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Factors Predicting Early Mortality After New Diagnosis of Myelodysplastic Syndrome (MDS): A Population Based Study

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Abstract

Objective: Little prospective data regarding factors determining patient outcomes in myelodysplastic syndromes (MDS) are available. To establish features of early mortality in MDS we compare characteristics of patients dying within one year of diagnosis with those surviving longer.

Methods: We prospectively enrolled adults with a new MDS diagnosis in a population-based case-control study. Logistic regression was used to calculate odds ratios and 95% confidence intervals for potential predictors of early mortality. Subgroup analyses were conducted within the following groups: High/Very High Risk IPSS-R; Very low/Low/Intermediate Risk IPSS-R; Treated Patients; and Supportive Care Only Patients.

Results: We observed early mortality in those with abnormal cytogenetics (OR: 3.36, 95% CI: 1.52-7.46), three or greater cytogenetic abnormalities (OR: 3.48, 95% CI: 1.51-7.99), treatment at a community medical center (versus academic) (OR: 2.55, 95% CI: 1.18-5.47), and with 2-3 concurrent medical comorbidities (OR: 2.14, 95% CI: 1.08-4.22). Similarly, in subgroup analyses, abnormal cytogenetics remained the main predictor of early mortality.

Conclusion: Complex cytogenetics and prognostic risk category have been associated with early mortality without intervention. Our data confirm these associations in a large, prospectively followed cohort and highlight the significance of cytogenetic abnormalities and complexity regardless of IPSS-R risk categorization or treatment.

Keywords

myelodysplastic syndrome; survival; prospective

Introduction

Myelodysplastic syndromes (MDS) are a heterogeneous collection of clonal disorders of hematopoietic stem cells characterized by ineffective hematopoiesis and dysplastic cell morphology with potential for clonal evolution to secondary acute myeloid leukemia (AML) in up to 30% of patients.¹ Prior to classification as a neoplasm by the National Cancer Institute in 2001, MDS was thought to be a “preleukemic” state.¹ Diagnosis of MDS requires the exclusion of non-MDS causes of cytopenias in the setting of some combination of increased bone marrow blast percentage, karyotypic abnormality, and morphologic dysplasia.² With the continual identification of associated genetic abnormalities and varied clinical presentations, refinement of pathologic classification is an ongoing challenge that has been addressed by the World Health Organization (WHO) in 2008³ and again in 2016.⁴ According to the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program, the incidence of MDS is approximately 2.6-4.3 per 100,000 individuals per year in the United States,⁵ making it one of the most common causes of acquired bone marrow failure in adults.¹ Five year survival rates range from 35-48%, with the highest 5-year-survival among blacks.⁵

The first prognostic tool for MDS, the International Prognostic Scoring System (IPSS) was published in 1997⁶ and revised (IPSS-R) in 2012.⁷ It is used at the time of diagnosis to categorize patients as lower- or higher-risk,⁷ and to direct treatment strategy based on accepted practice patterns and the guidelines of the National Comprehensive Cancer Network (NCCN).⁸⁻¹⁰ Lower-risk patients are usually managed with growth factors, blood transfusions, and the biologic agent lenalidomide. Higher-risk patients, having increased risk of leukemic transformation and lower overall survival,¹¹ are treated with chemotherapy, hypomethylating agents such as azacitidine and decitabine, or allogeneic hematopoietic stem cell transplant (HSCT). Despite all the recent advances mentioned above, HSCT remains the only curative therapy for MDS.^{1,8-10,12-14}

To gauge the impact of non-hematologic medical comorbidities on survival in MDS, the MDS Comorbidity Index (MDS-CI) was developed and can be combined with IPSS-R and the WHO Classification-Based Prognostic Scoring System (WPSS) to refine prognostication.^{15,16} This development represents one of the first probes into the relationship between patient and disease factors and survival in MDS. To further this body of evidence and to better elucidate the features of early mortality, we compare the characteristics of patients dying within one year of MDS diagnosis with the characteristics

of those surviving longer in our Adults in Minnesota with MDS (AIMMS) population based study.

