Infections in lower-risk myelodysplastic syndromes - prevalence and risk factors: a report from the European MDS Registry

Bente Houtman,[1] Adele Taylor,[2] Corine van Marrewijk,[1] Alexandra Smith,[2] Pierre Fenaux,[3] Catherine Cargo,[4] Argiris Symeonidis,[5] Moshe Mittelman,[6] Reinhard Stauder,[7] Jaroslav Čermák,[8] Guillermo Sanz,[9] Eva Hellström-Lindberg,[10] Luca Malcovati,[11,12] Lionel Adès,[3] Thibault Comont,[13] Dominic Culligan,[14] Ioannis Kotsianidis,[15] Theo de Witte,[16] Nicole Blijlevens,[1] Saskia Langemeijer[1] and Marlijn Hoeks[1] on behalf of the EUMDS Consortium

[1]Department of Hematology, Radboud University Medical Center, Nijmegen, the Netherlands; [2]Epidemiology and Cancer Statistics Group, Department of Health Sciences, University of York, York, UK; [3]Service d'Hématologie, Hôpital Saint-Louis, Assistance Publique des Hôpitaux de Paris (AP-HP) and Université Paris 7, Paris, France; [4]Haematological Malignancy Diagnostic Service, Leeds Cancer Centre, St James's University Hospital & Leeds Teaching Hospitals NHS Trust, Leeds, UK; [5]Department of Medicine, Division of Hematology, University of Patras Medical School and Olympion General Clinic, Patras, Greece; [6]Department of Hematology, Tel Aviv Sourasky (Ichilov) Medical Center and Medical Faculty, Tel Aviv University, Tel Aviv, Israel; [7]Department of Internal Medicine V (Hematology and Oncology), Innsbruck Medical University, Innsbruck, Austria; [8]Department of Clinical Hematology, Institute of Hematology & Blood Transfusion, Praha, Czech Republic; [9]Instituto de Investigación Sanitaria La Fe, Hospital Universitario y Politécnico La Fe and CIBERONC, Valencia, Spain; [10]Department of Medicine, Karolinska Institutet and Department of Hematology, Karolinska University Hospital, Stockholm, Sweden; [11]Department of Molecular Medicine, University of Pavia, Pavia, Italy; [12]Department of Hematology Oncology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; [13]Department of Internal Medicine – IUCT Oncopole – Toulouse University Hospital, Toulouse, France; [14]Department of Haematology, Aberdeen Royal Infirmary, Aberdeen, UK; [15]Department of Hematology, Democritus University of Thrace Medical School, University Hospital of Alexandroupolis, Alexandroupolis, Greece and [16]Department of Tumor Immunology - Nijmegen Center for Molecular Life Sciences, Radboud University Medical Center, Nijmegen, the Netherlands

Correspondence: M. Hoeks
marlijn.hoeks@radboudumc.nl

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Abstract

Infections are an important cause of morbidity and mortality in patients with lower-risk myelodysplastic syndromes (LR-MDS). Studies regarding risk factors for infections are, however, limited in this population. This study aimed to investigate the prevalence and risk factors for infections and infection-related death in patients with LR-MDS. The study included 2,552 patients from the European MDS (EUMDS) Registry, which prospectively collects observational data on newly diagnosed MDS patients from 17 countries. The prevalence of infections and infection-related death was determined. Risk factors for infections and infection-related death occurring within 1 year from diagnosis were analyzed in separate multivariable logistic regression models. A third model that only included LR-MDS patients who experienced an infectious episode within the first year after diagnosis was used to analyze risk factors associated with infection-related death in patients with an infectious episode. The prevalence of infections was 7.6%, and 24.6% of all deaths were due to infections. In multivariable analysis, an independent association with increased risk for infections was found for hemoglobin level <8 g/dL, platelet count <50x10^9/L, absolute neutrophil count <0.8x10^9/L, intermediate/poor/very poor cytogenetics, and having received red blood cell transfusions at baseline. An independent association with increased risk of infection-related death was found for older age at diagnosis, hemoglobin level <8 g/dL, and platelet count <50x10^9/L. Patients with an increased risk of infections could benefit from close monitoring, especially in the first months after diagnosis. Future research should focus on the causality and severity of infections and risk factors over time, to provide more guidance for monitoring.

