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Failure to reduce C-reactive protein levels more than 25% in the last 24 hours before intensive care unit discharge predicts higher in-hospital mortality: A cohort study☆,☆☆

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Abstract

Purpose: To discharge a patient from the intensive care unit (ICU) is a complex decision-making process because in-hospital mortality after critical illness may be as high as up to 27%. Static C-reactive protein (CRP) values have been previously evaluated as a predictor of post-ICU mortality with conflicting results. Therefore, we evaluated the CRP ratio in the last 24 hours before ICU discharge as a predictor of in-hospital outcomes.

Methods: A retrospective cohort study was performed in 409 patients from a 6-bed ICU of a university hospital. Data were prospectively collected during a 4-year period. Only patients discharged alive from the ICU with at least 72 hours of ICU length of stay were evaluated.

Results: In-hospital mortality was 18.3% (75/409). Patients with reduction less than 25% in CRP concentrations at 24 hours as compared with 48 hours before ICU discharge had a worse prognosis, with increased mortality (23% vs 11%, $P = .002$) and post-ICU length of stay (26 [7-43] vs 11 [5-27] days, $P = .036$). Moreover, among hospital survivors (n = 334), patients with CRP reduction less than 25% were discharged later (hazard ratio, 0.750; 95% confidence interval, 0.602-0.935; $P = .011$).

Conclusions: In this large cohort of critically ill patients, failure to reduce CRP values more than 25% in the last 24 hours of ICU stay is a strong predictor of worse in-hospital outcomes.

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1. Introduction

In-hospital mortality after intensive care unit (ICU) discharge has been reported to be as high as up to 27% [1,2]. Deaths occurring in the post-ICU period could be related to a premature discharge (in a patient with unresolved critical condition) or to a new process that occurred after ICU stay and that is not directly related to this period. An adequate evaluation of the patient before ICU discharge could probably detect individuals at high risk of unfavorable outcomes, therefore reducing readmissions to ICU and in-hospital mortality [3,4].

Discharging the patient from the ICU is a complex decision-making process. The 1999 American College of Critical Care Medicine Guidelines for Admission, Discharge and Triage of ICU patients [5] suggests that one should be discharged from the ICU when his "physiologic status has stabilized and the need for ICU monitoring and care is no longer necessary" but gives no information on objective parameters or markers that should be used to evaluate these individuals.

C-reactive protein (CRP) is an acute–phase protein that has been extensively evaluated in the ICU population [6]. Its concentrations correlate with ongoing organ dysfunction and ICU mortality [7] and have recently been evaluated as a predictor of mortality and readmission to ICU, with conflicting results [8-11]. All of the previous studies, however, evaluated static CRP values at discharge, and none reported the trend in CRP concentrations in this period.

Dynamic analysis of biologic variables seems more relevant than isolated values to predict outcomes in critical care illness [12-14]. Evaluation of CRP trend pattern in the first days of ICU admission has been reported as useful in discriminating outcomes in community-acquired pneumonia [15] and septic patients [16] and useful to help in the clinical decision-making process regarding ICU-acquired infections [17-19].

Therefore, we hypothesized that a reduction in the CRP values in the last 24 hours before ICU discharge would be useful to predict in-hospital outcomes.

2. Methods

2.1. Study subjects

This is a single-center retrospective cohort study consisting of 1043 consecutive critically ill patients admitted to the medical ICU of the emergency department of the Hospital das Clínicas of São Paulo in Brazil. Data were retrieved from January 2005 to December 2008, and all data were collected prospectively. However, hypotheses were generated before data analysis and after data collection. The present study was approved by the local research ethics committee (CAPPesq). Because of its strictly observational design, informed consent was waived.

We selected only patients who were discharged alive from the ICU and with at least 72 hours of length of stay (LOS). For patients with multiple ICU admissions, only the first admission was recorded. Exclusion criteria were patients with any missing data (Fig. 1) or patients transferred to other ICUs.

