Crit Care Shock (2021) 24:281-292

Thromboelastography (TEG) and hemostatic parameters as the diagnostic parameter of septic mortality in the intensive care unit

Isngadi[1], Aswoco Andyk Asmoro[1], Harjuna Atma Wiraharjanegara[1], Arie Zainul Fatoni[1]

Abstract

***Objective*: This study aimed to determine the relationship between thromboelastography (TEG) and hemostatic parameters and the Sequential Organ Failure Assessment (SOFA) score and mortality of septic patients, and found the potential of those parameters to be the mortality diagnostic parameters.**

***Design*: This was a prospective cohort study.**

***Setting*: This study was conducted in the Intensive Care Unit of Dr. Saiful Anwar General Hospital.**

***Patients and participant*: This study was conducted on thirty septic patients at the Intensive Care Unit.**

***Measurement and result*: Hemostatic parameters (prothrombin time [PT], activated partial thromboplastin time [aPTT], and international normalized ratio [INR]) and thromboelastography parameters (R time, K time, α angle, maximum amplitude [MA], G value, coagulation index [CI], and LY30) were analyzed using the normality test, homogeneity test, t-test, correlation test, and receiver operating characteristic (ROC) curve test in SPSS version 17.0. SOFA scores 8-11 and 12-20 had the highest mortality (100%). R time, K time, CI, α angle, MA, and G value, and all hemostatic parameters significantly correlated with SOFA score ($p<0.05$). R time, K time, α angle, CI, PT, aPTT, and INR of living patients significantly differed from death patients ($p<0.001$). K time, α angle, MA, CI, and all hemostatic parameters had an area under the curve (AUC) close to 1 ($p<0.05$). K time (69.2%) and aPTT (100%) had the highest sensitivity. The positive predictive value (PPV) of all TEG parameters was 100%. aPTT (100%) was the highest in the hemostatic parameters. The hemostatic parameters had a higher sensitivity than its specificity, while the TEG had higher specificity than its sensitivity.**

***Conclusion*: Most thromboelastography parameters and all hemostatic parameters significantly correlated with the SOFA score. K time had the highest sensitivity and specificity as the diagnostic parameter of septic mortality compared to the other thromboelastography parameters, while aPTT was the most sensitive diagnostic parameter of septic mortality compared to other hemostatic parameters.**

Key words: Hemostasis, Intensive Care Unit, mortality, sepsis, SOFA, thromboelastography (TEG).

Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Brawijaya University, Dr. Saiful Anwar General Hospital, Malang, Indonesia

Address for correspondence:
Isngadi
Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Brawijaya University
Jl. Jaksa Agung Suprapto No. 2, Malang, East Java, Indonesia
Tel: 0341-362101
Email: drisngadi@ub.ac.id

Introduction

Sepsis is a life-threatening organ dysfunction caused by abnormal regulation of the host's response to infection. Organ dysfunction is expressed as an acute change of the total score of Sequential Organ Failure Assessment (SOFA) ≥2 points as a sign of infection. In patients who are not known to have organ dysfunction, the SOFA value can be considered as zero. A SOFA score change ≥2 points is associated with a mortality rate of around 10% for hospitalized patients with suspected sepsis infec-

tions. A meta-analysis study by Jawad et al. (1) found that the incidence of sepsis in the population ranged from 22-240 cases per 100,000 people, severe sepsis 13-300 cases per 100,000 people, and septic shock 11 cases per 100,000 people, with mortality reaching 30% for sepsis, 50% for severe sepsis, and 80% for septic shock. Cases of sepsis in Indonesia ranged from 1.5-3.72%, with mortality between 37.09-80% in several referral hospitals in Indonesia, such as Cipto Mangunkusumo Hospital. (2) Based on the tracking of the medical records data from January 2012 to June 2013 at Dr. Saiful Anwar General Hospital Malang, Indonesia, overall found 1,026 patients diagnosed with sepsis, and 788 of them died (76.6%). Whereas, in the Intensive Care Unit (ICU) there were 168 septic patients, 78 of them died (46.4%). (3)

Sepsis can occur due to microbes that enter the bloodstream to trigger a systemic inflammatory response to cause organ dysfunction. (4) Septic patients can also experience the coagulation process disorders in the blood vessel system, such as hypercoagulopathy and coagulopathy. (5) Research conducted by Fenny et al. (6) suggested that there were impaired physiological parameters for hemostasis in septic patients such as prothrombin time (PT), activated partial thromboplastin time (aPTT), and international normalized ratio (INR). According to Levi and Opal (7) blood clotting time will prolong in many critically ill patients. Furthermore, a study by Pohan (8) said that septic patients had decreased organ function due to prolongation in PT, aPTT, and INR.

