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Original Research

CRITICAL CARE

Long-term Mortality Outcome Associated With Prolonged Admission to the ICU*

Kevin B. Laupland, MD, MSc; Andrew W. Kirkpatrick, MD, MSc; John B. Kortbeek, MD; and Danny J. Zuege, MD, MSc, FCCP

Study objectives: **Patients requiring prolonged admission to the ICU consume significant health-care resources and have a high rate of in-hospital death. The long-term mortality outcome of these patients has not been well defined in a nonselected cohort. The objective of this study was to describe the occurrence and factors predictive of prolonged ICU stay at admission, and to define the long-term (≥ 1 year) mortality outcome.**

Design: **Population-based cohort.**

Setting: **All adult multisystem and cardiovascular surgical ICUs in the Calgary Health Region (CHR) from July 1, 1999, to March 31, 2002.**

Patients: **Adult (≥ 18 years old) residents of the CHR admitted to regional ICUs.**

Interventions: **None.**

Measurements and results: **During the study, 4,845 patients had a median length of stay of 2 days (interquartile range, 1 to 4 days); 2,115 patients (44%) were admitted for < 2 days, 1,496 patients (31%) were admitted for 2 to 3 days; 1,018 patients (21%) were admitted from 4 to 13 days; and 216 patients (4%) had a prolonged (≥ 14 day) admission to the ICU. A higher severity of illness, the presence of shock, and bloodstream infection were independently associated with a prolonged ICU admission, and cardiovascular surgery was associated with a lower risk. Patients with prolonged ICU admissions were nearly twice as likely to die as patients with shorter ICU admissions: 53 of 216 patients (25%) vs 584 of 4,629 patients (13%) [p = 0.0001]. Among the 3,924 survivors to hospital discharge, the rates of mortality during the year following ICU admission were as follows: 59 deaths in 1,758 patients (3%) admitted < 2 days, 74 deaths in 1,267 patients (6%) with 2- to 3-day admissions, 78 deaths in 766 patients (10%) with 4- to 13-day admissions, and 10 deaths in 133 patients (8%) with admissions ≥ 14 days.**

Conclusions: **One in 25 critically ill patients will have prolonged ICU admission and higher ICU-related mortality. However, survivors of prolonged ICU admission have good long-term mortality outcome after acute illness.** ***(CHEST 2006; 129:954–959)***

Key words: ICU; mortality; risk factor

Abbreviations: APACHE = acute physiology and chronic health evaluation; BSI = bloodstream infection; CHR = Calgary Health Region; CVICU = cardiovascular surgery ICU; IQR = interquartile range

Although the majority of patients with a critical illness will only require admission to the ICU for a few days, some have particularly complicated courses requiring admission for prolonged periods. Prolonged ICU admission, as commonly defined by lengths of ICU stay > 2 to 3 weeks, have been associated with increased risk for infectious complications, adverse outcomes, and consumption of a considerable amount of ICU resources.[1–9] A number

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of studies have investigated the occurrence, risk factors, and/or outcome of prolonged admission to ICU, but a number of limitations exist. Prior studies[1–6,8,10,11] have typically been reported from highly selected patient subgroups or from single surgical or medical tertiary care ICUs such that they may not be readily generalized to critically ill populations at large. In addition, the majority of studies[1,2,4,5,11] to date have included relatively small numbers of patients and therefore are limited in statistical power. Furthermore, several studies[2,5,7,10,11] have had incomplete or limited duration of follow-up potentially underestimating the true impact of prolonged ICU admission.

No previous studies have utilized a population-based methodology to define the occurrence, risk factors, and long-term outcome of prolonged admission to ICU. We therefore studied all adults admitted to ICUs in our large Canadian health region in order to establish a minimally biased rate of and baseline risk factors for prolonged ICU admission, and to determine the long-term (≥ 1 year) mortality outcome of these patients.