Patients and Methods

Adults in Minnesota with MDS (AIMMS) is a statewide prospective population-based case-control study conducted by the University of Minnesota (UMN), Mayo Clinic, and the Minnesota Department of Health. Methods used in the study have previously been described in detail.^{17,18} Adults (age 20+ years) with a new diagnosis of MDS were identified by the Minnesota Cancer Surveillance System (MCSS) from April 2010 through October 2014. Patients were contacted for enrollment after physician approval. At study entrance, each patient completed a comprehensive questionnaire in order to compile retrospective epidemiologic data which was then compared to population-based controls (data not included in this analysis). Fifty-nine percent of patients referred to the study completed the interview.

After enrollment, we performed a central medical review starting from the time of MDS diagnosis. Pathologic review consisted of assessment of bone marrow and peripheral blood samples by two independent hematopathologists. Cytogenetic analyses were independently reviewed by a cytogeneticist. Reports were collated and a unifying subtype was determined through collaborative discussion for any discrepancies in WHO classification based on the 2008 revised criteria.³ We excluded cases without a confirmed diagnosis of MDS during the study eligibility period (N=165).

Patient charts were reviewed by an oncologist who assigned a prognostic risk score by IPSS and WPSS, and subsequently by IPSS-R.^{6-7,11} Risk scores were not calculated for patients lacking the required cytogenetic and hematologic data. Treatment exposures and responses were abstracted, including relevant exposures prior to formal diagnosis when available. Annual clinical review of all patients obtaining information on disease progression, treatment information and vital status is planned for four years after initial enrollment.

Patients enrolled in AIMMS with a confirmed diagnosis of MDS and at least one year of follow-up were included in this analysis (N=399). We compared the characteristics of patients who died within one year of diagnosis with those surviving longer. Medical comorbidities, family history, smoking status, benzene exposure, socioeconomic status, and race/ethnicity were identified by the questionnaire and by medical records. Academic centers were defined as the University of Minnesota and Mayo Clinic, with all other sites classified as community-based practices.

The association between risk factors and death within one year of MDS diagnosis was described using unconditional logistic regression. Variables were selected for assessment *a priori*, based on established associations with MDS. For all analyses, variables considered included sex (male, female), age at diagnosis as a dichotomous variable (≤ 60 years, > 60 years), smoking status (current smoker, former smoker, never smoker), family history of cancer, personal history of chemotherapy and/or radiation, treatment with hypomethylating agent (yes or no), supportive care only (yes or no), transplant (yes or no) treatment provider

(academic, community, both academic and community), cytogenetic complexity (3), cytogenetic categorization (normal, abnormal), 2008 WHO classification (RA/RN/RT/RARS, RCMD, RAEB 1/RAEB2, MDS with del(5q), MDS-unclassifiable, therapy related MDS), and a comorbidity index calculated from prior diagnosis of the following medical conditions (hyperthyroidism, hypothyroidism, peptic ulcer, ankylosing spondylitis, heart disease/angina/attack, high blood pressure, diabetes, rheumatoid arthritis, osteoarthritis, Crohn's disease, ulcerative colitis, celiac disease, Sjögren's disease, lupus, polymyositis, eczema, contact dermatitis, cirrhosis of liver, infectious mononucleosis, chronic fatigue syndrome, epilepsy). Covariates were first tested as effect modifiers and were only retained in the final model if they changed the ln(OR) estimate substantially (>10%). We also conducted stratified analyses to identify differences in survival within IPSS-R categories (High/Very High, Intermediate, Low/Very Low) and by treatment status (Treated Patients versus Supportive Care Only Patients). Statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

This analysis was completed after one year of clinical review was performed on all 399 cases enrolled to the AIMMS study. At one year of follow-up, 85 patients had died, a mortality rate of 21.3%. The median age at diagnosis was 71.5 (range 25-91). Males comprised 64% of patients. Active treatment was pursued in 40% of patients. Hypomethylating agents, azacitidine and decitabine, were the most common treatment versus a smaller subset undergoing transplant and a very small subset of patients received induction type chemotherapy. Fifty-eight percent of patients received supportive care only. Characteristics of the group of patients with early mortality and the group who survived at least one year past diagnosis are outlined in Table 1.

