

Mortality 7 years after prolonged treatment on a surgical intensive care unit

Barbara Meyer-Zehnder^a, Tobias E. Erlanger^b, Hans Pargger^c^a Clinic for Anaesthesia, Intermediate Care, Prehospital Emergency Medicine and Pain Therapy, University Hospital Basel, Switzerland^b Clinical Trial Unit, Department of Clinical Research, University Hospital Basel, University of Basel, Switzerland^c Intensive Care Unit, University and University Hospital Basel, Switzerland

Summary

AIMS OF THE STUDY: Long-term intensive care treatment confers a substantial physical, psychological and social burden on patients, their relatives and the treatment team. It is essential to know the outcome of patients with long-term treatment and to establish factors that possibly can predict mortality. Only few Swiss studies have previously addressed this issue.

METHODS: This retrospective observational study at a Swiss tertiary academic medical care centre included patients who were treated for ≥ 7 consecutive days at the surgical intensive care unit (ICU) between 1 January 2011 and 31 December 2012. Follow-up ended on 30 September 2018.

RESULTS: Two-hundred and fifty patients were included, and three were lost to follow-up. Fifty-two patients (21.1%) died in the ICU, 25 (10.1%) after transfer to the normal ward. Thirty-one patients (12.5%) died within one year after the beginning of intensive care treatment. Altogether, the one-year mortality was 43.7% (108 patients). At the end of follow-up, 99 patients (40.1%) were still alive. Polytrauma patients represent a special group with a survival of more than 90%. Median patient age was 66 years (interquartile range 56–75); two thirds were men. Patients who died within one year of beginning treatment in the ICU were significantly older (median 71 vs 63 years, $p < 0.001$), had a higher Charlson comorbidity index (mean 2.3 vs 1.2, $p < 0.001$), a longer intensive care stay (median 13.9 vs 10.6 days, $p = 0.001$), a higher SAPS-II score (mean 52.7 vs 45.6, $p = 0.001$), a higher NEMS score (mean 1772.4 vs 1230.4, $p < 0.001$) and more complications (mean 2.9 vs 2.0, $p < 0.001$) than patients who survived at least 1 year. Those who died within 1 year more often developed pneumonia (50.9% vs 29.5%, $p = 0.001$), pleural empyema (13.0% vs 2.9%, $p = 0.005$), septic shock (51.9% vs 20.1%, $p < 0.001$) or critical illness polyneuropathy (16.7% vs 2.9%, $p < 0.001$). Moreover, they more frequently (30.6% vs 15.1%, $p = 0.006$) required a renal replacement therapy.

CONCLUSIONS: Long-term mortality of patients with prolonged intensive-care treatment is high. Scores combined with factors shown to be associated with an increased

short- and long-term mortality can help to identify patients at risk for death within one year after ICU treatment.

Introduction

“An intensive care unit is an organized system for the provision of care to critically ill patients that provides intensive and specialized medical and nursing care, an enhanced capacity for monitoring, and multiple modalities of physiologic organ support to sustain life during a period of acute organ system insufficiency” is the definition of an intensive care unit (ICU) according to the Task Force of the World Federation of Societies of Intensive and Critical Care Medicine [1]. This definition clearly states the tasks of intensive care medicine and ICUs including the monitoring, maintenance and, if necessary, replacement of vital functions. Usually, patients are treated in an ICU for only a few days. However, a small proportion requires a longer treatment period, with 5–10% of all patients developing a persistent or chronic critical illness [2–5]. Reasons for prolonged intensive care treatment may include: (1) absence of efficacious therapy for an underlying long-term disease, which is not immediately lethal; (2) complications during the ICU stay (e.g., persistent single-organ failure, cascade of multiorgan failure, prolonged mechanical ventilation due to muscle weakness or persistent delirium); and (3) system factors (e.g., patients cannot be transferred to the ward, patients with unrealistic expectations, lack of palliative care facilities) [5].

Long-term treatment in an ICU confers a substantial physical, psychological and social burden on patients and their relatives [6]. The treatment team can also reach its limits, and the costs of long-term intensive care treatment are considerable [7–9]. Stricker et al. showed that 11% of patients (583 out of 4898) who were treated > 7 days in a mixed ICU consumed over 50% of the available resources [10]. A study from the USA found that patients (142 out of 2618, 5.4%) who received intensive care after heart surgery for 10 or more days accounted for 50% of the treatment days and caused 48% of the direct ICU costs [11]. Given these high costs in addition to the considerable burden on the patients receiving long-term intensive treatment, their families and caregivers, it is essential to know the outcome and to establish factors that possibly can predict mortality.

Correspondence:

Barbara Meyer-Zehnder,
MD
Department of Anaesthesiology
University Hospital Basel
Spitalstrasse 21
CH-4031 Basel
[barbara.meyer\[at\]usb.ch](mailto:barbara.meyer[at]usb.ch)

This study examined the mortality of patients who were treated continuously for 7 or more consecutive days in the surgical ICU of the University Hospital Basel and how survivors differ from the deceased in terms of various parameters. Only a few Swiss studies address this issue previously [10, 12, 13].

Methods

Design, setting and objectives

This retrospective observational study was performed in the 22-bed ICU of the University Hospital of Basel, a Swiss tertiary academic medical care centre, which treated approximately 2500 mainly surgical and trauma patients per year at the time of study. As there is no generally accepted definition of prolonged ICU stay [8, 14] (supplementary table S1 in the appendix), all patients who were treated in the surgical ICU for at least 7 consecutive days between 1 January 2011 and 31 December 2012 were included. The Ethics Committee of Northwest and Central Switzerland (EKNZ) approved this study (2018-00184). The objectives of this study were to assess mortality in the ICU and the nursing department in the year following the beginning of ICU treatment, and until the cut-off-date (30 September 2018) (fig. 1). We sought to identify factors associated with 1-year mortality.

Data collection

Patient data, including patient age and sex, main surgical and secondary diagnoses, admission status, severity of illness using the simplified acute physiology score (SAPS II) [15], measurement of the nursing workload according to the nine equivalents of nursing manpower use score (NEMS) [16], ICU complications, ICU treatments includ-

ing the duration, and hospital outcome, were collected from the patients' charts. Survival after discharge was determined by hospital records or by contact with registration office or the family doctor. Follow-up was closed on 30 September 2018.

