Vasopressor dependency index- A quick prognostic parameter of septic shock patient in emergency and intensive care unit in remote area

by Imamuddin Arif Wicaksono

Submission date: 15-Sep-2020 01:32PM (UTC+0800)
Submission ID: 1387484843
File name: patient_in_emergency_and_intensive_care_unit_in_remote_area.pdf (628.07K)
Word count: 4574
Character count: 21798

Crit Care Shock (2020) 23:85-94

Vasopressor dependency index: a quick prognostic parameter of septic shock patient in emergency and intensive care unit in remote area

Imamuddin Arif Wicaksono, Arie Utariani, Kuntaman

Abstract

***Objective*: The aim of the this study was to find out the outcome differences in septic shock patients based on the vasopressor dependency index (VDI) value at Dr. Soetomo General Hospital Surabaya.**

***Design*: This was an analytical observational research.**

***Setting*: Resuscitation Room of Dr. Soetomo General Hospital Surabaya from March to May 2019. This study was approved by the Research Ethics Committee of Dr. Soetomo General Hospital Surabaya.**

***Patients and participants*: The inclusion criteria was septic shock patient who met sepsis-3 criteria. There were 44 samples in the inclusion criteria.**

***Interventions*: Samples were taken by consecutive sampling. VDI was measured starting from 10 minutes, 1 hour, 6 hours, 12 hours, 24 hours, and 48 hours after the treatment of vasopressor drug.**

***Measurements and results*: The most common causes of sepsis was pneumonia (47.7%). Septic shock patients were given norepinephrine (80.0%) as the first line vasopressor drug. There were patient outcome differences within 7 days of treatment based on the VDI value. The VDI value at the 24th hour and the 48th hour were the most influential variable to the patient outcome (p=0.034). The VDI value threshold of the 24th hour was 0.176/mmHg (81.8% sensitivity; 85.2% specificity; 95% CI 0.818-1.000; p=0.000) and of the 48th hour was 0.150/mmHg (88.9% sensitivity; 92.6% specificity; 95% CI 0.859-1.000; p=0.000).**

***Conclusion*: There were significant differences in septic shock patient's outcome in the first 7 days of treatment based on VDI value. The VDI value at the 24th hour and the 48th hour were the most influential variables to the patient outcome (p=0.034). The threshold of VDI at the 24th hour was 0.176/mmHg. The threshold value of VDI at 48th hour was 0.150/mmHg.**

Key words: Sepsis, septic shock, vasopressor dependency index, outcome.

Introduction

Shock is an acute life-threatening circulation failure related to inadequate use of oxygen by cells as a result of a circulatory disorder in delivering sufficient oxygen quantity in order to meet tissue oxygen demand, leading to cellular dysfunction. Shock can cause an increase in lactate level, disruption of the microcirculation, and cellular death. (1) Shock can occur due to decreased venous return as a result of hypovolemia, cardiac pump failure due to ischemia, infarction and conduction disorder, obstruction due to pulmonary embolism, tension pneumothorax, and cardiac tamponade, loss of blood vessel tone due to sepsis, and anaphylaxis or spinal cord injury. (2) Shock can be identified based on clinical symptoms, hemodynamics, and biochemical changes. Shock identification is not only based on blood pressure changes. Blood pressure changes may come late due to the compensatory mechanism of baroreflex, which activates the sympathetic nervous system. (3)

Based on the etiology, the most common cause of shock is septic shock (62.2%), cardiogenic shock (16.7%), and hypovolemic shock (15.7%). (4) The occurrence of shock has increased yearly; the in-

From Department of Anesthesiology and Reanimation, Faculty of Medicine Universitas Airlangga - Dr. Soetomo General Hospital, Surabaya, Indonesia (Imamuddin Arif Wicaksono, Arie Utariani) and Department of Microbiology, Faculty of Medicine Universitas Airlangga - Dr. Soetomo General Hospital, Surabaya, Indonesia (Kuntaman).

Address for correspondence:
Arie Utariani
Department of Anesthesiology and Reanimation, Faculty of Medicine Universitas Airlangga - Dr. Soetomo General Hospital, Surabaya
Jl. Mayjend Prof. Dr. Moestopo No. 6-8, Airlangga, Gubeng, Surabaya, East Java, Indonesia 60285
Tel: (+6231) 5501503; 5501504
Email: arie.utariani@fk.unair.ac.id

crease rate has reached 2.7% per year. The average death rate due to shock in 7 days and 90 days were 23.1% and 40.7%. (5)

