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Septic shock: a major cause of hospital death after intensive care unit discharge

Choque séptico: importante causa de morte hospitalar após alta da unidade de terapia intensiva

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ABSTRACT

Objective: To assess the causes and factors associated with the death of patients between intensive care unit discharge and hospital discharge.

Methods: The present is a pilot, retrospective, observational cohort study. The records of all patients admitted to two units of a public/private university hospital from February 1, 2013 to April 30, 2013 were assessed. Demographic and clinical data, risk scores and outcomes were obtained from the Epimed monitoring system and confirmed in the electronic record system of the hospital. The relative risk and respective confidence intervals were calculated.

Results: A total of 581 patients were evaluated. The mortality rate in the intensive care unit was 20.8% and in the hospital was 24.9%. Septic shock was the cause of death in 58.3% of patients who died after being discharged from the intensive care unit. Of the patients from the public health system,

73 (77.6%) died in the intensive care unit and 21 (22.4%) died in the hospital after being discharged from the unit. Of the patients from the Supplementary Health System, 48 (94.1%) died in the intensive care unit and 3 (5.9%) died in the hospital after being discharged from the unit (relative risk, 3.87%; 95% confidence interval, 1.21 - 12.36; $p < 0.05$). The post-discharge mortality rate was significantly higher in patients with intensive care unit hospitalization time longer than 6 days.

Conclusion: The main cause of death of patients who were discharged from the intensive care unit and died in the ward before hospital discharge was septic shock. Coverage by the public healthcare system and longer hospitalization time in the intensive care unit were factors associated with death after discharge from the intensive care unit.

Keywords: Sepsis; Shock, septic; Patient readmission; Patient discharge; Death; Intensive care units

Conflicts of interest: None.

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INTRODUCTION

In recent years, intensive care units (ICU) have faced an increasing number of elderly patients with multiple comorbidities who are often subjected to prolonged and debilitating treatments. Although the mortality rates in the ICU have dropped for this group of patients, we still know little about the complications and causes of deaths that occur in the ward after ICU discharge.^(1,2)

With population aging, there is an increasing demand for ICU beds, which may hasten the discharge of patients who are not completely free from risk. The number of semi-intensive care beds, also called progressive care, is not

known in Brazil, but we know that it is far from meeting the needs, especially in public services.⁽²⁻⁴⁾ When placed in wards or other hospital units, these patients most likely do not receive support, treatment and care from personnel qualified to treat them, which may lead to higher rates of readmission to the ICU and mortality.⁽⁵⁻⁷⁾

The causes of death after ICU discharge and before hospital discharge and the factors that could influence these outcomes have not been studied yet. The present study aimed to assess the causes of death after ICU discharge and the characteristics of these patients when compared to patients who died in the ICU.

METHODS

The present is a pilot, retrospective, observational cohort study. The records of all patients admitted from February 1, 2013 to April 30, 2013 to two units with 20 and 23 beds, respectively, of a public/private university hospital were assessed. That is, the data were from patients admitted to an ICU dedicated (but not exclusive) to patients from the Supplementary Health System (SHS) and another ICU dedicated to patients from the Public Health System (PHS). The study was approved by the Ethics and Research Committee (ERC) of the aforementioned hospital under CAAE number 33417814.7.0000.5415. The need to obtain informed consent was waived by the ERC.

Demographic and clinical data, risk scores and outcomes (discharge or death) were obtained from the Epimed Monitoring System and confirmed in the electronic record system of the hospital. The type of patient hospitalization was discriminated between PHS and SHS. The recorded causes of death were classified into 12 categories. All cases of patients who died in the hospital after being discharged from the first ICU hospitalization were considered deaths after ICU discharge, regardless of the place of death.

For the statistical analysis, the Statistical Package for the Social Sciences (SPSS), version 11 was used. Categorical variables were addressed as proportions and analyzed by the chi-square test. Normally distributed continuous variables are presented as means and were evaluated by *Student's t* test, whereas variables that were not normally distributed were evaluated by Mann-Whitney's test and are presented as medians. The Kolmogorov-Smirnov test was used to test for normality. To study risk factors, the relative risk (RR) was calculated and its respective confidence intervals (CI). A *p* value < 0.05 was considered significant.

