Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Aberrant DNA repair signaling through NER, BER, and TC-NER pathways in Myelodysplastic Neoplasms

P. Katsiampoura

panagiotakats@gmail.com

Laiko General Hospital National and Kapodistrian University of Athens

C.-N. Kontandreopoulou

Laiko General Hospital National and Kapodistrian University of Athens

S. Douka

National and Kapodistrian University of Athens

P. Diamantopoulos

Laiko General Hospital National and Kapodistrian University of Athens

S. Chatzidavid

Laiko General Hospital National and Kapodistrian University of Athens

C. Stafylidis

Laiko General Hospital National and Kapodistrian University of Athens

D. Vlachopoulou

Laiko General Hospital National and Kapodistrian University of Athens

S. Syriopoulou

Laiko General Hospital National and Kapodistrian University of Athens

C. Tzavara

V. Pappa

National and Kapodistrian University of Athens, Attikon Hospital

I. Kotsianidis

Democritus University of Thrace

A. Symeonidis

University Hospital of Patras

P. Kollia

National and Kapodistrian University of Athens

N.-A. Viniou

Laiko General Hospital National and Kapodistrian University of Athens

Research Article

Keywords: DNA repair, Myelodysplastic neoplasms, Base Excision Repair (BER), Nucleotide Excision Repair (NER), RPA, MPG, ERCC8

Posted Date: August 4th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10482485/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Title: Aberrant DNA repair signaling through NER, BER, and TC-NER pathways in Myelodysplastic Neoplasms

P. Katsiampoura[1], C.-N. Kontandreopoulou[1], S. Douka[2], P. Diamantopoulos[1], S. Chatzidavid[1], C. Stafylidis[1], D. Vlachopoulou[1], S. Syriopoulou[1], C. Tzavara[3], V. Pappa[4], I. Kotsianidis[5], A. Symeonidis[6], P. Kollia[2], N.-A. Viniou[1]. Hellenic MDS Study Group

1. First Department of Internal Medicine, Haematology Unit, Laiko General Hospital National and Kapodistrian University of Athens, Greece

2. Department of Biology, National and Kapodistrian University of Athens, Greece

3. Biostatistician, Medical Researcher

4. Second Department of Internal Medicine, Haematology Unit, National and Kapodistrian University of Athens, Attikon Hospital, Greece

5. Haematology Clinic, Democritus University of Thrace, Alexandroupolis, Greece

6. Haematology Clinic, University Hospital of Patras, Greece

Abstract

Myelodysplastic neoplasms (MDS) comprise a heterogenous group of acquired myeloid disorders involving the haematopoietic stem cell. They are characterized by inefficient haematopoiesis and increased risk of progression to acute myeloid leukemia. Although the pathogenesis of MDS remains incompletely understood, accumulating evidence implicates defects in DNA repair mechanisms in disease development and progression. In this study, we evaluated the *RPA*, *MPG* and *ERCC8* mRNA levels in 46 MDS patients, which play critical role in nucleotide excision repair (NER), base excision repair (BER), and transcription coupled-nucleotide excision repair (TC-NER) pathways, respectively. Statistical analysis revealed a strong association between elevated *ERCC8* expression and high-risk MDS as well as progression to AML, whereas *RPA* and *MPG* expression showed no significant correlation with clinicopathological characteristics. These findings contribute to our better understanding of the MDS molecular biology and suggest a potential role in disease progression, with possible future therapeutic implications.

Keywords: DNA repair; Myelodysplastic neoplasms; Base Excision Repair (BER); Nucleotide Excision Repair (NER); RPA; MPG; ERCC8

1. Introduction

Myelodysplastic neoplasms (abbreviated MDS) are a heterogenous group of acquired myeloid disorders that derive from a mutated haematopoietic stem cell. They predominantly affect the elderly and are

characterized by dysplasia in one or more myeloid lineages, inefficient haematopoiesis and peripheral blood cytopenias. Clinically, MDS is associated with anaemia, infections, bleeding complications and a substantial risk of transformation to acute myeloid leukemia (AML). The rate of patients with MDS is increasing every year and it is considered to be a more common disease than previously believed.

The incidence of these clonal neoplasms increases with age and the majority of cases remain unexplained. However, several risk factors like ionizing and ultraviolet radiation, occupational exposure to solvents, and prior chemotherapy for previous malignancies (especially alkylating agents and purine analogs) have been implicated in the development of MDS through the induction of genetic mutations [3]. Emerging evidence indicates that MDS are associated with dysregulation of multiple DNA damage repair mechanisms [32].

DNA, the genetic material responsible for the perpetuation of life, is highly sensitive and constantly being threatened. Therefore, in order to maintain its integrity and genome stability, it has developed multiple protective strategies. Unrepaired lesions can lead to mutagenesis, genomic instability and development of cancer [17]. Consequently, cells rely on highly coordinated DNA repair pathways to minimize the detrimental effects of DNA damage and ensure proper cellular function. Among these, Nucleotide Excision Repair (NER) and Base Excision Repair (BER) constitute two major repair pathways responsible for the removal of bulky and non-bulky DNA lesions, respectively. Both pathways share three common steps: 1) damage recognition, 2) incision and removal of the damaged fragment and, 3) reconstruction with error-free nucleotides [38].

NER is a unique pathway responsible for the removal of bulky DNA lesions and includes two distinct subpathways: Global Genome NER (GG-NER) and Transcription-Coupled NER (TC-NER). Mutations in specific genes lead to rare genetic disorders: Xeroderma Pigmentosum (XP) results from defects in seven GG-NER proteins (XPA to XPG) characterized by extreme sensitivity to sunlight and predisposition to skin cancer. Cockayne Syndrome (CS) is caused by mutations in two TC-NER genes, ERCC8 gene or CSA and ERCC6 gene or CSB; affected individuals exhibiting developmental and neurological abnormalities despite having no increased cancer susceptibility. Trichothiodystrophy (TTD) is also a disease connected with defective TC-NER. TTD patients share similar clinical features with XP and CS patients, but are not cancer-prone [41].

Except from the initial step, both GG-NER and TC-NER share common downstream repair mechanisms. GG-NER eliminates lesions throughout the whole genome and repair occurs indepedently of transcription. It is initiated by XPC-RAD23B, often assisted by UV-DDB (UV damaged DNA binding protein) playing a crucial role in the recognition of a variety of DNA lesions [15,35] .

In TC-NER, lesions located within actively transcribed genes are initially detected by RNA polymerase II (RNAPII). In cooperation with CSA, CSB and XAB2 the lesion becomes accessible, allowing repair initiation. Subsequently, transcription initiation factor IIH (TFIIH) is recruited to unfold the DNA around the lesion. Together with XPA and replication protein A (RPA), TFIIH formulates the pre-incision complex. DNA excision is then carried out by XPF and XPG while DNA reconstruction is executed by the replication proteins proliferating cell nuclear antigen (PCNA), Polδ, Polε, DNA ligase 1 or XRCC1-DNA ligase 3 complex [37]. RPA, is a heterotrimeric protein that plays a central role in DNA metabolism. Post translational modifications and phosphorylation in particular are responsible for its proper function.