Introduction

Myelodysplastic syndromes (MDS) are a heterogeneous group of hematologic neoplasms that are characterized by dysplastic changes in the bone marrow and ineffective hematopoiesis, which results in cytopenias.[1] Treatment for patients classified as having lower-risk myelodysplastic syndromes (LR-MDS)[2,3] mainly consists of supportive care, aiming to minimize disease-related symptoms and morbidity associated with cytopenias.[4,5]

Infections are one of the leading causes of death in patients with LR-MDS, accounting for 17-38% of deaths,[6-8] and infections have also been associated with a reduced overall survival.[9] Previous studies in the general MDS population found that bacterial infections were the most common type of infection, followed by fungal infections, while viral infections were uncommon. The most commonly found bacterial pathogens include enterobacteria and coagulase-negative staphylococci. Pneumonia and fever of unknown origin were the most common manifestations of infections, followed by bloodstream infections, urinary tract infections, and sepsis.[6,9-11] Some of these infections might be associated with specific conditions or types of treatment, such as bacteremia or thrombophlebitis resulting from central catheter line infections. Opportunistic infections that are associated with immunosuppressive types of treatments, such as lenalidomide and cyclosporine A, are also present in patients with LR-MDS. Among the latter, reactivation of latent infections has been described. In this regard, it is worth recalling that patients with LR-MDS have inherent impairment of innate and adaptive immunity, which is not usually estimated and this factor might also contribute.[12,13]

Several studies have identified risk factors for infections and infection-related mortality in patients with high-risk MDS (HR-MDS), or patients with MDS who were treated with azacitidine, which is typically used in the HR-MDS group. However, risk factors are not yet precisely characterized in patients with LR-MDS. There are reasons to assume that the risk factors for infections in patients with LR-MDS might be different from those in patients with HR-MDS due to differences in disease pathophysiology, course and treatment. The risk of infections in patients with HR-MDS is increased mainly due to a higher risk of transformation to acute myeloid leukemia and more pronounced bone marrow suppression compared to that in patients with LR-MDS.[14,15] Patients with HR-MDS also receive more intensive types of treatments, which might independently increase the risk of infections, due to chemotherapy-induced neutropenia, treatment with hypomethylating agents and transient worsening of pre-existing cytopenias.[9,11,14,16,17]

Identifying risk factors for infections in patients diagnosed with LR-MDS could improve preventive strategies, monitoring, and treatment for patients at increased risk. Therefore, the purpose of this study was to investigate the prevalence of and risk factors for infections and infection-related deaths within the first year after diagnosis in patients diagnosed with LR-MDS, using data from the prospective European LeukemiaNet MDS (EUMDS) Registry.

Methods

Patients and data collection

Patients were included from the prospective longitudinal EUMDS Registry, which has been previously described.[18] This registry includes newly diagnosed patients with all subtypes of MDS classified according to the 2001 (and later the 2008 and 2016) World Health Organization (WHO) diagnostic criteria who were enrolled within 100 days after the initial MDS diagnosis.[19] Patients are enrolled from 146 hematology centers throughout 17 countries (Austria, Croatia, Czechia, Denmark, France, Germany, Greece, Israel, Italy, the Netherlands, Poland, Portugal, Romania, Serbia, Spain, Sweden, and the United Kingdom). Data are collected at baseline and at 6-month intervals thereafter, and include information regarding demographics, disease classification and prognostic categorization, clinical and laboratory parameters, disease management, treatment outcome, and quality of life. Data are collected until death, loss to follow-up, or withdrawal of informed consent. All included patients were ≥18 years old and had given informed consent to their participation in the study.

