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The predictive value of peripheral blood monocytic myeloid-derived suppressor cells for survival and immunotherapy responses in tumor patients

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Abstract

Background and objectives The identification of affordable and easily accessible indicators to predict overall survival is important for tumor immunotherapy. Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of immature myeloid cells, which promote tumor immune escape in the tumor microenvironment (TME). This study aimed to determine whether peripheral blood MDSCs could determine their potential as predictors of survival in tumor patients with immunotherapy.

Methods Flow cytometry was used to detect peripheral blood monocytic myeloid-derived suppressor cells (M-MDSCs) and granulocytic myeloid-derived suppressor cells (G-MDSCs) in 126 patients. Multivariate Cox regression analysis was conducted to examine the associations between peripheral blood MDSCs and patient survival. The receiver operating characteristic (ROC) curve determined the optimal cutoff value for peripheral blood MDSCs and grouped the indicators. The relationship between peripheral blood M-MDSCs and the prognosis and treatment outcome of tumor patients was explored.

Results The proportion of peripheral blood M-MDSCs was associated with the prognosis of patients with tumors, as were tumor metastasis, the red blood cell count, absolute neutrophil count, absolute monocyte count, and BMI. Multivariate Cox regression analysis revealed that M-MDSCs, absolute lymphocyte value, and tumor metastasis were independent risk factors affecting the prognosis of patients with tumors. Detection of peripheral blood M-MDSCs obtained high sensitivity and specificity for tumor diagnosis. Patients with high M-MDSCs percentage demonstrated reduced survival durations and diminished responses to immunotherapy compared to those with low M-MDSCs percentage.

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Conclusions Peripheral blood M-MDSCs may be used to predict overall survival and immunotherapy efficacy outcomes. This study provides a putative predictive biomarker for clinicians to choose from to predict tumor patients' survival and the selection of receiving immunotherapy regimens.

Keywords MDSCs, Peripheral blood, Predictive value, Overall survival, Immunotherapy response

Introduction

Recent data from the American Cancer Society on population-based cancer statistics indicate an increase in cancer incidence from 2015 to 2019 [1]. Specifically, breast, pancreas, and uterine corpus cancers exhibited an annual rise of 0.6–1%. In contrast, prostate, liver (female), kidney, and human papillomavirus-associated oral cancers, as well as melanoma, showed an annual increase of 2-3%. Additionally, cervical cancer in individuals aged 30–44 years and colorectal cancer in those under 55 years of age experienced an annual increase of 1–2% in young adults [2]. Globally, cancer remains a significant public health challenge [3]. From radiotherapy, chemotherapy, and targeted therapy to immunotherapy, continuous efforts have deepened our comprehension of the intricate nature of tumor pathogenesis and increased the standards of treatment [4–6]. However, not all patients with tumors benefit from immunotherapy [7]. Consequently, it is essential to identify and characterize novel biomarkers predicting the efficacy of tumor immunotherapy to develop precise immunotherapy strategies.

Myeloid cells are a group of heterogeneous immune cells produced by the bone marrow [8] and include monocytes, macrophages, granulocytes, and dendritic cells, which are the most abundant immune cells in the tumor microenvironment [9]. Myeloid cells play important roles in the tumor immune response and immune escape [10, 11]. Under pathological conditions, such as tumors, inflammation, and autoimmune diseases, the body can produce MDSCs [12], which can be classified into myeloid-derived suppressor cells (M-MDSCs) and granulocytic myeloid-derived suppressor cells (G-MDSCs) according to their phenotypes and functions [13]. There is a close relationship between MDSCs and tumors [14]. Existing reports have reported that MDSCs can inhibit immune response [15–17], promote angiogenesis, and enhance tumor invasion [18].

Meanwhile, the characteristics and clinical significance of M-MDSCs and G-MDSCs in clinical tumor patients who received remain to be further explored [19, 20]. According to the published literature, the functional phenotypes of MDSCs in mice and humans have been verified [21]. Many scholars have found that MDSCs are related to immunosuppression through studying MDSCs in tumor tissues and tumor microenvironments [22, 23]. However, the detection of peripheral blood MDSC has not been reported to predict the efficacy of immunotherapy and the overall survival in pan-cancer patients. Consequently, we revealed the predictive value of M-MDSCs for the response to immunotherapy and distant metastasis based on survival data. Our analysis indicated that M-MDSCs may be a reliable predictive biomarker for both prognosis and response to immunotherapy in patients with tumors.