Sepsis is a clinical syndrome characterized by life-threatening organ dysfunction caused by dysregulated body responses towards infection. (6) Septic shock is a result of the poor progression of sepsis condition with the death rate reaching 60.4% within 28 days and 65.1% within 90 days. (7) Mortality in septic shock patients is related to compliance in implementing the sepsis bundle. The implementation of the 3-hour sepsis bundles significantly reduces mortality compared to those who do not. (8) In the Resuscitation Room Dr. Soetomo Hospital, the implementation of sepsis bundle in the first three and six hours reached 46.88% with mortality rate <48 hours reached 31.25%. (9)

Shock, endothelial injury, and inflammatory mediators in sepsis have an impact on increasing the production of nitric oxide (NO) as well as decreasing the vascular response to catecholamines. Such conditions can cause vasoplegia and refractory shock. (10,11) Until recently, there is no any consensus regarding the definition of refractory shock. The proposed refractory shock definition includes failure to reach the mean arterial pressure (MAP) even though vasopressor therapy has been given, the need for vasopressor treatment or a condition requiring high-dose vasopressor. (12) Vasopressor can be measured using the vasopressor dependency index (VDI), an assessment of hemodynamic response disorder based on the relationship between the vasopressor doses and mean arterial pressure (MAP). The higher the VDI, the higher of the vasopressor doses. (13) In abdominal septic patients, the vasopressor dependency index is higher in the non-survivor group compared to the survivor group (p=0.046). The optimal threshold for VDI to predict the prognosis of 28-day survival is 0.499/mmHg (sensitivity 78.3%, specificity 83.3%). This result supports VDI as a prognostic factor in septic patients. (14) Low-dose corticosteroids are recommended in septic shock patients who depend on vasopressor, but this fact remains controversial. (15)

Materials and methods

This study was an observational analysis research using a prospective cohort design, which was conducted in the Resuscitation Room of Dr. Soetomo General Hospital from March to May 2019. This study has been approved by the Ethics Committee of Dr. Soetomo General Hospital. The sample was septic shock patients who met the criteria of sepsis-3 in the Resuscitation Room of Dr. Soetomo General Hospital. The sample size was calculated using consecutive sampling method. The exclusion criteria were patients aged <17 years, pregnant women, patients with malignancies, immunocompromised or HIV patients, hypothalamus pituitary and adrenal (HPA) insufficiency, long-term corticosteroid drug user, and who refused to be included.

The sepsis diagnosis was made by a doctor in charge of the Resuscitation Room in Dr. Soetomo General Hospital Surabaya. Patients who were diagnosed with sepsis were measured in terms of their MAP prior to receiving vasopressor treatment. MAP measurement used non invasive blood pressure (NIBP) on the left arm. The dosage of vasopressor and MAP were recorded at 10 minutes, 1 hour, 6 hours, 12 hours, 24 hours, and 48 hours after vasopressor administration. Vasopressor inotropic score (VIS) was calculated using the formula: (dose of dopamine x 1) + (dose of dobutamine x 1) + (dose of epinephrine x 100) + (dose of norepinephrine x 100) + (dose of phenylephrine x 100). The dosage was in µg/kgBW/min.

For patients who died before 48 hours, their last vasopressor dosage and MAP were recorded. The vasopressor dependency index was measured at 10 minutes, 1 hour, 6 hours, 12 hours, 24 hours, and 48 hours using the formula:

VDI=Vasopressor score/MAP

The 7 days outcome of all patients were recorded in data collection and research observation sheet. The data were analyzed using the logistic regression method with IBM SPSS version 20.0.

Results

There were 44 septic shock patients in the Resuscitation Room of Dr. Soetomo General Hospital Surabaya from March 2019 to May 2019 who met the inclusion criteria. The characteristics of the study subjects are presented in **Table 1**. The most common cause of sepsis condition was pneumonia, followed by intra-abdominal infection, and skin-tissue infection (**Table 2**).

The majority of septic shock patients received norepinephrine treatment (80.0%) as the initial vasopressor, which was used to achieve and maintain the MAP target of >65 mmHg. No patient received a single administration of dopamine or dobutamine as the initial vasopressor medicine to achieve and maintain the MAP target of >65 mmHg.

The percentage of septic shock patient, which survived were 61.4% whereas the percentage of septic

shock patient who died within 7 days was 38.6%. There was a different outcome of septic patients based on the VIS with the mean value of the alive patients were 7.28 (95% CI, 3.77-10.78, p=0.002), whereas the mean value of the dead patients was 18.11 (95% CI, 13.45-22.78, p=0.002). The outcome differences of septic patients based on the VDI were 0.106 (95% CI, 0.039-0.174, p=0.000) for alive patients, whereas 0.255 (95% CI, 0.199-0.310, p=0.000) for dead patients.