2.2. Data collection

Data were extracted from our electronic database, including demographics (age and sex), comorbidities (systemic arterial hypertension, diabetes mellitus, chronic renal failure, chronic obstructive pulmonary disease, chronic liver disease, chronic heart failure, acquired immunodeficiency syndrome, and cancer diagnosis), syndrome at admission, source of admission, type of admission, severity of illness (Acute Physiology and Chronic Health Evaluation II [APACHE II] [20] and Sequential Organ Failure Assessment [SOFA] [21]), use of noninvasive positive pressure ventilation, mechanical ventilation, renal replacement therapy, or vasoactive drugs. We also recorded the hour of discharge from the ICU, the LOS in the hospital before ICU admission, and the LOS during the ICU period. The follow-up of patients was extended to in-hospital death/survival, and the post-ICU hospital LOS was recorded. Any unscheduled ICU readmission in the same hospitalization after discharge from our unit was recorded. We were unable to

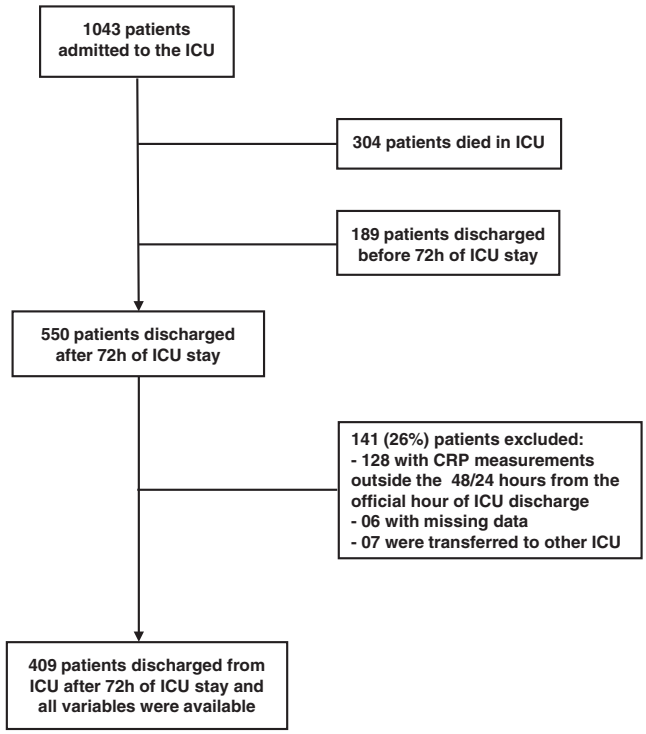

Fig. 1 Flow chart.

identify patients in our cohort who were discharged from the ICU with orders of no resuscitation or limitation of therapeutic efforts.

2.3. Laboratorial data

Blood samples were collected at 11 PM, according to our ICU standard of care, including daily CRP measurements and blood gas analysis. All samples were analyzed in the central laboratory of the institution. We collected the following laboratorial data at ICU discharge: arterial blood gas analysis, lactate, albumin, hemoglobin level, white blood cell and platelet counts, and CRP. C-reactive protein measurement was performed with an immunoturbidimetric method using a commercially available test (BIOTÉCNICA Indústria e Comércio Ltda, Minas Gerais, Brazil), with reference range less than 5 mg/L. We retrieved the following CRP values: at ICU admission, maximum value during ICU stay, and in the last 48 and 24 hours before ICU discharge. C-reactive protein ratio was calculated by dividing the CRP concentration at 24 hours before ICU discharge (CRP-24 h) to the CRP concentration at ICU admission, maximum value, and at 48 hours before the ICU discharge (CRP-48 h). To show the CRP trend as a percentage value, CRP variation was calculated by subtracting the CRP-24 h to CRP-48 h and dividing the result to CRP-48 h. C-reactive protein values were only included in the analysis if the result was inside a

