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# Risk factors for death in septic shock

## A retrospective cohort study comparing trauma and non-trauma patients

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### Abstract

The aim of this study was to compare septic shock directly associated-mortality between severe trauma patients and nontrauma patients to assess the role of comorbidities and age. We conducted a retrospective study in an intensive care unit (ICU) (15 beds) of a university hospital (928 beds). From January 2009 to May 2015, we reviewed 2 anonymized databases including severe trauma patients and nontrauma patients. We selected the patients with a septic shock episode. Among 385 patients (318 nontrauma patients and 67 severe trauma patients), the ICU death rate was 43%. Septic shock was directly responsible for death among 35% of our cohort, representing 123 (39%) nontrauma patients and 10 (15%) trauma patients ( $P < 0.0$ ). A sequential organ failure assessment score above 12 (odds ratio [OR]: 6.8; 95% confident interval (CI) [1.3–37],  $P = 0.025$ ) was independently associated with septic shock associated-mortality, whereas severe trauma was a protective factor (OR: 0.26; 95% CI [0.08–0.78],  $P = 0.01$ ). From these independent risk factors, we determined the probability of septic shock associated-mortality. The receiver-operating characteristics curve has an area under the curve at 0.76 with sensitivity of 55% and specificity of 86%. Trauma appears as a protective factor, whereas the severity of organ failure has a major role in the mortality of septic shock. However, because of the study's design, unmeasured confounding factors should be taken into account in our findings.

**Abbreviations:** CI = confident interval, ICU = intensive care unit, ISS = injury severity score, OR = odds ratio, ROC = receiver-operating characteristic, SAPS 2 = simplified acute physiology score 2, SD = standard deviation, SOFA = sequential organ failure assessment.

**Keywords:** age, comorbidities, death, septic shock, severe trauma

### 1. Introduction

Septic shock remains a major public health issue. Despite recent advances in the management of patients, there is still a high mortality and morbidity.<sup>[1–3]</sup> In a recent study, 84% of intensive care unit (ICU) patients had at least 1 organ failure at the time of death.<sup>[4]</sup> However, several factors can interfere with the outcomes of patients. However, the actual causes of death remain unclear in those patients. The respective role of severity of shock, comorbidities and age is uncertain.<sup>[5]</sup>

Trauma is the leading cause of mortality among young people. Trauma is associated with an impaired immune response, resulting in a significant rate of healthcare-associated infections.<sup>[6–8]</sup> Interestingly, the majority of trauma patients are young.<sup>[9]</sup> In blunt hemorrhagic shock, mortality was associated with increasing age. Multiple organ failure and cardiac arrest were the leading causes of death.<sup>[9]</sup> In most cases, the trauma patients do not exhibit comorbidities.<sup>[9,10]</sup> Then, they can serve as controls for assessing the role of age and comorbidities, as compared with those with other causes of admission.

We hypothesized that the mortality rate of trauma patients with septic shock was lower than that of non-trauma patients with septic shock. Our primary objective was to compare the mortality rate of nontrauma patients with septic shock and that of trauma patients who developed septic shock. Our secondary objective was to identify risk factors for septic shock associated-mortality.

### 2. Methods

We conducted a retrospective, observational, and noninterventional study from our database (from January 2009 to May 2015). The patients admitted to a 15-bed ICU in a tertiary hospital (928 beds) (North Hospital, Marseille, France) were screened. As our electronic data collection system was set up in 2009, we defined the study period from January 2009. All patients included were followed-up until death or discharge from the hospital.

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In our electronic database, we retrospectively selected among nontrauma patients and trauma patients those who developed septic shock. Of note, a sub-cohort of these patients was included in a previous study.<sup>[11]</sup> All the patients were treated according to local protocols derived from the successive editions of the “Surviving Sepsis Guidelines”.<sup>[11]</sup>

The inclusion criteria were: age  $\geq 18$  years and septic shock upon ICU admission or septic shock during the ICU stay. For the trauma group, the inclusion criteria were ICU admission for severe trauma defined by an Injury Severity Score (ISS)  $>15$ <sup>[12]</sup> and septic shock during the ICU stay. The patients transferred from another hospital were excluded from the analysis. We excluded the patients with shock states that were not related to sepsis and those requiring an extracorporeal membrane oxygenation device. For each patient, we considered only the first episode of septic shock.