Materials and Methods

Study Population

The Calgary Health Region (CHR) administers all publicly funded hospital care to the residents of the cities of Calgary and Airdrie and approximately 20 nearby small towns, villages, and hamlets (population 1 million) in the Province of Alberta, Canada. All critically ill adult patients in the CHR are managed in ICUs under the care of the Department of Critical Care Medicine, University of Calgary, and CHR. These ICUs are closed units staffed by fully trained intensivists and currently include a 14-bed cardiovascular surgery ICU (CVICU) and three multisystem ICUs: one 24-bed multisystem ICU that serves as the regional trauma and neurosurgical referral center; one 12-bed multisystem ICU that is also the vascular surgery referral center; and a 10-bed multisystem ICU. There are no generally predefined set criteria for admission to the regional ICUs, and the decision for admission and discharge remains with the attending intensivist. Patients after cardiac surgery are routinely admitted to the CVICU; an individualized decision is made regarding ICU admission for all other surgical patients. Postoperative neurosurgical and noncardiac vascular surgical patients may be admitted to specialized monitored wards, but these patients are transferred to ICU areas if physiologic supportive measures are required. Coronary care patients requiring ventilator support are always transferred to ICUs in two of the three regional coronary care units. However, if patients receiving mechanical ventilation who are managed in the third coronary care unit acquire multiorgan dysfunction, they are commonly transferred to an ICU. The base study population consisted of all adult (≥ 18 years old) residents of the CHR admitted to any multisystem or cardiovascular surgery ICU in the CHR between July 1, 1999, and March 31, 2002. The Conjoint Health Research Ethics Board at the University of Calgary and CHR approved this study.

Study Protocol

This study utilized a population-based inception cohort design that linked clinical, microbiologic, and outcome data from four large regional/provincial databases. The details of development of the study database have been previously reported in detail.[12] Briefly, demographic, clinical, and basic laboratory data collected on the first day of ICU admission and hospital outcome data were obtained on all patients in an uniform manner across all sites using a regional patient care and administrative ICU database. A primary diagnosis was defined as that listed by the attending physician as the main reason for ICU admission. Information on CHR residency status was obtained from a regional corporate data warehouse, and the presence of bloodstream infection (BSI) was established through a linkage with Calgary Laboratory Services, a regional-based laboratory that performs all basic microbiology testing on residents of the CHR. Mortality outcome information through March 31, 2003, was obtained through a linkage with the Alberta Health and Wellness database that maintains information on all residents of Alberta eligible for publicly funded health-care coverage (> 99% of the population of Alberta).

Definitions

The time of inception was the day of admission to ICU. A prolonged admission was defined by an ICU length of stay ≥ 14 days. The diagnosis of systemic inflammatory response syndrome was based on the presence of two or more modified consensus criteria.[13] A BSI was deemed to be present if a pathogenic organism was cultured from at least one set of blood specimens; at least two positive blood culture results were required to diagnose BSI with common skin contaminants.[14] Shock was deemed to be present if a vasopressor infusion was required to maintain a clinically adequate BP. A surgical patient was any patient recorded as having an operative diagnostic code or admitted from the trauma ward, postcardiac surgery care unit, or directly from the operating room. Severity of illness at inception was assessed using the APACHE (acute physiology and chronic health evaluation) II, and intensity of care was assessed using Therapeutic Intervention Scoring System scores.[15,16]

Statistical Analysis

Analysis was performed using statistical software (Stata version 8.0; StataCorp; College Station, TX). To avoid the assessment of multiple outcomes for a single patient, only first ICU presentations were analyzed from patients with multiple ICU admissions. Normally or near-normally distributed variables are reported as mean ± SD, and nonnormally distributed variables are reported as medians with interquartile range (IQR). Means were compared using the Student *t* test, and medians were compared using the Mann-Whitney *U* test. Differences in proportions among categorical data were assessed using a Fisher exact test. In comparisons of factors predictive of a prolonged ICU stay, an *a priori* decision was made to limit comparison to those patients requiring at least 2 days of admission to ICU in order to exclude patients admitted for routine postoperative monitoring.

A logistic regression model was developed to assess independent factors at ICU admission associated with a prolonged ICU length of stay. Variables initially included in the model were those potentially clinically relevant variables of age, gender, and surgical vs medical diagnosis, and those variables found to be significant to the $p \leq 0.2$ level in univariate analysis. Backward stepwise variable elimination was then performed to develop the final model. Discrimination was assessed using the area under the receiver operator characteristic curve and calibration using the

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Hosmer-Lemeshow goodness of fit test. Kaplan-Meier plots were used to display the survival functions of different ICU length of stay categories following ICU discharge.

Results

During the study period, 4,845 residents of the CHR were admitted to a regional adult ICU. Of the entire cohort, 2,913 patients (60%) were surgical patients, 3,007 patients (62%) were men, and the median age was 64.6 years (IQR, 50.7 to 74.4 years). The mean APACHE II score was 24.9 ± 8.8, and the median length of ICU stay was 2 days (IQR, 1 to 4 days). Two thousand one hundred fifteen patients (44%) were admitted for < 2 days; 1,496 patients (31%) were admitted for 2 to 3 days; 1,018 patients (21%) were admitted for 4 to 13 days; and 216 patients (4%) had a prolonged (≥ 14 days) admission to the ICU.