Table 1 Clinical features

	Whole group (n = 409)	Survivors (n = 334)	Nonsurvivors (n = 75)	*P* [a]
Characteristics				
Age, y (mean ± SD)	48.6 ± 19.4	46 ± 18.5	60.5 ± 19	<.001
Male sex, n (%)	210 (51)	174 (52)	36 (48)	.521
APACHE II score, median (IQR)	16 (10-21)	15 (10-20)	20 (14-27)	<.001
SOFA at admission, median (IQR)	5 (3-7)	4 (2-7)	6 (4-8)	<.001
SOFA at discharge, median (IQR)	2 (1-3)	2 (1-3)	3 (1-5)	<.001
Type of admission, n (%)				.591
Medical	318 (78)	258 (77)	60 (19)	.604
Scheduled surgery	13 (03)	12 (04)	01 (01)	.313
Urgent surgery	78 (19)	64 (19)	14 (19)	.921
Origin of patients, n (%)				.001
Ward	134 (33)	95 (28)	39 (52)	<.001
Emergency department	238 (58)	208 (62)	30 (30)	<.001
Other ICU	15 (04)	13 (04)	02 (03)	.610
Step-down unit	04 (01)	02 (01)	02 (03)	.100
Operating room	13 (03)	11 (03)	02 (03)	.563
Other hospital	05 (01)	05 (02)	–	.361
Comorbid conditions, n (%)	1 (0-2)	1 (0-2)	2 (1-3)	<.001
Systemic arterial hypertension	188 (46)	140 (42)	48 (64)	.001
Diabetes mellitus	86 (21)	65 (20)	21 (28)	.101
Chronic renal failure	60 (15)	45 (14)	15 (20)	.149
Chronic heart failure	53 (13)	35 (11)	18 (24)	.002
Chronic coronary disease	43 (11)	28 (08)	15 (20)	.003
Chronic obstructive pulmonary disease	32 (08)	18 (05)	14 (19)	<.001
Chronic liver disease	14 (03)	12 (04)	2 (3)	.510
AIDS	13 (03)	13 (04)	-	.138
Cancer	49 (12)	35 (11)	14 (19)	.048
Syndrome at admission, n (%)				.134
Respiratory failure	117 (29)	98 (29)	19 (25)	.942
Shock [b]	66 (16)	46 (14)	20 (27)	.006
Sepsis/severe sepsis	53 (13)	40 (12)	13 (17)	.212
CNS disorders	51 (13)	43 (13)	08 (11)	.601
Renal failure	16 (04)	14 (04)	02 (03)	.368
Electrolytes disturbances	16 (04)	15 (05)	01 (01)	.202
Severe trauma	12 (03)	12 (04)	–	.096
Exogenous intoxication	09 (02)	08 (02)	01 (01)	.486
Other	69 (16)	58 (17)	11 (15)	.573

AIDS indicates acquired immunodeficiency syndrome; CNS, central nervous system.

[a] *P* values refer to a comparison between survivors vs nonsurvivors.

[b] There were 57 patients (86%) with septic shock, 5 (08%) with hypovolemic shock, and 4 (06%) with cardiogenic shock.

predefined time window to avoid bias due to CRP half-life and sample-collect routine. Regarding the CRP-48 h, only results collected up to 50 hours (2 hours of difference) were considered valid. The same time window was used for the CRP-24 h. Intensive care unit discharge time was collected from the hospital's official system. All the laboratorial results were available to the intensivists before the discharge decision.

2.4. Statistical analysis

Data are presented as the mean ± SD or median and 25th and 75th percentiles (interquartile range [IQR]) if they are normal or skewed distributed, respectively. Baseline characteristics of the post-ICU survivors and nonsurvivors were compared using the Mann-Whitney *U* or unpaired *t* test, as appropriate. The Fisher exact test or χ^2 statistics were used for dichotomous variables. Binary logistic regression was used to evaluate the prognostic factors to in-hospital outcome. Variables with $P < .20$ on the univariate analysis were included in the multivariate analysis and selected using likelihood ratio backward elimination method. The backward elimination method was performed using $P < .05$ as statistical significant, and variables with $P < .10$ were retained in the final multivariate model after the likelihood ratio analysis. Single collinearity was evaluated with the Pearson correlation among the independent variable, and multicollinearity was evaluated with the variance inflation factor [22]. The odds ratio (OR) and corresponding 95% CI for each variable were computed. The discriminative ability of the model to predict the outcome of patients was assessed by the area under the

