Prognostic value of pro-BNP compared to procalcitonin as markers in patients with severe sepsis

Fayed AM[1], Megahed MM[1], Mahros AAEA[1], ELRakshy YM[2] and Mohammed AH[1]

[1]Department of Critical Care Medicine, Faculty of Medicine, University of Alexandria, Alexandria, Egypt.
[2] Department of Cardiology and Angiology, Alexandria University students Hospital, Alexandria, Egypt.
amira_bekh@yahoo.com

Abstract: Background: increased level of pro brainnatriuretic peptide (pro-BNP) has been defined as a predictor of left ventricular dysfunction. Different biomarkers had been used as prognostic markers of severe sepsis one of them was procalcitonin (PCT), but there was no information available about the prognostic value of pro brainnatriuretic peptide in those patients. **Objective:** To assess the prognostic value of pro brainnatriuretic peptide in patients with severe sepsis on day one and day three of ICU admission. We compared values of pro-BNP and PCT on day one and day three. **Patients & Methods:** This was a prospective observational study in 25 consecutive patients admitted to ICU with preliminary diagnosis of severe sepsis. Echocardiography was done to rule out left ventricular dysfunction. Cultures from suspected sites of infection were done. The blood levels of CRP, procalcitonin, and pro-BNP on day one and day three were measured for all patients. **Result:** Pro-BNP was measured on day one in survivor group of patients it was 102.0-16791.0pg/ml, while on day three it was 60.0-10200.0 pg/ml. While in non-survivors the pro-BNP level on day one was 361.0-24244.0 pg/ml and on day three it was 502.0-28560.0pq/ml. Level of pro-BNP showed statistically significant difference between that of day one and day three in survivor and non-survivor groups of patients, with (p=0.002 and p=0.004 respectively). Procalcitonin level in survivors was 0.72-17.80 ng /ml on day one and was 0.40-10.10ng/ml on day three, while in nonsurvivors PCT level was 0.50-12.40ng/ml on day one, and on day three it was 0.40-15.1ng/ml. PCT level showed statistically significant difference between day one and day three in survivors and nonsurvivors (p= 0.002and p=0.005 respectively). By comparing the percentage of change of pro-BNP and PCT and application of ROC curve we found that the specificity of percentage of change of pro-BNP was 100% which was higher than the specificity of percentage of change of PCT was 91.67%, while the sensitivity of both biomarkers was the same. **Conclusion:** Pro-BNP is a good prognostic marker of severity in patients with severe sepsis, the sensitivity and specificity of pro-BNP were comparable to those of PCT in the prognosis of severe sepsis. The predicting ability of APACHI II score improved when combined with pro-BNP and PCT levels.
[Fayed AM, Megahed MM, Mahros AAEA, EL Rakshy Y M and Mohammed AH. **Prognostic value of pro-BNP compared to procalcitonin as markers in patients with severe sepsis.** *J Am Sci* 2016;12(6):77-85]. ISSN 1545-1003 (print); ISSN 2375-7264 (online). http://www.jofamericanscience.org. 10. doi:10.7537/marsjas12061610.

Key words: Pro-BNP, procalcitonin, Prognostic value.

1. Introduction

Bacterial infection and sepsis are common problems in critically ill patients. Almost 1.5 million people in northern America and, another 1.5 million people in northern Europe present annually with severe sepsis and/or septic shock with an estimated mortality of 35-50%. (Becker *et al.,* 2009).

ACCP/SCCM Consensus Conference defined "sepsis" as SIRS plus infection, "severe sepsis" as sepsis associated with organ dysfunction, hypoperfusion or hypotension, and "septic shock" as sepsis with arterial hypotension despite "adequate" fluid resuscitation. (American College of Chest, 1992; Bone *et al.,* 1992)

In fact, sepsis compromises all levels of the cardiovascular system, resulting in cardiac dysfunction, vascular dysregulation, and microcirculatory damage. (Vincent, 2011)

Myocardial contractility is compromised shortly after the induction of sepsis. (Bouhemad *et al.,* 2009) This finding is confirmed in septic patients when a reduced ejection fraction is observed by echocardiograph. (Ognibene *et al.,* 1988) The drop in myocardial contractility is accompanied by diastolic dilatation of the left ventricle, which causes the left ventricular end-diastolic volume to rise. This mechanism allows the heart to maintain a sufficient stroke volume despite impaired contractility. Septic patients without compensatory left ventricular dilatation have a significantly greater risk of death. (Parrillo *et al.,*1985) Cardiac dysfunction is reversible if the patient recovers from sepsis. (Vincent, 2011)

Pro-BNP is part of the family of natriuretic peptides (NPs) which is present in the brain, cardiac atria and ventricles (although there is a higher concentration expressed in the ventricles than atria) (Parrillo and Richards, 1985).

