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Compatibility of Endocan Levels with SOFA Scorein Sepsis Patients at Dr.Wahidin Sudirohusodo Hospital Makassar

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ABSTRACT: Background:Sepsis is a life-threatening organ dysfunction and the leading cause of death in critically ill patients. The use of biomarkers and scoring systems is an attempt to assist in the diagnosis and assessing the severity of multi-organ dysfunction. C-reactive protein (CRP), procalcitonin (PCT), and the currently reported marker are endocan. Endocan is a biomarker for multiorgan dysfunction in sepsis. Endocan synthesis and release are triggered by proinflammatory cytokineswhich can increase endocan levels in sepsis while the Sequential (Sepsis-related) Organ Failure Assessment (SOFA) is a scoring method for identifying organ dysfunction in sepsis. A SOFA score ≥2 indicates organ dysfunction. Endocan and SOFA scores are both aimed at assessing multiorgan dysfunction and can determine the prognosis in sepsis. This study aims to determine the suitability of endocan levels with SOFA values in septic patients at Dr.WahidinSudirohusodoHospital Makassar.

Purpose: To determine the suitability of SOFA values with endocan levels in septic patients at the Dr.WahidinSudirohusodoHospital and its network hospital.

Methods: This cross-sectional observational study was conducted from December 2019-August 2020. The population of this study was all sepsis patients in the hospital. DR.

WahidinSudirohusodo. Data were analyzed descriptively. The compatibility of endocan levels with SOFA values in septic patients used the Spearman correlation test.
Results: From a total of 150 subjects, it was found that patients <60 years were 45 subjects (80.04%), men were 34 subjects (60.7%), patients with 2 comorbid were 21 subjects (37.5%), the mean Endocan levels were 361.9 ± 472.4 with tertileendocan 1 (<110.0) as many as 19 subjects (33.9%) and tertile 3 (> 232.0) as many as 19 subjects (33.9%) while SOFA scores Mean 5.6 ± 3.7 with SOFA scores 0-6 as many as 36 subjects (64.3%). The endocan level in sepsis was significantly lower than the control, namely 361.9 (p <0.01). Based on the Spearman correlation test, it was found that there was a significant negative correlation between endocan levels and the SOFA score (p <0.05). In women, there was a significant negative correlation between endocan levels and SOFA scores (p <0.05), at age <60 years, there was a significant negative correlation between endocan levels and SOFA scores (p <0.05). with the number of comorbid 1, there was a significant negative correlation between endocan levels and the SOFA score (p <0.05).
Conclusion: There is a significant negative correlation between endocan levels and SOFA score in septic patients at Dr.WahidinSudirohusodo Makassar.

Keywords: sepsis, endocan, SOFA (Sequential (Sepsis-related) Organ Failure Assessment)

1. INTRODUCTION

Sepsis is a life-threatening organ dysfunction resulting from dysregulation of the host response to infection and is the leading cause of death in critically ill patients despite modern antibiotics. The occurrence of sepsis is a very complex one that includes inflammatory and anti-inflammatory processes, humoral and cellular reactions, and circulatory disorders. Early diagnosis and severity of sepsis are essential for proper treatment.[1] According to the World Health Organization (WHO), sepsis is estimated to affect 30 million people worldwide each year and has the potential to cause 6 million deaths. Sepsis can be a clinical manifestation of infection. Based on the results of the 2013 Basic Health Research (Riskesdas) published by the Ministry of Health, the main infectious diseases in Indonesia includeAcute Respiratory Infection (ARI), pneumonia, tuberculosis, hepatitis, diarrhea, malaria. Where respiratory infection and tuberculosis are among the top 5 causes of death in Indonesia. [2]
Biomarkers can be used to determine the presence or absence of sepsis. In addition, biomarkers can distinguish bacterial, viral, and fungal infections and systemic sepsis from local infections. C-reactive protein (CRP) and procalcitonin (PCT) and the currently reported marker are endocan. Endocan is a proteoglycan that can be detected in human blood and expressed on the surface of the endothelial cells of the lungs and kidneys. Endocan is a marker of angiogenesis in several types of cancer. The synthesis and release of these molecules are triggered by proinflammatory cytokines such as tumor necrosis factor (TNF) -α and interleukin (IL) -1β. Endocan is increased in septic patients because the release of pro-inflammatory cytokines can increase endocan levels. The level of endocan gene expression is caused by lipopolysaccharide (LPS) from the cell wall of gram-negative bacteria. In vitro tests, it was found that increased interleukin-1, tumor necrosis factor-α and followed by LPS, increased endocan sex in endothelial cells.5,13 Several studies have shown that endocan is a

biomarker for endothelial dysfunction and multiorgan failure in sepsis and can determine the prognosis in sepsis. [3]

SOFA (Sequential (Sepsis-related) Organ Failure Assessment) is a scoring method used to identify the presence or absence of organ dysfunction and can determine the prognosis in sepsis. A SOFA score ≥2 indicates organ dysfunction.[4,5]An increase in the SOFA score is associated with the presence of organ dysfunction in sepsis. There are studies that suggest that patients treated with infections suspected of sepsis have an increase in the SOFA score which provides a greater prognostic risk for mortality than the qSOFA score.

