Readmissions to Intensive Care: A Prospective Multicenter Study in Australia and New Zealand

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Objectives: To determine factors independently associated with readmission to ICU and the independent association of readmission with subsequent mortality.

Design: Prospective multicenter observational study.

Setting: Forty ICUs in Australia and New Zealand.

Patients: Consecutive adult patients discharged alive from ICU to hospital wards between September 2009 and February 2010. **Interventions:** Measurement of hospital mortality.

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The data were collected by designated persons at each of the participating hospitals. In addition, a senior intensivist at each hospital held the position of chief investigator; this person provided a reference point for data collection.

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Measurements and Main Results: We studied 10,210 patients and 674 readmissions. The median age was 63 years (interguartile range, 49-74), and 6,224 (61%) were male. The majority of readmissions were unplanned (84.1%) but only deemed preventable in a minority (8.9%) of cases. Time to first readmission was shorter for unplanned than planned readmission (3.2 vs 6.9 d; p < 0.001). Primary diagnosis changed between admission and readmission in the majority of patients (60.2%) irrespective of planned (58.2%) or unplanned (60.6%) status. Using recurrent event analysis incorporating patient frailty, we found no association between readmissions and hospital survival (hazard ratios: first readmission 0.88, second readmission 0.90, third readmission 0.44; p > 0.05). In contrast, age (hazard ratio, 1.03), a medical diagnosis (hazard ratio, 1.43), inotrope use (hazard ratio, 3.47), and treatment limitation order (hazard ratio, 17.8) were all independently associated with outcome.

Conclusions: In this large prospective study, <u>readmission to ICU</u> <u>was not an independent risk factor for mortality.</u> (*Crit Care Med* 2016; XX:00–00)

Key Words: hospital mortality; intensive care units; readmission; recurrent events; risk factors

Readmission to ICUs during the same hospital admission is an uncommon event with a benchmark rate between 4.0 and 6.3 per 100 patient discharges (1). Furthermore, patients readmitted to ICU are reported to have increased mortality, longer ICU and hospital lengths of stay, and increased costs (2–4) compared to those not requiring readmission. Therefore, ICU readmissions are considered a failure of clinical care and included by authors and jurisdictions as ICU qualityof-care indicators (5, 6). Accordingly, identification of risk factors for ICU readmission is considered important and has been the subject of previous investigations (7–9).

Such investigations have attempted to identify risk factors for readmission on the assumption that readmissions are preventable and independently contribute to unfavorable outcomes. Such assumptions, however, have been challenged by

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evidence that the majority of readmissions may not be preventable (10, 11).

As a consequence, complex and costly interventions have been devoted to the prevention of readmission to ICU including rapid response teams (12); outreach services (13); and deliberately delaying ICU discharge. These efforts, however, have met with unclear benefits (14).

The Discharge and Readmission Evaluation study was undertaken to examine the impact of ICU discharge processes on hospital mortality and to characterize ICU readmissions in a prospective investigation as most previous large studies had been undertaken retrospectively and without collection of detailed discharge processes or conditions. We followed over 10,000 patients discharged from ICU to the ward and collected detailed information on their clinical condition at the time of discharge, their final outcome as well as all their readmissions to ICU. The impact of time of day of ICU discharge on hospital outcome has been previously reported (15). In this study, we aimed to describe the demographics and outcomes of patients readmitted to ICU and to determine whether readmission to ICU is an independent predictor of outcome.

MATERIALS AND METHODS

Forty ICUs in Australia (n = 33) and New Zealand (n = 7) participated in the study. Their characteristics have been previously reported (15) and are listed in **Table E1** (Supplemental Digital Content 1, http://links.lww.com/CCM/C152). The study was approved by the institutional ethics committees of the participating hospitals, which waived the need for informed consent.

Study outcomes included 1) readmission to ICU during the same hospital admission and 2) hospital mortality. We collected the following data at the time of each ICU discharge: demographic details (age, sex), admission and discharge dates and time, primary admission diagnosis (Australian modifications of Acute Physiology and Chronic Health Evaluation [APACHE] III-J codes [16]), and need for advanced therapies (mechanical ventilation, noninvasive ventilation, inotrope infusions, renal replacement therapies, intraaortic balloon pump) during each ICU admission.

