The Role of Procalcitonin (PCT) and Lactic Acid in Febrile Neutropenic Cancer Patients in an Oncological Emergency Center

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BACKGROUND:

Procalcitonin (PCT) is a biomarker that has been associated with bacterial infection and sepsis. It has been used along with clinical judgment to guide antibiotic therapy in antibiotic stewardship program particularly in patients with lower respiratory tract infections. Serial measurement of PCT may have a prognostic role as failure to decrease may predict mortality (6). Although PCT may be elevated in cancer patients, it can further increase in febrile cancer patients in the setting of bacteremia or sepsis.

Lactic acidosis has also been used as a prognostic biomarker in severe sepsis. Levels > 4 mmol/L have been associated with increased mortality. In hemodynamically stable patients, elevated levels has preceded the development of septic shock within 48 hours. Like PCT, lactic acidosis has also been associated with malignancies. In patients with hematological malignancies hospitalized for neutropenic fever, serum lactate levels (≥2 mmol/L) have been associated with development of septic shock.

Multinational Association for Supportive Care in Cancer (MASCC) risk index has been used as a tool to identify the risk of patients who present with chemotherapy-induced febrile neutropenia in order to dictate the management of patients, need for hospitalization and intravenous antibiotic therapy. A score < 21, predicts patients at high risk for complications and would indicate the need for admission. This risk index however could be difficult to use in a busy emergency center. Furthermore, some elements could be confusing (active chronic bronchitis) and others, such as the illness severity, are subject to the physician interpretation of the burden of the illness.

The objective of this study was to evaluate the role of serum PCT used alone or in combination with lactate and to compare it to the MASCC risk index to predict bloodstream infections (BSI), hospitalization and 14 days mortality in febrile neutropenic cancer patients presenting to the EC.

METHODS:

- We conducted a retrospective study of all febrile neutropenic cancer patients who presented to our EC between April 1, 2018 and April 30, 2019.
- We included patients who had a serum PCT and lactic acid levels measured at presentation. We calculated the Multinational Association for Supportive Care in Cancer (MASCC) risk index as follows:

  For burden of illness, all patients who presented to the emergency center had either moderate or severe symptoms. The patient status was considered outpatient given that all patients presented to the emergency center at the time of onset of the neutropenic fever. All patients received parenteral fluids and were therefore considered to have dehydration.

- **Definitions:**

  Fever was defined either as a documented temperature of ≥100.4° F or a chief complaint of fever reported at home.

  Neutropenia was defined as an absolute neutrophil count ≤500 cells/mL.

RESULTS:

Table 1. Patient characteristics

Characteristics	Patients
	(n= 550)
	N (%)
Study time period	4/2018 - 4/2019
Age (years), median (range)	56 (3 - 95)
Sex, male	285 (52)
Race	
White	389/541 (72)
African American	45/541 (8)
Asian	36/541 (7)
Other	71/541 (13)
Unknown	9
Type of cancer	
Hematological malignancy	385 (70)
Solid tumor	165 (30)
Procalcitonin level, median (IQR)	0.24 (0.13 - 0.64)
WBC, median (IQR)	0.4 (0.1 - 0.9)
ANC, median (IQR)	0.10 (0.03 - 0.22)
Lactate, median (IQR)	1.4 (0.95 - 1.8)
MASSC score, median (IQR)	19 (17-21)
CRP, median (IQR)	101.2 (55.9 - 186.6)
BSI (=Bacteremia)	116/544 (21)
Gram staining of organisms	
G +	33/109 (30)
G -	72/109 (66)
Both G + and G -	4/109 (4)
Inpatient length of stay (days), median (IQR)	5 (4-9)
Death within 14 days of EC admission	16/548 (3)
Death within 30 days of EC admission	32/548 (6)
Abbreviation: IQR= Interquartile range.	

