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Presepsin: A New Biomarker for Sepsis?

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Abstract

The number of different biomarkers used in patients admitted in ICU for SIRS, sepsis and septic shock is extremely high, but no single one has high specificity and sensitivity so it has been suggested that combinations of several biomarkers may be more effective than single biomarkers. The aim of this study was to investigate the use of Presepsin, a soluble fragment of the cluster of differentiation marker protein 14 (CD14), involved in pathogen recognition by innate immunity. In selected ICU patients and cardiac surgery patients we tried to investigate the diagnostic and prognostic value of Presepsin (PSP) compared to Procalcitonin (PCT), C-reactive Protein (CRP), White blood cells (WBC) and IL6. The assay for biomarkers were performed on whole venous or arterial blood, on days 1, 2, 4, and 7 from admission of patients eligible for the study. The diagnostic accuracy of the biomarkers studied was evaluated using the areas under the curve (AUCs). The accuracy of all biomarkers decreases with time until they are no longer useful. The use of Presepsin (PSP) to early detect the presence of infection could improve patient survival and outcome in distinguishing sepsis from SIRS in intensive care unit.

Keywords: Sepsis; Septic Shock; Biomarker; Presepsin; Procalcitonin; C-reactive Protein; Interleukin-6

Aim

Each year about 13 million people become ill with sepsis and more than 30% dies. Only 50% of patients with sepsis receives best standard of care with an early diagnosis and immediate therapeutic intervention. As reported by Vincent: [10].

- More than 170 different biomarkers have been assessed for potential use in sepsis, more for prognosis than for diagnosis.
- None has sufficient specificity or sensitivity to be routinely employed in clinical practice.
- Combinations of several biomarkers may be more effective than single biomarkers, but this requires further evaluation.

Early diagnosis and timely initiation of appropriate antibiotic therapy and resuscitation are keys to improve survival. Although many laboratory biomarkers are available for the diagnosis of sepsis, only few markers have proven to be beneficial in differentiate sepsis infectious disease and systemic inflammatory response syndrome of non-infectious origin. The most commonly used biomarkers are Plasma C-reactive protein (CRP) or Procalcitonin (PCT). Procalcitonin (PCT), as a biomarker in sepsis, has limited specificity and can also be elevated in other scenarios of systemic inflammatory response syndrome (SIRS). Presepsin is a soluble fragment of the cluster of differentiation marker protein 14 (CD14) involved in pathogen recognition by innate immunity. Available literature suggests that levels of presepsin are significantly higher in septic patients than in healthy individuals [1].

Cardiac surgery is specific because of the use of cardiopulmonary bypass machine (CPB), during which patients are in relative hypotensive state, moderate hypothermia leads to moderate systemic inflammatory response. This inflammatory response attenuates quickly after surgery. Presepsin levels are high in patients with acute heart failure and acute coronary syndrome without signs of infection. The use of volatile anesthetics and intravenous anesthetic-propofol, can lead to decreased expression of inflammatory biomarkers, which is important in interpreting results.

The aim of this study is to investigate the diagnostic and prognostic value of Presepsin (PSP) compared to Procalcitonin (PCT), C-reactive Protein (CRP), White blood cells (WBC), IL6 in patients with sepsis or septic shock in intensive care unit [2] and in more specific group of cardiac surgery patients [3].

Methods

This study was conducted at the San Filippo Neri Hospital in Rome, Italy, and consecutively continued at the Clinic for Cardiac Surgery, Clinical Center of Serbia, Belgrade, Serbia.

Patients were recruited from three critical areas: a general intensive care unit, interacting with the Emergency Room; a post-operative intensive care unit for general, orthopedic and vascular surgery; a neurosurgical intensive care, and a cardiac surgery intensive care unit.

Inclusion criteria were: age between 18 and 80 yr.; hospitalized due to major medical or surgical reasons (abdominal surgery, major vascular surgery, cardiac surgery, ENT major surgery, major orthopedic surgery, neurosurgery, other major surgery), burn victims, patients with exogenous intoxication, all subjects with traumas not mentioned in the exclusion criteria in this list, SAPS II score greater than or equal to 20, hospitalization, even in the in-patient area, for the minimum number of days required for observation (three days).

Female patients who are pregnant women or lactating mothers cannot be enrolled in the trial. Patients with kidney failure, even when treated with CRRT at the beginning of the observation, were eligible to participate. The assay for biomarkers were performed on whole venous or arterial blood, on days 1, 2, 4, and 7 from the admission of all the patients eligible for the study. Once the hematocrit value is known, the analysis was performed on the Mitsubishi Compact Immuno-Analyzer unit. Patients enrolled in the trial had to test - on the same day and within six hours after the PSP dosage - also the dosage of PCT, of Creatinine, of CRP, of IL6 and of the complete Blood Count, with or without the formula. The patient's information flow should include the outcome or the possible death if it occurs within the 7th day (the last day of observation). Statistical Analysis was performed by National Institute of Statistics. Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value were calculated for each biomarker. The diagnostic accuracy of the four biomarkers studied was evaluated using the areas under the curve (AUCs).