Septic shock was defined according to international definition.<sup>[11]</sup> Norepinephrine infusion was targeted to achieve at least a mean arterial pressure of 65 mmHg and a urine output  $>0.5$  mL/kg/h. Heart rate, mean arterial pressure, oxygen saturation, and expired carbon dioxide (if required) were continuously measured (Monitor Intellivue MP 70; Philips, Andover MA). All patients were equipped with invasive blood pressure and central venous catheter.

### 2.1. Data collection

Demographic and clinical data were extracted from our electronic medical charts including clinical and biological assessment. To this purpose, the number of patients was determined by the availability of the electronic system of our institution. At the ICU admission, we collected age, sex, Simplified Acute Physiology Score (SAPS) 2, and medical history to calculate the Charlson score.<sup>[13]</sup> As the Charlson score includes age, we computed the “modified Charlson score” (= Charlson score - age) to focus on comorbidities. We also reported the use of selective digestive decontamination, which was included in our protocols for the trauma patients requiring invasive mechanical ventilation.

At the onset of septic shock, we collected: cause of shock, site of infection, Sequential Organ Failure Assessment (SOFA) score, plasma lactate level, and the pathogens responsible for the infectious episode. The multidrug resistant pathogens that were defined according to the international definition (nonsusceptibility to at least 1 agent in  $\geq 3$  antimicrobial categories) were also collected.<sup>[14]</sup> We also noted the duration of mechanical ventilation as appropriate. We investigated the death in hospital, ICU and we identified septic shock as a direct cause of ICU mortality (i.e., death during the septic shock episode). The causes of death were evaluated in all patients. We also investigated whether a collective decision of limitations of life-sustaining treatments had been taken.

### 2.2. Ethical statement

All patients or their relatives were informed that their data were used anonymously, except if they expressed a disagreement. Our study obtained the agreement from the “Comité d’Ethique pour le Recherche en Anesthésie-Réanimation” (IRB 00010254-2016-145). According to the French law, we exploited electronic data after agreement from the “Correspondant Informatique et Libertés” N°2017-07.

### 2.3. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 20 (IBM SPSS Inc., Chicago, IL). Continuous data were

expressed as mean and standard deviation (SD) or median with interquartile. Qualitative data were expressed as absolute numbers and percentages. The comparisons were performed using a Student *t* test or Mann–Withney test according to their distribution.

Multivariate analysis was performed using multiple logistic regression. Variables that were found to be associated with the septic shock associated-mortality, or that marginally significant ( $P < .20$ ) in the univariate analysis, or that had clinical relevance were included into the logistic models. Calibration of the logistic model was assessed using the Hosmer-Lemeshow goodness-of-fit test to evaluate the discrepancy between observed and expected values. Odds ratios (ORs) were expressed with 95% confidence intervals (CIs). The area under the receiver-operating characteristic (ROC) curve was used to define a cutoff value according to predictive value of a positive test of the septic shock associated-mortality. All the tests were 2-sided, the statistical significance was defined as  $P < .05$ . Analysis was conducted only in patients with complete data for the primary objective. All secondary objectives should not include  $>5\%$  of missing data.

## 3. Results

Among 385 patients with septic shock (Table 1), we compared 318 (83%) nontrauma patients and 67 (17%) trauma patients (Fig. 1). They were 62 (49–74) years of age, with a SAPS2 score of 45 (33–61). At the onset of septic shock, the SOFA score was 8 (7–10). The main causes of septic shock were pneumonia (43% [ $n=168$ ]) and intra-abdominal infections (27% [ $n=105$ ]). In 64% of patients, pathogens responsible for the septic shock episode were identified. *Escherichia coli* (13%,  $n=50$ ), *Pseudomonas aeruginosa* (6%,  $n=23$ ) and methicillin-susceptible *Staphylococcus aureus* (8%,  $n=31$ ) were the predominant pathogens (Table 2). The rate of appropriate empirical antimicrobial therapy was similar in the nontrauma and the trauma patients (Table 2). In contrast, the rate of hospital-acquired infection was higher in the trauma patients, as compared with the nontrauma patients ( $P < .00$ ) (Table 2). The ICU and hospital mortality rates were 43% and 46%, respectively. Septic shock was directly responsible for death in 133 (35%) patients.

