

Validation and Modeling of Flow Cytometric CD36 Coefficient of Variation Analysis in the Diagnosis of Lower-Risk Myelodysplastic Syndrome

Düşük Risk Myelodisplastik Sendrom Tanısında Akım Sitometrik CD36 Varyans Katsayısı Analizinin Validasyonu ve Modellenmesi

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Abstract

Objective: Myelodysplastic syndrome (MDS) constitutes a group of clonal hematopoietic disorders in which flow cytometry plays a limited yet evolving role in diagnosis. Recent studies have identified the CD36 coefficient of variation (CV) as a potential marker of dyserythropoiesis. This study aimed to validate the diagnostic utility of the CD36 CV in a local cohort, establish control-based cut-off values, and assess the added value of the CD36 CV when integrated into the Ogata score for improved detection of lower-risk MDS.

Materials and Methods: In this retrospective study, 82 patients who underwent bone marrow aspiration for unexplained cytopenia were analyzed using multiparametric flow cytometry, cytogenetics, and morphological assessment. CD36 CV values were obtained from erythroid precursors and diagnostic thresholds were determined based on the distribution of values in the control group. Diagnostic models included CD36 CV alone, a combined binary model with the Ogata score, and an expanded five-point scoring system.

Results: CD36 CV values were numerically higher in patients with MDS (mean: 75.81) compared to the control group (mean: 65.84), although the difference was not statistically significant ($p=0.099$). For low-risk MDS, the 75th percentage cut-off yielded 60% sensitivity and 80% specificity. Integration of the CD36 CV into the Ogata score improved specificity from 33.3% to 80% at a ≥ 3 -point threshold, with an area under the curve of 0.754 ($p=0.003$). Models with higher cut-off values demonstrated lower sensitivity.

Conclusion: Incorporating the CD36 CV into flow cytometric evaluation enhances diagnostic specificity for lower-risk MDS without requiring additional antibody panels. This locally validated marker may improve diagnostic accuracy when combined with myelomonocytic immunophenotyping. Standardization across institutions remains necessary for broader applicability.

Keywords: Myelodysplastic syndromes, Flow cytometry, Diagnosis, CD36, Erythroid dysplasia

Öz

Amaç: Myelodisplastik sendrom (MDS) klinik, morfolojik ve sitogenetik özelliklerin bir arada değerlendirilmesi ile tanı konulan klonal hematopoetik bir hastalıktır. Kemik iliğinin akım sitometrik immünofenotipleme ve bu açıdan geliştirilen skorlama sistemleri tanıyı destekleyici bir rol üstlenmektedir. Son çalışmalar, CD36 varyans katsayısını (*coefficient of variation-CV*) diseritropoez için potansiyel bir biyobelirteç olarak tanımlamıştır. Bu çalışmanın amacı, CD36 CV'nin tanısıl değerini yerel bir kohortta doğrulamak, kontrol grubuna dayalı eşik değerler belirlemek ve CD36 CV'nin Ogata skoruna entegre edilmesiyle düşük riskli MDS'nin tanısıl performansına olan katkısını değerlendirmektir.

Gereç ve Yöntemler: Bu retrospektif çalışmaya, açıklanamayan sitopeni nedeniyle kemik iliği aspirasyonu yapılan 82 hasta dahil edildi. Hastalar multiparametrik akım sitometrisi, sitogenetik ve morfolojik inceleme ile değerlendirildi. CD36 CV değerleri eritroid öncüller üzerinde ölçülerek eşik değerler kontrol grubundaki dağılıma göre belirlendi. Tek başına CD36 CV, CD36 CV ile Ogata skorunun ikili kombinasyonu ve genişletilmiş beş puanlı bir skorlama sistemi şeklinde oluşturulan tanısıl modeller çeşitli eşik değerler üzerinden test edildi.

Bulgular: CD36 CV değerleri, MDS hastalarında (ortalama: 75,81) kontrol grubuna (ortalama: 65,84) kıyasla sayısal olarak daha yüksek olmasına rağmen, istatistiksel olarak anlamlı bulunmamıştır ($p=0,099$). Düşük riskli MDS için 75. persentil eşik değeri %60 duyarlılık ve %80 özgüllük sağlamıştır. CD36 CV'nin Ogata skoruna entegrasyonu, ≥ 3 puanlık eşik değerinde özgüllüğü %33,3'ten %80'e yükseltmiş ve eğri altındaki kalan alan değeri 0,754 ($p=0.003$) olarak bulunmuştur. Daha yüksek eşik değerleriyle oluşturulan modellerde duyarlılık daha düşük olmuştur.