Phosphorylation of RPA has been studied for many decades due to its great impact on cell cycle regulation, DNA repair and numerous metabolic pathways. Deficits in these reactions may lead to genome instability and high cancer risk [10].

BER represents another essential DNA repair pathway active throughout all stages of the cell cycle. This pathway is specialized to fix non-bulky single-base lesions that seem to have minimal effects on the helix but can be mutagenic. Alterations in BER-associated genes have been linked to human disease: cancer, neurodegenerative syndromes such as Alzheimer's disease, aging and inflammation [23]. The initial response starts with a specific DNA glycosylase that recognises and eliminates the damaged bases. DNA glycosylases can be either monofunctional or bifunctional. Monofunctional DNA glycosylases have only glycosylase activity and include: UNG, SMUG1, MBD4, TDG, MYH, MPG. In contrast, bifunctional DNA glycosylases exhibit AP (apurinic/apyrimidinic site) lyase activity and include OGG1, NTH1 and NEIL1. Following base excision, an AP site is generated and subsequently processed by AP endonuclease 1 (APE1). Finally, the resulting gap is filled by DNA polymerases and sealed by DNA ligases, completing the repair process [23]. MPG, also known as Alkyladenine DNA Glycosylase (AAG), is a prominent DNA glycosylase involved in BER that can recognize and excise alkylated purines. Increasing evidence suggests that MPG overexpression may contribute to carcinogenesis and could also have a role in chemotherapy resistance [46].

The present study aimed to investigate the involvement of DNA repair mechanisms in myelodysplastic neoplasms (MDS) through the evaluation of the expression of the *RPA*, *MPG* and *ERCC8* genes, which are critically involved in the NER, BER, and TC-NER pathways, respectively. Elucidating the role of these mechanisms may improve our understanding of MDS pathogenesis and facilitate the identification of potential therapeutic targets.

2. Patients and Methods

Patients

We collected bone marrow samples from 46 MDS patients at diagnosis, who were classified based on the 2016 revision of the WHO classification of haematolymphoid tumours (MDS-SLD: 18, MDS-RS-SLD: 2, MDS-MLD: 9, EB_1: 1, EB_2: 11, MDS-U: 5) and the FAB (RA: 27, RARS: 2, RAEB: 12 ,CMML: 5) [66]. The demographic, clinical, and haematological characteristics of the patients were retrospectively collected and recorded. Basic laboratory and clinical parameters were recorded during the diagnosis for each patient. Progression to AML was also evaluated. All the risk classification of the patients was based on the International Prognostic Scoring System (IPSS), the Revised IPSS (IPSS-R), and the WHO Classification Based Prognosis Scoring System (WPSS) for MDS. Written informed consent was obtained from all patients in accordance with the Declaration of Helsinki. The study was approved by the Institutional Ethics Committee.

Sample collection

Bone marrow samples were collected in Ethylene-Diamine-Tetraacetic Acid (EDTA) during a routine bone marrow aspiration at diagnosis and processed within 6 hours from the collection. Nucleic acid

extraction (Purelink RNA mini kit Invitrogen, Carlsbad, CA, USA) and cDNA synthesis (Invitrogen, Carlsbad, CA, USA) followed the standard protocols and the samples were kept at -80 ^{o}C.

Reverse transcription and real-time polymerase chain reaction (RT-PCR)

Total RNA was extracted from bone marrow cells using the PureLink RNA Mini Kit (Invitrogen, Carlsbad, CA, USA). Reverse transcription was performed using MMLV-derived reverse transcriptase enzyme (MMLV RT, Invitrogen, Carlsbad, CA, USA) following the manufacturer's recommendations. Quantitative real-time PCR using SYBR-Green technology (Bio-Rad Laboratories, Hercules, California, USA) was performed on the CFX-96 real-time PCR system (Bio-Rad Laboratories, Hercules, CA, USA). The reaction mixture contained specific primers for the genes of interest (*RPA*, *MPG* and *ERCC8*). B actin was used as the reference gene for normalization of gene expression levels.

3. Statistical analysis

Quantitative variables were expressed as mean values (Standard Deviation) or as median (interquartile range), while categorical variables were expressed as absolute and relative frequencies. Mann-Whitney test and Kruskal-Wallis test were used for the comparison of continuous variables between two or more groups, respectively. Bonferroni correction was used in order to control for type I error. Spearman correlations coefficients (rho) were used to explore the association of two continuous variables. The coefficient is considered very high when it is above 0.9, high when it is 0.7-0.9, moderate when it is 0.5-0.7, low when it is 0.3-0.5 and very low when it is below 0.3 [1]. Logistic regression analysis was used in order to examine if gene expression was significantly associated with having moderate/ high and very high risk according to IPSS-R score as well as with having a progression to AML, after adjusting for age, gender and FAB classification. Adjusted odds ratios (OR) with 95% confidence intervals (95% CI) were computed from the results of the logistic regression analyses. All reported p values are two-tailed. Statistical significance was set at $p<0.05$ and analyses were conducted using SPSS statistical software (version 27.0).

4. Results

The study population included 46 patients (63% male), with a mean age of 69.02 years (SD=13.75). Patient characteristics are presented in **Table 1**. A normal karyotype was identified in 77.8% of the patients, 58.7% were classified as refractory anaemia (RA) according to FAB criteria, and 45.7% were categorized as low risk based on the IPSS-R score. Progression to acute myeloid leukemia (AML) occured in 23.9% of patients.

ERCC8, as well as *MPG* expression, was significantly greater in patients with moderate/ high and very high risk according to IPSS-R score (**Table 2**). Patients with progression to AML had also significantly greater *ERCC8* expression, while *MPG* expression was found to be significantly different among FAB categories. After Bonferroni correction, it was found that in RA cases, *MPG* expression was significantly lower than in cases with other FAB category (p=0.006). Also, *RPA* expression was significantly lower in cases with normal karyotype.

Greater *MPG* expression was significantly associated with lower PLT (rho=-0.31; p=0.041) and greater BM blasts (rho=0.34; p=0.022); **Table 3**. Greater IPSS Score was significantly associated with

greater *MPG* (rho=0.33; p=0.026) and *RPA* expression (rho=0.30; p=0.045). No other significant correlation was found among gene expressions and patients' age, number of cytopenias and laboratory indexes (p>0.05).

