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Long-term outcome after renal replacement therapy in severe burns

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Abstract

Introduction: Acute kidney injury is a common sequela after major burn injury, but only a small proportion of patients need renal replacement therapy. In the majority of patients, need for renal replacement therapy subsides before discharge from the burn centre but limited literature exists on long-term outcomes. A few studies report an increased risk for chronic renal failure after burn injury. We investigated the long-term outcome of severely burned patients receiving renal replacement therapy during acute burn injury treatment.

Methods: Data on 68 severely burned patients that received renal replacement therapy in Helsinki Burn Centre between November 1988 and December 2015 were collected retrospectively. 32 patients survived and remained for follow-up after the primary hospital stay until 31st December 2016.

Results: 56.3% of discharged patients were alive at the end of follow-up. In 81.3% of discharged patients, need for renal replacement therapy subsided before discharge. Two patients received renal replacement therapy for longer than three months, however, need for renal replacement therapy subsided in both patients. One patient required dialysis several years later on after the need for renal replacement therapy had subsided.

Conclusions: This study showed that long-term need for renal replacement therapy is rare after severe burn injury. In the vast majority of patients, need for renal replacement therapy subsided before discharge from primary care. Acute kidney injury in association with burns is a potential but small risk factor for later worsening of kidney function in fragile individuals.

Keywords: Burn injury, Acute kidney injury, Renal replacement therapy, End-stage renal disease

1. Introduction

Acute kidney injury (AKI) often follows severe burn injury and significantly increases the risk of death. However, renal replacement therapy (RRT) is needed only in a minority of AKI cases. Among severely burned patients, the incidence of AKI is usually observed in tens of percents of cases, whereas the proportion of patients receiving RRT is only a few percent (1-6), although proportions as high as over 50% have been reported (7).

Modern RRT techniques were invented in the early 1960s to improve the prognosis of patients with loss of kidney function (8,9). Studies from recent decades revealed a high mortality of burn patients that received RRT, even up to 85% (5,10-12). Since then the prognosis has improved, with mortality still approximately 50% to 60% (13-16).

In the vast majority of burn patients that receive RRT, kidney function recovers during the hospital stay and RRT can be discontinued before discharge (17). Surprisingly, there are limited studies on the long-term outcome of these patients. To our knowledge there are only two register studies that have evaluated the risk of long-term deterioration of kidney function after severe burn injury. One study concluded that the risk for end-stage renal disease (ESRD) increased after burn injury compared to the general population (18), while the other study concluded that AKI is associated with risk for chronic dialysis and ESRD development one year after injury (19).

The purpose of this study was to investigate the long-term outcome of severely burned patients that received RRT during acute burn injury treatment.

2. Materials and methods

We retrospectively searched for data on all patients that received RRT in the Helsinki Burn Centre between November 1988 and December 2015. At the time of the study, the treatment of most severe burns was centralized into two burn centers in Finland (the burn centers of the Helsinki University Hospital and the Kuopio University Hospital). The Helsinki Burn Centre treated two thirds of the severe burn victims of Finland (population approximately 5 million).

The following parameters were collected: age, burned total body surface area (TBSA%), burn mechanism, length of hospital stay, Abbreviated Burn Severity Index (ABSI) (20) and Baux score (21) at admission, gender, any co-existing diagnosis at arrival, presence of inhalation injury, sepsis, rhabdomyolysis, type of AKI (early/late), and mortality. AKI was defined as early if diagnosed within five days after burn injury (12).

Data from patients that received long-term RRT (>3 months) were obtained from the Finnish Register for Kidney Diseases, which is maintained by the Finnish Kidney and Liver Association. The register covers up to 99% of patients receiving RRT for > 3 months in Finland (22). Cause of death (COD) was recorded from the Causes of Death registry maintained by Statistics Finland, which covers all deaths that occurred in Finland, recorded by individual national identification number (23). The underlying and immediate COD were recorded by the ICD-10 system. Some patients from the earlier period had diagnosis recorded by ICD-9; these diagnoses were converted into corresponding ICD-10 codes. The last date of verified data was 31 Dec 2016.

The Student's t-test was used for continuous variables and chi-square of Fischer's exact test for dichotomous variables. Normality of continuous variables was not violated. A Kaplan-Meier estimator was created to estimate survival after discharge. Data was analyzed with IBM SPSS Statistics for Macintosh, Version 22.0 (Armonk, NY, USA, IBM Corp.) and STATA (STATA v12.0, Stata Corp. LP College Station, TX, USA). A *P*-value less than 0.05 was considered statistically significant.

