

Background

Early sepsis diagnosis in cancer patients, which are a population at higher risk of developing infection or sepsis, is challenging, despite the use of serum biomarkers. With that in mind, our aim was to evaluate the performance of monocyte distribution width (MDW), in these patients and compare MDW with other sepsis biomarkers, namely procalcitonin (PCT) and C-reactive protein (CRP) along with leucocytes (LEU#), monocytes (MO#) and interleukine-6 (IL6).

Results

In total, 215 patients were screened, and 157 patients with valid laboratory test results were included in the analysis: 83 men and 74 women, ages ranging between 41 and 87. MDW and PCT presented statistically significant results on the comparison of analytical characteristics between patients with sepsis ($p < 0.001$). No parameter evaluated evidenced statistically significant results considering the infection group. Only MDW showed adequate logistic regression as an independent predictor of sepsis ($p < 0.001$) and presented the highest AUC for sepsis (0.735), whereas PCT was 0.718. Sepsis cutoff value obtained for MDW was 26.435 presenting an NPV of 0.935. Regarding PCT the cutoff obtained was 4.35 ng/mL with an NPV of 0.956. The association of PCT with MDW did not increased MDW performance on predicting sepsis.

Comparison of analytical characteristics between patients with blood infection and other infections (Median (range)) *** $p < 0.001$

	Total	Blood Infection			Other Infections		
		No	Yes	p	No	Yes	p
N	157	132	25		112	45	
WBC ($10^3/\mu\text{L}$)	9.9 (0.3 - 43.4)	9.55 (0.30 - 43.40)	10.15 (1.70 - 31.8)	0.662	9.00 (0.3 - 43.4)	10.50 (1.6 - 38.3)	0.204
MO#	0.70 (0.10 - 4.20)	0.75 (0.10 - 2.20)	0.55 (0.10 - 4.20)	0.254	0.60 (0.1 - 2.2)	0.8 (0.1 - 4.2)	0.682
MDW	25.07 (17.39 - 52.18)	24.74 (17.39 - 52.18)	30.15 (19.43 - 38.41)	0.000***	24.95 (17.39 - 52.18)	26.32 (19.43 - 38.3)	0.274
PCR	12.95 (0.12 - 43.20)	12.00 (0.12 - 43.20)	14.25 (0.44 - 30.2)	0.175	12.70 (0.12 - 40.50)	13.00 (0.44 - 43.20)	0.674
PCT	0.56 (0.02 - 97.80)	0.46 (0.02 - 97.80)	2.15 (0.07 - 46.82)	0.000***	0.43 (0.05 - 97.80)	0.77 (0.02 - 46.82)	0.137
IL6	91.2 (0.83 - 27185)	86.20 (0.83 - 27185)	168.25 (5.4 - 1107)	0.132	87.20 (0.83 - 27185)	92.80 (5.40 - 1107)	0.847

Logistic regression for independent predictors of blood infection
*** $p < 0.001$; ** $p < 0.01$, * $p < 0.05$, † $p < 0.1$

	Crude OR (95% CI)	Univariate p	Adjusted OR (95% CI)	Multivariate p
Gender (Male)	1.07 (0.58 - 1.97)	0.829	1.05 (0.28 - 3.96)	0.943
Age	1.02 (0.99 - 1.04)	0.217	1.01 (0.95 - 1.07)	0.837
CCI	0.86 (0.76 - 0.98)	0.024*	0.60 (0.44 - 0.82)	0.001**
CHF	3.29 (1.12 - 9.68)	0.030*	3.30 (0.14 - 76.31)	0.457
DM	2.17 (1.10 - 0.00)	0.025*	10.70 (2.11 - 54.15)	0.004**
qSOFA	0.71 (0.24 - 2.12)	0.537	0.05 (0.00 - 1.31)	0.073
WBC ($\times 10^3/\mu\text{L}$)	1.00 (0.97 - 1.05)	0.826	1.04 (0.93 - 1.17)	0.463
MO# ($10^3/\mu\text{L}$)	0.85 (0.51 - 1.41)	0.531	0.83 (0.23 - 2.95)	0.775
MDW	1.08 (1.03 - 1.14)	0.003**	1.26 (1.10 - 1.44)	0.001***
PCR < 0.3 mg/dL	1.02 (0.98 - 1.05)	0.359	0.93 (0.86 - 1.00)	0.052
[PCT] < 0.5 ng/mL	1.03 (1.00 - 1.06)	0.056†	1.17 (1.04 - 1.32)	0.011**
[IL6] < 7.0 pg/mL	1.00 (1.00 - 1.00)	0.810	1.00 (1.00 - 1.00)	0.990