We compared the clinical characteristics of patients who died within one year of diagnosis to those surviving longer than one year. We observed early mortality in those with abnormal cytogenetics (OR: 3.36, 95% CI 1.52-7.46), three or greater cytogenetic abnormalities (OR: 3.48, 95% CI 1.51-7.99), treatment at a community medical center only (versus academic) (OR: 2.55, 95% CI 1.18-5.47), and with 2-3 concurrent medical comorbidities (OR: 2.14, 95% CI 1.08-4.22) (Table 2). Treatment with a hypomethylating agent also correlated with early mortality (OR: 2.72, 95% CI 1.50-4.95), but when adjusted for WPSS and IPSS-R, this association was no longer significant.

We analyzed outcomes based primarily on IPSS-R adjusting for patient and disease variables also known to impact outcomes. Among patients with high or very high risk IPSS-R, the presence of 3 or more cytogenetic abnormalities was the only significant predictor of early mortality (OR: 5.81, 95% CI: 2.11-15.99) (Table 3). Similarly, in those with very low, low, or intermediate IPSS-R, abnormal cytogenetics was the factor nearing significance as a predictor of early mortality in an adjusted model (OR: 3.42, 95% CI 0.97-12.13) (Table 3).

Analysis on outcomes based on treatment approach, supportive care versus active treatment, we observed interesting trends. In patients receiving supportive care only, early mortality was seen in those who had diabetes (OR: 3.06, 95% CI 1.11-8.42), complex cytogenetics

(OR for 3 abnormalities: 4.94, 95% CI 1.25-19.46), and very high or high IPSS-R (OR: 4.20, 95% CI 1.43-12.34). In patients receiving any treatment, complex cytogenetics remained the sole significant predictor of early mortality (OR: 4.84, 95% CI 1.43-16.37). Table 4 outlines these findings.

Discussion

Despite the development and refinement of numerous prognostic scoring systems,^{6-7,15-16} few prospective data regarding the influence of these and other factors on patient outcomes are available. To our knowledge, early mortality in MDS has not been studied in a prospective cohort. In our large, prospectively followed cohort, cytogenetic abnormalities and complexity were clearly the most significant predictors of early mortality. We observed early mortality in patients with increased cytogenetic abnormalities and complexity regardless of their prognostic category, and regardless of whether they received treatment or supportive care only. The association of treatment with a hypomethylating agent and early mortality (Table 2) was not statistically significant when adjusted for WPSS and IPSS-R, and likely reflects the decision to treat more aggressive disease. These data are in agreement with published data where cytogenetic abnormalities have long been associated with poor prognosis.^{6-7,19-21}

Our research sheds new light on the role of cytogenetic abnormalities and complexity in early mortality in patients with low risk disease. Even among patients in our cohort with very low, low or intermediate risk, the presence of cytogenetic abnormalities or complex karyotype was the sole predictor of early mortality. With the current IPSS-R, a patient with normal hemoglobin, platelets, and blast percent, but with “very poor” cytogenetic category (>3 cytogenetic abnormalities) would be classified as having intermediate risk.²² Current guidelines suggest that treatment in this group should be pursued based on clinical signs of symptomatic anemia, clinically relevant neutropenia, or increased marrow blasts.^{8,10} The findings of our analysis suggest that individuals with abnormal or complex cytogenetics have increased mortality regardless of IPSS-R, thus early treatment prior to the development of these clinical signs or progression may be reasonable.

Consideration of earlier treatment is further supported by our observation of increased early mortality seen in patients receiving care only in a community (versus academic) center. A previous analysis of this cohort comparing treatment at academic to community centers has shown that care in an academic center results in more active treatment earlier in the disease course.²³ The increased mortality observed in our current expanded cohort in patients receiving care only in a community center may suggest that a less aggressive up front approach to treatment may result in earlier death, especially for those with higher risk features.