Markers of severity of illness at the time of ICU discharge included tracheostomy, inotropic drug infusion, noninvasive ventilation, renal replacement therapy, parenteral nutrition, impaired consciousness (Glasgow Coma Score, < 15), and the presence of documented orders that limited future medical treatments (not for emergency team or cardiopulmonary resuscitation, not for readmission to the ICU or mechanical ventilation). Discharges were determined to be premature or delayed by the intensivist on duty. The presence of written discharge summaries, clinical handovers, and timing of post-ICU nursing and medical review observations were also recorded.

Readmissions

At the time of readmission to ICU, clinicians were asked the following questions. First, was the readmission planned (e.g.,

booked for an ICU bed following surgery or procedure) or unplanned (e.g., following clinical deterioration or cardiac arrest on the ward). Second, was the original ICU discharge (in retrospect) premature and increased the risk of readmission. Third, if optimal care had been provided was the readmission preventable?

Readmissions were further categorized as an elective correction of an underlying problem; as management of the original medical or surgical problem; or as management of a new medical or surgical problem. Based on previous reports (14), readmissions were also categorized as early (\leq 72 hr of the previous ICU discharge) or late (> 72 hr). The full data definitions are listed in **Table E2** (Supplemental Digital Content 1, http:// links.lww.com/CCM/C152).

We commenced data collection in October 2009 and concluded at the end of February 2010 to enable recruitment of 10,000 patients, which was deemed necessary for the original study examining timing of discharge and subsequent hospital mortality. We included all patients 16 years and older discharged alive from the ICU to another ward in the same hospital. We assessed patient status at the time of hospital discharge by reference to each hospital's patient administration system or the written medical record.

We reported results according to the published guidelines (17).

Statistical Analysis

We expressed data as means and SD (normally distributed variables) and as median and interquartile range (IQR) for remaining continuous variables. We expressed categoric variables as numbers and percentages. We analyzed differences between groups by t tests or Kruskal-Wallis statistics or with chi-square and Fisher exact tests, respectively. We explored relationships between the outcome measures of readmission/mortality and patient factors with fixed effects logistic regression, where ICUs were parameterized as indicator variables and considered fixed effects; the latter were included to adjust for unmeasured confounders at the ICU and hospital levels. Independent variables included patient characteristics; features of the primary ICU admission (origin to ICU, duration in ICU, therapies received); conditions present at the time of discharge from ICU (tracheostomy, ongoing dialysis, parenteral nutrition, altered conscious state); and limitation of medical treatment orders, as well as process factors such as prematurity of discharge as assessed by the attending intensivist.

In order to evaluate the impact of ICU readmissions on inhospital mortality, we used a methodology for recurrent events specifically a frailty approach (18, 19). Frailty models take into account the heterogeneity that exists between individuals due to unmeasured covariates and which affects estimates of times to event such as subsequent mortality. We limited the number of readmissions to three. (A detailed description of the statistical approach is provided in the **supplemental data**, Supplemental Digital Content 1, http://links.lww.com/CCM/C152)

We performed analyses with Stata V14 (Stata, College Station, TX; 2013). A p value less than or equal to 0.05 was considered significant.

	All Readmissions (674)			First Readmission (581)		
Variable	Planned 107 (15.9%)	Unplanned 567 (84.1%)	p	Planned 91 (15.7%)	Unplanned 490 (84.3%)	p
New problem	22 (20.6%)	219 (38.6%)	< 0.001	20 (22.0%)	201 (41.0%)	0.001
Origin						
Operating room	89 (83.2%)	98 (17.3%)	< 0.001	78 (85.7%)	87 (17.8%)	< 0.001
General ward	16 (15.0%)	463 (81.7%)	< 0.001	12 (13.2%)	398 (81.2%)	< 0.001
Premature first discharge ^a	1 (1.0%)	61 (10.8%)	< 0.001	1 (1.1%)	54 (11.0%)	0.001
Preventable readmission	2 (1.9%)	58 (10.2%)	0.003	2 (2.2%)	53 (10.8%)	0.006
Interval to readmission, days ^b	15.6 (7.3–68.9)	3.2 (1.3–7.2)	< 0.001	6.9 (3.8–13.1)	3.2 (1.3–7.0)	< 0.001

TABLE 1. Characteristics of Planned and Unplanned Readmissions

^aAs assessed at the time of first readmission.