Blood clotting or hemostatic disorders can be evaluated using conventional coagulation tests using physiological parameters. However, there is a new tool used as a bed site. Thromboelastography (TEG), which can provide a global estimate of hemostasis, is a method of testing the efficiency of coagulation in the blood. TEG produces effective and precise overall blood coagulation supervision because it evaluates the blood's elastic properties and provides a global estimate of the function of hemostasis. (9)

TEG and hemostatic parameters can potentially be used as diagnostic parameters for mortality in septic patients. Therefore, this study aimed to determine the relationship between TEG parameters (R-time, K time, α angle, maximum amplitude [MA], G value, coagulation index [CI], and LY30) and hemostatic parameters (PT, aPTT, and INR) and SOFA score and mortality of septic patients, and to find the potential of those parameters to be the mortality diagnostic parameter in the ICU of Dr. Saiful Anwar General Hospital Malang, Indonesia.

Research design and method

Study subject

This study was a prospective cohort study on 30 septic patients treated in the Intensive Care Unit, conducted in March-September 2019. The study method has been approved by the Health Research Ethical Committee of Dr. Saiful Anwar General Hospital (No. 400/117/K.3/302/2019). The number of samples was calculated using the following formula:

$$n = \frac{\left(Z\alpha\sqrt{2V1} + Z\beta\sqrt{V1} + V2\right)^2}{(\emptyset 1 - \emptyset 2)^2}$$

Zα=1.64 (alpha standard deviation with type I error was set at 5%)

Zβ=1.28 (beta standard deviation with type II error was set at 10%)

$V1=Q_{11}+Q_{21}-2\theta_1^2=0.0174$

$V2=Q_{12}+Q_{22}-2\theta_2^2=0.0913$

$\emptyset 1$ =area under the curve (AUC) of the index studied (0.964)

$\emptyset 2$ =AUC of the known index (0.814)

Subjects were taken using a non-random sampling technique, namely consecutive sampling. The minimum number of subjects calculated based on this formula was 23 subjects. Research subjects met the inclusion criteria, including age 18-60 years old, diagnosed with sepsis, treated in the ICU of Dr. Saiful Anwar General Hospital Malang, Indonesia, and willing to be the subject of research. The subject was excluded from the study when the patient died less than 24 hours in the study period. Patients with hemostasis abnormalities history (both primary and secondary) taking antiplatelet drugs or oral anticoagulants were excluded from the study. The study was done for ten days after patients were diagnosed with sepsis.

Method

Nine milliliters fresh blood samples from vein or artery were taken and put into two tubes: citrate tube (trisodium citrate 3.2%:blood=1:9) and ethylenediaminetetraacetic acid tube. PT, aPTT, and INR were checked not more than 2 hours after sampling. Samples were centrifuged for 10 minutes at 2500 G. The plasma fraction was then examined by a coagulation analyzer according to the manufacturer's instructions. Platelets were examined with an automated hematology analyzer according to the manufacturer's instructions. TEG examination was carried out based on research methods by Yang and Wang. (10) TEG was examined using TEG® 5000 Thrombelastograph® (Haemonetics Corp., USA) with standard disposable cuvettes and pins. The device was run

according to the manufacturer's instructions. One milliliter of blood was taken from citrate tube and mixed with a kaolin vial and was shaken slowly. Zero point thirty-four milliliter of blood was taken with an automatic pipette and put into a TEG cuvette. Twenty microliters of 0.2 mol/l calcium were added to remove the effects of citrate. The test was run immediately.

Statistical analysis

The data obtained (TEG parameters and hemostatic parameters) were analyzed statistically using the normality test, homogeneity test, correlation test, difference test, and receiver operating characteristic (ROC) curve test on SPSS version 17.0 (IMB Statistics, Chicago, USA) with α=0.05.