Several new insights come from our analysis. Diabetes has recently been correlated with early mortality in lower-risk myelodysplastic syndrome in a retrospective cohort.¹⁶ Similarly in our prospective cohort, we observed increased mortality in patients with diabetes who received supportive care only; this group generally had low or very low IPSS-R, which validates this correlation by Falantes and colleagues. Our analysis included multiple medical

comorbidities and none other than diabetes showed a correlation with early mortality (data not shown), although patients with two or three comorbidities were more likely to die within one year of diagnosis. This alone is not surprising, however, patients in our cohort with four or more comorbidities did not experience early mortality, possibly due to small sample size.

One strength of our study was the high degree of diagnostic certainty through pathologic evaluation, due to a rigorous central review process. Further, because we utilized direct chart review of treatment strategy and independent calculation of risk scores, we effectively eliminated the recall bias that can be seen with a survey-based data collection approach as relied upon by several previously published studies.²⁴⁻²⁶ In addition to these strengths, several weaknesses must be considered. Selection bias is possible given the enrollment response rate (59%). While rapid case ascertainment was used to reduce this possibility, survival bias is also possible given the poor outcomes associated with MDS. Our exclusion of patients whose death preceded collection of all necessary preliminary data may bias toward lower risk disease. Finally, lack of molecular data for included cases does limit our conclusions. As other studies have shown that TP53 mutations are the major factor of poor outcome in those with complex cytogenetics, this information would be helpful in our analysis to allow for comparison.²¹

Complex cytogenetics and prognostic risk category (either by WPSS or IPSS-R) have previously been associated with higher risk disease and early mortality without intervention. Our data confirm this association in a large prospectively followed MDS cohort and highlight the significance of cytogenetic abnormalities and complexity regardless of IPSS-R risk categorization or treatment.

References

1. Bejar R & Steensma DP. Recent developments in myelodysplastic syndromes. *Blood* 2014;124:2793–2803. [PubMed: 25237199]
2. Steensma DP. Dysplasia has a differential diagnosis: Distinguishing genuine myelodysplastic syndromes (MDS) from mimics, imitators, copycats and impostors. *Curr Hematol Malig Rep* 2012 12;7(4):310–320. [PubMed: 23015360]
3. Vardiman JW, Thiele J, Arber DA, et al. The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: rationale and important changes. *Blood* 2009;114:937–951. [PubMed: 19357394]
4. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood* 2016;127:2391–2405. [PubMed: 27069254]
5. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Mortality - All COD, Aggregated With State, Total U.S. (1969-2015) <Katrina/Rita Population Adjustment>, National Cancer Institute, DCCPS, Surveillance Research Program, released 12/2017 Underlying mortality data provided by NCHS (www.cdc.gov/nchs).
6. Greenberg P, Cox C, LeBeau MM, et al. International scoring system for evaluating prognosis in myelodysplastic syndromes. *Blood*. 1997;89:2079–2088. [PubMed: 9058730]
7. Greenberg P, Tuechler H, Schanz J, et al. Revised international prognostic scoring system (IPSS-R) for myelodysplastic syndromes. *Blood* 2012 9 20;120(12):2545–2465. [PubMed: 22773386]
8. Santini V Treatment of low-risk myelodysplastic syndromes. *Hematology Am Soc Hematol Educ Program* 2016 12 2;2016(1), 462–469. [PubMed: 27913517]
9. Sekeres MA, Cutler C. How we treat higher-risk myelodysplastic syndromes. *Blood* 2014 2 6;123(6), 829–836. [PubMed: 24363399]

