Infection as an independent risk factor for mortality in the surgical intensive care unit

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OBJECTIVES: Medical and surgical intensive care unit patients represent two different populations and require different treatment approaches. The aim of this study was to investigate the parameters associated with mortality in medical and surgical intensive care units.

METHODS: This was a prospective cohort study of adult patients admitted to a medical and surgical intensive care unit teaching hospital over an 11-month period. Factors associated with mortality were explored using logistic regression analysis.

RESULTS: In total, 827 admissions were observed, and 525 patients >18 years old and with a length of stay >24 h were analyzed. Of these patients, 227 were in the medical and 298 were in the surgical intensive care unit. The surgical patients were older ($p < 0.01$) and had shorter lengths of stay ($p < 0.01$). The mortality in the intensive care unit (35.1 *vs.* 26.2, $p = 0.02$) and hospital (48.8 *vs.* 35.5, $p < 0.01$) was higher for medical patients. For patients in the surgical intensive care unit, death was independently associated with the need for mechanical ventilation, prognostic score (SAPS II), community-acquired infection, nosocomial infection, and intensive care unit-acquired infection. For patients in the medical intensive care unit, death was independently associated with the need for mechanical ventilation and prognostic score.

CONCLUSIONS: Although the presence of infection is associated with a high mortality in both the medical and surgical intensive care units, the results of this prospective study suggest that infection has a greater impact in patients admitted to the surgical intensive care unit. Measures and trials to prevent and treat sepsis may be most effective in the surgical intensive care unit population.

KEYWORDS: Sepsis; Cohort Studies; Infection Control; Nosocomial Infections; Intraabdominal Surgery.

◼ INTRODUCTION

Surgical and medical patients are two large groups of critically ill patients with differences in demographic characteristics, leading primary intensive care diagnoses upon admission, and mortality (1-4), suggesting that different treatment approaches may benefit both groups.

Surgical patients admitted to intensive care units (ICUs) are generally older, with a preexistent chronic condition and a poor nutritional status that could be associated with diverse mortality causes (1,5). Major postoperative complications are uncommon, occurring in less than 20% of patients, but these patients have a four-fold higher mortality rate than patients without complications (6). Infection is prominent among the surgical complications.

In a multicenter study, the ICU mortality rate of infected patients was more than twice that of non-infected patients (7). In the PROGRESS registry, the ICU mortality rate in patients with severe sepsis was 39.2% (8). In a prospective cohort study including 75 ICUs in Brazil, the mortality rates of patients with severe sepsis and septic shock were 34.4 and 65.3%, respectively (9). An observational study in surgical patients revealed incidences of severe sepsis and septic shock of 5 and 11.5%, respectively, while the mortality rates were 48.4% for severe sepsis and 70.8% for septic shock (5).

Although risk factors for mortality have been reported in the medical literature, there are few studies comparing differences in the risk factors for mortality in two different ICUs in the same institution. The aim of this study was to identify differences between patients admitted to a surgical and medical ICU through a prospective study comparing

Infection and mortality in intensive care
Toufen Jr C et al.

CLINICS 2013;68(8):1103-1108

demographic factors, severity scores, infection, and their association with ICU mortality in a medical and surgical ICU.

■ MATERIALS AND METHODS

We performed an observational prospective study for eleven months (from December 1, 2000, through October 31, 2001) in a medical ICU (11 beds) and a surgical ICU (12 beds) at the ''Hospital das Clínicas'' of the University of São Paulo Medical School, a major tertiary care referral center in São Paulo, Brazil. Both ICUs were closed units with the same patient to nurse ratio. This investigation was part of a longitudinal observational study designed to evaluate acute respiratory failure in Brazil (10). Patients with acute coronary syndromes and postoperative heart surgery occupied other ICUs in the hospital. During the study period, all consecutively admitted patients aged 18 years or older and with a length of stay (LOS) in the ICU of more than 24 hours were enrolled. This study was approved by the ethics committee of the Hospital das Clinicas of São Paulo University.

We prospectively collected the following information daily for each eligible patient: 1) demographic data (age, gender, dates of ICU admission and discharge, and dates of hospital admission and discharge); 2) prior health status (solid and hematologic malignancy; myocardial infarction, heart failure, or hypertensive vascular disease; restrictive, obstructive, or vascular pulmonary chronic disease; cirrhosis, upper GI bleeding, or bilirubin level>2 mg/dl; necessity of dialysis or creatinine level>2; AIDS; diabetes mellitus; and tuberculosis); 3) ICU admission diagnosis and therapeutic interventions in the ICUs, and 4) all variables necessary for computing the Simplified Acute Physiology Score (SAPS II) (11) and Logistic Organ Dysfunction Score (LODS) (12) for the first day in the ICU.