RESULTS

From February 1, 2013 to April 30, 2013, a total of 581 patients who were hospitalized or had been admitted to the intensive care unit were evaluated. The readmission rate was 7.75%. None of the patients received palliative care in this period. Of these patients, 121 died in the ICU and 24 died after being discharged from the first ICU hospitalization. The mortality rates were 20.8% in the ICU and 24.9% in the hospital.

Table 1 shows clinical and demographical data, support measures, prognostic scores and mortality rates of patients admitted in the studied period. The main comorbidities were hypertension and diabetes. Regarding the type of support used during ICU hospitalization, 201 patients (34.5%) received mechanical ventilation, 165 vasoactive drugs (28.3%), 50 dialysis support (8.6%), and 3 palliative care (0.5%). Sepsis, neurologic disease and respiratory failure were the most common causes for admission.

Table 2 shows the clinical characteristics of patients who died. Of patients who died after ICU discharge (24 patients), 10 (41.6%) died within 7 days after ICU discharge, 5 (20.8%) died between 8 and 14 days, 4 (16.6%) died between 15 and 21 days, and 5 (20.8%) died more than 21 days after discharge.

The length of stay in the hospital before ICU admission (in days) was significantly longer in the group that died after discharge [4 days (1.5 - 13.5 days)] compared to the group that died in the ICU [2 days (1 - 6 days)] (*p* = 0.008). The length of stay in the ICU was significantly higher in the group that died after discharge [9 days (5.5 - 20.5 days)] compared to the group that died in the ICU [5 days (2 - 9 days)] (*p* < 0.001). The median length of stay in the ICU of all patients who died was 6 days. The post-discharge mortality rate was significantly higher in patients whose length of stay in the ICU was longer than 6 days (25.8%) than in patients with a shorter length of stay in the ICU (9.9%) (RR 2.61; 95% CI 1.19 - 5.70; *p* < 0.05).

Table 3 shows the causes of death in the ICU and after discharge from this unit. The cause of death was septic shock in 51.2% of those who died in the ICU and in 58.3% of those who died after ICU discharge, followed by refractory shock or cardiopulmonary arrest in 18.1 and 25.0%, respectively. Other causes of death after discharge were hemorrhagic shock (4.1%), acute myocardial infarction (4.1%) and aspiration pneumonia (4.1%).

Of PHS patients, 73 (77.6%) died in the ICU and 21 (22.4%) died in the hospital after ICU discharge. Of SHS

Table 1 - Clinical and demographic data, support measures, prognostic scores and mortality rates of all patients

Variables	Results
Number of patients	581
Male	302 (51.9)
Age (years)	58.5 ± 19.2
Infection at admission to the unit	98 (16.8)
SAPS 3	49.9 ± 19.9
Type of ICU admission	
Medical	328 (60.07)
Elective surgery	120 (21.9)
Urgency/emergency surgery	72 (13.1)
Not informed	26 (4.7)
Care category	
PHS	241 (41.4)
SHS	340 (58.5)
Origin	
Emergency	236 (40.6)
Operating room	213 (36.6)
Ward/room	81 (13.9)
Other ICU/SIU of the hospital	11 (1.9)
Semi-intensive care unit	3 (0.51)
Catheterization laboratory	8 (1.3)
Other	29 (4.9)
Main hospitalization support measures	
Mechanical ventilation	201 (34.5)
Vasoactive drugs	165 (28.3)
Renal support	50 (8.6)
Decision for palliative care	3 (0.5)
Probability of death in the ICU - SAPS 3 score	
PHS	
General equation	33.9 ± 28.8
Adjusted equation for Latin America	41.8 ± 32.2
Standardized mortality rates of the unit (O/E)	0.91/0.74
SHS	
General equation	17.3 ± 20.3
Adjusted equation for Latin America	22.7 ± 24.5
Standardized mortality rates of the unit (O/E)	0.73/0.55
Probability of hospital death - SAPS 3 score	
PHS	
General equation	34.2 ± 28.5
Adjusted equation for Latin America	42.2 ± 31.9
Standardized mortality rates of the unit (O/E)	1.39/1.13
SHS	
General equation	14.6 ± 18
Adjusted equation for Latin America	14.6 ± 18
Standardized mortality rates of the unit (O/E)	1.22/0.92

