Presepsin and Procalcitonin Values to Determine The Prognosis of Urosepsis

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PRESEPSIN AND PROCALCITONIN VALUES TO DETERMINE THE PROGNOSIS OF UROSEPSIS

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ABSTRACT

Objective:To evaluate the prognostic value of presepsin and procalcitonin in patient with urosepsis.Material & Method: This is an observational prospective study. Patients who fulfilled the criteria for urosepsis at Soetomo Hospital Surabaya were enrolled. Presepsin and procalcitonin were measured at first admission. All patients were managed according to standard urosepsis therapy. At the 28th day of treatment, patients were evaluated and classified into survivor and non-survivor. The statistical analysis were tested with logistic regression test using software SPSS 23. Results: 30 urosepsis patients were included in this study withaverage age was 48.3 years (range 21-77 years).There were 23 survivor and 7 non-survivor. Mean presepsin values were higher in non-survivor than in survivor but the difference was not significant (4405 ± 4664 vs 4042 ± 2643, p=0.259). Mean procalcitonin value was significantly higher in non-survivor than in survivor (7.68 ± 6.81 vs 3.27 ± 2.74, p=0.013). Using the cut off value ≥2.24 ng/ml, procalcitonin can predict mortality in 28 days with sensitivity 71.4% and specificity 47.8%.Conclusion: Presepsin can not be used to determine the prognosis of urosepsis patients. Procalcitonin showed a significant correlation with outcome of urosepsis patients so it can be use to determine the prognosis of urosepsis.

Keywords: Urosepsis, prognostic, mortality, presepsin, procalcitonin.

ABSTRAK

Tujuan: Untuk mengevaluasi apakah presepsin dan procalcitonin dapat digunakan untuk menentukan prognosis pada pasien urosepsis.Bahan & Cara: Penelitian ini merupakan penelitian prospektif observasional dengan mengevaluasi pasien urosepsis di RSUD Dr. Soetomo Surabaya. Pemeriksaan presepsin dan procalcitonin dilakukan saat awal pasien didiagnosis urosepsis. Seluruh pasien mendapatkan penanganan standar urosepsis. Penilaian prognosis dilakukan pada hari ke-28 dengan kriteria hidup atau meninggal. Analisa statistik menggunakan regresi logistik dengan aplikasi SPSS 23.Hasil: Didapatkan sampel penelitian sebanyak 30 pasien dengan diagnosis urosepsis. Usia rerata sampel 48.3 tahun (rentang 21–77 tahun). Dalam observasi yang dilakukan selama 28 hari sebanyak 23 pasien urosepsis dalam kondisi hidup dan 7 pasien meninggal dunia. Rerata kadar presepsin pada pasien meninggal lebih tinggi dibanding pasien yang hidup namun tidak berbeda secara signifikan (4405 ± 4664 banding 4042 ± 2643, p=0.259) sedangkan rerata kadar procalcitonin pada pasien yang meninggal lebih tinggi dibanding pasien yang hidup dengan perbedaan yang signifikan (7.68 ± 6.81 banding 3.27 ± 2.74, p=0.013). Dengan nilai titik potong ≥2.24 ng/ml, procalcitonin dapat memprediksi mortalitas dalam observasi selama 28 hari dengan sensitivitas 71.4% dan spesifisitas 47.8%.Simpulan: Presepsin tidak dapat digunakan untuk menentukan prognosis pada pasien urosepsis. Procalcitonin menunjukkan korelasi yang signifikan terhadap outcome urosepsis sehingga dapat digunakan untuk menentukan prognosis pada pasien urosepsis.

Kata kunci: Urosepsis, prognosis, mortalitas, presepsin, procalcitonin.

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INTRODUCTION

Urosepsis is defined as sepsis caused by infection of the urinary tract.[1-3] Sepsis is a life-threatening organ dysfunction resulting from dysregulated host response to infection.[4] In urosepsis, as in other types of sepsis, the dysregulation of host response to infectioncan progress into severe sepsis and septic shock which correlates with increase risk of mortality.

The incidence rate of sepsis has increased about 8.7% per year.[5-7] There were 437 cases of sepsis

and 270 cases of severe sepsis per 100.000 population. Mortality occurred in 17% in sepsis and 26% in severe sepsis.[8] In a recent study in the UK within 10 years, the largest percentage of sepsis mortality occurred in urological disease by 17.8%, followed by respiratory tract disease 15.4%, gastrointestinal disease 14%, malignancy 13.4%, and blood stream infection 11.5%.[9] Retrospective Studyby Kusuma et al, at Soetomo Hospital between January 2013 and December 2014 found 171 urosepsis patients with mortality in 45 patients (26.3%).[10]

Blood culture as a gold standard for sepsis has limited usefulness for early detection of infection because it requires several days for results and often produces false-negative and bacterial contamination that will affect the diagnostic outcome.[11,12] Biomarkers can be used as an adjunct for the diagnosis of sepsis. C-reactive protein (CRP) has high sensitivity but low specificity whereas Procalcitonin (PCT) has better prognostic value than CRP.[13,14]

Presepsin (sCD14-ST) is a promising new sepsis biomarker in early sepsis diagnosis. It can assess the severity and predict the outcome/ prognosis in septic patients compared to other biomarkers such as CRP and procalcitonin.[12,15,16]

OBJECTIVE

There is currently no research that assesses the prognosis of urosepsis patients using presepsin and procalcitonin. Therefore, this study aim to evaluate the prognostic value of presepsin and procalcitonin in patient with urosepsis.