The features of trauma patients according to their survival are reported in Table 3. As compared with the nontrauma patients, those with trauma were younger (46 [28–63] vs. 64 [54–76] years of age,  $P < .001$ ) and had a lower modified Charlson’s score (0 [0–1] vs. 2 [1–4],  $P < .001$ ). The SAPS2 at admission (45 [33–61] vs. 45 [33–55],  $P = .4$ ) and the SOFA score at inclusion (8 [6–10] vs. 8 [7–10],  $P = .6$ ) were similar in both groups. The septic shock associated-mortality rate was 39% ( $n=123$ ) for the non-trauma patients and 15% ( $n=10$ ) for the trauma patients ( $P = .001$ ) (Table 1). The other causes of death were related to a decision of limitations of life-sustaining treatments in 14 (3.6%) patients, cardiac arrest in 7 (2%) patients and a severe bleeding in 5 (1.2%) patients (Table 4).

All trauma patients developed septic shock during the ICU stay, whereas 229 (72%) nontrauma patients were admitted to ICU for septic shock. To assess a potential role of the delay of treatment, we compared the mortality between patients hospitalized in ICU during the episode of septic shock (no delay of treatment) and those admitted to ICU for septic shock (potential delayed treatment). The ICU death rates were 50% and 38% for the patients who developed septic shock during the ICU stay and those admitted to ICU for septic shock, respectively ( $P = .03$ ). The results of the univariate analysis are shown in Table 5.

Using a multivariate analysis, a SOFA score above 12 (OR: 6.8; 95% CI [1.2–37],  $P < .03$ ) was an independent risk factor of

**Table 1****Features of patients.**

| Variables (n=385)  | Missing data | Nontrauma patients (n=318) | Severe trauma patients (n=67) | P    |
|--|--------------|----------------------------|-------------------------------|------|
| <b>Demographics</b>  |              |                            |                               |      |
| Age, y, median (Q25–Q75)                                     | 0            | 64 (54–76)                 | 46 (28–63)                    | <.0  |
| Sex (male) (%)   | 0            | 219 (69)                   | 51 (76)                       | .3   |
| SOFA score, median (Q25–Q75)                                 | 1            | 8 (6–10)                   | 8 (7–10)                      | .6   |
| SAPS2 score, median (Q25–Q75)                                | 0            | 45 (33–61)                 | 45 (33–55)                    | .4   |
| Charlson score, median (Q25–Q75)                             | 3            | 5 (3–6)                    | 0 (0–3)                       | <.0  |
| Charlson score – age, median (Q25–Q75)                       | 3            | 2 (1–4)                    | 0 (0–1)                       | <.0  |
| ISS score, median (Q25–Q75)                                  | 0            |                            | 26 (21–40)                    |      |
| Days in ICU (mean ± SD)                                      | 0            | 15 (±22)                   | 28 (±37)                      | <.0  |
| Days in hospital (mean ± SD)                                 | 3            | 26 (±28)                   | 52 (±69)                      | <.0  |
| <b>Cause of septic shock (%)</b>                             |              |                            |                               |      |
| Community-acquired pneumonia                                 |              | 31                         | 0                             |      |
| Hospital-acquired pneumonia                                  |              | 93                         | 44                            |      |
| Abdominal  |              | 96                         | 9                             |      |
| Urinary tract  |              | 27                         | 8                             |      |
| Gynecological  |              | 2                          | 0                             |      |
| Central nervous system                                       |              | 4                          | 0                             | <.0  |
| Skin and soft tissue   |              | 9                          | 2                             |      |
| Surgical site infection                                      |              | 30                         | 0                             |      |
| Catheter-related infections                                  |              | 3                          | 2                             |      |
| Bones infections   |              | 1                          | 0                             |      |
| Unknown  |              | 22                         | 2                             |      |
| <b>Variables</b>   |              |                            |                               |      |
| Plasma lactate level at the onset of shock, median (Q25–Q75) | 1            | 2.9 (2–4.7)                | 1.9 (1.5–2.4)                 | <.0  |
| Duration of mechanical ventilation, days, median (Q25–Q75)   | 0            | 4 (1–10)                   | 13 (7–23)                     | <.0  |
| Limitation of life-sustaining treatments, n (%)              | 3            | 61 (19.4)                  | 15 (22.4)                     | .6   |
| Use of selective digestive decontamination, n (%)            | 0            |                            | 44 (65.6)                     |      |
| <b>Death</b>   |              |                            |                               |      |
| Hospital mortality, n (%)                                    | 0            | 156 (49)                   | 22 (33)                       | .02  |
| ICU mortality, n (%)   | 0            | 147 (46)                   | 20 (30)                       | .02  |
| Septic shock as the direct cause of ICU mortality, n (%)     | 8            | 123 (39)                   | 10 (15)                       | .001 |

