048-1054.
38. Branas CC, MacKenzie EJ, Williams JC, et al. Access to Trauma Centers in the United States. *JAMA.* 2005;293(21):2626-2633.

39. Keeves J, Ekegren CL, Beck B, Gabbe BJ. The relationship between geographic location and outcomes following injury: A scoping review. *Injury.* 2019.
40. Simon R, Stone M, Cucuzzo J. The Impact of a New Trauma Center on an Existing Nearby Trauma Center. *Journal of Trauma and Acute Care Surgery.* 2009;67(3):645-650.
41. Cole E, Lecky F, West A, Smith N, Brohi K, Davenport R. The Impact of a Pan-regional Inclusive Trauma System on Quality of Care. *Ann Surg.* 2016;264(1):188-194.
42. Carr BG, Geiger J, McWilliams N, Reilly PM, Wiebe DJ. Impact of adding Level II and III trauma centers on volume and disease severity at a nearby Level I trauma center. *Journal of Trauma and Acute Care Surgery.* 2014;77(5):764-768.
43. Taheri PA, Butz DA, Lottenberg L, Clawson A, Flint LM. The cost of trauma center readiness. *Am J Surg.* 2004;187(1):7-13.
44. van Rein EAJ, Jochems D, Lokerman RD, et al. Diagnostic value of emergency medical services provider judgement in the identification of head injuries among trauma patients. *European journal of neurology.* 2019;26(2):274-280.
45. Newgard CD, Nelson MJ, Kampp M, et al. Out-of-hospital decision making and factors influencing the regional distribution of injured patients in a trauma system. *The Journal of trauma.* 2011;70(6):1345-1353.
46. Voskens FJ, van Rein EAJ, van der Sluijs R, et al. Accuracy of Prehospital Triage in Selecting Severely Injured Trauma Patients. *JAMA surgery.* 2018;153(4):322-327.
47. van Rein EAJ, van der Sluijs R, Houwert RM, et al. Effectiveness of prehospital trauma triage systems in selecting severely injured patients: Is comparative analysis possible? *The American journal of emergency medicine.* 2018.
48. van der Sluijs R, Debray TPA, Poeze M, Leenen LPH, van Heijl M. Development and validation of a novel prediction model to identify patients in need of specialized trauma care during field triage: design and rationale of the GOAT study. *Diagn Progn Res.* 2019;3:12.
49. van Rein EAJ, van der Sluijs R, Voskens FJ, et al. Development and Validation of a Prediction Model for Prehospital Triage of Trauma Patients. *JAMA surgery.* 2019;154(5):421-429.
50. Bennett KM, Vaslef S, Pappas TN, Scarborough JE. The volume-outcomes relationship for United States Level I trauma centers. *J Surg Res.* 2011;167(1):19-23.
51. Brown JB, Rosengart MR, Kahn JM, et al. Impact of Volume Change Over Time on Trauma Mortality in the United States. *Ann Surg.* 2016.
52. Freeman J, Nicholl J, Turner J. Does size matter? The relationship between volume and outcome in the care of major trauma. *J Health Serv Res Policy.* 2006;11(2):101-105.
53. Nathens AB, Jurkovich GJ, Maier RV, et al. Relationship between trauma center volume and outcomes. *Jama.* 2001;285(9):1164-1171.
54. Minei JP, Fabian TC, Guffey DM, et al. Increased trauma center volume is associated with improved survival after severe injury: results of a Resuscitation Outcomes Consortium study. *Ann Surg.* 2014;260(3):456-464; discussion 464-455.
55. Caputo LM, Salottolo KM, Slone DS, Mains CW, Bar-Or D. The relationship between patient volume and mortality in American trauma centres: a systematic review of the evidence. *Injury.* 2014;45(3):478-486.
56. Demetriades D, Martin M, Salim A, Rhee P, Brown C, Chan L. The effect of trauma center designation and trauma volume on outcome in specific severe injuries. *Ann Surg.* 2005;242(4):512-517; discussion 517-519.

57. Celso B, Tepas J, Langland-Orban B, et al. A systematic review and meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems. *J Trauma.* 2006;60(2):371-378; discussion 378.
58. MacKenzie EJ, Rivara FP, Jurkovich GJ, et al. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med.* 2006;354(4):366-378.
59. Nguyen NT, Paya M, Stevens CM, Mavandadi S, Zainabadi K, Wilson SE. The relationship between hospital volume and outcome in bariatric surgery at academic medical centers. *Annals of surgery.* 2004;240(4):586-594.
60. Gooiker GA, van Gijn W, Wouters MW, et al. Systematic review and meta-analysis of the volume–outcome relationship in pancreatic surgery. *British Journal of Surgery.* 2011;98(4):485-494.
61. Billingsley KG, Morris AM, Dominitz JA, et al. Surgeon and hospital characteristics as predictors of major adverse outcomes following colon cancer surgery: understanding the volume-outcome relationship. *Archives of surgery.* 2007;142(1):23-31.
62. Chowdhury M, Dagash H, Pierro A. A systematic review of the impact of volume of surgery and specialization on patient outcome. *British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery.* 2007;94(2):145-161.
63. Sava J, Kennedy S, Jordan M, Wang D. Does volume matter? The effect of trauma surgeons' caseload on mortality. *J Trauma.* 2003;54(5):829-833; discussion 833-824.
64. Haut ER, Chang DC, Efron DT, Cornwell EEI. Injured Patients Have Lower Mortality When Treated by "Full-Time" Trauma Surgeons vs. Surgeons Who Cover Trauma "Part-Time". *Journal of Trauma and Acute Care Surgery.* 2006;61(2):272-279.
65. Piontek FA, Coscia R, Marselle CS, Korn RL, Zarling EJ. Impact of American College of Surgeons verification on trauma outcomes. *J Trauma.* 2003;54(6):1041-1046; discussion 1046-1047.
66. DiRusso S, Holly C, Kamath R, et al. Preparation and achievement of American College of Surgeons level I trauma verification raises hospital performance and improves patient outcome. *J Trauma.* 2001;51(2):294-299; discussion 299-300.
67. Calland JF, Stukenborg GJ. Trauma centre patient volume and inpatient mortality risk reconsidered. *Injury.* 2016;47(5):1072-1077.
68. Ursic C, Curtis K, Zou Y, Black D. Improved trauma patient outcomes after implementation of a dedicated trauma admitting service. *Injury.* 2009;40(1):99-103.
69. Davis KA, Cabbad NC, Schuster KM, et al. Trauma team oversight improves efficiency of care and augments clinical and economic outcomes. *Journal of Trauma and Acute Care Surgery.* 2008;65(6):1236-1244.
70. Nederlandse Vereniging voor Traumachirurgie. *Visiedocument 2016-2020.* Utrecht2016.
71. Holbrook TL, Anderson JP, Sieber WJ, Browner D, Hoyt DB. Outcome after major trauma: 12-month and 18-month follow-up results from the Trauma Recovery Project. *Journal of Trauma and Acute Care Surgery.* 1999;46(5):765-773.
72. Holbrook TL, Hoyt DB, Anderson JP. The importance of gender on outcome after major trauma: functional and psychologic outcomes in women versus men. *Journal of Trauma and Acute Care Surgery.* 2001;50(2):270-273.
73. Polinder S, van Beeck EF, Essink-Bot ML, et al. Functional outcome at 2.5, 5, 9, and 24 months after injury in the Netherlands. *Journal of Trauma and Acute Care Surgery.* 2007;62(1):133-141.
74. Holbrook TL, Hoyt DB, Anderson JP. The impact of major in-hospital complications on functional outcome and quality of life after trauma. *Journal of Trauma and Acute Care Surgery.* 2001;50(1):91-95.