The NPs are released in response to myocardial stress and have several physiologic actions, the most important being (a) vasodilation; (b) promotion of natriuresis and diuresis; (c) inhibition of the sympathetic nervous system and of the renin-

angiotensin-aldosterone system, endothelins, cytokines, and vasopressin; (d) inhibition of the pathophysiologic mechanisms responsible for ventricular and vascular hypertrophy and remodeling; and (e) beneficial effects on endothelial dysfunction secondary to the atherosclerotic process, including blunting of shear stress and regulation of coagulation and fibrinolysis, as well as inhibition of platelet activation (Levin *et al.,* 1998; Maisel, 2003).

PCT is synthesized in various extrathyroidal neuroendocrine tissues. PCT is a precursor of the hormone calcitonin and is synthesized physiologically by thyroid C cells. In normal physiological conditions, PCT levels in the serum are low (<0.1 ng/mL). However, in bacterial infection Systemic PCT secretion is a component of the inflammatory response that appears to be relatively specific to systemic bacterial infections (Shehabi *et al.,* 2008; Dahab *et al.,* 2009).

Procalcitonin have been used as prognostic biomarker of severe sepsis (Nakamura *et al*., 2009).

Aim of the Work

The aim of the present work was to evaluate the prognostic value of pro-BNP in severe sepsis patients, and to compare between pro-BNP and procalcitonin as biochemical markers to assess patient with severe sepsis.

2. Patients and Methods

Patients:

The approval of the medical ethics committee of Alexandria faculty of Medicine was taken. An informed consent from the patients' next of kin was obtained before conducting the study.

This prospective observational study was carried out on 25 patients consecutively admitted to department of critical care medicine with the preliminary diagnosis of severe sepsis defined according to American college of chest physicians.

Inclusion criteria:

Patients who fulfilled the criteria of severe sepsis according to American college of chest physician' 1992; and International Sepsis Definition Conference were included (Levy *et al*., 2003).

Exclusion criteria:

1. Age <18 years.
2. Patients who were known to have heart failure.
3. Patients who were known to have left ventricular dysfunction (LVD).
4. Patients who were known to have renal failure.

Methods:

All the patients studies were subjected on admission to the followings:

- Demographic data: age and sex.
- Complete history taking: including the etiology of sepsis.
- Complete physical examination.
- Routine laboratory investigations.
- Arterial blood gasses were sampled in a heparinized syringe on admission.
- Acute Physiologic and Chronic Health Evaluation II scoring system (APACHE II) was calculated for all patients. They ranged from12.0–25.0.
- Sequential organ failure assessment score (SOFA score) was calculated on admission and on third day.
- Sepsis work-up included cultures from suspected sites of infection (blood, urine, and sputum).
- The blood level of C-reactive protein as a marker of sepsis on admission, and third day for patients with severe sepsis was analyzed by immunediffusion assay by using kits from Roche diagnostic company, Germany, using cobas 6000 device.
- The blood level of pro-BNP was measured on admission and on third day for patients with severe sepsis. It was collected in serum bottle and analyzed by chemiluminescence immunoassay using kits from Roche diagnostic company, Germany, using Cobas-E601 device.
- The blood level of Procalcitonin was measured on admission and on third day for patients with severe sepsis by using serum of the patient collected in serum bottle and analyzed by chemiluminescence immunoassay using kits from Roche diagnostic company, Germany, using Cobas-E601 device.
- Echocardiography was done on admission by using Echocrdiography Vivid 3, GE health care, milwaukee, WI, USA. Systolic dysfunction is defined as an LVEF less than 40 % (Maeder *et al.,* 2009).

Statistical analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. The significance of the obtained results were judged at the 5% level.

3. Results:

The baseline characteristic data of severe sepsis patientsregarding the age, sex, vital signs, laboratory investigation, arterial blood gasses (ABG), APACHE II score, SOFA score, echocrdiographic findings (EF%), outcome, CRP, PCT and pro-BNP levels day one and day three. Table (1).

