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Mortality and causes of death in a burn centre

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Chapter 7

ABSTRACT

Mortality rates are important outcome parameters after burn, and can serve as objective end points for quality control. Causes of death after severe burn have changed over time; in the international literature, multisystem organ failure is seen as the most important cause, but the exact distribution of causes of death remains unknown. Insight into underlying agents of mortality can be directive in research and prevention programs. This comparison between results from the Rotterdam Burn Centre (RBC) and the American National Burn Repository (NBR) examines the most important predictive parameters for fatal outcome, i.e. age, total body surface area involved and presence of inhalation injury. Causes of death were attributed for all fatal outcomes treated in the RBC from 1996 to 2006.

The mortality rate at the RBC was 6.9% and at the NBR was 5.6%, with almost no differences in age or total body surface area involved. The discrepancy in mortality rate might have been due to the high incidence of inhalation injury among the RBC population. However, the mortality rate at the RBC after admission with intention to treat decreased to 4.9%. The most frequent cause of death appeared to be multisystem organ failure, in 64.9% of cases; 93% of these had systemic inflammatory response syndrome at time of death and, in 45.9%, infection was deemed responsible for the fatal clinical deterioration (in 21.3% sepsis was proved and in 24.6% was highly suspected).

To compare mortality rates between different burn centres and periods of time, uniform classifications are needed, particularly for presence of inhalation injury and for causes of death. Prevention of multisystem organ failure, by better management of infection and systemic inflammatory response syndrome, might do most to decrease mortality after burn.
1. INTRODUCTION

Outcome measures are the first step in evaluating consequences of trauma and in following health care. In potentially life-threatening conditions, mortality is the outcome measure of greatest concern[1]. Furthermore, mortality rates are used in evaluating new therapeutic interventions and establishing standards of burn survival. The predictive power for mortality is known for age, total body surface area (TBSA) involved and presence of inhalation injury[2–4]. However, in decisions about treatment withdrawal, these parameters should be handled with great care; for example, among severely burned children it has been shown that outcome cannot be predicted by demographic and injury characteristics alone [5]. During the past 50 years, mortality rates following burn have dramatically decreased. Half a century ago, approximately 50% of victims survived if burns involved more than 40% TBSA[6]. Nowadays, burns involving >90% TBSA are sometimes survived by young and healthy people. In the Western world, overall mortality rates following burn have decreased to 5–6% [2,7–9]. This remarkable fall can be attributed to the establishment of specialised burn centres, therapeutic developments including advances in critical care and anesthetic procedures, vigorous fluid resuscitation[10], excision of burn wounds [11], a dynamic, aggressive approach to nutritional management [12,13] and use of topical antimicrobial agents and systemic antibiotics. There has also been a shift in time and cause of death following burn. Historically, a fatal outcome followed burn in the first few days and was primarily caused by burn shock, respiratory insufficiency and wound sepsis [14]. Today, the first few days after burn are almost always survived and factors such as systemic inflammatory response syndrome (SIRS), sepsis and other complications contribute to later fatality. Despite their importance for quality control and comparison of results, uniform data on causes of death are surprisingly scarce in the literature. We performed a retrospective review in order to describe our population, compare results and analyse causes of death following burn.

2. MATERIALS AND METHODS

2.1. Principles of treatment

Standard treatment protocols in the Rotterdam Burn Centre (RBC) from 1996 to 2006 included fluid resuscitation with hypertonic crystalloids (0.45% NaHCO3 in 500 ml 0.9% NaCl; total Na content 202 mmol/l) according to the Parkland formula. Partial-thickness burns involving <10% TBSA were covered with dressings (hydrocolloids, alginates, hydrofibres); larger defects and full-thickness burns were initially treated with topical agents (silver sulfadiazine,
cerium nitrate–silver sulfadiazine). In full-thickness burns, delayed primary excision and biological closure with autographs or allografts or both were started within 7 days. Isolated one-patient intensive care units were equipped with a laminar downflow system, sluices and overpressure to prevent cross-infection. Inhalation injury was diagnosed on the basis of suspicion after exposure to smoke or fire, and considered proven in the presence of signs of airway obstruction or carbon particles in sputum or by bronchoscopy. Suspected and proven inhalation injuries were treated by endotracheal intubation and mechanical ventilation. Antibiotics were not routinely administered at admission apart from selective decontamination of the digestive tract in the presence of burns involving >30% TBSA. Further indications for antibiotic prophylaxis included artificial ventilation in cases of inhalation injury, bacteraemia when the area to be excised exceeded 1% TBSA (one dose preoperatively) and change of a central line. Antibiotics were used therapeutically in the presence of contamination with group Lancefield A haemolytic streptococci or clinically suspected or proven infection. The choice of antibiotic was adjusted according to results of culture of the microorganism. Enteral feeding was started within 24 h after admission and nutritional requirements were calculated using a modified Curreri formula. Gastric mucosal protection was administered if TBSA involved exceeded 20%.