10. National Comprehensive Cancer Network, I. NCCN guidelines version 2.2017, myelodysplastic syndromes. 11 10, 2016 Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds_blocks.pdf. (Accessed: 12th December 2018).
11. Malcovati L, Germing U, Kuendgen A, et al. Time-dependent prognostic scoring system for predicting survival and leukemic evolution in myelodysplastic syndromes. *J Clin Oncol*. 2007;25:3503–3510. [PubMed: 17687155]
12. Warlick ED, Cioc A, Defor T, et al. Allogeneic stem cell transplantation for adults with myelodysplastic syndromes: importance of pretransplant disease burden. *Biol Blood Marrow Transplant*. 2009 1;15(1):30–8. [PubMed: 19135940]
13. Ustun C, Trottier BJ, Sachs Z, et al. Monosomal karyotype at the time of diagnosis or transplantation predicts outcomes of allogeneic hematopoietic cell transplantation in myelodysplastic syndrome. *Biol Blood Marrow Transplant*. 2015 5;21(5):866–72. [PubMed: 25620751]
14. Pourhassan H, DeFor T, Trottier B, et al. MDS disease characteristics, not donor source, predict hematopoietic stem cell transplant outcomes. *Bone Marrow Transplant*. 2016 12 12.
15. Della Porta MG, Malcovati L, Strupp C, et al. Risk stratification based on both disease status and extra-hematologic comorbidities in patients with myelodysplastic syndrome. *Haematologica*. 2011 3;96(3):441–9. [PubMed: 21134982]
16. Falantes JF, Marquez-Malaver FJ, Knight T, et al. The incorporation of comorbidities in the prognostication of patients with lower-risk myelodysplastic syndrome. *Leuk Lymphoma*. 2016 12 12:1–10.
17. Poynter JN, Richardson M, Roesler M, et al. Chemical Exposures and Risk of Acute Myeloid Leukemia and Myelodysplastic Syndromes in a Population-Based Study. *Int J Cancer* 2017 1 1;140(1):23–33. [PubMed: 27603749]
18. Poynter JN, Richardson M, Blair CK, et al. Obesity over the Life Course and Risk of Acute Myeloid Leukemia and Myelodysplastic Syndromes. *Cancer Epidemiol* 2016 2;40:134–40. [PubMed: 26720913]
19. Itzykson R, Thepot S, Quesnel B, et al. Prognostic factors for response and overall survival in 282 patients with higher-risk myelodysplastic syndromes treated with azacitidine. *Blood* 2011 1 13;117(2):403–411. [PubMed: 20940414]
20. Visconte V, Tiu RV, Rogers HJ. Pathogenesis of myelodysplastic syndromes: An overview of molecular and non-molecular aspects of the disease. *Blood Res* 2014;49(4):216–227. [PubMed: 25548754]
21. Bejar R, Stevenson KE, Caughey B, et al. Somatic mutations predict poor outcome in patients with myelodysplastic syndrome after hematopoietic stem-cell transplantation. *J Clin Oncol* 2014 9 1;32(25):2691–2698. [PubMed: 25092778]
22. MDS Foundation IPSS-R calculator. <https://www.mds-foundation.org/ipss-r-calculator>
23. Pease DF, Ross JA, Poynter JN, et al. Differences in community and academic practice patterns for newly diagnosed myelodysplastic syndromes (MDS) patients. *Cancer Epidemiol*. 2015 4; 39(2): 222–228. [PubMed: 25701277]
24. Sekeres MA, Schoonen WM, Kantarjian H, et al. Characteristics of US patients with myelodysplastic syndromes: results of six cross-sectional physician surveys. *J Natl Cancer Inst* 2008 11 5;100(21):1542–1551. [PubMed: 18957672]
25. Sekeres MA. Epidemiology, natural history, and practice patterns of patients with myelodysplastic syndromes in 2010. *J Natl Compr Canc Netw* 2011 1;9(1):57–63. [PubMed: 21233244]
26. Gatterman N, Kundgen A, Kellermann L, et al. Diagnosis and therapy of myelodysplastic syndromes in Germany: a retrospective multicenter analysis. *Onkologie* 2012;35(6):350–356. [PubMed: 22722455]

Table 1:

Selected characteristics of the study population

Characteristic	Survived < 1 year N (%)	Survived 1 year N (%)	p- value ^I
Total	85	314	
Male Sex	57 (67.1)	198 (63.1)	0.50
Age Group 60	73 (85.9)	278 (88.5)	0.51
Race - Non-Hispanic White	82 (96.5)	309 (98.4)	-
Marital status			
Married/Cohabiting	64 (75.3)	223 (71.0)	
Widow/Divorced/Separated/Never Married	21 (24.7)	91 (29.0)	0.44
Education			0.82
HS	30 (36.1)	116 (36.3)	
Post-HS	25 (30.1)	84 (26.8)	0.65
College graduate	28 (33.7)	114 (36.3)	0.86
Income			0.60
\$40,000	37 (44.6)	135 (44.1)	0.71
\$40,000 – \$80,000	33 (39.8)	109 (35.6)	
> \$80,000	13 (15.7)	62 (20.3)	0.31
BMI category – 2 years before diagnosis			0.87
Normal/Under weight	24 (28.2)	83 (26.5)	
Overweight	30 (35.3)	120 (38.3)	0.64
Obese	31 (36.5)	110 (35.1)	0.93
Smoking history			0.86
Current Smoker	6 (7.1)	28 (8.9)	0.65
Former Smoker	44 (52.4)	159 (50.6)	0.90
Never Smoker	34 (40.5)	127 (40.5)	
Personal history of cancer	38 (44.7)	117 (37.4)	0.22
Personal history of chemotherapy	23 (27.1)	43 (13.7)	0.004
Personal history of radiation	19 (22.4)	37 (11.8)	0.01
Family history of cancer	62 (72.9)	207 (65.9)	0.22

^IWald Chi-square for individual levels and Type 3 Wald Chi-Square for overall test

Table 2.

Comparison of clinical characteristics in MDS patients who did and did not die within 1 year of diagnosis

Characteristic	Survived < 1 year N (%)	Survived year 1 N (%)	Unadjusted OR (95% CI)	p-value ²	Multivariable Adjusted ¹ OR (95% CI)	p-value ²
Total	85	314				
Treatment						
Hypomethylating agent	25 (30.1)	43 (14.0)	2.72 (1.50-4.95)	0.001	1.24 (0.55-2.78)	0.61
Transplant	10 (12.1)	36 (11.7)	1.27 (0.58-2.75)	0.55	0.57 (0.17-1.94)	0.37
Supportive Care only	41 (49.4)	192 (62.5)	<i>Ref</i>		<i>Ref</i>	
Other ⁵	7 (8.4)	36 (11.7)	0.91 (0.38-2.19)	0.83	0.46 (0.14-1.49)	0.20
Treatment provider						
Community only	44 (51.8)	143 (45.7)	1.33 (0.78-2.28)	0.29	2.55 (1.18-5.47)	0.02
Academic and Community	27 (31.8)	116 (37.1)	<i>Ref</i>		<i>Ref</i>	
Academic only	14 (16.5)	54 (17.3)	1.12 (0.55-2.31)	0.75	1.01 (0.39-2.58)	0.99
Comorbidities						
0-1	28 (32.9)	140 (44.7)	<i>Ref</i>		<i>Ref</i>	
2-3	46 (54.1)	119 (38.0)	1.95 (1.15-3.31)	0.01	2.14 (1.08-4.22)	0.03
4	11 (12.9)	54 (17.3)	1.03 (0.48-2.20)	0.95	0.74 (0.28-1.97)	0.55
Cytogenetics						
Normal	14 (17.5)	153 (51.5)	<i>Ref</i>		<i>Ref</i>	
Abnormal	66 (82.5)	144 (48.5)	5.04 (2.71-9.37)	<.0001	3.36 (1.52-7.46)	0.003
Complex karyotype ³ (≥ 3 abnormalities)	33 (38.8)	22 (7.0)	8.03 (4.37-14.75)	<.0001	3.48 (1.51-7.99)	0.003
IPSS-R Risk Category						
High/ Very High	53 (67.1)	79 (27.2)	7.54 (3.87-14.66)	<.0001	2.64 (0.87-8.06)	0.09
Intermediate	13 (16.5)	66 (22.8)	2.21 (0.97-5.03)	0.06	1.76 (0.61-5.11)	0.30
Low/ Very Low	13 (16.5)	146 (50.0)	<i>Ref</i>		<i>Ref</i>	
WHO Subtype						
RA / RN / RT/ RARS	4 (4.7)	67 (21.4)	0.25 (0.08-0.77)	0.02	0.60 (0.16-2.18)	0.44
RCMD	20 (23.5)	86 (27.5)	<i>Ref</i>		<i>Ref</i>	
RAEB (1 and 2)	37 (43.5)	91 (29.1)	1.75 (0.94-3.25)	0.08	1.56 (0.63-3.89)	0.34
MDS with del(5q)	3 (3.5)	24 (7.7)	0.54 (0.15-1.96)	0.35	1.01 (0.22-4.66)	0.99
MDS, unclassifiable	5 (5.9)	21 (6.7)	1.02 (0.34-3.05)	0.35	0.97 (0.25-3.77)	0.97