After adjusting for age, gender and FAB classification, it was found that *ERCC8* expression remained significantly associated with moderate/ high and very high risk MDS according to IPSS-R score (OR=1.23; 95% CI:1.03 – 1.46; p=0.022, **Figure 1**) as well as with progression to AML (OR=1.19; 95% CI:1.02 – 1.38; p=0.026, **Figure 2**); **Table 4**. On the contrary, *MPG* and *RPA* expressions were no longer significantly associated with moderate/ high and very high risk MDS according to IPSS-R score, after adjusting for age, gender and FAB (p>0.05).

Table 1. Sample characteristics

n=46		n (%)
Gender	Females	17 (37.0)
	Males	29 (63.0)
FAB category	RA	27 (58.7)
	RAEB	12 (26.1)
	Other	7 (15.2)
WHO category	MDS-SLD	20 (43.5)
	MDS-MLD	9 (19.6)
	EB-1/ EB-2	12 (26.1)
	Other	5 (10.9)
Normal karyotype		35 (77.8)
IPSS-R Risk Group	Very low (< 1.5)	9 (19.6)
	Low (1.5-3)	21 (45.7)
	Moderate (3-4.5)	5 (10.9)
	High (4.5-6)	8 (17.4)
	Very high (>6)	3 (6.5)
Progression to AML		11 (23.9)
		Mean (SD)
Age (years)		69.02 (13.75)
IPSS-R Score		3.12 (1.8)
		Median (IQR)
ERCC8/ACTIN-β		0.017 (0.005 ─ 0.068)
MPG/ACTIN-β		0.003 (0.001 ─ 0.008)
RPA/ACTIN-β		0.007 (0.004 ─ 0.032)

Table 2. Association of *ERCC8/ACTIN-β*, *MPG/ACTIN-β* and *RPA/ACTIN-β* with patients' characteristics

	ERCC8/ACTIN-β	P	MPG/ACTIN-β	P	RPA/ACTIN-β	P

	Median (IQR)		Median (IQR)		Median (IQR)	
Gender						
Females	0.012 (0.008 — 0.043)	0.724+	0.002 (0.001 — 0.006)	0.446+	0.007 (0.003 — 0.035)	0.759+
Males	0.019 (0.005 — 0.070)		0.003 (0.001 — 0.008)		0.007 (0.004 — 0.032)	
FAB						
RA	0.013 (0.003 — 0.031)	0.065++	0.001 (0.001 — 0.004)	0.004++	0,007 (0,003 — 0,032)	0.149++
RAEB	0.052 (0.009 — 0.084)		0.006 (0.002 — 0.012)		0,012 (0,007 — 0,221)	
Other	0.070 (0.008 — 0.144)		0.006 (0.004 — 0.971)		0,001 (0,000 — 0,024)	
Normal karyotype						
No	0.031 (0.008 — 0.091)	0.353+	0.004 (0.001 — 0.019)	0.530+	0,018 (0,008 — 0,480)	0.027+
Yes	0.014 (0.004 — 0.061)		0.003 (0.001 — 0.006)		0,007 (0,002 — 0,018)	
IPSS-R Risk Group						
Very low (< 1.5) / Low (1.5-3)	0.012 (0.004 — 0.032)	0.034+	0.002 (0.001 — 0.004)	0.050+	0.007 (0.003 — 0.032)	0.299+
Moderate (3-4.5) / High (4.5-6) / Very high (>6)	0.052 (0.009 — 0.107)		0.007 (0.002 — 0.033)		0.010 (0.005 — 0.221)	
Progression to AML						
No	0.014 (0.003 — 0.034)	0.016+	0.003 (0.001 — 0.008)	0.652+	0.007 (0.003 — 0.035)	0.887+
Yes	0.070 (0.012 — 0.144)		0.003 (0.001 — 0.009)		0.008 (0.004 — 0.018)	

Table 3. Spearman's correlation coefficients (rho) of *ERCC8/ACTIN-β*, *MPG/ACTIN-β* and *RPA/ACTIN-β* with patients' characteristics

	ERCC8/ACTIN-β	MPG/ACTIN-β	RPA/ACTIN-β
Age	0.21	0.09	0.26
Hb (g/dl)	-0.16	-0.17	-0.19
WBC x 10^9/l	-0.08	0.09	-0.26
NEUT x 10^9/l	-0.01	0.00	-0.26
LYMPH x 10^9/l	-0.14	0.16	-0.18
MONO x 10^9/l	0.00	0.21	-0.33
PLT x 10^9/l	-0.02	-0.31*	-0.09
BM blasts %	0.12	0.34*	0.10
Number of cytopenias	-0.06	0.13	0.16

IPSS Score	0.28	0.33*	0.30*

*p<0.05; **p<0.01; ***p<0.001

Table 4. Association of *ERCC8/ACTIN-β*, *MPG/ACTIN-β* and *RPA/ACTIN-β* with IPSS-R Risk Group and Progression to AML via logistic regression

Dependent variables	Independent variables	OR (95% CI)+	P
IPSS-R Risk Group	ERCC8/ACTIN-β	1.23 (1.03 – 1.46)	0.022
	MPG/ACTIN-β	0.74 (0.22 -2.46)	0.620
	RPA/ACTIN-β	0.91 (0.67 – 1.24)	0.564
Progression to AML	ERCC8/ACTIN-β	1.19 (1.02 – 1.38)	0.026
	MPG/ACTIN-β	0.20 (0.00 -296.87)	0.663
	RPA/ACTIN-β	0.97 (0.74 – 1.25)	0.763