Table 3. Comparing performance of outcome prediction between PCT, Lactate and MASSC scores

a) Bloodstream infection			
BSI	PCT ≥ 0.25	PCT ≥ 0.25 or Lactate > 2.2	MASSC score < 21
Sensitivity	0.78	0.77	0.74
95% CI	0.69 to 0.84	0.68 to 0.84	0.65 to 0.81
Specificity	0.59	0.54	0.44
95% CI	0.54 to 0.63	0.50 to 0.59	0.39 to 0.48
PPV	0.34	0.31	0.26
95% CI	0.28 to 0.40	0.26 to 0.36	0.22 to 0.31
NPV	0.91	0.90	0.86
95% CI	0.87 to 0.94	0.86 to 0.93	0.81 to 0.90
b) 14-Day mortality			
BSI	PCT ≥ 0.25	PCT ≥ 0.25 or Lactate > 2.2	MASSC score < 21
Sensitivity	0.88	0.93	1.00
95% CI	0.64 to 0.97	0.70 to 0.99	0.81 to 1.00
Specificity	0.52	0.49	0.41
95% CI	0.48 to 0.56	0.45 to 0.54	0.37 to 0.45
PPV	0.05	0.05	0.05
95% CI	0.03 to 0.09	0.03 to 0.08	0.03 to 0.08
NPV	0.99	1.00	1.00
95% CI	0.97 to 1.00	0.98 to 1.00	0.98 to 1.00

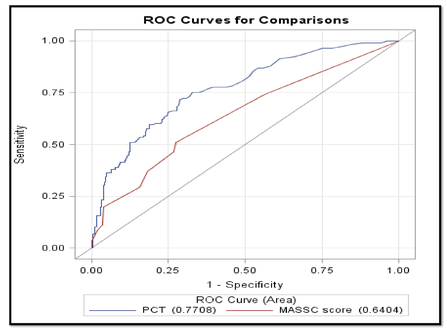
Table 2. Comparing patients with different PCT levels

Outcomes	PCT < 0.25	PCT ≥ 0.25	p-value
	(n=280)	(n=270)	
	N (%)	N (%)	
BSI	26/277 (9)	90/267 (34)	< .0001
Hospital admission	211 (75)	229 (85)	0.006
Length of hospital stay > 7 days	51 (18)	96 (36)	< .0001
Mortality within 14 days	2 (0.7)	14/268 (5.2)	0.002
Mortality within 30 days	7 (2.5)	25/268 (9.3)	< .001

Table 4. Logistic regression models of outcomes

a) Hospital admssion			
Variables	OR	95% CI	p-value
Type of cancer			< .0001
Hematological malignancy	3.30	(2.13, 5.11)	
Solid tumir	Referene		
PCT level			0.031
< 0.25	Reference		
≥ 0.25	1.63	(1.05, 2.53)	
Abbreviations: OR=Odds ratio. 95% CI = 95% Confidence Interval.			
b) LOS > 7 days			
Variables	OR	95% CI	p-value
Type of cancer			< .0001
Hematological malignancy	4.88	(2.75, 8.69)	
Solid tumir	Referene		
PCT level			< .0001
< 0.25	Reference		
≥ 0.25	2.27	(1.52, 3.41)	
c) Death within 14 days since EC visit			
Variables	OR	95% CI	p-value
Age	1.10	(1.04, 1.17)	0.002
Lactate level			< .001
0.5 -2.2 mmol/L	Reference		
> 2.2 mmol/L	9.19	(2.70, 31.26)	
CRP	1.01	(1.004, 1.02)	0.002
After adjuting for the factors above in the multivariate analysis, PCT was no longer associated with death within 14 days since EC visit (p=0.32).			
d) BSI			
Variables	OR	95% CI	p-value
Type of cancer			0.049
Hematological malignancy	1.96	(1.002, 3.82)	
Solid tumir	Referene		
PCT level			0.01
< 0.25	Reference		
≥ 0.25	2.24	(1.21, 4.15)	
Lactate level			0.006
0.5 -2.2 mmol/L	Reference		
> 2.2 mmol/L	2.64	(1.33, 5.25)	
WBC	0.19	(0.09, 0.42)	<.0001
CRP	1.003	(1.000, 1.006)	0.047

Figure 1. ROC curves for prediction of bloodstream infection by PCT and MASSC score



ROC curve analysis showed that PCT was a better predictor of bloodstream infection (BSI) than MASSC score. The areas under the receiver-operating characteristics (ROC) curves (AUCs) were 0.77 (95% CI: 0.72 to 0.82) for PCT and 0.64 (95% CI: 0.58 to 0.70) for MASSC score for predicting BSI, with a significant difference (p<0.001).

CONCLUSIONS:

- A PCT ≥ 0.25 was associated with BSI, LOS and 14 day mortality.
- The combination of PCT / serum lactate have a better sensitivity and high negative predictive value for BSI and mortality compared to the MASCC score index.
- This combination could be useful in a busy emergency center to identify high risk febrile patients requiring hospital admission and is less labor intensive than the MASCC score index.