Decision-making in severe traumatic brain injury: patient outcome, hospital costs, and research practice

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CHAPTER 10

GENERAL SUMMARY

Humans have sustained traumatic brain injuries (TBI) from the beginning of their existence and will most likely be confronted with this devastating disease until their extinction. Even after thousands of years of experience in treating patients with TBI, decisions regarding the optimal treatment strategy remain difficult for both healthcare workers as policy makers. In this thesis, consisting of two parts, we aimed to describe and improve the acute treatment decision-making process and research practice in patients with TBI.

Part I investigated the challenges of the treatment decision-making process in patients with (severe) TBI and focussed on three factors considered to be important in this process: patient outcome, in-hospital healthcare consumption, and in-hospital costs.

Chapter 2 was a literature review of acute neurosurgical management in patient with very severe TBI (Glasgow Coma Scale 3-5). It showed major variation in treatment strategies between forty-five included studies. Mortality rates were high, and the chance to reach a so called 'favourable outcome' was low. Some studies however, did report favourable outcome rates for specific patient groups (lower age, lower TBI severity and absence of pupillary abnormalities). In addition to patient and injury related factors, also the type and timing of an intervention appeared to be related with outcome. It was not possible to establish causality due to the high variation between studies and due to the methodological limitations of individual studies.

Chapter 3 was a systematic review that investigated the in-hospital costs of patients after sustaining severe TBI (Glasgow Coma Scale 3-8). The twenty-five included articles showed generally high in-hospital healthcare costs (median €44,660; range €1,720 – €324,660; mean €70,810). The in-hospital costs were primarily driven by costs related to both general ward (12% – 38%) and ICU (51% – 79%) length of stay and surgical interventions (4% – 8%). The length of stay (LOS) in the ICU ranged from 8 to 26 days and hospital LOS ranged from 10 to 37 days. Consumption and costs increased with higher TBI severity. Drawing firm conclusions was difficult, due to the inadequate quality of the included studies and variation of study results, caused by methodological and clinical heterogeneity. It was concluded that future economic evaluations could improve their quality, accuracy of cost calculation, and reporting of costs, by using guideline recommendations and common data elements.

Chapter 4 and *chapter 5* reported on patient outcome and on in-hospital healthcare consumption and in-hospital costs of two different patient cohorts. The first cohort consisted of 108 consecutive patients with a traumatic acute subdural hematoma and

the second cohort consisted of 486 TBI patients that were regionally included in the CENTER-TBI study. Following the recommendations made in *chapter 3*, we used the Dutch guidelines for economic healthcare evaluations to ascertain the quality of costs calculation. Both studies reported high rates of mortality and unfavourable outcome, as defined by the Glasgow Outcome Scale score. These rates increased with higher TBI severity, presence of intracranial abnormalities, extracranial injury and need for surgical intervention. Despite high rates of mortality and unfavourable outcome, both studies also showed that patients with severe TBI could achieve favourable outcome. Even the most severely injured patients were able to achieve favourable outcome.

Both studies found substantial in-hospital healthcare consumption and generally high in-hospital costs, even in patients with mild TBI (Glasgow Coma Score 13-15). Average in-hospital costs were €7,800 for mild, €20,210 for moderate €26,600 for severe, and €26,350 for very severe TBI patients *(chapter 5)*. Increase in healthcare consumption and costs was associated with several factors, including higher TBI severity (lower Glasgow Coma Score), presence of pupillary abnormalities, presence of major extracranial injury, presence of intracranial abnormalities on CT scan, use of intracranial pressure monitoring, and performed surgical interventions(s). In-hospital costs were primarily driven by costs related to admission and surgical intervention. This was in accordance with the results from *chapter 3*.

Chapter 6 was the result of multiple focus group sessions with medical professionals in the field of neurosurgery, intensive care medicine, rehabilitation, chronic care, anthropology and medical ethics. It described the process and reasoning of decision-making and proposed several reasons that could legitimize treatment-limiting decisions in patients with severe TBI (initial Glasgow Coma Score of 3-8). We also discussed the professional code of physicians, treatment-limiting decision, unacceptability of patient outcome, prognostic uncertainty, shared decision-making difficulties, healthcare costs, societal perspective, and importance of specialized rehabilitation and long-term care. Despite multiple efforts to improve care and outcome of TBI patients, it was concluded that decision-making remains highly complicated. The majority of uncertainty was caused by a lack of high-quality scientific evidence on treatment effectiveness and inaccurate outcome prediction. But there was also uncertainty on the acceptability of outcome, due to different societal and individual values.

Part II analysed procedural difficulties in TBI research efficiency by focussing on the process of institutional review board approval and the use of informed consent procedures in patients with TBI with an inability to provide informed consent.

Chapter 7 analysed the process of institutional review board approval around Europe. Major variation was found in how the CENTER-TBI study protocol was reviewed and approved by 66 European institutional review boards. The reported variation between and within European countries with regard to submission and approval requirements, number of review rounds and total duration was not beneficial for study efficiency. It was concluded that future research initiatives could benefit from the implementation of more uniform legislation and regulation while acknowledging local cultural and ethical arrangements between countries.

Chapter 8 and *chapter 9* focussed on the use of informed consent procedures in patients with traumatic brain injury with an inability to provide informed consent for emergency research.

Chapter 8 showed variation and discordance between reported and observed informed consent procedures in intensive care patients that were believed to have an inability to provide informed consent between and within European countries from the CENTER-TBI study. Proxy informed consent and deferred consent procedures appeared to be essential informed consent alternatives in studying TBI patients with an acute inability to provide informed consent. However, the deferred consent procedure was only actively used in a third of the centers where it was considered to be a valid method of consent. The study concluded that the reported European variation in informed consent procedures indicated inconsistencies in clear legislation or knowledge of such legislation among researchers. This could be optimized for the benefit of future research initiatives.

Chapter 9 was an extensive overview that discussed all relevant aspects on the use of informed consent procedures in emergency interventional research in patients with TBI and stroke that have an acute inability to provide informed consent. It was found that currently accepted consent alternatives such as deferred consent and exception/waiver of consent appear under-utilized, despite being ethically permissible, socially acceptable, and regulatory compliant. We concluded that when the requirements for medical urgency are properly balanced with legal and ethical conduct, the increased use of these alternatives has the potential to improve efficiency and quality of future emergency interventional studies in patients with an inability to provide informed consent.

The general discussion of this thesis will elaborate on the role of patient outcome and in-hospital costs in the acute treatment decision-making process in patients with s-TBI