Original Article

Prognosis of patients with shock receiving vasopressors

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BACKGROUND: Consensus guidelines suggested that both dopamine and norepinephrine may be used, but specific doses are not recommended. The aim of this study is to determine the predictive role of vasopressors in patients with shock in intensive care unit.

METHODS: One hundred and twenty-two patients, who had received vasopressors for 1 hour or more in intensive care unit (ICU) between October 2008 and October 2011, were included.There were 85 men and 37 women, with a median age of 65 years (55–73 years). Their clinical data were retrospectively collected and analyzed.

RESULTS: The median simplified acute physiological score 3 (SAPS 3) was 50 (42–55). Multivariate analysis showed that septic shock (P=0.018, relative risk: 4.094; 95% confidential interval: 1.274–13.156), SAPS 3 score at ICU admission (P=0.028, relative risk: 1.079; 95% confidential interval: 1.008–1.155), and norepinephrine administration (P<0.001, relative risk: 9.353; 95% confidential interval: 2.667–32.807) were independent predictors of ICU death. Receiver operating characteristic curve analysis demonstrated that administration of norepinephrine ≥0.7 μg/kg per minute resulted in a sensitivity of 75.9% and a specificity of 90.3% for the likelihood of ICU death. In patients who received norepinephrine ≥0.7 μg/kg per minute there was more ICU death (71.4% vs. 44.8%) and in-hospital death (76.2% vs. 48.3%) than in those who received norepinephrine <0.7 μg/kg per minute. These patients had also a decreased 510-day survival rate compared with those who received norepinephrine <0.7 μg/kg per minute (19.2% vs. 64.2%).

CONCLUSION: Septic shock, SAPS 3 score at ICU admission, and norepinephrine administration were independent predictors of ICU death for patients with shock. Patients who received norepinephrine ≥0.7 μg/kg per minute had an increased ICU mortality, an increased in-hospital mortality, and a decreased 510-day survival rate.

KEY WORDS: Vasopressors; Intensive care; Shock

World J Emerg Med 2013;4(1):59–62
DOI: 10.5847/ wjem.j.issn.1920–8642.2013.01.011

INTRODUCTION

Critically ill patients with shock had a mortality of 27.5% to 50.2%.[1–3] In addition to sufficient volume resustitation, vasopressors are frequently used to restore tissue perfusion. A multicenter randomized study[3] revealed that there is no significant difference in patients with shock who are treated with dopamine or norepinephrine. Dopamine administration is associated with greater arrhythmic events. Hence, norepinephrine administration is preferred to dopamine administration. Povoa et al[4] found that norepinephrine administration could be associated with worse outcomes in patients with septic shock. On the other hand, there is no consensus on the maximal dose of vasopressors. Consensus guidelines suggested that both dopamine and norepinephrine may be used, but not recommended on specific doses.[5] Recently, Benbenishty et al[2] found that patients with shock who received norepinephrine or epinephrine more than 0.5 μg/kg per minute showed 96% likelihood of intensive care unit (ICU) death. The purpose of this study was to determine

the predictive role of vasopressors and maximal dosage of vasopressors in patients with shock in ICU.

METHODS

This retrospective study was conducted at the department of ICU of Cancer Hospital (Institute), the Chinese Academy of Medical Sciences and Peking Union Medical College in Beijing, China. The ICU is a 10-bed medical-surgical unit. Informed consent was obtained because of the observational nature of the study. One hundred and twenty-two patients who had received vasopressors between October 2008 and October 2011 were included in this study. There were 85 men and 37 women, with a median age of 65 years (55–73 years). The median SAPS 3 score of the patients was 50 (42–55).

The following clinical data were retrospectively analyzed: age, gender, simplified acute physiological score 3 (SAPS) on day of ICU admission,[6] type of vasopressors (dopamine or norepinephrine), maximal dosage of vasopressors, duration of infusion, laboratory values (white blood cell count, ratio of PaO_2 to FiO_2, serum total bilirubin, serum creatinine level, platelet count) on the day of admission, cause of shock, mechanical ventilation treatment, duration of mechanical ventilation, length of ICU stay, ICU mortality, length of hospitalization, and in-hospital mortality. Shock was defined as mean blood pressure being less than 65 mmHg despite an adequate amount of fluids (at least 1000 mL of crystalloids or 500 mL of colloids) had been administered.