Sonuç: CD36 CV'nin akım sitometrik değerlendirmeye dahil edilmesi, ek antikor panellerine ihtiyaç duymadan düşük riskli MDS tanısına katkı sağlamaktadır. Lokal validasyonu sağlanan bu belirteç, myelomonositik immünofenotipleme ile birlikte kullanıldığında tanısıl doğruluğu iyileştirilebilir. Ancak bu yöntemin daha geniş ölçekte uygulanabilmesi için kurumlar arası standardizasyon gereklidir.

Anahtar Sözcükler: Myelodisplastik sendromlar, Akım sitometri, Tanı, CD36, Eritroid displazi



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Introduction

Myelodysplastic syndrome (MDS) constitutes a group of clonal hematopoietic disorders diagnosed through an integrated assessment of clinical, morphological, and cytogenetic features. Risk stratification is based on the percentage of bone marrow blasts and the presence of specific molecular and cytogenetic abnormalities [1]. Due to the lack of global standardization in flow cytometric analysis, immunophenotyping currently plays only a supportive role in MDS diagnostics. Most flow cytometric scoring systems are based on evaluating the myelomonocytic lineage, and standardized protocols for assessing dyserythropoiesis remain under development [2].

The Ogata score is one of the most widely used flow cytometric tools for the diagnosis of MDS [3]. It evaluates four parameters, each of which is assigned one point if the abnormal threshold is met: the proportion of CD34⁺ myeloid progenitors among total nucleated cells ($\geq 2\%$), the percentage of B-cell precursors among CD34⁺ cells ($\leq 5\%$), the mean fluorescence intensity (MFI) ratio of CD45 in lymphocytes to myeloblasts (≤ 4 or ≥ 7.5), and the side scatter (SSC) ratio of granulocytes to lymphocytes (≤ 6). A total score of 2 to 4 points is considered supportive of MDS, with reported sensitivity of approximately 69% and specificity of 92% [3,4]. The enriched or extended Ogata score incorporates additional aberrant immunophenotypic features, adding 1 point when CD5 or CD7 is expressed on myeloid progenitors or CD56 on monocytes with a threshold of 30% positive cells, thereby improving the sensitivity for MDS [5]. More recent studies have confirmed the prognostic relevance of the Ogata score and validated its diagnostic performance in different patient cohorts [6,7].

During normal erythropoiesis, early erythroid progenitors express high levels of transferrin receptor (CD71) and stem cell factor receptor (CD117), which progressively decrease as cells mature, while thrombospondin receptor (CD36) expression becomes more homogeneous. In parallel, the MFI of CD71 declines and the proportion of CD117-positive cells is reduced as differentiation proceeds, reflecting the transition from immature to mature erythroid stages [8]. CD36 is a transmembrane glycoprotein expressed on various hematopoietic and non-hematopoietic cells. It is involved in angiogenesis, lipid metabolism, apoptosis, and thrombosis, depending on its ligands [9]. During erythropoiesis, CD36 is expressed in the proerythroblast stage, progressively downregulated during maturation, and absent in reticulocytes. Increased flow cytometric coefficient of variation (CV) values of CD36, indicating surface expression heterogeneity, have been identified as potential markers of dyserythropoiesis [10].

In patients with MDS, these physiological patterns are altered. An increased CV value for CD36 or CD71 indicates broader heterogeneity of antigen expression among erythroid precursors, consistent with dysplastic maturation. A decreased CD71 MFI reflects abnormally low transferrin receptor density, suggesting

impaired proliferative activity or defective iron uptake. Similarly, an increased proportion of CD117-positive cells denotes a relative accumulation of immature erythroid progenitors, a hallmark of ineffective erythropoiesis [2]. A multicenter study identified CD36 CV, CD71 CV, CD71 MFI, and CD117 positivity as key markers associated with erythroid dysplasia, and incorporating these variables into myelomonocytic flow cytometric evaluation improved the diagnostic sensitivity of the Ogata score from 76% to 84% [2,11]. In this study, we aimed to validate the diagnostic relevance of elevated CD36 CV values in MDS patients in a local cohort, establish a locally applicable cut-off value through comparisons with an anemic control group, and evaluate the performance of a revised scoring model integrating the CD36 CV into the Ogata system.