Methodological Notes

Test Result	*Truth*		
		Disease	**Not Disease**
	Positive	True positive	False positive
	Negative	False negative	True negative

Sensitivity: is the probability that a test will indicate 'disease' among those with the disease.
Specificity: is the fraction of those without disease who will have a negative test result.
Positive predictive value is the probability that subjects with a positive screening test truly have the disease.
Negative predictive value is the probability that subjects with a negative screening test truly don't have the disease.
ROC curve: Total area under ROC curve is a single index for measuring the performance a test. The larger the AUC, the better is overall performance of the medical test to correctly identify diseased and non-diseased subjects. Equal AUCs of two tests represents similar overall performance of tests but this does not necessarily mean that both the curves are identical.

AUC 1	***Perfect test***
0,9 < AUC ≤ 0,99	*Highly accurate test*
0,8 < AUC ≤ 0,89	*Accurate test*
0,7 < AUC ≤ 0,79	*Moderately accurate test*
0,51< AUC ≤ 0,69	*Inaccurate test*
AUC ≤ 0,5	*Not informative test*

Results

Biomarker Day 1 (Not Cardiac Surgery Intensive Care Unit Patients)

PSP

PSP\Sepsis	***Infected***	***Not Infected***	***TOT***
Infected	9	15	24
Not Infected	0	20	20
TOT	9	35	44

Biomarkers	***PSP***	
Sensitivity	100%	*100% of infected individuals were positive*
Specificity	57%	*57% of not infected individuals were negative*
Positive Predictive Value	38%	*38% of individuals positive resulted are really sick*
Negative Predictive Value	100%	*100% of individuals negative resulted are really healthy*
AUC	0,89	*Accurate test*
P-Value	0,003667	*The test is statistically significant*

PCR

PCR\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	7	18	25
Not Infected	2	17	19
TOT	9	35	44

Biomarkers	*PCR*	
Sensibility	78%	*Il 78% of infected individuals were positive*
Specificity	77%	*77% of not infected individuals were negative*
Positive Predictive Value	47%	*47% of individuals positive resulted are really sick*
Negative Predictive Value	93%	*93% of individuals negative resulted are really healthy*
AUC	0,84	*Accurate test*
P-Value	0,01856	*The test is not statistically significant*

PCT

PCT\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	7	8	15
Not Infected	2	27	29
TOT	9	35	44

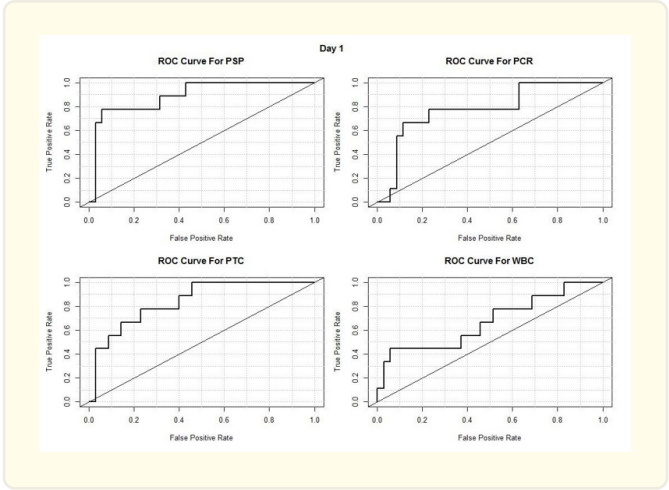
Biomarkers	*PCT*	
Sensitivity	63%	*63% of infected individuals were positive*
Specificity	66%	*66% of not infected individuals were negative*
Positive Predictive Value	29%	*29% of individuals positive resulted are really sick*
Negative Predictive Value	88%	*88% of individuals negative resulted are really healthy*
AUC	0,74	*Moderately accurate test*
P-Value	0,09901	*The test is not statistically significant*

WBC

WBC Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	5	15	20
Not Infected	4	20	24
TOT	9	35	44

Biomarkers	*WBC*	
Sensitivity	56%	*56% of infected individuals were positive*
Specificity	57%	*57% of not infected individuals were negative*
Positive Predictive Value	25%	*25% of individuals positive resulted are really sick*
Negative Predictive Value	83%	*83% of individuals negative resulted are really healthy*
AUC	0,66	*Inaccurate test*
P-Value	0,1032	*The test is not statistically significant*

Roc Curve Day 1 (Not Cardiac Surgery Intensive Care Unit Patients)



Biomarkers	***PSP***	***PCR***	***PCT***	***WBC***
Sensitivity	100%	78%	78%	56%
Specificity	57%	49%	77%	57%
Positive Predictive Value	38%	28%	47%	25%
Negative Predictive Value	100%	89%	93%	83%
AUC	0,89	0,77	0,84	0,66

The PSP biomarker resulted being the best indicator to identify True Positive and True Negative. PSP is also the only one with a statistically significant T-test. Observing Roc curve analysis PSP seems to be better than other biomarkers [5, 6].