3. Results

From November 1988 to December 2015, 68 patients received RRT during their stay at the Helsinki Burn Centre. Of these patients, 52.9% (n=36) died during their stay. Patients who died, had higher ABSI, Baux score, and TBSA% than survivors, and all parameters between survivors and non-survivors are presented in Table 1. In 81.3% (26/32) of survivors, the need for RRT subsided before discharge. In these patients, later long-term RRT (> 3 months) was not necessary. Six patients (18.8% of survivors) required RRT after discharge. Of these patients four died and three of them within 50 days after discharge and one after more than 10 years (Figure 1). Only two patients required RRT for >3 months; these patients received intermittent RRT 10.5 and 17 months before the need for RRT subsided, respectively. However, the other patient developed chronic kidney failure several years later (Figure 1). None of the patients had at admission pre-existing diagnosed reduced kidney function based on available medical records.

Of the discharged patients, 56.3% (18/32) were alive at the end of the follow-up period in 2016; 14 patients died during this time. Kaplan-Meier analysis of patient survival is presented in Figure 2. Of 14 patients, five died due to burns (ICD-10: T20-32.9); these events occurred within 50 days of discharge. The one-year mortality after discharge was 18.8% (6/32). The patients who died within one year from discharge had a mean age of 57 years, a Baux score of 99, an ABSI score of 8.7, and TBSA 42%. In 50% (3/6) of these patients, RRT was still ongoing at time of discharge.

Of those eight patients, who died after first year, only one patient died due to chronic kidney failure, more than 10 years after discharge. In the rest of the seven patients, COD was unrelated to burns or kidney failure. These events occurred on average 7.4 years after discharge (range 6-7622 days) at an average age of 60 years. The average follow-up time of patients (discharge-death/end of follow-up) was 7.4 years (range 5-7622 days) and 9.3 years (range 367-7607 days) in those who were alive at the

end of follow up. The total follow-up years was 238. A flowchart of patient follow-up is presented in Figure 1.

4. Discussion

This single-center study on all renal replacement therapy patients treated at Helsinki Burn Centre between 1988-2015 showed a notable mortality (52.9%) among patients with major burns. However, if burn patients with severe AKI survived beyond the primary hospital stay, the prognosis was good and the risk for long-term ESRD and need for RRT was small. The estimated incidence for need for RRT was 1.5% to 1.9% of all patients admitted to the burn unit during the study period, which is comparable to previous studies (24,25). ~~The majority of patients that succumbed had higher TBSA% and ABSI and Baux scores than survivors (Table 1).~~ Even though the mortality rate of RRT patients was high (52.9%), it is lower than that presented in earlier studies among burn patients that received RRT (12,24,26).

Need for RRT after primary hospital stay

In 81.3% (26/32) of survivors, need for RRT subsided before discharge from the burn unit. Two of 32 patients (6.3% of the survivors) developed chronic kidney ~~disease~~ failure. However, in both cases, after 10.5 and 17 months, the need for RRT subsided. In our study, the normalizing rate of kidney function was higher and the incidence of chronic kidney disease one year after injury was lower than that observed in a cohort of 959 general intensive care unit (ICU) patients that received RRT (27). In that cohort, those who remained dialysis dependent had elevated baseline serum creatinine and a higher incidence of pre-existing diabetes mellitus. In contrast, in our study no patients had known weakened kidney function before burn injury.

In a study of 1213 general ICU patients, early initiation of RRT did not reduce long term mortality risk in end stage renal disease or risk for development of chronic kidney disease. In our study in-hospital mortality, need for RRT at discharge and need for RRT six months after injury were nearly equal with that observed in a recent American study on a cohort of 170 burn patients who received RRT (15).

Long term risk for ESRD

To our knowledge, there are only two register studies that investigated the association between burns and ESRD. Both studies concluded that the risk is increased after burn injury (18,19). One study (a Finnish register study) had a somewhat overlapping study population as the present study; this study investigated 41 179 patients that received treatment for burns as in- or outpatients between 1998 and 2011 in any health care facility of the country. The study concluded that the risk for ESRD is increased compared to general population. The authors reported five patients (out of 41 179) who developed ESRD after burn injury and who had no coexisting diagnosis that would explain the weakened kidney function. Out of the five patients who developed ESRD after treatment due to burns without a coexisting diagnosis, RRT was initiated in only two patients within one year of burn injury admission. There was no information on the severity of the burn injury or AKI or whether these five patients had AKI related to burns or if they were treated as in or outpatients (18). These omissions discredit the proposed causality between ESRD and burn injury though this was noted at the group level. The study was conducted via registers without access to the patient medical records, which is a notable weakness when evaluating causality between burn injury and AKI.