Methods

Study design

To determine the relationship between peripheral blood MDSCs and tumor prognosis, we collected clinical data from 126 tumor patients at the Department of Oncology, Affiliated Hospital of Jiangsu University from September 2021 to September 2022. In this investigation, all patients were Chinese. The median age of patients was 69 years. Study enrollment conditions:1.Patients with pathologically confirmed solid tumors after diagnosis and before treatment; 2. Patients who have received an MDSC examination before medical therapy; 3. The inspection period is between September 2021, and September 2022; 4. Exclusion criteria: (a) unevaluable lesions; (b) Patients with severe infections and autoimmune diseases; (c) Have previously been diagnosed with other tumors; (d) Damage to functional organs (e) Complicated with serious medical diseases, such as heart dysfunction, liver, and kidney dysfunction; (f) Persons with cognitive impairment or mental illness; (g) Drug or alcohol abusers. Moreover, we collected clinical data from the patients, which included age, sex, counts of white blood cells, red blood cells, and platelets, as well as the absolute values of neutrophils, lymphocytes, and monocytes, BMI, tumor metastasis status, and pathological classification. The presence of regional lymph node metastasis or distant metastasis was confirmed through pathological examination or imaging techniques.

Flow cytometry analysis of blood samples and data collection

We took patient blood draws with pathologically confirmed solid tumors after diagnosis and before treatment. 4 ml of venous blood was collected from the patient's elbow fossa vein with an intravenous blood collection needle, and M-MDSCs and G-MDSCs were detected by flow cytometry. Specific steps: First, peripheral blood was collected in EDTA anticoagulant tubes. According to the manufacturer's instructions, the sample was treated with red blood cell lysis buffer (BD, Cat.# 555899) and incubated at room temperature for 15 min to lysis

red blood cells. Next, the mixture underwent centrifugation at 200×g for 5 min, after which the supernatant was carefully discarded. The cell lysates were washed by resuspending them in PBS buffer, followed by a repeat centrifugation step to remove residual impurities. The sample was fixed with Fc blocker(BD, Cat.#564219) at room temperature for 10 min followed by specific surface antigens of M-MDSCs and G-MDSCs were labeled with specific antibodies, including APC-Cy7 anti-human CD14(BD, Cat.#557831,1:200), FITC anti-human CD15(BD, Cat.# 555401,1:200), PE anti-human CD11b(BD, Cat.#555388,1:200), APC HLA-DR(BD, Cat.# 559866,1:200). For LOX-1(R&D, Cat.#FAB1798P,1:200) staining, the LOX-1 antibody was incubated with cells, and then PerCP secondary antibody was used to label LOX-1. M-MDSCs were gated as $CD14^+/CD15^-/HLA\text{-}DR^{-/lo}$, and G-MDSCs were gated as $CD11b^+/CD14^-/CD15^+/LOX\text{-}1^+$. The labeled cell samples were analyzed by flow cytometry in BD FACS CANTO 10 C. The outcomes were presented as a percentage(Fig. S1). The specific values of M-MDSCs and G-MDSCs can be obtained according to the analysis data of flow cytometry. Data on numerical results of MDSCs, clinically relevant indicators, and pathological features were collected from all relevant patients.

Statistical analysis

In this research, statistical evaluations were carried out using SPSS (version 27.0, NY, USA) and GraphPad Prism (version 10.0, CA, USA). The results are expressed as the means ± standard deviations, and the Kruskal–Wallis test was used to test for clinical parameters among multiple subgroups. The Mann-Whitney U test was applied to assess differences in continuous variables, and the results were subsequently plotted via the GraphPad Prism 10.0 software. The ROC curve was used to select the best cut-off value for peripheral blood MDSCs and to stratify the indicators. The Kaplan–Meier method was applied to plot survival curves. Univariate analysis was performed to determine variables that were associated with the survival of patients with tumors. Multivariate Cox regression analysis was used to identify predictors of cancer in patients. A p-value below 0.05 was deemed to indicate statistical significance.

Evaluation strategy

The primary endpoint of this study was overall survival (OS). For participants who missed their follow-up visits before death, their last recorded follow-up was considered the date of death. The secondary assessment endpoints included progression-free survival (PFS), which was defined as the period from the start of randomization to the progression of tumorigenesis or death due to any cause.

Ethics statement

The study was approved by the Ethics Committee of the Affiliated Hospital of Jiangsu University. Samples were taken from patients after obtaining informed consent and with the approval of the Affiliated Hospital of Jiangsu University Ethics Committee.