Biomarker Day 2 (Not Cardiac Surgery Intensive Care Unit Patients)

PSP

PSP\Sepsis	***Infected***	***Not Infected***	***TOT***
Infected	7	15	22
Not Infected	1	20	21
TOT	9	35	44

Biomarkers	***PSP***	
Sensitivity	88%	*88% of infected individuals were positive*
Specificity	57%	*57% of the non-infected individuals were negative*
Positive Predictive Value	32%	*32% of individuals positive resulted are really sick*
Negative Predictive Value	95%	*95% of individuals negative are really healthy*
AUC	0,77	*Moderately accurate test*
P-Value	0,1321	*The test is not statistically significant*

PCR

PCR\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	7	18	25
Not Infected	1	17	18
TOT	8	35	43

Biomarkers	*PCR*	
Sensitivity	88%	*Il 88% of infected individuals were positive*
Specificity	49%	*49% of the non-infected individuals were negative*
Positive Predictive Value	28%	*28% of individuals positive resulted are really sick*
Negative Predictive Value	94%	*94% of individuals negative resulted are really healthy*
AUC	0,68	*Inaccurate test*
P-Value	0,1022	*The test is not statistically significant*

PCT

PCT\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	5	12	17
Not Infected	3	23	26
TOT	8	35	43

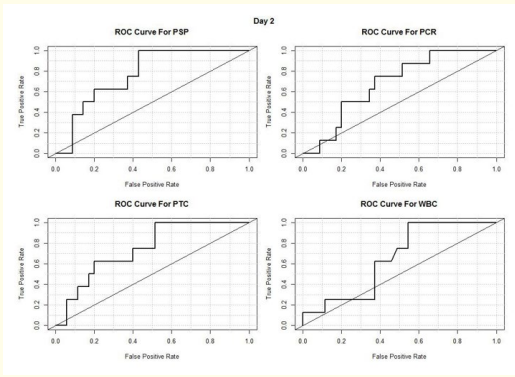
Biomarkers	*PCT*	
Sensitivity	63%	*63% of infected individuals were positive*
Specificity	66%	*66% of the non-infected individuals were negative*
Positive Predictive Value	29%	*29% of individuals positive resulted are really sick*
Negative Predictive Value	88%	*88% of individuals negative resulted are really healthy*
AUC	0,74	*Moderately accurate test*
P-Value	0,3263	*The test is not statistically significant*

WBC

WBC Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	5	15	20
Not Infected	4	20	24
TOT	9	35	44

Biomarkers	*WBC*	
Sensitivity	56%	*56% of infected individuals were positive*
Specificity	57%	*57% of the non-infected individuals were negative*
Positive Predictive Value	25%	*25% of individuals positive resulted are really sick*
Negative Predictive Value	83%	*83% of individuals negative resulted are really healthy*
AUC	0,66	*Inaccurate Test*
P-Value	0,1812	*The test is not statistically significant*

Roc Curve Day 2 (Not Cardiac Surgery Intensive Care Unit Patients)



Biomarkers	***PSP***	***PCR***	***PCT***	***WBC***
Sensitivity	88%	88%	63%	38%
Specificity	57%	49%	66%	63%
Positive Predictive Value	32%	28%	29%	19%
Negative Predictive Value	95%	94%	88%	81%
AUC	0,77	0,68	0,74	0,65

PCR and PSP biomarkers resulted being the best indicator to identify True Positive Predictive Value while PCT biomarker resulted being the best indicator to identify True Negative. Observing Roc curve analysis PSP seems to be better than other biomarkers. T-test was not statistically significant for all biomarkers.

Biomarker Day 4 (Not Cardiac Surgery Intensive Care Unit Patients)

PSP

PSP\Sepsis	***Infected***	***Not Infected***	***TOT***
Infected	6	10	16
Not Infected	2	18	20
TOT	8	28	36

Biomarkers	***PSP***	
Sensitivity	75%	*75% of infected individuals were positive*
Specificity	64%	*64% of the non-infected individuals were negative*
Positive Predictive Value	38%	*38% of individuals positive resulted are really sick*
Negative Predictive Value	90%	*90% of individuals negative resulted are really healthy*
AUC	0,76	*Moderately accurate test*
P-Value	0,1504	*The test is not statistically significant*

PCR

PCR\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	7	17	24
Not Infected	1	11	12
TOT	8	28	36

Biomarkers	*PCR*	
Sensitivity	88%	*Il 88%of infected individuals were positive*
Specificity	39%	*39% of non-infected individuals were negative*
Positive Predictive Value	29%	*29% of individuals positive resulted are really sick*
Negative Predictive Value	92%	*92% of individuals negative resulted are really healthy*
AUC	0,5	*Not informative test*
P-Value	0,9232	*The test is not statistically significant*

PCT

PCT\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	4	7	11
Not Infected	4	21	25
TOT	8	28	36

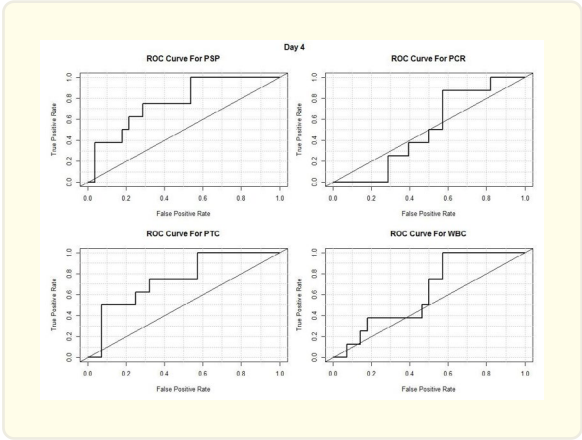
Biomarkers	*PCT*	
Sensitivity	50%	*50% of infected individuals were positive*
Specificity	75%	*75% of the non-infected individuals were negative*
Positive Predictive Value	36%	*36% of individuals positive resulted are really sick*
Negative Predictive Value	84%	*84% of individuals negative resulted are really healthy*
AUC	0,75	*Moderately accurate test*
P-Value	0,1619	*The test is not statistically significant*

