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ORIGINAL ARTICLE

Predictors of Adverse Outcome Early After ICU Discharge

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Abstract

Objective: Clinicians are often confronted with the timely discharge decision, in order to avoid readmission and escalation of costs. Aim of the present study was to determine potential risk factors for ICU readmission or death early after ICU discharge.

Methods: One hundred fifty-four ICU discharged patients were divided into three outcome groups according to whether they were readmitted (Group A, n = 13), or died within 72 h after ICU discharge (Group B, n = 11), or were not readmitted or died within 72 h (Group C, n = 130).

Results: Patients being readmitted to the ICU had significantly longer prior length of stay in a ward compared to the group with positive outcome after ICU discharge (median: 12 vs. 2 days, p = 0.023). Patients with early post discharge death had received vasopressor support with norepinephrine for significantly longer period of time and were significantly more severely diseased at the day of discharge, based on APACHE II calculation. Rates of tracheostomy, central venous catheter, nasogastric nutrition and colonization with an MDR organism, along with hemodynamic and respiratory parameters at ICU discharge were similar among the outcome groups. Nonetheless, the prevalence of patients with Glasgow Coma Scale (GCS) < 13 was significantly higher in Group B. The principal cause of ICU readmission was sepsis (8/13 patients), whereas of early mortality was acute respiratory failure (9/11 patients).

Conclusions: Patients with higher disease severity at discharge and moderately altered mental status, especially those with prolonged hospitalization and vasopressor support are at increased risk for ICU readmission or early post discharge mortality.

Keywords

Intensive care unit, Patient readmission, Post discharge mortality, Predictors

Introduction

The Intensive Care Unit (ICU) is the designated department in the hospital for the care of the most unstable and sickest patients. Depending on ICU availability, it is possible these intubated and critically ill patients are being hospitalized in other areas (e.g. general ward, emergency department) for varying periods of time. Since delays in providing intensive care are associated with worse outcomes [1], prompt ICU admission is desirable. Consequently, some patients might be subjected to a demand-driven discharge from the ICU and therefore face the potential risks of deterioration and necessity of readmission. Readmission to the ICU during the same hospital stay has been associated with a greater risk of in-hospital mortality and has been suggested as a marker of quality of care [2,3]. If intensive care patients are discharged before they can be safely cared for in a lower acuity unit, they are at risk for complications and delayed recognition of clinical deterioration. The former may result in unplanned readmission, while the latter may contribute in patient death. On the other hand, a readmission rate that is significantly lower than might be expected may represent an inability to discharge ICU patients in a timely fashion, resulting in unjustifiable prolongation of ICU stay. Thus, clinicians are often confronted with the timely discharge decision, in order to avoid readmission and escalation of costs. However, the criteria used to decide the patients' discharge are quite subjective, contributing to inappropriate and excessive indications along with risk for patients [2].

Approximately 1 in 10 patients discharged from ICU in developed countries will be readmitted during the same hospital stay [2,4]. This emphasizes the need for knowledge of which patients are at risk of ICU



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readmission. Awareness of patient- level factors along with intensive care related factors could enable the ICU team to best plan both the discharge and the ongoing care outside the ICU [5-7].

The aim of the present study was to determine potential risk factors for ICU readmission or death early after ICU discharge, and thus improving the ability to predict the readiness for discharge and improve ICUs' efficiency.

Materials/Methods

We prospectively studied 154 patients being hospitalized and successfully discharged from the 9-bed general ICU of Konstantopouleio-Patission in Athens during an 18-month period. The study was approved by the institutional review board of the hospital. No informed consent was obtained from patients' next of kin, due to the observational and non-interventional nature of the study.

Patients were divided into three outcome groups according to whether they were readmitted to the ICU (Group A, n = 13), or died within 72 h after ICU discharge (Group B, n = 11), or were not readmitted or died within 72 h (Group C, n = 130). Data compiled for each patient included demographics; co morbidities; primary admission diagnosis; severity of illness (Acute Physiology and Chronic Health Evaluation II score, APACHE II; Sequential Organ Failure Assessment score, SOFA); Physiological (arterial blood pressure; heart rate; arterial blood gases) and laboratory parameters (blood lactate; white blood cell count, WBC) at ICU admission and discharge. We also recorded intensive care factors: Length of stay (LOS); days of central venous catheterization and mechanical ventilation; days on vasopressor agent (norepinephrine) during ICU stay;

colonization with multidrug-resistant (MDR) organism during ICU hospitalization; presence of tracheostomy or central venous catheter (CVC) and nutrition route at discharge; after hours (16:00 hours to 08:00 hours) and weekend discharge; in-hospital or out-hospital discharge.