A nosocomial infection was defined as an infection that became evident 48 hours or more after hospital admission. Infections that become evident 48 hours or more after admission in the ICU were classified as ICU-acquired infections. Infections that started before hospital admission were classified as community-acquired infections. Surgeries indicated 24 hours before the procedure were defined as urgent surgeries. All other surgeries were classified as elective surgeries.

Analyses were performed using SPSS 10.0 software for windows (SPSS, Chicago, IL). The numerical values are expressed as the means $\pm$ SD of the mean, except when otherwise specified. Significance was set at $p \leq 0.05$. The data

were analyzed using the chi-square test for categorical variables and Student's t-test for continuous variables. We performed a univariate analysis to identify variables associated with an outcome at $p < 0.05$ to be included in a multinomial logistic regression procedure to indicate independent variables for ICU mortality. Odds ratios (ORs) were estimated from the β coefficients, and the 95% confidence intervals (CIs) were calculated. We generated Kaplan-Meier curves and used Mantel-Cox log rank tests to compare survival distributions of infected and non-infected patients admitted to the SICU and MICU. A $p < 0.05$ was considered significant in all procedures.

■ RESULTS

A total of 827 patients were consecutively admitted to the medical (MICU) and surgical (SICU) ICUs. Of these patients, 525 were over 18 years old and had occupied an ICU bed for more than 24 hours, and they were therefore included in the study.

The characteristics of all 525 patients (227 patients admitted to the MICU and 298 patients admitted to the SICU) are presented in Table 1. Only 58.9% of the patients admitted to the surgical ICU have the postoperative period as the cause of admission; most of the other patients were admitted to the SICU from surgical wards or emergency rooms for causes other than the early postoperative period. The mean age of SICU patients was higher than that of MICU patients. The hospital and ICU length of stay and mortality were higher in the MICU patients. LODSs were higher in the MICU patients. There was no difference in the SAPS II score or the need for mechanical ventilation between the medical or surgical ICU patients. The main reasons for ICU admission are presented in Figure 1.

There were no differences in comorbidities between the patients in the medical and surgical ICUs (77.0% vs. 71.4%, respectively, $p = 0.34$). Of the 227 MICU patients, 73 (32.1%) presented with a cardiovascular comorbidity, 43 with a renal comorbidity (18.9%), 34 with a respiratory comorbidity (14.9%), and 30 with diabetes (13.2%). Of the 298 SICU patients, 100 (33.5%) presented with a solid malignancy (26% with metastasis), 85 with a cardiovascular comorbidity (28.5%), 42 with diabetes (14.0%), and 31 with a renal comorbidity (10.4%).

Some therapeutic interventions were utilized more frequently in the medical ICU, including pulmonary artery catheterization (30.7% of 205 patients vs. 9.1% of 263 patients, $p < 0.01$) and endotracheal intubation (65.2% of 207 patients vs. 53.9% of 267 patients, $p = 0.01$). Urinary

Table 1 - The characteristics of patients admitted to the medical and surgical ICUs who were included in the study.

	All cases (n = 525)	SICU (n = 298)	MICU (n = 227)	p-value
Male gender n (%)	291 (55.4)	161 (54.0)	130 (57.2)	0.45
Age (yr)	56.3 $\pm$ 18.2	59.3 $\pm$ 17.6	52.3 $\pm$ 18.3	<0.01
Elective postoperative admission n (%)	127 (24.1)	115 (38.5)	12 (5.2)	<0.01
Postoperative admission due to urgency n (%)	68 (12.9)	61 (20.4)	7 (3.0)	<0.01
Mechanical ventilation n (%)	279 (47.0) (n = 474)	144 (53.9) (n = 267)	135 (65.2) (n = 207)	0.01
SAPS II in 1 to 24 hrs	31.7 $\pm$ 15.6 (n = 479)	30.6 $\pm$ 15.5 (n = 272)	33.2 $\pm$ 15.7 (n = 207)	0.06
LODS in 1 to 24 hrs	3.38 $\pm$ 2.65 (n = 481)	2.97 $\pm$ 2.47 (n = 274)	3.94 $\pm$ 2.77 (n = 207)	<0.01
LOS in ICU (days) - median (percentile 25-75)	4 (2-10)	4 (2-8)	6 (3-13)	<0.01
Mortality in ICU n (%)	158 (30.0)	78 (26.1)	80 (35.2)	0.02
Mortality in hospital n (%)	217 (41.3)	106 (35.5)	111 (48.8)	<0.01

SICU - Surgical ICU, MICU - Medical ICU, LOS - Length of stay.