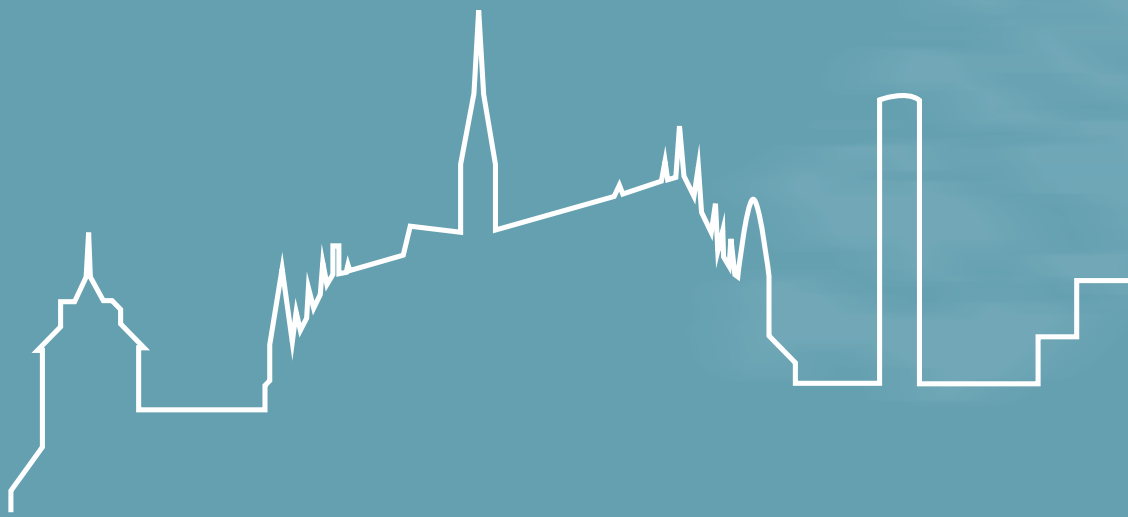
75. Kiely JM, Brasel KJ, Weidner KL, Guse CE, Weigelt JA. Predicting Quality of Life Six Months After Traumatic Injury. *Journal of Trauma and Acute Care Surgery.* 2006;61(4):791-798.
76. Vles WJ, Steyerberg EW, Essink-Bot ML, van Beeck EF, Meeuwis JD, Leenen LP. Prevalence and determinants of disabilities and return to work after major trauma. *J Trauma.* 2005;58(1):126-135.
77. Holtslag HR, Post MW, van der Werken C, Lindeman E. Return to work after major trauma. *Clin Rehabil.* 2007;21(4):373-383.
78. Livingston DH, Tripp T, Biggs C, Lavery RF. A fate worse than death? Long-term outcome of trauma patients admitted to the surgical intensive care unit. *J Trauma.* 2009;67(2):341-348; discussion 348-349.
79. Geurtsen GJ, van Heugten CM, Martina JD, Geurts ACH. Comprehensive Rehabilitation Programmes in the Chronic Phase after Severe Brain Injury: A Systematic Review. *Journal of Rehabilitation Medicine.* 2010;42(2):97-110.
80. Wiertsema SH, van Dongen JM, Geleijn E, et al. Evaluation of a new Transmural Trauma Care Model (TTCM) for the rehabilitation of trauma patients: a study protocol. *BMC Health Serv Res.* 2017;17(1):99-99.
81. Wiertsema SH, van Dongen JM, Geleijn E, et al. Cost-Effectiveness of the Transmural Trauma Care Model (TTCM) for the Rehabilitation of Trauma Patients. *Int J Technol Assess Health Care.* 2019;35(4):307-316.
82. Wu J, Faux SG, Harris I, Poulos CJ. Integration of trauma and rehabilitation services is the answer to more cost-effective care. *ANZ J Surg.* 2016;86(11):900-904.
83. Bouman AI, Hemmen B, Evers SM, et al. Effects of an Integrated 'Fast Track' Rehabilitation Service for Multi-Trauma Patients: A Non-Randomized Clinical Trial in the Netherlands. *PLoS One.* 2017;12(1):e0170047.
84. Mock C. WHO releases Guidelines for trauma quality improvement programmes. In: BMJ Publishing Group Ltd; 2009.
85. Zehtabchi S, Nishijima DK, McKay MP, Clay Mann N. Trauma registries: history, logistics, limitations, and contributions to emergency medicine research. *Academic Emergency Medicine.* 2011;18(6):637-643.
86. O'Reilly GM, Joshipura M, Cameron PA, Gruen R. Trauma registries in developing countries: a review of the published experience. *Injury.* 2013;44(6):713-721.
87. O'Reilly GM, Gabbe B, Moore L, Cameron PA. Classifying, measuring and improving the quality of data in trauma registries: A review of the literature. *Injury.* 2016;47(3):559-567.
88. Gabbe BJ, Simpson PM, Sutherland AM, et al. Functional measures at discharge: are they useful predictors of longer term outcomes for trauma registries? *Ann Surg.* 2008;247(5):854-859.
89. Williamson OD, Gabbe BJ, Sutherland AM, Wolfe R, Forbes AB, Cameron PA. Comparing the responsiveness of functional outcome assessment measures for trauma registries. *J Trauma.* 2011;71(1):63-68.
90. Rosenberg GM, Stave C, Spain DA, Weiser TG. Patient-reported outcomes in trauma: a scoping study of published research. *Trauma Surgery & Acute Care Open.* 2018;3(1):e000202.
91. Attenberger C, Amsler F, Gross T. Clinical evaluation of the Trauma Outcome Profile (TOP) in the longer-term follow-up of polytrauma patients. *Injury.* 2012;43(9):1566-1574.
92. Wanner JP, deRoon-Cassini T, Kodadek L, Brasel K. Development of a trauma-specific quality of life measurement. *The journal of trauma and acute care surgery.* 2015;79(2):275.
93. Rios-Diaz AJ, Herrera-Escobar JP, Lilley EJ, et al. Routine inclusion of long-term functional and patient-reported outcomes into trauma registries: The FORTE project. *Journal of Trauma and Acute Care Surgery.* 2017;83(1):97-104.