Table (1): Demonstration of baseline characteristic in studied cases(n=25)

	No.	%
Sex		
Male	9	36.0
Female	16	64.0
Age (years)		
≤50	8	32.0
>50	17	68.0
Min. – Max.	27.0 – 85.0	
Mean ± SD	56.92 ± 13.34	
Median	60.0	
Past medical history		
History of DM	12	48.0
History of HTN	15	60.0
Respiratory tract infection	12	48.0
Urinary tract infection	7	28.0
Intraabdomial sepsis	2	8.0
Other sites	7	28.0
Culture		
I.Mini BAL	11	44.0
II. Urine	7	28.0
III. Blood	1	4.0
IV. Other	7	28.0
Outcome		
Survival	12	48.0
Died	13	52.0

Table (2): presentation of vital signs, laboratory findings and scores in studied patients(n=25)

	Min -Max	Mean ± SD	Median
Mean arterial blood pressure	39.0 – 100.0	62.08 ± 13.84	60.0
Heart rate	60.0 – 160.0	100.28 ± 23.62	96.0
Respiratory rate	18.0 – 40.0	30.40 ± 6.0	30.0
Temperature	36.0 – 40.0	38.01 ± 0.89	38.0
Haemoglobin	6.50 – 14.0	9.55 ± 2.11	9.40
White cell count	9.60 – 47.0	18.96 ± 7.58	17.60
Pletelet	65.0 – 505.0	242.88±117.35	240.0
Urea	8.0 – 272.0	114.0 ± 79.68	90.0
Creatinine	0.90 – 4.20	2.08 ± 0.89	1.90
Blood PH	7.19 – 7.43	7.33 ± 0.06	7.34
PCO_2	28.0 – 46.0	34.0 ± 4.49	34.0
PO_2	48.0 – 74.0	60.12 ± 7.57	61.0
HCO_3	11.50 – 20.0	15.50 ± 2.58	15.50
SGOT	10.0 – 300.0	56.56 ± 68.38	33.0
SGPT	11.0 – 350.0	67.20 ± 71.51	46.0
GCS	9.0 – 15.0	11.44 ± 2.08	11.0
APACHII	12.0 – 25.0	20.36 ± 3.16	21.0

Table (3): presentation of pro-BNP, CRP, PCT, SOFA score on day one and day three (n=25)

	Day 1	Day 3
Pro-BNP		
Min - Max	102.0 – 24244.0	60-28560.0
Mean ± SD	3435.4 ± 5433.8	3103.72±5634.02
Median	1906.0	1670.0
Z(p)	1.063 (0.288)	
CRP		
Min - Max	63.0 – 355.0	6.0 – 285.0
Mean ± SD	137.40 ± 62.31	140.96 ± 79.03
Median	120.0	130.0
Z(p)	0.215 (0.830)	
Procalcitonin		
Min - Max	0.50 – 17.80	0.40 – 15.10
Mean ± SD	5.08 ± 4.63	5.08 ± 4.84
Median	3.0	3.0
Z(p)	0.676	
SOFA		
Min - Max	7.0 – 14.0	5.0 – 18.0
Mean ± SD	10.80 ± 1.87	10.76 ± 3.98
Median	11.0	11.0
t(p)	0.676	

There was statistically significant positive correlation between level of pro-BNP and the outcome either on day one and day three P=0.002 and P= 0.004 respectively) for survivors and non-survivorsgroup of patients.

Table (4): Prognostic value of Pro- BNP

	Outcome		Z	*P*
	Survived	**Died**		
Day 1	**(n= 12)**	**(n= 13)**		
Min – Max	102.0 – 16791.0	361.0 – 24244.0		
Mean ± SD	3652.9 ± 4464.29	3234.5 ± 6379.08	1.523	0.128
Median	2226.00	1400.0		
Day 3	**(n= 12)**	**(n= 13)**		
Min – Max	60.0 – 10200.0	502.0 – 28560.0		
Mean ± SD	2365.3 ± 2668.76	3785.4 ± 7477.10	0.381	0.703
Median	1637.50	1855.0		
p_1	0.002*	0.004*		

There was also statistically significant positive correlation between level of procalcitonin and outcome on day one and day three either in survivor or non-survivors (p= 0.002 and p= 0.005 respectively).