Result

The characteristic of research subjects can be seen in **Table 1**. Research subjects were dominated by male. Research subjects experienced sepsis (n=12) and septic shock (n=18) with the most infection originated from lungs. The mean age of the subject was 46.2 years and the mean body mass index (BMI) was 23.7 kg/m^2.

Most of the TEG and hemostatic parameters showed an exceed from normal values. Several TEG parameters, including R time, K time, CI, and LY30, had higher values than normal values in subjects with septic shock, while α angle, MA, and G values were still in the normal range. The TEG parameter was mostly still in the normal range in septic patients, except for the R time variable and CI. All hemostatic parameters in septic shock subjects were higher than the normal range, while in septic subjects, all hemostatic parameters were still in the normal range (**Table 2**).

SOFA score of research subjects were divided into five groups: SOFA 0-3, SOFA 4-7, SOFA 8-11, SOFA 12-20, and SOFA 21-25. The research subjects were mostly classified as SOFA 4-7 (11 patients). The subjects in SOFA score 8-11 and 12-20 had the highest mortality rate (100%), while the SOFA 0-3 group had the lowest mortality rate (60%) (**Figure 1**).

A correlation test was performed to determine the relationship between TEG and hemostatic parameters on the SOFA score. Most TEG parameters significantly had a strong to very strong correlation with the SOFA score ($p<0.05$), except for LY30 variable ($p>0.05$). All hemostatic parameters also had a significant correlation with the SOFA score (**Table 3**).

Hemostatic parameters such as PT, aPTT, and INR underwent several changes. PT and aPTT lengthened in SOFA 8-11 and SOFA 12-20 group subjects. INR also increased in those groups. In SOFA 0-3 group, all parameters were still within the normal range (100%). While in SOFA 4-7 group, most of the hemostatic parameters were also still in the normal range, except for INR value (**Figure 2**).

The final condition of the subjects was 4 patients alive and 26 patients died. Based on the difference test, most of the TEG parameters had a significant difference between the living patients and deceased ones ($p<0.001$), except for LY30 ($p>0.05$). Compared with the normal range, some TEG parameters (R time, K time, α angle, and CI) of the dead patients had values outside the normal range, while MA, G values, and LY30 were still in the normal range. R time and K time were higher than the normal range, while α angle and CI were lower than the normal range. The hemostatic parameters (PT, aPTT, and INR) were outside the normal range in patients who died. In the living patient group, all TEG parameters were within the normal range. However, PT and aPTT were outside the normal range. INR parameter was still within the normal range. R time of the dead patients was higher than living ones, while α angle, MA, G values, CI, and LY30 of the patients who died were lower than the patients who still alive (**Table 4**).

Thromboelastography and hemostatic parameters had the potency to be diagnostic parameters of mortality in septic patients. A sensitivity and specificity test of those parameters have been done to find the most accurate diagnostic parameter. Based on the ROC analysis, TEG parameters (including K time, α angle, MA, and CI) and all hemostatic parameters significantly could be used as diagnostic parameters because they had an AUC value close to 1 ($p<0.05$). Among these parameters, K time became the best diagnostic parameter with a sensitivity of 69.2% and specificity of 100% at a cut-off value of 2.95 minutes (confidence interval 95%). Other parameters such as R time, α angle, MA, and CI had a specificity that reached 100% but had sensitivity less than K time. In the hemostatic parameters, aPTT parameter was the best diagnostic parameter with the highest sensitivity (100%) and specificity of 65.4% at a cut-off value of 34.3 minutes (**Table 5**).

The possibility of the true positive (suffering from the disease) of all subjects found suffering from illness by a diagnostic test was indicated by a positive predictive value (PPV). The PPV value of each TEG parameter was 100%. The highest PPV value of the hemostatic parameters was aPTT, which was 100%. Negative predictive value (NPV) was the magnitude of the possibility that the subjects found were true negative (did not suffer from the disease) of all

those found not to have the disease. The highest NPV value of the TEG parameter was K time, which was 33.3%, while the highest NPV value of the hemostatic parameters was aPTT, which was 30.8%.
The likelihood ratio (LR) value of subjects suffering from the disease would get positive diagnostic test results using the combined parameters of the five components of the TEG equal to 2.615. The LR value for INR separately was 2.615, and the LR from PT was 2.462. However, for other parameters, the LR value cannot be calculated (**Table 5**).