The distribution of primary admitting diagnostic categories was significantly ($p < 0.001$) different among the patients who had intermediate (from 2 to 13 days) as compared to prolonged (≥ 14 days) ICU admissions as shown in Table 1. This was due to lower rates of cardiovascular ($p < 0.0001$) and endocrine/metabolic diagnoses ($p = 0.02$), and higher rates of respiratory (< 0.001), shock ($p < 0.01$), and trauma ($p < 0.0001$) diagnoses among patients requiring prolonged ICU admission. The proportions of admissions to the multisystem units that were prolonged were not different among each of the three multisystem ICUs, but these were significantly different from the CVICU (87 of 881 admissions, 59 of 574 admissions, and 57 of 496 admissions for the three multisystem ICUs, vs 13 of 779 admissions for the CVICU; $p < 0.001$).

A number of different factors at presentation (as determined within the first day of ICU admission) were associated with a prolonged ICU length of stay as compared to an intermediate ICU length of stay and are shown in Table 2. A multivariable logistic regression model was developed (2,706 observations) that had fair discrimination (area under receiver operator characteristic curve, 0.71; 95% confidence interval, 0.69 to 0.73) and good calibration (goodness of fit $p = 0.9$) to determine independent factors at baseline associated with a subsequent prolonged ICU admission. The variables and their parameters are shown in Table 3.

In the overall cohort, 637 patients (13%) died during the ICU admission at a median of 3 days (IQR, 2 to 6 days) after ICU admission. Among those who died in the ICU, 297 patients (47%) died within the first 2 days, 143 patients (22%) died from 2 to 3 days, 144 patients (23%) died from 4 to 13 days, and 53 patients (8%) died ≥ 14 days of ICU admission. Among the 4,208 patients who survived admission to the ICU, the in-hospital death rate was 64 deaths (22%) for those admitted for < 2 days, 89 deaths (30%) for those admitted from 2 to 3 days, 111 deaths (37%) for those admitted from 4 to 13 days, and 33 deaths (11%) for those admitted ≥ 14 days. Among the 3,924 survivors to hospital discharge, the rates of mortality during the year following ICU admission were as follows: 59 deaths in 1,758 patients (3%) admitted < 2 days, 74 deaths in 1,267 patients (6%) admitted from 2 to 3 days, 78 deaths in 766 patients (10%) admitted from 4 to 13 days, and 10 deaths in 133 patients (8%) admitted for ≥ 14 days. Figure 1 shows the survival of patients stratified according to ICU length of stay.

Discussion

This study demonstrates that patients with prolonged critical illness have high mortality rates in the acute phase, but if they survive ICU admission they have a subsequent long-term mortality rate that is

Table 1—*Admission Diagnoses Among Patients With Intermediate and Prolonged ICU Length of Stay

Diagnostic Category	Length of Stay: Intermediate (2 to 14 d; n = 2,514)	Length of Stay: Prolonged (≥ 14 d; n = 216)	p Value
Respiratory	605 (24)	77 (36)	< 0.001
Cardiovascular	1,077 (43)	46 (21)	< 0.0001
Shock	155 (6)	23 (11)	< 0.01
Trauma	115 (5)	20 (9)	< 0.0001
GI	128 (5)	15 (7)	0.3
Neurologic	184 (7)	13 (6)	0.6
Poisoning	33 (1)	6 (3)	0.1
Genitourinary	19 (1)	2 (1)	0.7
Endocrine/metabolic	56 (2)	0	0.02
Other	142 (6)	14 (6)	0.6

*Data are presented as No. (%).

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Table 2—*Presenting Clinical and Demographic Features Associated With Intermediate and Prolonged ICU Length of Stay