Results

Analysis of clinical relevance of M-MDSCs and G-MDSCs to tumor patients

This study comprised 126 patients. The specific clinical and pathological features of the patients are presented in Tables 1 and 2. We investigated the relationship between the percentage of tumor patient peripheral blood M-MDSCs and G-MDSCs and clinical characteristics, including age, sex, white blood cell count (WBC), red blood cell count (RBC), platelets (PLT), absolute neutrophil count, absolute lymphocyte count, absolute monocyte count, body mass index (BMI), tumor location, tumor metastasis, and pathological classification. The results showed that the percentage of M-MDSCs and G-MDSCs had no significant differences in age, sex, WBC, PLT, absolute lymphocyte value, tumor location, and pathological classification ($p > 0.05$). G-MDSCs did not show significant differences in RBC, absolute neutrophil count, absolute monocyte count, BMI, and tumor metastasis ($p > 0.05$). However, statistical differences in M-MDSCs were observed in RBC, absolute neutrophil count, absolute monocyte count, BMI, and tumor metastasis ($p < 0.05$).

Peripheral blood M-MDSCs are associated with distant metastasis in tumor patients

The tumor metastasis types include lymph node metastasis and distant metastasis. Utilizing the TNM staging results from the eighth edition of AJCC [24], patients were stratified into the no metastasis group ($n = 63$), lymph node metastasis group ($n = 25$), and distant metastasis group ($n = 38$). Mann-Whitney U tests were used to analyze the relationship between MDSCs and tumor metastasis. Results showed that M-MDSCs (Fig. 1A) were associated with tumor metastasis. Comparison between groups indicated no significant variation of M-MDSCs between the lymph node metastasis and non-metastatic group ($p > 0.05$). However, the proportion of M-MDSCs in the distant metastasis group was significantly increased than the no metastatic and lymph node metastasis groups ($p < 0.05$). Next, metastasis was analyzed in patients with esophageal tumors and NSCLC (Fig. 1B&C), which have sufficient sample size for statistical analysis. Similar results were obtained, showing no significant differences between no metastasis and lymph node metastasis groups. In contrast, significant

Table 1 Basic physiological and clinicopathological parameters of 126 tumor patients in comparison with the M-MDSCs percentage

Characteristic	*N*(%)	M-MDSC(%)	*p*-value
Age			0.1289
< 60 years	27(21.4%)	11.0 ± 16.5	
≥ 60 years	99(78.6%)	6.0 ± 8.1	
Sex			0.1494
Male	63(50.0%)	8.9 ± 13.4	
Female	63(50.0%)	5.3 ± 6.5	
WBC			0.5272
$< 4 \times 10^9$/L	8(6.3%)	6.6 ± 10.4	
$\geq 4 \times 10^9$/L	118(93.7%)	7.1 ± 10.7	
RBC			0.0463
$< 4.0 \times 10^9$/L	64(50.8%)	8.6 ± 12.2	
$\geq 4.0 \times 10^9$/L	62(49.2%)	5.6 ± 8.5	
PLT			0.1382
$< 150 \times 10^9$/L	25(19.8%)	4.9 ± 6.4	
$\geq 150 \times 10^9$/L	101(80.2%)	7.7 ± 11.4	
Absolute neutrophil count			0.0024
$\leq 6.3 \times 10^9$/L	111(89.1%)	5.9 ± 8.1	
$> 6.3 \times 10^9$/L	15(11.9%)	15.8 ± 19.9	
Absolute lymphocyte count			0.0989
$< 0.8 \times 10^9$/L	30(23.8%)	12.6 ± 18.2	
$\geq 0.8 \times 10^9$/L	96(76.2%)	5.4 ± 5.9	
Absolute monocyte count			0.0079
$\leq 0.6 \times 10^9$/L	108(85.7%)	6.2 ± 10.0	
$> 0.6 \times 10^9$/L	18(14.3%)	12.5 ± 12.9	
BMI			0.0364
< 18.5	18(14.3%)	12.5 ± 19.7	
18.5–23.9	72(57.1%)	7.0 ± 9.3	
≥ 24	36(28.6%)	4.7 ± 4.4	
Tumor location			0.5018
Esophagus cancers	34(26.98%)	9.5 ± 15.8	
Gynecological cancers	34(26.98%)	5.1 ± 4.4	
Head & neck cancers	17(13.49%)	3.6 ± 2.8	
Lung cancers	27(21.42%)	9.7 ± 12.6	
Other locations	14(11.11%)	5.2 ± 3.8	
Tumor metastasis			< 0.0001
No metastatic	63(50.0%)	4.2 ± 0.04.0	
Lymph node metastasis	24(19.0%)	4.9 ± 8.0	
Distant metastasis	39(31.0%)	13.3 ± 15.9	
Pathological classification			0.4609
Squamous carcinoma	84(66.7%)	7.0 ± 11.8	
Adenocarcinoma	33(26.2%)	8.2 ± 8.4	
Other classifications	9(7.1%)	4.4 ± 5.9	

differences were obtained between lymph node metastasis and distant metastasis groups.