^bResults are median and interquartile range.

p values are comparisons between planned and unplanned readmissions.

RESULTS

Patient Characteristics

There were 10,884 discharges from ICU, and 581 patients were readmitted to ICU. Of these, 510 had two ICU admissions, 56 had three admissions, 11 had four admissions, two had five admissions, and one patient each had six and seven admissions. The patient characteristics are presented in Tables E3 and E4 (Supplemental Digital Content 1, http:// links.lww.com/CCM/C152). The median age was 63 (IQR, 49-74) years, 61% were male, and the median APACHE III risk of death on first admission was 9% (IQR, 3-25%). Fiftytwo percent came from operating or recovery rooms, 25% from emergency departments, 14% from general wards, and 8% from interhospital transfers; 20% had undergone cardiac surgery. During the first admission, 56% required mechanical ventilation, 42% needed inotrope administration, and 5% had renal replacement therapy. At the time of discharge from ICU, 16% had an altered conscious state, and 5.3% had limits



Figure 1. Interval in hours to first readmission stratified by elective/ unplanned readmission.

of medical treatment orders. Overall, 5.2% died before hospital discharge.

Nature of the Readmission

The 581 patients (5.7%) had 674 ICU readmissions, which were classified as planned (107 all readmissions, 91 first readmission) or unplanned (538 all readmissions, 490 first readmission). Unplanned readmissions were more likely to be due to a new problem and to have come from the general ward sometimes following an emergency call or cardiac arrest. Clinicians assessed unplanned readmissions to be potentially preventable in 58 (10.2%). Readmission rates also varied with primary diagnosis and disease (**Table 1**; and **Table E5**, Supplemental Digital Content 1, http://links.lww. com/CCM/C152).

Timing of Readmission

Limiting the analysis to the first ICU readmission (581 patients), the median interval between primary discharge and readmission was 3.7 (IQR, 1.45–7.90) days. As shown in **Figure 1** and **Figure E1** (Supplemental Digital Content 1, http://links.lww.com/CCM/C152), unplanned ICU readmissions occurred significantly earlier (median, 76hr) than planned readmissions (median, 165 hr; p < 0.001). Furthermore, planned readmissions occurred more often in the afternoon or evening, whereas unplanned readmissions were spread more evenly throughout the 24 hours (p = 0.014; **Fig. E2**, Supplemental Digital Content 1, http://links.lww.com/CCM/C152). The interval from admission to first readmission was similar for patients who survived or died (p = 0.22; **Fig. E3**, Supplemental Digital Content 1, http://links.lww.com/CCM/C152).

Patients readmitted early (≤ 72 hr) following original ICU discharge were more likely to have been an unplanned admission; to have come from the general wards; to have been discharged (in retrospect) prematurely from ICU; and to have had opportunities to prevent readmission (Table E6,

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Supplemental Digital Content 1, http://links.lww.com/CCM/C152).

Comparisons Between Readmitted and Nonreadmitted Patients

Readmitted patients were older, had greater severity of illness at admission to ICU, had more organ support therapies during their initial admission, had longer ICU admissions, and were more likely to have been discharged from ICU prematurely. Furthermore, they had more ongoing organ dysfunction (tracheostomy, dialysis, altered conscious state) following ICU discharge; had primary medical reasons for admission; and were less likely to have limitation of treatment orders and to have undergone cardiac surgery. Those with unplanned readmissions were seen earlier by a doctor after their first ICU discharge than other patients. They required more assessments by a medical emergency/rapid response team (45.3%) between discharge and readmission and had experienced more cardiac arrests (5.9%). Their hospital mortality was substantially higher than those not readmitted (23.3% vs 4.3%) (Table E7, Supplemental Digital Content 1, http://links.lww.com/CCM/C152).