Based on log regression bivariate analysis (**Table 3**), the 10th minute and 1st hour of VIS, the 10th minute VDI, the 1st hour VDI, and the average VDI did not have significant effect on patient outcomes within 7 days of treatment, while the other values of VIS and VDI had significant effect on patient outcomes. Based on backward stepwise log regression analysis (**Table 4**), the 24th hour and 48th hour VIS had the most significant effect on patient outcomes within 7 days of treatment. In the VDI, the result of backward stepwise log regression analysis (**Table 4**) showed that the 24th hour and 48th hour VDI had the most significant effect on patient outcomes within 7 days of treatment.

Figure 1 shows the threshold value of VIS at 24 hour was 12.5 with a sensitivity of 81.8% and specificity of 81.5% (AUC 0.901, 95% CI 0.803-0.998, p=0.000), while the threshold value of VIS at 48 hour was 8.75 with a sensitivity of 88.9% and a specificity of 88.9% (AUC 0.934, 95% CI 0.853-1.000, p=0.000) (**Figure 2**).

Figure 3 shows the threshold value of VDI at 24 hour was 0.176/mmHg with a sensitivity of 81.8% and specificity of 81.5% (AUC 0.909, 95% CI 0.818-1.000, p=0.000), while the threshold value of VDI at 48 hour was 0.150/mmHg with a sensitivity of 88.9% and a specificity of 92.6% (AUC 0.938, 95% CI 0.859-1.000, p=0.000) (**Figure 4**).

Discussion

VIS is an alternative calculation method to measure the cumulative doses of vasopressor. This is considered to be necessary because the medicines are given continuously with titration dosages. VIS is obtained from the calculation using the formula: (dose of dopamine x 1) + (dose of dobutamine x 1) + (dose of epinephrine x 100) + (dose of norepinephrine x 100) + (dose of phenylephrine x 100). The dosage is in µg/kg BW/min.

Based on the VIS, there were different outcomes in septic shock patients. The mean vasopressor inotropic score in the alive patients was lower than in the dead patients at the 10th minute, 1st hour, 6th hour, 12th hour, 24th hour, and 48th hour VIS. It was indicated that in non-survivor septic shock patient needed a higher cumulative dose of vasopressor than the survivor septic shock patient. Other studies stated that VIS could be used as 28 day mortality discrimination method in septic shock patients. (16)

The VDI can be used as an alternative to calculating the vasopressor medicine effect towards mean arterial pressure increase. VDI is calculated from the ratio of inotropic/vasopressor score to MAP. In this study, there were outcome differences in septic shock patients based on their VDI. The mean VDI in the survivor septic shock patients was lower than in the non-survivor septic shock patient. Statistically, the VIS and VDI significantly influence the outcome of septic shock patients within 7 days of treatment.

This study was in line with the Early Use of Polymyxin B Hemoperfusion in Abdominal Sepsis (EUPHAS) Trial, which stated that in patients with abdominal sepsis the vasopressor dependency index value is higher in the non-survivor group compared to the survivor group (p=0.046). Based on the receiver operating characteristic (ROC) curve and the determination of the area under the curve (AUC), the VDI optimal threshold to predict 28 day survival prognostic was 0.499/mmHg (sensitivity 78.3%, specificity 83.3%). (14)

In septic condition, endothelial dysfunction occurs as a result of nitric oxide excessive production by inducible nitric oxide synthase (INOS), which results in the shifting of intravascular fluid to the extravascular compartment.

Excessive increment of NO can cause hypotension, cardiac depression, and vascular hyporeactivity (vasoplegia) in septic shock, which leads to catecholamine refractory shock and a need of high dose catecholamine. (17)

Resuscitation in shock conditions can be done by administering fluids. In septic patients, the fluid administration protocol for patients with hypotension (MAP<65 mmHg) or hypoperfusion (lactate>4 mmol) is 30 ml/kgBW of crystalloid fluid.

Early fluid administration of <45 ml/kgBW can reduce the lactate level and may potentially reduce mortality. (18) It indicates that the early administration of fluid in sepsis management may not be significant on patient outcomes if it is not followed by a decrease in lactate level or improvement in microcirculation and tissue perfusion.

The 2018 Surviving Sepsis Campaign guideline mentioned that the MAP target for sepsis resuscitation is >65 mmHg, but it can vary according to the conditions of each patient. (19) In this study, the mean MAP in survivor septic patients was higher than in non-survivor septic patients. The result of

the Sepsis and Mean Arterial Pressure Study suggested that the MAP target of <65-75 mmHg was sufficient for septic shock patients, but a higher MAP target of 75-85 mmHg may be needed in septic patients with chronic hypertension. The study also mentioned that the MAP of <60-65 mmHg could adversely affect the outcomes of septic shock patients. (20)