ICU complications were defined as follows: delirium as a transient, usually reversible, global cognitive dysfunction (screening for delirium was made using the Intensive Care Delirium Screening Checklist (ICDSC) every 8 hours); stroke as new ischaemic or haemorrhagic cerebral event evidenced on computed tomography (CT); tracheobronchitis as an inflammation of the airways between the larynx and the bronchioles; pneumonia as an inflammation of the lung tissue accompanied by infiltration of alveoli; pleural empyema as a collection of pus in the pleural cavity; acute respiratory distress syndrome (ARDS) as acute onset of respiratory failure, bilateral infiltrates on chest radiograph, and hypoxaemia; septic shock as persisting hypotension requiring vasopressors, and a serum lactate level >2 mmol/l (18 mg/dl) despite adequate volume resuscitation; acute renal failure as an acute increase of creatinine of >26.4 $\mu\text{mol/l}$ (0.3 mg/dl), a percentage increase creatinine $>50\%$, or a reduction of urine output; acute on chronic renal insufficiency as increased serum creatinine by 50% or more from index serum creatinine prior to this acute illness, critical illness polyneuropathy as a peripheral neuropathy involving both motor and sensory fibres accompanied by limb and respiratory muscle weakness.

Statistical analysis

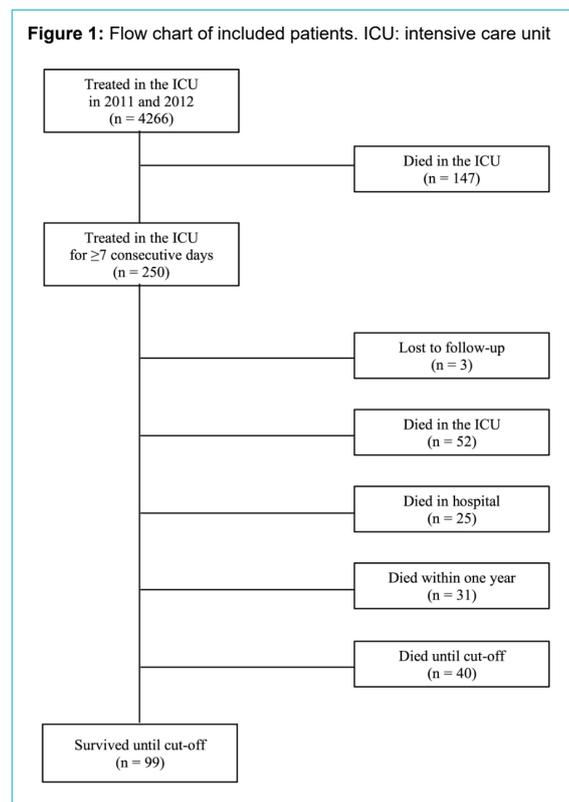
Variables were summarised by comparing patients who survived less than one year with patients who survived longer than one year. We compared between these groups using the chi-square test for nominal variables. Continuous variables were compared using t-tests or, if strongly skewed, using the non-parametric Kruskal-Wallis test. No correction for multiple testing (i.e., alpha inflation) was performed. For normally distributed numerical variables, mean and standard deviation (SD) were calculated. For non-normal numerical data, median and interquartile range (IQR) were computed. Categorical data are summarised in percent. Kaplan-Meier curves including a table for number at risk were fit to compare survival of groups concerning age, with and without comorbidities, complications, and treatment. All statistical analyses were performed using R Statistical Language and Environment.

Results

In the years 2011 and 2012, a total of 4926 patients were treated in the examined ICU. Of the 4676 patients (94.9%) requiring short-term care, 147 (3.2%) died during their ICU stay. A total of 250 patients (5.1%) needed a treatment of ≥ 7 consecutive days, three of whom were lost to follow up. Therefore, further evaluation included 247 patients (fig. 1).

Fifty-two long-term patients (21.1%) died in the ICU, 25 (10.1%) after transfer to the normal ward (table 1). Thirty-one patients (12.5%) died within 1 year after the beginning of intensive care treatment. Altogether, the 1-year mortality was 43.7% (108 patients) (table 2). At the end of follow-up

Figure 1: Flow chart of included patients. ICU: intensive care unit



after 6 to 7 years, 99 patients (40.1%) were still alive (table 1).

The median age of all long-term patients was 66 years (IQR 56–75) and two thirds were men. Almost 70% of them were admitted to the hospital as emergency patients. The median length of stay of was 12.7 days (IQR 9.0–18.6), the mean SAPS-II was 48.7 points (SD 17.3) and the mean NEMS 1467.4 points (SD 1092.1). Eighty-four patients (34%) were treated more than once in the ICU. Ninety-nine patients (40.1%) underwent heart surgery; 39 (15.8%) were post-abdominal surgery patients. A total of 42 patients suffered a polytrauma (31 patients, 12.6%) or isolated traumatic brain injury (11 patients,

4.5%). All other diagnosis groups included less than 10% of patients for each group. More than 90% of patients with polytrauma survived until the cut-off date. Among cardiac surgery patients, 37 of 99 patients (37.4%), and after abdominal surgery, 11 of 39 patients (28.2%) survived. All 15 patients who underwent lung surgery died.

Delirium occurred in more than half of the patients (140 patients, 56.7%). Eighty-four patients (34.0%) suffered from septic shock, 62 (25.1%) from tracheobronchitis, 96 (38.9%) from pneumonia, and 74 (30.0%) from acute renal failure. On average, 2.4 complications occurred per patient. Almost all patients (232 patients, 93.9%) were transferred intubated to the ICU or were intubated at least once

Table 1:
Patient characteristics and outcomes.