+Odds Ratio (95% Confidence Interval) adjusted for age, gender and FAB level

Figure 1. *ERCC8/ACTIN-β* by IPSS-R Risk Group

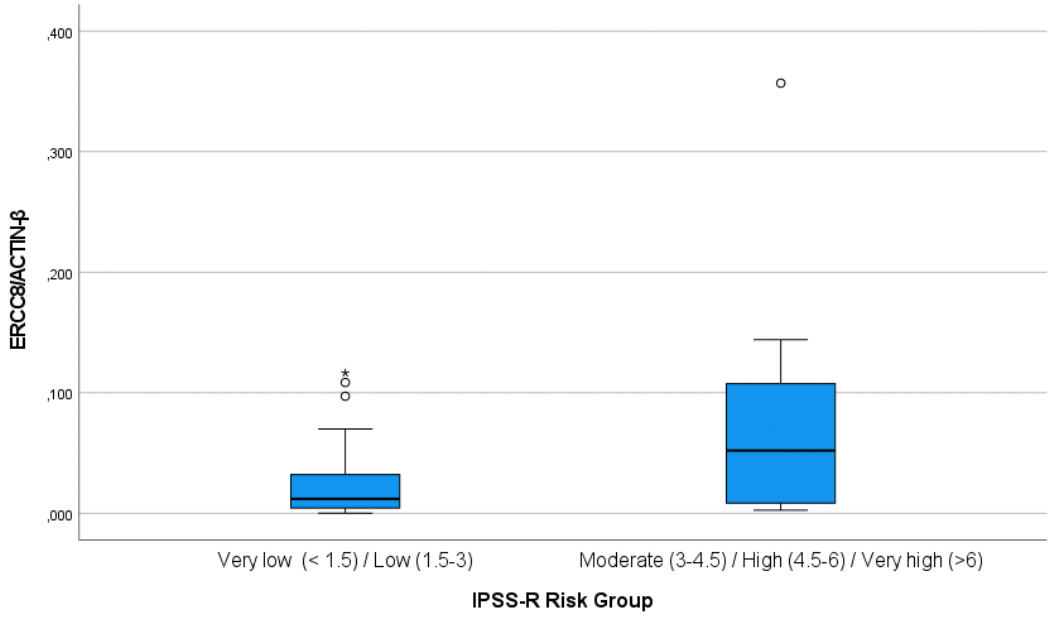
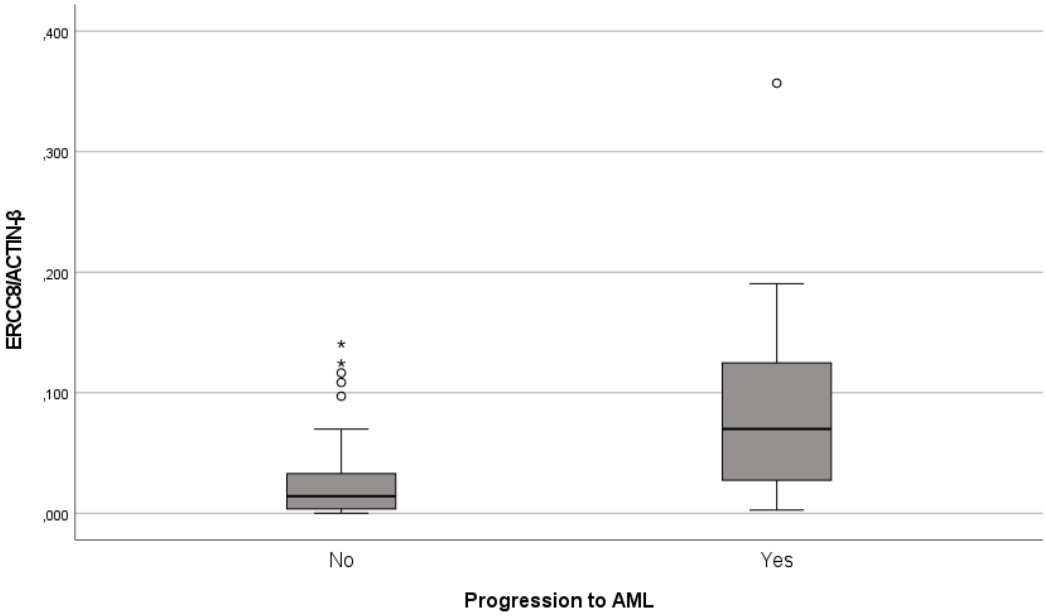


Figure 2. *ERCC8/ACTIN-β* by having or not progression to AML



5. Discussion

MDS is clonal haematopoietic stem cell disorder, previously considered as proleukemic condition. Although the aetiology of MDS is not fully understood, there is increasing evidence that this entity is related with defects in DNA repair mechanisms.The present study attempted to investigate the involvement of RPA, MPG, ERCC8 key genes of the NER, BER, and TC-NER repair pathways in the pathophysiology of MDS.

RPA is a heterotrimeric protein that has an essential role in the the cell cycle regulation, DNA repair mechanisms, and other metabolic pathways. Its phosphorylation is very important, as it enhances its ability to interact with numerous proteins. In our study, RPA expression was associated with sex, age, laboratory measurements, cytopenias, karyotype, FAB classification, WHO classification (2016), the IPSS , and IPSS-R prognostic systems, as well as progression to AML in patients with MDS. A higher IPSS score was correlated with increased RPA expression levels. However, after adjusting for age, gender, and FAB, RPA expression was no longer significantly associated with moderate/high and very high risk MDS as determined by the IPSS score. Furthermore, low RPA levels were correlated with a normal karyotype. These findings suggest that low levels of RPA expression are associated with low-risk MDS, although further studies are needed to confirm this observation. No other significant correlations between RPA expression and the other clinical or laboratory parameters were observed. The existing literature indicates that RPA plays an important role in carcinogenesis, but there is no evidence that it is involved in the biology of MDS. Indeed, increased RPA expression assessed by immunohistochemistry has been reported in ovarian [52], colorectal [53], and esophageal [54] cancers, where it has been associated with poor prognosis and has been proposed as a potential therapeutic target. On the other hand, elevated RPA levels of expression, as determined by immunohistochemistry, have been associated with a favorable prognosis and low-grade disease in bladder cancer [55] and gastric cancer [56] . Moreover, low transcriptional levels of RPA have been associated with aggressive forms of breast cancer, poor prognosis, and sensitivity to cisplatin [57]. The multiple roles of RPA may reflect its extensive interactions with numerous proteins and its involvement in a wide range of cellular pathways. With respect to MDS, the precise role of RPA remains unclear and further research is required to fully elucidate its biological and clinical significance.

MPG is an important DNA glycosylase that recognizes and eliminates alkylated purines. In our study, MPG expression was associated with sex, age, laboratory parameters, cytopenias, karyotype, FAB classification, WHO classification (2016), the IPSS, and IPSS-R prognostic systems, as well as progression to AML in patients with MDS. MPG expression was significantly higher in patients with moderate/high/very high risk MDS based on the IPSS-R, compared with patients classified as very low/low risk. However, after adjusting for age, gender, and FAB classification, MPG expression was not significantly associated with moderate/high or very high risk MDS. Increased MPG expression was also observed in MDS with low platelet counts and increased percentage of blasts. These findings suggest that patients with higher-risk MDS and adverse laboratory parameters, exhibit elevated MPG expression levels. Conversely, low MPG expression was observed in the RA category implying an association with low- or very low-risk MDS. No other significant correlations between MPG expression and the other parameters were identified. The existing literature has not described any correlation between MPG and MDS, except for solid tumors. Indeed, the overexpression of MPG enzymatic activity, as well as that of other enzymes involved in BER pathway, paradoxically does not contribute to cellular protection against endogenous and exogenous mutagenic factors. Instead, it may promote genomic instability and carcinogenesis [6]. Increased MPG activity has been reported in breast [59] and lung cancer [8]. In colorectal cancer, elevated MPG expression has also been associated with poor prognosis. Furthermore, accumulating evidence suggests that increased MPG levels, in combination with mismatch repair deficiency, sensitize colorectal cancer cells to 5-FU and temozolomide. MPG overexpression may alter DNA repair and cellular metabolism and has been proposed as a therapeutic strategy to overcome chemoresistance [60]. Consequently, the role of MPG in the pathogenesis of MDS remains unclear and appears to be limited based on the current evidence. Larger studies may be required to further clarify its biological and clinical role in MDS.