Table (5): Prognostic value of Procalcitonin

	Out come		Z	*p*
	Survived	**Died**		
Day 1	**(n= 12)**	**(n= 13)**		
Min – Max	0.72 – 17.80	0.50 – 12.40		
Mean ± SD	5.03 ± 4.53	5.13 ± 4.91	0.435	0.663
Median	4.05	2.50		
Day 3	**(n= 12)**	**(n= 13)**		
Min – Max	0.40 – 10.10	0.40 – 15.10		
Mean ± SD	2.90 ± 2.69	7.10 ± 5.58	2.016*	0.044*
Median	2.10	5.60		
p_1	0.002*	0.005*		

By observing all patients in this study, levels of both biomarkers, pro-BNP and procalcitonin were changed in survivors and non-survivors groups of patients from day one to day three. This change was by increasing their levels in non survivors or by decreasing their levels in survivor group of patients.

The percent of change of the levels of both biomarkers showed statistically significant positive correlation with the clinical out come.

Table (6): Relation between clinical outcome with percent of change in levels of pro-BNP and PCT.

% of Change	Out come		Z	*p*
	Survived (n = 12)	**Died (n = 13)**		
Pro- BNP				
Min – Max	↓21.60 - ↓41.18	↓45.71 -↑144.77		
Mean ± SD	↓32.45 ± 6.15	↑35.46 ± 48.40	3.318*	0.001*
Median	↓33.24	↑39.06		
Procalcitonin				
Min – Max	↓26.67 - ↓75.0	↓53.33 - ↑520.0		
Mean ± SD	↓43.50 ± 14.42	↑106.01 ± 157.45	3.264*	0.001*
Median	↓41.63	↑30.0		

ROC curve was applied to change in levels of procalcitonin and pro-BNP and was found the AUC for percent of change of pro-BNP was 0.891with sensitivity 84.62% and specificity 100%,while the AUC for percent of change of procalcitonin was 0.885with sensitivity 84.62%and specificity 91.67%.

Table (7): Agreement (sensitivity, specificity, and accuracy) for % of change pro-BNP and procalcitonin

% of change	AUC	p	Sensitivity	Specificity	PPV	NPV	Accuracy
Pro BNP (>↑14 %)	0.891*	0.001	84.62	100.0	100.0	85.71	92.0
Procalcitonin (>↑26 %)	0.885*	0.001	84.62	91.67	91.67	84.62	88.0

Table (8): Relation between Percent of change in either pro-BNP or Procalcitonin and outcome

	Outcome					*P*
	Survived (n = 12)		Died (n =13)			
	No.	%	No.	%		
PRO – BNP						
Decreased	12	100.0	2	15.4	18.132*	<0.001*
Increased	0	0.0	11	84.6		
Procalcitonin						
Decreased	12	100.0	2	15.4	18.132*	<0.001*
Increased	0	0.0	11	84.6		

χ^2: Chi square test

There was statistically significant positive correlation between the percent of change of procalcitonin and pro-BNP and clinical outcome.

ROC curve applied to pro-BNP in day three to evaluate cut off point in day 3 it was found that AUC 0.545 with cut-off value 2000 pg /ml**.**

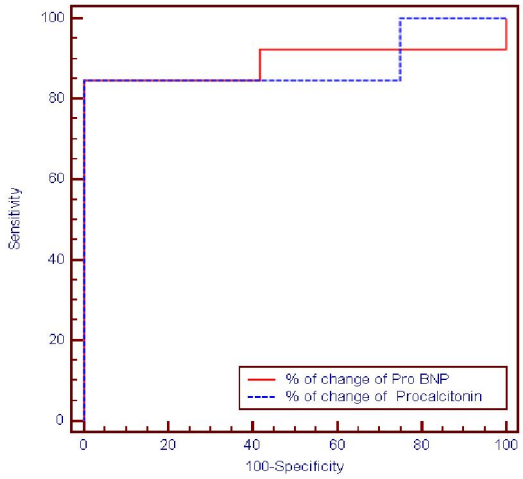

Figure (1): Agreement (sensitivity, specificity, and accuracy) for % of change pro-BNP and procalcitonin