SAPS 3 - Simplified Acute Physiology Score 3; ICU - intensive care unit; PHS - Public Health System; SHS - Supplementary Health System; SIU - semi-intensive care unit; O/E - observed/expected. Results expressed as number (%) or mean ± standard deviation.

patients, 48 (94.1%) died in the ICU and 3 (5.9%) died in the hospital after ICU discharge (RR 3.87; 95% CI 1.21 - 12.36; $p < 0.05$) (Figure 1).

DISCUSSION

Information on the complications and deaths that occur in the short and long term after ICU discharge has attracted great interest, as evidenced by the increasing number of published studies.⁽⁸⁻¹⁰⁾ However, few investigations have assessed the causes of death during the same hospitalization after ICU discharge. In the present study, we found that the main cause of death between discharge from the ICU and discharge from the hospital was septic shock.

We must also consider that most of the cases classified as refractory shock and cardiopulmonary arrest may have occurred due to sepsis. The post-discharge mortality rate was almost four times as high in the group of patients from the PHS. A few hypotheses for possible causes of this scenario can be discussed.

First, it is possible that PHS press for higher turnover of beds because of the high demand for beds for new admissions, which could cause early ICU discharges in the PHS, with greater possibility of adverse outcomes. In institutions with great demand for beds, the chances of readmission after ICU discharge are greater. We must also consider that given the need for readmission and the scarcity of beds, patients have to face new priority lines, and the wait for readmission may be longer in public units.⁽⁴⁾ The time between the appearance of an organ dysfunction and admission to the ICU is twice as long in public as in private units for patients with sepsis.⁽³⁾

It is also likely that post-discharge care may be different because of the financial coverage offered by PHS and by SHS. Health expenses are different between countries, and the results vary according to the gross domestic product.^(11,12) Because the present study did not assess differences such as time between the need for intensive care and ICU admission, physical area, size of healthcare staff and availability of ICU beds in case of readmission to the unit, among other factors, it is not possible to indicate the cause of such differences in results. It is possible that all of these factors play a role and should be analyzed in further studies so that the resizing and remodeling needs of PHS can be identified.

The length of stay of patients who died after ICU discharge was approximately 30 days in this unit, but with better results obtained these days, many are discharged alive but extremely fragile and with major physical and cognitive sequelae. Severe malnutrition, old age, muscle atrophy, diaphragmatic dysfunction and delirium are

Table 2 - Clinical characteristics of patients who died in the intensive care unit and after discharge from this unit