Characteristic	Survived < 1 year N (%)	Survived 1 year N (%)	Unadjusted OR (95% CI)	p-value ²	Multivariable Adjusted ¹ OR (95% CI)	p-value ²
Therapy related	16 (18.8)	24 (7.7)	2.87 (1.29-6.37)	0.01	1.03 (0.32-3.29)	0.96
WPSS at Diagnosis⁴						
Very High	23 (27.4)	21 (6.8)	16.43 (5.09-53.06)	<.0001		
High	35 (41.7)	100 (32.6)	5.25 (1.78-15.50)	0.003		
Intermediate	5 (6.0)	38 (12.4)	1.97 (0.50-7.82)	0.33		
Low	8 (9.5)	57 (18.6)	2.11 (0.60-7.38)	0.24		
Very Low	4 (4.8)	60 (19.5)	<i>Ref</i>			
Cannot calculate	9 (10.7)	31 (10.1)	4.36 (1.24-15.28)	0.02		

* Numbers may not sum to total due to missing values OR: Odds Ratio; 95% CI: 95% Confidence Interval; NC: not calculated

¹ Adjusted for sex, age at diagnosis, smoking status, personal and family history of cancer, treatment, treatment provider, comorbidities, cytogenetics, WHO classification, and IPSS-R

² Wald Chi-square

³ Includes a subset of cases with abnormal karyotype

⁴ Due to high correlation with IPSS-R, WPSS category was not included in adjusted model

⁵ Other treatment included induction chemotherapy, revlimid, and miscellaneous. In those that Survived < 1 Year (Induction chemo (n=3), Lenalidomide (n=2), Misc (n=2). In those that Survived 1 year (Induction chemo (n=6), Lenalidomide (n=22), Misc (n=3)

Table 3.

Comparison of MDS patients who did and did not die within 1 year of diagnosis – stratified by IPSS-R Risk Category

Factor	Survived < 1 year N (%)	Survived ≥ 1 year N (%)	Multivariable Adjusted ¹ OR (95% CI)	p-value ²
IPSS-R High/Very High				
Total	53	79		
Treatment				
Hypomethylating agent	18 (34.6)	21 (26.6)	0.88 (0.30-2.64)	0.82
Transplant	6 (11.5)	19 (24.1)	0.29 (0.06-1.53)	0.15
Supportive Care only	22 (42.3)	27 (34.2)	<i>Ref</i>	
Other	6 (11.5)	12 (15.2)	0.39 (0.08-1.90)	0.24
Treatment provider				
Community only	25 (47.2)	24 (30.4)	1.81 (0.61-5.38)	0.29
Academic and Community	21 (39.6)	37 (46.8)	<i>Ref</i>	
Academic only	7 (13.2)	18 (22.8)	0.41 (0.11-1.51)	0.18
Comorbidities				
0-1	20 (37.7)	36 (45.6)	<i>Ref</i>	
2-3	26 (49.1)	30 (38.0)	1.00 (0.37-2.72)	0.99
4	7 (13.2)	13 (16.5)	0.46 (0.11-1.87)	0.28
Cytogenetics				
Normal	5 (9.6)	24 (30.8)	<i>Ref</i>	
Abnormal	47 (90.4)	54 (69.2)	3.42 (0.97-12.13)	0.06
Complex karyotype ³ (≥ 3 abnormalities)	31 (58.5)	20 (25.3)	5.81 (2.11-15.99)	0.0006
IPSS-R Very Low/Low/Intermediate				
Total	26	212		
Treatment				
Hypomethylating agent	7 (26.9)	20 (9.4)	0.88 (0.30-0.30)	0.83
Transplant	2 (7.7)	17 (8.0)	0.29 (0.06-1.53)	0.15
Supportive Care only	16 (61.5)	151 (71.2)	<i>Ref</i>	
Other	1 (3.9)	24 (11.3)	0.39 (0.08-1.90)	0.24
Treatment provider				
Community only	15 (57.7)	105 (49.5)	1.81 (0.61-5.38)	0.29
Academic and Community	5 (19.2)	74 (34.9)	<i>Ref</i>	
Academic only	6 (23.1)	33 (15.6)	0.41 (0.11-1.51)	0.18