2.2. Study design

Mortality was studied for the total population admitted to the RBC and for the subgroup admitted with intention to treat (ITT) over the 10-year period from 1996 to 2006. The decision for tender loving care (TLC) only was always a patient-tailored judgement made by an experienced team of burn specialists on the basis of the important criteria of age, TBSA burned, inhalation injury and also comorbidity. These characteristics were recorded in all cases and are presented for the total population as well as for the subgroups with ITT and TLC (Tables 1 and 2).

For quality control, our overall mortality rate from 1996 to 2006 was compared with results derived from an extensive multicentre database published in the National Burn Repository (NBR) 2005 [9]. These results were derived from 70 centres in the USA plus the District of Colombia from 1995 to 2005.

Causes of death were analysed for burn victims admitted from 1996 to 2006 to the RBC with an ITT. Categorisation included dysfunction of organ system(s), SIRS, sepsis and underlying causes. The concept of MOF as cause of death was defined by dysfunction of more than one organ system responsible for fatal outcome despite organ support.
In recording dysfunction, definitions[15–17] were modified for the following organ systems:
respiratory, defined by the requirement for mechanical ventilation for >72 h; cardiovascular, defined by inotropic dependency to keep mean arterial pressure above 60 mmHg; renal, defined by the use of continuous veno-venous or arterio-venous haemofiltration; hepatic, defined by transaminase level >1.5 of normal; and haematological, defined by a platelet count below 100,000/ml.

For SIRS and sepsis, definitions proposed by the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference were used[16,17]. SIRS, regardless of cause, was defined and diagnosed if the patient showed more than one of the following clinical features:
- body temperature >38 °C or <36 °C
- heart rate >90/min
- respiratory rate >20/min or PaCO2 <32 mmHg
- white blood cell count >12,000 cells/ml or <4000 cells/ml.

Sepsis was defined as the clinical syndrome of a systemic inflammation in response to infection. In the International Sepsis Definitions Conference no single specific criterion for sepsis was proposed, but rather a combination of criteria including proven or at least highly suspected infection[18]. In our study, sepsis was proved by positive blood culture or was suspected in, for example, the presence of a new radiographic infiltrate together with an overall clinical impression.
Chapter 7

Data expression and statistical analyses were performed using SPSS version 15.0. Descriptive statistics included means for continuous variables and proportions for categorical variables, which were compared using \( \chi^2 \) tests.

3. RESULTS

3.1. Burn centre mortality

Causes of burn among victims admitted to the RBC are shown in Fig. 1; flames (48%) or scalds (43%) were the agent of injury in 91% of cases. Demographic and injury characteristics and mortality rates among people admitted to the RBC together with data derived from the NBR are presented in Table 1. From 1996 to 2006, 1946 victims of burn were admitted to the RBC with a mean age of 29 years (range 0–98 years) and a mean TBSA involved of 10.9% (range 0–99%); 243 (12.5%) had suspected or proven inhalation injury according to the criteria mentioned in 2.1. Overall mortality rate among this population was 6.9%.

During almost the same decade, from 1995 to 2005, 121,930 people with burns were admitted to the 70 participating burn centres summarised in the NBR data. Demographic and injury characteristics included a mean age of 33 years and a mean TBSA involved of 11.9%, and 6.5% of cases had inhalation injury. Overall mortality rate in the NBR during this period was 5.6%. Differences between the RBC and the NBR in overall mortality rate and in incidence of inhalation injury proved to be statistically significant (\( p<0.05 \)).