Materials and Methods

Patients

This retrospective study included patients who underwent bone marrow aspiration between January 2019 and June 2024 due to unexplained cytopenia and were evaluated by multiparametric flow cytometry. Cytogenetic and morphological analyses were also performed as part of the diagnostic workup. Following the diagnostic workup, according to the 2016 classification of the World Health Organization (WHO), a diagnosis of MDS was established if morphological evaluation of the bone marrow aspirate revealed $\geq 10\%$ dysplasia in at least one myeloid lineage, or, in cases of equivocal dysplasia, if one of the defining cytogenetic/molecular genetic markers described in the same WHO criteria was present [12]. Clinical, demographic, and laboratory data were extracted from electronic medical records. Patients who received a diagnosis of MDS formed the study group, while those for whom MDS was excluded based on alternative, non-hematological causes of anemia constituted the control group. The anemic control group consisted of patients with cytopenia and pathological findings suggestive of a preliminary diagnosis of MDS; a healthy control group was not included in the study. Upon retrospective evaluation, 15 patients with flow cytometry data deemed sufficient for analysis were allocated to the control group, whereas 67 patients were included in the MDS cohort that constituted the study group. Risk stratification was performed using the Revised International Prognostic Scoring System (IPSS-R) [13].

The study was approved by the Tekirdağ Namık Kemal University Ethics Committee (protocol no: 2025.16.01.16, date: 28.01.2025).

Flow Cytometry

Bone marrow aspirates were processed within 24 hours (most often within 1 hour) and analyzed using the Navios EX Flow Cytometer (Beckman Coulter, Brea, CA, USA), acquiring a minimum of 20,000 events per sample. A two-tube, 10-color antibody panel was used (Tube 1: CD11b-FITC, CD117-PE, CD10-

ECD, CD33-PC5.5, CD34-PC7, CD13-APC, CD123-A700, CD38-A750, HLA-DR-PB, CD45-KO; Tube 2: CD15-FITC, CD16-PE, CD19-ECD, CD56-PC7, CD36-APC, CD7-A700, CD64-A750, CD14-PB, CD45-KO). Antibodies were prepared in sequence according to the manufacturer's instructions (FITC/PE/ECD/PC5/PC7/APC/A750/A700/PB/KO). Following antibody preparation, 100 µL of sample was added to the antibody tube, vortexed, and incubated in the dark at room temperature for 15 minutes. After addition of 500 µL of OptiLyse C (Beckman Coulter) and a 10-minute incubation for red blood cell lysis, 500 µL of phosphate-buffered saline (PBS) was added and incubated for another 10 minutes. Cells were then washed twice with PBS (300 g, 5 min) and finally resuspended in 500 µL of PBS for flow cytometric analysis. Quality control procedures were implemented at each step according to the manufacturer's calibration protocols, and results were systematically recorded and reported. Using Kaluza analysis software (Beckman Coulter), CD36-positive events were gated from SSC^{low}CD45^{dim} populations to calculate CD36 CV values (Figure 1). Ogata scores were calculated and recorded for each patient (Figure 2).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics 23 (IBM Corp., Armonk, NY, USA). Depending on the variable type, comparisons utilized the chi-square test, Fisher's exact test, independent samples t-test, Mann-Whitney U test, and/or receiver operating characteristic (ROC) curve analysis. Three cut-off values for CD36 CVs were derived from the control group: (i) the 75th percentile (P75), (ii) the 90th percentile (P90), and (iii) the 90th percentile as calculated using the method described by Westers et al. [11] (WP90). The modeling approaches included the modeling of the CD36 CV alone, the combination of CD36 CV positivity with Ogata score positivity, and an expanded 5-point scoring system adding one point for CD36 CV positivity to the original Ogata score. Sensitivity, specificity, and ROC analyses were performed for all models and cut-off thresholds.