Table 2 Clinical features

	Whole group (n = 409)	Survivors (n = 334)	Nonsurvivors (n = 75)	*P* [a]
Support during ICU stay, n (%)				
Noninvasive positive ventilation	75 (18)	60 (18)	15 (20)	.681
Mechanical ventilation	214 (52)	167 (50)	47 (63)	.047
Renal replacement therapy	75 (18)	53 (16)	22 (29)	.006
Vasoactive drugs	152 (37)	110 (33)	42 (56)	<.001
Hour of discharge, n (%)				.719
Night (22:00-06:59)	60 (14.7)	48 (14.4)	12 (16)	
Day (07:00-21:59)	349 (85.6)	286 (85.6)	63 (84)	
Readmission, n (%)				
Unplanned readmission	71 (17)	35 (11)	36 (48)	<.001
LOS, d (IQR)				
Preadmission	2 (0-6)	1 (0-6)	4 (1-11)	<.001
ICU	7 (4-12)	6 (4-11)	9 (5-15)	.002
Post-ICU	14 (7-31)	13 (6-28)	21 (7-39)	.158
Hospital	29 (17-50)	26 (16-48)	38 (24-57)	.001
Laboratorial data at ICU discharge, median (IQR)				
pH	7.42 (7.39-7.45)	7.42 (7.39-7.45)	7.42 (7.39-7.45)	NS
pCO_2 (mm Hg)	36.4 (32.1-40.9)	36.4 (32.6-40.4)	36.3 (31.8-43.2)	NS
SBE (mEq/L)	−0.5 (−2.6 to 1.9)	−0.5 (−2.8 to 1.6)	0.5 (−3.0 to 3.7)	.146
Lactate (mmol/L)	1.8 (11.3-2.3)	1.8 (1.3-2.3)	1.9 (1.2-2.6)	.127
Hemoglobin level (g/dL)	9.1 (7.9-11.0)	9.5 (8.1-11.2)	8.6 (7.6-9.6)	<.001
White blood cell count (per L)	10.0 (6.7-13.5) × 10^9	9.9 (6.6-13.3) × 10^9	10.4 (7.0-13.7) × 10^9	NS
Platelets (per L)	249.0 (166.0-365.0) × 10^9	254.0 (169.7-370.5) × 10^9	214.0 (149.0-338.0) × 10^9	.117
Creatinine (μmol/L)	70.7 (53.0-114.9)	69.8 (53.0-106.1)	87.5 (61.9-152.1)	.004
Albumin (g/L)	27 (23-31)	27 (23-32)	24 (21-28)	<.001
CRP at admission (mg/L)	102.0 (33.5-180.5)	98.3 (33.1-176.3)	108.0 (37.6-200.0)	.128
CRP maximum (mg/L)	162.0 (95.4-236.5)	160.0 (93.2-226.8)	170.0 (102.0-268.0)	.109
CRP-48 h (mg/L)	65.2 (31.8-130.0)	64.8 (31.4-128)	72.4 (33.3-142)	.184
CRP-24 h (mg/L)	48.9 (26.7-112.0)	47.0 (25.3-107.8)	75.9 (36.4-136)	.022
CRP-24 h/CRP at admission	0.65 (0.28-1.28)	0.65 (0.26-1.27)	0.66 (0.40-1.40)	.419
CRP-24 h/CRP maximum	0.43 (0.22-0.72)	0.40 (0.21-0.72)	0.49 (0.28-0.69)	.350
CRP-24 h/CRP-48 h	0.84 (0.65-1.03)	0.80 (0.63-1.01)	0.91 (0.75-1.06)	.012
CRP reduction > 25%, [b] n (%)				.002
Yes	163 (40.0)	145 (43.4)	18 (24.0)	
No	246 (60.0)	189 (56.6)	57 (76.0)	

NS indicates not significant; SBE, standard base excess.

[a] *P* values refer to a comparison between survivors vs nonsurvivors.

[b] Patients who had a reduction more than 25% in CRP values between 48 and 24 hours before ICU discharge.

