ORIGINAL ARTICLE

Clinical Characteristics and Outcomes of Myelodysplastic Syndromes: A Single Center Study in Thailand

Theerin Lanamtieng, MD[1], Nattiya Teawtrakul, MD[1], Chinadol Wanitpongpun, MD[1], Pisa Phiphitaporn, MD[1], Pornpim Tuntibundit, MD[1]

[1] Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Background: In Thailand, myelodysplastic syndrome (MDS) characteristics differ from existing literature. There is a compelling need for the study, the clinical characteristics, outcomes, and prognostic factors within the context.

Objective: To demonstrate the characteristics, overall survival (OS) outcome and factors associated with OS of myelodysplastic syndromes in a university hospital in Thailand.

Materials and Methods: A retrospective cohort was performed. Newly diagnosed MDS from 2014 to 2023 were reviewed. Kaplan-Meier curve was used to illustrate OS and Cox regression analysis was performed to demonstrate factors associated with OS.

Results: The present study revealed 145 newly diagnosed MDS cases, with a median age of 72 years. About 70% exhibited at least one comorbidity. eighty-nine percent of the cohort revealed normal cytogenetics. Only 10% underwent gene sequencing, with TET2 and SF3B1 mutations were the most prevalent. Employing the Revised International Prognostic Scoring System (IPSS-R), our findings illustrated that higher-risk patients (>3.5 score of IPSS-R) experienced poorer OS than lower-risk groups. Multivariable Cox regression analysis identified that absolute neutrophil count (ANC) $<0.8\times10^3/\mu L$ (hazard ratio (HR) 2.40 (1.28 to 4.50)), blast count ≥5% (HR 3.89 (2.17 to 6.97)) and the presence of at least one comorbidity (HR 1.70 (1.01 to 2.88)), were predictors of inferior OS.

Conclusion: The present study demonstrated some different disease features from previous literature. Higher-risk groups in IPSS-R can predict inferior outcomes. Low ANC, increased blast count, and the presence of at least one comorbidity were identified as significant factors associated with poor outcomes.

Keywords: Myelodysplastic syndromes; Outcomes; Prognosis

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Myelodysplastic syndromes (MDS) represent a group of clonal hematopoietic neoplasms characterized by cytopenia and morphologic dysplasia[1]. The clinical presentation and survival outcomes of MDS are heterogeneous. The Revised International Prognostic Scoring System (IPSS-R) has been applied for prognostication in clinical practice[2]. Multiple statistically weighted clinical features were used to generate the model. Bone marrow cytogenetics, marrow blast percentage, and cytopenia were used for scoring and the model defined 5 prognostic categories. More than 3.5 score of IPSS-R is considered as a higher-risk group and need more intensive treatment due to dismal outcomes[3]. Although the IPSS-R is widely utilized for prognostication, it primarily draws data from western countries.

Multiple studies involving the Asian population have distinctions in clinical features of MDS compared to the Western countries[4-6]. A systematic review that collected epidemiological data from Western and Asian countries for the past 20 years suggested that the Asian population exhibited a lower incidence, an earlier age of onset, and a higher percentage of individuals categorized as higher risk[6]. In the specific case of Thailand, prior studies have revealed unique characteristics among MDS patients, deviating from the western countries' literature. Research conducted by Intragumtornchai et al.[7] reported that Thai MDS patients tended to be younger but the distribution of MDS subtypes and overall survival rates were found to be comparable. A more recent study by Polprasert et al.[8] reported a lower proportion of higher-risk group.

Given the evident heterogeneity and discrepancies

Correspondence to:

Lanamtieng T.

Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

Phone: +66-43-363664

Email: theela@kku.ac.th

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in disease phenotype attributed to ethnic factors, there is a compelling need for the development of a tailored prognostic model within the specific context of the Asian population. This would not only enhance the accuracy of prognostic predictions but also contribute to more effective and personalized management strategies for individuals diagnosed with MDS in this region.

Materials and Methods

The present study aimed to investigate the characteristics, overall survival (OS) outcomes, and factors associated with the outcomes of adult Thai patients diagnosed with myelodysplastic syndromes (MDS). The study focused on the population of newly diagnosed MDS patients at Srinagarind Hospital, a tertiary hospital in the northeast of Thailand, Faculty of Medicine, Khon Kaen University. Eligible participants were MDS patients aged 18 years or older who were diagnosed at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University between January 2014, and October 2023.

A retrospective cohort was performed. Clinical characteristics, including gender, complete blood count, cytogenetic profiles, genetic mutations, and survival outcomes from medical records were retrospectively reviewed.

The Kaplan-Meier curve is used to estimate survival probabilities over time, stratified by different groups of a categorical variable, without considering the effects of other covariate. The Cox regression analysis was utilized to identify factors associated with time-to-death outcomes. All statistical analyses were conducted using R Statistical Software (v 4.3.2; R Core Team, 2023)[9]. The graphical representation in the Figure was generated using the packages: survival[10], survminer[11], and dplyr[12].