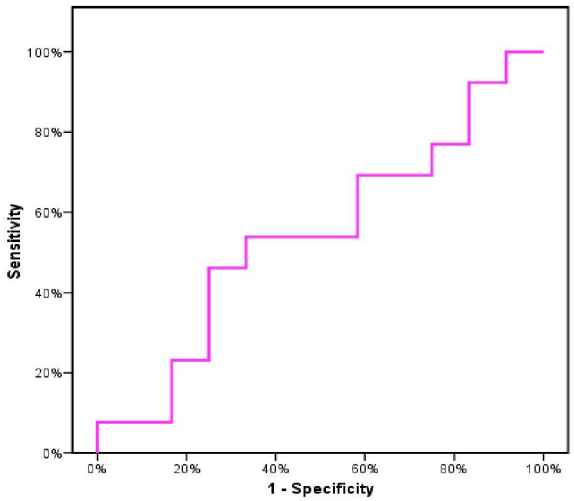

Figure (2): Cut of value of pro-BNP

Table (9):Cut of value of pro-BNP

	AUC	p	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
PRO-BNP for 3rd day	0.545	0.703	2000	46.15	75.0	66.67	56.25	60.0

It was observed that there were statistically significant positive correlation in patients who had a positive history of diabetes and their clinical outcome (p=0.003).

Table (10): Relation between outcomes and history of diabetes

	Outcome				χ^2	*p*
	Survived (n=12)		Died (n=13)			
	No.	%	No.	%		
History of diabetes						
Positive	2	16.7	10	76.9	9.077*	0.003*
Negative	10	83.3	3	23.1		

χ^2 and p values for Chi-square test; *: Statistically significant at $p \leq 0.05$

It was found that there was a statistically significant negative correlation between ejection fraction and pro-BNP level in day one (*p*-value = <0.001).

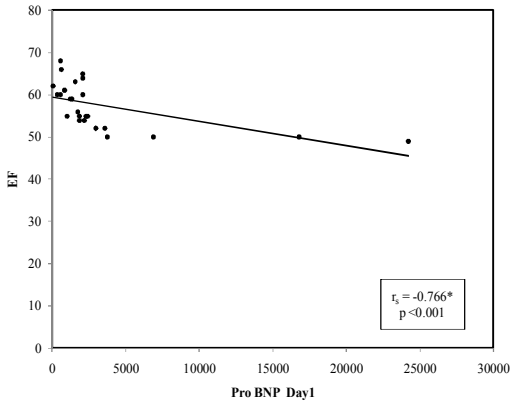

Figure (3): Relation between pro-BNP level and EF.

Table (11): Correlation between pro- BNP level in day 1 and EF

	Pro- BNP Day1	
	r_s	*P*
EF	-0.766*	<0.001*

It was observed that there was no statistically significant correlation between APACHE II, CRP, and WBCs.

It was also observed that there was no statistically significant correlation between the change in procalcitonin level and CRP either on day one or on day three.

Also, there was no statistically significant correlation between CRP and pro-BNP either in day one or in day three.

There was a statistically significant negative and positive correlation between level of SOFA score and clinical outcome in survivor and in non survivors groups (*p*=0.001, *p*=0.001 respectively).

Table (12): Correlation between WBCs and APACHE II and CRP level in total cases

	WBCS	
	r_s	p
APACHE II	-0.139	0.506
CRP day1	-0.078	0.712
CRP day 3	-0.178	0.395

r_s: Spearman coefficient

Table (13): Correlation between CRP level and Procalcitonin level on day one and day three

	Correlation between CRP and procalcitonin	
	r_s	*P*
Day 1	0.314	0.127
Day 3	0.229	0.270

r_s: Spearman coefficient

Table (14): Correlation between CRP level and Pro-BNP level on day one and day three

	Correlation between CRP and pro BNP	
	r_s	*p*
Day 1	0.185	0.375
Day 3	0.202	0.332

r_s: Spearman coefficient

Table (15): Prognostic value of SOFA score

	SOFA score		t	*p*
	Survived	**Died**		
Day 1	**(n= 12)**	**(n= 13)**		
Min – Max	8.0 – 12.0	7.0 – 14.0		
Mean ± SD	10.42 ± 1.24	11.15 ± 2.30	0.984	0.336
Median	10.0	11.0		
Day 3	**(n= 12)**	**(n= 13)**		
Min – Max	5.0 – 10.0	11.0 – 18.0		
Mean ± SD	7.08 ± 1.56	14.15 ± 1.86	10.226*	<0.001*
Median	7.0	14.0		
p_1	<0.001*	<0.001*		

t, p: t and p values for Student t-test; p_1: p value for paired t test for comparing between day 1 and day 3 in each group; *: Statistically significant at $p \leq 0.05$

4. Discussion

In this study the mean age of patients admitted to ICU with severe sepsis was 56.92 ±13.3 years. This mean age was close to that detected by Charpentier*et al.,* 2004 (55± 016.3 years) and Brueckmann et al., 2005 (56 ± 15.7 years).