ICU=intensive care unit, ISS=Injury severity score, SAPS2=Simplified acute physiology score, SD=Standard deviation, SOFA=Sequential organ failure assessment.

septic shock associated-mortality, while being a severe trauma patient (OR: 0.26; 95% CI [0.08–0.70],  $P=.017$ ) who was a protective factor. Based on these findings, we generated a score to determine the probability of septic shock associated-mortality ( $P$ ). We computed the following formula:  $P = \exp(z)/(1 + \exp[z])$  with  $z = 0.098 + 1.337 \times \text{trauma} + 0.02 \times \text{age} - 0.332 \times \text{SOFA (1)} + 0.035 \times \text{SOFA (2)} + 1.925 \times \text{SOFA (3)}$ .

trauma: 0 = nonsevere trauma patient, 1 = severe trauma patient

SOFA (1): SOFA score 7 to 9,

SOFA (2): SOFA score 10 to 11,

SOFA (3): SOFA score  $\geq 12$ .

This score has an area under the ROC curve at 0.76 (95% CI [0.68–0.82]), resulting in a sensitivity of 55% and a specificity of 86% (Fig. 2).

To reinforce our results, in a secondary analysis, we assessed the risk factors for septic shock survivors ( $n=252$ ) and septic shock nonsurvivors ( $n=133$ ) (Table 6). Being trauma (OR: 0.4; 95% CI [0.1–0.7],  $P=.01$ ), being older (OR: 1.02; 95% CI [1.01–1.04],  $P=.002$ ), and increased SOFA scores (OR: 1.5; 95% CI [1.3–1.7],  $P<.01$ ) were found independent risk factors of septic shock associated-death.

#### 4. Discussion

Here our results suggest that the rate of septic shock associated-mortality was lower in the trauma patients than in the nontrauma

patients. A high SOFA score is an independent risk factors of septic shock associated-mortality, while being a severe trauma patient was a protective factor. This last result should be carefully interpreted because of unmeasured confounding factors that should be taken into account in our findings.

Only few studies investigated whether the patient's features play a role in the septic shock directly associated-mortality.<sup>[5,15]</sup> In our cohort, the septic shock directly associated-mortality was 39% for nontrauma patients, which is in line with previous studies.<sup>[16,17]</sup> In the trauma patients, the septic shock directly associated-mortality was 15%. Nevertheless, the initial severity of patients, assessed by the SOFA score, was similar in both groups. This suggests that the intensity of shock did not explain the difference of mortality between the 2 groups. One may hypothesize that this difference could be associated with age or comorbidities.

We used the Charlson score to compare the comorbidities between the 2 groups. This is a comorbidity score including the patient's age. It provides a mortality risk determination based upon the patient comorbidity. This score has been validated in large patient populations.<sup>[18–21]</sup> In the surgical patients, it was used to determine the risk of developing a postoperative sepsis.<sup>[22]</sup> In agreement with our hypothesis, this score differed between the nontrauma patients and the trauma patients, but this finding was not confirmed in the multivariate analysis. Interestingly, the result was similar for global analysis including septic shock survivors and septic shock non-survivors. Thus, our

