

CIRCULATING BIOMARKERS (MR-PROADM, CRP, PCT) FOR RISK STRATIFICATION OF CANCER PATIENTS WITH CHEMOTHERAPY ASSOCIATED FEBRILE NEUTROPENIA



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BACKGROUND

Febrile neutropenia (FN) is one of the most common and severe complications in cancer patients. Although the Multinational Association for Supportive Care in Cancer (MASCC) score is the predominant approach for distinguishing low and high-risk episodes of FN, it relies on clinical indicators (1,2). Biomarkers of inflammation could provide additional information in the emergency department (ED) (3). Hence, **mid-regional proadrenomedullin** (MR-proADM) has emerged as a useful tool when infection is suspected (4).

AIM

Evaluate the **role of MR-proADM** for risk stratification of FN episodes, **compared to MASCC score, C-reactive protein (CRP) and procalcitonin (PCT)**, in predicting the development of serious complications.

METHODS

This retrospective study included chemotherapy-related FN episodes in patients with solid tumors presenting to the ED in our Hospital (Santa Lucía, Cartagena). On admission, a blood sample was collected to determine CRP, PCT and MR-proADM levels. The main outcome was ICU admission and/or death.

To evaluate the discriminatory ability of biomarkers and MASCC score for outcome, Receiver Operating Characteristic (ROC) curve analysis was used and optimal cutoffs were calculated through Youden index (5).

RESULTS

During the study period (2017 – 2022), **173 episodes** were included (Table 1). ICU admission and/or death occurred in 17 (9.8%) episodes.

Median CRP, PCT and MR-proADM levels were **significantly higher** in patients requiring **ICU management and/or deceased** ($p < 0.001$). Additionally, Median MASCC score was significantly lower, $p < 0.001$ (Table 2).

In ROC curve analysis (Figure 1), **MR-proADM** had the **highest discriminatory ability** (AUC 0.94), without a significant difference with PCT (0.94 vs 0.92; $p = 0.47$). This **difference** was significant in **comparison with CRP** (0.83; $p = 0.03$) and **MASCC score** (0.82; $p = 0.01$) (Table 3). Optimal cutoffs are described in Table 4.

CONCLUSION

In our study, in chemotherapy-associated FN patients, **PCT** and **MR-proADM** achieved a high performance for risk stratification and could assist us in the management in the management in the ED.

REFERENCES

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3. Ozgar HS, Senol E. Use of infection biomarkers in the emergency department. *Turk J Emerg Med*. 2022;22:169-76.
4. Saeed K, et al. Mid-regional pro-adrenomedullin as a supplementary tool to clinical parameters in cases of suspicion of infection in the emergency department. *Expert Rev Mol Diagn*. 2021;21(4):397-404.
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RESULTS

	Total population N = 173
Age, years (median age (IQR))	61 (52-69)
Gender, n (%). Female	105 (60.7)
Cancer type, n (%)	
Breast	70 (40.5)
Lung	47 (27.2)
Urological	11 (6.4)
Non-colorectal digestive	9 (5.2)
Gynecological	9 (5.2)
Sarcoma	7 (4.0)
Colorectal	6 (3.5)
Other	14 (8.0)
Tumor staging, n (%)	
I	20 (11.5)
II	28 (16.2)
III	38 (22.0)
IV	87 (50.3)
Suspected source of infection in ED, n (%)	
No apparent focus	60 (34.7)
Respiratory	43 (24.9)
Gastrointestinal	22 (12.7)
Urinary	18 (10.4)
Oral / mucositis	12 (6.9)
Other	18 (10.4)
MASCC score ≥ 21 , n (%)	132 (76.3)
MASCC score, median (IQR)	24 (21-26)
Hospital admission, n (%)	106 (96)
ICU admission, n (%)	9 (5.2)
Death, n (%)	10 (5.8)
ICU admission and/or death, n (%)	17 (9.8)

Table 1. Basic characteristics.