94. Bruce PJ, Helmer SD, Osland JS, Ammar AD. Operative volume in the new era: a comparison of resident operative volume before and after implementation of 80-hour work week restrictions. *Journal of surgical education.* 2010;67(6):412-416.
95. Ulmer C. Committee on Optimizing Graduate Medical Trainee (Resident) Hours and Work Schedules to Improve Patient Safety for the Institute of Medicine. *Resident duty hours: Enhancing sleep, supervision, and safety.* 2008.
96. Mackenzie CF, Tisherman SA, Shackelford S, Sevdalis N, Elster E, Bowyer MW. Efficacy of Trauma Surgery Technical Skills Training Courses. *Journal of Surgical Education.* 2019;76(3):832-843.
97. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr.* 2016;40(2):159-211.
98. Wischmeyer PE. Tailoring nutrition therapy to illness and recovery. *Critical care (London, England).* 2017;21(Suppl 3):316.
99. Rice TW, Wheeler AP, Thompson BT, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. *Jama.* 2012;307(8):795-803.
100. Braunschweig CA, Sheean PM, Peterson SJ, et al. Intensive nutrition in acute lung injury: a clinical trial (INTACT). *JPEN J Parenter Enteral Nutr.* 2015;39(1):13-20.
101. Arabi YM, Aldawood AS, Haddad SH, et al. Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults. *New England Journal of Medicine.* 2015;372(25):2398-2408.
102. Alberda C, Gramlich L, Jones N, et al. The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study. 2009;35(10):1728-1737.
103. Wischmeyer PE, Hasselmann M, Kummerlen C, et al. A randomized trial of supplemental parenteral nutrition in underweight and overweight critically ill patients: the TOP-UP pilot trial. *Critical care (London, England).* 2017;21(1):142.
104. Meijers JMM, van Bokhorst-de van der Schueren MAE, Schols JMGA, Soeters PB, Halfens RJG. Defining malnutrition: Mission or mission impossible? *Nutrition.* 2010;26(4):432-440.
105. Robinson MK, Mogensen KM, Casey JD, et al. The relationship among obesity, nutritional status, and mortality in the critically ill. *Critical care medicine.* 2015;43(1):87-100.
106. Jensen GL, Hsiao PY. Obesity in older adults: relationship to functional limitation. *Curr Opin Clin Nutr Metab Care.* 2010;13(1):46-51.
107. Kaidar-Person O, Person B, Szomstein S, Rosenthal RJ. Nutritional deficiencies in morbidly obese patients: a new form of malnutrition? Part B: minerals. *Obes Surg.* 2008;18(8):1028-1034.
108. Schweiger C, Weiss R, Berry E, Keidar A. Nutritional deficiencies in bariatric surgery candidates. *Obes Surg.* 2010;20(2):193-197.
109. Kaidar-Person O, Rosenthal RJ. Malnutrition in morbidly obese patients: fact or fiction? *Minerva Chir.* 2009;64(3):297-302.
110. Kaidar-Person O, Person B, Szomstein S, Rosenthal RJ. Nutritional deficiencies in morbidly obese patients: a new form of malnutrition? Part A: vitamins. *Obes Surg.* 2008;18(7):870-876.
111. Brown CVR, Neville AL, Rhee P, Salim A, Velmahos GC, Demetriades D. The Impact of Obesity on the Outcomes of 1,153 Critically Injured Blunt Trauma Patients. *Journal of Trauma and Acute Care Surgery.* 2005;59(5):1048-1051.
112. Liu T, Chen JJ, Bai XJ, Zheng GS, Gao W. The effect of obesity on outcomes in trauma patients: a meta-analysis. *Injury.* 2013;44(9):1145-1152.
113. Choi KM. Sarcopenia and sarcopenic obesity. *Korean J Intern Med.* 2016;31(6):1054-1060.

114. Sieber CC. Malnutrition and sarcopenia. *Aging Clin Exp Res.* 2019;31(6):793-798.
115. Barazzoni R, Bischoff S, Boirie Y, et al. Sarcopenic obesity: Time to meet the challenge. *Obesity facts.* 2018;11(4):294-305.
116. Montano-Loza AJ, Angulo P, Meza-Junco J, et al. Sarcopenic obesity and myosteatosis are associated with higher mortality in patients with cirrhosis. *J Cachexia Sarcopenia Muscle.* 2016;7(2):126-135.
117. Honda H, Qureshi AR, Axelsson J, et al. Obese sarcopenia in patients with end-stage renal disease is associated with inflammation and increased mortality. *Am J Clin Nutr.* 2007;86(3):633-638.
118. Prado CM, Lieffers JR, McCargar LJ, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *Lancet Oncol.* 2008;9(7):629-635.
119. White JV, Guenter P, Jensen G, Malone A, Schofield M. Consensus statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *JPEN J Parenter Enteral Nutr.* 2012;36(3):275-283.
120. Malone A, Hamilton C. The Academy of Nutrition and Dietetics/the American Society for Parenteral and Enteral Nutrition consensus malnutrition characteristics: application in practice. *Nutr Clin Pract.* 2013;28(6):639-650.
121. Mogensen KM, Malone A, Becker P, et al. Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition Consensus Malnutrition Characteristics: Usability and Association With Outcomes. *Nutr Clin Pract.* 2019;34(5):657-665.
122. Matos LC, Tavares MM, Amaral TF. Handgrip strength as a hospital admission nutritional risk screening method. *Eur J Clin Nutr.* 2007;61(9):1128-1135.
123. Flood A, Chung A, Parker H, Kearns V, O'Sullivan TA. The use of hand grip strength as a predictor of nutrition status in hospital patients. *Clin Nutr.* 2014;33(1):106-114.
124. Norman K, Stobaus N, Gonzalez MC, Schulzke JD, Pirlich M. Hand grip strength: outcome predictor and marker of nutritional status. *Clin Nutr.* 2011;30(2):135-142.
125. Khalil SF, Mohktar MS, Ibrahim F. The theory and fundamentals of bioimpedance analysis in clinical status monitoring and diagnosis of diseases. *Sensors (Basel).* 2014;14(6):10895-10928.
126. Barbosa-Silva MC, Barros AJ, Post CL, Waitzberg DL, Heymsfield SB. Can bioelectrical impedance analysis identify malnutrition in preoperative nutrition assessment? *Nutrition.* 2003;19(5):422-426.
127. Gupta D, Lis CG, Dahlk SL, et al. The relationship between bioelectrical impedance phase angle and subjective global assessment in advanced colorectal cancer. *Nutr J.* 2008;7:19.
128. Parent B, Seaton M, O'Keefe GE. Biochemical Markers of Nutrition Support in Critically Ill Trauma Victims. *JPEN J Parenter Enteral Nutr.* 2016.
129. Smith SH. Using albumin and prealbumin to assess nutritional status. *Nursing.* 2017;47(4):65-66.
130. Parent BA, Seaton M, Sood RF, et al. Use of Metabolomics to Trend Recovery and Therapy After Injury in Critically Ill Trauma Patients. *JAMA surgery.* 2016;151(7):e160853.
131. Mao H, Wang H, Wang B, et al. Systemic metabolic changes of traumatic critically ill patients revealed by an NMR-based metabonomic approach. *Journal of proteome research.* 2009;8(12):5423-5430.
132. Zivkovic AM, German JB. Metabolomics for assessment of nutritional status. *Curr Opin Clin Nutr Metab Care.* 2009;12(5):501-507.
133. Lee R, West D, Phillips SM, Britz-McKibbin P. Differential Metabolomics for Quantitative Assessment of Oxidative Stress with Strenuous Exercise and Nutritional Intervention: Thiol-Specific

Regulation of Cellular Metabolism with N-Acetyl-l-Cysteine Pretreatment. *Analytical Chemistry.* 2010;82(7):2959-2968.

134. Abbondante S, Eckel-Mahan KL, Ceglia NJ, Baldi P, Sassone-Corsi P. Comparative Circadian Metabolomics Reveal Differential Effects of Nutritional Challenge in the Serum and Liver. *Journal of Biological Chemistry.* 2016;291(6):2812-2828.
135. Christopher KB. Nutritional metabolomics in critical illness. *Curr Opin Clin Nutr Metab Care.* 2018;21(2):121-125.
136. Bear DE, Griffith D, Puthucheary ZA. Emerging outcome measures for nutrition trials in the critically ill. *Curr Opin Clin Nutr Metab Care.* 2018;21(6):417-422.
137. de Vries MC, Koekkoek WK, Opdam MH, van Blokland D, van Zanten AR. Nutritional assessment of critically ill patients: validation of the modified NUTRIC score. *Eur J Clin Nutr.* 2018;72(3):428-435.
138. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Critical care (London, England).* 2011;15(6):R268.
139. Mendes R, Policarpo S, Fortuna P, Alves M, Virella D, Heyland DK. Nutritional risk assessment and cultural validation of the modified NUTRIC score in critically ill patients-A multicenter prospective cohort study. *Journal of critical care.* 2017;37:45-49.