Characteristics of the First and Second Admission

The second admission (first readmission) differed from the first admission in several ways. The former more often came from the ward, had greater severity of illness, had longer stay in ICU, and were less likely to be prematurely discharged and more likely to have their ICU discharge delayed. Medical diagnoses were more common in those readmitted (**Table 2; Table E8**, Supplemental Digital Content 1, http://links.lww.com/CCM/C152). Even the 290 patients with an initial surgical diagnosis were more often readmitted with a medical condition (165; 59.6%). The three most common medical categories were respiratory, cardiovascular, and neurologic conditions.

Changes in diagnostic category between first admission and readmission did not depend upon the nature of readmission and occurred in 56.3% of elective readmissions, 68.3% of readmissions with a new problem, and 50.7% of readmissions with an old problem.

Statistical Modeling of Unplanned First Readmission

A summary of the results is shown in **Table 3** and complete details in **Table E9** (Supplemental Digital Content 1, http://links. lww.com/CCM/C152). Patient and illness factors were strongly associated with readmission; the area under the receiver operating characteristic (ROC) curve for this model was 0.70.

Impact of Multiple Readmissions on Hospital Outcome

To account for multiple readmissions, we used a recurrent event analysis (incorporating frailty) adjusted for patient factors to assess the impact of readmissions on mortality. Age, illness, illness severity during and on discharge from ICU, and limitations of medical treatment orders were significantly associated with mortality, but the need for readmission was not a predictor of outcome after adjustment for these factors, and, furthermore, the point estimates (hazard ratios) for each readmission were all below one (**Table 4**; **Table E10**, Supplemental Digital Content 1, http://links.lww.com/CCM/C152).

DISCUSSION

Key Findings

We conducted a prospective multicenter observational study to describe the demographics and outcomes of patients readmitted to ICU during the same hospital admission and to determine whether readmission is an independent predictor of outcome. We found that the majority of readmissions to ICU were unplanned and often due to a new problem (cardiorespiratory in nature). Readmission occurred earlier if unplanned but still more than 3 days after primary ICU discharge. Readmission was not associated with subsequent mortality, whereas patient factors were far more significant. Crucially, after adjusting for these patient-related factors and for multiple ICU admissions, there was no independent statistical association between readmission to ICU and subsequent hospital mortality.

Relationship to Previous Studies

Our readmission rate was similar to other large studies (Renton et al [4], 5.5%; Chen et al [20], 4.79%; Ho et al [21], 3.9%; Metnitz et al [22], 5.1%; Kramer et al [23], 5.9%) and to the recent benchmark of 5.6–6.9% suggested by Hosein et al (1). The median time between ICU discharge and first readmission was 90.5 hours also in keeping with previous studies (20–22). Furthermore, patient characteristics in this study were also similar to previously described cohorts (2, 4, 21–23) as was their mortality rate (2, 4, 21–24).

Importantly, previous studies used a change in diagnostic code to identify unplanned admissions (2). In our study, diagnostic codes changed more than 50% of the time irrespective of planned or unplanned readmission, or whether the readmission was for a new or old problem suggesting that identification based on coding is highly inaccurate. Of unplanned readmissions, 4.5% had been prematurely discharged, and only 8.9% of all readmissions were deemed potentially preventable. Nishi et al (10) reported similar results with premature ICU discharge rates of 5%, anticipated readmission in 11%, and preventable readmission in a higher 22%.

Other large studies (2, 3) had looked at factors associated with readmission to ICU. In general, these authors found similar impacts of age, severity of illness in ICU, therapies delivered, and duration of original admission. However, by the nature of such retrospective analyses, the authors were not able to assess the effects of organ dysfunction at discharge or the unplanned nature of the readmission, and only one study (2) had information on limitation of medical treatment orders.