An American register study of 18 155 patients conducted between 2009 and 2013 concluded that the risk for ESRD and chronic dialysis was increased in burn patients with AKI one year after injury when adjusted for confounding factors (age, size of burn injury, comorbidities, gender) (19). It reported that 4.58% of all AKI patients were receiving dialysis one year after injury, whereas ours

corresponding proportion was 3.8% (1/26 patients), which is lower although we included only RRT patients, who suffered from a very severe form of kidney injury.

In our study, need for RRT subsided in all patients, which indicates that patients benefited from RRT and none of the patients remained ~~instantly~~ permanently dialysis dependent following burn injury and AKI. Burn-induced AKI and AKI for any reason may though worsen underlying weakened kidney function (acute on chronic) and increase the risk for ESRD. The risk for ESRD is increased even after complete recovery of kidney function in non-burn population (28,29). We did not observe such a development in the current study; patient's survival after 50 days after discharge was deemed fair.

Mortality during follow-up

Even though the mortality rate of RRT patients was high, 53% (36/68) during ICU-stay, it is lower than that presented in many earlier studies among burn patients that received RRT (12,24,26). During follow-up further five patients (5/14) died of sustained burns within 50 days after discharge and one patient of chronic kidney failure several years later on, although not directly related to burn injury. There were another 8 patients (57%, (8/14)), who died after discharge, but whose death was not related to burns or kidney deterioration. In this cohort we did not observe a clear trend between premature death and life expectancy predicted by year of birth and gender compared to general population in Finland. In half of the deaths not related to burns or kidney failure (4/8), the underlying COD was due to cardiovascular events (ICD-10: I20-24.9, I60-64). An American register study of 17 325 hospitalized patients with AKI revealed an increased later risk for cardiovascular disease; the risk increased with the severity of AKI (30). Moreover, cardiac dysfunction of burn patients and the hospitalized burn patients' increased risk for later myocardial infarction has been documented (19,31).

Only one patient (3.1%) died during the follow-up period of chronic kidney disease (underlying COD: ICD-10: N08, N18-N19). This occurred more than 10 years after the primary ICU stay. Although the patient received intermittent dialysis several years before death, the need for RRT had subsided nine months after discharge from the primary burn center stay and renal function remained normal for

many years. Based on medical records and COD, the worsening of kidney function was most probably affected by later events (unstable diabetes) not directly related to the original burn injury, whose impact on the final outcome is impossible to evaluate.

In this study, the one-year mortality after discharge from the burn unit was 19%, which is clearly higher than that reported among burn patients admitted to intensive care (32). The mortality rate is, however, comparable to the one-year mortality after discharge from a general intensive care unit ICU after need for RRT (27). All deaths within the first year after discharge from the burn unit (n=6) occurred within 50 days from discharge and 83% (5/6) were due to sustained burns (COD, ICD-10: T20-32.9). These deaths occurred in hospitals where they had been discharged from the Helsinki Burn Centre prematurely due to a shortage of acute ICU beds. The cases revealed a trend of pneumonia (ICD-10: J12-18.9) or acute respiratory distress syndrome (ICD-10: J80) as the immediate COD. The immediate CODs were similar to those who died during burn centre stay except in one case, where the patient died due to a rare transfusion complication related to treatment. These rapid deaths after discharge were investigated individually. In all cases, discharge from the burn center occurred when patient was still in critical condition. In some cases (three patients), RRT was still in progress, which underlines the severity of injury and may have contributed to the poor outcome. This observation emphasizes the importance of continuing acute burn treatment in a specialized ward until recovery has reached a level where general wound treatment and rehabilitation can safely be continued. In addition to these five prematurely discharged patients only one patient died within 1 year after discharge from the burn center.

In these early deaths, we observed that the patients were older and had more severe burn injury, which corresponds partly to the results from a Swedish cohort of burn patients, where older age increased the risk of rapid death after discharge (33). Two population-based cohort studies followed burn patients for many years after hospital discharge and revealed increased all-cause mortality compared to matched controls. One study had age limit >45 years and no TBSA limit while the other study had a TBSA limit >10% (34,35). Moreover, younger age and good pre-existing medical

condition are associated with long-term survival after burn injury (36). Due to small number of patients, we were unable to investigate in detail the factors that affected survival.