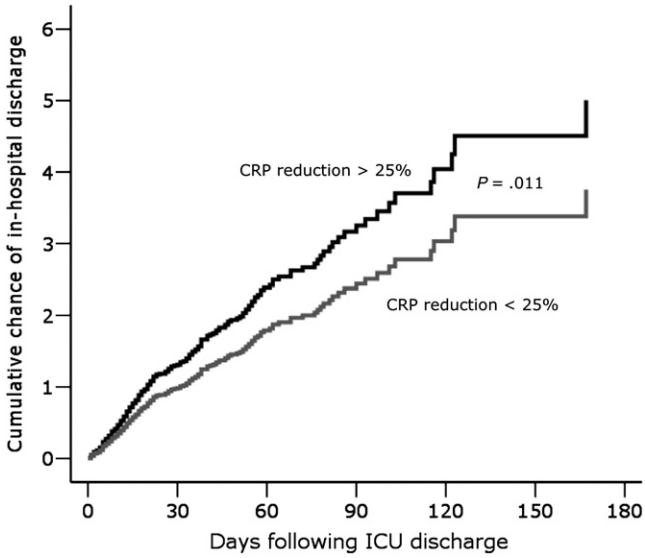

Fig. 2 Time to hospital discharge. Time to discharge from the hospital after ICU discharge. Assessed by cumulative hazard estimates and Cox proportional hazards analysis, with adjusting for age, SOFA at discharge, admission from ward, comorbidities, shock status at ICU admission, and hemoglobin level at ICU discharge (HR, 0.750; 95% CI, 0.602-0.935; $P = .011$).

receiver operating characteristic curve. Calibration ability for the model was evaluated by Hosmer-Lemeshow goodness-of-fit statistic. Receiver operating characteristic curves were used to identify the optimal cutoff values for outcome associations. The *optimal cutoff* was defined as the value associated with the highest sum of sensitivity and specificity − 1.

The effect of CRP variation on time to hospital discharge after ICU discharge was assessed by cumulative hazard ratio (HR) estimates and adjusted Cox proportional hazards analysis [23], adjusting for age, SOFA at ICU discharge, admission from ward, shock status at ICU admission, comorbidities, and hemoglobin level concentrations at ICU discharge.

Significance was considered as $P < .05$ (2 tailed). All statistical tests were performed using the commercial package SPSS 13.0 for Windows (SPSS Inc, Chicago, Ill).

3. Results

During the study period, a total of 550 patients fulfilled the inclusion criteria. Of these, 128 patients (23%) had CRP measurements outside the time range mentioned above, 6 had data missing, and 7 patients were transferred to another ICU. Thus, 409 patients were included in the analysis (Fig. 1). There were no differences among patients included or not in the analysis regarding disease severity and outcomes (APACHE II, $P = .581$; age, $P = .114$; ICU LOS, $P = .985$; unplanned readmission, $P = .088$; and in-hospital death, $P = .490$).

Overall in-hospital mortality was 18.3% (n = 75). Two hundred ten patients were male (51%), and mean age was 48.6 years (±19.4 years). Most of the patients were admitted from the emergency department (58%) or ward (33%) because of a medical condition (78%). Median APACHE II score was 16 (IQR, 10-21). The most common syndromes at admission were respiratory failure (29%) and shock (16%). Table 1 summarizes other demographic data. The 75 patients who died after ICU discharge were older (60.5 ± 19 vs 46 ± 18.5, $P < .001$), had a more severe disease at ICU admission (APACHE II score, 20 [IQR, 14-27] vs 15 [IQR, 10-20], $P < .001$), were more likely to have a chronic disease before ICU admission (2 [IQR, 1-3] vs 1 [IQR, 0-2], $P < .001$], were more often admitted from the ward (52% vs 28%, $P < .001$), and more likely to have a shock status at admission (27% vs 14%, $P = .006$). As expected, patients who required more support during the ICU stay were more prone to have a poor prognosis, as shown on Table 2.