WBC

WBC Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	3	10	13
Not Infected	5	18	23
TOT	8	28	36

Biomarkers	*WBC*	
Sensitivity	38%	*38% of infected individuals were positive*
Specificity	64%	*64% of the non-infected individuals were negative*
Positive Predictive Value	23%	*23% of individuals positive resulted are really sick*
Negative Predictive Value	78%	*78% of individuals negative resulted are really healthy*
AUC	0,62	*Inaccurate test*
P-Value	0,2504	*The test is not statistically significant*

Roc Curve Day 4 (Not Cardiac Surgery Intensive Care Unit Patients)



Biomarkers	***PSP***	***PCR***	***PCT***	***WBC***
Sensitivity	75%	88%	50%	38%
Specificity	64%	39%	75%	64%
Positive Predictive Value	38%	29%	36%	23%
Negative Predictive Value	90%	92%	84%	78%
AUC	0,76	0,5	0,75	0,62

The PCR biomarker resulted being the best indicator to identify True Positive, while PCT biomarker resulted being the best indicator to identify True Negative. The PSP biomarker resulted being the best indicator to identify Positive Predictive Value and observing Roc curve analysis seems to be better than other biomarkers.

Biomarker Day 7 (Not Cardiac Surgery Intensive Care Unit Patients)

PSP

PSP\Sepsis	***Infected***	***Not Infected***	***TOT***
Infected	4	14	18
Not Infected	4	10	14
TOT	8	24	32

Indicators	***PSP***	
Sensitivity	50%	*50% of infected individuals were positive*
Specificity	42%	*42% of the non-infected individuals were negative*
Positive Predictive Value	22%	*22% of individuals positive resulted are really sick*
Negative Predictive Value	71%	*71% of individuals negative resulted are really healthy*
AUC	0,53	*Inaccurate test*
P-Value	0,2845	*The test is not statistically significant*

PCR

PCR\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	4	14	18
Not Infected	4	10	14
TOT	8	24	32

Biomarkers	*PCR*	
Sensitivity	50%	*Il 50% of infected individuals were positive*
Specificity	42%	*42% of the non-infected individuals were negative*
Positive Predictive Value	22%	*22% of individuals positive resulted are really sick*
Negative Predictive Value	71%	*71% of individuals negative resulted are really healthy*
AUC	0,42	Not informative test
P-Value	0,9528	*The test is not statistically significant*

PCT

PCT\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	0	5	5
Not Infected	8	19	27
TOT	8	24	32

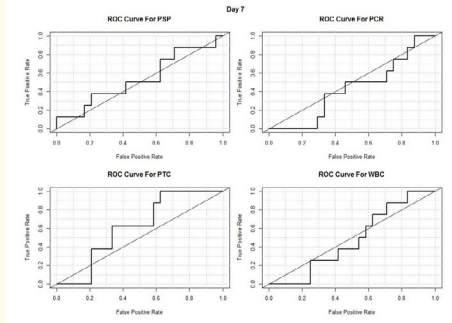
Biomarkers	*PCT*	
Sensitivity	0%	*0% of infected individuals were positive*
Specificity	79%	*79% of the non-infected individuals were negative*
Positive Predictive Value	0%	*0% of individuals positive resulted are really sick*
Negative Predictive Value	70%	*70% of individuals negative resulted are really healthy*
AUC	0,61	*Inaccurate test*
P-Value	0,8992	*The test is not statistically significant*

WBC

WBC Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	2	9	11
Not Infected	6	15	21
TOT	8	24	32

Biomarkers	*WBC*	
Sensitivity	25%	*25% of infected individuals were positive*
Specificity	63%	*63% of the non-infected individuals were negative*
Positive Predictive Value	18%	*18% of individuals positive resulted is really sick*
Negative Predictive Value	71%	*71% of individuals negative resulted are really healthy*
AUC	0,47	*Not informative test*
P-Value	0,7623	*The test is not statistically significant*

Roc Curve Day 7 (Not Cardiac Surgery Intensive Care Unit Patients)



Biomarkers	***PSP***	***PCR***	***PCT***	***WBC***
Sensitivity	50%	50%	0%	25%
Specificity	42%	42%	79%	63%
Positive Predictive Value	22%	22%	0%	18%
Negative Predictive Value	71%	71%	70%	71%
AUC	0,53	0,42	0,61	0,47

PSP and PCR biomarkers resulted being the best indicator to identify True Positive, Positive Predictive Value and Negative Predictive Value. PCT biomarker resulted being the best indicator to identify True Negative but has 0% sensitivity. Generally observing Roc curve analysis all biomarkers seems to be not informative with AUC values close to 0.5 and curves very close to the bisector. T-test is not statistically significant for all biomarkers.