MATERIAL & METHODS

This study was performed at Soetomo Hospital Surabaya.Patients who fulfilled the criteria for urosepsis at Soetomo Hospital Surabaya were enrolled. The inclusion criteria were the presence of urosepsis and agreed to be involved in this study. The exclusion criteria were the presence of sepsis from another organ system, evidence of decreased immunity, received prior antibiotic therapy within 2 weeks, refused any standard treatment.

All patients who had fullfiled the sample criterias were assessed for SOFA scores, mean arterial pressure (MAP), blood leukocytes, blood urea nitrogen (BUN), creatinine serum, PaO2/FiO2, total bilirubin, urinalysis, presepsin, procalcitonin (PCT), and microbiological examination. Each patient was treated with standard therapy for urosepsis according to the European Association of Urology (EAU) guidelines. All patients were followed up until 28th day of admission. Patients were assessed for prognosis/outcome on the last day with provision for survive or non-survive. Then a statistic test was performed to determine the correlation between presepsin and PCT levels on the prognosis/outcome of the urosepsis patients with logistic regression test using software SPSS 23.

RESULTS

This study was performed at Soetomo Hospital Surabaya from August – November 2017. There were 30 urosepsis patients included in this study. The average age was 48.3 years (range 21–77 years). Most of the patient were male 18 patients (60%), while the female were 12 patients (40%) (table 1).

Mostly the patients of this study diagnosed with urolithiasis with 43.33% (renal stone 30%, ureteral stone 10%, and bladder stone 3.33%). The other were urosepsis patients with blood clot retention caused by malignancies 20%, retroperitoneal abscess 13.33%, stenosis of ureteropelvic junction 6.66%, Fournier gangrene 6.66%, urethral stricture 3.33%, vesicorectal fistula 3.33% and, testes carcinoma 3.33% (table 2).

Microbiological examination was done in all samples including blood culture and urine culture. We also performed pus culture in 6 patients. The result showed that Escherischia coli was the dominant bacteria that caused urosepsis in this study (table 3).

In this study there were 23 (76.67%) survivors and 7 (23.33%) nonsurvivors. From 23 survivors consist of 15 male patients and 8 female patients. While from 7 nonsurvivors consist of 3 male patients and 4 female patients. Presepsin levels were higher in nonsurvivor than survivor, but the correlation was not significant (p=0.446). Procalcitonin levels in this study were significantly higher in nonsurvivor than survivor (p=0.039) (table 4).

Receiver operating characteristic (ROC) curve showed the ability of procalcitonin to predict mortality in urosepsis patients at the time of 28 day follow up. The Area Under Curve (AUC) was 0.64 (95% CI: 0.319-0.960). Procalcitonin by cut-off value of ≥ 2.24 ng/ml predict mortality in urosepsis with sensitivity 71.4% and specificity 47.8% (Figure 1).

Table 1. Patients characteristics.

Characteristic	Value	Amount	
		n	%
Sex			
Male	-	18	60
Female	-	12	40
Age (years)	48.3 (21 – 77)	30	100
Leucocyte (/ml)	19.189 (5.900 – 42.690)	30	100
SOFA Scores	4.23 (2 – 9)	30	100
PaO_2 / FiO_2 (mmHg)	370.6 (50 – 642)	30	100
Platellete ($x10^3$/ml)	420 (154 – 993)	30	100
Total Bilirubin (mg/dl)	1.13 (0.14 – 5.90)	30	100
MAP (mmHg)	91.43 (65 – 132)	30	100
GCS	15*	30	100
Creatinine serum (mg/dl)	7.31 (0.70 – 30.97)	30	100

* Constant

Table 2. Description of sample study based on diagnosis.

Diagnosis	Amount	Percentage
Urolithiasis	13	43.33%
Renal stone	9	30%
Ureteral stone	3	10%
Bladder stone	1	3.33%
Blood clot retention	6	20%
Cervix carcinoma	4	13.33%
Bladder carcinoma	2	6.66%
Retroperitoneal abscess	4	13.33%
Stenosis UPJ	2	6.66%
Fournier gangrene	2	6.66%
Urethral stricture	1	3.33%
Vesicorectal fistula	1	3.33%
Testis carcinoma	1	3.33%
Total	30	100%

Table 3. Microbiological examination.

Microorganism	Urine	Pus	Blood
Escherichia coli	8	3	4
Proteus mirabilis	2	-	1
Staphylococcus hominis	1	-	1
Klebsiella pneumonia	2	-	1
Pseudomonas aeroginosa	3	-	2
Enterococcus faecium	1	1	-
Streptococcus spp	1	1	-
Acinetobacter spp	1	-	-
Sterile	11	1	21
Total	30	6	30

Table 4. Outcome characteristics based on clinical data and biomarker.