For the current analysis, all patients diagnosed with low- and intermediate-1-risk MDS according to the International Prognostic Scoring System (IPSS) were included.[2] Patients with a history of organ transplantation and those with a previous history or post-diagnosis administration of an allogeneic hematopoietic stem cell transplant were excluded, since these conditions are known to increase the risk of infections. Follow-up data up to 1 year after inclusion, defined as 15 months from diagnosis due to the potential 100-day gap between diagnosis and inclusion, were used in the analyses. At baseline and at each follow-up visit, it was registered whether the patient had an infection. However, the exact date of infection was not recorded in the EUMDS Registry. Therefore, only baseline data were used, and follow-up was restricted to 1 year, since a longer follow-up time might have introduced more uncertainty regarding the potential associations found. Infection was defined as all types of infections that were recorded in the EUMDS Registry, including infection-related death. Infections were reported at the discretion of the physician at follow-up visits, without the use of any specific report form and the type or site of infection could not be retrieved. Cause of death was classified by the EUMDS investigators, and could be classified as one of the following reasons: acute myeloid leukemia, MDS, infection, cardiovascular, pulmonary, hemorrhage, hepatic, renal failure, other malignancy or accident. If the cause of death did not fall into any of these categories, it was classified as 'other'. If the cause of death was not available, this was recorded as

'not known'.[7] Since the establishment of the EUMDS Registry, the revised IPSS (IPSS-R) was implemented in the registry, which includes more cytogenetic profiles, different categorization of bone marrow blast cell percentage, and also takes into consideration the depth of cytopenias.[18] This can lead to identification of a higher IPSS-R risk profile in some of the IPSS low- and intermediate-1-risk patients.[18] The EUMDS Registry (Clinical Trials.gov identifier: NCT00600860) was approved by each institution's ethics committee in accordance with national legislation and written informed consent was obtained from each patient.

Statistical analysis

Continuous variables are presented as means and standard deviations, and compared using a two-sample *t* test. Categorical variables are presented as percentages, and compared using χ^2 analysis. Risk factors for infections and infection-related death within the first year of follow-up were assessed in univariable logistic regression analysis, including age at diagnosis, sex, level of hemoglobin, platelet and neutrophil counts, percentages of lymphocytes, monocytes, and bone marrow blasts, cytogenetics, ferritin level, IPSS and IPSS-R classification, MDS-specific comorbidity index (MDS-CI) and having received red blood cell transfusions. Significant variables from the univariate analysis were included in the multivariable logistic regression model, which was adjusted for age and sex. A model was made to analyze associations with infections in general, and infection-related death occurring within the first year of follow-up in the full cohort. A subgroup analysis, including only patients who had at least one infectious episode, was performed to analyze potential associations with infection-related death in patients who had an infectious episode in the first year of follow-up. A *P* value <0.05 was considered statistically significant. All analyses were performed in Stata version 17.

Results

Study population and infectious events

A total of 2,552 patients registered in the EUMDS Registry between January 2008 and November 2022 were included (Figure 1). The median age at diagnosis was 74 years (range, 18-97), and IPSS-defined risk group was low in 1,074 (42.1%) and intermediate-1 in 1,026 (40.2%) patients (Table 1). The exact IPSS risk score could not be properly determined in 452 (17.7%) patients because of a lack of cytogenetic testing. However, based on the number of cytopenias (score: zero [0/1 cytopenia]) and bone marrow blasts (<5%) it could be determined that these patients fell into the LR-MDS group. Within the first year of follow-up after inclusion in the EUMDS Registry, 220 infectious episodes were reported in 193 patients (7.6%, 1.14 episodes per infected patient). Of these, 95 (43.2%) infectious episodes had occurred within the first