Based on backward stepwise log regression analysis of VIS variables, it is obtained that the VIS at the 24th hour and at the 48th hour had the most influences to the outcome of septic shock patients in the 7 day treatment period. From the ROC curve, the VIS threshold at the 24th hour was 12.5, which equivalent to the use of norepinephrine at a dose of 0.125 µg/kgBW/min, while the VIS threshold at the 48th hour was 8.75, which equivalent to the use of norepinephrine at a dose of 0.0875 µg/kgBW/min. Other studies found that administration of norepinephrine or epinephrine at a dose of 0.5 µg/kgBW/min can be used as sepsis mortality predictor with sensitivity of 96% and specificity of 76%. Patients with norepinephrine or epinephrine at a dose of <0.5 µg/kgBW/min had 6 years life expectancy of 60%. All patients who received norepinephrine at a dose of >3.8 µg/kgBW/min or epinephrine at a dose of >9.6 µg/kgBW/min died, while the duration of vasopressor did not affect the survival rate (p=0.4). (21)

Another study found that vasopressor at a dose of 0.75 µg/kgBW/min can be used as a predictor of mortality with a sensitivity of 73% and a specificity of 74%. The mortality would increase to 86.4% if the dose of vasopressor was >0.75 µg/kgBW/min. (7)

Based on backward stepwise log regression analysis of the VDI variables, it was obtained that the VDI value at the 24th hour and at the 48th hour had the most influence affect to the outcome of septic shock patients in the 7 day treatment period. From the ROC curve, the VDI threshold value at the 24th hour was 0.176/mmHg with sensitivity of 81.8% and specificity of 85.2% (AUC 0.909, 95% CI 0.818-1000, p=0.000), while the VDI threshold value at the 48th hour was 0.150/mmHg with a sensitivity of 88.9% and specificity of 92.6% (AUC 0.938, 95% CI 0.859-1000, p=0.000). Matsukuma, et al (2015) found that the VDI threshold value to predict 28 days mortality rate in septic shock patients was 0.499/mmHg (sensitivity 78.3%, specificity 83.3%). (14)

Multivariate analysis to compare variables that affect septic patient outcomes between VIS at the 24th hour and 48th hour, VDI at the 24th hour and 48th hour, and Sequential Organ Failure Assessment (SOFA) scores showed that SOFA scores were the most influential variables on septic patient outcomes. A number of studies mentioned that SOFA score were the best prognostic predictor of septic patients. In this study, the threshold value for SOFA score was 11. Gunes Ozaydin, et al (2017) found the value of the SOFA score as a prediction of mortality of septic patients was >4.5 with sensitivity of 44% and specificity of 95% (AUC 0.80, 95% CI 0.65-0.94). Their study also found that all patients with SOFA scores of >10 died. (22)

Conclusion

There were outcome differences in the septic shock patients within the 7 days of treatment based on the vasopressor dependency index value. The VDI that mostly affected the patient outcome within 7 days of treatment were at the 24th and 48th hour with the VDI threshold at the 24th hour was 0.176/mmHg (sensitivity 81.8%, specificity 85.2%, AUC 0.909, 95% CI 0.818-1000, p=0.000) and the VDI threshold at the 48th hour was 0.150/mmHg (88.9% sensitivity, 92.6% specificity, AUC 0.938, 95% CI 0.859-1000, p=0.000). The VDI value can predict the outcome of septic shock patients in 7 days of treatment in addition to the SOFA score.

Table 1. Subjects characteristics

Variable	Patient outcome in 7th day		p value
	Survival	Non survival	
Sex: - Male, n - Female, n	 13 14	 9 8	1.000*
Ethnicity: - Javanese, n - Maduranese, n - Other, n	 18 5 4	 14 2 1	0.894*
Age (based on Ministry of Health of Indonesia): - Teen, n - Adult, n - Elderly, n	 1 16 6	 0 12 9	0.342*
Body weight (kg)	64.11±13.414	64.35±14.204	0.955**
BMI	25.15±5.07	25.34±6.26	0.736***
Respiratory rate: - Normal, n - Tachypnea, n	 6 21	 1 16	0.220*
Heart rate (bpm)	116.22±19.170	116.00±19.862	0.971**
Temperature (°C)	37.20±0.92	37.39±1.38	0.726***
Intubated	22	16	0.380*
History of illness: - Asthma, n - COPD, n - TBC, n - Hypertension, n - CAD, n - Arrhythmias, n - Heart failure, n - CVA, n - CKD, n - Diabetes mellitus, n - Gastritis, n	 4 1 4 8 1 0 0 1 1 7 2	 2 1 0 8 2 1 2 2 0 6 1	 0.111* 0.396* 0.549* 0.386* 0.144* 0.549* 1.000* 0.746* 1.000*

Legend: BMI=body mass index; COPD=chronic obstructive pulmonary disease; TBC=tuberculosis; CAD=coronary artery disease; CVA=cerebrovascular accident; CKD=chronic kidney disease; p<0.05=significant.
*chi-square test, significant p value <0.05
**T-test, significant p value <0.05
***Mann-Whitney test, significant p value <0.05

Table 2. Source of infection caused sepsis

Sources of infection	Number (n)	Percetage (%)
Pneumonia	21	47.7
Abdomen	11	25.0
CNS	1	2.3
UTI	1	2.3
Skin and soft tissue	9	20.4
Blood stream infection	1	2.3

Legend: CNS=central nervous system; UTI=urinary tract infection.