Characteristics	Survivor	Nonsurvivor	P value**
Sex	23	7	
Male	15 (50)*	3(10)*	
Female	8 (26.67)*	4 (13.33)*	
Age (years)	49.09 ± 13.36	45.71 ± 13.41	0.604
Leucocyte (/ml)	18.92 ± 9.3	20.06 ± 5.58	0.820
SOFA score	4.22 ± 1.59	4.29 ± 1.60	0.422
Creatinine serum (mg/dl)	7.45 ± 7.82	6.85 ± 5.35	0.568
Presepsin (pg/ml)	4042 ± 2643	4405 ± 4664	0.446
Procalcitonin (ng/ml)	3.27 ± 2.74	7.68 ± 6.81	0.039

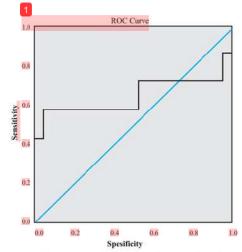* Percentage (%)
** logistic regression

Figure 1. ROC curve of procalcitonin.

DISCUSSION

The characteristics of urosepsis patients in this study 60% were male, and the average patient age was 48.3 years. This was similar with another sepsis study that found male were more dominant.[17] However the percentage of mortality associated with sepsis were higher in females than males and this also consistent with another study.[13,14,18]

SOFA score, leucocyte, and creatinine serum levels did not show significant correlation with outcome in urosepsis patients, although the value were more higher in nonsurvivor than survivor, except creatinine serum. This result similar with the previous study.[15,16,19]

Urosepsis in this study mostly caused by urinary obstruction resulted from urolithiasis 43.33% (renal stone 30%, ureteral stone 10%, and bladder stone 3.33%). The other were urosepsis patients with blood clot retention caused by malignancies 20%, retroperitoneal abscess 13.33%, stenosis of ureteropelvic junction 6.66%, Fournier gangrene 6.66%, urethral stricture 3.33%, vesicorectal fistula 3.33% and, testes carcinoma 3.33%. Based on study by serniak et al, from 205 analyzed case histories of urosepsis, 43% resulted from urolithiasis, 25% from prostatic adenoma, 18% from urologic malignancies, and 14% suffered from other urologic diseases.[3]

Initial presepsin levels were higher in nonsurvivor than survivor, but the correlation was not significant (p=0.446). Therefore presepsin can not be used to determine the prognosis of urosepsis. This result is different with previous studies which performed on other sepsis condition.[19-21] Masson et al reported mean values of initial presepsin in nonsurvivor was 2269, significantly higher than in survivor 1184. This contradiction may be caused by the difference of sample criteria.

Chenevier et al reported that presepsin was increased significantly in patient aged >70 years than in younger and also increased in the patient with kidney dysfunction (eGFR<60ml/min/1.73m²).[22] Older patient can suffered from glomerulosclerosis which can increase the presepsin level. In this study the majority of the urosepsis patients also suffered from kidney dysfunction. As presepsin is a 13kDa protein, it is freely filtered by the glomerolus and almost completely reabsorbed and catabolized within proximal tubular cells, with that result in

patient with kidney dysfunction the presepsin level will be found increased although there were no sepsis condition.[22] Therefore the results of presepsin levels in this study which different from the other might be caused by the sample age and kidney dysfunction.

In this study initial procalcitonin significantly higher in nonsurvivor than in survivor. Procalcitonin levels has correlation in the outcome of urosepsis patients (p=0.039). This result is similar with previous study.[23-26] ROC curve showed the ability of procalcitonin to predict mortality in urosepsis patients at the time of 28 day follow up. The Area Under Curve (AUC) was 0.64 (95% CI: 0.319-0.960). Procalcitonin by cut-off value of ≥2.24 ng/ml can predict mortality in urosepsis with sensitivity 71.4% and specificity 47.8%. From the meta-analysis study by Liu et al, reported the prognostic value of procalcitonin in adult patient with sepsis. The sensitivity varied between 55-100% and the specificity between 14.4 - 91.5%.[27]

Procalcitonin has widely observed as diagnostic and prognostic biomarker for sepsis. Several researches showed different results depends on sample characteristics. Currently there is no study which evaluate the prognostic value of procalcitonin only in urosepsis patients. The study about procalcitonin had been performed in sepsis patient caused by pneumonia and the results was procalcitonin could predict outcome in sepsis patients.[28,29] In other study procalcitonin found to be strongest predictor in mortality on ventilator-associated pneumonia.[30]

Procalcitonin level had been investigated in patients with kidney dysfunction by Meisner et al in 2000. The research reported that the plasma elimination rate of procalcitonin does not depend on renal function and the age of the patients.[31] Based on that data, procalcitonin measurements can provide valid information used for prognostic reasons in patients with different age and with kidney dysfunction as it showed in this study.

CONCLUSION

Initial presepsin value has no significant correlation with outcome of urosepsis patients so presepsin can not be used to determine the prognosis of urosepsis. On the other side initial procalcitonin significantly correlated with outcome of urosepsis patients so procalcitonin can be used to determine the prognosis of urosepsis.

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