		Died in ICU (n = 52)	Died in hospital (n = 25)	Died after discharge (n = 71)	Survived to follow-up (n = 99)	All patients (n = 247)
Age (years), median (IQR)		69 (62.5–75)	71 (62–79)	71 (61–76)	59 (42–67)	66 (56–75)
Sex, n (%)	Male	35 (67.3)	15 (60.0)	43 (60.6)	70 (70.7)	163 (66.0)
	Female	17 (32.7)	10 (40.0)	28 (39.4)	29 (29.3)	84 (34.0)
Charlson comorbidity index, mean (SD)		2.0 (1.8)	2.4 (1.8)	2.3 (1.9)	0.9 (1.4)	1.7 (1.8)
Emergency admission, n (%)		29 (55.8)	18 (72.0)	49 (69.0)	75 (75.8)	171 (69.2)
Length of stay (days), median (IQR)		16.0 (10.4–23.3)	12.1 (9.0–20.1)	11.0 (8.9–18.9)	11.5 (8.6–16.9)	12.7 (9.0–18.6)
Main diagnosis, n (%)	Traumatic brain injury	1 (9.1)	1 (9.1)	2 (18.2)	7 (63.6)	11 (4.5)
	Polytrauma	1 (3.2)	1 (3.2)	1 (3.2)	28 (90.3)	31 (12.6)
	Internal disease	1 (20.0)	2 (40.0)	0	2 (40.0)	5 (2.0)
Type of surgery, n (%)	Cardiac	24 (24.2)	7 (7.1)	31 (31.3)	37 (37.4)	99 (40.1)
	Neurological	2 (13.3)	4 (26.7)	3 (20.0)	6 (40.0)	15 (6.1)
	Pulmonary	6 (40.0)	2 (13.3)	7 (46.7)	0	15 (6.1)
	Abdominal	10 (25.6)	5 (12.8)	13 (33.3)	11 (28.2)	39 (15.8)
	Vascular	2 (11.8)	2 (11.8)	8 (47.1)	5 (29.4)	17 (6.9)
	Maxillofacial	2 (40.0)	0	2 (40.0)	1 (20.0)	5 (2.0)
	Orthopaedic	1 (14.3)	1 (14.3)	3 (42.9)	2 (28.6)	7 (2.8)
	Urological	2 (66.7)	0	1 (33.3)	0	3 (1.2)
SAPS-II, mean (SD)		53.2 (15.7)	52.2 (14.4)	51.9 (18.0)	43.2 (16.9)	48.7 (17.3)
NEMS, mean (SD)		2061.0 (1432.1)	1442.2 (1244.1)	1338.2 (868.8)	1254.5 (873.5)	1467.4 (1092.1)
ICU complications, n (%)	Delirium	22 (42.3)	11 (44.0)	47 (66.2)	60 (60.6)	140 (56.7)
	Stroke	2 (3.8)	2 (8.0)	7 (9.9)	7 (7.1)	18 (7.3)
	Tracheobronchitis	11 (21.2)	6 (24.0)	14 (19.7)	31 (31.3)	62 (25.1)
	Pneumonia	31 (59.6)	9 (36.0)	28 (39.4)	28 (28.3)	96 (38.9)
	Pleural empyema	9 (17.3)	1 (4.0)	5 (7.0)	3 (3.0)	18 (7.3)
	ARDS	9 (17.3)	2 (8.0)	2 (2.8)	9 (9.1)	22 (8.9)
	Septic shock	29 (55.8)	13 (52.0)	23 (32.4)	19 (19.2)	84 (34.0)
	Acute renal insufficiency	22 (42.3)	9 (36.0)	21 (29.6)	22 (22.2)	74 (30.0)
	Acute on chronic renal insufficiency	15 (28.8)	7 (28.0)	21 (29.6)	10 (10.1)	53 (21.5)
	Critical illness polyneuropathy	11 (21.2)	2 (8.0)	8 (11.3)	1 (1.0)	22 (8.9)
Number of complications, mean (SD)		3.0 (1.6)	2.4 (1.7)	2.5 (1.4)	1.9 (1.3)	2.4 (1.5)
Requiring mechanical ventilation n (%)		51 (98.1)	23 (92.0)	65 (91.5)	93 (93.9)	232 (93.9)
Days of ventilation, median (IQR)		10 (6–13)	5 (3–10)	6 (4–11)	7 (4–11)	7 (4–11)
Requiring tracheostomy, n (%)		17 (32.7)	5 (20.0)	24 (33.8)	27 (27.3)	73 (29.2)
Requiring RRT, n (%)		22 (42.3)	5 (20.0)	12 (16.9)	15 (15.2)	54 (21.9)
Days of RRT, median (IQR)		6.5 (3–14)	5 (2–6)	6.5 (4.5–16)	7 (4–13)	6 (3.75–14)
Requiring IABP, n (%)		7 (13.5)	0	7 (9.9)	11 (11.1)	25 (10.1)
Days of IABP, median (IQR)		8 (5–9)	0	3 (1–5)	2 (2–4)	3 (2–5.5)
Requiring ECMO, n (%)		4 (7.7)	0	2 (2.8)	3 (3.0)	9 (3.6)
Days of ECMO, median (IQR)		8.5 (8–11.5)	0	4.5 (2–7)	4 (2–5)	7 (3–8.5)
Requiring ICP monitoring, n (%)		1 (1.9)	4 (16.0)	4 (5.6)	19 (19.2)	28 (11.3)
Days of ICP monitoring, median (IQR)		8	7 (3.5–19.5)	9 (7–10)	7 (4–10)	8 (4.25–10)
Number of ICU treatments, mean (SD)		1.6 (1.5)	1.7 (1.2)	1.8 (1.2)	1.3 (0.6)	1.56 (1.1)

ARDS: acute respiratory distress syndrome; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; ICP: intracranial pressure; IQR: interquartile range; NEMS: nine equivalents of nursing manpower score; ICU: intensive care unit; RRT: renal replacement therapy; SAPS: simplified acute physiological score; SD: standard deviation

during the course of treatment. Median ventilation time was 7 days (IQR 4–11). Seventy-three patients (29.2%) had to be tracheotomised. Renal replacement therapy (RRT) was necessary in 54 patients (21.9%), an intra-aortic balloon pump (IABP) in 25 (10.1%, corresponding to 25% of the cardiac surgery patients), an extracorporeal membrane oxygenation (ECMO) device in 9 (3.6%), and an intracranial pressure (ICP) measurement in 28 (11.3%) (table 1).

Patients who died within one year of beginning treatment in the ICU were significantly older (median 71 vs 63 years, $p < 0.001$), had a higher Charlson comorbidity index (CCI) (mean 2.3 vs 1.2, $p < 0.001$), a longer ICU stay (median 13.9 vs 10.6 days, $p = 0.001$), a higher SAPS-II (mean 52.7 vs 45.6, $p = 0.001$), a higher NEMS (mean 1772.4 vs

1230.4, $p < 0.001$) and more complications (mean 2.9 vs 2.0, $p < 0.001$) compared with those surviving at least one year. Moreover, the deceased more frequently developed pneumonia (50.9% vs 29.5%, $p = 0.001$), pleural empyema (13.0% vs 2.9%, $p = 0.005$), septic shock (51.9% vs 20.1%, $p < 0.001$), or critical illness polyneuropathy (16.7% vs 2.9%, $p < 0.001$). They also more frequently required RRT (30.6% vs 15.1%, $p = 0.006$) (table 2).

Supplementary table S1 (appendix) lists patients with different treatment times. Ninety-two patients (37.2%) received intensive care for 7–9 days, 60 patients (24.3%) for 10–14 days, 49 patients (19.8%) for 15–20 days, and 46 patients (18.6%) for ≥ 21 days. The mortality among the four groups in the ICU or after transfer to the normal ward

Table 2:
Patient characteristics and survival.