Table 3. Log regression bivariate analysis on outcome in 7 days

Variable	Wald	Exp (B)	B	95% CI exp (B)	p value
MAP	4.982	0.948	-0.054	0.904-0.993	0.026
SOFA score	11.756	1.976	0.681	1.339-2.917	0.001
VIS groups:					
- VIS at the 10th minute	1.866	1.041	0.040	0.983-1.102	0.172
- VIS at the 1st hour	2.740	1.050	0.049	0.991-1.112	0.098
- VIS at the 6th hour	7.321	1.085	0.082	1.023-1.152	0.007
- VIS at the 12th hour	10.691	1.150	0.140	1.058-1.251	0.001
- VIS at the 24th hour	9.153	1.223	0.201	1.073-1.393	0.002
- VIS at the 48th hour	9.059	1.174	0.161	1.058-1.304	0.003
- VIS average	6.153	1.152	0.141	1.030-1.288	0.013
VDI groups:					
- VDI at the 10th minute	1.128	4.535	1.512	0.279-73.825	0.288
- VDI at the 1st hour	1.341	6.050	1.800	0.287-127.324	0.247
- VDI at the 6th hour	5.139	123.141	4.813	1.919-7902.594	0.023
- VDI at the 12th hour	9.687	10151.951	9.225	30.449-3384795.029	0.002
- VDI at the 24th hour	8.232	3683317.467	15.119	120.443-112640600288.671	0.004
- VDI at the 48th hour	7.619	39112.779	10.574	21.454-71306764.664	0.006
- VDI average	3.361	651.668	6.480	0.639-664242.255	0.067

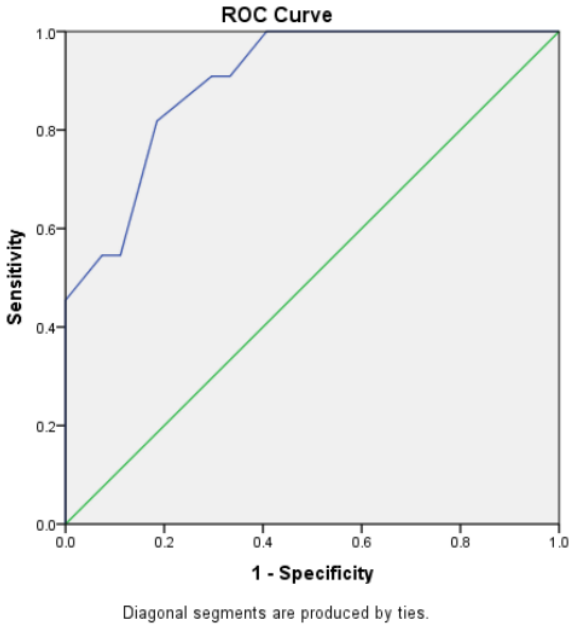
Legend: MAP=mean arterial pressure; SOFA=sequential organ failure assessment; VIS=vasopressor inotropic score; VDI=vasopressor dependency index; Wald=Wald test; Exp (B)=exponentiation of the β coefficient; B=β coefficient. Significant if p value <0.05.

Table 4. Backward stepwise log regression analysis VIS and VDI groups on the 7 days outcome

Variable	Wald	Exp (B)	B	95%CI	P Value
VIS Groups: - VIS at the 24th hour - VIS at the 48th hour	 4.414 4.667	 1.212 1.119	 0.192 0.113	 1.013-1.451 1.011-1.240	 0.036 0.031
VDI Groups:					
• VDI at the 24th hour	4.512	3062313.776	14.935	3.173-2955949692696.163	0.034
• VDI at the 48th hour	4.500	1012.736	6.920	1.693-605857.847	0.034
All component (MAP, SOFA Score, VIS, VDI)					
• SOFA Score	4.667	1.119	0.113	1.110-3.584	0.021