Factors	Length of Stay: Intermediate (2 to 14 d; n = 2,514)	Length of Stay: Prolonged (≥ 14 d; n = 216)	Relative Risk (95% Confidence Interval)	p Value
CVICU admission vs other ICU	766 (30)	13 (6)	0.20 (0.12–0.34)	< 0.0001
Admitted via emergency department vs other	619 (25)	69 (32)	1.30 (1.06–1.60)	0.02
Surgical vs medical	1,441 (57)	88 (41)	0.71 (0.60–0.84)	<0.0001
Median age (IQR), yr	66.3 (51.7–75.4)	64.25 (51–74.7)		0.2
Male gender	130 (60)	1,498 (60)	1.01 (0.90–1.13)	0.9
APACHE II score	25.7 ± 8.1	27.4 ± 8.5		<0.01
Therapeutic Intervention Scoring System score	44.7 ± 18.3	42.6 ± 15.2		0.1
BSI	145 (6)	36 (17)	2.89 (2.06–4.05)	<0.0001
Shock	1,486 (59)	144 (67)	1.13 (1.02–1.25)	0.03
Systemic inflammatory response syndrome	2,271 (90)	202 (94)	1.04 (1.00–1.07)	0.14
Receiving invasively ventilation at admission	1,495 (59)	138 (64)	1.07 (0.97–1.19)	0.2

*Data are presented as No. (%) or mean ± SD unless otherwise indicated.

only marginally increased above patients with shorter lengths of ICU stay. These observations support the existing literature conducted in other selected populations. Montuclard and colleagues[1] studied 75 elderly patients admitted to a single tertiary care surgical ICU for > 30 days and found that these patients had substantially lower survival after ICU discharge than the general population but that this became comparable after 1 year. Lipsett and colleagues[3] conducted a study in a single surgical ICU and found that patients with an ICU stay ≥ 7 days had an overall rate of death of 55%; however, they similarly found that the survival rate reached a plateau after 6 to 12 months. In contrast, Bapat et al[17] reported on outcomes of 89 cardiac surgical patients after > 5-day ICU postoperative stays and found that 33% of survivors past 30 days subsequently died during 1 year of follow-up.

We identified that higher severity of illness, shock, and BSI were independently associated with a prolonged ICU admission and that cardiovascular surgery was associated with a lower risk among all patients admitted to ICUs in our population. Several other studies[7,10,11] have investigated factors associated with prolonged admission to the ICU. Most notably, Higgins et al[7] conducted a multicentered study in 34 ICUs and found that higher severity of disease, middle age, infection, ventilation, male gender, emergency surgery, trauma, critical care fellows, and longer pre-ICU lengths of hospital stay were associated with longer ICU stays, and that the presence of full-time ICU physicians, do-not-resuscitate orders, and coma were associated with shorter admissions. In contrast, we did not find that gender, age, ventilation at admission, and pre-ICU hospital length of stay were independently associated with a prolonged ICU admission. This may in part either reflect the smaller size of the present study and therefore lower statistical power, or use of differing study methodologies and definitions.

Our study focused on long-term mortality as the primary outcome, but it must be recognized that this is only one of several potential outcomes of interest after prolonged ICU admission. Niskanen et al[18] compared quality of life in stays ≥ 4 days against the general population and found a generally acceptable but reduced quality of life. These findings have been echoed by others.[1,6] Lipsett et al[3] and Miller et al[2] also found that most patients with prolonged surgical and trauma ICU admissions had generally acceptable functional recovery. Bapat et al[17] found a significantly reduced quality-of-life scores in their cohort of patients after cardiac surgery with lengths of stay > 5 days as compared to control subjects, which may in part represent the specific features of their population. In addition to quality-of-life assess-

Table 3—*Logistic Regression Modeling of Baseline Factors Predictive of Prolonged ICU Length of Stay*

Variables	Odds Ratio	95% Confidence Interval	p Value
CVICU, vs multisystem	0.122	0.068–0.219	< 0.001
Age, per yr	0.993	0.984–1.001	0.08
APACHE II score, per point	1.035	1.016–1.055	< 0.001
Shock	1.570	1.130–2.182	0.007
BSI	1.825	1.206–2.761	0.004