Regarding CRP, in the univariate analysis, the values at ICU admission, maximum, and CRP-48 h were not significantly different between post-ICU survivors and nonsurvivors. By contrast, higher CRP-24 h value was associated with in-hospital death (75.9 [IQR, 36.4-136] vs 47 [IQR, 25.3-107.8] mg/L, $P = .022$). When adjusted by CRP values at ICU admission and maximum, the CRP ratio was similar between survivors and nonsurvivors. However, the relative change of CRP between 48 and 24 hours before discharge was different between the 2 groups (0.80 [IQR, 0.63-1.01] vs 0.91 [IQR, 0.75-1.06], $P = .012$), as shown on Table 2. Considering the area

Table 3 Bivariate and multivariate (independent) predictors of in-hospital mortality after ICU discharge

Variable	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*	VIF
Age	1.043 (1.028-1.058)	<.001	1.035 (1.016-1.054)	<.001	1.399
SOFA at discharge	1.359 (1.202-1.538)	<.001	1.220 (1.056-1.409)	.007	1.117
Admission from ward	2.725 (1.634-4.546)	<.001	2.745 (1.502-5.017)	.001	1.065
Comorbidities	1.519 (1.272-1.814)	<.001	1.292 (1.025-1.630)	.030	1.393
Shock status at ICU admission	2.277 (1.251-4.144)	.006	2.594 (1.257-5.355)	.010	1.040
Hemoglobin level at ICU discharge	0.782 (0.683-0.895)	<.001	0.776 (0.664-0.906)	.001	1.080
CRP reduction <25% [a]	2.427 (1.370-4.310)	.002	2.703 (1.387-5.291)	.004	1.025

[a] Patients who had a reduction less than 25% in CRP values between 48 and 24 hours before ICU discharge. Hosmer-Lemeshow χ^2, 5.000; $P = .758$; C-statistic, 0.821 (0.769-0.872); $P < .001$.

Table 4 Univariate analysis of CRP reduction less than 25% as a predictor of unplanned readmission at ICU

Variable	OR (95% CI)	*P*
Unplanned readmission (n = 71)	2.415 (1.344-4.340)	.003
After 7 d (n = 33)	3.226 (1.301-7.999)	.008
After 14 d (n = 52)	1.944 (1.017-3.717)	.042
After 21 d (n = 62)	2.113 (1.151-3.879)	.014

Patients who had a reduction less than 25% in CRP values between 48 and 24 hours before ICU discharge.

under the curve for different CRP variables, just the values at discharge have significantly results. For CRP-24 h, the discriminating ability to in-hospital death was 0.584 (0.514-0.654, P = .022), and for CRP-24 h/CRP-48 h, it was 0.593 (0.523-0.662, P = .012). The best cutoff for the CRP ratio was a decrease of 25% in CRP value when comparing 24- from 48-hour values. Patients who had CRP reduction less than 25% had a worse prognosis, with an increased mortality (23% vs 11%, P = .002) and post-ICU LOS (26 [IQR, 7-43] vs 11 [IQR, 5-27] days, P = .036). More notably, even among hospital survivors (n = 334), patients in the CRP-reduction-less-than-25% group were discharged later from hospital (HR, 0.750; 95% CI, 0.602-0.935; P = .011; Fig. 2).

Independent predictors of post-ICU mortality after a backward stepwise multivariate logistic regression analysis were age, SOFA score at ICU discharge, admission from ward, chronic comorbidities, shock status at ICU admission, hemoglobin level at ICU discharge, and CRP reduction less than 25%. Among these, hemoglobin level at ICU discharge was a protective factor to in-hospital mortality. This model has an excellent discrimination (C-statistic, 0.821) and is well calibrated (Hosmer-Lemeshow P = .758, Table 3).

Regarding unplanned ICU readmission, a secondary and prognostic end point after ICU discharge, CRP-48 h and CRP-24 h (static values) were not able to differentiate readmitted from not-readmitted patients (P = .622 and P = .710, respectively). By contrast, CRP reduction less than 25%, a dynamic variable, was a good tool to predict this unfavorable outcome, both early and late (Table 4).