Statistical analysis

Continuous variables were expressed as mean \pm standard deviation (SD) or median (interquartile range). Categorical variables were evaluated with the Chi-square test. Continuous variables were compared with one-way analysis of variance. When analysis of variance revealed a significant difference, all pair wise multiple comparison procedures were executed with Dunn's method or Holm-Sidak method. All tests were two-tailed and a p-value of < 0.05 was considered to indicate statistical significance.

Results

During the study period, a total of 154 ICU discharged patients were included in the study. Thirty-six patients (23.4%) of the study cohort died after ICU discharge: 7.2% within 72 h and 16.2% within 28 days after discharge. No difference in 28-day mortality between readmitted (4/13) and not readmitted patients (21/130) was identified (p = 0.347). The anthropometric and clinical characteristics of study population are depicted in Table 1. After patients' allocation in three groups according to their post-ICU discharge outcome, the sex distribution and mean age were similar between the groups. Primary admission diagnosis was mainly medical in all groups, including acute respiratory failure, cardiac or neurological events and sepsis. Patients being readmitted to the ICU had significantly longer prior length of stay in a ward compared to the group with

Table 1: Anthropometric and clinical characteristics of study population.

Factor	Group A (n = 13)	Group B (n = 11)	Group C (n = 130)	p-value
Demographics				
Age (years)	68 (66-75)	75 (58-80)	71 (59-78)	0.809
Male sex	9 (69.2)	6 (54.5)	81 (62.3)	0.760
Medical admission	9 (69.2)	11 (100)	85 (65.4)	0.061
Prior LOS in ward (days)	12 (1-37) [*]	3 (1-5)	2 (1-4)	0.023
APACHE II ^a	19.5 \pm 6.3	22.7 \pm 5.9	18.7 \pm 6.9	0.162
SOFA ^a	8 (7.5-11)	9 (8-11)	8 (6-10)	0.168
Comorbidities				
Diabetes mellitus	5 (38.5)	2 (18.2)	48 (36.9)	0.450
Chronic renal failure	3 (23.1)	1 (9.1)	21 (16.1)	0.650
Chronic lung disease	0 [#]	5 (45.5)	39 (30)	0.032
Chronic heart failure	6 (46.1)	2 (18.2)	27 (20.7)	0.107
Chronic neuro-psychiatric disorders	0	2 (18.2)	19 (14.6)	0.309
Immunosuppression ^b	0	1 (9.1)	4 (3.1)	0.440

^{*}Significantly different compared to Group C; [#]Significantly different compared to Group B; Data are no. (%) of patients or median (IQR) unless otherwise stated.

LOS: Length of Stay; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; IQR: Interquartile Range.

^aAt ICU admission; ^bNeutropenia (neutrophil count < 1000/mm³); immunosuppressant medication (including corticosteroids), splenectomy.

Table 2: Intensive care-related risk factors of adverse outcome early after ICU discharge.

Factor	Group A (n = 13)	Group B (n = 11)	Group C (n = 130)	p-value
ICU LOS (days)	13 (7-26)	21 (14-34)	11 (6-19)	0.061
Length of CVC (days)	13 (7-33)	21 (14-35)	11 (6-21)	0.068
Length of MV (days)	8 (4-12)	13 (5-26)	7 (3-13)	0.324
Length of norepinephrine support (days)	5 (4-15)	15 (2-21)*	3 (0-8)	0.012
CVVHDF	3 (23.1)	1 (9.1)	15 (11.5)	0.456
Tracheostomy ^a	3 (23.1)	3 (27.3)	21 (16.1)	0.557
CVC ^a	13 (100)	11 (100)	112 (86.1)	0.152
Nasogastric tube ^a	8 (61.5)	8 (72.7)	58 (44.6)	0.120
Colonization with MDR pathogen ^a	9 (69.2)	7 (63.6)	60 (46.1)	0.175
Weekday discharge ^a	11 (84.6)	11 (100)	115 (88.4)	0.439
Morning shift discharge ^a	10 (76.9)	10 (90.1)	100 (76.9)	0.560
In hospital discharge	10 (76.9)	6 (54.5)	86 (66.1)	0.513

*Significantly different compared to Group C; Data are no. (%) of patients or median (IQR).

LOS: Length of Stay; CVC: Central Venous Catheter; MV: Mechanical Ventilation; CVVHDF: Continuous Veno-Venous Hemodiafiltration; MDR: Multidrug-Resistant; IQR: Interquartile Range.

^aAt ICU discharge.

Table 3: Physical and laboratory factors of study population on the discharge day.