This was possibly because elderly individuals were at an increased risk of developing sepsis compared to younger patients. This risk steadily increased with age, because of frequent comorbidities, institutionalization, declining performance status, and altered immune function. The clinical presentation of older patients with sepsis was often atypical, leading to a difficult and delayed diagnosis. Although increasing age appeared to confer a high risk of death due to severe sepsis. (Girard *et al.,* 2005)

Diabetics had a higher incidence of death compared to nondiabetic patients with a percent of 76.9 % (p=0.003) this was in agreement with the result of Bertoni *et al.,* 2001; Muller *et al.,* 2005; Koh *et al.,* 2012.

Diabetes predisposes to infection due to abnormalities of the host response, particularly in neutrophil chemotaxis, adhesion and intracellular killing, defects that have been attributed to the effect of hyperglycemia. There was also evidence for defects in humoral immunity, and this could have played a larger role than previously recognized.

Respiratory tract infection and urinary tract infection were the most common primary sites of infection with an incidence of 48% and 28% respectively, while intraabdominal sites accounted for 8% and other sites of infection like blood stream, gluteal abcess, psoas abcess constituted about 28%. Respiratory tract infection was primary site of infection in a study by Brueckman *et al., (2005)* and accounted for 49% of infection.

Different scores were applied to patients on our study to evaluate the severity of illness. One of these scores was by APACHI II score. This score included the person's age, underlying condition, and various physiologic variables for estimation of risk of non survival in patient with severe sepsis. Which ranged from 12-25. This range was close to what was observed by Brueckmann *et al.,* 2005. 26 (19–30).

Another scoring system was applied to patients in the study, which was SOFA score it was 10.8±1.87. This level was the highest level detected by Acharya et al., 2007 who applied SOFA score in prediction of mortality in patient with SIRS, They showed that high SOFA score of ≥ 11 predict mortality.

The pro-BNP level was measured in the patients on day one and on day three after excluding left ventricular dysfunction. As pro-BNP was released mainly from ventricles, it was found that this level increased in patient with severe sepsis who didn't survive from first day to third day. However in patients who survived, the pro-BNP level was decreased in day three. So there was statistically significant correlation between pro-BNP and outcome. In survived p=0.002, while in non-survivor p= 0.004.

A cutoff value of pro-BNP for prognosis of severe sepsis according to ROC curve was 2000 pq /ml with sensitivity of 46.15 % and specificity of 75.0%.

This result was also detected by Li *et al.,* 2013 which was a systematic review and meta-analysis that suggested that an elevated pro-BNP level was a powerful predictor of mortality in patients with sepsis. This test appeared to represent a rapid and relatively in expensive method to improve mortality prediction in septic patients.

The increased level of pro-BNP in non-survivors was explained by dysfunction of the cardiovascular system in response to systemic inflammation. Hence, pro-BNP could be used as a predictor of myocardial depression secondary to sepsis. This was like wise detected by Brueckmann *et al.,* 2005. They studied 57 patients presenting with severe sepsis, selected according to the criteria of the American College of

Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) consensus conference, 1992. They observed that pro-BNP level increased in patients of severe sepsis due to myocardial depression and it also was used as useful laboratory marker to predict time to death in patient with severe sepsis.

Procalcitonin was another biomarker, it had been widely used for prognosis of severe sepsis as was also confirmed in our study. Procalcitonin blood levels were differed significantly on day one and on day three in survivors and non-survivors with severe sepsis (p=0.002, p=0.005 respectively).

Procalcitonin level increased from day one to day three in non survivors, while it decreased in survivors. This change in the level of procalcitonin was by 26% either by being increased in non-survivor or by being decreased in survivors. Application of ROC curve to this percent showed sensitivity of 84.62%, and specificity of 91.67%. There was statistically significant correlation between procalcitonin level and mortality.

This result was also detected by Karlsson *et al.,*2010; Azevedo *et al.,* 2012; Poddar *et al.,* 2015.

Karlsson*et al.,* 2010 conducted a prospective observational study in about 242 patient with severe sepsis. Procalcitonin level was sampled on day one and on day three, they showed that a decrease in procalcitonin level was associated with favorable outcome.