Clinical characteristics	Survivors (N = 436)	Death in the ICU (N = 121)	Death after discharge (N = 24)
Male	223 (51.1)	68 (56.1)	11 (45.8)
Age (years)	58.0 ± 20.0	63.1 ± 16.1	62.8 ± 16.0
SAPS 3	43.8 ± 16.2	65.4 ± 16.6	60.9 ± 16.6
Mechanical ventilation	95 (21.7)	89 (73.5)	17 (70.8)
Vasoactive drug	71 (16.2)	83 (68.5)	11 (48.5)
Dialysis	12 (2.7)	35 (28.9)	3 (12.5)
Origin before first ICU admission			
Emergency room	169 (38.7)	58 (47.9)	9 (37.5)*
Operating room	167 (38.3)	36 (29.7)	10 (41.6)
Ward	60 (13.7)	17 (14.0)	4 (16.6)
Other ICU	8 (1.8)	3 (2.4)	0 (0)
Catheterization room	7 (1.6)	0 (0)	1 (4.1)
Not informed	25 (5.7)	7 (5.7)	0 (0)
Diagnosis at admission			
Sepsis	64 (14.6)	36 (29.7)	6 (25.0)
Neurosurgery/neurologic	64 (14.6)	22 (18.1)	8 (33.3)
Acute abdomen	23 (5.2)	8 (6.6)	3 (12.5)
Respiratory failure	37 (8.4)	10 (8.2)	1 (4.1)
Shock/cardiopulmonary arrest	3 (0.6)	4 (3.3)	0 (0)
Upper gastrointestinal bleeding	13 (2.9)	4 (3.3)	0 (0)
Elective surgery	68 (15.5)	2 (1.6)	2 (8.3)
Trauma	31 (7.1)	2 (1.6)	1 (4.1)
Complicated chronic renal failure	8 (1.8)	3 (2.4)	0 (0)
Acute myocardial infarction	13 (2.9)	2 (1.6)	0 (0)
Pulmonary thromboembolism	2 (0.4)	2 (1.6)	0 (0)
Liver disease complications	1 (0.2)	2 (1.6)	0 (0)
Seizures	10 (2.2)	2 (1.6)	0 (0)
Cholecystitis/acute cholangitis	0 (0)	1 (0.8)	0 (0)
Coma/torpor	8 (1.8)	1 (0.8)	0 (0)
Other	91 (20.8)	19 (15.7)	3 (12.5)
Comorbidities			
Hypertension	171 (39.2)	50 (41.3)	14 (58.3)
DM with and without complications	63 (14.4)	22 (18.2)	4 (16.6)
Neoplasia	35 (8.02)	14 (11.5)	6 (25.0)
Liver cirrhosis (Child A-C)	14 (3.2)	18 (14.8)	1 (4.1)
Chronic renal failure	31 (7.1)	13 (10.7)	4 (16.6)
CHF (NYHA II-IV)	3 (0.7)	11 (9.1)	2 (8.3)
Cardiac arrhythmias	31 (7.1)	8 (6.6)	0 (0)
Morbid obesity	4 (0.9)	6 (4.9)	0 (0)
Cerebrovascular accident	25 (5.7)	5 (4.1)	2 (8.3)
Previous acute myocardial infarction	17 (3.9)	4 (3.3)	1 (4.1)
AIDS	6 (1.3)	1 (0.8)	0 (0)
Smoking	36 (8.2)	10 (8.2)	1 (4.1)
Alcoholism	7 (1.6)	7 (5.7)	2 (8.3)
Corticosteroids	5 (1.1)	1 (0.8)	0 (0)
Immunosuppression	7 (1.6)	4 (3.3)	0 (0)

ICU - intensive care unit; SAPS 3 - Simplified Acute Physiology Score 3; DM - diabetes mellitus; CHF (NYHA) - congestive heart failure (New York Heart Association); AIDS - acquired immunodeficiency syndrome. Results expressed as number (%) or mean ± standard deviation. * p < 0.05 versus death in the intensive care unit.

Table 3 - Characteristics, outcomes and causes of death in the intensive care unit and after discharge from the intensive care unit

Groups	Death in the ICU (N = 121)	Death after ICU discharge (N = 24)
Septic shock	62 (51.2)	14 (58.3)
Refractory shock/cardiopulmonary arrest	23 (19.0)	6 (25.0)
Respiratory failure	9 (7.4)	0 (0)
Intracranial hypertension	8 (6.6)	0 (0)
Hemorrhagic shock	5 (4.1)	1 (4.1)
Cardiogenic shock	5 (4.1)	0 (0)
Aspiration pneumonia	3 (2.4)	1 (4.1)
Mesenteric ischemia	2 (1.6)	0 (0)
Decompensated liver disease	2 (1.6)	0 (0)
Acute myocardial infarction	1 (0.8)	1 (4.1)
Pulmonary thromboembolism	1 (0.8)	0 (0)
Cardiac arrhythmia	0 (0)	1 (4.1)
Length of stay before ICU (days)	2.0 [0 - 6.0]	3.5 [1.0 - 11.7]*
Length of stay in the ICU (days)	6 [2.0 - 12.0]	8.5 [5.2 - 19]*
Length of stay in the hospital (days)	12 [5.0 - 26.0]	29.5 [17.0 - 38.0]*

ICU - intensive care unit. Values represent the number of patients (%). * $p < 0.05$.