The study has been reviewed by the Khon Kaen University Ethics Committee (HE631251) for Human Research based on the Declaration of Helsinki and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use - Good Clinical Practice Guidelines.

Results

One hundred forty-five newly diagnosed MDS cases were included, revealing a median age of 72 years. Baseline characteristics are demonstrated in Table 1. Approximately 70% exhibited at least one comorbidity, predominantly diabetes and renal disease. Only 10.3% displayed abnormal cytogenetics, while only 10% underwent gene sequencing, with TET2 and SF3B1 mutations being the most prevalent.

Employing IPSS-R, our findings illustrated that higher-risk patients (>3.5 score of IPSS-R) experienced significantly poorer OS than lower-risk groups (≤3.5 score of IPSS-R), as shown in Figure 1. Distinctions in OS among lower-risk IPSS-R groups were not detectable. Multivariable Cox regression analysis identified that absolute neutrophil count (ANC) $<0.8\times10^3/\mu L$, blast count ≥5%, and the presence of at least one comorbidity were associated with inferior OS (Table 2).

Discussion

In comparison to the database utilized in the IPSS-R study[2], this investigation revealed a comparable median age and male/female ratio. However, there was a notably higher prevalence of severe anemia (hemoglobin <8 g/dl). Although the proportion of the higher-risk group was lower than in prior studies conducted in other Asian countries, it was consistent with more recent studies in Thailand[8,13,14]. A lower proportion of MDS with SF2B1 mutation or MDS with ring sideroblast and MDS with isolated 5q deletion was observed in the study, aligning with findings in the Asian population[7,15].

Notably, approximately 90% of our cohort exhibited normal cytogenetics, a different feature from preceding studies. Some studies from Eastern Asian countries also reported a higher proportion of normal chromosomes than the Western countries[5,6,15]. The limitation of detecting abnormal chromosomes in the study could be attributed to cell culture techniques, low resolution, and the diminished sensitivity of conventional karyotyping[15]. Given the low prevalence of abnormal chromosomes, the risk categories defined by cytogenetic risk may not be reliable predictors in our setting. Gene sequencing emerges as a valuable tool for enhancing diagnostic accuracy and prognostic capabilities. For instance, the absence of clonal driver mutations in unexplained cytopenia, termed idiopathic cytopenia of undetermined significance, holds a high negative predictive value for MDS[16]. A study by Polprasert et al.[17] highlighted that unexplained cytopenia and lower-risk Thai MDS patients without genetic abnormalities exhibited a superior outcome than those with mutations.

In terms of overall survival (OS), higher-risk patients (>3.5 score of IPSS-R) exhibited significantly poorer outcomes compared to lower-risk groups (≤3.5 score of IPSS-R). However, distinctions in OS among lower-risk IPSS-R groups were not detectable. Adopting a two-category risk group may be more comprehensible and suitable for treatment planning in our context. However, the intermediate and lower-risk groups may benefit from additional information for outcome prediction. The Molecular International Prognostic Scoring[18] has been proposed and validated in Asian MDS patients[9,15]. Gene sequencing will be more important in making more precise prognostication.

A blast count of ≥5% was the strongest factor correlated

Table 1. Baseline characteristic of 145 Myelodysplastic syndromes patients

Characteristics	Patient, n=145
Median age at diagnosis (years old)	72
Gender,	
Male	76 (52.4%)
Female	69 (47.6%)
Median hemoglobin	8 g/dl
Median white blood cell count	$3.78\times10^3/\mu L$
Median platelet count	$98\times10^3/\mu L$
Median blast count	1%
Hemoglobin <8 g/dl	72 (49.7%)
Absolute neutrophil count $<0.8\times10^3/\mu L$	24 (16.6%)
Platelet $<50\times10^3/\mu L$	35 (24.1%)
At least one comorbidity	101 (69.7%)
Comorbidities	
Renal disease	38 (26.2%)
Diabetes mellitus	33 (22.8%)
Liver disease	7 (4.8%)
Autoimmune disease	6 (4.1%)
Blast count ≥5%	25 (17.2%)
Abnormal cytogenetics	15 (10.3%)
Revised International Prognostic Scoring System	
Very low	15 (10.3%)
Low	81 (55.7%)
Intermediate	24 (16.6%)
High	17 (11.7%)
Very high	8 (5.5%)
Diagnosis (World Health Organization 2022 criteria)	
MDS with low blast	93 (64.1%)
MDS with increased blasts	24 (16.6%)
MDS, hypoplastic	15 (10.3%)
MDS with low blasts and SF2B1 mutation or MDS with ring sideroblast	12 (8.3%)
MDS with low blasts and isolated 5q deletion	1 (0.7%)