ERCC8, also known as Cockayne syndrome A (CSA), is a critically important protein involved in the transcription-coupled NER (TC-NER) repair pathway. In our study, we compared ERCC8 gene expression with the demographic and clinical characteristics of the patients. A significant association was observed based on the IPSS-R prognostic classification, with ERCC8 expression being significantly higher in patients with intermediate/high/very high risk MDS compared with those classified as very low or low risk. Additionally, patients who progressed to AML had significantly higher ERCC8 gene expression levels. After adjusting for age, gender, and FAB classification, ERCC8 expression remained significantly correlated with moderate/high and very high risk MDS (OR=1.23; 95% CI: 1.03–1.46; $p = 0.022$) as well as with progression to AML (OR = 1.19; 95% CI: 1.02–1.38; $p = 0.026$). These findings are in agreement with the current literature. The role of ERCC8 has been extensively studied in recent years particularly in solid tumors. Elevated levels of ERCC8 has been associated with poor prognosis in gastric cancer, suggesting that this molecule may serve as a therapeutic target [61]. Similarly, increased mRNA levels of ERCC8, together with ERCC1 have been correlated with reduced overall survival in patients with ovarian cancer, particularly in advanced-stage and low-grade disease [62]. In lung adenocarcinoma, increased expression of ERCC8 and ERCC6 showed a negative correlation with good prognosis, highlighting their potential prognostic value. Moreover, ERCC8 expression has been linked to variable responses to antineoplastic therapy, while in vitro studies have demonstrated that ERCC8 inhibition may attenuate the malignant phenotype of lung adenocarcinoma cells [63]. Research on ERCC8 has also expanded to haematological malignancies. Specifically, in hypoplastic MDS, reduced expression of

ERCC8 has been associated with chromosomal abnormalities suggesting that this gene may be involved in the pathogenesis of MDS [64]. Furthermore, the ERCC8 rs158572 genotype appeared to be associated with refractory AML and positive minimal residual disease (MRD), highlighting that genetic polymorphisms in DNA repair pathway genes may contribute to its chemosensitivity [65].

In conclusion, although further investigation is required to fully elucidate their biological significance, the DNA repair genes *RPA* and *MPG* appeared to have a limited role in the pathophysiology of MDS. On the other hand, our study demonstrated a significant correlation between *ERCC8* expression, higher risk MDS and progression to AML. Nevertheless, larger studies are required to validate these findings and further clarify the role of *ERCC8* in disease progression. Future research should also explore the potential development of *ERCC8*-targeting therapies for the treatment of MDS and possibly AML.

6. Conclusion

In summary, cells have evolved highly efficient DNA repair mechanisms to prevent DNA damage. Defects in these pathways may result in the accumulation of mutations, genomic instability and cancer. In the present study, we tried to investigate the role of *RPA*, *MPG* and *ERCC8* repair genes in the pathophysiology of MDS. Our findings suggest that *RPA* and *MPG* seem to have a limited contribution to MDS pathogenesis. In contrast, elevated ERCC8 expression was strongly associated with intermediate/high/very high risk MDS as well as with progression to AML. Although larger studies are needed to validate these findings, our results provide new insights into the biology of MDS and may contribute to the therapeutic landscape for the MDS patients in the future.

Conflicts of interest: The authors declare no conflicts of interest

References

1. Mukaka, Mavuto. (2012). Statistics Corner: A guide to appropriate use of Correlation coefficient in medical research. Malawi medical journal : the journal of Medical Association of Malawi. 24. 69-71.

2. Ma X. Epidemiology of myelodysplastic syndromes. Am J Med.2012 Jul;125(7 Suppl):S2-5. doi: 10.1016/j.amjmed

3. Nisse C, Haguenoer JM, Grandbastien B, Preudhomme C, Fontaine B, Brillet JM, Lejeune R, Fenaux P. Occupational and environmental risk factors of the myelodysplastic syndromes in the North of France. Br J Haematol. 2001 Mar; 112 (4): 927-35. doi: 10.1046/j.1365-2141.2001.02645.x.

4. Mc Kinnon PJ. DNA repair deficiency and neurological disease. Nat Rev Neurosci. 2009. Feb;10(2):100-12. doi: 10.1038/nrn2559.

5. Hofseth LJ, Khan MA, Ambrose M, Nikolayeva O, Xu-Welliver M, Kartalou M, Hussain SP, Roth RB, Zhou X, Mechanic LE, Zurer I, Rotter V, Samson LD, Harris CC. The adaptive imbalance in base excision-repair enzymes generates microsatellite instability in chronic inflammation. J Clin Invest. 2003 Dec;112(12):1887-94. doi: 10.1172/JCI19757.

6. Frosina G. Overexpression of enzymes that repair endogenous damage to DNA. Eur J Biochem. 2000 Apr;267(8):2135-49. doi: 10.1046/j.1432-1327.2000.01266.x.

7. Klapacz J, Lingaraju GM, Guo HH, Shah D, Moar-Shoshani A, Loeb LA, Samson LD. Frameshift mutagenesis and microsatellite instability induced by human alkyladenine DNA glycosylase. Mol Cell. 2010 Mar 26;37(6):843-53. doi: 10.1016/j.molcel.2010.01.038.

8. Crosbie PA, Watson AJ, Agius R, Barber PV, Margison GP, Povey AC. Elevated N3-methylpurine-DNA glycosylase DNA repair activity is associated with lung cancer. Mutat Res. 2012 Apr 1;732(1-2):43-6. doi: 10.1016/j.mrfmmm.2012.01.001

9. Meira LB, Moroski-Erkul CA, Green SL, Calvo JA, Bronson RT, Shah D, Samson LD. Aag-initiated base excision repair drives alkylation-induced retinal degeneration in mice. Proc Natl Acad Sci U S A. 2009 Jan 20;106(3):888-93. doi: 10.1073/pnas.0807030106.

10. Fousek-Schuller VJ, Borgstahl GEOThe Intriguing Mystery of RPA Phosphorylation in DNA Double-Strand Break Repair. Genes. 2024. Genes (Basel). 2024 Jan 27;15(2):167. doi: 10.3390/genes15020167.

11. Bastin-Shanower, S.A.; Brill, S.J. Functional analysis of the four DNA binding domains of replication protein A. The role of RPA2 in ssDNA binding. J Biol Chem. 2001 Sep 28;276(39):36446-53. doi: 10.1074/jbc.M104386200

12. Borgstahl, G.E.; Brader, K.; Mosel, A.; Liu, S.; Kremmer, E.; Goettsch, K.A.; Kolar, C.; Nasheuer, H.P.; Oakley, G.G. Interplay of DNA damage and cell cycle signaling at the level of human replication protein A. DNA Repair (Amst). 2014 Sep:21:12-23. doi: 10.1016/j.dnarep.2014.05.005

13. Zou,Y.; Liu, Y.; Wu, X.; Shell, S.M. Functions of human replication protein A (RPA): From DNA replication to DNA damage and stress responses. J Cell Physiol. 2006 Aug;208(2):267-73. doi: 10.1002/jcp.20622.