Results

A total of 82 patients were analyzed in this study, including 67 diagnosed with MDS and 15 assigned to the anemic control group. In the MDS group, 12 (17.9%) cases were of high risk, while 55 (82.1%) were classified as low or intermediate risk according to the IPSS-R (Table 1). In the control group, after exclusion of MDS by morphology and cytogenetics, the etiologies of anemia included renal failure (26.6%), rheumatological disease (20%), drug-induced anemia (20%), chronic liver disease (13.3%), iron deficiency due to gastrointestinal bleeding (6.6%), cytomegalovirus infection secondary to prolonged steroid use (6.6%), and chronic inflammation (6.6%). The mean CD36 CV value in the control group was 65.84 (range: 57.99-92.19), while it was 75.81 (range: 46.23-139.57) among

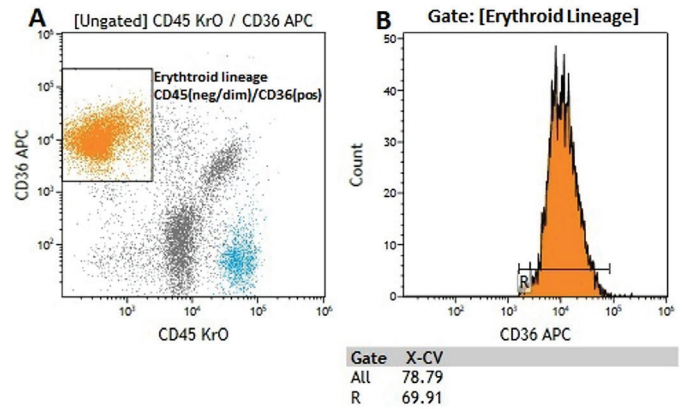
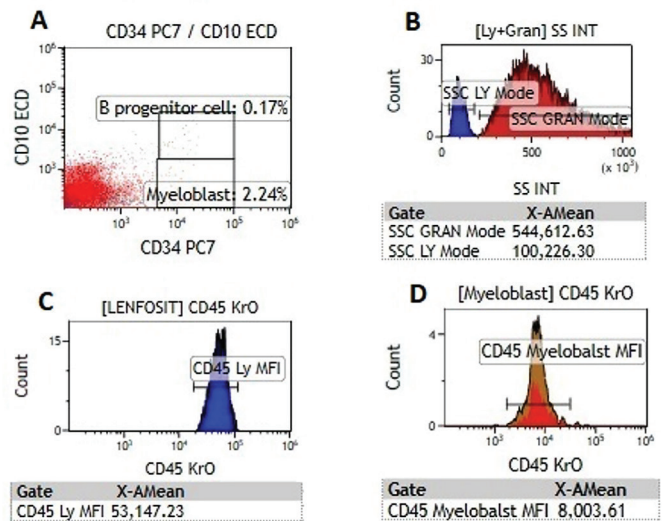


Figure 1. Flow cytometric gating strategy for CD36 coefficient of variation (CV) analysis. (A) Erythroid lineage cells were identified as CD45^{negative/dim}/CD36^{positive} events (orange) within the CD45 KrO vs. CD36 APC dot plot. (B) Histogram representation of CD36 APC expression in the gated erythroid population, where a region (R) was defined to calculate the coefficient of variation (X-CV) of CD36 expression.



Parameter	Cut-off values	Score
Myeloblast(% of CD45+cells)	>2%	1
B-Progenitor-related cluster size(% of CD34+)	<5%	1
Lymphocyte to myeloblast CD45 ratio	<4 or >7.5	1
Granulocyte to lymphocyte SSC ratio	<6	1

Figure 2. Representative example of Ogata score calculation. (A) CD34 vs. CD10 plot showing 2.24% myeloblasts and 0.17% B-progenitor cluster size. (B) Side scatter (SSC) histogram displaying granulocyte (red) and lymphocyte (blue) peaks, used to calculate a granulocyte-to-lymphocyte SSC ratio of 5.43. (C) Histogram of lymphocyte CD45 expression with mean fluorescence intensity (MFI) of 53,147. (D) Histogram of myeloblast CD45 expression with MFI of 8004. The resulting lymphocyte-to-myeloblast CD45 ratio was 6.64. According to these parameters, the Ogata score for this case is 3 (myeloblasts >2%, 1 point; B-progenitor cluster size <5%, 1 point; granulocyte-to-lymphocyte SSC ratio <6, 1 point; lymphocyte-to-myeloblast CD45 ratio between 4 and 7.5, 0 points).