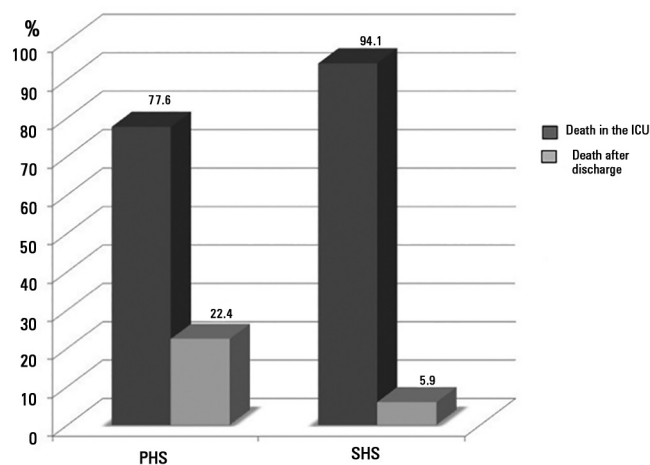


Figure 1 - Mortality rates (%) in the intensive care unit and in the hospital after discharge from the intensive care unit for patients from the Public Health System and the Supplementary Health System. ICU - intensive care unit; PHS - Public Health System; SHS - Supplementary Health System.

some of the sequelae of prolonged immobilization time and metabolic response to the disease.⁽¹³⁾ It is possible that these patients are not receiving the required comprehensive and specialized care for their degree of fragility. Causes and proposals for improvements in comprehensive care must be urgently reviewed, considering the large and increasing demand placed on our health services. Analyzing differences in care provided to those who have supplementary health assistance and equalization is an urgent measure to end social injustice in a country in which healthcare still should be universal.

Some limitations of the present study must be considered. In addition to the retrospective nature of the study, the small sample size with a limited number of outcomes did not allow us to establish a cause-and-effect relationship by multivariate analysis, which must be assessed in studies with greater observation time and, if possible, multicentric studies. However, the present study assessed very important issues, which must be confirmed with larger populations. Our findings suggest that more beds and better care should be extended to the level of care with greater complexity, which includes ICUs and semi-intensive care as well as physical and nutritional rehabilitation units. In addition, the present study highlights the importance of recognizing septic shock patients and treating them early, both in the intensive care environment and in other hospitalization sectors.

CONCLUSION

Septic shock was the main cause of hospital death after discharge from the ICU. Prolonged length of stay in the intensive care unit and discharge to the ward in the Public Health System were associated with higher hospital mortality rates.

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RESUMO

Objetivo: Avaliar as causas e os fatores associados a mortes de pacientes na enfermaria que receberam alta de unidades de terapia intensiva.

Métodos: Estudo piloto, retrospectivo, observacional, de coorte. Foram avaliados os registros de todos os pacientes admitidos no período de 1º de fevereiro de 2013 a 30 de abril de 2013 em duas unidades de um hospital universitário público/privado. Dados demográficos, clínicos, escores de risco e desfechos foram retirados do Sistema de Monitorização Epimed e confirmados no sistema de registro eletrônico do hospital. Foram calculados o risco relativo e seus respectivos intervalos de confiança.

Resultados: Um total de 581 pacientes foi avaliado. A taxa de mortalidade na unidade de terapia intensiva foi 20,8% e, no hospital, de 24,9%. A principal causa de óbito foi choque séptico em 58,3% dos que faleceram após a alta da unidade de terapia intensiva. Dos pacientes do sistema público de

saúde, 73 (77,6%) morreram na unidade de terapia intensiva e 21 (22,4%) morreram no hospital, após a alta da unidade. Dos pacientes do Sistema Suplementar de Saúde, 48 (94,1%) morreram na unidade de terapia intensiva e 3 (5,9%) morreram no hospital, após a alta da unidade (risco relativo de 3,87; intervalo de confiança de 95% de 1,21 - 12,36; $p < 0,05$). A taxa de mortalidade pós-alta foi significativamente maior em pacientes com tempo de internação em unidade de terapia intensiva superior a 6 dias.