5. Strengths and limitations

One strength of this study is that on those patients that received RRT, the need for RRT long-term and possible COD was tracked at the individual patient level. The availability of medical records after ICU stay for key individuals was also a clear strength when evaluating relationships between burn injury and later adverse outcomes. Despite a long study period, the number of analyzed patients (n=32) was small, which is a notable limitation for making fundamental conclusions. It also limits some aspects of data evaluation at the group level. Although in some patients the follow-up time exceeded 20 years, we emphasize that the shortest period was slightly over a year in patients that did not die during follow up.

In our institute, RRT is not initiated on every patient with severe AKI if the patient's ability to survive and recover is evaluated to be very poor; no universal criteria for this decision exists and they may differ from one ICU to another. This aspect potentially improves the survival rates of RRT patients (or worsens the survival of those not receiving RRT) in this study.

It must be noted that late worsening of kidney function without need for RRT (CKD gradings 1-4) is possible and these patients were not included to the follow-up, which is a limitation.

6. Conclusions

This study showed that long-term need for renal replacement therapy is rare after severe burn injury. In the vast majority of the burn patients that received RRT, need for RRT subsided before discharge from the burn center. Nearly all deaths within first year after discharge occurred due to burns and majority of these may have been avoided by keeping patients in specialized burn center until the critical stage was over. In this study, we observed that chronic dialysis after severe burn injury is rare and need for RRT subsides over time in all patients without pre-existing reduced renal function. AKI associated with burn injury may be a potential risk factor for later worsening of kidney function in fragile individuals but the risk is small. No trend of premature deaths were observed during follow-up compared to general population in Finland.

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7. Conflict of interest statement

The authors declare no conflict of interests.

8. Statement of funding

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9.

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Table 1 Demographic data of patients

Variable	All patients (n=68)	Survived (n=32)	Succumbed (n=36)	P
Age	49.0 ± 13.1 (17-76)	47.4 ± 12.7 (19-76)	50.5 ± 13.4 (17-75)	NS
Burned TBSA	43.0 ± 19.2 (7-90)	37.3 ± 17.2 (7-77)	47.9 ± 19.6 (10-90)	0.03
Burn mechanism				NS
Flame	52 (76.5 %)	22 (68.8 %)	30 (83.3 %)	
Sauna (hot air)	6 (8.8 %)	4 (12.5 %)	2 (5.6 %)	
Electrical	3 (4.4 %)	3 (9.4 %)	0 (0 %)	
Liquid	3 (4.4 %)	1 (3.1 %)	2 (5.6 %)	
Scald	2 (2.9 %)	1 (3.1 %)	1 (2.8 %)	
Explosion	1 (1.5 %)	1 (3.1 %)	0 (0 %)	
Other	1 (1.5 %)	0 (0 %)	1 (2.8 %)	
Hospital stay (days)	36.9 ± 24.8 (2-111)	54.0 ± 20.6 (15-111)	21.7 ± 17.2 (2-65)	< 0.001
ABSI score	8.7 ± 2.0 (5-14)	8.2 ± 1.8 (5-11)	9.2 ± 2.0 (5-14)	0.04
Baux score	91.5 ± 19.1 (46-138)	84.1 ± 17.8 (46-113)	97.8 ± 18.1 (50-138)	0.003
Male sex	58 (85.3 %)	26 (81.3 %)	32 (88.9 %)	NS
Inhalation injury	17 (25 %)	9 (28.1 %)	8 (22.2 %)	NS
Pre-existing co-morbidity	25 (36.8 %)	13 (40.6 %)	12 (33.3 %)	NS
Sepsis	25 (36.8 %)	11 (34.4 %)	14 (38.9 %)	NS
Rhabdomyolysis	22 (32.4 %)	9 (28.1 %)	13 (36.1 %)	NS
Early AKI (<5 days)	36 (52.9 %)	25 (78.1 %)	22 (61.1 %)	NS
Non-survivors	36 (52.9 %)			

Data are reported as mean ± SD, (range) or percentage, when appropriate. P-values are calculated between survived and succumbed patients. ABSI, Abbreviated Burn Severity Index, AKI, acute kidney injury; NS, not significant; RRT, renal replacement therapy; TBSA, total body surface area. **Statistically significant, p < 0.05**

Figure 1 Flow chart of patients' outcome during follow-up period (until 31th Dec 2016)

1) ICD-10: T20-32.9. All deaths due to burns occurred within 50 days after discharge from burn center.

2) ICD-10: N03, N18-19. Death occurred >10 years after discharge.

3) Death not related to kidney failure or burns.

ICD, International Classification of Diseases; RRT, renal replacement therapy

Figure 2 Kaplan-Meier estimator for cumulative survival of RRT patients after discharge (n=32)

RRT, renal replacement therapy