Discussion

This study was a prospective cohort of 30 septic patients treated in the ICU. The majority of subjects were male with the most infection originating from lungs. The mean age of the subject was 46.2 years, and the mean BMI was 23.7 kg/m^2. The mortality rate in female patients was higher than male patients. This was in contrast to the study of Melamed and Sorvillo, (11) which stated that men were 27% higher in experiencing death due to sepsis than women.
Based on TEG and hemostatic parameters, most of the parameters exceeded the normal range. In septic shock, several TEG parameters, including R time, K time, CI, and LY30, were higher than normal, while the α angle, MA, and G values were still in the normal range. In the septic patients, the average TEG parameter was still normal, except for the R time and CI.
SOFA scores of research subjects were divided into five groups: SOFA 0-3, SOFA 4-7, SOFA 8-11, SOFA 12-20, and SOFA 21-25. Most research subjects were classified into SOFA 4-7. SOFA 8-11 and SOFA 12-20 had the highest mortality rate (100%), while SOFA 0-3 group had the lowest mortality rate. The mortality rate in SOFA 8-11 and SOFA 12-20 was higher than the mortality rate found in Tee et al. (2019) study, which stated that the mortality rate of SOFA 8-11 was 20-40% and SOFA 12-20 is 40-75%. (12)
TEG and hemostatic parameters were closely associated with sepsis and had the potency to be diagnostic parameters. A correlation test was performed to determine the relationship between TEG and hemostatic parameters on the SOFA score. Most of the TEG parameters (R time, K time, CI, α angle, MA, and G values) significantly had strong to very strong correlation with SOFA score ($p<0.05$), except for LY30 variable ($p>0.05$). All hemostatic parameters also had significant correlation with the SOFA score. Based on correlation analysis between SOFA score and TEG, the increase of SOFA score significantly correlated with R values elevation and CI decline, indicating that the body was experiencing hypocoagulant. Increasing in K value and decreasing in α angle indicated a decrease in fibrinogen function. The decrease in MA value also indicated platelet function reduction. Therefore, it can be concluded that TEG can show the functional status of clotting factors in patients with sepsis and overall blood coagulation, and it follows the occurrence and development of sepsis.
Hemostatic parameters such as PT, aPTT, and INR of the subjects underwent several changes. In SOFA 8-11 and SOFA 12-20 groups, PT and aPTT lengthened, and INR increased. In SOFA 0-3 group, all parameters were still in the normal range. In SOFA 4-7 group, most of the hemostatic parameters were still in the normal range except for the INR value.
The final results of the study showed that 26 patients died and 4 patients alive. Based on the difference test, it was known that most of the TEG parameters had significant difference between the groups of living patients and deceased ones ($p<0.001$), except for LY30 parameter ($p>0.05$). Compared with the normal range, some TEG parameters in the dead patients such as R time, K time, α angle, and CI had values outside the normal range, while MA, G values, and LY30 were still within the normal range. R time and K time were higher than the normal range, whereas α angle and CI were lower than the normal range. The same thing happened to the hemostatic parameters: in dead patients the hemostatic parameters (PT, aPTT, and INR) had values outside the normal range.
In the living patients, all TEG parameters were within the normal range. However, hemostatic parameters (PT and aPTT) were outside the normal range, while INR was still within the normal range. The comparison between the dead and the living patients found out that the parameters of K time and R time of dead patients were higher than living ones, while the α angle, MA, G values, CI, LY30 of dead patients were lower than living patients. This study supports the study by Zhou et al. (13) that compared patients who lived and died due to sepsis. The clot formation speed (K time) and reaction time (R time) were higher in dead patients, while MA and α angle were lower in the dead patients than in the living ones. This showed the occurrence of hypercoagulable ($p<0.01$). This study supported the study by Panigada et al., (14) which stated that septic patients also showed a decrease in MA and LY30.
Hemostatic parameters of living patients significantly differed from the dead patients. The majority of dead patients who experienced lengthening of PT and aPTT also experienced an increase in INR. In the living patients, the patient still had normal PT,

aPTT, and INR. This study supported the study by Walborn et al., (15) where there was an increase in PT or INR in 90% or more patients with sepsis and severe disease. High PT and INR values associated with increased mortality and poor clinical outcomes in patients with sepsis and other critically ill or injured patients. This study also supported the study by Walborn et al., (15) which stated that the majority of increased INR was about 1.6 to 2.5 in global coagulation parameters.