Factor	Survived < 1 year N (%)	Survived ≥ 1 year N (%)	Multivariable Adjusted ¹ OR (95% CI)	p-value ²
Comorbidities				
0-1	7 (26.9)	92 (43.4)	<i>Ref</i>	
2-3	16 (61.5)	83 (39.2)	1.00 (0.37-2.72)	0.99
4	3 (11.5)	37 (17.5)	0.46 (0.11-1.87)	0.28
Cytogenetics				
Normal	8 (32.0)	124 (60.5)	<i>Ref</i>	
Abnormal	17 (68.0)	81 (39.5)	3.42 (0.97-12.13)	0.06
Complex karyotype ³ (≥ 3 abnormalities)	1 (3.9)	3 (1.4)	NC	

Numbers may not sum to total due to missing values OR: Odds Ratio; 95% CI: 95% Confidence Interval; NC: not calculated

¹ Adjusted for sex, age at diagnosis, smoking status, personal and family history of cancer, treatment, treatment provider, comorbidities, cytogenetics, WHO classification

² Wald Chi-square

³ Includes a subset of cases with abnormal karyotype

Table 4.

Comparison of MDS patients who did and did not die within 1 year of diagnosis – stratified by initial treatment received (supportive care only or any active treatment)

	Died < 1 Year	Died 1 Year		
Supportive Care Only				
Total	41	192		
Cytogenetics				
Normal	6 (15.8)	99 (54.7)	<i>Ref</i>	
Abnormal	32 (84.2)	82 (45.3)	4.01 (1.41-11.43)	0.009
Diabetes	17 (42.5)	34 (17.8)	3.06 (1.11-8.42)	0.03
Complex karyotype³ (≥ 3 abnormalities)	11 (26.8)	6 (3.1)	4.94 (1.25-19.46)	0.02
IPSS-R				
High/ Very High	22 (57.9)	27 (15.2)	4.20 (1.43-12.34)	0.009
Intermediate	4 (10.5)	32 (18.0)	1.01 (0.26-3.99)	0.99
Low/ Very Low	12 (31.6)	119 (66.9)	<i>Ref</i>	
Received Active Treatment				
Total	42	116		
Cytogenetics				
Normal	8 (20.0)	52 (46.4)	<i>Ref</i>	
Abnormal	32 (80)	60 (53.6)	2.94 (0.87-9.95)	0.08
Complex karyotype³ (≥ 3 abnormalities)	21 (50)	17 (14.7)	4.84 (1.43-16.4)	0.01
IPSS-R				
High/ Very High	30 (75.0)	52 (46.0)	0.96 (0.31-2.95)	
Intermediate	9 (22.5)	34 (30.1)	<i>Ref</i>	
Low/ Very Low	1 (2.5)	27 (23.9)	0.11 (0.01-1.03)	

OR: Odds Ratio; 95% CI: 95% Confidence Interval; NC: not calculated

¹ Adjusted for sex, age at diagnosis, smoking status, personal and family history of cancer, treatment, treatment provider, comorbidities, cytogenetics, WHO classification

² Wald Chi-square

³ Includes a subset of cases with abnormal karyotype