![Fig. 1 - Causes of burn among patients admitted to the Rotterdam Burn Centre from 1996 to 2006.](image)

Of the 1946 burn victims admitted to the RBC, 41 (2.1%) received TLC only. Mean age was 61.1 years, mean TBSA involved was 62.3% and 95.1% of these patients had inhalation injury. Therefore, 1905 people (97.9%) were admitted to the RBC with ITT. Mean age was 27.9 years, mean TBSA involved was 9.7%, inhalation injury was present in 10.7% and mortality rate was
4.9%. Divided into survivors and non-survivors, their demographic and injury characteristics are shown in Table 2. Mean age among the non-survivors was 58.2 years compared with 26.3 years among the survivors. Compared with survivors, TBSA involved was three times higher among the non-survivors (29.1% versus 8.7%) and the incidence of inhalation injury was five times higher (44.7% versus 8.9%).

3.2. Causes of death following burn

All burn victims receiving TLC died of irreversible shock, as resuscitation was withheld. Among the 4.9% of patients with ITT who died, cause of death could be retrieved in 89 (94.7%), as presented in Table 3. As categorised by organ system, circulatory failure resulted in lethal outcome for eight patients, i.e. four (4.3%) sustained cardiac arrest, three (3.2%) died of burn shock and one (1.1%) died of an uncontrollable haemorrhage.

A further six people did not survive respiratory problems, i.e. pneumonia in two cases (2.1%) and aspiration in four cases (4.3%). Neurological problems were the cause of death of eight people, i.e. cerebral stroke in three cases (3.2%) and neurological deterioration in five cases (5.3%). For 61 people (64.9%) MOF resulted in fatal outcome; the remaining six died of toxic shock syndrome (two cases), carbon monoxide intoxication (one case), crush syndrome (one case), refusal of dialysis (one case) and refusal of blood transfusion (one case).

With respect to the inflammatory state among those who died from MOF, almost all (93%) showed signs of SIRS before death; among 28 of these (45.9%) an infectious source was
concurrently identified. In 13 of these 28 cases (46.4%), sepsis was proved by positive blood cultures, a further 14 had a diagnosis of pneumonia and 1 had a diagnosis of infected ascites. From 41 (67.2%) of those who died from MOF, blood cultures were drawn during their final septic episode; 17 microorganisms were cultured from 13 different blood samples, 12 cultures showed Gram-negative strains (Klebsiella, Acinetobacter, Pseudomonas) and 5 cultures yielded Gram-positive strains (Staphylococcus, Streptococcus, Enterococcus).

4. DISCUSSION

4.1. Mortality

This study aimed to describe, first, the demographic and clinical features of the study population, comparing mortality rates with those published in a multicentre database from 70 burn centres in the USA and the District of Colombia. The number of admissions (1946) for burn to the RBC from 1996 to 2006 was slightly higher than the average number (1742) of admissions (121,930/70) to the participating burn centres in the NBR from 1995 to 2005. The 6.9% mortality rate from the RBC was significantly higher than the 5.6% mortality rate from the NBR and deserves a closer look, not least because mortality is one of the most important outcome parameters following life-threatening trauma and can serve as a measure for quality of care. Before being conclusive about quality of care, an evaluation of the most predictive parameters of fatal outcome should be taken into account.

Even with a higher mean age and higher mean TBSA involved, a 1.3% lower mortality rate was found in the NBR. The differences in age and TBSA involved are too small to explain the differing mortality rates, the reason which is probably the significant difference in incidence of inhalation injury, one of the three most powerful predictive parameters for fatal outcome (12.5% in the RBC compared with 6.5% in the NBR). Unfortunately, the comparison is complicated by the lack of definition in the NBR and by the criteria used in the RBC (see Section 2.1). From 1996 to 2006, burn victims were frequently admitted to the RBC as a tertiary referral centre and intubation had already taken place in another hospital. Bronchoscopy to prove inhalation injury was performed only if there had been no such previous intubation. In 12.5% of cases inhalation injury was diagnosed by suspicion, and in only 16.5% of these was proven by bronchoscopy. The number of cases where inhalation injury was diagnosed on the basis of signs of airway obstruction or carbon particles found in sputum unfortunately could not be retrieved. Because some of the criteria used are less specific than bronchoscopy, this may have resulted in an overestimation of inhalation injury among the RBC population. Nevertheless, the odds are that the difference in incidence of inhalation injury, with its high morbidity and mortality, is the most likely explanation for the difference in mortality rates between the RBC and the NBR. A uniform definition of
Mortality and causes of death in a burn centre

Inhalation injury is recommended for future comparisons, and the most reliable and specific definition would be positive findings at bronchoscopy. Thus it is also recommended that clinical findings and bronchoscopy results indicating inhalation injury should be mentioned in handovers to tertiary referral centres, and that referred patients should undergo bronchoscopy for suspected inhalation injury even after previous intubation.