We observed that there was no statistically significant correlation between APACHE II score and CRP level on day one as detected by Wilhelm *et al.,* 2012; Hegazy *et al.,* 2014

Hegazy *et al.,* 2014 conducted a prospective observational study on 138 patients with severe sepsis. They found that there was no statistically significant correlation between APACHE II score and CRP. It was also found that there was no statistically significant correlation between the change in CRP level and procalcitonin level. This was due to the fact that CRP wasn'tsensitive to sepsis-like procalcitonin and it's elevation was affected by many other conditions that caused inflammation and not mainly caused by sepsis. This result was also noted by Suberviolae *et al.,* 2012; He verified that PCT is an earlier and more specific marker of infection than CRP. The PCT values increased faster than those of CRP in response to infection and likewise, decrease faster as infection subsided.

Limitation of the study:

The results of this study clearly showed that pro-BNP was a promising biomarker in prognosis of severe sepsis, yet the study had some limitations. First, the study was a single-center study and the sample size was small and heterogeneous due to financial constraints. Second, infection was established on the basis of clinical features, laboratory findings, and imaging tests according to SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference and not according to culture results which might have introduced some bias.

5. Conclusion

Pro-BNP is a good prognostic biomarker in patients with severe sepsis, The specificity and sensitivity of pro BNP in prognosis of severe sepsis were comparable to those of PCT, Procalcitonin is a good prognostic marker of severe sepsis than CRP Lastly The predicting ability of APACHI II score improved when combined with pro-BNP and PCT levels.

References

1. Acharya, S.P., Pradhan, B., and Marhatta, M.N., 2007, Application of “the sequential organ failure assessment (SOFA) score” in predicting outcome in ICU patients with SIRS: Kathmandu Univ Med J (KUMJ), v. 5, p. 475-483.
2. American College of Chest, 1992, Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis: Crit Care Med, v.20, p. 864-874.
3. Azevedo, J.R., Torres, O.J., Czeczko, N.G., Tuon, F.F., Nassif, P.A., and Souza, G.D., 2012, Procalcitonin as a prognostic biomarker of severe sepsis and septic shock. Rev Col Bras Cir, v. 39, p.456-461.
4. Becker, J.U., Theodosis, C., Jacob, S.T., Wira, C.R., and Groce, N.E., 2009, Surviving sepsis in low income and middle-income countries: New directions for care and research: Lancet Infect Dis, v.9, p.577–582.
5. Bertoni, A.G., Saydah, S., and Brancati, F.L., 2001, Diabetes and the risk of infection-related mortality in the U.S: Diabetes Care, v. 24, p. 1044–1049.
6. Bone, R.C., Balk, R.A., Cerra, F.B., Dellinger, R.P., Fein, A.M., Knaus, W.A., Schein, R.M., and Sibbald, W.J., 1992, Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee American College of Chest Physicians/Society of Critical Care Medicine: Chest, v. 101, p.1644-1655.
7. Bouhemad, B., Nicolas-Robin, A., Arbelot, C., Arthaud, M., Feger, F., and Rouby, J.J., 2009, Acute left ventricular dilatation and shock-induced myocardial dysfunction: Crit Care Med, v.37, p.441-447.