Patients who were younger than 18 years of age were excluded.

Statistical analysis

The SPSS software package 16.0 for Windows was used for statistical analysis. Data were presented as median (interquartile range) for continuous variables, and percentages for dichotomous variables. Continuous variables were analyzed using Student's *t* test, and categorical variables were analyzed using the Chi-square test. Univariate or multivariate Cox regression was used to define the predictors of ICU mortality. The area under the receiver operating characteristic curve (AUROC) was used to ascertain the dosage of vasopressors that determine patients who died in ICU or not. Survivals were estimated using the Kaplan-Meier method, and the log-rank test was used to analyze differences between curves. A *P* value less than 0.05 was considered statistically significant.

RESULTS

In the 122 patients with shock, dopamine was the most commonly used vasopressor (94.3%). It was used as a single agent in 73 patients. Norepinephrine was used in 49 patients, and it was used as a single agent in 7 patients. Forty-two patients received both dopamine and nonepinephrine. The median concentration of dopamine was 10 (6–16) μg/kg per minute and the median concentration of nonepinephrine was 1.3 (0.5–2.1) μg/kg per minute.

Twenty-nine patients died in ICU. Sixteen patients died from septic shock, 11 patients died from gastrointestinal bleeding, and 2 patients died from myocardial infarction. Other characteristics of the patients are shown in Table 1.

Univariate analysis showed that cause of shock, SAPS 3 score at ICU admission, mechanical ventilation treatment, and norepinephrine administration were

Table 1. Baseline characteristics of shock patients receiving vasopressors in intensive care unit

Variables	Survivors (*n*=93)	Non-survivors (*n*=29)	*P* value
Age (yr)	66 (53–72)	63 (57–76)	0.555
Male sex (%)	67 (72.0)	18 (62.1)	0.357
Cause of shock			<0.001
Hypovolemic (%)	81 (87.1)	11 (37.9)	
Septic (%)	11 (11.8)	16 (55.2)	
Cardiogenic (%)	1 (1.1)	2 (6.9)	
SAPS 3 score at admission	46 (40–53)	55 (51–64)	<0.001
White blood cell count (G/L)	11.5 (8.2–15.6)	12.3 (8.8–22.0)	0.061
Serum total bilirubin (μmol/L)	11.6 (6.7–21.5)	13.7 (9.7–24.5)	0.697
Ratio of PaO_2 to FiO_2 (mmHg)	254 (147–376)	185 (146–377)	0.552
Serum creatinine (μmol/L)	61 (51–94)	68 (42–100)	0.969
Platelet count (G/L)	166 (124–245)	263 (186–542)	0.419
Mechanical ventilation treatment (%)	65 (69.9)	27 (93.7)	0.012
Duration of mechanical ventilation (d)	2 (0–6)	4 (2–12)	0.109
Dopamine administration (%)	88 (94.6)	27 (93.1)	0.670
Norepinephrine administration (%)	25 (26.9)	24 (82.8)	<0.001

SAPS: simplified acute physiology score.

predictive factors of ICU death (Table 1). Multivariate analysis showed that septic shock, SAPS 3 score at ICU admission, and norepinephrine administration were independent predictors of ICU death (Table 2).

The results of receiver operating characteristic curve analysis are shown in Figure 1. Administration of norepinephrine ≥0.7 μg/kg per minute resulted in a sensitivity of 75.9% and a specificity of 90.3% for the likelihood of ICU death, with area under the curve of 0.844±0.048 (P<0.001, 95% confidential interval: 0.750–0.938).

Compared with patients receiving norepinephrine <0.7 μg/kg per minute, those receiving norepinephrine ≥0.7 μg/kg per minute demonstrated more severe diseases as reflected by SAPS 3, more ICU deaths and more in-hospital deaths (Table 3). The Kaplan-Meier survival curves of patients with shock are shown in Figure 2. We found that patients receiving norepinephrine <0.7 μg/kg per minute exhibited a 510-day survival rate of 64.2%, while those receiving norepinephrine ≥0.7 μg/kg per minute showed a 510-day survival rate of 19.2% (log rank =9.348; P=0.002).