	Died within 1 year (n = 108)	1-year survivor (n=139)	p-Value
Age (years), median (IQR)	71 (63–71)	63 (47–71)	<0.001
Sex, n (%)	Male	71 (65.7)	92 (66.2)
	Female	37 (34.3)	47 (33.8)
Charlson comorbidity index, mean (SD)	2.3 (1.8)	1.2 (1.6)	<0.001
Emergency admission, n (%)	65 (60.2)	106 (76.3)	0.010
Length of stay (days), median (IQR)	13.9 (10.2–21.2)	10.6 (8.5–17.1)	0.001
Main surgical diagnosis, n (%)	Traumatic brain injury	3 (27.3)	8 (72.7)
	Polytrauma	2 (6.5)	29 (93.5)
	Internal disease	3 (60.0)	2 (40.0)
Type of surgery, n (%)	Cardiac	42 (42.4)	57 (57.6)
	Neurological	7 (46.7)	8 (53.3)
	Pulmonary	13 (86.7)	2 (13.3)
	Abdominal	20 (51.3)	19 (48.7)
	Vascular	9 (52.9)	8 (47.1)
	Maxillofacial	4 (80.0)	1 (20.0)
	Orthopaedic	3 (42.9)	4 (57.1)
	Urological	2 (66.7)	1 (33.3)
SAPS-II, mean (SD)	52.7 (16.0)	45.6 (17.6)	0.001
NEMS, mean (SD)	1772.4 (1275.7)	1230.4 (857.3)	<0.001
ICU complications, n (%)	Delirium	51 (47.2)	89 (64.0)
	Stroke	8 (7.4)	10 (7.2)
	Tracheobronchitis	26 (24.1)	36 (25.9)
	Pneumonia	55 (50.9)	41 (29.5)
	Pleural empyema	14 (13.0)	4 (2.9)
	ARDS	12 (11.1)	10 (7.2)
	Septic shock	56 (51.9)	28 (20.1)
	Acute renal insufficiency	41 (38.0)	33 (23.7)
	Acute on chronic renal insufficiency	32 (29.6)	21 (15.1)
Critical illness polyneuropathy	18 (16.7)	4 (2.9)	
Number of complications, mean (SD)	2.9 (1.6)	2.0 (1.2)	<0.001
Requiring mechanical ventilation n (%)	102 (94.4)	130 (93.5)	0.026
Days of ventilation, median (IQR)	8 (5–12)	7 (4–11)	0.038
Requiring tracheostomy, n (%)	36 (33.3)	37 (26.6)	0.314
Requiring RRT, n (%)	33 (30.6)	21 (15.1)	0.006
Days of RRT, median (IQR)	6 (3–14)	5 (4–11)	1.000
Requiring IABP, n (%)	9 (8.3)	16 (11.5)	0.543
Days of IABP, median (IQR)	6 (5–8)	2 (2–3.2)	<0.001
Requiring ECMO, n (%)	4 (3.7)	5 (3.6)	1.000
Days of ECMO, median (IQR)	8.5 (8–10.2)	4 (2–5)	0.014
Requiring ICP monitoring, n (%)	6 (5.6)	22 (15.8)	0.020
Days of ICP monitoring, median (IQR)	8.5 (5–9.8)	7.5 (5–9.8)	0.866
Number of ICU treatments, mean (SD)	1.7 (1.5)	1.4 (0.7)	0.026

ARDS: acute respiratory distress syndrome; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; ICP: intracranial pressure; IQR: interquartile range; NEMS: nine equivalents of nursing manpower score; ICU: intensive care unit; RRT: renal replacement therapy; SAPS: simplified acute physiological score; SD: standard deviation

was 18.5%, 32.7%, 40.8% and 43.4% and increased until follow-up to 53.3%, 60%, 59.2% and 73.9%, respectively. The four Kaplan-Meier curves comparing patient mortality in age groups >65 years and <66 years, patients with a CCI ≤3 or >4, patients with or without septic shock, and patients who received ≥2 treatments compared with just one are shown in figure 2. Short vertical lines crossing the curves indicate censoring (i.e., right censoring indicates end of follow-up). Tables below each Kaplan-Meier curve indicate the number of patients “at risk”, which corresponds to the number of patients still alive at this time point. The numbers at the 7-year time point are fragmentary, as not all patients were observed for 7 years in total.