TEG and hemostatic parameters had the potency to be diagnostic parameters of mortality in septic patients. Based on the results of ROC analysis, TEG parameters including K time, α angle, MA, and CI could be used as significant diagnostic parameters with the AUC value close to 1 ($p<0.05$). Among these parameters, K time became the best diagnostic parameter with a sensitivity of 69.2% and specificity of 100% at a cut-off value of 2.95 minutes. Other parameters such as R time, α angle, MA, and CI had a specificity that reached 100%, but had sensitivity below the K time variable. Among the hemostatic parameters, the aPTT parameter was the best diagnostic parameter with the highest sensitivity (100%), and the specificity reached 65.4% at a cut-off value of 34.3 minutes. K time and aPTT were considered the ideal diagnostic parameter for the mortality rate of sepsis and sepsis shock. The hemostatic parameters was useful as an initial evaluation or screening because it had a greater sensitivity rate than its specificity. Overall, the TEG parameter had a higher specificity than its sensitivity, so that TEG could replace the hemostatic parameters as the diagnosis tool. The limitation of this study was the limited number of research subjects. Further research needs to use more specific intrinsic and extrinsic factors to suppress cofounding factors. Besides, research needs to be done with routine TEG sampling to determine the TEG trends.

Conclusion

Most TEG parameters and all hemostatic parameters significantly have a strong to very strong correlation with the SOFA score. Most of the patients who died also experienced significant changes in hemostatic and TEG parameters. K time has the highest sensitivity and specificity as the diagnostic parameter of septic mortality among the other TEG parameters, while aPTT is the most sensitive as the diagnostic parameter of septic mortality among other hemostatic parameters.

Conflict of interest

The authors declare there is no conflict of interest.

Table 1. The characteristics of the subject

Characteristics	Total (n=30)	Diagnosis	
		Sepsis (n=12)	Septic shock (n=18)
Gender, n (%) - Male - Female	 16 14	 7 (43.75) 5 (35.71)	 9 (56.25) 9 (64.28)
Age (years), mean	46.2	43.08±3.7	48.3±3.0
BMI (kg/m^2), mean	23.7	23.04±1.4	23.90±1.2
Infection source, n - Lungs - Abdomen - Brain	 27 1 2	 11 - 1	 16 1 1

Legend: BMI=body mass index.

Table 2. TEG and hemostasis in sepsis and septic shock patients

Parameters	Normal range	Sepsis (mean±SD)	Septic shock (mean±SD)
Thromboelastography - R time (minute) - K time (minute) - α angle (degree) - Maximum amplitude (mm) - G value (Kdynes/cm^2) - Coagulation index - LY30 (%)	 5-7 1-3 53-67 50-68 4.5-11.5 -3 - 3 0-8	 7.94±3.10 2.75±1.13 53.97±13.21 56.85±5.91 7.45±2.16 -1.25±3.08 4.95±9.02	 8.11±2.09 3.05±1.04 54.51±11.51 58.01±6.59 7.87±2.10 -1.60±2.67 16.67±5.93
Hemostasis - PT (second) - aPTT (second) - INR	 17.1-15.3 39.3-37.2 <1.5	 15.966±5.46 36.77±12.71 1.45±0.49	 16.67±5.93 38.76±12.45 1.64±0.52

Legend: TEG=thromboelastography; LY30=percentage decrease in amplitude 30 minutes after maximum amplitude and gives a calculated fibrinolysis rate; PT=prothrombin time; aPTT=activated partial thromboplastin time; INR=international normalized ratio.