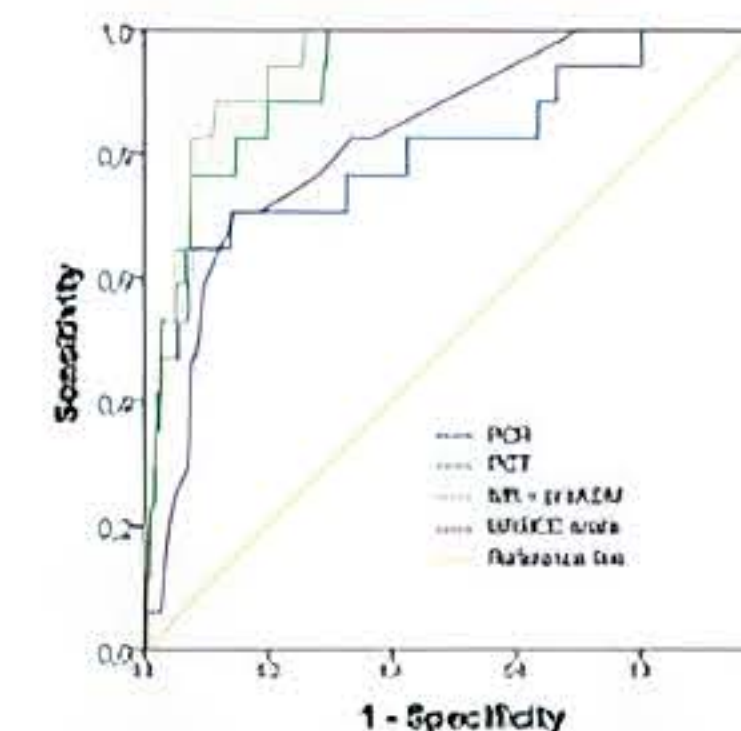


Figure 1. ROC curve analysis.

	No ICU admission or death occurred N = 156 (90.2%)	ICU admission and/or death N = 17 (9.8%)	p
Age, years (median age (IQR))	61 (52-68)	68 (58-72)	0.175
Gender, n (%)			0.001
Female	101 (64.7)	4 (23.5)	
Male	55 (35.3)	13 (76.5)	
ECOG ≥ 2 , n (%)	40 (25.6)	13 (76.5)	< 0.001
MASCC score, n (%)			< 0.001
≥ 21 (low risk)	127 (81.4)	5 (29.4)	
< 21 (high risk)	29 (18.6)	12 (70.6)	
MASCC score, median (IQR)	24 (21-26)	18 (16-21)	< 0.001
CRP, mg/dl (median (IQR))	82.5 (33.0 – 132.5)	303.0 (105.8 – 344.0)	< 0.001
PCT, ng/dl (median (IQR))	0.17 (0.09 – 0.45)	7.45 (1.01 – 26.11)	< 0.001
MR-proADM, nmol/L median (IQR)	1.02 (0.70 – 1.42)	3.14 (2.23 – 0.39)	< 0.001

Table 2. Characteristics, levels of biomarkers and MASCC score in relation to the occurrence of ICU admission or death. ECOG: Eastern Cooperative Oncology Group.

	AUC	95% IC	p-value	p ¹
MR-proADM	0.938	0.896 – 0.979	< 0.001	Ref.
PCT	0.920	0.869 – 0.972	< 0.001	0.468
CRP	0.826	0.678 – 0.934	< 0.001	0.031
MASCC score	0.820	0.730 – 0.922	< 0.001	0.014

Table 3. AUC values of biomarkers and MASCC score.

p¹: p-value for comparison with MR-proADM. AUC: area under the curve.

	Cut off point	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Negative predictive value (%) (95% CI)	Positive predictive value (%) (95% CI)
MASCC score	≥ 21 ¹	70.6 (44.0 – 89.7)	81.4 (74.4 – 87.2)	96.2 (91.4 – 98.6)	29.3 (16.1 – 45.5)
CRP, mg/dl	> 250 ²	64.7 (38.3 – 85.8)	92.3 (86.9 – 96.0)	96.0 (91.5 – 98.5)	47.8 (26.4 – 69.9)
PCT, ng/dl	> 0.34 ²	100 (85 – 100)	70.5 (62.7 – 77.5)	100 (96.7 – 100)	27.0 (16.5 – 39.8)
MR-proADM, nmol/L	> 1.82 ²	88.2 (63.6 – 98.5)	88.5 (82.4 – 93.0)	98.6 (94.9 – 99.8)	45.5 (28.1 – 63.6)
	< 0.87 ³	100 (80.5 – 100)	-	100 (93.7 – 100)	-
	≥ 1.54 ³	-	80.1 (73.0 – 86.1)	-	32.6 (19.4 – 48.2)

Table 4. Performance of biomarkers and MASCC score for outcome.

¹ Cut-off point recommended by ASCO/IDSA and ESMO international guidelines.

² Optimal cut-off point according to Youden index.

³ Optimal cut-off point recommended as criteria for discharge from the Emergency Department and hospital admission with close clinical monitoring by Saeed et al (4).