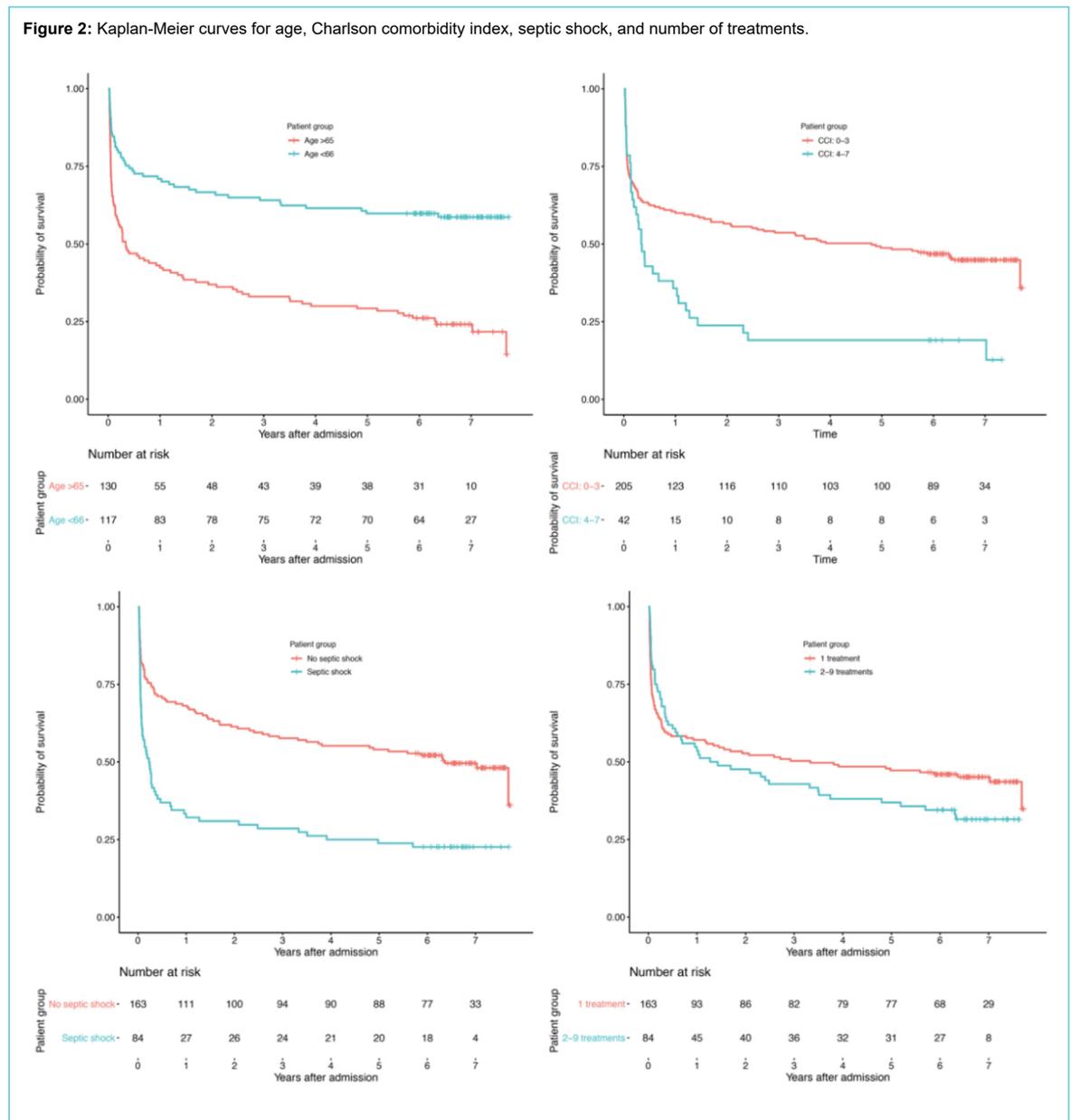
Discussion

This study examines mortality after an ICU treatment of 7 or more consecutive days. Seventy-six of the 247 (30.8%) patients died in hospital, and another 32 (12.9%) within one year. At the end of follow-up, at least 6.6 years after the beginning of intensive care treatment, 99 patients

(40.1%) were still alive. One-year mortality was significantly higher with increased age, higher CCI, longer length of ICU treatment, higher SAPS-II and NEMS score, the occurrence of pneumonia, sepsis or critical illness polyneuropathy, the need for RRT, and a higher number of complications.

As there is no generally accepted definition of prolonged ICU stay (PrLOS) [8, 14], we selected 7 days as the cut-off for long-term ICU treatment in this study. If the disease is more severe or if complications occur, ICU treatment can be prolonged, sometimes massively. The acute critical illness then turns into a persistent or chronic critical illness. Iwashyna et al. [17] defined a persistent critical illness as “when a patient’s reason for being in ICU is now more related to their ongoing critical illness than their original reason for admission to the ICU.” In a single-centre cohort study in Australia, Williams et al. found the long-term mortality to reach a plateau after 10 days of ICU treatment [18]. Baghsaw et al. determined this transition point to be approximately 9 days after ICU admission in a cohort of

Figure 2: Kaplan-Meier curves for age, Charlson comorbidity index, septic shock, and number of treatments.



about 18,000 patients in 12 Canadian ICUs [19]. This point can show a wide range. Iwashyna and colleagues found it between day 7 and day 22 across diagnosis-based subgroups and between day 6 and day 15 across risk-of-death-based subgroups [8]. A retrospective observational cohort study of three large Anglo-American intensive care databases showed that the probability of future survival does not decrease further after 5 to 10 days, except for patients older than 75 years [14]. A cut-off of 7 days, therefore, seems to be an adequate threshold for PrLOS.

Obviously, this is not the first study examining the outcome of patients with a PrLOS. Supplementary table S2 summarises 32 of these studies. Only studies that also investigated factors associated with short- or long-term mortality were included. This includes 11 studies from the USA [9, 11, 20–28], six from Germany [29–34], three from Canada [35–37], two from Sweden [38, 39], and one each from Scotland [40], Switzerland [12], Italy [41], Israel [42], France [43], Austria [44], Belgium [45], New Zealand [46] and Taiwan [47]. Nine studies examined a mixed ICU [20, 34, 36, 40, 43–46, 48], three a surgical ICU [30, 32, 47] and five studies examined the outcome after trauma [9, 23, 24, 26, 28]. Most studies investigated patients after heart surgery [11, 12, 21, 22, 25, 27, 29, 33, 35, 37–39, 41, 42]. The definition of a PrLOS shows a wide variation. The number of days defined as cut-off varies from 3 to 90 days. A stay of at least 7 days [22, 29, 33, 41, 46] and more than 30 days were chosen most often [9, 26, 36, 40, 44]. Eight studies compared different groups of days [21, 23, 25, 27, 28, 31, 34, 45]. Despite a rather wide variation in hospital mortality, there is a trend towards increasing mortality with longer treatment time. If the length of stay is <10 days, hospital mortality is most often less than 18%. Exceptions include very old patients (hospital mortality 23.8%) [35] and patients on mechanical ventilation for longer than 7 days (hospital mortality) [41]. All but seven studies had a follow-up after 6 months to 5 years. Except for a few studies, total mortality at follow-up exceeded 50%, sometimes considerably. Trauma patients represent an exception, having a good short- and long-term prognosis, with a survival rate of usually over 90% [23, 28].

Many factors were shown to be associated with short or long-term mortality. Age [9, 20, 23, 24, 26, 28–30, 32, 34, 36, 39–42, 46, 48] and acute renal failure with or without renal replacement therapy [12, 20–23, 26, 27, 30, 31, 33, 36, 37, 39, 42–47] were found most frequently. Length of mechanical ventilation was associated with mortality in 10 studies [12, 22, 29, 32, 33, 36, 37, 41, 43, 45]. Length of the ICU or hospital stay was shown to be associated with short- or long-term mortality five times [33–35, 37, 42], and APACHE-II score [32, 35, 46, 48] and perioperative stroke four times [22, 23, 25, 42]. Other associated factors such as perioperative infarction [23, 29, 42], or the CCI [31] were reported less often.