11

Summary

Annually around 5 million people die as a consequence of injuries and many more suffer from livelong disabilities. Although implementation of trauma care systems and structured trauma training has led to decreased mortality and disability in several countries, controversies remain to exist. The awareness of the current trauma burden and its expected increase has led to new initiatives for scientific research in an attempt to eventually improve trauma care worldwide. Despite the improvements there is room for further optimization of care. The primary aim of this thesis was to analyze the presence and structure of trauma systems, evaluate specific care-delivery processes, and focus on patient-centered and clinically important parameters and outcomes. The second aim is to evaluate one of these parameters, the role of the nutritional status in the outcome of polytrauma patients.

In **chapter 1** the historic development of trauma systems and the trauma system in the Netherlands is discussed. In addition, background information about malnutrition in polytrauma patients is described.

Chapter 2 gives an overview of the recent literature on the state of trauma systems globally. Despite the presence of seemingly sufficient resources and the evidence-based benefits of trauma systems, only nine of the 23 high-income countries in this review had a well-defined and documented national trauma system according to the identified studies. Although 90% of all lethal traumatic injuries occur in middle and low income countries, according to the literature, to which our study is limited to, only few of these countries hold a formal trauma system and/or trauma registry. Much improvement in the trauma systems in these countries might be achieved, but unfortunately the economic situation of many countries may render trauma systems not at their top priority list.

The review showed that there are still many differences in trauma care worldwide. By studying these differences, factors of influence on outcome of care may be identified. **Chapters 3** and **4** describe the differences in patient characteristics, outcomes and processes of trauma care between the Netherlands and the United States. **Chapter 3** discusses the characteristics and outcomes of 1367 blunt polytrauma patients (Injury Severity Score≥16) admitted to a level I trauma center in the US (USTC) or in the Netherlands (NLTC). Although several outcome parameters differed between the two urban area trauma centers in the USA and the Netherlands, such as a higher injury severity and more comorbidity in the USTC patients, the in-hospital survival of the trauma patients in these trauma centers was similar. Other outcome parameters, such as the length of stay in hospital and in the Intensive Care Unit, varied between the trauma centers, suggesting that differences in local policies and processes do influence the care system, but not so much the outcome of care as reflected by in-hospital mortality. Similar results were seen in the study described in **chapter 4**, on the characteristics and clinical outcomes of 1331 patients with penetrating injuries treated at urban Level-1 trauma centers in the USA (USTC) or the Netherlands (NLTC). Despite the higher incidence of penetrating trauma,

particularly firearm-related injuries, and higher hospital volumes in the USTC compared to the NLTC, the in-hospital mortality was similar. In this study, outcome of care was not significantly influenced by differences in incidence of firearm-related injuries.

Since the introduction of trauma systems in the Netherlands, the trade-off between centralization of care with sufficient hospital volumes on one hand and adequate trauma center access in terms of transport times and population coverage by means of more but smaller centers on the other hand is an important but complex issue. **Chapter 5** discusses the use of geographical information system (GIS) technology as a potential methodology for objectifying trauma access. The goal of this study was to determine the influence of trauma center distribution (the number and geographical location) during high and low traffic flow in a densely-populated region with 3 trauma centers in the Netherlands using GIS-technology. Not only was the current three trauma center scenario analyzed, but also six other scenarios with a varying number of trauma centers on different locations. This study showed that a GIS-model for trauma center access offered a quantifiable and objective method to evaluate trauma system distribution in areas with different geography and demography. Applying this technology to one of the most densely populated areas in the Netherlands shows that the transport time from accident to trauma center would remain acceptable if the current situation with three trauma centers would be changed to a scenario with two geographically well-spread trauma centers.

In 1998, after years of discussion, an inclusive trauma system was implemented in the Netherlands. The objective of the study, described in **chapter 6**, was to evaluate the impact of structured trauma care on the concentration of polytrauma patients over time in the Netherlands. This study shows that over the past 20 years trauma care has been progressively centralized, with more polytrauma patients primarily being brought to a trauma center. During the entire study period, the patients primarily brought to a trauma center were more severely injured, reflected by a higher median Injury Severity Score and higher median total Abbreviated Injury Score than the patients that were primarily brought to a non-trauma center. However, despite the well-organized Dutch EMS system, still roughly 30% of the polytrauma patients were primarily brought to a non-trauma center, indicating a need for improving pre-hospital triage.

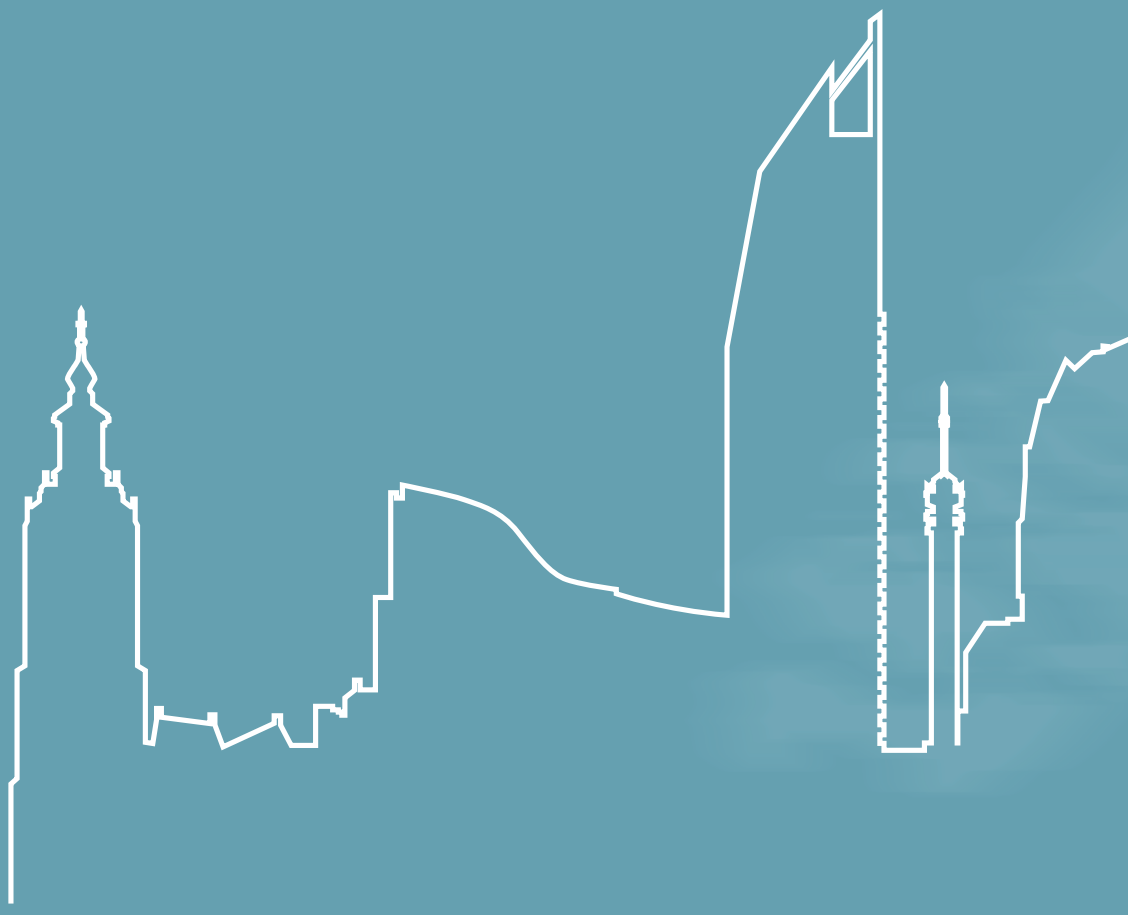
The second part of this thesis focuses on the individualized care of polytrauma patients and more specifically on the role of malnutrition in severely injured patients admitted to the intensive care unit (ICU). **Chapter 7** gives an overview of the current knowledge about the pathophysiology, prevalence, and effects of malnutrition in severely injured patients. This review showed that despite the widespread belief about the importance of nutrition in severely injured patients, the quantity and quality of available evidence is sparse, mainly of low-quality, and outdated. Based on the malnutrition-associated

adverse outcomes, the nutritional status of severely injured trauma patients should be routinely and carefully monitored.