4. Discussion

Defining the appropriate time to discharge a patient from the ICU is an important decision that has a direct impact on in-hospital mortality. This study showed that, in a retrospective cohort evaluation of 409 critically ill patients, a decrement in CRP concentration lower than 25% considering CRP concentrations 24 and 48 hours before ICU discharge is associated with an increase in-hospital mortality, unplanned ICU readmission, post-ICU LOS, and later hospital discharge.

Several studies have evaluated the utility of CRP measurements on the ICU [6,7,17]. In this study, we found that, at ICU discharge, the predischarge CRP concentrations were associated with in-hospital mortality in a univariate analysis. However, in the multivariate analysis, this finding did not persist. C-reactive protein and other biologic variables are dynamic because their concentrations depend on the intensity of the inflammatory stimulus. The result of reduced in-hospital mortality with CRP decrease more than 25% may be due to an improved resolution of latent inflammation in these subjects. Interestingly, the best value of CRP reduction in this study was 25%, similar to the results of Yentis et al [16] and Claeys et al [24] that evaluated the trend of CRP during a septic shock event on the ICU. Coelho et al [15], which evaluated 53 patients with community-acquired pneumonia, also identified that a reduction in CRP concentrations after 3 days of antibiotic treatment was a marker of good clinical outcome. This conjunct of findings emphasizes the opinion that the trend appears much more important for the clinical evaluation of a biologic variable during critical illness scenarios than the absolute values.

The lack of an association between the static values of CRP at ICU discharge and the prediction of post-ICU outcomes has been reported in other studies [10,11]. Comparing the present study with the previous ones, ours was predominantly composed of medical patients, and our cohort had more severe disease at admission and longer ICU LOS. Conversely, in 2 large prospective cohorts that have also evaluated the static CRP values, medical patients with higher CRP values at discharge were more prone to death at both short- [9] and long-term evaluations [8]. The different measurement techniques across the studies could partially account for these disparate findings. Because every patient may have a self-pattern of response to inflammatory stimulus, the use of CRP variation can possibly decrease the bias of individual differences and the influence of these confounders [25]. Another interesting finding of the present study is that CRP reduction less than 25% was a good marker of risk of ICU readmission. Static values of CRP have been described as markers for readmission in surgical patients [26] and in a case-control study [27,28], but as far as we are aware, predischarge CRP variation was not used for this purpose. Intensive care unit readmission is a major factor independently associated with in-hospital mortality and also with burden costs and increased hospital LOS [28]. Another intriguing finding is that, among patients who were discharged alive, those with CRP reduction less than 25% were discharged from hospital later, corroborating this hypothesis.

Some of the strengths of this study shall be emphasized. First, this is a large cohort of critically ill patients, and the data were prospectively collected in a period of 4 years. Second, we intentionally removed patients who remained in the ICU for less than 72 hours from the analysis, thus selecting a subgroup of more severely ill individuals. In

addition, the indexes described here are easy to interpret, reasonably inexpensive, and may be readily implemented in ICUs worldwide. However, despite these strengths, this study has some shortcomings that must be acknowledged. First, it is a retrospective and single-center analysis, thus subjected to biases. Second, we were unable to identify the cause of in-hospital death and the main reason for readmission after ICU discharge. Regarding readmission, it is possible that some patients returned to the ICU for a reason unrelated to the previous medical condition, including need for observation in a monitored setting. On the other hand, it is also possible that few discharged patients died in the wards while waiting for an ICU bed. Both situations could have interfered with our results. Third, we did not identify orders of withdrawing and withholding at the ICU discharge, although Azoulay et al [29] consider that these patients must be included in the analysis of post-ICU mortality. Fourth, potential confounders regarding CRP production and patients who achieved a plateau with low CRP values earlier than the moment of ICU discharge were not evaluated. For clinical purposes, we advise that this new variable should be evaluated in other critically ill patients and other centers.

In this large retrospective cohort of complex critically ill patients (ICU LOS >72 hours), we identified a new useful tool to help the physician in identifying patients at high risk of death after ICU discharge in addition to classical risk factors. Moreover, patients with a CRP reduction less than 25% had more than two and a half times the odds of dying in hospital after ICU discharge when compared with patients with a CRP reduction greater than 25%.

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