all patients diagnosed with MDS. When stratified by risk group, the mean CD36 CV was 73.16 (range: 46.23-122.56) in the low-to-intermediate-risk MDS subgroup and 80.25 (range: 47.67-139.57) in the high-risk subgroup. Although the mean CD36 CV values were numerically higher in all MDS subgroups compared to the control group, these differences did not reach the level of statistical significance ($p=0.099$ for all MDS patients vs. control group, $p=0.146$ for low-risk patients vs. control, and $p=0.083$ for high-risk patients vs. control), as shown in Table 1. To assess diagnostic thresholds, upper cut-off values for CD36 CVs were calculated based on the control group distribution. These values were 70.9 for the 75th percentile, 87.16 for the 90th percentile, and 95.47 using the 90th percentile as defined

Table 1. Patient characteristics.

	MDS (n=67)	LR-MDS (n=55)	Control group (n=15)	p (MDS vs. control, LR-MDS vs. control)
Sex				
Male	42 (62.7%)	35 (63.6%)	5 (33.3%)	$p=0.047$, $p=0.036$
Female	25 (37.3%)	20 (36.4%)	10 (66.7%)	
Age	70.42	71.11	67.93	$p<0.01$, $p<0.01$
Hb (g/dL)	8.67	8.73	10.52	$p<0.01$, $p<0.01$
Neu (/μL)	2368	2575	4469	$p<0.01$, $p<0.01$
PLT ($\times 10^3/\mu\text{L}$)	177	201	226	$p<0.01$, $p<0.01$
CD36 CV	75.81	73.16	65.84	$p=0.099$, $p=0.146$
Ogata score				
1	10 (14.9%)	8 (14.5%)	5 (33.3%)	$p=0.014$, $p=0.04$
2	17 (25.4%)	17 (30.9%)	8 (53.3%)	
3	34 (50.7)	29 (52.7%)	2 (13.3%)	
4	6 (9%)	1 (1.8%)	0 (0%)	
Dysplasia				
SLD	20 (29.9%)	20 (36.4%)	NA	NA
MLD	47 (70.1%)	35 (63.6%)	NA	NA
IPSS-R				
Very low	8 (11.9%)	NA	NA	NA
Low	27(40.3%)	NA	NA	NA
Intermediate	20 (29.9%)	NA	NA	NA
High	5 (7.5%)	NA	NA	NA
Very high	7 (10.4%)	NA	NA	NA
Mean values are given for age, Hb, Neu, PLT, and CD36 CV. MDS: Myelodysplastic syndrome; LR-MDS: low-to-intermediate risk MDS; Hb: hemoglobin; Neu: neutrophil count; PLT: platelet count; CV: coefficient of variation; SLD: single-lineage dysplasia; MLD: multilineage dysplasia; IPSS-R: Revised International Prognostic Scoring System; NA: not applicable.				

by the method described by Westers et al. [11] (WP90). For the diagnosis low-risk MDS, corresponding sensitivities were 60%, 18.2%, and 3.6% and specificities were 80%, 93.3%, and 100%, respectively (Table 2). CD36 CV alone was not statistically significant in ROC analysis (area under the ROC curve: 0.623, 95% confidence interval: 0.475-0.771, $p=0.146$). Using an Ogata score threshold of ≥ 2 yielded 85.5% sensitivity and 33.3% specificity for low-risk MDS (area under the ROC curve: 0.720, 95% confidence interval: 0.584-0.856, $p=0.009$) (Tables 2 and 3). A revised 5-point scoring model was developed by adding one point for a CD36 CV above the specified cut-off. ROC analysis showed statistical significance for all three cut-offs values. The model using the 75th percentile cut-off achieved the best performance, with 72.7% sensitivity and 80% specificity at a ≥ 3 -point threshold (Supplementary Table 1).

Discussion

MDS diagnosis relies on morphological and cytogenetic analysis, along with exclusion of secondary causes of cytopenia. Unlike acute leukemias or chronic lymphocytic leukemia, flow cytometry lacks definitive diagnostic power for MDS [14]. Most current flow cytometry-based strategies focus on the myelomonocytic lineage, despite erythroid dysplasia being the most common dysplastic feature.