Malnutrition is associated with, but not only due to, calorie and protein deficits. It is customary to initiate enteral nutrition at a low rate and slowly increase the delivery rate to goal rate (RAMP-UP-protocol). Increasing evidence suggests that RAMP-UP may contribute to iatrogenic malnutrition. In **chapter 8** it was determined which proportion of total Surgical Intensive Care Unit calorie/protein deficit is attributable to RAMP-UP. In Surgical Intensive Care Unit patients initiating enteral nutrition, the RAMP-UP period accounted for 41% and 53% of the overall caloric and protein deficits, respectively. Starting enteral nutrition immediately at goal rate may therefore prevent a significant proportion of macronutrient deficit in the SICU.

It seems that polytrauma patients are at risk of considerable harm from malnutrition due to the metabolic response to trauma. However, little is known about (the risk of) malnutrition and its consequences in these patients. Recognition and acknowledgment of sub-optimally nourished polytrauma patients and their nutritional needs is crucial to prevent complications and optimize their clinical outcomes. Therefore, the trauma department of the LUMC initiated a multicenter international observational prospective cohort study. This Malnutrition in Polytrauma Patient (MaPP) study aims to gain more insight into the effect and consequences of malnutrition in polytrauma patients admitted to the ICU. The research protocol of the study is described in **chapter 9.** The objective is to investigate whether polytrauma patients admitted to the Intensive Care Unit, who are already malnourished before admission or develop malnutrition during admission, have a higher complication rate than patients who are and remain well-nourished. This study is performed at three Level-1 trauma centers in the United States and two Level-1 trauma centers in the Netherlands.

The general discussion in **chapter 10** presents an overview of issues that remain to be studied and future perspectives both on the organization of trauma care worldwide as well as malnutrition in polytrauma patients. Although substantial improvements were seen in the care for the injured in the past few decades, there are still many opportunities for improvement. In the future, we need to further focus on the continuum of trauma care, recognizing that strengthening each element of the trauma care chain improves outcomes for the severely injured patient. Malnutrition is still an underestimated problem in the polytrauma patient population, especially severely injured patients who are particularly susceptible to malnutrition and its related complications. New studies should focus on better defining the optimal nutritional treatment of severely injured patients. However, standardized data dictionaries and reasonable outcome measures are required for meaningful interpretation and application of results in malnutrition related research.



12

Samenvatting

Elk jaar sterven ongeveer 5 miljoen mensen als gevolg van ongevallen. Een aanzienlijk deel van deze ongeval slachtoffers krijgt te maken met levenslange invaliditeit in verschillende gradaties van ernst. De implementatie van traumasystemen en gestructureerde opleidingen binnen de traumazorg hebben geleid tot lagere sterfte en minder invaliditeit. Deze kennis in combinatie met de te verwachten groei in het aantal slachtoffers van ongevallen heeft geleid tot nieuwe wetenschappelijke initiatieven wereldwijd ter verbetering van de traumazorg. Ondanks de gemaakte vorderingen is verdere verbetering mogelijk.

Het primaire doel van dit proefschrift is het analyseren van de aanwezigheid en structuur van traumasystemen, specifieke zorgverleningsprocessen en hiermee gerelateerde belangrijke patiëntgerichte en klinische parameters en uitkomsten. Het secundaire doel is om een van deze parameters verder uit te lichten en te evalueren, namelijk de rol en het effect van de voedingsstatus op de uitkomsten van polytrauma patiënten

In **hoofdstuk 1** wordt als introductie de historische ontwikkeling van traumasystemen wereldwijd en in Nederland besproken. Tevens wordt de rol van ondervoeding bij traumapatiënten nader toegelicht.

Hoofdstuk 2 geeft een overzicht van de recente literatuur over de status van traumasystemen wereldwijd. Ondanks de aanwezigheid van ogenschijnlijk voldoende middelen en de bewezen voordelen van traumasystemen, hadden slechts negen van de drieëntwintig landen met een hoog- inkomen volgens de studies in deze review een goed gedefinieerd en gedocumenteerd nationaal traumasysteem. Hoewel 90% van alle dodelijke traumatische ongevallen plaatsvindt in midden- en laag- inkomen landen, is, volgens de beschikbare literatuur, slechts in een beperkt aantal van deze landen een formeel traumasysteem en/of een traumaregistratie aanwezig. Vooral in deze landen kan nog veel verbetering in de traumazorg worden gerealiseerd op het gebied van prehospitale zorg, intramurale organisatie, scholing en registratie.

Uit de literatuurstudie in **hoofdstuk 2** bleek dat, ondanks internationaal geaccepteerde standaarden, er nog veel verschillen zijn in de organisatie van traumazorg wereldwijd. Door deze verschillen te herkennen en erkennen, kunnen mogelijke factoren van invloed op de uitkomst geïdentificeerd worden. In de **hoofdstukken 3 en 4** zijn de verschillen in patiëntkarakteristieken, organisatie van traumazorg en uitkomsten van trauma patiënten in Nederland en de Verenigde Staten bestudeerd. **Hoofdstuk 3** bespreekt de kenmerken en uitkomsten van 1367 polytrauma patiënten (Injury Severity Score ≥ 16) met stomp letsel die zijn opgenomen in stedelijk gelegen level 1-traumacentra in de VS (USTC) en in Nederland(NLTC). Hoewel de uitkomsten van meerdere parameters verschilden tussen de twee traumacentra in de VS en Nederland, zoals een hogere letselernst en meer comorbiditeit bij de USTC-patiënten, was de ziekenhuismortaliteit bij de traumapatiënten in de traumacentra gelijk. De variatie in de andere uitkomsten, zoals duur van ziekenhuis- en intensive care opname, suggereert dat verschillen in

lokaal beleid en zorgprocessen invloed hebben op het zorgsysteem, maar niet zozeer op de uitkomst van zorg zoals weerspiegeld in de ziekenhuismortaliteit. Vergelijkbare resultaten werden gezien in **hoofdstuk 4** waarin een studie naar de patiëntkarakteristieken en uitkomsten van 1331 patiënten met penetrerend letsel die werden behandeld in stedelijk gelegen level-1 traumacentra in de VS (USTC) en Nederland (NLTC), wordt beschreven. Ondanks de hogere volume van penetrerend letsel, met name schotwonden, en de hogere ziekenhuisvolumes in de USTC's in vergelijking tot de NLTC's, was de ziekenhuismortaliteit in beiden landen vergelijkbaar.