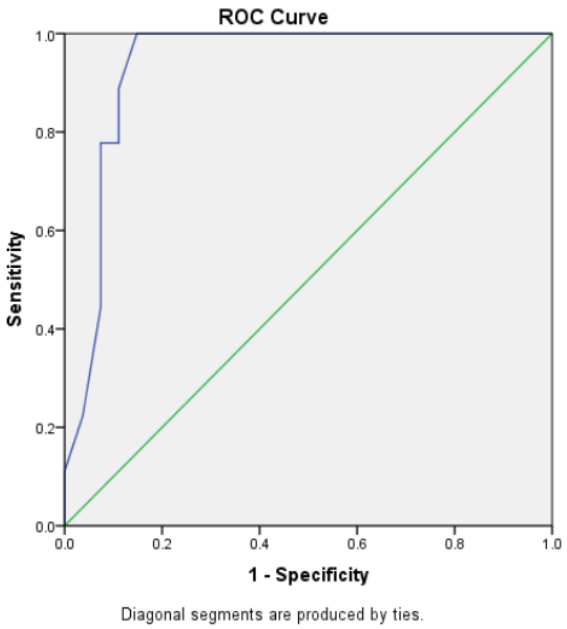
Legend: VIS=vasopressor inotropic score; VDI=vasopressor dependency index; Wald=Wald test; Exp (B)=exponentiation of the β coefficient; B=β coefficient. Significant if p value <0.05.

Figure 1. VIS ROC curve at 24th hour



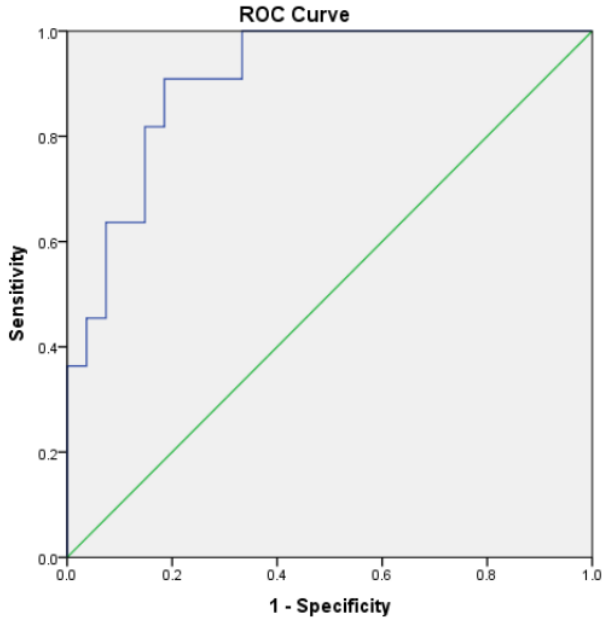
Legend: VIS=vasopressor inotropic score; ROC=receiver operating characteristic.

Figure 2. VIS ROC curve at 48th hour



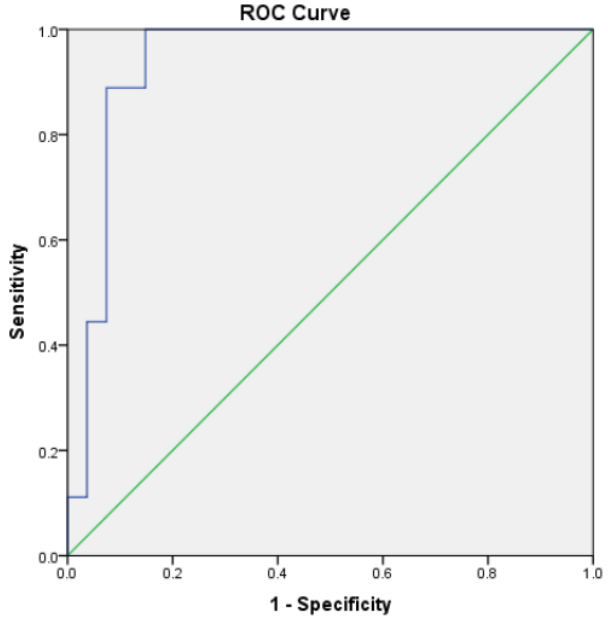
Legend: VIS=vasopressor inotropic score; ROC=receiver operating characteristic.

Figure 3. VDI ROC curve at 24th hour



Legend: VDI=vasopressor dependency index; ROC=receiver operating characteristic.

Figure 4. VDI ROC curve at 48th hour



Legend: VDI=vasopressor dependency index; ROC=receiver operating characteristic.