Endocan and SOFA scores are both aimed at assessing multiorgan dysfunction and can determine the prognosis in sepsis. In this study, we wanted to determine the suitability of endocan levels with SOFA values in septic patients at Dr. WahidinSudirohusodo Makassar

2. MATERIAL AND METHODS

Research Design This is a cross-sectional analytic study conducted at the DrWahidinSudirohusodo Hospital.

Research Subjects All sepsis patients at DR. WahidinSudirohusodo from December 2019-August 2020

Research Data Collection The inclusion criteria were sepsis patients who were treated at Dr.WahidinSudirohusodoHospital and his network hospital, subjectswho are>18 years old.

Research Data Analysis .Data analysis was performed using SPSS version 22. The statistical analysis performed was descriptive statistical calculations and frequency distribution as well as Kappa statistical tests and Spearman's Correlation test. The test results are significant if the p value <0.05

Ethical Clearance This study protocol was approved by Health Research Ethics Commission of Hasanuddin University, Medical Faculty, with approval letter number 146/UN4.6.4.5.31/PP36/2020.

3. RESULTS

Subject's Characteristics

From a total of 150 subjects obtained from December 2019-August 2020, it was found that the age of the subjects was between 18-77 years with a mean of 46.5 ± 14.6 years, patients <60 years were 45 subjects (80.04%) and ≥60 years as many as 11 subjects (19.6%). Subjects consisted of 34 men (60.7%) and 22 women (39.3%). Patients with 1 comorbid were 19 subjects (33.9%), with 2 comorbid was 21 subjects (37.5%), with 3 comorbid was 10 subjects (17.9%), and >3 comorbid was 6 subjects. (10.7%). The mean endocan level was 361.9 ± 472.4 with tertileendocan 1 (<110.0) as many as 19 subjects (33.9%), tertile 2 (110.0-232.0) as many as 18 subjects (32.1%), and tertile3 (> 232.0) as many as 19 subjects (33.9%) while the mean SOFA score was 5.6 ± 3.7 with a SOFA score 0-6 as many as 36 subjects (64.3%),

7-9 as many as 10 subjects (17.9%), and 10-14 as many as 10 subjects (17.9%) (Table 1).

Comparison of Endocan Sepsis with Control

This study classified patients into 2 groups, namely the sepsis group as many as 56 subjects with a mean of 361.9 ± 472.4 and the control group as many as 28 subjects with a mean of 868.4 ± 866.1. Based on Figure 1, it was found that the endocan level in sepsis was significantly lower than the control, which was 361.9 compared to the control 868.4 ($p < 0.01$) (Figure 1)

SOFA Score Conformity with Endocan

There was a significant negative correlation between tertileeendocan levels and SOFA scores ($p < 0.01$), where the low SOFA scores were more frequent 2 and 3 endocan, while the high SOFA scores were more common in endocan 1 and 2 (Table 2).). The Spearman correlation test was conducted to clarify the meaning of the suitability between endocan levels and SOFA scores, indicating that there was a significant negative correlation between endocan levels and SOFA scores, where the lower the endocan level, the higher the SOFA score ($p < 0.05$).

In women, there was a significant negative correlation between endocan levels and SOFA scores ($p < 0.05$), while in men, there was no match between endocan levels and SOFA scores ($p > 0.05$) (Table 3).

At age <60 years, there was a significant negative correlation between endocan levels and SOFA scores ($p < 0.05$), while at age ≥60 years, there was no match between endocan levels and SOFA scores ($p > 0.05$) (Table 3).

The compatibility of endocan levels with the SOFA score according to the number of comorbid was found that in subjects with 1 comorbid, there was a significant negative correlation between endocan levels and SOFA scores ($p < 0.05$), in subjects with 2 comorbids, there was no match between endocan levels with a SOFA score ($p > 0.05$), whereas, in subjects with 3 and >3comorbidscould not be interpreted because none of the subjects had endocan in table 2 (Table 3).