Sinds de introductie van traumasystemen in Nederland is de afweging tussen centralisatie van zorg door grotere traumacentra met hogere patiëntvolumes enerzijds en een goede bereikbaarheid van traumacentra voor de bevolking middels meer maar kleinere traumacentra een belangrijke maar lastige discussie. In **hoofdstuk 5** wordt het gebruik van geografische informatie systeem(GIS) technologie als een potentiële methode voor het evalueren van de bereikbaarheid van traumacentra besproken. Het doel van deze studie was het evalueren van de invloed van de verkeersdrukte en geografische ligging van drie traumacentra in de Traumaregio West op de aanrijtijden naar het dichtstbijzijnde traumacentrum op basis van gegevens verkregen met GIS-technologie. Hierbij werden naast de huidige situatie, de drie traumacentra, zes andere scenario's geanalyseerd met een verschillend aantal traumacentra op verschillende locaties. Deze studie liet zien dat de op GIS-technologie gebaseerde analyse een manier biedt om de toegankelijkheid van de traumasystemen in verschillende omstandigheden, zoals wisselende verkeersdrukte en mogelijke structurele traumasysteemwijzigingen, zoals geografische TC-spreiding, te objectiveren. In de geanalyseerde traumaregio zijn de aanrijtijden naar het dichtstbijzijnde traumacentrum acceptabel in het huidige 3-traumacentrum-scenario en zouden dat blijven indien gekozen werd voor een 2-traumacentrum-scenario met goede geografische spreiding van deze centra.

In 1998 werd er, na jaren van discussie, in Nederland een inclusief traumasysteem ingevoerd. In **hoofdstuk 6** wordt de evaluatie van de impact van gestructureerde traumazorg op de concentratie van polytrauma patiënten over de afgelopen 20 jaar beschreven. In de afgelopen 20 jaar is de traumazorg in Nederland geleidelijk gecentraliseerd, waarbij steeds meer polytrauma patiënten primair naar een trauma centrum werden gebracht. Gedurende de gehele onderzoeksperiode waren de patiënten die primair naar een traumacentrum werden gebracht, zwaarder gewond, weergegeven door een hogere mediane ISS en een hogere mediane totale AIS, dan de patiënten die primair naar een niet-traumacentrum werden gebracht. Ondanks het goed georganiseerde Nederlandse ambulance systeem werd echter nog steeds ongeveer 30% van de polytrauma patiënten primair naar een niet-traumacentrum gebracht, wat aangeeft dat er behoefte is aan verbetering van de prehospitale triage in het veld.

Het tweede deel van dit proefschrift richt zich op individuele traumazorg en meer specifiek op de rol van ondervoeding bij ernstig gewonde patiënten die werden opgenomen op de intensive care. **Hoofdstuk 7** geeft een overzicht van de huidige kennis over de pathofysiologie, prevalentie en effecten van ondervoeding bij ernstig gewonde patiënten. Dit literatuuroverzicht laat zien dat, ondanks de wijdverbreide overtuiging dat een goede voedingsstatus essentieel is voor een goed herstel van ernstig gewonde patiënten, de kwantiteit en kwaliteit van beschikbare literatuur over dit onderwerp schaars, grotendeels van lage kwaliteit en verouderd is. Gezien de vele met ondervoeding geassocieerde complicaties, met name voor traumapatiënten, is het van belang de voedingsstatus van ernstig gewonde traumapatiënten routinematig en zorgvuldig te monitoren.

Ondervoeding is geassocieerd met, maar niet alleen ten gevolge van, calorie- en eiwittekorten. In de klinische praktijk is het gebruikelijk om enterale voeding met een lage toedieningssnelheid te initiëren en deze vervolgens langzaam te verhogen tot doelsnelheid (RAMP-UP- protocol). Toenemend bewijs suggereert dat RAMP-UP kan bijdragen aan iatrogene ondervoeding. In **hoofdstuk 8** is geprobeerd om te bepalen welk deel van het totale calorie- en eiwittekort ten tijde van een opname op de Surgical Intensive Care Unit (SICU) kan worden toegeschreven aan RAMP-UP. Bij SICU-patiënten waarbij enterale voeding was gestart, droeg de RAMP-UP-periode bij aan respectievelijk 41% en 53% van de totale calorie- en eiwittekorten. Indien de RAMP-UP periode wordt overgeslagen en enterale voeding direct volgens behoefte wordt gegeven, kan een aanzienlijk deel van het tekort aan macronutriënten verkregen tijdens de SICU-opname, worden voorkomen.

De literatuur suggereert dat polytrauma patiënten een hoger risico hebben op het ontwikkelen van ondervoeding als gevolg van de metabole reactie op letsel. Er is echter weinig kennis over zowel het risico op als de gevolgen van ondervoeding voor deze patiënten. Herkennen en erkennen van een suboptimale voedingsstatus bij polytrauma patiënten en hun hogere voedingsbehoeften is cruciaal om complicaties te voorkomen en hun klinische uitkomsten te optimaliseren. Daarom is door de afdeling Traumachirurgie van het LUMC een internationale multicenter observationele prospectieve cohortstudie geïnitieerd. Deze Manutrition in Polytrauma Patient (MaPP) -studie heeft als doel te evalueren of polytrauma patiënten die op de intensive care unit zijn opgenomen en die dan wel bij opname al ondervoed zijn dan wel ondervoeding ontwikkelen gedurende opname, meer complicaties hebben dan patiënten die een goede voedingsstatus hebben en deze ook behouden gedurende opname. Het onderzoeksprotocol van deze studie wordt beschreven in **hoofdstuk 9.** In de studie wordt onderzocht of Dit onderzoek wordt uitgevoerd in drie level-1 traumacentra in de Verenigde Staten en twee level-1 traumacentra in Nederland.

In de algemene discussie van het proefschrift (**hoofdstuk 10**) worden de resultaten uit alle hoofdstukken van dit proefschrift en toekomstperspectieven besproken. Hoewel in de afgelopen decennia grote verbeteringen zijn gerealiseerd in de zorg voor traumapatiënten, zijn er nog veel mogelijkheden voor verdere optimalisatie van de zorg en zorgprocessen. In de toekomst moet er verder geconcentreerd worden op het verbeteren van de ketenzorg bij de ernstig gewonde patiënt, waarbij het van belang is om elk element van de traumaketen te optimaliseren om zo de uitkomsten voor traumapatiënten verder te verbeteren. Ondervoeding is een onderschat probleem in de traumapopulatie, vooral omdat deze bijzonder vatbaar is voor ondervoeding en de bijbehorende complicaties. Nieuwe studies moeten gericht zijn op het beter definiëren van de optimale voedingsstatus van ernstig gewonde patiënten. Gestandaardiseerde datasets en universeel gedefinieerde klinisch relevante uitkomstmaten zijn echter vereist voor een zinvolle interpretatie en toepassing van de resultaten van nieuwe en internationale studies wat betreft ondervoeding.

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Curriculum Vitae

Suzan Dijkink was born on July 25, 1992 in Hengelo (Ov.) and grew up in Markelo. After graduating cum laude from her secondary school "De Waerdenborch" in Holten, she started her medical studies at Leiden University in 2010.

Suzan completed her Bachelor's degree in medicine in three years. In 2012, after her second year, she went to New York City, United States of America, for three months to participate in a clinical internship at the Department of Bariatric Surgery at the New York Presbyterian Hospital / Weill Cornell Medical Center under supervision of Dr. Alfons Pomp. After completing her bachelor's degree in 2013, she spent three months in Berlin where she combined a clinical internship with a scientific internship at the neurosurgery department of the Charité Hospital in Berlin. In addition to her studies, Suzan has completed the "Bachelor's Honors College Medicine" and the "Leiden Leadership Program", part of the Leiden University's Honors Program. She was also an active member of the student association L.V.V.S. Augustinus and participated in various committees of the Medical Faculty for Leiden Students.