Factor	Group A (n = 13)	Group B (n = 11)	Group C (n = 130)	p-value
APACHE II (mean ± S.D.)	11.5 ± 3.1	13.5 ± 3.9*	9.6 ± 4.4	0.007
SOFA	3 (2-4)	5 (3-6)	3 (2-4)	0.102
Systolic arterial pressure (mmHg)	115 (110-150)	120 (116-136)	130 (115-140)	0.676
Heart rate (bpm)	90 (75-97)	80 (70-95)	86 (80-95)	0.493
Glasgow Coma Scale (< 13)	1 (7.7)	4 (36.4)*	11 (8.5)	0.014
PaO ₂ /FiO ₂ (mmHg)	312 ± 114	276 ± 86	273 ± 87	0.330
Blood lactate concentration (mmol/L)	0.85 (0.7-0.9)	0.8 (0.7-1.15)	0.8 (0.6-1.1)	0.832
White blood cell count (cells/mcL)	9,400 (7,675-12,645)	9,190 (8,050-14,225)	10,435 (7,700-12,800)	0.971

*Significantly different compared to Group C; Data are no. (%) of patients or median (IQR) unless otherwise stated.

APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; PaO₂/FiO₂: Arterial partial pressure of oxygen to fraction of inspired oxygen ratio; IQR: Interquartile Range.

positive outcome after ICU discharge [12 (1-36.5) vs. 2 (1-4) days, p = 0.023]. Patients readmitted to ICU after 4 (2-6) days post discharge.

Evaluation of various chronic comorbidities among the three study groups did not reveal significant differences, apart from the significantly lower prevalence of chronic lung disease in the readmission group. Severity of disease and organ dysfunction at ICU admission, as determined by APACHE II and SOFA scores respectively were also similar.

The intensive care - related risk factors are presented on [Table 2](#). Patients with early post discharge death had received vasopressor support with norepinephrine for significantly longer period of time (median: 5 vs. 15 vs. 3 days, p = 0.012). Although this group displayed longer ICU LOS and duration of central venous catheterization, these differences marginally did not reach statistical significance. Rates of tracheostomy, CVC, nasogastric nutrition and colonization with an MDR organism at ICU discharge were similar among the outcome groups. Patients in all groups were mainly discharged from ICU during weekdays and during morning shifts. Whether patients were discharged to in-hospital or to other hospitals' wards did not have any impact on their outcome.

The physical and laboratory factors on the discharge day are presented on [Table 3](#). Patients that died early after ICU discharge were significantly more severely diseased at the day of discharge compared to not readmitted patients, based on APACHE II calculation (13.5 ± 3.9 vs. 9.6 ± 4.4, p = 0.007), while number of organ failures, based on SOFA score calculation, was similar. Hemodynamic and respiratory parameters at discharge were also similar among the study groups. Nonetheless, the prevalence of patients with Glasgow Coma Scale (GCS) < 13 was significantly higher in Group B (7.7% vs. 36.4% vs. 8.45%, p = 0.014). Values of blood lactate concentration (lac) and WBC count did not significantly differ among the three groups. We also calculated the change of each variable at ICU admission and discharge (Δ value) and examined their interaction with the post discharge outcome. Apart from Δ lac values that approached statistical significance [0.85 (0.4-3) vs. 0.5 (0.2-1) vs. 0.9 (0.4-2) mmol/L, p = 0.068], no other differences were identified.

Regarding the reasons for readmission, the majority of patients readmitted to ICU (8/13) due to sepsis. More specifically, 5 patients readmitted postoperatively after emergency surgery that was related to their initial primary diagnosis, 2 patients suffered from catheter related bloodstream infections (CRBSIs)

and 1 patient from complicated skin and soft tissue infection. The rest of patients readmitted to ICU due to acute pulmonary edema (2 patients) due to ischemic heart disease; hypoglycemic coma (1 patient); acute respiratory failure (1 patient); neurologic impairment (1 patient). Concerning the reasons for early death after ICU discharge, the majority of patients died due to acute respiratory failure (9/11 patients), including both hypoxemic and inadequate ventilatory respiratory failure. The rest of patients died due to sudden cardiac arrest (1 patient); septic shock due to bloodstream infection from MDR pathogen (1 patient).

Discussion

Decisions on discharge from ICU are currently based on clinical judgment rather than objective criteria. Through the present study, we prospectively studied various demographic, clinical, laboratory and intensive care factors that might be implicated in an adverse outcome early after ICU discharge. The interval between ICU discharge and readmission or death was defined the 72 h post discharge, based on previous workers that studied early readmissions [8-11]. Our findings are compatible with previous studies [12] and identified that the sick and chronically unwell patients, who had already longer prior hospitalization in the ward, to have greater odds of readmission or early death. Notably, patients died within 72 h after discharge had received vasopressor support for significantly longer period, indicating slower resolution of septic events. They disclosed higher utilization of ICU resources, as demonstrated by longer ICU LOS, central venous catheterization and mechanical ventilation, despite that these differences marginally did not reach statistical significance. Moreover, the prevalence of patients with GCS < 13 was significantly higher in this group. The leading cause of death in this patient group was respiratory failure and might be associated with inadequate pulmonary toilet. Their altered mental status along with the polyneuropathy and myopathy that often involve critically ill patients [13], might have impaired their ability to manage their bronchial secretions. Presence of tracheostomy did not prevent ventilator insufficiency. The use of dedicated teams of respiratory therapists actively following upon selected patients after ICU discharge have been associated with decreased mortality [14]. These patients received nutrition mainly via nasogastric tube (72.7%). Nasogastric tube feeding may be a marker for sicker patients with poor central nervous system recovery, suggesting that a higher demand for support either by medical/nurse staff or by relatives is needed. The introduction of an intermediate care or step-down unit would allow the admission of these ICU discharged patients before their transfer in a general ward and thus might reduce their mortality rate [15].