These findings correlate well with the present study. Age, acute renal failure and the length of ICU stay were dominant in our data as well as in other studies, and the mortality of our patients – short- and long-term – was comparable. It is not surprising that age is associated with 1-year mortality. Some studies focussed particularly on outcome of older patients. Octogenarians after cardiac surgery and

an ICU stay of at least 5 days have higher hospital mortality than those with a shorter stay (23.8% vs 5.5%) and a significantly lower 1- and 5-year functional survival [35]. In a review article, Conti et al. examined the outcome of elderly patients after intensive care treatment [49]. The 22 included studies had very different definitions to describe “elderly”, ranging from 65 to 90 years. Long-term mortality increased with older age. If mortality is adjusted according to disease severity and comorbidities, the difference diminishes. In recent years, the concept of frailty (i.e., the combination of decreased mobility, weakness, reduced muscle mass, poor nutritional status and diminished cognitive function) has received increasing attention and has been shown to have a prognostic value [50]. In a 2017 systematic review by Muscedere et al., both hospital and long-term mortality of frail patients was higher and discharge home less likely in 10 observational studies examining the outcome of frail patients after intensive care treatment [51]. Acute renal failure – particularly if RRT is needed – is the second important factor that can indicate a bad outcome after PrLOS [52]. It is often the result of septic shock and triggers a cascade of systemic effects by release of cytokines and inflammatory mediators [53]. In recent years several strategies to prevent acute renal failure have been proposed that have the potential to improve outcome [54, 55]. Surprisingly, delirium was more often observed in the group of 1-year survivors. In a systematic review of 42 studies, Salluh et al. found increased hospital mortality in ICU patients with delirium [56]. One possible explanation for our contradictory results is the longer period of mechanical ventilation in those patients who died in the ICU compared with those who survived at least one year (median 10 vs 7 days). A delirium could have been masked by intubation and sedation.

Efforts were made to identify patients at risk for PrLOS or increased mortality. Wesch et al. presented a risk score assessed at day 7 for predicting a PrLOS for more than 20 days. This score includes the factors mechanical ventilation for >14 hours (98 points), need for parenteral nutrition on day 7 (36 points), lowest albumin <20 g/l (28 points), and a CCI >2 (23 points) with a cut-off at 100 points (sensitivity 88%, specificity 75%) [57]. The ProVent risk model uses the variables age >65 years (2 points), age 50–64 years (1 point), platelet count <150,000/ml (1 point), vasopressors (1 point), haemodialysis (1 point) for patients requiring at least 21 days of mechanical ventilation [20]. A score >2 identifies patients who are at high risk of death within one year. For patients at risk for PrLOS, multimodal care management can optimise care and treatment [3, 57]. An evidence-based assessment and treatment plan includes early mobilisation, adapted nutrition, neurorehabilitation, scheduling daily activities and maintaining a diary. Ethical case discussions support the critical care team in end-of-life decision making for patients at high risk of death in hospital or soon after discharge [58, 59].

This study has some limitations. As a retrospective observational study involving one institution, the results cannot be generalised. It is possible that factors specific to this ICU will not be found in other ICUs. Our study focused on mortality, but this is only one important outcome. In recent years, quality of life after prolonged treatment in ICU has gained increasing attention.

Conclusion

Sixty percent of the patients who are treated for 7 or more consecutive days on a surgical ICU die within 7 years. One-year mortality (43.7%) is associated with age, CCI, length of ICU treatment, SAPS-II and NEMS scores, the occurrence of pneumonia, sepsis, critical illness polyneuropathy, the need for RRT and the number of complications. Scores combined with factors shown to be associated with increased short- and long-term mortality can help to identify patients at risk to die within one year after ICU treatment.

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

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Appendix: Supplementary tables

Table S1:

Patient characteristics and outcome of different LOS-groups.

		7–9 days (n = 92)	10–14 days (n = 60)	15–20 days (n = 49)	≥21 days (n = 46)	All patients (n = 247)
Outcome, n (%)	Died in ICU	10 (10.9)	14 (23.3)	14 (28.6)	14 (30.4)	52 (21.1)
	Died in hospital	7 (7.6)	10 (16.7)	2 (4.1)	6 (13.0)	25 (10.1)
	Died after discharge	32 (34.8)	12 (20.0)	13 (26.5)	14 (30.4)	71 (28.7)
	Survived at least 1 year	66 (71.7)	29 (48.3)	25 (51.0)	19 (41.3)	139 (56.3)
	Survived to follow-up	43 (46.7)	24 (40.0)	20 (40.8)	12 (26.1)	99 (40.1)
Age (years), median (IQR)	67 (48–74)	66.5 (56.5–73.5)	72 (60–76)	63 (56–70)	66 (56–75)	
Sex, n (%)	Male	58 (63.0)	45 (75.0)	30 (61.2)	30 (65.2)	163 (66.0)
	Female	34 (37.0)	15 (25.0)	19 (38.8)	16 (34.8)	84 (34.0)
Charlson comorbidity index, mean (SD)		1.5 (1.8)	1.7 (1.7)	1.8 (2.0)	2.0 (1.7)	1.7 (1.8)
Emergency admission, n (%)		62 (67.4)	50 (83.3)	32 (65.3)	27 (58.7)	171 (69.2)
Length of stay (days), median (IQR)		8.4 (7.7–9.2)	12.7 (10.8–13.6)	17.6 (16.7–18.9)	32.2 (25.2–40.5)	12.7 (9.0–18.6)
Main diagnosis, n (%)	Traumatic brain injury	7 (63.6)	3 (27.3)	1 (9.1)	0	11 (4.5)
	Polytrauma	10 (32.3)	10 (32.3)	7 (22.6)	4 (12.9)	31 (12.6)
	Internal disease	1 (20.0)	2 (40.0)	2 (40.0)	0	5 (2.0)
Type of surgery, n (%)	Cardiac	39 (39.4)	25 (25.3)	15 (15.2)	20 (20.2)	99 (40.1)
	Neurological	5 (33.3)	5 (26.7)	2 (13.3)	3 (20.0)	15 (6.1)
	Pulmonary	4 (26.7)	2 (13.3)	2 (13.3)	7 (46.7)	15 (6.1)
	Abdominal	18 (46.2)	1 (2.6)	10 (25.6)	10 (25.6)	39 (15.8)
	Vascular	1 (5.9)	9 (52.9)	5 (29.4)	2 (11.8)	17 (6.9)
	Maxillofacial	1 (20.0)	1 (20.0)	3 (60.0)	0	5 (2.0)
	Orthopaedic	5 (71.4)	1 (14.3)	1 (14.3)	0	7 (2.8)
	Urological	1 (33.3)	1 (33.3)	1 (33.3)	0	3 (1.2)
SAPS-II, mean (SD)	44.3 (17.0)	50.9 (15.0)	49.6 (15.1)	53.9 (20.8)	48.7 (17.3)	
NEMS, mean (SD)	735.1 (155.5)	1134.1 (208.7)	1645.1 (314.2)	3177.5 (1428.2)	1467.4 (1092.1)	
ICU complications, n (%)	Delirium	52 (56.5)	34 (56.7)	28 (57.1)	26 (56.5)	140 (56.7)
	Stroke	7 (7.6)	3 (5.0)	4 (8.2)	4 (8.7)	18 (7.3)
	Tracheobronchitis	15 (16.3)	20 (33.3)	13 (26.5)	14 (30.4)	62 (25.1)
	Pneumonia	21 (22.8)	23 (38.3)	32 (44.9)	30 (65.2)	96 (38.9)
	Pleural empyema	1 (1.1)	3 (5.0)	3 (6.1)	11 (23.9)	18 (7.3)
	ARDS	4 (4.3)	2 (3.3)	7 (14.3)	9 (19.6)	22 (8.9)
	Septic shock	22 (23.9)	18 (30.0)	18 (36.7)	26 (56.5)	84 (34.0)
	Acute renal insufficiency	16 (17.4)	14 (23.3)	17 (35.7)	27 (58.7)	74 (30.0)
	Acute on chronic renal insufficiency	19 (20.7)	15 (25.0)	10 (20.4)	9 (19.6)	53 (21.5)
Critical illness polyneuropathy	0	3 (5.0)	1 (2.0)	18 (39.1)	22 (8.9)	
Number of complications, mean (SD)	1.7 (1.0)	2.3 (1.5)	2.5 (1.3)	3.7 (1.4)	2.4 (1.5)	
Requiring mechanical ventilation, n (%)	80 (87.0)	57 (95.0)	49 (100)	46 (100)	232 (93.9)	
Days of ventilation, median (IQR)	4 (2–6)	8 (4–11)	10 (8–13)	13.5 (10–21)	7 (4–11)	
Requiring tracheostomy, n (%)	14 (15.2)	12 (20.0)	19 (38.8)	28 (60.9)	73 (29.2)	
Requiring RRT, n (%)	9 (9.8)	12 (20.0)	13 (26.5)	20 (43.5)	54 (21.9)	
Days of RRT, median (IQR)	4 (3–5)	4 (3–11.5)	6 (4–10)	13.5 (7–18)	6 (3.75–14)	
Requiring IABP, n (%)	5 (5.4)	7 (11.7)	6 (12.2)	7 (15.2)	25 (10.1)	
Days of IABP, median (IQR)	6 (4–8)	4 (3–5)	2 (2–5)	2 (1–5)	3 (2–5.5)	
Requiring ECMO, n (%)	4 (4.3)	2 (3.3)	2 (4.1)	1 (2.2)	9 (3.6)	
Days of ECMO, median (IQR)	5 (2–8.5)	11 (8–14)	4.5 (4–5)	7	7 (3–8.5)	
Requiring ICP monitoring, n (%)	10 (10.9)	11 (18.3)	5 (10.2)	2 (4.3)	28 (11.3)	
Days of ICP monitoring, median (IQR)	6.5 (5–10)	6 (4–9)	12 (9–15)	20 (11–29)	8 (4.25–10)	
Number of ICU treatments, mean (SD)	1.3 (0.6)	1.6 (1.1)	1.5 (1.1)	2.1 (1.7)	1.56 (1.1)	