DISCUSSION

Our data suggested that septic shock, SAPS 3 score at ICU admission, and norepinephrine administration were independent predictors of ICU death for patients with shock. Patients who received norepinephrine ≥0.7 μg/kg per minute were more likely to have ICU

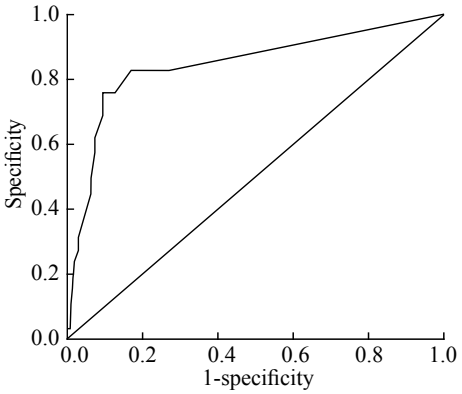

Figure 1. Receiver operating characteristic curve of patients receiving norepinephrine.

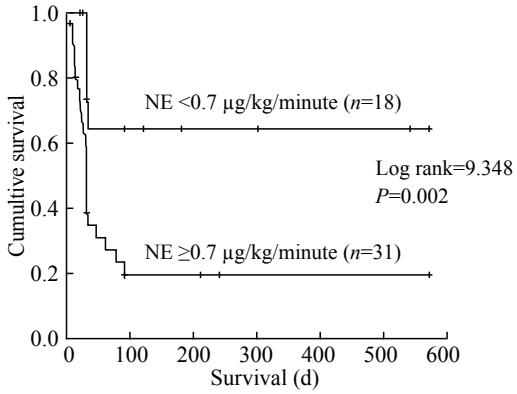

Figure 2. Long-term survival of patients receiving norepinephrine greater or less than 0.7 μg/kg per minute.

Table 2. Multivariate analysis of predictors of intensive care unit death

Variables	*B*	*S.E.*	*Wald*	*P* value	Relative risk (95%CI)
Hypovolemic shock (reference)					1.000
Septic shock	1.410	0.596	5.602	0.018	4.094 (1.274–13.156)
Cardiogenic shock	2.461	1.430	2.964	0.085	11.722 (0.711–193.167)
SAPS 3 (per point)	0.076	0.035	4.815	0.028	1.079 (1.008–1.155)
Mechanical ventilation treatment	1.194	0.889	1.805	0.179	3.300 (0.578–18.839)
Norepinephrine administration	2.236	0.640	12.193	<0.001	9.353 (2.667–32.807)

SAPS:simplified acute physiology score; CI: confidential interval.

Table 3. Comparison of short-term outcomes of patients receiving norepinephrine greater or less than 0.7 μg/kg per minute

Variables	Norepinephrine <0.7 μg/kg per minute (*n*=18)	Norepinephrine ≥0.7 μg/kg per minute (*n*=31)	*P* value
Age (yr)	63 (51–65)	63 (55–73)	0.232
Male sex (%)	14 (77.8)	19 (61.3)	0.346
SAPS 3 score at admission	48 (38–52)	54 (50–64)	0.001
Mechanical ventilation treatment (%)	12 (66.7)	28 (90.3)	0.058
Duration of mechanical ventilation (d)	2 (0–4)	2 (2–9)	0.795
ICU death (%)	2 (11.1)	22 (71.0)	<0.001
ICU length of stay (d)	4 (3–7)	5 (3–11)	0.328
In-hospital death (%)	3 (16.7)	23 (74.2)	<0.001
Length of hospitalization (d)	21 (16–47)	21 (11–32)	0.778

SAPS: simplified acute physiology score; ICU: intensive care unit.

death and in-hospital death than those who received norepinephrine <0.7 μg/kg per minute. These patients also had a decreased 510-day survival rate compared with those who received norepinephrine <0.7 μg/kg per minute. SAPS 3 score as the fourth-generation adult ICU prognostic model has good discrimination and calibration for critical ill patients.[6] The role of SAPS 3 prognostic model in predicting ICU mortality has validated.[7] Póvoa et al[4] and Patel et al[8] reported that SAPS II and Acute Physiology and Chronic Health Evaluation II prognostic model were both predictive of ICU death in patients with shock. In our study, we found that the new generation prognostic model for critical ill patients suits well for patients with shock.