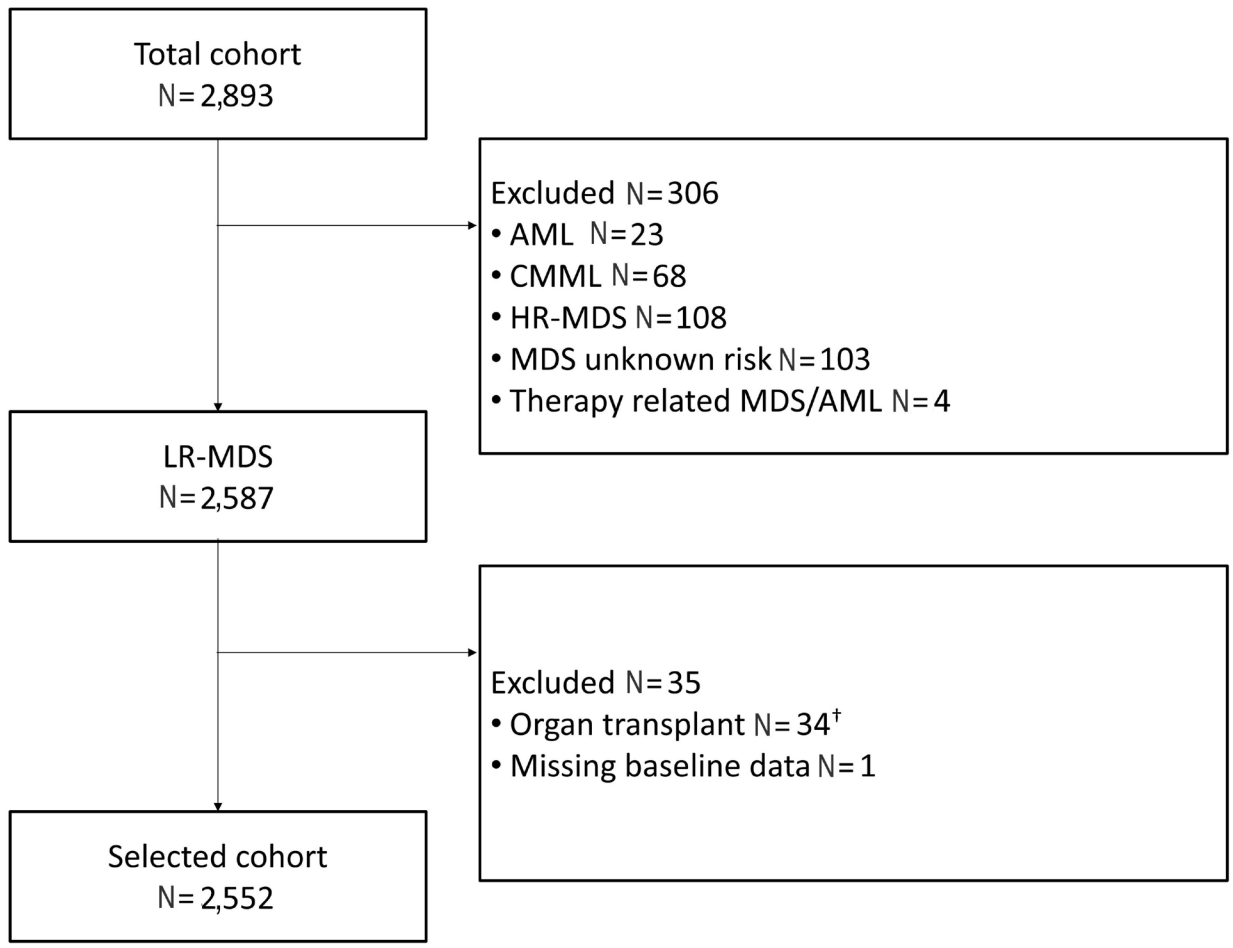

Figure 1. Patients' inclusion in the study. †Includes 27 patients for whom it was unknown whether they received an organ transplant. AML: acute myeloid leukemia; CMML: chronic myelomonocytic leukemia; HR-MDS: higher-risk myelodysplastic syndrome; LR-MDS: lower-risk myelodysplastic syndrome.

Table 1. Characteristics of newly diagnosed cases of lower-risk myelodysplastic syndrome by infection and death due to infection.