Conclusão: A principal causa de morte de pacientes que receberam alta da unidade de terapia intensiva e morreram na enfermaria antes da alta hospitalar foi o choque séptico. A cobertura pelo sistema público de saúde e o maior tempo de internação na unidade de terapia intensiva foram fatores associados à morte, após a alta da unidade de terapia intensiva.

Descritores: Sepsis; Choque séptico; Readmissão do paciente; Alta hospitalar; Morte; Unidades de terapia intensiva

REFERENCES

- Hermans G, Van Mechelen H, Clerckx B, Vanhullebusch T, Mesotten D, Wilmer A, et al. Acute outcomes and 1-year mortality of intensive care unit-acquired weakness. A cohort study and propensity-matched analysis. *Am J Respir Crit Care Med.* 2014;190(4):410-20.
- Simchen E, Sprung CL, Galai N, Zitser-Gurevich Y, Bar-Lavi Y, Gurman G, et al. Survival of critically ill patients hospitalized in and out of intensive care units under paucity of intensive care unit beds. *Crit Care Med.* 2004;32(8):1654-61.
- Conde KA, Silva E, Silva CO, Ferreira E, Freitas FG, Castro I, et al. Differences in sepsis treatment and outcomes between public and private hospitals in Brazil: a multicenter observational study. *PLoS One.* 2013;8(6):e64790.
- Caldeira VM, Silva Júnior JM, Oliveira AM, Rezende S, Araújo LA, Santana MR, et al. Critérios para admissão de pacientes na unidade de terapia intensiva e mortalidade. *Rev Assoc Med Bras.* 2010;56(5):528-34.
- Rosenberg AL, Watts C. Patients readmitted to ICUs: a systematic review of risk factors and outcomes. *Chest.* 2000;118(2):492-502.
- Araújo TG, Rieder MM, Kutchak FM, Franco Filho JW. Readmissões e óbitos após a alta da UTI - um desafio da terapia intensiva. *Rev Bras Ter Intensiva.* 2013;25(1):32-8.
- Rosenberg AL, Hofer TP, Hayward RA, Strachan C, Watts CM. Who bounces back? Physiologic and other predictors of intensive care unit readmission. *Crit Care Med.* 2001;29(3):511-8.
- Lone NI, Walsh TS. Impact of intensive care unit organ failures on mortality during the five years after a critical illness. *Am J Respir Crit Care Med.* 2012;186(7):640-7.
- Contrim LM, Paschoal VD, Beccaria LM, Cesarino CB, Lobo SM. Quality of life of severe sepsis survivors after hospital discharge. *Rev Latinoam Enferm.* 2013;21(3):795-802.
- Pandharipande PP, Girard TD, Ely EW. Long-term cognitive impairment after critical illness. *N Engl J Med.* 2014;370(2):185-6.
- Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, Lipman J, Reinhart K, Antonelli M, Pickkers P, Njimi H, Jimenez E, Sakr Y; ICON investigators. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. *Lancet Respir Med.* 2014;2(5):380-6.
- Sogayar AM, Machado FR, Rea-Neto A, Dornas A, Grion CM, Lobo SM, Tura BR, Silva CL, Cal RG, Beer I, Michels V, Safi J, Kayath M, Silva E; Costs Study Group - Latin American Sepsis Institute. A multicentre, prospective study to evaluate costs of septic patients in Brazilian intensive care units. *Pharmacoeconomics.* 2008;26(5):425-34.
- Cardoso LT, Grion CM, Matsuo T, Anami EH, Kauss IA, Seko L, et al. Impact of delayed admission to intensive care units on mortality of critically ill patients: a cohort study. *Crit Care.* 2011;15(1):R28.