Relationship between peripheral blood M-MDSCs and prognosis of tumor patients

Multivariate Cox regression analysis (Table 3) was performed with the indicators that showed statistical significance in the univariate Cox regression analysis, and the results suggested that the level of M-MDSCs (HR 2.005 (95% CI 1.035–3.882), $p = 0.039$), absolute lymphocyte count, and tumor metastasis were independent risk factors affecting the prognosis of patients with tumors. Patients with low M-MDSCs percentage exhibited longer survival than patients with high M-MDSCs percentage.

ROC curve (Fig. 2A) was used to evaluate the values of statistically significant variables in the Cox regression model for M-MDSCs. The area under the curve for M-MDSCs was 0.710 ($p < 0.001$), and the optimal cutoff value for M-MDSCs was 4.2%.

Table 2 Basic physiological and clinicopathological parameters of 126 patients in comparison with the G-MDSCs percentage

Characteristic	*N*(%)	G-MDSC(%)	*p*-value
Age			0.2412
< 60 years	27(21.4%)	2.8 ± 2.4	
≥ 60 years	99(78.6%)	2.0 ± 1.3	
Sex			0.7492
Male	63(50.0%)	2.0 ± 0.9	
Female	63(50.0%)	2.5 ± 2.1	
WBC			0.7589
$< 4 \times 10^9$/L	8(6.3%)	2.0 ± 0.6	
$\geq 4 \times 10^9$/L	118(93.7%)	2.2 ± 1.7	
RBC			0.2469
$< 4.0 \times 10^9$/L	64(50.8%)	2.2 ± 1.9	
$\geq 4.0 \times 10^9$/L	62(49.2%)	2.3 ± 1.2	
PLT			0.1382
$< 150 \times 10^9$/L	25(19.8%)	2.3 ± 1.7	
$\geq 150 \times 10^9$/L	101(80.2%)	2.1 ± 0.8	
Absolute neutrophil count			0.9967
$\leq 6.3 \times 10^9$/L	111(89.1%)	2.3 ± 1.7	
$> 6.3 \times 10^9$/L	15(11.9%)	2.2 ± 1.2	
Absolute lymphocyte count			0.9557
$< 0.8 \times 10^9$/L	30(23.8%)	1.9 ± 0.8	
$\geq 0.8 \times 10^9$/L	96(76.2%)	2.3 ± 1.8	
Absolute monocyte count			0.6493
$\leq 0.6 \times 10^9$/L	108(85.7%)	2.3 ± 1.7	
$> 0.6 \times 10^9$/L	18(14.3%)	2.2 ± 0.9	
BMI			0.4494
< 18.5	18(14.3%)	1.8 ± 0.9	
18.5–23.9	72(57.1%)	2.3 ± 1.2	
≥ 24	36(28.6%)	2.3 ± 2.4	
Tumor location			0.1424
Esophagus cancers	34(26.98%)	2.0 ± 1.0	
Gynecological cancers	34(26.98%)	2.2 ± 2.1	
Head & neck cancers	17(13.49%)	2.4 ± 2.5	
Lung cancers	27(21.42%)	2.0 ± 1.0	
Other locations	14(11.11%)	1.6 ± 0.9	
Tumor metastasis			0.4032
No metastatic	63(50.0%)	2.4 ± 2.1	
Lymph node metastasis	24(19.0%)	2.1 ± 0.9	
Distant metastasis	39(31.0%)	2.0 ± 1.1	
Pathological classification			0.1424
Squamous carcinoma	84(66.7%)	2.3 ± 1.5	
Adenocarcinoma	33(26.2%)	1.8 ± 1.1	
Other classifications	9(7.1%)	3.0 ± 3.2	

Kaplan–Meier analysis was used to construct survival curves. According to the optimal cutoff value for M-MDSCs, 66 patients were included in the low M-MDSC group (M-MDSCs ≤ 0.042), and 60 patients were included in the high M-MDSC group (M-MDSCs > 0.042). PFS was significantly greater in the patients with low M-MDSCs percentage than in those with high M-MDSCs percentage ($p < 0.001$) (Fig. 2B). Furthermore, patients in the low M-MDSCs group presented significantly higher OS rates than did those in the high M-MDSCs group ($p < 0.001$) (Fig. 2C).