Methods

We prospectively enrolled all consecutive patients with blood cultures, evaluated the LEU#, MO# and MDW on a DXH900 (Beckman Coulter) and PCT, CRP, and IL6 from serum analysis. Two groups were defined, sepsis (isolation of at least one microorganism from positive blood cultures) and infection (isolation of microorganisms from other products). Mann-Whitney test was applied to compare the characteristics of the different parameters, and univariate and multivariate logistic regression, to examine the impact of each parameter on sepsis or infection. Receiver operating characteristic curve (ROC) analysis for predicting sepsis and infection (area under curve - AUC), and optimal cutoff values (Youden's index). Statistically significant differences were considered for $p < 0.05$.

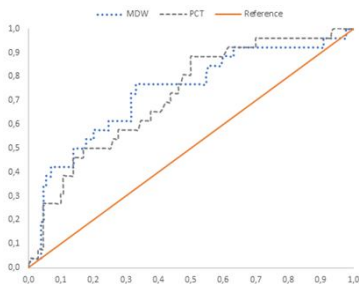
Comparison of demographic and clinical characteristics between patients with Blood cultures (Median (IQR))

		Total	Blood culture		p
			Negative	Positive	
Gender	Female	115 (38.3)	95 (38.6)	20 (37)	0.829
	Male	185 (61.7)	151 (61.4)	34 (63)	
Age, Median (IQR)		66 (57 - 74)	65 (56 - 74)	68 (59 - 77)	0.113
Cancer type	Unknown	1 (0.3)	1 (0.4)	0 (0)	0.236
	Brain (Neurology)	5 (1.7)	4 (1.6)	1 (1.9)	
	Head and Neck	29 (9.7)	22 (8.9)	7 (13)	
	Breast	19 (6.3)	16 (6.5)	3 (5.6)	
	Vagina and uterus	16 (5.3)	14 (5.7)	2 (3.7)	
	Others (Gynecology)	6 (2)	5 (2)	1 (1.9)	
	Lung	33 (11)	31 (12.6)	2 (3.7)	
	Skin	17 (5.7)	14 (5.7)	3 (5.6)	
	Stomach and esophagus	39 (13)	33 (13.4)	6 (11.1)	
	Colon and rectal	59 (19.7)	45 (18.3)	14 (25.9)	
	Liver, gallbladder and pancreas	20 (6.7)	17 (6.9)	3 (5.6)	
	Prostate, urethra and testicles	8 (2.7)	3 (1.2)	5 (9.3)	
	Kidneys and urothelium	11 (3.7)	10 (4.1)	1 (1.9)	
	Hematological	24 (8)	21 (8.5)	3 (5.6)	
Soft tissue and bone	7 (2.3)	5 (2)	2 (3.7)		
Thyroid and supra	6 (2)	5 (2)	1 (1.9)		

Spearman Correlation between analytical variables

	WBC ($\times 10^3$)	MO# ($\times 10^3$)	MDW	RCP	[PCT]	[IL6]
WBC ($\times 10^3$)	1					
MO# ($\times 10^3$)	0.641	1				
MDW	0.003	-0.091	1			
CRP < 0.3 mg/dL	0.313	0.188	0.290	1		
[PCT] < 0.5 ng/mL	0.261	0.007	0.435	0.577	1	
[IL6] < 7.0 pg/mL	0.178	0.054	0.570	0.380	0.447	1

Area Under Curve (AUC) univariate



		AUC
		Blood Infection
	MO#	0.429
	MDW	0.735
	PCR	0.577
	PCT	0.718
	IL6	0.594
Other Infections	WBC	0.562
	MO#	0.520
	MDW	0.553
	PCR	0.512
	PCT	0.569
	IL6	0.500

Sensitivity, specificity, PPV, PNV of MDW and PCT in predicting positive/negative blood cultures.

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Conclusions

MDW alone had the best performance on detecting sepsis. We suggest the introduction of MDW as a systematic screening test, together with other sepsis biomarkers, in order to improve the accuracy of sepsis diagnosis regarding oncology patients.