References

1. Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intensive Care Med 2014;40:1795-815.
2. Thomovsky E, Johnson PA. Shock pathophysiology. Compend Contin Educ Vet 2013;35:E2.
3. Carrara M, Bollen Pinto B, Baselli G, Bendjelid K, Ferrario M. Baroreflex Sensitivity and Blood Pressure Variability can Help in Understanding the Different Response to Therapy During Acute Phase of Septic Shock. Shock 2018;50:78-86.
4. 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. N Engl J Med 2010; 362:779-89.
5. Holler JG, Jensen HK, Henriksen DP, Rasmussen LM, Mikkelsen S, Pedersen C, et al. Etiology of Shock in the Emergency Department: A 12 Year Population Based Cohort Study. Shock 2019;51:60-7.
6. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Crit Care Med 2017;45:486-552.
7. Auchet T, Regnier M-A, Girerd N, Levy B. Outcome of patients with septic shock and high-dose vasopressor therapy. Ann Intensive Care 2017;7:43.
8. Lynn NB, Gupta C, Vaaler M, Held J, Leon L. Severe sepsis 3-hour bundle compliance and mortality. Am J Infect Control 2018;46:1299-300.
9. Utariani A, Semedi BP, Anestesia R, Hamzah, Rahardjo E, Hanindito E. Analysis of sepsis and septic shock 3- and 6-hour management at resuscitation room in Dr. Soetomo General Hospital. Crit Care Shock 2019;22:122-30.
10. Burgdorff A-M, Bucher M, Schumann J. Vasoplegia in patients with sepsis and septic shock: pathways and mechanisms. J Int Med Res 2018;46:1303-10.
11. Jentzer JC, Vallabhajosyula S, Khanna AK, Chawla LS, Busse LW, Kashani KB. Management of Refractory Vasodilatory Shock. Chest 2018;154:416-26.
12. Bassi E, Park M, Azevedo LCP. Therapeutic Strategies for High-Dose Vasopressor-Dependent Shock. Crit Care Res Pract 2013; 2013:1-10.
13. Cruz DN, Antonelli M, Fumagalli R, Foltran F, Brienza N, Donati A, et al. Early Use of Polymyxin B Hemoperfusion in Abdominal Septic Shock: The EUPHAS Randomized Controlled Trial. JAMA 2009;301:2445-52.
14. Matsukuma S, Sakamoto K, Nishiyama M, Tamesa T, Yoshino S, Hazama S, et al. Prognostic factors in patients with septic shock in digestive surgery who have undergone direct hemoperfusion with polymyxin B-immobilized fibers: a retrospective observational study. J Intensive Care 2015;3:13.
15. Guzman JA, Guzman CB. Adrenal exhaustion in septic patients with vasopressor dependency. J Crit Care 2007;22:319-23.
16. Vallabhajosyula S, Jentzer JC, Kotecha AA, Murphree Jr DH, Barreto EF, Khanna AK, et al. Development and performance of a novel vasopressor-driven mortality prediction model in septic shock. Ann Intensive Care 2018; 8:112.
17. Peters K, Unger RE, Brunner J, Kirkpatrick CJ. Molecular basis of endothelial dysfunction in sepsis. Cardiovasc Res 2003;60:49-57.
18. Liu V, Morehouse JW, Soule J, Whippy A, Escobar GJ. Fluid Volume, Lactate Values, and Mortality in Sepsis Patients with Intermediate Lactate Values. Ann Am Thorac Soc 2013;10:466-73.
19. Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 update. Crit Care Med 2018;46:997-1000.
20. Leone M, Asfar P, Radermacher P, Vincent J-L, Martin C. Optimizing mean arterial pressure in septic shock: a critical reappraisal of the literature. Crit Care 2015;19:101.
21. Benbenishty J, Weissman C, Sprung CL, Brodsky-Israeli M, Weiss Y. Characteristics of patients receiving vasopressors. Hear Lung 2011;40:247-52.
22. Ozaydin MG, Guneysel O, Saridogan F, Ozaydin V. Are scoring systems sufficient for predicting mortality due to sepsis in the emergency department? Turk J Emerg Med 2017;17:25-8.

Vasopressor dependency index- A quick prognostic parameter of septic shock patient in emergency and intensive care unit in remote area

ORIGINALITY REPORT

17%	13%	13%	0%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	link.springer.com Internet Source	1%
2	Y. Heper, E. H. Akalın, R. Mıstık, S. Akgöz, O. Töre, G. Göral, B. Oral, F. Budak, S. Helvacı. "Evaluation of serum C-reactive protein, procalcitonin, tumor necrosis factor alpha, and interleukin-10 levels as diagnostic and prognostic parameters in patients with community-acquired sepsis, severe sepsis, and septic shock", European Journal of Clinical Microbiology & Infectious Diseases, 2006 Publication	1%
3	www.dovepress.com Internet Source	1%
4	www.researchsquare.com Internet Source	1%
5	archive2016.eusemcongress.org Internet Source	1%