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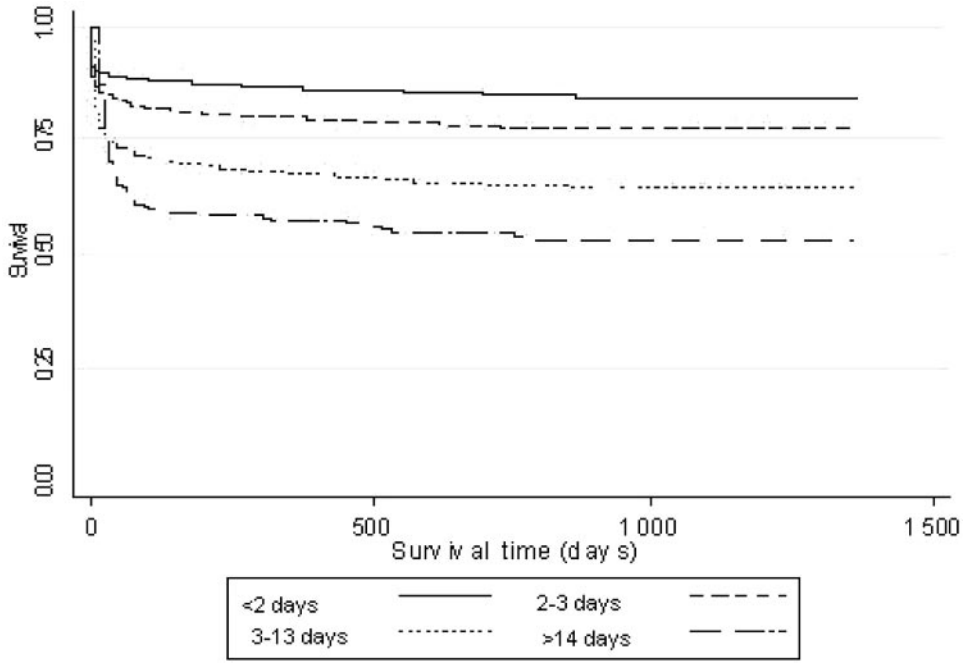

FIGURE 1. Kaplan-Meier survival estimates according to ICU admission length of stay.

ments, several studies[2–4] have evaluated the charges/costs associated with prolonged admission to ICU. Heyland et al[4] estimated that in their single mixed medical/surgical ICU, the incremental cost-effectiveness of continued care for patients with prolonged ICU admission > 2 weeks as compared to a hypothesized policy of withdrawal of care was $65,219 (1992 Canadian dollars). This study, in addition to the body of published literature, suggests that although many patients with a prolonged ICU admission will die acutely and consume considerable health-care resources, those that survive their prolonged admission may expect an overall generally good outcome.

There are a number of methodologic strengths of the current study that merit discussion. First, we studied all critically ill residents of a well-defined population; since sampling was not performed, selection bias was minimized. Previous studies have been limited by selection bias as a result of being reported from single, tertiary care, university-affiliated ICUs,[1–6,10,11] or selected critically ill subpopulations such as elderly,[1] trauma,[2,5] surgical,[3] or long-term ventilator unit patients.[8] While these are important studies, the results obtained from within these specific critically ill patient subgroups must be generalized to other critically ill populations at large with great caution. Not only did we study all adult medical, surgical, trauma, and cardiovascular surgical ICU patients, we excluded those patients who were nonresidents of the base study population so as to minimize "referral" bias.[19,20] While our results should also be generalized to other critically ill populations elsewhere with care, we believe that our study is a better reflection of critical illness in populations at large. A second important aspect of our study is that it represents one of the largest studies to date investigating the epidemiology of prolonged ICU admission. Only two other studies[6,7] have included larger cohorts of patients. A final important strength of our study is that we assessed long-term outcome with follow-up for at least 1 year in all patients.

While our study does have many methodologic strengths, there are some important limitations. First, the diagnostic categories as listed in Table 1 were based on the impression of the most important problem necessitating ICU admission and were not *a priori* defined. It is possible that independent intensivists may classify a similar patient differently, for example, a patient with septic shock due to pneumonia could be classified by one intensivist as "respiratory" and by another as "shock." As a result, there exists the possibility for misclassification in these primary diagnoses, and this should be considered in interpretation of our results. Second, the multivariable regression model we developed requires validation in a second independent cohort of patients. Third, it would have been of value to compare our long-term survival rates with other hospitalized and nonhospitalized populations to see if the prolonged ICU admission led to a persistent excess increased

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mortality. However, we do not have that data to enable such a comparison. Fourth, because this was an analysis of a previous established database, we were limited in the clinical detail available. It would have been useful to assess other potential confounding variables such as body mass index, specific diagnostic categories, and ICU staffing. Finally, our assessment of follow-up was dependent on patients remaining within the Province of Alberta, and patients who moved elsewhere and died would have been missed. Given that Alberta is currently experiencing a large net influx of people from elsewhere in the country, we suspect this is only a minor bias overall.

In conclusion, we present novel population-based data on the occurrence of, risk factors for, and outcome of prolonged ICU admission. While prolonged ICU admission is not uncommonly required and patients are at high risk for death as a result, those that survive their acute illness have a generally good long-term outcome. Further study is needed to better define the determinants and clinical outcomes associated with prolonged admission to the ICU.

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