Probably more interesting than the outcome parameter of overall mortality is a comparison of mortality rates after admission with an ITT. Unfortunately, no data about this subgroup were available in the NBR and therefore no comparison with the RBC results could be made in this respect. However, comparisons with the NBR results are still of great value because of the multicentre character of the repository and its large amount of data [9]. The mortality rate for burn victims admitted to the RBC with an ITT was 4.9%, and this outcome parameter is in our opinion the most important and should be used in future evaluations of quality of care. Finally, the importance of taking into account the most important risk factors for fatal outcome in evaluation of mortality rates is shown by dividing the patients admitted for burn to the RBC with ITT into survivors and non-survivors.

This division shows that among non-survivors compared with survivors, age is twice, TBSA involved is three times and incidence of inhalation injury five times higher.

4.2. Causes of death

The second goal of this retrospective study was analysis of causes of death following burn. According to the literature, MOF is the leading cause of death [16,19]. However, recent studies of the distribution of causes of death are lacking, and therefore we have attempted to categorise causes of death in the RBC from 1996 to 2006. Despite intense investigation the aetiology of MOF remains largely unclear, although all cases seem to exhibit episodes of an uncontrolled inflammatory response (SIRS). A variety of conditions can lead to this response after burn, and underlying causes can be infectious as well as non-infectious [16]. Infectious causes include sepsis [20], bacteraemia following manipulation of colonised wounds, small repetitive infections [21] and bacterial translocation from the gut [22]. In non-infectious aetiology the crucial pathophysiological event is thought to be the tissue damage itself [23]. Several factors can be responsible for this tissue damage and for the prolongation of a systemic inflammatory response to it. After burn, the presence of necrotic tissue, resuscitation failure, ischaemic–reperfusion injury and translocation of endotoxins across the bowel [24] can all lead to SIRS. Sheridan et al. [19] reported MOF to be cause of death after burn injury in 67% of cases. They referred to these fatal cases of MOF as being sterile because no clinical infection was suspected at time of death. In the RBC population MOF was the leading cause of death after burn in 64.9% of cases; 28 of these 61 people (21.8%) had sepsis proved by bacteriological culture, and 15 (24.6%) had highly suspected sepsis. Therefore, in almost half of the RBC population dying from fatal MOF, death could, at
least partially, be attributed to a final infection. Decreased mortality after burn, and decreased death from MOF in particular, could be achieved with improvement of infection prevention and therapy and prevention of other causes of SIRS. Theoretically, ability to establish an immunological balance between pro-inflammatory and anti-inflammatory biological signals would be the most promising development [25]. However, so far the best approach in practice remains infection prevention and treatment together with patient and organ support to prevent organ failure[26]. A minority of people in our population died from theoretically preventable causes of death; in three cases (3.2%) fatal burn shock could not be relieved despite vigorous fluid resuscitation, and in four cases (4.3%) fatal aspiration could not be prevented despite precautions such as no tube feeding at night and sleep in a reverse Trendelenburg position for those without intubation.

5. CONCLUSION

The availability of demographic and injury characteristics together with outcome variables is necessary for making meaningful comparisons. Risk factors such as age, TBSA involved and the presence of inhalation injury should be taken into account when mortality rates are compared. With respect to comparison of results between the RBC and NBR, the difference in mortality rates can most probably be attributed to differing incidences of inhalation injury, although criteria for its diagnosis were dissimilar. A uniform definition for the diagnosis inhalation injury will be mandatory for reliable comparison of results in future reports and demographic and injury characteristics, not only for the total population but also for the subgroups with and without ITT. After admission to the RBC during the period from 1996 to 2006, overall mortality rate was 6.9%; on an ITT basis, mortality rate was 4.9%. MOF was the most common cause of death, and its fatality was due to a final infection in 45.9% of cases. Decrease in mortality rates after burn is most likely to be achieved by development of better prevention programmes and treatments for infection and of methods for establishing immunological balance.
REFERENCES