ARDS: acute respiratory distress syndrome; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; ICP: intracranial pressure; IQR: interquartile range; NEMS: nine equivalents of nursing manpower score; ICU: intensive care unit; RRT: renal replacement therapy; SAPS: simplified acute physiological score; SD: standard deviation

Table S2:

Studies examining the outcome after prolonged ICU length of stay and associated factors.

Reference, year, country	Type pat./ICU	Definition of Pr-LOS	Patients (n)	Follow-up period	Mortality	Factors associated with short- or long-term mortality
Arora et al. [35], 2017, Canada	Cardiac surgery	Age >80 y and >5 d	105	1 and 5 y	25 (23.8%) in-hospital; another 11 (10.5%) within 1 y; another 38 (36.2%) within 5 y	Diabetes / APACHE II \geq 20 / Days in hospital / More physician visits within 30 d
Bashour et al. [11], 2000, USA	Cardiac surgery	>10 d	142	16–37 mo	47 (33%) in-hospital; another 44 (31%) until follow-up	Previous myocardial infarction / Preoperative hypalbuminaemia / History of congestive heart failure
Elfstrom et al. [21], 2012, USA	Cardiac surgery	(a) <3 d; (b) 3-7 d; (c) 7-14 d; (d) >14 d	(a) 8666; (b) 1625; (c) 405; (d) 388	1 y	One-year: (a) 259 (3%); (b) 144 (8.9%); (c) 49 (12.1%); (d) 123 (31.7%)	Postoperative renal failure / Reintubation
Engoren et al. [22], 2000, USA	Cardiac surgery	Mechanical ventilation \geq 7 d	123	5 y	19 (15%) in-hospital; Another 51 (41%) until follow-up	Aortic valve surgery / Pre- or postoperative stroke / Admitting creatinine / Postoperative renal failure / Days of mechanical ventilation / Discharge on tube feeding
Gersbach et al. [12], 2006, Switzerland	Cardiac surgery	>5 d	194	1 and 3 y	17 (8.7%) in-hospital; Another 19 (9.8%) until follow-up	Mechanical ventilation >5 d / Renal replacement therapy
Grothausen et al. [29], 2013, Germany	Cardiac surgery	>7 d	230	5 y	28 (12%) in-hospital; Another 91 (39.5%) until follow-up	Age >70 y / Preoperative atrial fibrillation / Myocardial infarction / Mechanical ventilation >8 d
Hellgren et al. [38], 2005, Sweden	Cardiac surgery	>8 d	225	1–5 y	27 (12%) in-hospital; Another 44 (19.5%) until follow-up	NYHA \geq III
Lagercrantz et al. [39], 2010, Sweden	Cardiac surgery	>10 d	141	1, 3 and 5 y	46 (33%) in-hospital; Another 19 (14%) until follow-up;	Renal replacement therapy / Age
Manji et al. [37], 2016, Canada	Cardiac surgery	>5 d	728	1 and 5 y	132 (18%) in-hospital; Another 300 (41%) until follow-up	Age >80 y / Preoperative dialysis / Cerebrovascular disease / Peripheral vascular disease / Preoperative infection / ECMO/VAD / Days in ICU / Ventilator days / Renal replacement therapy
Pappalardo et al. [41], 2004, Italy	Cardiac surgery	Mechanical ventilation >7 d	148	36 \pm 12 mo	67 (45.3%) in-hospital; Another 11 (7.4%) until follow-up	Age / Diabetes / Mechanical ventilation >21 d
Ryan et al. [27], 1997, USA	Cardiac surgery	(a) >14 d; (b) >28 d	(a) 324; (b) 166	None	In-hospital: (a) 141 (43.5%); (b) 74 (45%)	Reduced GCS / Vasopressors / Renal replacement therapy / Lower platelet count / Lower serum albumin
Schöttler et al. [33], 2011, Germany	Cardiac surgery	>7 d	223	1 y	28 (12.6%) in-hospital; Another 60 (26.9%) until follow-up	Preoperative atrial fibrillation / Preoperative pulmonary hypertension / Days in ICU / Days with vasopressors / Days with mechanical ventilation / Tracheostomy / Pneumonia / Renal replacement therapy
Silberman et al. [42], 2013, Israel	Cardiac surgery	>14 d	331	5 y	131 (40%) in-hospital; Another 96 (29%) until follow-up	Days in ICU / Age / Female sex / COPD / Sepsis / Stroke / Perioperative myocardial infarction / Renal deterioration
Yu et al. [25], 2016, USA	Cardiac surgery	(a) 1-2 wk; (b) 2-4 wk; (c) >4 wk	(a) 162; (b) 79; (c) 142	2 y	In-hospital: (a) 18 (11.1%); (b) 21 (26.6%); (c) 44 (31%); Total mortality after 2 y: (a) 24.7% ; b) 25.9% ; c) 58.9%	Preoperative low haematocrit / Postoperative stroke / Peripheral vascular disease
Carden et al. [46], 2008, New Zealand	Mixed	>7d	207	1 y	60 (28%) in-hospital; Another 24 (12%) within 1 y	Age / APACHE II score / Sepsis / Renal replacement therapy / Cardiac arrest in ICU
Carson et al. [20], 2012, USA	Mixed	Mechanical ventilation >21 d	260	1 y	72 (28%) in-hospital; Another 52 (20%) until follow-up	Age / Platelet count >150 / Vasopressors / Renal replacement therapy
Combes et al. [43], 2003, France	Mixed	Mechanical ventilation >14 d	347	3 y	150 (43%) ICU; Another 58 (29%) until follow-up	Age >65 y / NYHA \geq III / Preadmission immunocompromised status / Septic shock and nosocomial septicemia / Renal replacement therapy / Mechanical ventilation >35 d
Delle Karth et al. [44], 2006, Austria	Mixed	>30 d	135	1–4 y	46 (34%) in-hospital; Another 46 (34%) until follow-up	Renal replacement therapy
Friedrich et al. [36], 2006, Canada	Mixed	>30 d	182	6 mo	76 (42%) in-hospital; Another 15 (8%) until follow-up	Age / Immunosuppression / Mechanical ventilation >90 d / Vasopressor for >3 d / Renal replacement therapy
Hermans et al. [45], 2019, Belgium	Mixed	(a) <8 d; (b) >8 d	(a) 3410; (b) 1209	5 y	In-hospital: (a) 146 (4.3%); (b) 158 (13.1%); Another until follow-	Hypoglycaemia in ICU / Infection in ICU / Mechanical ventilation >2 d / Renal replacement therapy