Relationship between peripheral blood M-MDSCs and treatment outcome of tumor patients

M-MDSCs are closely related to tumor immune suppression [25]. Among the follow-up patients, 31 patients received single anti-PD-1 ICB immunotherapy, according to patients' tolerance and therapeutic schedule, the duration of treatment ranged from one month to

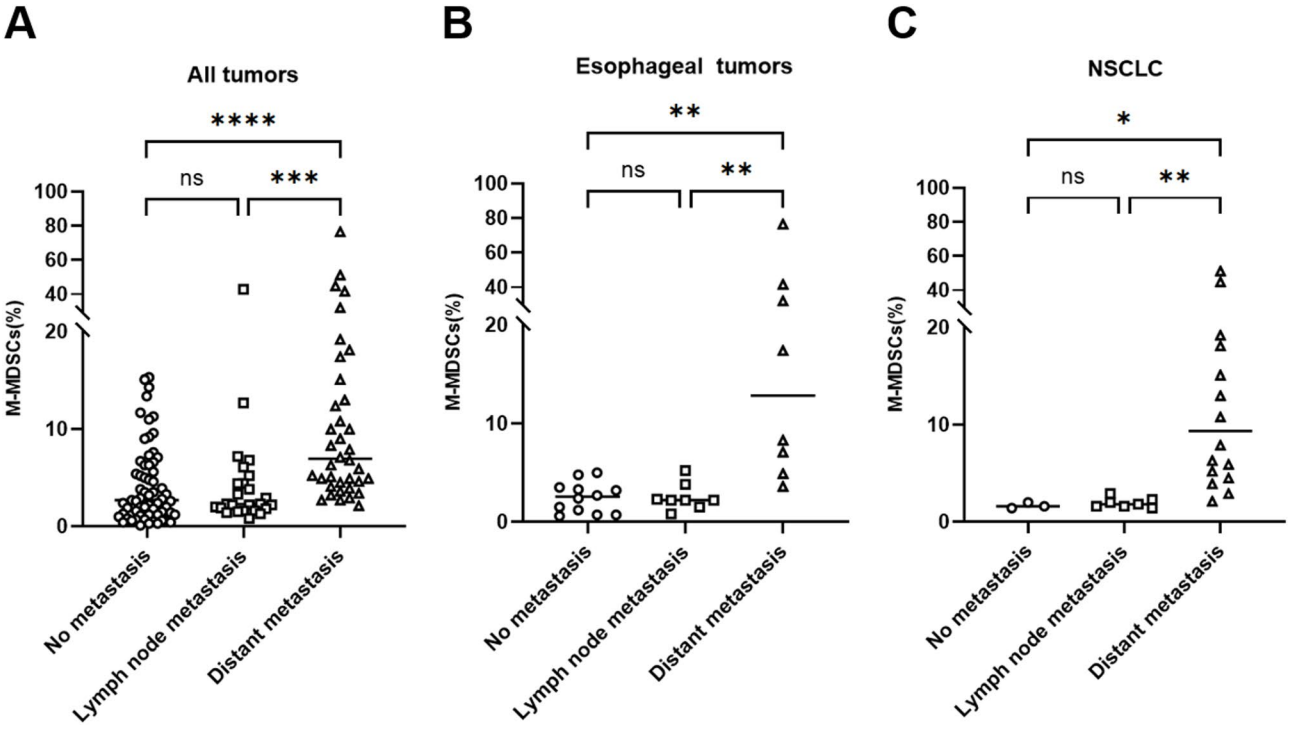

Fig. 1 Peripheral blood M-MDSCs are associated with distant metastasis in patients with tumors: **A**-**C** Metastasis in all patients with tumors (**A**), patients with esophageal tumors (**B**), and patients with NSCLC (**C**)

Table 3 Univariate and multivariate Cox regression analyses of the relationships between clinical variables and patient survival