4. DISCUSSION

Subject's Characteristics

This study included 56 study subjects aged between 18-77 years with a mean of 46.5 ± 14.6 years. Patients aged <60 years were 45 subjects (80.04%) and ≥60 years were 11 subjects (19.6%). The results of this study are not in line with previous studies. The incidence of sepsis is not clearly influenced by age, but age is one of the risks that aggravate sepsis. Research conducted by Chen Ming et al in 2014 in Taiwan found 63.8% of patients aged ≥65 years and mortality would increase with age. This is because immunity has begun to decline and the number of comorbid in patients aged ≥65 years.[6]

The research subjects consisted of 34 men (60.7%) and 22 women (39.3%). This is in line with a study conducted by Nasir et al. in 2015 in Pakistan, which found that 97 sepsis patients, 54% were male and 46% female. In addition, the death rate from sepsis increased by

70% in men compared to women. This may be due to differences in the severity of sepsis. However, gender did not have a clear significance for sepsis. [7]

Patients with 1 comorbid were 19 subjects (33.9%), 2 comorbids was 21 subjects (37.5%), 3 comorbids was 10 subjects (17.9%), and >3 comorbids was 6 subjects. (10.7%). The results of this study are in line with previous studies. Comorbid or basic disease is important to diagnose and find the cause of sepsis. Research conducted by Rheza et al in 2014 at Prof.Dr. R. D. Kandou Manado found that the most common cause of sepsis infection was lung, urinary tract, and surgical scars and the most common cause of sepsis was pneumonia (71.4%). [8] In addition, sepsis patients with many comorbid mortality rates will increase.[9]

The average SOFA score was 5.6 ± 3.7 with a SOFA score of 0-6 as many as 36 subjects (64.3%), 7-9 as many as 10 subjects (17.9%), and 10-14 as many as 10 subjects (17.9 %). The results of this study are not in line with previous studies. The SOFA score is used to determine the prognosis of sepsis, especially to determine its mortality.[10] Research conducted by Iskandar et al in 2018 at Dr.Saiful Anwar obtained a SOFA score greater than equal to 7, a 3.8-fold greater risk for mortality due to sepsis.[11]

The mean endocan level was 361.9 ± 472.4 with tertileendocan 1 (<110.0) as many as 19 subjects (33.9%), tertile 2 (110.0-232.0) as many as 18 subjects (32.1%), and number 3 (> 232.0) as many as 19 subjects (33.9%). This is in line with previous research. Research conducted by Nathalie et al in 2018 found that there was an increase in endocan levels in sepsis patients.[12]

Comparison of Endocan Sepsis with Control

The endocan level in sepsis was significantly lower than the control, namely 361.9 compared to 868.4 ($p < 0.01$). This is not in line with previous research. Research by Katharine et al. 2012 found that in their prospective study, endocan was higher in patients with sepsis compared to SIRS or healthy control patients.[13]

SOFA Score Conformity with Endocan

There was a significant negative correlation between endocantertile levels and SOFA scores ($p < 0.01$), where low SOFA scores were more in endocan 2 and 3, while high SOFA scores were more common in endocan 1 and 2. In the correlation test, there was a significant negative correlation between endocan levels and SOFA scores, where the lower the endocan level, the higher the SOFA score ($p < 0.05$). This is not in line with previous research. Research conducted by Loakeimidou in 2014 found that endocan levels in patients with sepsis increased, which means that there was organ dysfunction, this is also related to the increased SOFA score.[14]

The compatibility of endocan levels with the SOFA score according to gender was found that in women, there was a significant negative correlation between endocan levels and SOFA scores ($p < 0.05$), while in men, there was no match between endocan levels and SOFA scores ($p > 0.05$). Research conducted by Diego et al. In 2017 found that there was an increase in endocan levels followed by an increase in the SOFA score.[15] Gender was not clear.[7]

The suitability of endocan levels with SOFA scores according to age was found that at age <60 years, there was a significant negative correlation between endocan levels and SOFA scores ($p < 0.05$) while at age ≥60 years, there was no match between endocan levels and

SOFA score (p> 0.05). Research conducted by Loakeimidou in 2014 found that endocan levels in septic patients increased, which means that there was organ dysfunction, this is also associated with an increased SOFA score.[14] However, it was not clearly influenced by age.[6]
The compatibility of endocan levels with the SOFA score according to the number of comorbid was found that in subjects with a 1 comorbid, there was a significant negative correlation between endocan levels and SOFA scores (p <0.05), in subjects with 2 comorbids, there was no match between endocan levels with a SOFA score (p> 0.05), whereas in subjects with 3and >3 comorbids could not be interpreted because none of the subjects had endocan at table 2. This is in line with previous studies. Research conducted by Diego et al. In 2017 found that there was an increase in endocan levels followed by an increase in SOFA scores.[15] Comorbid increases the risk of sepsis and organ dysfunction which will later affect endocan levels and SOFA scores.[16]

5. CONCLUSION

There is a significant negative correlation between endocan levels and SOFA score in septic patients at Dr. WahidinSudirohusodo Makassar.