Table 3. Relationship of TEG and hemostatic parameters and SOFA score

Parameter	Variable	Normal range	SOFA 0-3 (mean±SD)	SOFA 4-7 (mean±SD)	SOFA 8-11 (mean±SD)	SOFA 12-20 (mean±SD)	p value	R value
TEG	R time (minute)	5-7	5.08±1.1	6.95±2.2	10.4±0.7	9.9±0.3	<0.001*	0.715
	K time (minute)	1-3	1.42±0.2	2.52±0,5	3.77±0.4	4.03±0.6	<0.001*	0.892
	α angle (degree)	53-67	70.1±2.5	57.9±9.8	48.3±3.9	40.7±6.6	<0.001*	-0.848
	MA (mm)	50-68	63.1±1.6	61.0±5.4	52.8±3.4	51.3±2.6	<0.001*	-0.773
	G value (Kdynes/cm^2)	4.5-11.5	10.4±0.6	8.1±1.6	6.98±1.2	54.8±1.8	<0.001*	-0.753
	CI	-3 - 3	1.70±1.0	-0.24±1.4	-2.67±1.3	-5.11±2.5	0.003*	-0.901
	LY30 (%)	0-8	7.76±10.6	2.39±5.6	5.22±13.8	3.91±8.8	0.903	-0.011
Hemostasis	PT (second)	17.1-15.3	10.5±0.6	13.9±5.1	21.6±2.9	20.0±3.5	<0.001*	0.673
	aPTT (second)	39.3-37.2	24.9±1.1	31.9±12	49.6±1.8	47.2±3.0	<0.001*	0.686
	INR	<1.5	1.01±0.1	1.34±0.4	1.98±0.2	2.00±0.3	<0.001*	0.700

Legend: TEG=thromboelastography; SOFA=sequential organ failure assessment; MA=maximum amplitude; CI=coagulation index; PT=prothrombin time; aPTT=activated partial thromboplastin time; INR=international normalized ratio; R value=correlation coefficient.
*Significant correlation test.

Table 4. Relationship of TEG and hemostatic parameters and mortality of septic patients during the study

Parameter	Variable	Normal range	Normal range (mean±SD)	Died (n=17) (mean±SD)	Alive (n=13) (mean±SD)	p value
TEG	R time (minute)	5-7	8.04±2.4	10.1±0.9	5.63±1.0	<0.001*
	K time (minute)	1-3	2.93±1.09	3.73±0.6	2.02±0.6	<0.001*
	α angle (degree)	53-67	54.2±12	45.1±6.4	64.7±7.4	<0.001*
	MA (mm)	50-68	57.2±6.2	52.8±3.6	62.8±3.8	<0.001*
	G value (Kdynes/cm^2)	4.5-11.5	7.70±2.1	6.50±1.6	9.08±1.2	<0.001*
	CI	-3 - 3	-1.46±2.7	-3.40±2.1	0.76±1.3	<0.001*
	LY30 (%)	0-8	4.25±9.21	3.75±10.3	4.82±8.1	0.728
Hemostasis	PT (second)	17.1-15.3	16.30±5.6	20.8±2.9	11.2±3.0	<0.001*
	aPTT (second)	39.3-37.2	37.9±12.3	48.6±2.9	25.7±5.4	<0.001*
	INR	<1.5	1.57±0.5	1.97±0.2	1.10±0.2	<0.001*

Legend: TEG=thromboelastography; SOFA=sequential organ failure assessment; MA=maximum amplitude; CI=coagulation index; PT=prothrombin time; aPTT=activated partial thromboplastin time; INR=international normalized ratio.
*significant t-test ($p<0.05$).

Table 5. The results of sensitivity and specificity test of TEG and hemostatic parameters for septic mortality

Parameter	Variable	AUC	p value	Cut-off value	Sensitivity	Specificity	PPV	NPV	Likelihood ratio (LR)
TEG	R time	0.688	0.081	≥9.05	57.7%	100.0%	100.0%	26.7%	~
	K time	1.000	0.000*	≥2.95	69.2%	100.0%	100.0%	33.3%	~
	α angle	0.941	0.000*	≥54.85	65.4%	100.0%	100.0%	30.8%	~
	MA	0.936	0.002*	≥53.25	34.6%	100.0%	100.0%	19.0%	~
	CI	1.000	0.000*	≥-2.85	26.9%	100.0%	100.0%	17.4%	~
Hemostasis	PT	1.000	0.000*	≥16.9	75.0%	61.5%	94.1%	23.1%	2.462
	aPTT	0.944	0.000*	≥34.3	100.0%	65.4%	100.0%	30.8%	~
	INR	1.000	0.000*	≥1.39	75.0%	65.4%	94.4%	25.0%	2.615

Legend: TEG=thromboelastography; MA=maximum amplitude; CI=coagulation index; PT=prothrombin time; aPTT=activated partial thromboplastin time; INR=international normalized ratio; AUC=area under the curve; PPV=positive predictive value; NPV=negative predictive value.