Before starting her clinical rotations, Suzan completed her LUMC scientific internship at the Division of Trauma, Emergency Surgery and Surgical Critical Care Department at Massachusetts General Hospital(MGH) / Harvard Medical School in Boston. During the seven months she spent in Boston, she worked on several studies about the organization of trauma care and the outcomes of polytrauma patients. After her return to the Netherlands, she continued her research during her clinical rotations under the supervision of Prof. Dr. I.B. Schipper. This ultimately resulted in an MD / PhD scholarship. After her graduation in 2017, Suzan started as a fulltime PhD student at the LUMC with Prof. Dr. I.B. Schipper (LUMC) and Prof. Dr. G.C. Velmahos (MGH) as her primary thesis advisors. She had the opportunity to present her studies at several national and international conferences, such as the Trauma- and Chirurgendagen, the European Congress of Trauma and Emergency Surgery, the American College of Surgeons Clinical Congress and at the American Association for the Surgery of Trauma.

After working for two years in the LUMC Trauma Research Group, she returned in September 2019 to Boston to complete several studies. In January 2020 she started as a surgical resident not in training (ANIOS) at the Haaglanden Medical Center in The Hague.

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List of publications,
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PUBLICATIONS

Dijkink S. Winchell RJ, Krijnen P, Schipper IB. Quantification of trauma center accessibility using GIS-based technology. *Value in Health. 2020; 23(8):1020–1026*

Nejad S, Nisavic M, Larentzakis A, **Dijkink S**, Chang Y, Levin AR, DeMoya M, Velmahos GC. Phenobarbital for Acute Alcohol Withdrawal Management in Surgical Trauma Patients – A Retrospective Comparison Study, *Psychosomatics. 2020;61(4):327-335.*

Dijkink S, Meier K, Krijnen P, Yeh DD, Velmahos GC, Schipper IB. The effect of malnutrition in polytrauma patients: a systematic review. *European Journal of Trauma and Emergency Surgery*. 2020 Jan 23.

Dijkink S, Meier K, Krijnen P, Yeh DD, Velmahos GC, Arbous MS, Salim A, Hoogendoorn JM, Schipper IB. Malnutrition in Polytrauma Patients (MaPP) Study: Research Protocol. *Nutrition and Health. 2019 Dec;25(4):291-301.*

Chesser TJS, Moran C, Willett K, Bouillon B, Sturm J, Flohé S, Rucholtz S, **Dijkink S**, Schipper IB, Rubio-Suarez JC, Chana F, De Caso J, Guerado E. Development of Trauma Systems in Europe – reports from England, Netherlands, Germany and Spain. *International Orthopaedic Trauma Association (2019) e019.*

Dijkink S, Krijnen P, Hage A, Van der Wilden GM, Kasotakis G, Den Hartog D, Salim A, Goslings JC, Bloemers FW, Rhemrev S, King DR, Velmahos GC, Schipper IB. Differences in characteristics and outcome of patients with penetrating injuries in the U.S. and the Netherlands: A multi-institutional comparison. *World Journal of Surgery. 2018 Nov;42(11):3608-3615.*

Dijkink S, Van der Wilden GM, Krijnen P, Dol L, Rhemrev S, King DR, DeMoya MA, Velmahos GC, Schipper IB. Polytrauma patients in the Netherlands and the USA: A bi-institutional comparison of processes and outcomes of care. *Injury. 2018 Jan;49(1):104-109.*

Dijkink S, Krijnen P, Schipper IB. Re: Trauma systems around the world: A systematic overview. *Journal of Trauma and Acute Care Surgery. 2018 Sep;85(3):649-650.*

Dijkink S, Nederpelt CJ, Krijnen P, Velmahos GC, Schipper IB. Trauma systems around the world: a systematic overview. *Journal of Trauma and Acute Care Surg. 2017 Nov;83(5):917-925.*

Yeh DD, Nazarian RM, Demetri L, Mesar T, **Dijkink S**, Larentzakis A, Velmahos GC, Sadik KW. The effect of OASIS Ultra on critical sized wound healing: a pilot study. *Journal of Cutaneous Pathology. 2017 Jun;44(6):523-529*.

Dijkink S, Fuentes E, Quraishi SA, Cropano C, Kaafarani HM, Lee J, King DR, DeMoya M, Fagenholz P, Butler K, Velmahos G, Yeh DD. Nutrition in the Surgical Intensive Care Unit: The Cost of Starting Low and Ramping Up Rates. *Nutrition in Clinical Practice*. 2016 Feb;31(1):86-90.

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Dijkink S. Winchell RJ, Krijnen P, Schipper IB. Identifying objective measures to assess trauma center access using GIS-based methodology. *Poster presentation Annual Meeting of the Dutch Trauma Society 2019, November 28-29, Amsterdam, The Netherlands*

Dijkink S. Winchell RJ, Krijnen P, Schipper IB. Identifying objective measures to assess trauma center access using GIS-based methodology. *Quickshot oral presentation, 78th Annual meeting American Association for the Surgery of Trauma 2019, 18-21 September, Dallas, TX, US*

Dijkink S. Winchell RJ, Krijnen P, Schipper IB. Identifying objective measures to assess trauma center access using GIS-based methodology. *Oral presentation Annual Meeting of the Dutch Surgical Society 2019, 16-17 may, Veldhoven, The Netherlands*

Dijkink S. Winchell RJ, Krijnen P, Schipper IB. Identifying objective measures to assess trauma center access using GIS-based methodology. *Poster presentation, 20th European Congress of Trauma & Emergency 2019, May 5-7, Prague, Czech Republic*

Dijkink S, Meier K, Krijnen P, Yeh DD, Velmahos GC, Schipper IB**.** The effect of malnutrition in polytrauma patients: a systematic review. *Poster presentation 20th European Congress of Trauma & Emergency 2019, May 5-7, Prague, Czech Republic*

Dijkink S. Winchell RJ, Krijnen P, Schipper IB**.** Identifying objective measures to assess trauma center access using GIS-based methodology *Oral presentation, Resident Symposium, Dutch Trauma Society 2019, January 25, Amersfoort, The Netherlands*

Dijkink S, Meier K, Krijnen P, Yeh DD, Velmahos GC, Schipper IB. The effect of malnutrition in polytrauma patients: a systematic review. *Oral presentation, Resident Symposium, Dutch Trauma Society 2019, January 25, Amersfoort, The Netherlands*

Dijkink S. Malnutrition and the metabolic response in severely injured trauma patients: a vicious circle. *Keynote lecture, Annual Meeting of the Dutch Trauma Society 2018, November 22-23, Amsterdam, The Netherlands*

Dijkink S, Meier K, Krijnen P, Yeh DD, Velmahos GC, Schipper IB. The effect of malnutrition in polytrauma patients: a systematic review. *Poster presentation, Annual Meeting of the Dutch Trauma Society 2018, November 22-23, Amsterdam, The Netherlands*

Dijkink S. Trauma systems in the Netherlands. *Keynote lecture. Surgical Intensive Care Unit Talks, Massachusetts General Hospital/Harvard Medical School, October 31 2018, Boston, MA, United States of America*

Dijkink S, Meier K, Krijnen P, Yeh DD, Velmahos GC, Schipper IB**.** The effect of malnutrition in polytrauma patients: a systematic review. *Quick shot presentation, 104th Annual American College of Surgeons Clinical Congress 2018, October 21-25, Boston, MA, United States of America.*