Norepinephrine administration was predictive of ICU death in patients with shock. Póvoa et al[4] reported that norepinephrine administration was associated with worst outcomes in patients with septic shock, with a 3.5 increase of the 28-day mortality risk. After adjusting for SAPS II, norepinephrine administration was still significantly associated with an increased death rate. In this study, after adjusting for SAPS 3, norepinephrine administration was associated with a 9.353 increase of ICU mortality risk in patients with shock. However, controversy exists regarding the maximal dosage of norepinephrine predictive of death. Benbenishty et al[2] reported that patients receiving norepinephrine or epinephrine ≥0.5 μg/kg per minute had a 96% possibility of death in a cohort with shock receiving vasopressors. Sakr et al[1] found that in 1058 patients with shock due to any cause, the median dosage of norepinephrine in non-survivors (n= 405) was 0.7 μg/kg per minute, which was significantly higher than 0.5 μg/kg per minute in survivors (n=653). Póvoa et al[4] reported that norepinephrine administration was associated with worst outcome in patients with septic shock; however, the maximal dosage of norepinephrine was not mentioned in their study. In our study, the patients who received norepinephrine ≥0.7 μg/kg per minute showed a sensitivity of 75.9% and a specificity of 90.3% for the likelihood of ICU death, and these patients had a poor 510-day survival rate compared with those receiving norepinephrine <0.7 μg/kg per minute. Benbenishty et al[2] also found that patients who received norepinephrine ≥0.5 μg/kg per minute had a 6-year survival rate of 20%, which is close to the result of this study.

Our study has several limitations. First, this study is retrospective. Second, the sample of this study is relatively small. Third, our results were obtained from a single medical center and may not be generalized to other medical centers.

In conclusion, in this study, septic shock, SAPS 3 score at admission and norepinephrine administration were independent predictors of ICU death for patients with shock. Patients who received norepinephrine ≥0.7 μg/kg per minute had an increased ICU mortality, an increased in-hospital mortality, and a decreased 510-day survival rate compared with patients who received norepinephrine <0.7 μg/kg per minute. As Benbenishty et al[2] pointed out, that knowing the maximum effective dose of drugs such as norepinephrine that can be administered while patients have a chance for survival is crucial, which could aid physicians in treatment decision-making.

Funding: None.

Ethical approval: Not needed.

Conflicts of interest: No competing interests.

Contributors: Xing XZ and Sun KL designed the research. Xing XZ analyzed the data, and wrote the paper. All authors read and approved the final version.

REFERENCES

1 Sakr Y, Reinhart K, Vincent JL, Sprung CL, Moreno R, Ranieri VM, et al. Does dopamine administration in shock influence outcome? results of the sepsis occurrence in acutely ill patients (SOAP) Study. Crit Care Med 2006; 34: 589–597.

2 Benbenishty J, Weissman C, Sprung CL, Brodsky-Israeli M, Weiss Y. Characteristics of patients receiving vasopressors. Heart Lung 2011; 40: 247–252.

3 De Backer D, Biston P, Devriendt J, Madl C, Chochrad D, Aldecoa C, et al. Comparison of dopamine and norepinephrine in the treatment of shock. New Engl J Med 2010; 362: 779–789.

4 Póvoa PR, Carneiro AH, Ribeiro OS, Pereira AC. Influence of vasopressor agent in septic shock mortality. Results from the Portuguese Community-Acquired Sepsis Study (SACiUCI study). Crit Care Med 2009; 37: 410–416.

5 Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med 2008; 36: 296–327.

6 Moreno RP, Metnitz PG, Almeida E, Jordan B, Bauer P, Campos RA, et al. SAPS 3-From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. Intensive Care Med 2005; 31: 1345–1355.

7 Keegan MT, Gajic O, Afessa B. Severity of illness scoring systems in the intensive care unit. Crit Care Med 2011; 39: 163–169.

8 Patel GP, Grahe JS, Sperry M, Singla S, Elpern E, Lateef O, et al. Efficacy and safety of dopamine versus norepinephrine in the management of shock. Shock 2010; 33: 375–380.

Received August 25, 2012
Accepted after revision December 21, 2012