	Univariate Cox		Multivariate Cox	
	HR(95%CI)	*p*-value	HR(95%CI)	*p*-value
Age(≤ 60y vs. > 60y)	1.001(0.978–1.024)	0.963		
Sex(Men vs. Women)	0.353(0.199–0.626)	< 0.001	0.657(0.304–1.422)	0.287
RBC(≥ 4.0×10^9/L vs. < 4.0×10^9/L)	1.408(0.826–2.399)	0.209		
WBC(≥ 4.0×10^9/L vs. < 4.0×10^9/L)	0.757(0.233–2.431)	0.640		
PLT(≥ 150×10^9/L vs. < 150×10^9/L)	0.981(0.506–1.902)	0.956		
Absolute neutrophil count (>6.3×10^9/L vs. ≤ 6.3×10^9/L)	1.052(0.558–1.986)	0.875		
Absolute lymphocyte count (≥ 0.8×10^9/L vs<0.8×10^9/L)	1.772(1.015–3.096)	0.044	1.999(1.102–3.604)	0.021
Absolute monocyte count (> 0.6×10^9/L vs. ≤ 0.6×10^9/L)	1.022(0.529–2.376)	0.765		
BMI(<18.5 vs. 18.5–23.9 vs. ≥ 24)	0.780(0.511–1.191)	0.249		
Tumor location(Esophagus tumors vs. Gynecological cancers vs. Head & neck cancers vs. Lung cancers vs. Other locations)	0.711(0.488–1.034)	0.074		
Tumor metastasis (non-distant metastasis vs. distant metastasis)	3.465(2.036–5.897)	< 0.001	3.370(1.845–6.156)	<0.001
Pathological classification(Squamous carcinoma vs. Adenocarcinoma vs. Other classifications)	0.961(0.649–1.574)	0.961		
M-MDSCs(low M-MDSCs vs. high M-MDSCs)	3.106(1.750–5.512)	< 0.001	2.005(1.035–3.882)	0.039

twenty-seven months. Blood was always drawn before the treatment, and we did not assess the patient whose treatment prior to the blood draw. We found that PFS was significantly higher in patients with low M-MDSCs compared to those with high M-MDSCs ($p < 0.001$) (Fig. 3A). Patients in the low M-MDSCs group exhibited significantly higher OS compared to those in the high M-MDSCs group ($p < 0.001$) (Fig. 3B). Furthermore, to exclude the effect of distant metastasis on prognostic differences in immunotherapy patients, 11 patients without distant metastasis were excluded for further analyses. Similarly, in distant metastasis patients, we found that PFS was significantly higher in patients with low M-MDSCs compared to those with high M-MDSCs ($p < 0.05$) (Fig. 3C). Patients in the low M-MDSCs group showed noticeably greater OS compared to those in the high M-MDSCs group ($p < 0.05$) (Fig. 3D). The findings suggest that M-MDSCs are associated with the efficiency of anti-PD-1 immunotherapy. We further evaluated 16 patients who underwent radical chemoradiotherapy.

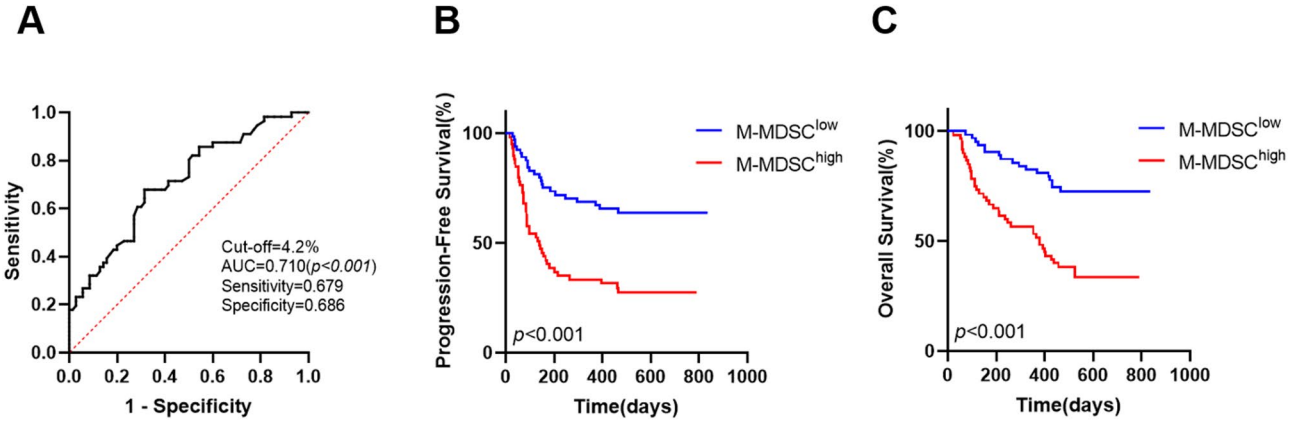

Fig. 2 **A** Receiver operating characteristic (ROC) curve was plotted to determine the values of statistically significant variables in the Cox regression model for M-MDSCs ($n=126$). According to the ROC analysis, the area under the curve for M-MDSCs was 0.710, and the optimal cutoff point was 0.042. **B**-**C** Kaplan-Meier analysis of patients with low M-MDSCs percentage ($n=66$) vs. high M-MDSCs percentage ($n=60$). PFS (**B**) and OS (**C**) according to M-MDSC levels in all patients with tumors

The analysis revealed no significant difference in PFS and OS between patients with low M-MDSCs or high M-MDSCs ($p>0.05$), suggesting a limited relationship between M-MDSCs results and radical chemoradiotherapy (Fig. 3E-F).