Biomarker Day 1 (cardiac surgery intensive care unit Patients)

PSP

PSP\Sepsis	***Infected***	***Not Infected***	***TOT***
Infected	17	18	35
Not Infected	4	19	23
TOT	21	37	58

Indicators	***PSP***	
Sensitivity	81%	*81% of infected individuals were positive*
Specificity	51%	*51% of the non-infected individuals were negative*
Positive Predictive Value	49%	*49% of Individuals positive resulted are really sick*
Negative Predictive Value	83%	*83% of Individuals positive are really healthy*
AUC	0,66	*accurate test*
P-Value	0,0085	*The test is statistically significant*

PCR

PCR\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	19	20	39
Not Infected	2	17	19
TOT	21	37	58

Biomarkers	*PCR*	
Sensitivity	90%	*90% of infected individuals were positive*
Specificity	46%	*46% of the non-infected individuals were negative*
Positive Predictive Value	49%	*49% of Individuals positive resulted are really sick*
Negative Predictive Value	89%	*89% of Individuals positive are really healthy*
AUC	0,68	*Inaccurate test*
P-Value	0,0025	*The test is statistically significant*

PCT

PCT\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	9	11	20
Not Infected	9	24	33
TOT	18	35	53

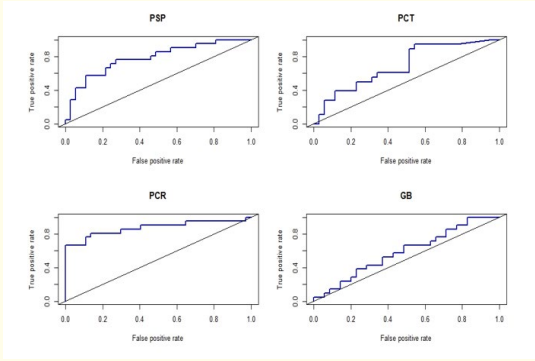
Biomarkers	*PCT*	
Sensitivity	50%	*50% of infected individuals were positive*
Specificity	69%	*69% of the non-infected individuals were negative*
Positive Predictive Value	45%	*45% of Individuals positive resulted are really sick*
Negative Predictive Value	73%	*73% of Individuals positive are really healthy*
AUC	0,59	*Inaccurate test*
P-Value	0,0973	*The test is not statistically significant*

WBC

WBC Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	11	15	26
Not Infected	10	20	30
TOT	21	35	56

Biomarkers	*WBC*	
Sensitivity	52%	*52% of infected individuals were positive*
Specificity	57%	*57% of the non-infected individuals were negative*
Positive Predictive Value	42%	*42% of Individuals positive resulted are really sick*
Negative Predictive Value	67%	*67% of Individuals positive are really healthy*
AUC	0,55	*Inaccurate test*
P-Value	0,2496	*The test is not statistically significant*

Roc Curve Day 1 (cardiac surgery intensive care unit Patients)



Biomarkers	*PSP*	*PCR*	*PCT*	*WBC*
Sensitivity	81%	90%	50%	52%
Specificity	51%	46%	69%	57%
Positive Predictive Value	49%	49%	45%	42%
Negative Predictive Value	83%	89%	73%	67%
AUC	0,66	0,68	0,59	0,55

The PCR biomarker resulted being the best indicator to identify True Positive and Negative Predictive Value, while PCR and PSP biomarkers resulted being the best indicator to identify Positive Predictive Value. In the end PCT biomarker resulted being the best indicator to identify True Positive [4]. PSP and PCR tests were statistically significant. Observing Roc curve analysis PCR seems to be better than other biomarkers.

Biomarker Day 2 (cardiac surgery intensive care unit Patients)

PSP

PSP\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	15	18	33
Not Infected	5	19	24
TOT	20	37	57

Indicators	*PSP*	
Sensitivity	75%	*75% of infected individuals were positive*
Specificity	51%	*51% of the non-infected individuals were negative*
Positive Predictive Value	45%	*45% of Individuals positive resulted are really sick*
Negative Predictive Value	79%	*79% of Individuals positive are really healthy*
AUC	0,63	*Inaccurate test*
P-Value	0,0290	*The test is statistically significant*

PCR

PCR\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	19	20	39
Not Infected	1	17	18
TOT	20	37	57

Biomarkers	*PCR*	
Sensitivity	95%	*95% of infected individuals were positive*
Specificity	46%	*46% of the non-infected individuals were negative*
Positive Predictive Value	49%	*49% of Individuals positive resulted are really sick*
Negative Predictive Value	94%	*94% of Individuals positive are really healthy*
AUC	0,68	*Inaccurate test*
P-Value	0,0009	*The test is statistically significant*

PCT

PCT\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	12	13	25
Not Infected	7	23	30
TOT	19	36	55

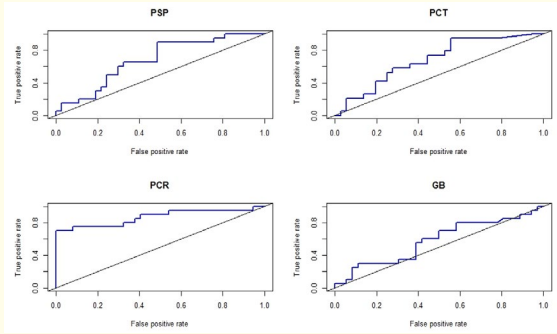
Biomarkers	*PCT*	
Sensitivity	63%	*63% of infected individuals were positive*
Specificity	64%	*64% of the non-infected individuals were negative*
Positive Predictive Value	48%	*48% of Individuals positive resulted are really sick*
Negative Predictive Value	77%	*77% of Individuals positive are really healthy*
AUC	0,70	*Moderately accurate test*
P-Value	0,0295	*The test is not statistically significant*