CLINICS 2013;68(8):1103-1108

Infection and mortality in intensive care
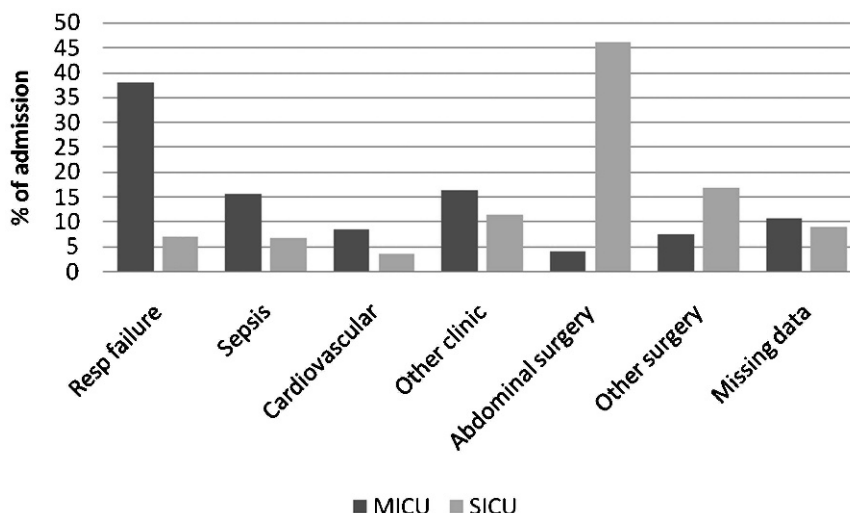Toufen Jr C et al.

Figure 1 - The main reasons for 298 surgical intensive care unit (SICU) and 227 medical intensive care unit (MICU) admissions during the study period. Legend: Respiratory failure: admission due to respiratory failure; Sepsis: admission due to sepsis; Cardiovascular: admission due to cardiovascular reasons; Other clinic: admission due to another clinical reason; Other surgery: admission due to surgery other than abdominal surgery.

catheters were more frequently utilized in the surgical ICU (93.1% of 263 patients *vs.* 84.3% of 204 patients, *p*<0.01). There was no statistically significant difference in the use of central venous catheters between the surgical and medical ICU (74.1% of 263 patients *vs.* 73.5% of 204 patients, *p* = 0.88).

Patients admitted to the medical ICU presented more overall infections (72.1% *vs.* 55.0%, *p*<0.01), community infections (38.4% *vs.* 16.7%, *p*<0.01), and ICU-acquired infections (22.6% *vs.* 14.1%, *p* = 0.01) than the surgical ICU patients, as demonstrated in Table 2. There was no difference in the frequency of nosocomial infections between SICU and MICU patients (30.9 and 29.5, respectively). Mortality in patients with community-, nosocomial-, and ICU-acquired infections was similar between the MICU and SICU patients. Among the patients with no infection, the mortality rate among the surgical ICU patients was lower than that among the medical ICU patients (6 [5.1%] *vs.* 11 [19.2%], *p*<0.01; Figure 2).

To identify risk factors for death in patients admitted to the SICU and MICU, we first performed a bivariate analysis to identify possible risk factors, including the SAPS II score, LODS score, need for mechanical ventilation, community-acquired infection, nosocomial-acquired infection, ICU-acquired infection, age, renal failure at admission, urgent surgery, gender, cardiovascular comorbidity, and diabetes. Predictor variables associated with the outcome at *p*<0.05 were eligible for inclusion in the logistic regression model. From the multivariate analysis, the independent risk factors for death in MICU patients were the SAPS II score and the need for mechanical ventilation. For SICU patients, the

independent risk factors for death were the SAPS II score, the need for mechanical ventilation, community-acquired infection, nosocomial-acquired infection, and ICU-acquired infection (Table 3).