14. Henricksen, L.A.; Umbricht, C.B.; Wold, M.S. Recombinant replication protein A: Expression, complex formation, and functional characterization. J Biol Chem. 1994 Apr 15;269(15):11121-32.

15. Schärer OD. Nucleotide excision repair in eukaryotes. Cold Spring Harb Perspect Biol. 2013 Oct 1;5(10):a012609. doi: 10.1101/cshperspect.a012609.

16. Spivak G. Nucleotide excision repair in humans. DNA Repair (Amst). 2015 Dec;36:13-18. doi: 10.1016/j.dnarep.2015.09.003.

17. Chatterjee N, Walker GC. Mechanisms of DNA damage, repair, and mutagenesis. Environ Mol Mutagen. 2017 Jun;58(5):235-263. doi: 10.1002/em.22087.

18. Iyama T, Wilson DM. DNA repair mechanisms in dividing and non-dividing cells. DNA Repair (Amst). 2013 Aug;12(8):620-36. doi: 10.1016/j.dnarep.2013.04.015.

19. Wood RD. DNA repair in eukaryotes. Annu Rev Biochem. 1996;65:135-67. doi: 10.1146/annurev.bi.65.070196.001031.

20. Carter RJ, Parsons JL Base Excision Repair, a Pathway Regulated by Posttranslational Modifications. Mol Cell Biol. 2016 May 2;36(10):1426-37. doi: 10.1128/MCB.00030-16.

21. Seeberg E, Eide L, Bjørås M. The base excision repair pathway. Trends Biochem Sci. 1995 Oct;20(10):391-7. doi: 10.1016/s0968-0004(00)89086-6.

22. Limpose KL, Corbett AH, Doetsch PW. BERing the burden of damage: Pathway crosstalk and posttranslational modification of base excision repair proteins regulate DNA damage management. DNA Repair (Amst). 2017 Aug:56:51-64. doi: 10.1016/j.dnarep.2017.06.007.

23. Gohil D, et al. Base Excision Repair: Mechanisms and Impact in Biology, Disease, and Medicine. Int J Mol Sci. 2023 Sep 16;24(18):14186. doi: 10.3390/ijms241814186.

24. D'Souza A, Blee AM, Chazin WJ.Mechanism of action of nucleotide excision repair machinery. Biochem Soc Trans. 2022 Feb 28;50(1):375-386. doi: 10.1042/BST20210246.

25. Baiken Y, Kanayeva D, Taipakova S, Groisman R, Ishchenko AA, Begimbetova D, Matkarimov B, Saparbaev M. Role of Base Excision Repair Pathway in the Processing of Complex DNA Damage Generated by Oxidative Stress and Anticancer Drugs. Front Cell Dev Biol. 2021 Jan 22:8:617884. doi: 10.3389/fcell.2020.617884.

26. Quiñones JL, Demple B. When DNA repair goes wrong: BER-generated DNA-protein crosslinks to oxidative lesions. DNA Repair (Amst). 2016 Aug:44:103-109. doi: 10.1016/j.dnarep.2016.05.014.

27. Piscone A, Gorini F, Ambrosio S, Noviello A, Scala G, Majello B, Amente S. Targeting the 8-oxodG Base Excision Repair Pathway for Cancer Therapy. Cells. 2025 Jan 14;14(2):112. doi: 10.3390/cells14020112.

28. Hafsi W, Saleh HM. Cockayne Syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan. 2024 Jan 11.

29. Carnie CJ, Acampora AC, Bader AS, Erdenebat C, Zhao S, Bitensky E, van den Heuvel D, Parnas A, Gupta V, D'Alessandro G, Sczaniecka-Clift M, Weickert P, Aygenli F, Götz MJ, Cordes J, Esain-Garcia I, Melidis L, Wondergem AP, Lam S, Robles MS, Balasubramanian S, Adar S, Luijsterburg MS, Jackson SP, Stingele J. Transcription-coupled repair of DNA-protein cross-links depends on CSA and CSB. Nat Cell Biol. 2024 May;26(5):797-810. doi: 10.1038/s41556-024-01391-1

30. D' Errico M, Pascucci B, Iorio E, Van Houten B, Dogliotti E. The role of CSA and CSB protein in the oxidative stress response. Mech Ageing Dev. 2013 May-Jun;134(5-6):261-9. doi: 10.1016/j.mad.2013.03.006.

31. Fousteri M, Mullenders LH. Transcription-coupled nucleotide excision repair in mammalian cells: molecular mechanisms and biological effects. Cell Res. 2008 Jan;18(1):73-84. doi: 10.1038/cr.2008.6.

32. Kuramoto K, Ban S, Oda K, Tanaka H, Kimura A, Suzuki G.Chromosomal instability and radiosensitivity in myelodysplastic syndrome cells. Leukemia. 2002 Nov;16(11):2253-8. doi: 10.1038/sj.leu.2402703.

33. Laugel V. Cockayne Syndrome.2000 Dec 28 [updated 2024 Aug 29]. In: Adam MP, Bick S, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2026.

34. Chen J, Li L, Sun L, Yuan Y, Jing J. Associations of individual and joint expressions of ERCC6 and ERCC8 with clinicopathological parameters and prognosis of gastric cancer. PeerJ. 2021 Jul 15:9:e11791. doi: 10.7717/peerj.11791

35. Sugasawa K. Molecular mechanisms of DNA damage recognition for mammalian nucleotide excision repair. DNA Repair (Amst). 2016 Aug;44:110-117. doi: 10.1016/j.dnarep.2016.05.015

36. Lans H, Hoeijmakers JHJ, Vermeulen W, Marteijn JA. The DNA damage response to transcription stress. Nat Rev Mol Cell Biol. 2019 Dec;20(12):766-784. doi: 10.1038/s41580-019-0169-4.

37. Pascucci B, D' Errico M, Parlanti E, Giovannini S, Dogliotti E. Role of nucleotide excision repair proteins in oxidative DNA damage repair: an updating. Biochemistry (Mosc). 2011 Jan;76(1):4-15. doi: 10.1134/s0006297911010032.

38. Lee TH, Kang T.DNA Oxidation and Excision Repair Pathways. Int J Mol Sci. 2019 Dec 3;20(23):6092. doi: 10.3390/ijms20236092.

39. Marteijn JA, Lans H, Vermeulen W, Hoeijmakers JH. Understanding nucleotide excision repair and its roles in cancer and ageing. Nat Rev Mol Cell Biol. 2014 Jul;15(7):465-81. doi: 10.1038/nrm3822.