WBC

WBC Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	11	14	25
Not Infected	9	22	31
TOT	20	36	56

Biomarkers	*WBC*	
Sensitivity	55%	*55% of infected individuals were positive*
Specificity	61%	*61% of the non-infected individuals were negative*
Positive Predictive Value	44%	*44% of Individuals positive resulted are really sick*
Negative Predictive Value	71%	*71% of Individuals positive are really healthy*
AUC	0,58	*Inaccurate test*
P-Value	0,1268	*The test is not statistically significant*

Roc Curve Day 2 (cardiac surgery intensive care unit Patients)



Biomarkers	*PSP*	*PCR*	*PCT*	*WBC*
Sensitivity	75%	95%	63%	55%
Specificity	51%	46%	64%	61%
Positive Predictive Value	45%	49%	48%	44%
Negative Predictive Value	79%	94%	77%	71%
AUC	0,77	0,68	0,74	0,65

The PCR biomarker resulted being the best indicator to identify True Positive, Positive Predictive Value and Negative Predictive Value, while PCT biomarker resulted being the best indicator to identify True Negative. PSP and PCR tests were statistically significant. Observing Roc curve analysis PSP seems to be better than other biomarkers [7].

Biomarker Day 4 (cardiac surgery intensive care unit Patients)

PSP

PSP\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	14	13	27
Not Infected	5	7	12
TOT	19	20	39

Indicators	*PSP*	
Sensitivity	74%	*74% of infected individuals were positive*
Specificity	35%	*35% of the non-infected individuals were negative*
Positive Predictive Value	52%	*52% of Individuals positive resulted are really sick*
Negative Predictive Value	58%	*58% of Individuals positive are really healthy*
AUC	0,65	*Moderately accurate test*
P-Value	0,0203	*The test is statistically significant*

PCR

PCR\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	17	19	36
Not Infected	1	11	12
TOT	18	30	48

Biomarkers	*PCR*	
Sensitivity	94%	*94% of infected individuals were positive*
Specificity	37%	*37% of the non-infected individuals were negative*
Positive Predictive Value	47%	*47% of Individuals positive resulted are really sick*
Negative Predictive Value	92%	*92% of Individuals positive are really healthy*
AUC	0,66	*Inaccurate test*
P-Value	0,0089	*The test is statistically significant*

PCT

PCT\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	11	9	20
Not Infected	7	21	28
TOT	18	30	48

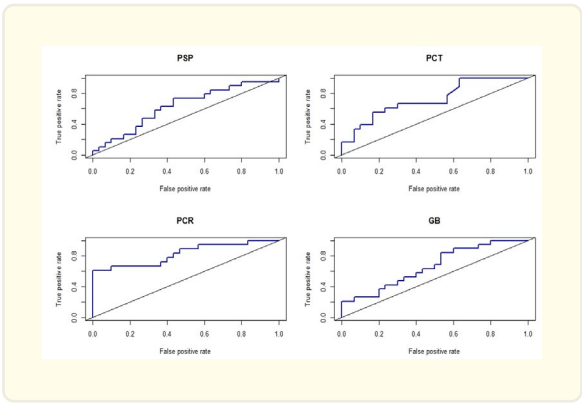
Biomarkers	*PCT*	
Sensitivity	61%	*61% of infected individuals were positive*
Specificity	70%	*70% of the non-infected individuals were negative*
Positive Predictive Value	55%	*55% of Individuals positive resulted are really sick*
Negative Predictive Value	75%	*75% of Individuals positive are really healthy*
AUC	0,66	*Inaccurate test*
P-Value	0,0187	*The test is statistically significant*

WBC

WBC Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	10	11	21
Not Infected	9	19	28
TOT	19	30	49

Biomarkers	*WBC*	
Sensitivity	*53%*	*53% of infected individuals were positive*
Specificity	*63%*	*63% of the non-infected individuals were negative*
Positive Predictive Value	*48%*	*48% of Individuals positive resulted are really sick*
Negative Predictive Value	*68%*	*68% of Individuals positive are really healthy*
AUC	*0,5798*	*Inaccurate test*
P-Value	*0,1407*	*The test is not statistically significant*

Roc Curve Day 4 (cardiac surgery intensive care unit Patients)



Biomarkers	*PSP*	*PCR*	*PCT*	*WBC*
Sensitivity	74%	61%	94%	53%
Specificity	35%	70%	37%	63%
Positive Predictive Value	52%	55%	47%	48%
Negative Predictive Value	58%	75%	92%	68%
AUC	0,65	0,66	0,66	0,58

The PCT biomarker resulted being the best indicator to identify True Positive and Negative Predictive Value, while PCR biomarker resulted being the best indicator to identify True Negative and Positive Predictive Value. PSP, PCR and PCT tests were statistically significant. Observing Roc curve analysis PCR, PCT and PSP seems to be better than other biomarkers.