Aberrant CD36 expression is a recognized dysplastic marker in both granulocytic and erythroid cells. The European LeukemiaNet Working Group considers CD36 upregulation on granulocytes as a dysplastic feature [15]. Interpretation, however, is complicated by factors such as eosinophil or apoptotic cell contamination and CD36 variability on monocytes. On erythroid cells, expression variability of CD36 and CD71 is diagnostically valuable. The “Red score,” which combines the CVs of CD36 and CD71 with hemoglobin levels, achieved 77.5% sensitivity and 90% specificity for erythroid dysplasia [16]. Lu et al. [17] investigated the expression of CD36 on CD105⁺ nucleated erythroid cells using multiparameter flow cytometry to differentiate MDS from megaloblastic anemia. Their key findings indicated that the relative MFI of CD36 was significantly decreased in MDS compared to megaloblastic anemia and anemia controls. Additionally, CD36 CV values were increased in MDS versus controls [17]. Westers et al. [11] conducted a comprehensive analysis of erythroid markers including CD36, CD71, CD105, CD117, and CD235a to evaluate CV, MFI, and antigen positivity. Among these, CD36 CV, CD71 CV, CD71 MFI, and CD117 positivity were considered feasible for routine use. Cremers et al. [2] later demonstrated that adding erythroid parameters to myeloid scoring significantly enhanced sensitivity from 74% to 86% without reducing specificity. In a more comprehensive recent study comparing five flow cytometric diagnostic criteria, the sensitivity of the Ogata score, focused on the myeloid lineage,

was reported as 57%, while the Red score, focused on the erythroid lineage, demonstrated sensitivity of 43% [18]. The integrated score proposed by Cremers et al. [2], incorporating both lineages, achieved sensitivity of 79%. However, their combined scoring system is time-consuming and highly antibody-intensive for daily routine practice, requiring either 13 tubes with 4-color or 7 tubes with 8-color panels [2]. Therefore, there is a need to develop diagnostic algorithms that rely on fewer parameters. Combined immunophenotypic analysis of CD36 with other erythroid markers such as CD71 may allow a clearer distinction. However, due to the retrospective nature of the present study, only routinely processed antibody panels were available; therefore, the validation in this study focused specifically on CD36. In our cohort, integrating the CD36 CV into the Ogata score improved specificity for low-risk MDS from 33.3% to 80%, though sensitivity decreased from 85.5% to 72.7%.

Despite promising results, technical variability in flow cytometry limits the global standardization of CV and MFI values. Local standardization using institutional control groups is essential [19]. Furthermore, assessing erythroid dysplasia by flow cytometry has additional challenges. Red blood cell lysis during sample preparation may variably affect nucleated erythroid precursors and alter antigen expression, potentially leading to misinterpretation [20]. As in this study, immunophenotypic assessment from lysed samples is generally limited to erythroid precursors and nucleated red blood cells, whereas mature erythrocytes cannot be analyzed. Similarly, while sample preparation and scatter-based gating strategies minimize platelet contamination, a complete distinction between erythroid precursors and residual platelets cannot be fully ensured with the currently available antibody panels.

Table 2. Sensitivity and specificity of the Ogata score, CD36 coefficient of variation cut-offs, and the revised 5-point model for the diagnosis of all cases of myelodysplastic syndrome and lower-risk cases.

	Threshold value	All MDS cases		Lower-risk MDS	
		Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Ogata score					
	≥2/4	85.1	33.3	85.5	33.3
	≥3/4	59.7	86.7	54.5	86.7
CD36 coefficient of variation (CV)					
	>P75	61.2	80	60	80
	>P90	22.4	93.3	18.2	93.3
	>WP90	9	100	3.6	100
5-point model					
CD36 CV Cut-off: P75	≥3/5	74.6	80	72.7	80
	≥4/5	38.8	93.3	32.7	93.3
CD36 CV Cut-off: P90	≥3/5	61.2	86.7	56.4	86.7
	≥4/5	20.9	100	12.7	100
CD36 CV Cut-off: WP90	≥3/5	59.7	86.7	54.5	86.7
	≥4/5	14.9	100	5.5	100

MDS: Myelodysplastic syndrome; CV: coefficient of variation; P75: the 75th percentile of the control group's CD36 CV; P90: the 90th percentile of the control group's CD36 CV; WP90: the 90th percentile of the control group's CD36 CV as calculated using the method described by Westers et al. [11]; 5-point model: 5-point scoring system adding one point for CD36 CV positivity (with respective cut-off values for P75, P90, and WP90) to the Ogata score.

Table 3. ROC curve analysis results of selected diagnostic models.