40. Friedberg EC. DNA damage and repair. Nature. 2003 Jan 23;421(6921):436-40. doi: 10.1038/nature01408.

41. Kraemer KH, Patronas NJ, Schiffmann R, Brooks BP, Tamura D, DiGiovanna JJ. Xeroderma pigmentosum, trichothiodystrophy and Cockayne syndrome: a complex genotype-phenotype relationship. Neuroscience. 2007 Apr 14;145(4):1388-96. doi: 10.1016/j.neuroscience.2006.12.020.

42. Faghri S, Tamura D, Kraemer KH, DiGiovanna JJ. Trichothiodystrophy: a systematic review of 112 published cases characterises a wide spectrum of clinical manifestations. J Med Genet. 2008 Oct;45(10):609-21. doi: 10.1136/jmg.2008.058743

43. Cleaver JE. Cancer in xeroderma pigmentosum and related disorders of DNA repair. Nat Rev Cancer. 2005 Jul;5(7):564-73. doi: 10.1038/nrc1652.

44. Grundy, G.J.; Parsons, J.L. Base Excision Repair and Its Implications to Cancer Therapy.Essays Biochem. 2020 Oct 26;64(5):831-843. doi: 10.1042/EBC20200013.

45. Li, L.; Guan, Y.; Chen, X.; Yang, J.; Cheng, Y. DNA Repair Pathways in Cancer Therapy and Resistance. Front Pharmacol. 2021 Feb 8:11:629266. doi: 10.3389/fphar.2020.629266.

46. Dixon M, Woodrick J, Gupta S, Karmahapatra SK, Devito S, Vasudevan S, Dakshanamurthy S, Adhikari S, Yenugonda VM, Roy R.Naturally occurring polyphenol, morin hydrate, inhibits enzymatic activity of N-methylpurine DNA glycosylase, a DNA repair enzyme with various roles in human disease. Bioorg Med Chem. 2015 Mar 1;23(5):1102-11. doi: 10.1016/j.bmc.2014.12.067

47. Rose, M.; Burgess, J.T.; O'Byrne, K.; Richard, D.J.; Bolderson, E. PARP Inhibitors: Clinical Relevance, Mechanisms of Action and Tumor Resistance. Front Cell Dev Biol. 2020 Sep 9:8:564601. doi: 10.3389/fcell.2020.564601.

48. Hopkins, T.A.; Ainsworth, W.B.; Ellis, P.A.; Donawho, C.K.; DiGiammarino, E.L.; Panchal, S.C.; Abraham, V.C.; Algire, M.A.; Shi,Y.; Olson, A.M.; et al. PARP1 Trapping by PARP Inhibitors Drives Cytotoxicity in Both Cancer Cells and Healthy Bone Marrow. Mol Cancer Res. 2019 Feb;17(2):409-419. doi: 10.1158/1541-7786.

49. Wang, R.; Sun, Y.; Li, C.; Xue, Y.; Ba, X. Targeting the DNA Damage Response for Cancer Therapy. Int J Mol Sci. 2023 Nov 2;24(21):15907. doi: 10.3390/ijms242115907.

50. Lee, K.J.; Piett, C.G.; Andrews, J.F.; Mann, E.; Nagel, Z.D.; Gassman, N.R. Defective Base Excision Repair in the Response to DNA Damaging Agents in Triple Negative Breast Cancer. PLoS One. 2019 Oct 9;14(10):e0223725. doi: 10.1371/journal.pone.0223725

51. Lodovichi, S.; Cervelli, T.; Pellicioli, A.; Galli, A. Inhibition of DNA Repair in Cancer Therapy: Toward a Multi-Target Approach. Int J Mol Sci. 2020 Sep 12;21(18):6684. doi: 10.3390/ijms21186684.

52. Levidou G, Ventouri K, Nonni A, Gakiopoulou H, Bamias A, Sotiropoulou M, Papaspirou I, Dimopoulos MA, Patsouris E, Korkolopoulou. Replication protein A in nonearly ovarian adenocarcinomas: correlation with MCM-2,

MCM-5, Ki-67 index and prognostic significance. Int J Gynecol Pathol. 2012 Jul;31(4):319-27. doi: 10.1097/PGP.0b013e31823ef92e.

53. Givalos N, Gakiopoulou H, Skliri M, Bousboukea K, Konstantinidou AE, Korkolopoulou P, Lelouda M, Kouraklis G, Patsouris E, Karatzas G. Replication protein A is an independent prognostic indicator with potential therapeutic implications in colon cancer. Mod Pathol. 2007 Feb;20(2):159-66. doi: 10.1038/modpathol.3800719.

54. Dahai Y, Sanyuan S, Hong L, Di Z, Chong Z. A relationship between replication protein A and occurrence and prognosis of esophageal carcinoma. Cell Biochem Biophys. 2013 Sep;67(1):175-80. doi: 10.1007/s12013-013-9530-y.

55. Levidou G, Gakiopoulou H, Kavantzas N, Saetta AA, Karlou M, Pavlopoulos P, Thymara I, Diamantopoulou K, Patsouris E, Korkolopoulou. Prognostic significance of replication protein A (RPA) expression levels in bladder urothelial carcinoma. BJU Int. 2011 Jul;108(2 Pt 2):E59-65. doi: 10.1111/j.1464-410X.2010.09828.x.

56. Fourtziala E, Givalos N, Alexakis N, Griniatsos J, Alevizopoulos N, Kavantzas N, C Lazaris A, Korkolopoulou P, Gakiopoulou. Protein A (RPA1, RPA2 and RPA3) expression in gastric cancer: correlation with clinicopathologic parameters and patients' survival. J BUON. 2020 May-Jun;25(3):1482-1489.

57. Algethami M, Toss MS, Woodcock CL, Jaipal C, Brownlie J, Shoqafi A, Alblihy A, Mesquita KA, Green AR, Mongan NP, Jeyapalan JN, Rakha EA, Madhusudan S. Unravelling the clinicopathological and functional significance of replication protein A (RPA) heterotrimeric complex in breast cancers. NPJ Breast Cancer. 2023 Mar 30;9(1):18. doi: 10.1038/s41523-023-00524-3.

58. Bélanger F, Fortier E, Dubé M, Lemay JF, Buisson R, Masson JY, Elsherbiny A, Costantino S, Carmona E, Mes-Masson AM, Wurtele H, Drobetsky E. Replication Protein A. Availability during DNA Replication Stress Is a Major Determinant of Cisplatin Resistance in Ovarian Cancer Cells. Cancer Res. 2018 Oct 1;78(19):5561-5573. doi: 10.1158/0008-5472.CAN-18-0618.