Readmission rate in our general ICU was 8.4%, similar to data from review studies that reported values from

0.9% to 19% [2,12]. The readmission rates reported in the literature for surgical ICU patients also ranged from 0.89% to 9.4% [10,16]. The only factors associated with early readmission were hospitalization time prior ICU first admission and vasopressor support during ICU stay. Hospitalization time before ICU may reflect a failure to respond to treatment on a general ward or late referral to ICU [9]. The principal cause of readmission was sepsis, as defined by the Surviving Sepsis Campaign definitions [17]. In the majority of the cases, the septic status of the patient was associated with emergency surgery related to patients' primary diagnosis. This finding highlights the need for definitive treatment of surgical problems during patients' hospitalization in the ICU. A study of 97 early readmissions to a surgical ICU concluded that the majority of readmissions were due to respiratory and neurologic deterioration, 22% were preventable and 5% might have been prematurely discharged [10]. Moreover, all readmitted patients had a CVC when discharged from the ICU. Given that CRBSIs represented the second septic cause of readmission, removal of CVC before patient's transfer to the ward is required. Unlike previous workers [18], we could not demonstrate a correlation between raised peripheral WBC at discharge and readmission, although sepsis was the leading readmission cause. We also studied systolic pressure and lactate concentration as markers of unresolved underlying pathology, particularly of insidious sepsis, but no correlation was found. Readmission to the ICU has been associated with poor outcomes, such as increased ICU and hospital length of stay and increased mortality [2,4]. In our series, readmitted patients revealed almost double 28-day mortality compared to not readmitted patients (30.7% vs. 16.1%). However, this difference did not reach statistical significance, probably due to the small patient sample size.

Unplanned readmissions within 48 h of discharge have been used as leading indicator of the quality of ICU care [11,19]. More than a half of our patients readmitted after ≥ 72 h of discharge, probably indicating an optimal quality of care. However, there is no clear evidence indicating that longer ICU stay would prevent readmission. The factors contributed to our patients' ICU readmission were not clinically observable at the time of discharge. Patient's readmission might be related to organizational factors outside the ICU, such as substandard care after ICU discharge. Presumable contributing factors might include the increased demand for support from relatives and the low nurse to patient ratio in the ward. Moreover, inadequate vigilance for clinical deterioration or failure by resident doctors to interpret signs of an impending medical emergency, along with delays in prompt medical treatment, could result in ICU readmission. Development of critical care outreach teams, who monitor patients after ICU discharge, provide early warning of deterioration and suggest interventions to prevent further deterioration, might provide benefit in

survival and readmission rates [20].

Scoring systems such as the patient at risk [21] and modified early warning scores [22] are designed to detect promptly subtle deterioration in physiology and evoke a graded response depending in the degree of the abnormality, in order to lower ICU readmission rates. However, multi-component scoring systems may be institutional dependent and modified by clinical judgment and institutional practices, resulting in inapplicability across different ICUs.

Our study has some limitations. It is a single-center study and management practices might have influenced our conclusions. The small number of patients in our series might have impeded statistical significance. Detailed recording of more physiological variables at discharge and at time prior to readmission or death might have provided more data about the reasons of patients' deterioration.

In conclusion, precise prediction of patients at risk for readmission or early death after ICU discharge continues to remain unfeasible target. Previous workers report that up to 40% of readmissions may have been associated with premature discharge [2]. Such results are not easily extrapolated to different ICUs due to varying organizational factors and policies especially between countries. Nevertheless, persisting organ dysfunction and patient's primary diagnosis for admission seem to be of signal importance. Patients with higher disease severity at discharge and moderately altered mental status, especially those with prolonged hospitalization in ICU are at increased risk for early death and demand a closer vigilance for clinical deterioration. Identification of these high-risk patients may allow extra resources to be targeted towards them, such as delayed discharge [23,24], discharge to a step-down unit before transfer to ward [15] or more aggressive follow-up on the wards [20], and thus improve their outcome.

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Competing Interests

None declared.

Ethical Approval

Not required.

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