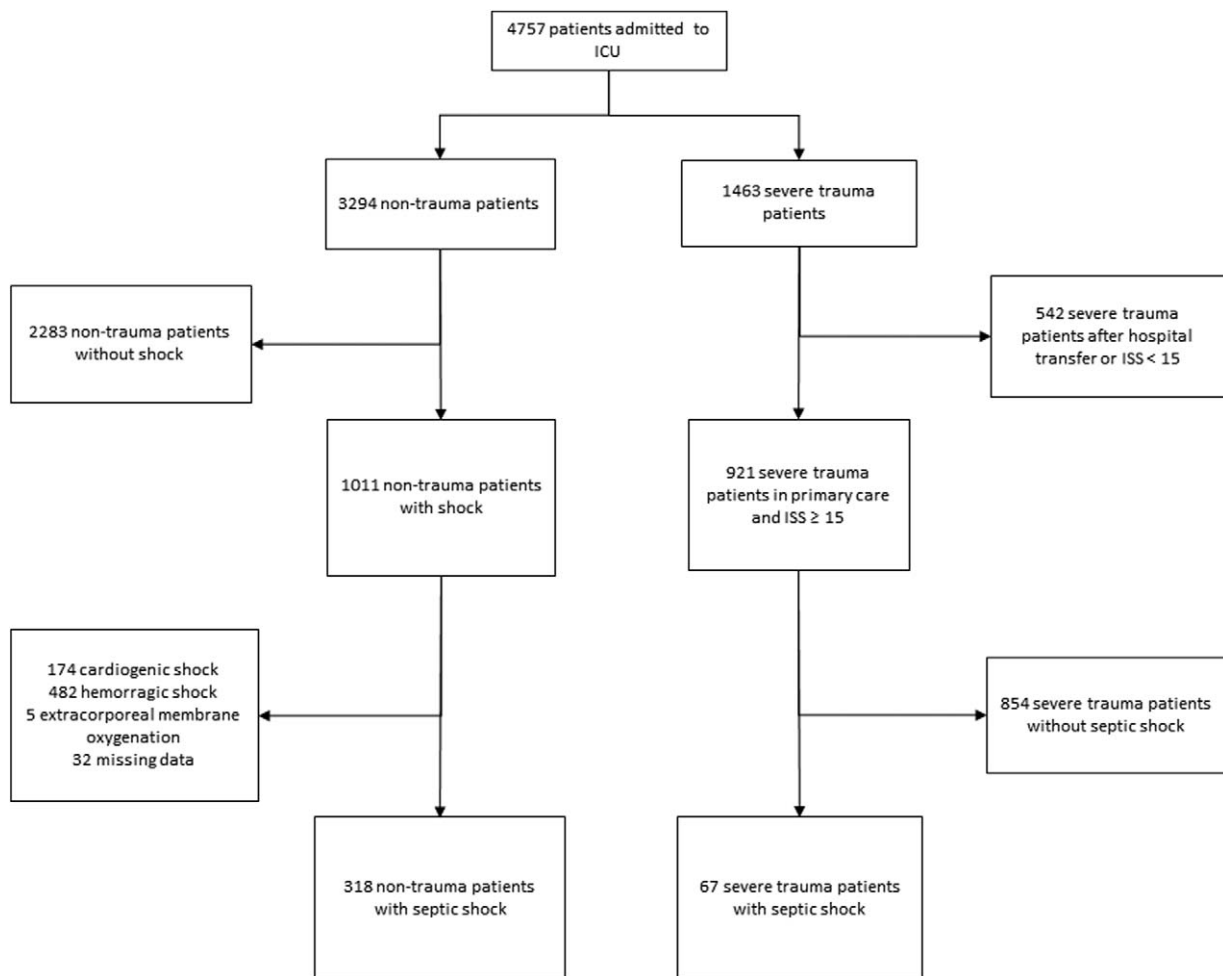


Figure 1. Flowchart.

results do not support a major role of comorbidities in the septic shock directly associated-mortality.

Age was not identified as an independent risk factor in the multivariate analysis. Our first aim was to compare septic shock

directly associated-mortality and nonseptic shock associated-mortality. We used this comparison to better define the independent risk factors directly associated with septic shock mortality. Our results, albeit provocative, are in line with those

Table 2

Pathogens et resistances.

| Variables                                   | All patients (n=385) | Nontrauma patients (n=318) | Severe trauma patients (n=67) | P    |
|---|----------------------|----------------------------|-------------------------------|------|
| Positive culture with identification, n (%) | 247 (64)             | 199 (62)                   | 48 (70)                       | .16  |
| Available antibiogram, n (%)                | 226 (58)             | 178 (56)                   | 48 (70)                       | .018 |
| Appropriate empirical antibiotics           | 197 (51)             | 152 (48)                   | 45 (67)                       | .15  |
| Multidrug resistant bacteria, n (%)         | 76 (30)              | 66 (21)                    | 10 (15)                       | .06  |
| Hospital-acquired infection                 | 275 (71)             | 214 (67)                   | 61 (91)                       | <.0  |
| Most frequently identified pathogens (n)    |                      |                            |                               |      |
| <i>Escherichia coli</i>                     | 50                   | 41                         | 9                             | .90  |
| <i>Pseudomonas aeruginosa</i>               | 23                   | 18                         | 5                             | .57  |
| <i>Klebsiella pneumoniae</i>                | 19                   | 17                         | 2                             | .54  |
| MSSA  | 31                   | 21                         | 10                            | .02  |
| MRSA  | 11                   | 8                          | 3                             | .31  |
| <i>Enterobacter aerogenes</i>               | 9                    | 7                          | 2                             | .66  |
| <i>Enterobacter cloacae</i>                 | 11                   | 7                          | 4                             | .10  |
| <i>Enterococcus faecalis</i>                | 13                   | 12                         | 1                             | .70  |
| <i>Enterococcus faecium</i>                 | 5                    | 5                          | 0                             | .59  |
| <i>Streptococcus pneumoniae</i>             | 11                   | 8                          | 3                             | .41  |

MRSA = methicillin-resistant *Staphylococcus aureus*, MSSA = methicillin-sensitive *Staphylococcus aureus*.