We also assessed the 30-day survival after ICU admission in SICU and MICU patients stratified by infection or non-infection at admission or during the ICU stay. The Kaplan-Meyer survival was significantly different between infected and non-infected patients in the SICU, with a non-statistically significant difference in MICU patients. The Kaplan-Meyer survival was significantly different between non-infected MICU and SICU patients (Figure 3).

◼ DISCUSSION

Our study identified infection as an independent risk factor for ICU mortality in SICU, but not MICU, patients. We found that among infected patients, the risk for mortality was similarly increased for both medical and surgical ICU patients, while the mortality rate was higher among non-infected medical ICU patients.

Infection is an important and common problem in ICUs world-wide, with a strong relationship with length of ICU stay and mortality (7). We found that although infection is related to mortality in both medical and surgical ICU patients, it has a greater impact on patients admitted to the surgical ICU. Infection remains an independent risk factor for mortality after adjusting for prognostic scores, age, urgent surgery, renal failure, and other variables. In previous clinical studies, some interventions related to

Table 2 - Infection in medical ICU (MICU) and surgical ICU (SICU) patients during the nine months of the study, expressed as the total number (percent).

	All cases (n = 465)	SICU (n = 262)	MICU (n = 203)	*p*-value
Community-acquired infection	122 (26.2)	44 (16.7)	78 (38.4)	<0.01
Nosocomial-acquired infection	141 (30.3)	81 (30.9)	60 (29.5)	0.75
ICU-acquired infection	83 (17.8)	37 (14.1)	46 (22.6)	0.01

SICU - Surgical ICU; MICU - Medical ICU.

Infection and mortality in intensive care
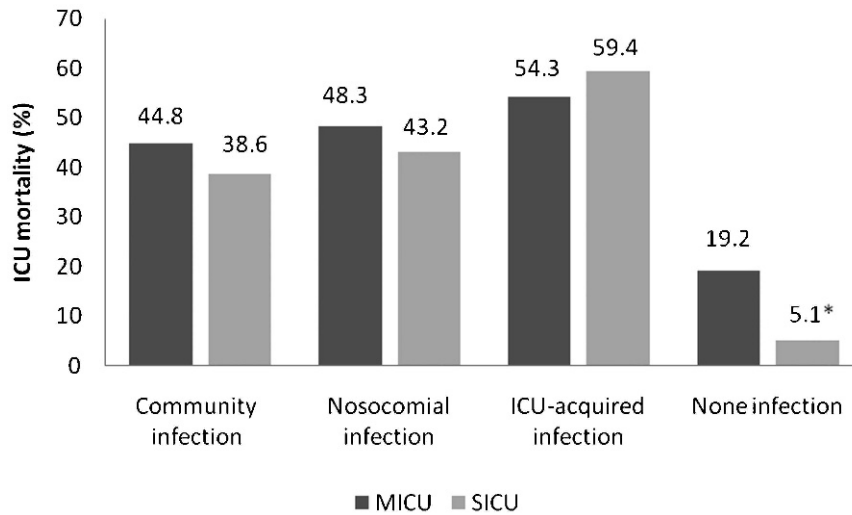Toufen Jr C et al.

CLINICS 2013;68(8):1103-1108

Figure 2 - The mortality of SICU and MICU patients associated with community-, nosocomial-, and ICU-acquired infections in non-infected patients. Legend: MICU = medical ICU, SICU = surgical ICU, *p<0.01.

infection in the ICU, such as hyperglycemic control, seemed to have greater impact in surgical ICU patients (13,14).

We believe the main reason for these findings is that the mortality in non-infected surgical ICU patients was lower than that in medical ICU patients (5.1% *vs.* 19.2%, respectively, *p*<0.01), thereby increasing the impact of infection in the surgical ICU. Patients admitted to the surgical ICU without infection are usually admitted for monitoring prior to elective operations and usually have no significant organic dysfunction. When surgical ICU patients acquire an infection, their mortality risk increases, becoming similar to that of medical ICU patients, demonstrating how infectious complications may increase mortality especially in the SICU (mortality of 5.1% without infection *vs.* 59.4% in ICU-acquired infection patients).

In our study, patients admitted to the surgical ICU were older, admitted primarily for surgical procedures (abdominal surgery was the most common), and had solid malignancies and cardiovascular disease as major comorbidities. These characteristics may contribute to the independent association

between infection and ICU mortality. Cancer is the most common medical comorbidity in patients with sepsis (15,16) and was identified as an independent risk factor in the acquisition of and mortality from sepsis in a longitudinal study (17). In our study, 33.5% of the SICU patients presented with a solid malignancy, compared with 11.5% of the MICU patients. Although pulmonary infection is the most frequent ICU infection, intra-abdominal sepsis may be associated with a higher mortality rate (18). In our study, abdominal surgery was the main surgical procedure in patients admitted to the SICU.

