



Evaluation of Monocyte Distribution Width as an Early Marker for Diagnosis of Sepsis

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BACKGROUND

Since sepsis has a high mortality rate, early diagnosis and treatment can increase the survival rate and improve prognosis. However, it is difficult to diagnose sepsis accurately in actual clinical practice. Determination of Procalcitonin (PCT) or C-reactive protein (CRP) levels, which are conventionally used for diagnosing sepsis, are time-consuming. Recent studies have shown that monocyte distribution width (MDW), which is observed simultaneously during the complete blood count (CBC)/diff test in Beckman Coulter DxH900, is a potential marker for the early detection of patients with or developing sepsis. This study evaluated MDW for early detection of sepsis in patients visiting emergency department.

METHODS

This study enrolled a total of 1,167 patients (>18 and ≤ 80 years of age) who visited the emergency department from August 4, 2020 to March 31, 2021, whose initial evaluation included CBC with differential tests and other blood tests (CRP and PCT). Samples for CBC and MDW were collected in K3-EDTA tubes and analyzed in a UniCel DxH 900 analyzer (Beckman Coulter, Inc., USA). Sepsis was diagnosed according to sepsis-3 definition through medical record review. All patients were grouped into no sepsis, sepsis and septic shock. The diagnostic performance of MDW and other biomarkers for detection of sepsis was evaluated through statistical analysis. The subgroup analysis for diagnostic performance was performed in subjects with malignancy or without malignancy. All statistical analyses were carried out using Analyze-it, and $P < 0.05$ was considered statistically significant.

RESULTS

1. Baseline characteristics of the patients

Variables	Total	No sepsis	Sepsis	Septic shock	P value
N	1167	1011 (86.6%)	135 (11.6%)	21 (1.8%)	
Age	1167	1011	135	21	
Median (IQR)		65.0 (65.0-73.0)	70.0 (60.2-76.0)	69.0 (63.7-73.7)	<0.05
Sex	1167	1011	135	21	
Male (n, (%))	747 (64%)	654 (64.7%)	84 (62.2%)	9 (42.9%)	0.107
Female (n, (%))	420 (36%)	357 (35.3%)	51 (37.8%)	12 (57.1%)	
Malignancy	1167	1011	135	21	
No (n, (%))	415 (35.5%)	344 (34.0%)	60 (44.4%)	11 (52.4%)	<0.05
Yes (n, (%))	752 (64.5%)	667 (66.0%)	75 (55.6%)	10 (47.6%)	
qSOFA score	1167	1011	135	21	
Median (IQR)		0.0 (0.0-0.0)	0.0 (0.0-1.0)	1.0 (1.0-1.0)	<0.05
SOFA score	1167	1011	135	21	
Median (IQR)		0.0 (0.0-2.0)	3.0 (2.0-4.0)	8.0 (6.0-9.0)	<0.05
WBC	1166	1010	135	21	
Median (IQR)		8.30 (5.90-11.60)	9.90 (6.72-14.58)	13.60 (9.07-19.70)	<0.05
CRP	1161	1006	134	21	
Median (IQR)		1.82 (0.35-7.26)	8.84 (4.17-15.93)	20.44 (12.74-29.83)	<0.05
PCT	563	445	98	20	
Median (IQR)		0.19 (0.07-0.45)	1.72 (0.52-5.44)	18.20 (2.78-54.92)	<0.05
MDW	1167	1011	135	21	
Median (IQR)		19.70 (17.80-22.40)	27.20 (23.93-31.88)	31.10 (26.77-35.47)	<0.05

Shapiro-Wilk's test was employed for test of normality assumption. P values were derived from chi-square test for categorical variables (sex and malignancy) and from Kruskal-Wallis test for continuous variables.

2. Microbiological testing for patients diagnosed with sepsis

Patients	Culture : ordered		Culture : not ordered
	Positive culture result	Negative culture result	
1167	667 (57.1%)		500 (42.9%)
	Sepsis N=73	Sepsis N=68	

Sepsis group	Positive culture result	No culture result
156	73 (46.8%)	83 (53.2%) Culture-negative: 68 (43.6%) Culture-not ordered: 15 (9.6%)

➢ Among sepsis patients, patients with positive culture results were 46.8%, and the rest of the patients either had negative culture results (43.6%) or did not proceed with culture testing (9.6%).