					up: (a) 673 (19.7%); (b) 449 (37.2%)	
Hughes et al. [40], 2001, Scotland	Mixed	>30 d	322	None	129 (40.1%) in-hospital	Age >70 y
Steenbergen et al. [48], 2015, Netherlands	Mixed	>72 h	740	1 y	191 (26%) in-hospital; Another 175 (28%) until follow-up;	Age / APACHE-IV PM Score / Comorbidity / ICU readmission
Weiler et al. [34], 2012, Germany	Mixed	(a) 5–19 d; (b) >20 d	(a) 87; (b) 67	1 y	In-hospital: (a) 38 (43.7%); (b) 29 (43.2%); Total mortality after 1 y: (a) 49 (56.3%); (b) 41 (61.2%)	Age / Days in ICU / SAPS II
Hartl et al. [32], 2007, Germany	Surgical	>28 d	390	1, 3 and 5 y	186 (47.7%) in-hospital; Survival of discharged patients: 1 y 61.8%; 3 y 44.7%; 5 y 37.0%	Age / APACHE II score / Thoracic surgery / Palliative surgery / Mechanical ventilation >50 d / Number of surgical revisions / Pneumonia
Huang et al. [47], 2010, Taiwan	Surgical	>16 d	377	1 y	132 (35%) in-hospital; Another 66 (14.4%) until follow-up	Renal replacement therapy
Martini et al. [30], 2017, Germany	Surgical	>90 d	19	1 y	10 (52%) in-hospital; Another 4 (21%) until follow-up	Age / Renal replacement therapy
Chaudhary et al. [28], 2019, USA	Trauma	(a) 2–9 d; (b) >9 d	(a) 4346; (b) 1043	1 y	Until follow-up: (a) 154 (3.5%); (b) 50 (4.8%)	Age
Eschbach et al. [31], 2016, Germany	Hip-fracture, Age >60 y	(a) <3 d; (b) >3 d	(a) 275; (b) 61	1 y	In-hospital: (a) 9 (3.2%); (b) 16 (26.2%); Another until follow-up: (a) 60 (21.8%); (b) 33 (54.1%)	ASA class / Charlson Comorbidity Index / Renal replacement therapy
Kisat et al. [23], 2016, USA	Trauma	(a) 1 d; (b) 2–9 d; (c) 10–40 d; (d) >40 d	(a) 168,604; (b) 324,419; (c) 8,334; (d) 4,794	None	In-hospital: (a) 9.9%; (b) 4.9%; (c) 6.6%; (d) 9.8%	Age >35 y / Higher ISS / Lower GCS / Myocardial infarction / Stroke / Renal failure
Miller et al. [24], 2000, USA	Trauma	>3 wk	115	NA	In-hospital: 25 (22%); After discharge another: 11 (9.6%)	Age
Ong et al. [26], 2009, USA	Trauma	>30 d	205	None	25 (12%) in-hospital	Age >64 y / Preexisting cardiac or renal disease / ARDS / Renal replacement therapy
Trottier et al. [9], 2007, USA	Trauma	>30 d	339	None	45 (13.3%) in-hospital	Age >50 y

APACHE II: acute physiology and chronic health evaluation; ARDS: acute respiratory distress syndrome; ASA = American Society of Anesthesiologists; COPD: chronic obstructive pulmonary disease; d: day, ECMO: extracorporeal membrane oxygenation; GCS: Glasgow Coma Scale; ICU: intensive care unit; ISS: injury severity score; mo: month; NYHA: New York Heart Association; PM: predicted mortality; PrLOS: prolonged ICU stay; SAPS II: simplified acute physiological score; VAD: ventricular assist device; wk: week; y: year