Biomarker Day 7 (cardiac surgery intensive care unit Patients)

PSP

PSP\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	7	15	22
Not Infected	5	11	16
TOT	12	26	38

Indicators	*PSP*	
Sensitivity	58%	*58% of infected individuals were positive*
Specificity	42%	*42% of the non-infected individuals were negative*
Positive Predictive Value	32%	*32% of Individuals positive resulted are sick*
Negative Predictive Value	69%	*69% of Individuals positive are really healthy*
AUC	0,50	*Inaccurate test*
P-Value	0,4927	*The test is not statistically significant*

PCR

PCR\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	9	16	25
Not Infected	3	11	14
TOT	12	27	39

Biomarkers	*PCR*	
Sensitivity	75%	*75% of infected individuals were positive*
Specificity	41%	*41% of the non-infected individuals were negative*
Positive Predictive Value	36%	*36% of Individuals positive resulted are really sick*
Negative Predictive Value	79%	*79% of Individuals positive are really healthy*
AUC	0,58	*Inaccurate test*
P-Value	0,1800	*The test is not statistically significant*

PCT

PCT\Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	5	5	10
Not Infected	7	22	29
TOT	12	27	39

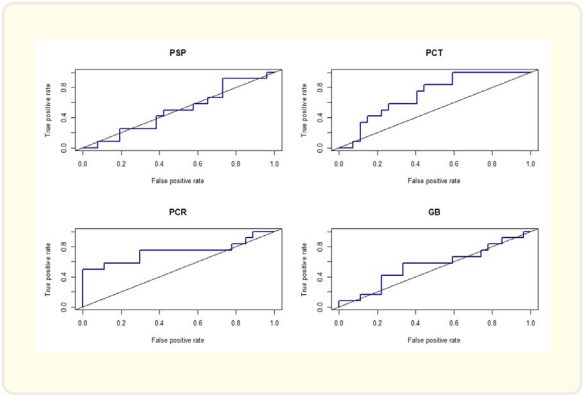
Biomarkers	*PCT*	
Sensitivity	42%	*42% of infected individuals were positive*
Specificity	81%	*81% of the non-infected individuals were negative*
Positive Predictive Value	50%	*50% of Individuals positive resulted are really sick*
Negative Predictive Value	76%	*76% of Individuals positive are really healthy*
AUC	0,62	*Inaccurate test*
P-Value	0,0684	*The test is not statistically significant*

WBC

WBC Sepsis	*Infected*	*Not Infected*	*TOT*
Infected	5	9	14
Not Infected	7	18	25
TOT	12	27	39

Biomarkers	*WBC*	
Sensitivity	42%	*42% of infected individuals were positive*
Specificity	67%	*67% of the non-infected individuals were negative*
Positive Predictive Value	36%	*36% of Individuals positive resulted are really sick*
Negative Predictive Value	72%	*72% of Individuals positive are really healthy*
AUC	0,55	*Not informative test*
P-Value	0,3171	*The test is not statistically significant*

Roc Curve Day 7 (cardiac surgery intensive care unit Patients)



Biomarkers	*PSP*	*PCR*	*PCT*	*WBC*
Sensitivity	58%	42%	75%	42%
Specificity	42%	81%	41%	67%
Positive Predictive Value	32%	50%	36%	36%
Negative Predictive Value	69%	76%	79%	72%
AUC	0,50	0,62	0,58	0,55

The PCT biomarker resulted being the best indicator to identify True Positive, Negative Predictive Value, while PCR biomarker resulted being the best indicator to identify True Negative and Positive Predictive Value. All biomarkers results tests were statistically significant. Observing Roc curve analysis PCR seems to be better than other biomarkers.

Results

The data are showed in table 1.1 (cardiac surgery intensive care unit Patients).

table 1.2 (Not Cardiac Surgery Intensive Care Unit Patients).

	Day	*PSP*	*CRP*	*PCT*	*WBC*
Sensitivity	1	81%	90%	50%	52%
	2	75%	95%	63%	38%
	4	74%	61%	94%	53%
	7	58%	42%	75%	42%
Specificity	1	51%	46%	69%	57%
	2	51%	46%	64%	61%
	4	35%	70%	37%	63%
	7	42%	81%	41%	67%
PPV	1	49%	49%	45%	42%
	2	45%	49%	48%	44%
	4	52%	55%	47%	48%
	7	32%	50%	36%	36%
NPV	1	83%	89%	73%	67%

	2	79%	94%	77%	71%
	4	58%	75%	92%	68%
	7	69%	76%	79%	72%
AUC	1	0,66	0,68	0,59	0,55
	2	0,77	0,68	0,74	0,65
	4	0,65	0,66	0,66	0,58
	7	0,50	0,62	0,58	0,55
PSP = Presepsin; CRP = C-Reactive Protein, PCT = ProCalcitonin; WBC = White Blood Cells; PPV = Positive Predictive Value; NPV = Negative Predictive Value; AUC = Area Under CURVE.					

Table 1.1: Parameters analyzed of the four biomarkers studied (cardiac surgery intensive care unit Patients).