**Table 3**  
**Features of trauma patients.**

| Variables  | All trauma | Survivors (n=47) | Nonsurvivors (n=20) | P     |
|--|------------|------------------|---------------------|-------|
| Age, y (mean ± SD)   |            | 44 ± 20          | 50 ± 17             | .233  |
| Sex (male) (%)   | 51 (76)    | 36 (76)          | 15 (75)             | .889  |
| SAPS2 score, median (Q25–Q75)                              |            | 44 (33–55)       | 46 (33–60)          | .430  |
| SOFA score, median (Q25–Q75)                               |            | 7 (6–9)          | 10 (8–11)           | <.001 |
| ISS score, median (Q25–Q75)                                |            | 26 (22–39)       | 25 (17–41)          | .555  |
| Charlson's score (mean ± SD)                               |            | 1.6 ± 2.4        | 2.1 ± 2.7           | .458  |
| Charlson's score – age (mean ± SD)                         |            | 0.8 ± 1.6        | 1.2 ± 2.2           | .489  |
| Days in ICU, median (Q25–Q75)                              |            | 21 (14–40)       | 13 (8–23)           | .018  |
| Duration of mechanical ventilation, days, median (Q25–Q75) |            | 13 (7–24)        | 12 (7–23)           | .924  |
| Limitation of life-sustaining treatments, n (%)            | 15 (22)    | 2 (4.2)          | 13 (65)             | <.001 |
| Antimicrobial therapy and pathogens                        |            |                  |                     |       |
| Use of selective digestive decontamination, n (%)          | 44 (67)    | 33 (70)          | 11 (55)             | .268  |
| Appropriate empirical antimicrobial therapy, n (%)         | 45 (67)    | 30 (63)          | 15 (75)             | .99   |
| Multidrug resistant pathogens, n (%)                       | 10 (15)    | 5 (11)           | 5 (25)              | .218  |
| Site of injury   |            |                  |                     |       |
| Brain, n (%)   | 37 (55)    | 24 (51)          | 13 (65)             | .421  |
| Chest, n (%)   | 44 (66)    | 35 (74)          | 9 (45)              | .027  |
| Abdominal, n (%)   | 22 (33)    | 20 (43)          | 2 (10)              | .011  |
| Pelvis, n (%)  | 12 (18)    | 9 (19)           | 3 (15)              | .99   |
| Spine, n (%)   | 29 (43)    | 22 (47)          | 7 (35)              | .428  |
| Bones, n (%)   | 23 (34)    | 16 (34)          | 7 (35)              | .99   |
| Blood transfusions above 4, n (%)                          | 18 (26)    | 16 (34)          | 2 (10)              | .069  |
| Mechanism of injury  |            |                  |                     |       |
| Motor vehicle accidents, n (%)                             | 57 (85)    | 39 (83)          | 18 (90)             | .711  |
| Other etiologies, n (%)                                    | 10 (15)    | 8 (17)           | 2 (10)              |       |

ICU=intensive care unit, ISS=Injury severity score, SAPS2=Simplified acute physiology score, SD=Standard deviation, SOFA=Sequential organ failure assessment.

obtained in an experimental model of trauma followed by sepsis. This experimental model concluded that the role of age in post-traumatic sepsis was undefined.<sup>[2,3]</sup> However, in a secondary analysis comparing nonsurvivors and survivors, we found that age had a probable minor role in ICU associated-mortality. Elsewhere, advanced age was identified as a predictor of mortality.<sup>[24,25]</sup> In a systematic review, Mann et al<sup>[26]</sup> also found that elderly patients had higher mortality rate. Hence, age has probably an undeniable minor role in the mortality of patients with septic shock.

Our study highlights the importance of organ failure in the mortality of septic shock. Indeed, a SOFA score >12 increased the risk of death with an OR of 6.8. According to previous studies, several studies showed its relevance—with an excellent correlation to the ICU outcome.<sup>[27,28]</sup> Leone et al<sup>[29]</sup> found that age and SOFA score at diagnosis were risk factors for mortality in

acute mesenteric ischemia. In routine, one can suggest that the initial severity of patients is the major determinant of outcomes. Thus, the organ failures have a critical role in the patient's outcomes, other factors playing only a supplementary role.