8. Brueckmann, M., Huhle, G., Lang, S., Haase, K.K., Bertsch, T., Weiss, C., Kaden, J.J., Putensen, C., Borggrefe, M., and Hoffmann, U., 2005, Prognostic value of plasma Nterminalpro-brain natriuretic peptide in patients with severe sepsis. Circulation, v.112, p. 527-534.
9. Charpentier, J., Luyt, C.E., Fulla, Y., Vinsonneau, C., Cariou, A., Grabar, S., Dhainaut, J.F., Mira, J.P. and Chiche, J.D., 2004, Brain natriuretic peptide: A marker ofmyocardial dysfunction and prognosis during severe sepsis: Crit Care Med, v. 32, p. 660-665.
10. Dahaba, A.A. and Metzler, H., 2009, Procalcitonin's role in the sepsis cascade. Is procalcitonin a sepsis marker or mediator: Minerva Anestesiologica, v. 75, p.447-452.
11. Girard, T.D., Opal, S.M., and Ely, E.W., 2005, Insights into severe sepsis in older patients: from epidemiology to evidence-based management. Clin Infect Dis, v. 40(5), p.719-727.
12. Hegazy, M.A., Omar, A.S., Samir, N., Moharram, A., Weber, S., and Radwan, W.A., 2014, Amalgamation of procalcitonin, C-reactive protein, and sequential organ failure scoring system in predicting sepsis survival: Anesth Essays Res, v. 8, p. 296-301.
13. Karlsson, S., Heikkinen. M., Pettilä, V., Alila, S., Väisänen, S., Pulkki, K., Kolho, E., and Ruokonen, E., 2010, Predictive value of procalcitonin decrease in patients with severe sepsis: Crit Care, v.14, p. R205.
14. Koh, G.C., Peacock, S.J., van der Poll, T., and Wiersinga, W.J., 2012, The impact of diabetes on the pathogenesis of sepsis: Eur J Clin Microbiol Infect Dis, v. 31, p. 379-388.
15. Levin, E.R., Gardner, D.G., and Samson, W.K., 1998, Natriuretic peptides: N Engl J Med, v. 339: p. 321–328.
16. Levy, M.M., Fink, M.P., Marshall, J.C., Abraham, E., Angus, D., Cook, D., Cohen, J., Opal, S.M. Vincent, J.L., and Ramsay, G., 2003, 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference: Intensive Care Med, v. 29, p.530-538.
17. Li, N., Zhang, Y., Fan, S., Xing, J., and Liu, H., 2013, BNP and NT-proBNP levels in patients with sepsis: Front Biosci (Landmark Ed), v. 18, p.1237-1243.
18. Maeder, M.T., and Kaye, D.M., 2009, Heart failure with normal left ventricular ejection fraction: J Am Coll Cardiol, v. 53, p, 905-918.
19. Maisel, A.S., 2003, The diagnosis of acute congestive heart failure: role of BNP measurements: Heart Fail Rev, v. 8, p.327–334.
20. Martinez-Rumayor, A., and Richards, A.M., 2008, Biology of the natriuretic peptides. Am J Cardiol, v. 101, p. 3-8.
21. Muller, L.M., Gorter, K.J., Hak, E., Goudzwaard, W.L., Schellevis, F.G., Hoepelman, A.L., and Rutten, G.E., 2005, Increased risk of common infections in patients with type 1 and type 2 diabetes mellitus: Clin Infect Dis, v. 41, p. 281–288.
22. Nakamura, A., Wada, H., Ikejiri, M., Hatada, T., Sakurai, H., Matsushima, Y., Nishioka, J., Maruyama, K., and Isaji, S., 2009, Takeda Efficacy of procalcitonin in the early diagnosis of bacterial infections in a critical care unit: Shock, v. 31, p. 586–591.
23. Ognibene. F.P., Parker, M.M., Natanson, C., Shelhamer, J.H., and Parrillo, J.E., 1988, Depressed left ventricular performance. Response to volume infusion in patients with sepsis and septic shock: Chest, v. 93, p.903-910.
24. Parrillo, J.E., Burch, C., Shelhamer, J.H., Parker, M.M., Natanson, C., and Schuette, W., 1985, A circulating myocardial depressant substance in humans with septic shock. Septic shock patients with a reduced ejection fraction have a circulating factor that depresses in vitro myocardial cell performance: J Clin Invest, v.76, p. 1539-1553.
25. Poddar, B., Gurjar, M., Singh, S., Aggarwal, A., Singh, R., Azim, A., and Baronia, A., 2015, Procalcitoninkinetics as a prognostic marker in severe sepsis/septic shock: Indian J Crit Care Med, v.19, p. 140-146.
26. Shehabi, Y., and Seppelt, I., 2008, Pro/con debate: is procalcitonin useful for guiding antibiotic decision making in critically ill patients: Crit Care, v.12:p.211-216.
27. Suberviola, B., Castellanos-Ortega, A., Gonzalez-Castro, A., Garcia-Astudillo, L.A., Fernandez-Miret, B., 2012, Prognostic value of procalcitonin, C-reactive protein and leukocytes in septic shock: Med Intensiva, v. 36,177-184.
28. Vincent, J.L., 2011, Textbook of critical care: 6thed. Philadelphia: Elsevier/Saunders.
29. Wilhelm, J., Hettwer, S., Hammer, D., Schürmann, M., Christoph, A., Amoury, M. Klöss, T., Finke, R., Ebelt, H., and Werdan, K., 2012, Outcome prediction using clinical scores and biomarkers in patients with presumed severe infection in the emergency department: Med Klin Intensivmed Notfme, v. 107, p.558-563.

5/18/2016