59. Cerda SR, Turk PW, Thor AD, Weitzman SA. Altered expression of the DNA repair protein, N-methylpurine-DNA glycosylase (MPG) in breast cancer. FEBS Lett. 1998 Jul 10;431(1):12-8. doi: 10.1016/s0014-5793(98)00697-8.

60. Leguisamo NM, Gloria HC, Kalil AN, Martins TV, Azambuja DB, Meira LB, Saffi J. Base excision repair imbalance in colorectal cancer has prognostic value and modulates response to chemotherapy. Oncotarget. 2017 Jan 31;8(33):54199-54214. doi: 10.18632/oncotarget.14909.

61. Luo SS, Liao XW, Zhu XD. Prognostic Value of Excision Repair Cross-Complementing mRNA Expression in Gastric Cancer. Biomed Res Int. 2018 Oct 17:2018:6204684. doi: 10.1155/2018/620468

62. Zhao M, Li S, Zhou L, Shen Q, Zhu H, Zhu X. Prognostic values of excision repair cross-complementing genes mRNA expression in ovarian cancer patients. Life Sci. 2018 Feb 1:194:34-39. doi: 10.1016/j.lfs.2017.12.018

63. Lu Z, Hou G. Characterization of the function and clinical value of ERCC family genes in lung adenocarcinoma. Front Oncol. 2024 Nov 8:14:1476100. doi: 10.3389/fonc.2024.1476100.

64. Ribeiro HL Jr, Maia ARS, de Oliveira RTG, Costa MB, Farias IR, de Paula Borges D, de Sousa JC, Magalhães SMM, Pinheiro RF. DNA repair gene expressions are related to bone marrow cellularity in myelodysplastic syndrome. J Clin Pathol. 2017 Nov;70(11):970-980. doi: 10.1136/jclinpath-2016-204269.

65. Zhang A, Liu W, Guo X, Jia H, Wei Y, Can C, He N, Ji C, Ma D. Genetic variations in DNA excision repair pathway contribute to the chemosensitivity and prognosis of acute myeloid leukemia. Clin Chim Acta. 2024 May 15:558:117899. doi: 10.1016/j.cca.2024.117899

66. Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, Bejar R, Berti E, Busque L, Chan JKC, Chen W, Chen X, Chng WJ, Choi JK, Colmenero I, Coupland SE, Cross NCP, De Jong D, Elghetany MT, Takahashi E, Emile JF, Ferry J, Fogelstrand L, Fontenay M, Germing U, Gujral S, Haferlach T, Harrison C, Hodge JC, Hu S, Jansen JH, Kanagal-Shamanna R, Kantarjian HM, Kratz CP, Li XQ, Lim MS, Loeb K, Loghavi S, Marcogliese A, Meshinchi S, Michaels P, Naresh KN, Natkunam Y, Nejati R, Ott G, Padron E, Patel KP, Patkar N, Picarsic J, Platzbecker U, Roberts I, Schuh A, Sewell W, Siebert R, Tembhare P, Tyner J, Verstovsek S, Wang W, Wood B, Xiao W, Yeung C, Hochhaus A.The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia. 2022 Jul;36(7):1703-1719. doi: 10.1038/s41375-022-01613-1.

66. Arber DA, Orazi A, Hasserjian R, et al, The 2016 revision to the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19;127(20):2391-405. doi: 10.1182/blood-2016-03-643544.

67. Garcia-Manero G. Myelodysplastic syndromes: 2023 update on diagnosis, risk-stratification, and management. Am J Hematol. 2023 Aug;98(8):1307-1325. doi: 10.1002/ajh.26984.

68. Nachtkamp K, Kobbe G, Gattermann N, Germing U.Myelodysplastic Syndromes: New Methods of Diagnosis, Prognostication, and Treatment. Dtsch Arztebl Int. 2023 Mar 24;120(12):203-210. doi: 10.3238/arztebl.m2023.0005.

69. Xiaomei Ma , Monique Does, Azra Raza, Susan T Mayne (2007). Myelodysplastic syndromes: incidence and survival in the United States. Cancer. 2007 Apr 15;109(8):1536-42. doi: 10.1002/cncr.22570

70. Hasserjian RP, Orazi A, Orfao A, Rozman M, Wang SA. The International Consensus Classification of myelodysplastic syndromes and related entities.Virchows Arch. 2023 Jan;482(1):39-51. doi: 10.1007/s00428-022-03417-1.

71. Rollison DE, Howlader N, Smith MT, Strom SS, Merritt WD, Ries LA, Edwards BK, List AF.Epidemiology of myelodysplastic syndromes and chronic myeloproliferative disorders in the United States, 2001-2004, using data from the NAACCR and SEER programs. Blood. 2008 Jul 1;112(1):45-52. doi: 10.1182/blood-2008-01-134858.

72. Hasserjian RP, Germing U, Malcovati L. Diagnosis and classification of myelodysplastic syndromes. Blood. 2023 Dec 28;142(26):2247-2257. doi: 10.1182/blood.2023020078.

73. Greenberg PL, Tuechler H, Schanz J, Sanz G, Garcia-Manero G, Solé F, Bennett JM, Bowen D, Fenaux P, Dreyfus F, Kantarjian H, Kuendgen A, Levis A, Malcovati L, Cazzola M, Cermak J, Fonatsch C, Le Beau MM, Slovak ML, Krieger O, Luebbert M, Maciejewski J, Magalhaes SM, Miyazaki Y, Pfeilstöcker M, Sekeres M, Sperr WR, Stauder R, Tauro S, Valent P, Vallespi T, van de Loosdrecht AA, Germing U, Haase D. Revised international prognostic scoring system for myelodysplastic syndromes. Blood. 2012 Sep 20;120(12):2454-65. doi: 10.1182/blood-2012-03-420489.

74. Papaemmanuil E, Gerstung M, Malcovati L, Tauro S, Gundem G, Van Loo P, Yoon CJ, Ellis P, Wedge DC, Pellagatti A, Shlien A, Groves MJ, Forbes SA, Raine K, Hinton J, Mudie LJ, McLaren S, Hardy C, Latimer C, Della Porta MG, O'Meara S, Ambaglio I, Galli A, Butler AP, Walldin G, Teague JW, Quek L, Sternberg A, Gambacorti-Passerini C, Cross NC, Green AR, Boultwood J, Vyas P, Hellstrom-Lindberg E, Bowen D, Cazzola M, Stratton MR, Campbell PJ; Chronic Myeloid Disorders Working Group of the International Cancer Genome Consortium. Blood. 2013 Nov 21;122(22):3616-27; quiz 3699. doi: 10.1182/blood-2013-08-518886

75. Jankowska AM, Gondek LP, Szpurka H, Nearman ZP, Tiu RV, Maciejewski JP.Base excision repair dysfunction in a subgroup of patients with myelodysplastic syndrome. Leukemia. 2008 Mar;22(3):551-8. doi:

10.1038/sj.leu.2405055.