Discussion

In the follow-up of tumor patients, we found that peripheral blood M-MDSCs were associated with the prognosis of tumor patients, as well as tumor metastasis and absolute neutrophil count, absolute monocyte count, and BMI. These findings remained significant after controlling for clinical features, suggesting an association of peripheral blood M-MDSCs with these adverse outcomes.

The association between peripheral blood MDSCs and outcomes of tumor patients remains unclear. MDSCs consist of two large groups of cells termed granulocytic or polymorphonuclear (G-MDSCs), which are phenotypically and morphologically similar to neutrophils, and monocytic (M-MDSCs), phenotypically and morphologically similar to monocytes [26]. We found that peripheral blood M-MDSCs are associated with prognosis and immunotherapy efficacy. Analysis of the prognostic predictive power of OS and PFS showed a significant association between the M-MDSCs percentage and prognosis in patients with tumors. A high M-MDSCs percentage was identified as a risk factor for tumorigenesis and tumor progression. Analysis of patients who received anti-PD-1 immunotherapy showed associations between the M-MDSCs percentage and immunotherapy efficacy in various tumors, indicating that M-MDSCs may play a role in modulating the TME. MDSCs accumulated within the TME were recognized as a major obstacle to tumor immunotherapy [27]. Based on the analysis of patients who received immunotherapy, we found that patients with high M-MDSCs had shorter survival times and lower response rates than those with low M-MDSCs. These results confirm the predictive value of M-MDSCs for the response to immunotherapy. In our present study, no significant difference was observed between G-MDSCs and clinical data. The following reasons may account for this result: (1) A relatively small sample size in the present study; (2) Given the lack of directly labeled LOX-1 antibody for flow cytometry, we used the indirect labeling method for LOX-1 staining, which may weaken the specificity of the flow cytometry results; (3) According to published studies [28], we used LOX-1 to identify G-MDSCs in human blood, which may need more supporting evidence. Therefore, more investigations are needed to explore the relationship between G-MDSCs and tumor prognosis.

Due to the difficulty in obtaining pathological specimens in certain tumor metastatic patients, and the expensive and time-consuming of imaging metastasis [29], the forecast of distant metastases can be assisted by liquid biopsy [30]. At present, the liquid biopsy includes circulating extracellular nucleic acids (cell-free DNA; cfDNA), circulating tumor DNA (ctDNA), and circulating tumor cells (CTCs) [31], which can be used to assess tumor distant metastasis [32]. However, due to the difficulty of these detections, many medical facilities lack the necessary facilities to conduct testing, which limits their application [33]. In the present study, we revealed the associations between M-MDSCs and clinical features in tumor patients. Consistent with the survival analysis results, patients with low M-MDSCs percentage presented a lower probability of distant metastasis and a lower TNM stage. We found that detecting peripheral blood M-MDSCs with flow cytometry can effectively predict the metastasis of pan-cancer. Given the accessibility and affordability of flow cytometry [34], we suggest