Several authors have attempted to develop statistical models to predict the likelihood of readmission to ICU (7–9, 25, 26); these studies have been the subject of a recent

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TABLE 2. Comparisons Between the First and Second ICU Admission in 581 Patients Who Were Readmitted

Variable	First Admission	Second Admission	p
ICU origin, <i>n</i> (%)			
Emergency	122 (21.0)		
Operating room	274 (47.2)	165 (28.4)	< 0.001
Ward	139 (23.9)	416 (71.6)	
Interhospital	46 (7.9)		
Mechanical ventilation, n (%)			
Any	346 (59.6)	324 (55.8)	0.21
Last 24 hr	109 (18.8)	109 (18.8)	1.00
Inotropes, <i>n</i> (%)			
Any	275 (47.3)	263 (45.3)	0.52
Last 24 hr	70 (12.0)	82 (14.1)	0.34
Noninvasive ventilation, <i>n</i> (%)			
Any	99 (17.0)	110 (18.9)	0.45
Last 24 hr	39 (6.7)	37 (6.4)	0.91
Renal replacement therapy, n (%)			
Any	47 (8.1)	59 (10.2)	0.26
Last 24 hr	16 (2.8)	24 (4.1)	0.26
Discharge, n (%)			
Premature	26 (4.5)	5 (0.9)	< 0.001
Delay > 8 hr	155 (26.7)	215 (37.0)	< 0.001
Delay > 24 hr	6 (1.0)	57 (9.8)	< 0.001
After 6 PM	110 (18.9)	122 (21.0)	0.42
After 10 PM	45 (7.8)	41 (7.1)	0.74
Therapy on discharge, <i>n</i> (%)			
Tracheostomy	46 (7.9)	56 (9.6)	0.35
Noninvasive ventilation	10 (1.7)	15 (2.6)	0.42
Ongoing dialysis	22 (3.8)	18 (3.1)	0.63
Inotropes	8 (1.4)	8 (1.4)	1.00
Altered conscious	142 (24.4)	137 (24.7)	0.95
Other factors, <i>n</i> (%)			
Discharge to general ward	267 (46.0)	235 (40.4)	0.07
Treatment limits	19 (3.3)	58 (9.9)	< 0.00
Cardiac surgery	67 (11.5)	34 (5.8)	0.001
Medical diagnosis	291 (50.1)	385 (66.3)	< 0.001
Acute Physiology and Chronic Health Evaluation III risk of death (median, IQR)	0.16 (0.05–0.38)	0.23 (0.09–0.50)	< 0.001
ICU length stay (days, median, IQR)	2.58 (1.1–5.57)	3.01 (1.52–5.87)	0.052
IQR = interquartile range.			

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Variable	OR	95% CI	р
Age (yr)	1.01	1.01-1.02	< 0.0001
Cardiac surgery	0.53	0.38-0.73	< 0.001
Original admission from general ward	1.84	1.49-2.36	< 0.001
Days in ICU during primary admission	1.02	1.01-1.03	< 0.001
Discharge prematurely from original admission	3.73	2.28-6.12	< 0.001
Treatment limitation at time of transfer from ICU	0.36	0.22-0.60	0.011
Tracheostomy	1.64	1.12-2.43	0.11
Altered conscious state (Glasgow Coma Scale, < 15)	1.59	1.26-2.01	< 0.001
Ongoing dialysis	2.09	1.27-3.41	0.003
Parenteral nutrition	2.32	1.55-3.46	< 0.001
Mechanical ventilation during admission	1.27	1.02-1.60	0.036

TABLE 3. Odds ratios (95% CIs) of Clinical Factors Associated With Unplanned First Readmission Following ICU Discharge

OR = odds ratio.

The full statistical model is included in the supplemental digital content.

systematic review (27). Discrimination, as assessed by the area under the ROC curve, varied between 0.66 and 0.75, and our logistic model yielded a similar value (0.70). Such analyses have linked demographic factors, severity of illness during ICU, origin of admission, and underlying

TABLE 4. Hazard Ratios (95% CIs) of Prediction of Mortality Taking Into Account Demographic and Clinical Factors as Well as Adjustment for Readmission