Figure 1. Distribution of research subjects based on SOFA score

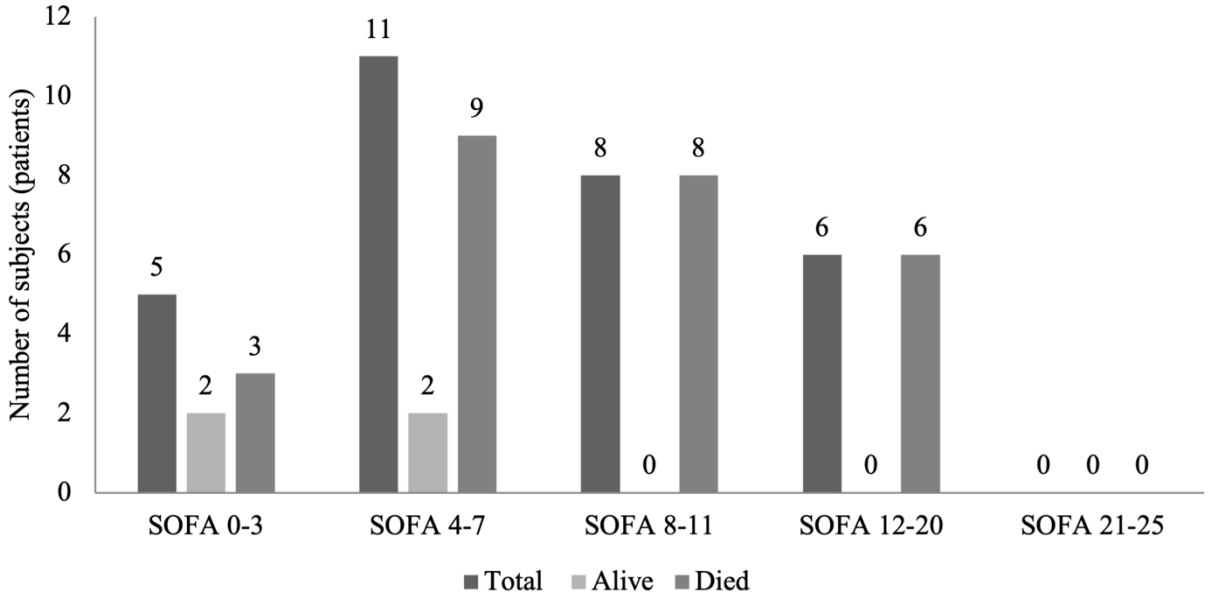
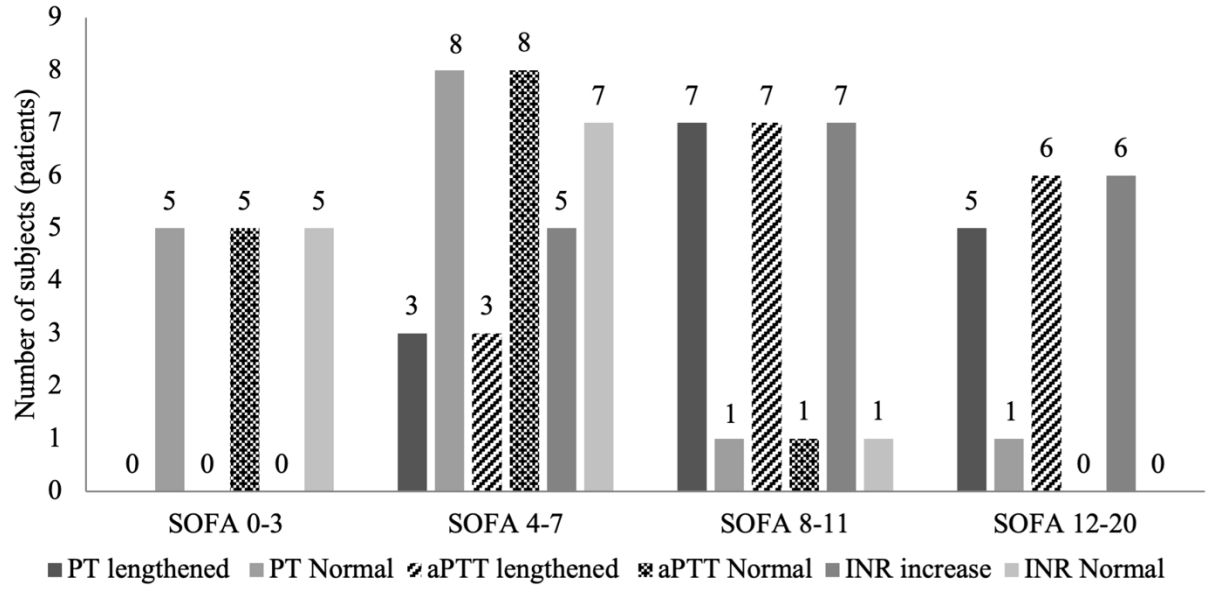