In the present study, infection was an important complication in patients admitted to the ICU and was found at a higher rate than that described in the literature (1,5,7,19). Previously, two observational studies reported an infection frequency of 29.3 and 24.7% in the SICU (5,20). The mortality rate in surgical ICU patients with an ICU-acquired infection was 39% (21). Some factors may be related to this mortality rate, including the selection of more severely ill patients who stayed in the ICU more than 24 hours, the

Table 3 - Variables independently associated with ICU mortality based on the multivariate logistic regression in the medical (n = 192) and surgical (n = 248) ICUs during the nine-month study period. Uni: univariate analysis; OR: Odds ratio; CI: Confidence interval.

	Surgical ICU			Medical ICU		
	Uni	Multivariate analysis		Uni	Multivariate analysis	
	p-value	*p-value*	OR (95% CI)	*p*-value	*p-value*	OR (95% CI)
SAPS II	<0.01	0.02	1.07 (1.04-1.10)	< 0.01	<0.01	1.03 (1.01-1.05)
Mechanical ventilation	<0.01	<0.01	5.3 (1.8-15.2)	<0.01	< 0.01	10.7 (3.9-29.1)
Community-acquired infection	0.02	0.01	5.9 (2.0-17.6)	0.10	-	
Nosocomial-acquired infection	<0.01	<0.01	5.2 (2.1-12.9)	0.04	0.34	
ICU-acquired infection	<0.01	0.02	6.3 (2.2-17.5)	<0.01	0.21	
LODS	<0.01	0.12		<0.01	0.45	
Age	<0.01	0.86		0.05	—	
Gender	0.52	—		0.71	—	
Renal failure at admission	<0.01	0.73		0.98	—	
Diabetes	0.16	—		0.79	—	
Cardiovascular comorbidity	0.90	—		0.16	—	
Urgent surgery	0.11	—		0.81	—	

CLINICS 2013;68(8):1103-1108

Infection and mortality in intensive care
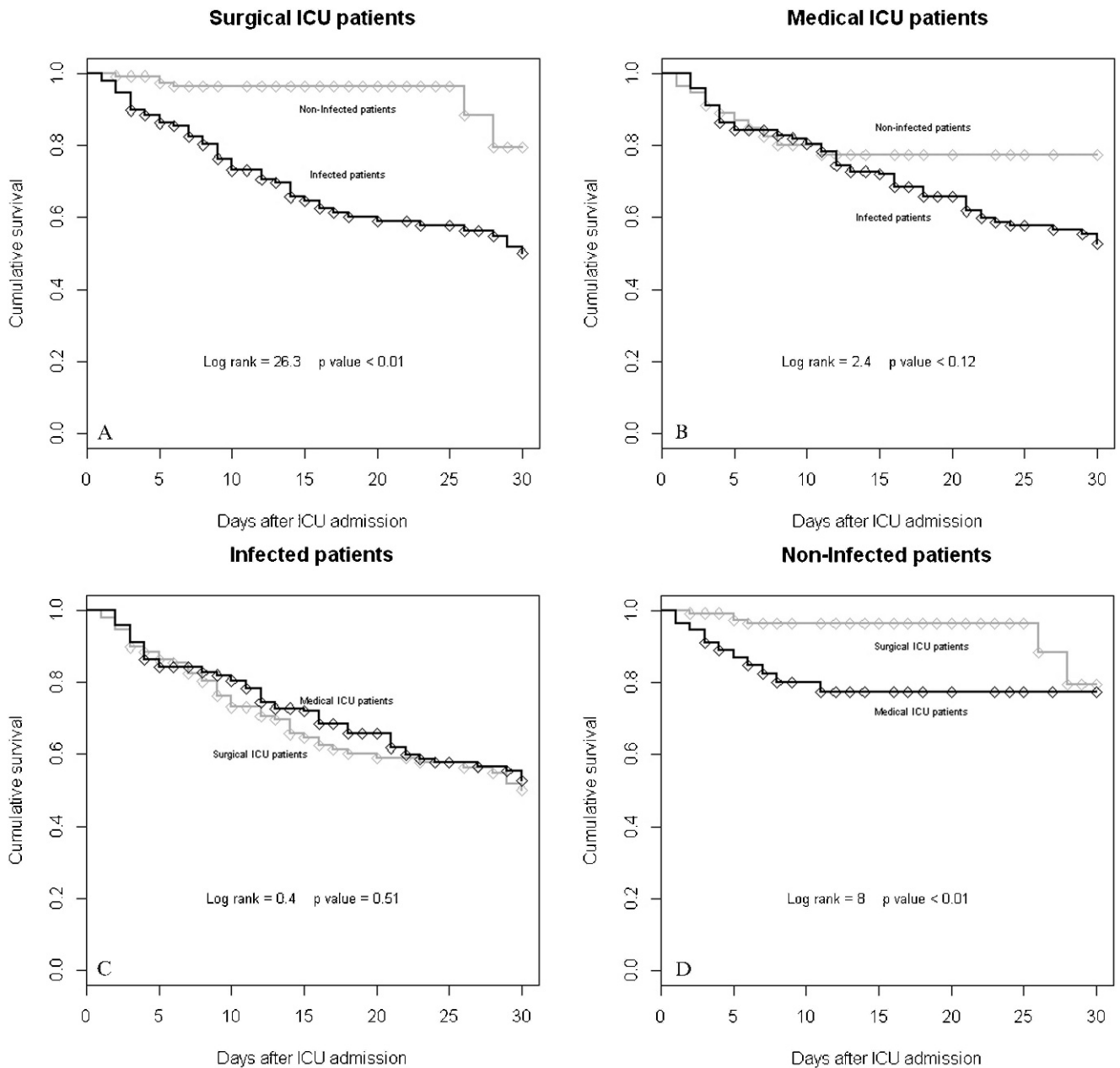Toufen Jr C et al.