Variable	Hazard Ratio	95% CI	p
Initial ICU admission	1.000		
First readmission	0.88	0.62-1.26	0.493
Second readmission	0.90	0.41-2.01	0.804
Third readmission	0.44	0.04-4.99	0.503
Age (yr)	1.03	1.02-1.03	< 0.001
Cardiac surgical patient	0.52	0.29-0.91	0.022
Medical patient	1.43	1.11-1.85	0.007
Limitation of medical treatment order	17.78	13.72-23.05	< 0.001
Tracheostomy	0.38	0.25-0.58	< 0.001
Inotrope history	3.47	1.65-7.28	0.001
Renal replacement therapy	1.56	0.94-2.57	0.080
Ward origin of readmission	1.70	1.32-2.19	< 0.001
Frailty (<i>q</i>); Log-Hazard Scale	0.82	0.67-0.96	< 0.001

The full statistical model is included in the supplemental digital content.

comorbidities with subsequent readmission, but these prediction models, exemplified by the Stability and Workload Index for Transfer (8), have not proven helpful when applied to different populations leading some authors to warn against their use for routine patient care (9, 24). Although these statistical models have reasonable discrimination, their sensitivity/specificity relationship and positive predictive value are poor, suggesting the presence of unmeasured factors. Furthermore, such an approach does not address the adjusted impact of readmission per se on subsequent clinical outcome nor do the studies address the issue whether readmission is a failure of ICU care.

The vast majority of ICU readmissions are unexpected and not preventable. In the study reported by Kramer et al (23), readmission rates varied markedly across the 105 ICUs studied but, after casemix adjustment, there were no differences in standardized mortality rates or casemix-adjusted lengths of stay. We have taken the analysis of survival further by taking into account the changes in covariates over time and all readmissions to ICU (not just the first). We found no association between subsequent mortality and readmission per se once the adjustment was made for factors known to influence outcome such as ongoing organ dysfunction and limitation of medical treatment orders.

Implications of Study Findings

Our study strongly suggests that <u>readmission per se is not</u> a <u>risk factor for subsequent mortality</u> and that readmissions are commonly unplanned or unexpected and <u>not</u> <u>preventable</u>.

This implies that <u>there is no statistical or clinical ratio-</u> <u>nale for using ICU readmission as a quality indicator</u> of ICU care. <u>Recent editorials (28, 29)</u> also <u>support</u> this observation.

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Accordingly, the <u>Australian</u> Council on Healthcare Standards removed readmission as a quality indicator (30).

In an article published in 2000, Rosenberg et al (11) suggested that unexpected readmission was due to failed resolution of the primary condition predominantly cardiac and respiratory. Our study supports the conclusion that patient factors are the strongest predictors of readmission.

We agree that less attention should be given to reducing readmission rates, and more emphasis should be placed on the need to achieve resolution of the primary condition.

Strengths and Limitations

The current study has a number of strengths. It was a large multicenter prospective investigation in 40 ICUs across two countries. There were no exclusions, and data were collected prospectively to examine readmissions. Our results also confirm that patient information present at the time of discharge from ICU is very important and should be included in future studies of readmissions along with completeness of data collection and appropriate modeling and statistical analyses.

The current study does have limitations. It is observational and descriptive which means that causation cannot be attributed to the factors associated with readmission. However, it is unlikely that a randomized control trial will be undertaken making large prospective studies the best available evidence. Our study was carried out in a range of mostly metropolitan and tertiary referral hospitals in Australia and New Zealand so that its applicability to smaller rural hospitals with different models of care may be limited. As we noted previously, the discharge of a patient from ICU is not a random event, and there may be organizational issues such as ward bed availability, electronic monitoring and clinical information systems, nursing intensity and medical cover that might influence readmissions, and subsequent mortality. We have tried to minimize these sources of bias by including a large number of hospitals and adjusting for as many factors as possible. Finally, we did not follow these patients after hospital discharge to know if some were readmitted to hospital or ICU for ongoing management of their primary condition.

CONCLUSIONS

This large prospective multicenter study of patients discharged from ICU found that approximately one in 20 required readmission to ICU and that readmission was associated with higher mortality and longer length of stay. The majority of readmissions to ICU were unexpected and unpreventable, likely to be the consequence of patientrelated factors, and that readmission per se was not an independent risk factor for subsequent mortality. These findings reinforce the view that readmission rates <u>cannot be logically</u> considered <u>indicators of clinical performance</u> within ICU, and that the focus of care must be on the resolution of the primary condition.

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