One may expect that the rate of limitations of life-sustaining treatments differed between the 2 groups. Surprisingly, we did not confirm this expectation. Next, we determined whether the location of onset of septic shock affected the outcome of patients. We compared the mortality rate between patients for whom the onset of septic shock occurred during ICU stay and those admitted to ICU for septic shock. We observed an increased mortality in the patients developing septic shock during the ICU stay, that is, 100% of trauma patients and 28% of nontrauma patients. A possible explanation was that the ICU patients developed an immunoparalysis during their ICU stay.<sup>[30]</sup>

**Table 4**  
**Causes of death.**

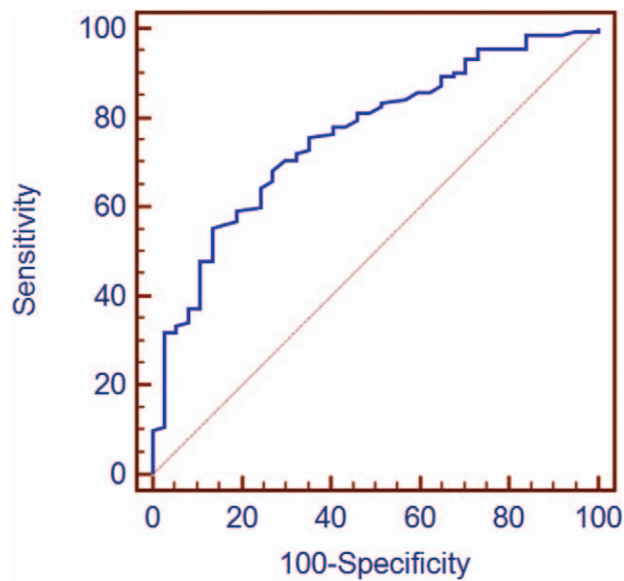
| Causes of death                                  | Nontrauma patients (n=156) | Severe trauma patients (n=22) | P    |
|--|----------------------------|-------------------------------|------|
| Septic shock with multiple organ failures, n (%) | 123 (78.8)                 | 10 (45.5)                     | <.0  |
| Limitations of life-sustaining treatment, n (%)  | 8 (5.1)                    | 6 (27.3)                      | .03  |
| Cardiac arrest, n (%)                            | 5 (3.2)                    | 2 (9.1)                       | .21  |
| Hemorrhagic shock, n (%)                         | 4 (2.6)                    | 1 (4.5)                       | .48  |
| ARDS, n (%)                                      | 2 (1.3)                    | 0 (0)                         | .99  |
| Brain death, n (%)                               | 0 (0)                      | 2 (9.1)                       | .015 |
| Missing data, n (%)                              | 14 (9)                     | 1 (4.5)                       | .69  |

ARDS=acute respiratory distress syndrome.

**Table 5**  
**Univariate analysis comparing septic shock associated-mortality and nonseptic shock-associated mortality.**

| Variables                          | Septic shock associated-mortality (n=133) | Non-septic shock associated-mortality (n=37) | P    |
|------------------------------------|---|--|------|
| Age mean ± SD                      | 64 ± 15                                   | 58 ± 15                                      | .024 |
| Sex, male, n (%)                   | 97 (73)                                   | 31 (84)                                      | .176 |
| Female, n (%)                      | 36 (27)                                   | 6 (16)                                       |      |
| Severe trauma, n (%)               | 10 (8)                                    | 11 (30)                                      | .001 |
| SOFA, mean ± SD                    | 10 ± 3                                    | 8 ± 2  | .007 |
| SAPS2 score, mean ± SD             | 54 ± 22                                   | 50 ± 21                                      | .286 |
| Modified Charlson score, mean ± SD | 2.8 ± 2                                   | 2 ± 2  | .049 |

SAPS2=Simplified acute physiology score, SD=Standard deviation, SOFA=sequential organ failure assessment.



**Figure 2.** ROC curve. ROC curve: AUC = 0.76 (95% CI: 0.68–0.82), Se 55%, Sp 86%, Youden index J = 0.41, associated criterion >0.801. AUC=area under the curve, CI=confidence interval, ROC=receiver-operating characteristics.

Our results suggest that being a trauma patient may be a protective factor of septic shock associated-mortality. We do not have clear explanation for this finding. Unmeasured variables may have affected our findings. In those patients, the effect of a

double hit injury, consisting on trauma followed by sepsis, remains uncertain.<sup>[23]</sup>

From the multivariate analysis, we generated a probability score of septic shock associated-mortality. Using age, SOFA score at the onset of septic shock and the presence or absence of trauma, we determined the probability of death. If the result of the calculation is above 0.80, a major risk of septic shock associated-mortality was identified.