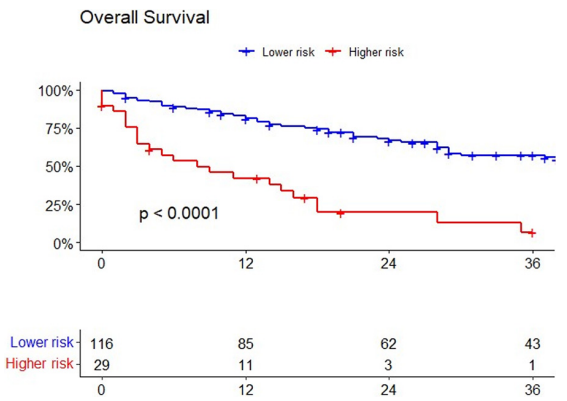

Figure 1. Kaplan-Meier curve demonstrated the estimation of survival probabilities over time, stratified by higher-risk and lower-risk groups.

with diminished overall survival in the present study. It is well-established that increased blast count represents advanced disease and associated inferior outcomes[2,20]. Blast count still be a crucial predictive factor in a novel molecular prognostic score when combined with genetic mutations[18]. Although morphological examination is the standard for myeloblast identification[20], there was a brief report about the discrepancy in blast count[21]. We need more objective and valid assessment tools for myeloblast detection in MDS.

In addition, our study identified an association between lower ANC and unfavorable survival outcomes. Neutropenia is associated with higher potential infectious risk and poor survival outcome, which aligns with the findings of several prior studies[22-24]. this observation resonates with a study investigating genetic mutations linked to blood count abnormalities in Thai myeloid neoplasm patients[25]. From previous literature, severe anemia and thrombocytopenia were associated with increased morbidity and poor survival[2,26,27]. Our study did not yield significant evidence supporting such associations. This finding resembled a

Table 2. Cox regression analysis for overall survival (time to death)

	Hazard ratio (univariable)		Hazard ratio (multivariable)	
Hemoglobin <8 g/dl	1.10 (0.73 to 1.70)	p=0.61	0.97 (0.61 to 1.56)	p=0.92
Absolute neutrophil count $<0.8\times10^3/\mu L$	2.10 (1.20 to 3.50)	p<0.01*	2.40 (1.28 to 4.50)	p<0.01*
Platelet $<50\times10^3/\mu L$	0.87 (0.52 to 1.40)	p=0.58	0.64 (0.37 to 1.13)	p=0.12
At least one comorbidity	1.40 (0.84 to 2.30)	p=0.19	1.70 (1.01 to 2.88)	p=0.04*
Blast count ≥5%	4.00 (2.30 to 6.80)	p<0.01*	3.89 (2.17 to 6.97)	p<0.01*

large-scale study conducted in China, which similarly failed to demonstrate these connections through multivariable analysis[5].

The last associated factor from multivariable Cox regression analysis was the comorbidities. This finding suggested that geriatric assessments become more important tools in prognosis and treatment decisions. Several studies reported the significance of comorbidity. Starkman et al.[28] proposed an MDS-specific frailty index added to clinical prognostic scoring. A combination of frailty Status and comorbidity score could Improve the stratification of survival[29]. Moreover, A study of older MDS patients who received azacitidine reported that a comprehensive geriatric assessment could predict azacitidine treatment duration and survival[30,31].

While this study contributes evidence for a two-category-risk model in the clinical context, it is important to acknowledge several limitations. One significant limitation is the lack of genetic data in our analysis. Genetic profiling plays a crucial role in understanding the underlying mechanisms and predicting outcomes in MDS. A larger dataset with complete genetic information would be invaluable for developing a more comprehensive predictive model tailored to our specific clinical context. The gene profiles in MDS are highly sophisticated, and their analysis may require more advanced computational methods, particularly when dealing with big datasets. Future research efforts should focus on incorporating genetic data into prognostic models, employing advanced computational analyses to unravel complex gene interactions and their implications on disease progression and treatment outcomes.

Conclusion

Multiple studies involving the Asian population have distinctions in clinical features compared to the Western countries. Our study revealed distinctive disease features among Thai MDS patients, deviating from established patterns observed in western countries' literature. The disease phenotype in our cohort resembled that of the Eastern Asian population, marking a significant regional variance. Furthermore, a lower prevalence of the higher-risk group was evident, with a predominant occurrence of normal cytogenetics among our patients. The application of the two-category-risk model, derived from the IPSS-R, demonstrated its efficacy in predicting unfavorable outcomes within our setting. Low ANC, increased blast count, and the presence of at least one comorbidity were identified as significant factors associated with poor survival outcomes.

What is already known on this topic?

Asian population have distinctions in clinical features compared to the Western countries. Five-categories IPSSR was widely used for prognostication.

What this study adds?

Our study revealed distinctive features, deviating from Western countries. Adopting a two-category risk group may be more comprehensible and suitable in our context.

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Conflicts of interest

The authors declare no conflict of interest.

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