6	repozitorij.svkst.unist.hr Internet Source	1 %
7	librarysearch.aut.ac.nz Internet Source	1 %
8	eprints.whiterose.ac.uk Internet Source	1 %
9	ufdc.ufl.edu Internet Source	1 %
10	content.sciendo.com Internet Source	<1 %
11	www.frontiersin.org Internet Source	<1 %
12	Sean M. Bagshaw, Rinaldo Bellomo, Prasad Devarajan, Curtis Johnson et al. "Article de synthèse: La suppléance rénale en cas de maladie grave", Canadian Journal of Anesthesia/Journal canadien d'anesthésie, 2010 Publication	<1 %
13	vbn.aau.dk Internet Source	<1 %
14	"Supplement 2 September 2011", Intensive Care Medicine, 2011 Publication	<1 %
15	www.ncbi.nlm.nih.gov Internet Source	

		<1%
16	www.atsjournals.org Internet Source	<1%
17	journals.sagepub.com Internet Source	<1%
18	Marc Leone, Pierre Asfar, Peter Radermacher, Jean-Louis Vincent, Claude Martin. "Optimizing mean arterial pressure in septic shock: a critical reappraisal of the literature", Critical Care, 2015 Publication	<1%
19	annalsofintensivecare.springeropen.com Internet Source	<1%
20	www.tandfonline.com Internet Source	<1%
21	bmcurol.biomedcentral.com Internet Source	<1%
22	endojournals.ru Internet Source	<1%
23	worldwidescience.org Internet Source	<1%
24	jmir.org Internet Source	<1%
	medicine.missouri.edu	

25	Internet Source	<1%
26	Daisuke Kasugai, Mitsuaki Nishikimi, Kazuki Nishida, Michiko Higashi et al. "Timing of administration of epinephrine predicts the responsiveness to epinephrine in norepinephrine-refractory septic shock: a retrospective study", Journal of Intensive Care, 2019 Publication	<1%
27	N. D'Arpa, A. Accardo-Palumbo, G. Amato, L. D'Amelio, D. Pileri, V. Cataldo, R. Mogavero, C. Lombardo, B. Napoli, F. Conte. "Circulating dendritic cells following burn", Burns, 2009 Publication	<1%
28	hdl.handle.net Internet Source	<1%
29	www.siaarti.it Internet Source	<1%
30	www.thieme-connect.com Internet Source	<1%
31	"Handbook of Sepsis", Springer Science and Business Media LLC, 2018 Publication	<1%
32	"Intensive Care for Emergency Surgeons", Springer Science and Business Media LLC,	<1%

2019
Publication

33	Raúl J. Gazmuri, Cristina Añez de Gomez. "From a pressure-guided to a perfusion-centered resuscitation strategy in septic shock: Critical literature review and illustrative case", Journal of Critical Care, 2020 Publication	<1 %
34	Xing Li, Zexiang Zhu, Tinghong Zhou, Xiaoyu Cao, Ting Lu, Jiafen He, Yan Liang, Chuankai Liu, Zhoulin Dou, Bin Shen. "Predictive value of combined serum FGF21 and free T3 for survival in septic patients", Clinica Chimica Acta, 2019 Publication	<1 %
35	onlinelibrary.wiley.com Internet Source	<1 %
36	Danni Wang, Xin Liang, Shiyu Xia, Fei Song, Huangyao Ru, Hui Yin, Lixia Li, Zhiguo Pan, Liangcheng Dai, Lei Su. "Impact of obesity on short- and long-term mortality in patients with sepsis: A retrospective analysis of the large clinical database MIMIC-III", Research Square, 2020 Publication	<1 %
37	"ESICM LIVES 2018", Intensive Care Medicine Experimental, 2018 Publication	<1 %

38	"Sepsis", Springer Science and Business Media LLC, 2017 Publication	<1%
39	Didier Payen, Anne-Claire Lukaszewicz, Matthieu Legrand, Etienne Gayat et al. "A Multicentre Study of Acute Kidney Injury in Severe Sepsis and Septic Shock: Association with Inflammatory Phenotype and HLA Genotype", PLoS ONE, 2012 Publication	<1%
40	L. Bos, L. Schouten, L. van Vught, M. Wiewel et al. "ESICM LIVES 2016: part one", Intensive Care Medicine Experimental, 2016 Publication	<1%
41	Manuel Garay-Fernández. "Chapter 9 Sepsis Management: Non-antibiotic Treatment of Sepsis and Septic Shock", Springer Science and Business Media LLC, 2018 Publication	<1%
42	jurnal.ugm.ac.id Internet Source	<1%

Exclude quotes	On	Exclude matches	Off
Exclude bibliography	On		

Vasopressor dependency index- A quick prognostic parameter of septic shock patient in emergency and intensive care unit in remote area

GRADEMARK REPORT

FINAL GRADE

/100

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7

PAGE 8

PAGE 9

PAGE 10