Our study has several limitations. First, this is a retrospective study comparing 2 different phenotypes of patients. Hence, our choices for the statistical approach can be a matter of discussion. Second, the number of patients is relatively small, requiring to reproduce this study in a large database. Third, this is a single-center study, which may have affected the management of patients based on their age and comorbidities. However, the rate of limitation orders did not differ between the 2 populations. Fourth, we used selective digestive decontamination only in trauma patients. This procedure has been associated with improved survival in several studies.<sup>[31]</sup> Finally, as our study was performed in a single center, there is a need to replicate our study design in other ICUs to determine whether our results are generalizable.

**5. Conclusion**

The mortality of patients with septic shock patients remains high. Here we show that organ failures and being a trauma patient can be associated with septic shock directly associated-mortality. Conversely, comorbidities do not play a major role as a cause of mortality in septic shock. The use of our calculation to determine

**Table 6**

**Feature of septic shock survivors and nonsurvivors.**

| Variables  | Missing data (n=8) | Septic shock survivors (n=252) | Septic shock nonsurvivors (n=133) | P   |
|--|--------------------|--------------------------------|-----------------------------------|-----|
| Age, y, median (Q25–Q75)                                     |                    | 59 (46–71)                     | 65 (57–78)                        | .00 |
| Sex (male) (%)   |                    | 167 (66)                       | 97 (73)                           | .5  |
| SOFA score, median (Q25–Q75)                                 |                    | 7 (6–9)                        | 10 (8–12)                         | .00 |
| SAPS2 score, median (Q25–Q75)                                |                    | 42 (33–55)                     | 53 (36–68)                        | .00 |
| Charlson’s score, median (Q25–Q75)                           |                    | 3 [1–5]                        | 5 (4–6)                           | .00 |
| Charlson’s score – age, median (Q25–Q75)                     |                    | 2 (0–3)                        | 2 (1–4)                           | .00 |
| ISS score, median (Q25–Q75)                                  |                    | 27 (24–41)                     | 22 (16–28)                        | .03 |
| Severe trauma patients, n (%)                                |                    | 56 (22)                        | 10 (8)                            | .00 |
| Days in ICU, median Q25–Q75)                                 |                    | 10 (5–22)                      | 8 (2–16)                          | .00 |
| Days in hospital, median Q25–Q75)                            |                    | 28 (17–49)                     | 8 (2–20)                          | .00 |
| Cause of septic shock (%)                                    |                    |                                |                                   |     |
| Community-acquired pneumonia                                 |                    | 20 (8)                         | 9 (7)                             |     |
| Hospital-acquired pneumonia                                  |                    | 84 (33)                        | 51 (38)                           |     |
| Abdominal  |                    | 62 (25)                        | 40 (30)                           |     |
| Urinary tract  |                    | 29 (12)                        | 5 (3.7)                           |     |
| Gynecological  |                    | 2 (1)                          | 0 (0)                             | .02 |
| Central nervous system                                       |                    | 3 (1.2)                        | 1 (1)                             |     |
| Skin and soft tissue   |                    | 9 (3.5)                        | 2 (1.5)                           |     |
| Surgical site infection                                      |                    | 20 (8)                         | 10 (8)                            |     |
| Catheter-related infections                                  |                    | 5 (2)                          | 0 (0)                             |     |
| Bones infections   |                    | 0 (0)                          | 1 (1)                             |     |
| Unknown  |                    | 10 (4)                         | 14 (10.5)                         |     |
| Variables:   |                    |                                |                                   |     |
| Duration of mechanical ventilation, days, median (Q25–Q75)   |                    | 6 (1–15)                       | 5 (2–13)                          | .6  |
| Limitation of life-sustaining treatments, n (%)              |                    | 24 (9.5)                       | 51 (38)                           | .00 |
| Use of selective digestive decontamination, n (%)            |                    | 40 (16)                        | 4 (3)                             | .00 |
| Plasma lactate level at the onset of shock, median (Q25–Q75) |                    | 2.5 (1.7–3.7)                  | 3.1 (2–6.1)                       | .00 |

ICU= intensive care unit, ISS=injury severity score, SAPS2=simplified acute physiology score, SOFA=sequential organ failure assessment.

the risk of septic shock directly associated with mortality may help in clinical practice.

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