RESULTS

3. Comparison of biomarkers among patient group

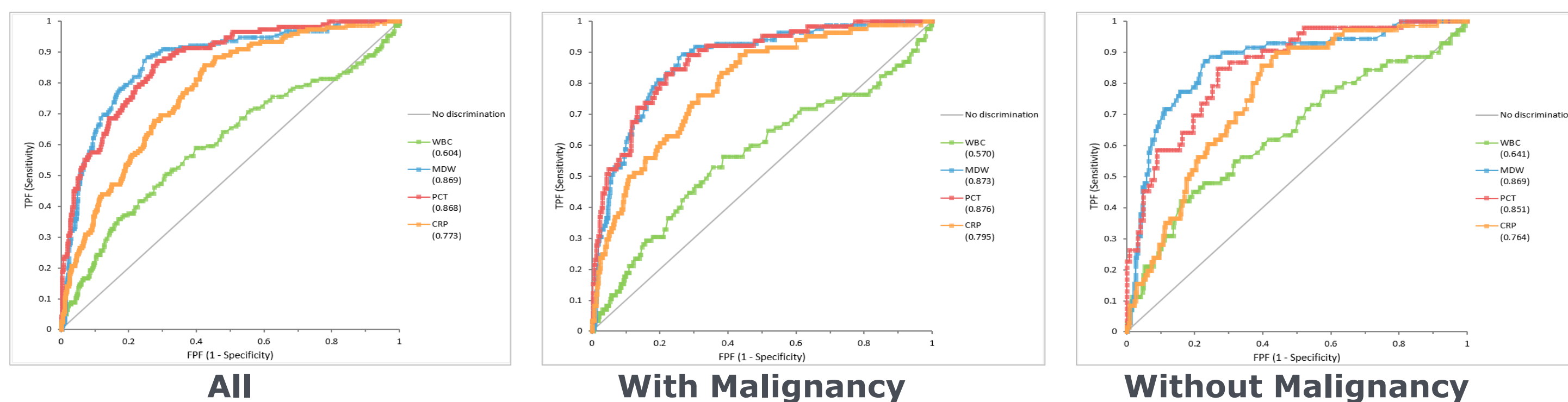
Population	Biomarker	Patient No.				Median (IQR)			P value
		Total	No sepsis	Sepsis	Septic shock	No sepsis	Sepsis	Septic shock	
All	MDW	1167	1011	135	21	19.70 (17.80-22.40)	27.20 (23.93-31.88)	31.10 (26.77-35.47)	<0.05
	WBC	1166	1010	135	21	8.30 (5.90-11.60)	9.90 (6.72-14.58)	13.60 (9.07-19.70)	<0.05
	CRP	1161	1006	134	21	1.82 (0.35-7.26)	8.84 (4.17-15.93)	20.44 (12.74-29.83)	<0.05
	PCT	563	445	98	20	0.19 (0.07-0.45)	1.72 (0.52-5.44)	18.20 (2.78-54.92)	<0.05
With malignancy	MDW	752	667	75	10	19.80 (18.00-22.60)	26.70 (23.72-32.10)	30.05 (28.21-35.27)	<0.05
	WBC	751	666	75	10	8.20 (5.90-11.31)	9.80 (6.13-13.58)	11.25 (6.83-19.63)	0.096
	CRP	746	662	74	10	2.33 (0.46-7.77)	10.38 (4.94-18.86)	25.86 (14.36-30.16)	<0.05
	PCT	387	322	55	10	0.18 (0.07-0.45)	1.62 (0.62-5.44)	13.51 (0.99-32.59)	<0.05
Without malignancy	MDW	415	344	60	11	19.40 (17.50-22.00)	27.25 (24.44-31.08)	31.10 (23.43-38.15)	<0.05
	WBC	415	344	60	11	8.60 (6.04-11.76)	10.45 (7.47-15.90)	14.70 (10.70-24.80)	<0.05
	CRP	415	344	60	11	1.12 (0.25-6.18)	7.02 (3.22-12.24)	16.54 (9.99-29.67)	<0.05
	PCT	176	123	43	10	0.20 (0.08-0.47)	1.83 (0.45-5.16)	34.20 (3.28-66.29)	<0.05

➢ The MDWs of the no sepsis group, sepsis group, and septic shock group were 19.70, 27.20, and 31.10, respectively, CRPs were 1.82, 8.84, and 20.44, and PCTs were 0.19, 1.72, and 18.20 (median, $P < 0.05$). All biomarkers showed a higher value in the sepsis group compared to the no sepsis group.

➢ Median MDW showed an increasing trend in patients with malignancy and without malignancy.

4. Diagnostic performance of biomarkers in predicting sepsis

Population	Biomarker	Total	No sepsis	Sepsis	AUC	Cutoff	Sensitivity	Specificity	PPV	NPV
All	MDW	1167	1011	156	0.869	22.3	88.5	74.5	35	98
	WBC	1166	1010	156	0.604	10.4	50.6	68.9	20	90
	CRP	1161	1006	155	0.773	3.09	85.8	57.7	24	96
	PCT	563	445	118	0.868	0.40	87.3	71.7	32	97
With malignancy	MDW	752	667	85	0.873	22.3	89.4	73.2	30	98
	WBC	751	666	85	0.570	9.4	56.5	61.4	16	92
	CRP	746	662	84	0.795	3.26	89.3	56.6	21	98
	PCT	387	322	65	0.876	0.52	83.1	78.3	33	97
Without malignancy	MDW	415	344	71	0.869	22.3	87.3	77.0	44	97
	WBC	415	344	71	0.641	14.0	42.3	84.0	35	88
	CRP	415	344	71	0.764	2.42	85.9	60.5	31	95
	PCT	176	123	53	0.851	0.42	84.9	73.2	40	96



➢ The AUCs of MDW, WBC, CRP, and PCT for the prediction of sepsis were 0.869, 0.604, 0.773, and 0.868, respectively ($P < 0.05$), which showed similar diagnostic performance with MDW and PCT. At the cutoff of MDW (21.5), the sensitivity was 91.0% and the NPV was 98%.

➢ The diagnostic performance of MDW showed similar results in cancer patients and cancer-negative patients (AUC 0.873 vs 0.869).

CONCLUSION

MDW, which is automatically measured in Beckman coulter DxH900 hematology analyzer without requirement of additional reagents during CBC with differential tests, has high accuracy in detecting patients with sepsis and could be a reliable tool for early detection of patients with sepsis in the emergency department compared to results of culture or other biomarkers which take longer time to get result. Furthermore, high NPV may help clinicians rule out sepsis.