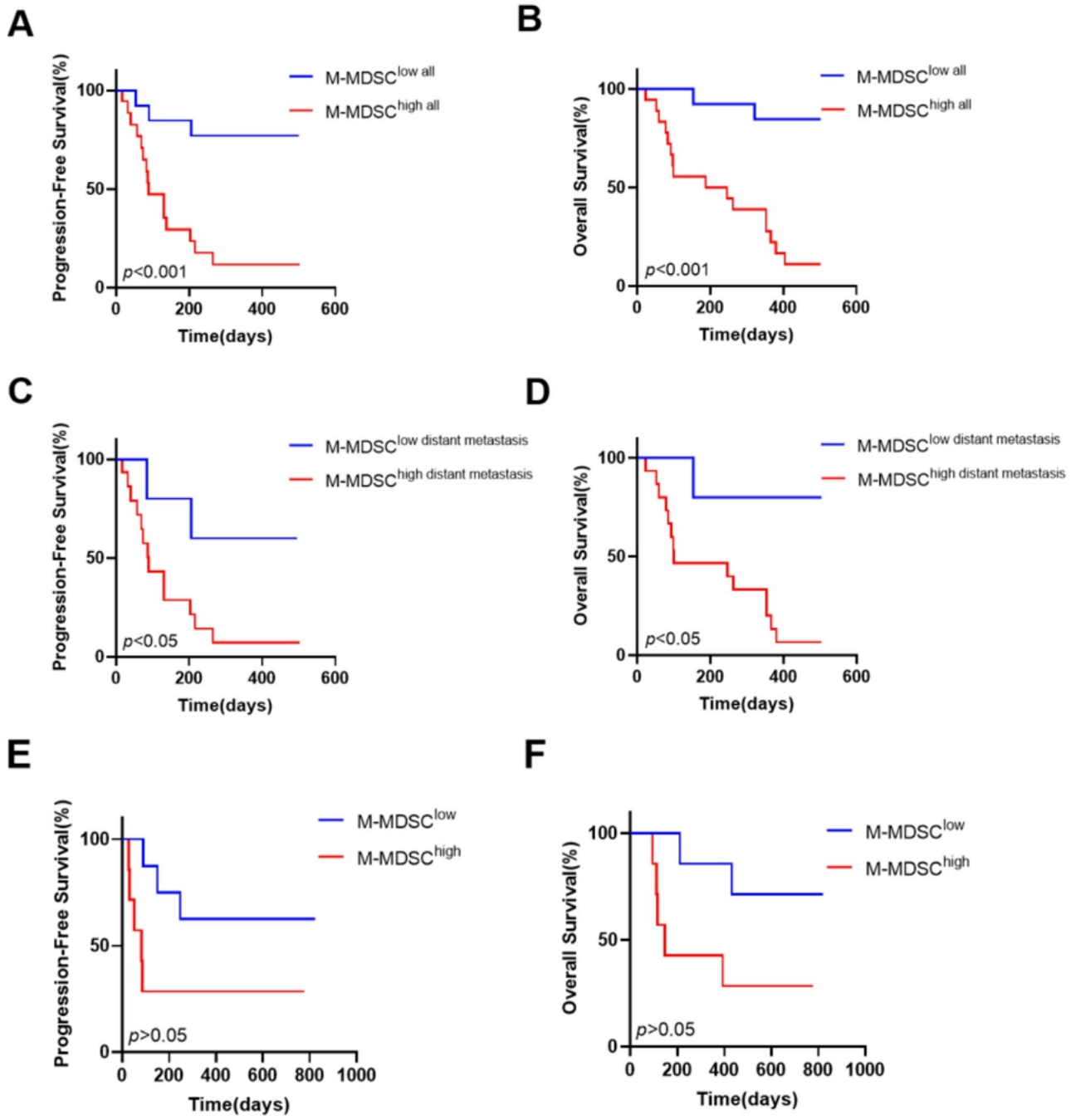

Fig. 3 Peripheral blood M-MDSCs are associated with treatment outcomes in patients with tumors: **A**-**B** PFS (**A**) and OS (**B**) according to the percentage of M-MDSCs in patients receiving immunotherapy ($n=31$). **C**-**D** PFS (**C**) and OS (**D**) according to the percentage of M-MDSCs in patients with distant metastasis receiving immunotherapy ($n=20$). **E**-**F** PFS (**E**) and OS (**F**) according to the number of M-MDSCs in patients receiving radical chemoradiotherapy ($n=16$)

that the peripheral blood M-MDSC is an important biomarker for evaluating metastasis in tumor patients.

Despite our data being accurately processed and analyzed, this study has several limitations. First of all, the small cohort size of 126 patients was examined in this study, which may lead to bias. Secondly, we excluded patients with comorbid diseases such as heart dysfunction, and liver, and kidney dysfunction, due to patients with comorbid diseases cannot tolerate conventional chemoradiotherapy and immunotherapy. This may lead to insufficient population representation and limit the guiding value for the real world. Thirdly, our study verified the predictive value of M-MDSCs for patient survival, and we need to establish animal and cell

experimental models before moving to the clinic. Last, this was a single-center and retrospective study, and all the included patients were from a single hospital, and the conclusions were not verified in other centers. Therefore, further prospective trials at multiple centers are needed to confirm the reproducibility of the results in heterogeneous populations.

Conclusion

Overall, M-MDSCs are predictors of overall survival and immunotherapy efficacy in patients with tumors. This study provides a putative predictive biomarker for clinicians to choose from to predict tumor patients' survival and the selection of receiving immunotherapy regimens.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12865-025-00722-7.

Supplementary Material 1.

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Authors' contributions
WYS contributed to data analysis and manuscript writing. YD, YTS, JH, and LW contributed to the collection and assembly of data. MJG and XY contributed to the supervision. DQW, CHD, and XW contributed to the study design and critical revision of the manuscript. All authors read and approved the final manuscript.

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Data availability
The data are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Affiliated Hospital of Jiangsu University. (ethical review report number: KY2021K0902). All the experiments were performed in accordance with the Helsinki Declaration. Informed consent was obtained from all subjects.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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