Model	All MDS cases			LR-MDS		
	AUC	95% CI	p	AUC	95% CI	p
Ogata score	0.740	0.617-0.864	0.004	0.720	0.584-0.856	0.009
CD36 CV	0.637	0.500-0.774	0.099	0.623	0.475-0.771	0.146
5p-WP90	0.744	0.624-0.864	0.003	0.722	0.589-0.856	0.009
5p-P90	0.760	0.644-0.875	0.002	0.742	0.614-0.871	0.004
5p-P75	0.800	0.680-0.919	<0.001	0.794	0.663-0.924	0.001

ROC: Receiver operating characteristic; MDS: myelodysplastic; LR-MD: low-to-intermediate risk MDS; CV: coefficient of variation; AUC: area under the curve; CI: confidence interval; P75: the 75th percentile of the control group's CD36 CV; P90: the 90th percentile of the control group's CD36 CV; WP90: the 90th percentile of the control group's CD36 CV as calculated using the method described by Westers et al. [11]; 5p: 5-point scoring system adding one point for CD36 CV positivity (with respective cut-off values for P75, P90, and WP90) to the Ogata score.

Conclusion

Our findings suggest that incorporating the CD36 CV into flow cytometric evaluation can enhance diagnostic performance in lower-risk cases of MDS, particularly when used alongside myelomonocytic immunophenotyping, without incurring extra costs or needing additional antibody panels. The limitations of this study include its retrospective design, small sample size, and lack of a healthy control group. Future research will focus on standardization and validation in larger prospective cohorts.

Ethics

Ethics Committee Approval: The study was approved by the Tekirdağ Namık Kemal University Ethics Committee (protocol no: 2025.16.01.16, date: 28.01.2025).

Informed Consent: Informed consent was obtained from all subjects or, when not possible due to the retrospective nature of the study, from their legal representatives or next of kin, in accordance with institutional and ethical standards.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.A., Ş.Ç., M.B., S.A., B.T.; Concept: E.A., B.T.; Design: E.A.; Data Collection or Processing: E.A., Ş.Ç., S.A.; Analysis or Interpretation: E.A., M.B.; Literature Search: E.A., M.B.; Writing: E.A., M.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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Supplementary Table 1. Sensitivity and specificity for considered models.

Model	All MDS cases		Lower-risk MDS	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Ogata score of ≥ 2	85.1	33.3	85.5	33.3
Ogata score of ≥ 3	59.7	86.7	54.5	86.7
Ogata score of 4	9	100	1.8	100
CV of >WP90	9	100	3.6	100
CV of >P90	22.4	93.3	18.2	93.3
CV of >P75	61.2	80	60	80
Ogata score of $\geq 2+$ CV of >WP90	9	100	3.6	100
Ogata score of $\geq 2+$ CV of >P90	17.9	100	12.7	100
Ogata score of $\geq 2+$ CV of >P75	52.2	86.7	49.1	86.7
Ogata score of $\geq 3+$ CV of >WP90	9	100	3,6	100
Ogata score of $\geq 3+$ CV of >P90	16.4	100	10.9	100
Ogata score of $\geq 3+$ CV of >P75	37.3	93.3	30.9	93.3
Ogata score of 4+ CV of >WP90	3	100	0	100
Ogata score of 4+ CV of >P90	4.5	100	0	100
Ogata score of 4+ CV of >P75	7.5	100	0	100
5p-WP90 of ≥ 3	59.7	86.7	54.5	86.7
5p-P90 of ≥ 3	61.2	86.7	56.4	86.7
5p-P75 of ≥ 3	74.6	80	72.7	80
5p-WP90 of ≥ 4	14.9	100	5.5	100
5p-P90 of ≥ 4	20.9	100	12.7	100
5p-P75 of ≥ 4	38.8	93.3	32.7	93.3

MDS: Myelodysplastic syndrome; CV: coefficient of variation; P75: the 75th percentile of the control group's CD36 CV; P90: the 90th percentile of the control group's CD36 CV; WP90: the 90th percentile of the control group's CD36 CV as calculated using the method described by Westers et al. [11]; 5p: 5-point scoring system adding one point for CD36 CV positivity (with respective cut-off values for P75, P90, and WP90) to the Ogata score. Models with significance of $p < 0.05$ according to chi-square tests are indicated in bold.