Figure 3 - The Kaplan-Meyer survival curve for patients admitted to the surgical intensive care unit (A) and medical intensive care unit (B) stratified by infected and non-infected patients, and the Kaplan-Meyer survival curve for infected (C) and non-infected (D) patients stratified by intensive care unit type (surgical or medical).

selection of ICUs in a tertiary hospital with problems related to overcrowding, and a delay between identification of the need for ICU admission and the time of ICU admission (10).

The correlation between mortality and the SAPS II score has been demonstrated in the literature for general (1,21) and surgical ICUs (1) and was confirmed in both ICU types. We included prognostic scores in the multivariate analysis to assess whether infection remained an independent risk factor for ICU mortality after adjusting for the prognosis at admission. When we performed the same analysis without prognostic scores, the result remained the same for infection. The need for mechanical ventilation is associated with respiratory failure, an important risk factor for death in the ICU that has already been described in the literature (10).

Our study has some limitations. Although this study was performed in a single center, we have generalized these results. Our study may be underpowered to detect a difference in mortality between infected and non-infected patients admitted to the medical ICU. We believe that even after increasing the study power, the main result regarding the difference in the impact of infections between the two ICU populations would remain the same. Although both ICUs belong to the same hospital, unquantified variables may have influenced the results. The logistic regression model was limited to pre-existing variables in the database, and several confounding factors may have been missed, such as therapeutic interventions and the timing of those interventions.

Infection and mortality in intensive care
Toufen Jr C et al.

CLINICS 2013;68(8):1103-1108

Clinical studies investigating risk factors for mortality do not usually include the presence and origin of infection among the studied risk factors for mortality and rarely differentiate medical and surgical ICU patients, despite the differences between these populations. Our study attempted to fill this gap by identifying the differential importance of infection in the mortality of patients in the surgical ICU. This finding may be responsible for the increased effectiveness of procedures, such as tight glycemic control (13,14), performed in surgical ICU patients and should be considered in future studies involving measures linked to infection.

In conclusion, although the presence of infection is associated with a high mortality rate in both medical and surgical ICU patients, the results of this prospective study suggest that infection has a greater impact on patients admitted to the surgical ICU, indicating the importance of preventable measurements and early detection and treatment of infection in this population. Measures to prevent and treat infection may be more effective in the surgical ICU population.

■ ACKNOWLEDGMENTS

■ AUTHOR CONTRIBUTIONS

Toufen Jr C and Carvalho CRR designed the study, analyzed and interpreted the data, and drafted and revised the manuscript. Franca SA designed the study, interpreted the data, and revised the manuscript. Okamoto VN and Salge JM acquired data and revised the manuscript.

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