Study Strength and Limitations: The results of this study is an information about Compatibility of Endocan Levels with SOFA Score in Sepsis Patients at Dr.WahidinSudirohusodo Hospital Makassar which can be used as a basis for further research. However, this study only had a limited number of samples, namely 56 subjects, so the results could not be generalized to a large number of subjects.

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Table 1. Distribution of Research Variable Categories (n = 56)

Variable		N	%
Gender	Men	34	60,7
	Women	22	39,3
Age	<60 years old	45	80,4
	≥60 years old	11	19,6
Comorbidities	1	19	33,9
	2	21	37,5
	3	10	17,9
	>3	6	10,7
SOFA Score	0-6	36	64,3
	7-9	10	17,9
	10-14*	10	17,9
TertileeEndocan	Tertilee1 (<110,0)	19	33,9
	Tertilee 2 (110,0 - 232,0)	18	32,1
	Tertilee 3 (>232,0)	19	33,9

*Score of SOFA 10-12 dan 13-14 was combined, because of limited samples

Table 2. SOFA Score Conformity with Endocan

SOFA Score	TertileEndocan			Total
	Tertile 1	Tertile 2	Tertile 3	
0-6	9	14	13	36

7-9	5	0	5	10
10-14	5	4	1	10
Total	19	18	19	56

Kappa=-0,237 (p=0,005)

Table 3. Suitability of SOFA and Endocan Scores based on Sex, Age, and Number of Comorbids

Variables	Score of SOFA	TertileEndocan			Total P
		Tertile 1	Tertile 2	Tertile 3	
Gender					
Men[1)]	0-6	5	7	12	24 [1)]Kappa=-0,233 (p=0,020)
	7-9	3	0	1	4 [2)]Kappa=-0,261 (p=0,077)
	10-14	3	2	1	6
Women[2)]	0-6	4	7	1	12
	7-9	2	0	4	6
	10-14	2	2	0	4
Age					
<60 years old	0-6	8	9	13	30 [1)]Kappa=-0,211 (p=0,017)
	7-9	3	0	5	8 [2)]Kappa=-0,269 (p=0,165)
	10-14	3	4	0	7
≥60 tahun	0-6	1	5	0	6
	7-9	2	0	0	2
	10-14	2	0	1	3
Number of Comorbidities					
1	0-6	1	7	4	12 [1)]Kappa=-0,320 (p=0,020)
	7-9	2	0	2	4 [2)]Kappa=-0,155 (p=0,179)
	10-14	1	2	0	3[3)]Can not be analyzed
2	0-6	4	7	4	15[4)]Can not be analyzed
	7-9	0	0	2	2
	10-14	2	2	0	4
3	0-6	4	0	3	7
	7-9	1	0	0	1
	10-14	1	0	1	2
>3	0-6	0	0	2	2
	7-9	2	0	1	3
	10-14	1	0	0	1

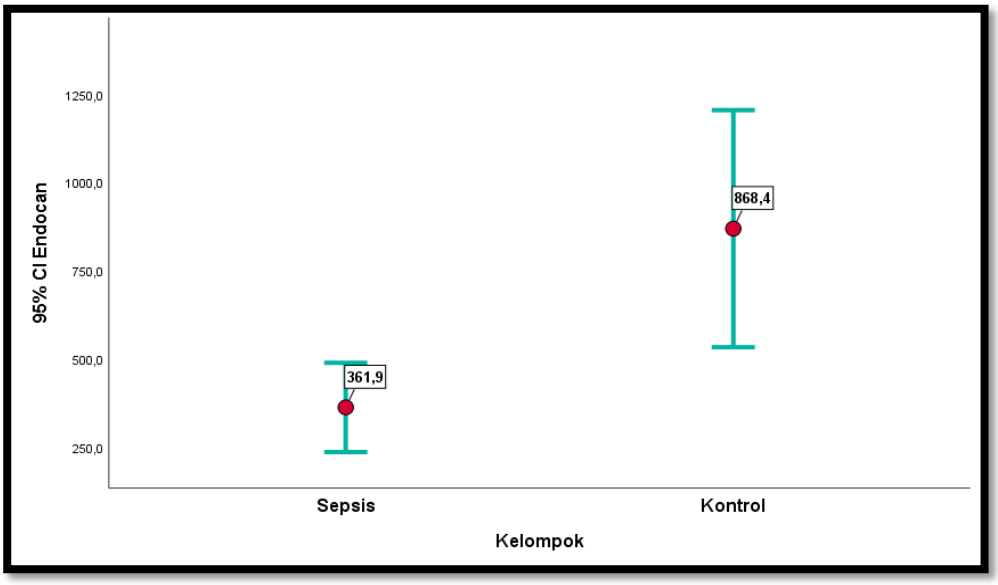

Figure 1. Comparison of Endocan Sepsis and Control