	Day	***PSP***	***CRP***	***PCT***	***WBC***
Sensitivity	1	100%	78%	78%	56%
	2	88%	88%	63%	38%
	3	75%	88%	50%	38%
	7	50%	50%	0%	25%
Specificity	1	57%	49%	77%	57%
	2	57%	49%	66%	63%
	3	64%	39%	75%	64%
	7	42%	42%	79%	63%
PPV	1	38%	28%	47%	25%
	2	32%	28%	29%	19%
	3	38%	29%	36%	23%
	7	22%	22%	0%	18%
NPV	1	100%	89%	93%	83%
	2	95%	94%	88%	81%
	3	90%	92%	84%	78%
	7	71%	71%	70%	71%
AUC	1	0,89	0,77	0,84	0,66
	2	0,77	0,68	0,74	0,65
	3	0,76	0,5	0,75	0,62
	7	0,53	0,42	0,61	0,47
PSP = Presepsin; CRP = C-Reactive Protein, PCT = ProCalcitonin; WBC = White Blood Cells; PPV = Positive Predictive Value; NPV = Negative Predictive Value; AUC = Area Under CURVE.					

Table 1.2: Parameters analyzed of the four biomarkers studied (Not Cardiac Surgery Intensive Care Unit Patients).

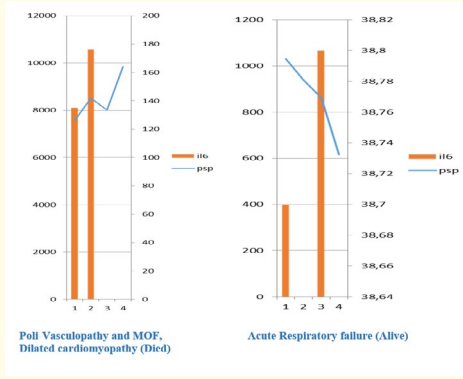


Table 2

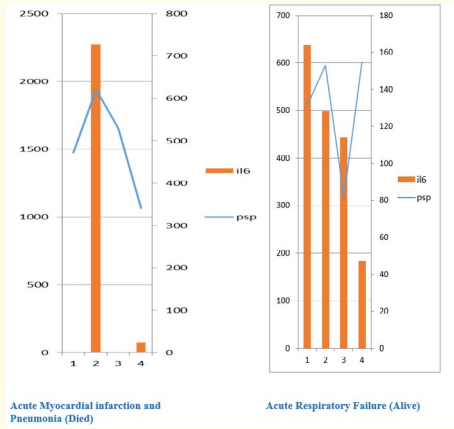


Table 3

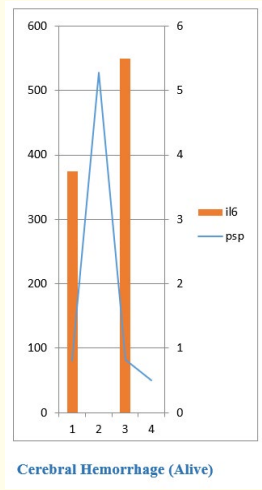


Table 4

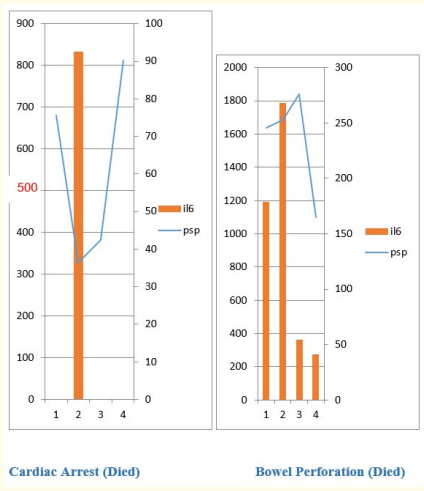


Table 5

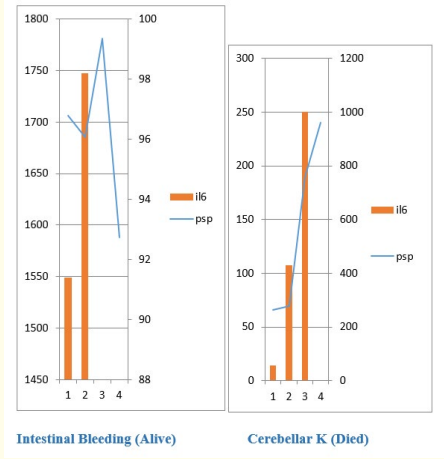


Table 6

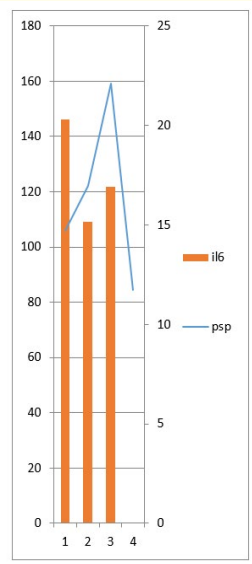


Table 7

Discussion

The accuracy of all the biomarkers decreases with time until they are no longer useful [7].

We found highest predictive values in the first measurements on day 1, with PSP reaching the value AUC of 0.66 (CRP = 0.68 and PCT = 0.59). Being that CRP is increased in patients after surgery, this is a valuable result because using PSP to early detect presence of infection could improve patient's survival [8-9].

Conclusion

In our experience, presepsin could be useful in the early diagnosis of infection in patients and distinguishing sepsis from SIRS in intensive care. The early detection of the disease could allow a rapid targeted therapy and an improved outcome.

Competing Interests

The authors declare no competing interests.

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