Figure 2. Relationship between hemostatic parameters and SOFA score



References

1. Jawad I, Lukšić I, Rafnsson SB. Assessing available information on the burden of sepsis: Global estimates of incidence, prevalence and mortality. J Glob Health 2012;2:010404.
2. Aulia D, Sanjaya AI, Timan IS. The Use of Immatane to Total Neutrophil (IT) Ratio to Detect Bacteriemia. J Lab Med Qual Assur 2003;25:237-42.
3. Asmoro AA, Vitraludyono R, Sindharta R, Widodo MA, Saleh SC, Widjayanto E. In vitro study on the inhibitory effect of ketamine to LPS-induced apoptosis in HUVEC culture. Asian Pac J Trop Dis 2015;5:968-70.
4. Sagy M, Al-Qaqaa Y, Kim P. Definitions and pathophysiology of sepsis. Curr Probl Pediatr Adolesc Health Care 2013;43:260-3.
5. Simmons J, Pittet J-F. The coagulopathy of acute sepsis. Curr Opin Anaesthesiol 2015;28: 227-36.
6. Fenny, Dalimoenthe NZ, Noormartany, Pranggono E, Dewi NS. Prothrombin Time, Activated Partial Thromboplastin Time, Fibrinogen, dan D-dimer Sebagai Prediktor Decompensated Disseminated Intravascular Coagulation Sisseminated pada Sepsis. Majalah Kedokteran Bandung 2011;43:49-54.
7. Levi M, Opal SM. Coagulation abnormalities in critically ill patients. Crit Care 2006;10:222.
8. Pohan HT. Assessment of clinical and laboratory parameters that reflect inflammatory response and organ function in sepsis. Med J Indones 2005;14:26-32.
9. Thakur M, Ahmed AB. A review of thrombo-elastography. Int J Perioper Ultrasound Appl Technol 2012;1:25-9.
10. Yang W, Wang C, Chen J, Xu X, Gong H, Zhu C. Thrombelastography and coagulation parameters in septic patients and their clinical significance. Int J Clin Exp Med 2016;9:20197-203.
11. Melamed A, Sorvillo FJ. The burden of sepsis-associated mortality in the United States from 1999 to 2005: An analysis of multiple-cause-of-death data. Crit Care 2009;13:1-8.
12. Tee Y-S, Fang H-Y, Kuo I-M, Lin Y-S, Huang S-F, Yu M-C. Serial evaluation of the SOFA score is reliable for predicting mortality in acute severe pancreatitis. Medicine (Baltimore) 2018; 97:1-6.
13. Zhou W, Zhou W, Bai J, Ma S, Liu Q, Ma X. TEG in the monitoring of coagulation changes in patients with sepsis and the clinical significance. Exp Ther Med 2019;17:3373-82.
14. Panigada M, Zacchetti L, L'Acqua C, Cressoni M, Anzoletti MB, Bader R, et al. Assessment of fibrinolysis in sepsis patients with urokinase modified thromboelastography. PLoS One 2015;10:1-17.
15. Walborn A, Williams M, Fareed J, Hoppensteadt D. International Normalized Ratio Relevance to the Observed Coagulation Abnormalities in Warfarin Treatment and Disseminated Intravascular Coagulation. Clin Appl Thromb Hemost 2018;24:1033-41.

This page is intentionally left blank