Dijkink S, Meier K, Krijnen P, Yeh DD, Velmahos GC, Schipper IB**.** The effect of malnutrition in polytrauma patients: a systematic review. *Oral presentation, Annual Meeting of the Dutch Surgical Society 2018, May 24-25, Veldhoven, The Netherlands*

Dijkink S, Krijnen P, Hage A, Van der Wilden GM, Kasotakis G, Den Hartog D, Salim A, Goslings JC, Bloemers FW, Rhemrev S, King DR, Velmahos GC, Schipper IB. Differences in acute treatment and outcome of patients with penetrating injuries in the Netherlands and the USA: A multi-institutional comparison. *Oral presentation, Annual Meeting of the Dutch Surgical Society 2018, May 24-25, Veldhoven, The Netherlands*

Dijkink S. Career path of a young researcher: from medical student to PhD. *Oral presentation European Summer School for Emergency and Trauma Surgery (ESSETS), July 16-19 2018, Leiden, The Netherlands*

Dijkink S, Nederpelt CJ, Krijnen P, Velmahos GC, Schipper IB**.** Trauma systems around the world: a systematic review. *Oral presentation ATLS symposium, 19th European Congress of Trauma & Emergency 2018, May 6-8, Valencia, Spain*

Dijkink S, Nederpelt CJ, Krijnen P, Velmahos GC, Schipper IB**.** Trauma systems around the world: a systematic review. *Oral presentation, Annual Meeting of the Dutch Trauma Society 2017, november 30 - 1 december, Amsterdam, The Netherlands*

Dijkink S, Nederpelt CJ, Krijnen P, Velmahos GC, Schipper IB**.** Trauma systems around the world: a systematic review. *Oral presentation 18th European Congress of Trauma & Emergency 2017,May 7-9, Bucharest, Romania*

Dijkink S, Krijnen P, Hage A, Van der Wilden GM, Kasotakis G, Den Hartog D, Salim A, Goslings JC, Bloemers FW, Rhemrev S, King DR, Velmahos GC, Schipper IB. Differences in acute treatment and outcome of patients with penetrating injuries in the Netherlands

and the USA: A multi-institutional comparison. *Oral presentation 18th European Congress of Trauma & Emergency 2017, May7-9, Bucharest, Romania*

Dijkink S, Van der Wilden GM, Krijnen P, Dol L, Rhemrev S, King DR, DeMoya MA, Velmahos GC, Schipper IB**.** Polytrauma patients in the Netherlands and the USA: A bi-institutional comparison of processes and outcomes of care. *Oral presentation 17th European Congress of Trauma & Emergency Surgery 2016, April 24-26, Vienna, Austria.*

Dijkink S, Fuentes E, Quraishi SA, Cropano C, Kaafarani HM, Lee J, King DR, DeMoya M, Fagenholz P, Butler K, Velmahos G, Yeh DD. Nutrition in the Surgical Intensive Care Unit: The Cost of Starting Low and Ramping Up Rates. *Poster presentation 16th European Congress of Trauma & Emergency Surgery 2015, May 10-12, Amsterdam, The Netherlands*

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Acknowledgements

To start with a cliché, a very important one nevertheless, finishing a PhD is not something you can achieve on your own. There are many people I would love to thank. Most importantly, a big thank you to all the patients, and their loved ones, who were willing to participate in our MaPP-study during these difficult and uncertain times to help future severely injured patients.

Dear Prof. Schipper, Dear Inger, I am very grateful that you initially saw the potential in me after finishing my scientific internship, prior to my PhD. You have been and remain a big inspiration, a female professor in Trauma surgery, even in this day-in-age is something special and I am very honored to work under your supervision.

Dear Prof. Velmahos, Dear George, it has been a great honor working with you over the past few years. Your passion for trauma surgery, your ability to make everyone feel included in the team, but most importantly, your sincere interest in everyone around you is what makes you a great inspiration to me.

Dear Dr. Krijnen, Dear Pieta, the spider in the web of the trauma surgery department, the one who keeps everyone together. Your extensive suggestions for projects, your willingness to always discuss papers but mostly the random small talks about almost anything are very much appreciated.

Members of the PhD committee, Prof. Aarts, Prof. Leenen, Prof. Goslings, Dr. Arbous, Dr. Yeh and Prof. De Jonge, thank you for your genuine interest in this thesis and the willingness to take a seat in the committee.

Geachte dr. Arbous, Beste Sesmu, en **alle medewerkers van de IC van het LUMC**, dank voor jullie inzet, jullie enthousiasme en bereidheid mee te helpen met de MaPP-studie. Het heeft soms wat voeten in de aarde gehad, maar samen hebben we een mooi aantal patiënten kunnen includeren!

Geachte Dr. Peters, Beste Ron, **beste Femke** en **alle medewerkers van de IC in het HMC**, dank voor jullie tomeloze inzet en enthousiasme voor de MaPP-studie. Zonder jullie inzet, alertheid en doorzettingsvermogen was het niet gelukt zoveel patiënten te includeren!

Geachte dr. Hoogendoorn, beste Jochem en iedereen van de **afdeling trauma chirurgie van het HMC** vanaf het begin betrokken bij de MaPP-studie en altijd bereid mee te denken over hoe we de studie nog meer onder de aandacht konden brengen. Dank voor het vertrouwen en de steun.

Dear Dr. Yeh, Dear Dante, it is amazing to see what you have built since we met. From finding your own niche in trauma research, to being the chair of the Nutritional Support Department and having your own research group. Your never-ending enthusiasm, your great help in writing my thesis and your ability to keep doing fun things beside your crazy work schedule is astonishing.

Dear dr. Winchell, Dear Robert, it has been a great honor for me to work with you on our trauma system projects. It is impressive to see how you combine your work in the clinic, research and for the ACS altogether.

Dear dr. Kaafarani, Dear Haytham, over the years you have become a good friend. It is impressive to see how the research department grew under your supervision, the amazing new collaborations you started, but moreover how much you enjoy everything you do.

Alle collega's van de afdeling traumachirurgie van het LUMC en in het speciaal **Ingeborg** dank voor jullie steun, enthousiasme en gezelligheid. Soms kwam ik met veeleisende vragen en lastige verzoeken, maar jullie dachten altijd met me mee.

Aan alle **"Actieve Menschen"** en in het bijzonder **Karin, Michelle, Fenna en Ruth**, zonder jullie was het afronden van een PhD lang niet zo leuk geweest.

Dear Boston Friends, both old and new you all have made my time in Boston unforgettable. Especially, **dear Elie**, I never could have imagined that my time in Boston would give me such a good friend.

"Lot!", nu beter bekend als de "Bende van Ellende" dank voor al jullie gezelligheid, wijnavondjes en weekendjes weg! Bijna een decennium sinds het allemaal begon bij Augustinus en ik kijk uit naar nog vele memorabele momenten!

Anne-Marijke, vriendinnen sinds onze babytijd en ik hoop nog totdat we bejaard zijn. Dank voor goede gesprekken, slappe lach momenten, maar vooral voor een zeer gewaardeerde vriendschap.

Laura en Margo, wat ben ik onwijs trots op jullie als grote kleine zus! Allebei jullie eigen pad gekozen en wat gaat het goed. Af en toe was jullie ontnuchterende advies precies wat ik nodig had, maar vooral jullie te zien groeien in wat jullie doen is geweldig om te zien!

Pap en Mam, het was een avontuur en zonder jullie had ik het niet gekund! Zo vaak kwam ik weer met bijzondere en soms enigszins ambitieuze plannen, maar jullie stonden altijd achter me. Jullie nuchtere blik, onvoorwaardelijke vertrouwen en support waren onmisbaar! Dankjewel!