Characteristics	Included cohort	Infection	*P*	Infection led to death	*P**	*P***
Total, N	2,552	193	-	73	-	-
Age at diagnosis in years, median (range)	74 (18-97)	76 (18-93)	0.24	77 (52-89)	<0.01	<0.01
Sex, N (%)						
Males	1,590 (62.3)	126 (65.3)	0.37	44 (60.3)	0.71	0.24
Females	962 (37.7)	67 (34.7)		29 (39.7)		
Country, N (%)						
Austria	165 (6.5)	15 (7.8)	<0.01	3 (4.1)	<0.01	<0.01
Croatia	18 (0.7)	0 (0.0)		0 (0)		
Czechia	139 (5.4)	13 (6.7)		1 (1.4)		
Denmark	65 (2.5)	3 (1.6)		1 (1.4)		
France	512 (20.1)	31 (16.1)		6 (8.2)		
Germany	62 (2.4)	4 (2.1)		1 (1.4)		
Greece	362 (14.2)	16 (8.3)		12 (16.4)		
Israel	239 (9.4)	25 (13.0)		10 (13.7)		
Italy	96 (3.8)	2 (1.0)		0 (0)		
Netherlands	111 (4.3)	17 (8.8)		7 (9.6)		
Poland	58 (2.3)	4 (2.1)		2 (2.7)		
Portugal	38 (1.5)	2 (1.0)		2 (2.7)		
Romania	45 (1.8)	7 (3.6)		3 (4.1)		
Serbia	31 (1.2)	7 (3.6)		2 (2.7)		
Spain	131 (5.1)	12 (6.2)		12 (16.4)		
Sweden	106 (4.2)	7 (3.6)		3 (4.1)		
UK	374 (14.7)	28 (14.5)		8 (11.0)		
IPSS category, N (%)						
Low risk	1,074 (42.1)	52 (26.9)	<0.01	19 (26.0)	0.01	0.79
Intermediate-1	1,026 (40.2)	96 (49.7)		35 (48.0)		
Unknown	452 (17.7)	45 (23.3)		19 (26.0)		
IPSS-R, N (%)						
Very low	655 (25.7)	37 (19.2)	<0.01	8 (11.0)	<0.01	0.17
Low	1,115 (53.7)	60 (31.1)		22 (30.1)		
Intermediate	446 (17.5)	50 (25.9)		23 (31.5)		
High	98 (3.8)	15 (7.8)		7 (9.6)		
Very high	11 (0.4)	4 (2.1)		2 (2.7)		
Unknown	227 (8.9)	27 (14.0)		11 (15.1)		
MDS-CI, N (%)						
Low risk	1,509 (59.1)	100 (51.8)	0.03	40 (54.8)	0.74	0.49
Intermediate risk	877 (34.4)	83 (43.0)		28 (38.4)		
High risk	166 (6.5)	10 (5.2)		5 (6.8)		
Hemoglobin <8 g/dL, N (%)	241 (9.4)	35 (18.1)	<0.01	21 (28.8)	<0.01	<0.01
Platelets <50x10^9/L, N (%)	203 (8.0)	29 (15.0)	<0.01	17 (23.3)	<0.01	0.01
ANC <0.8x10^9/L, N (%)	288 (11.3)	40 (20.7)	<0.01	15 (20.6)	0.01	0.91
Bone marrow blasts ≥5%, N (%)	415 (17.3)	37 (20.3)	0.27	11 (16.2)	0.79	0.28
Lymphocytes, %, mean (SD)	32.6 (15.1)	33.9 (18.6)	0.21	32.1 (15.7)	0.78	0.29
Monocytes, %, mean (SD)	9.2 (6.3)	8.2 (6.4)	0.04	9.1 (8.1)	0.98	0.13
Ferritin ≥1,000 g/dL, N (%)	188 (7.4)	22 (11.4)	<0.01	12 (12.4)	<0.01	0.13
Cytogenetics, N (%)						
Very poor	19 (0.7)	3 (1.6)	<0.01	2 (2.7)	<0.01	0.73
Poor	36 (1.4)	7 (3.6)		3 (4.1)		
Intermediate	291 (11.4)	27 (14.0)		12 (16.4)		
Good	1,778 (69.7)	125 (64.8)		44 (60.3)		
Very good	217 (8.5)	6 (3.1)		2 (2.7)		
Unknown	211 (8.3)	25 (13.0)		10 (13.7)		

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Characteristics	Included cohort	Infection	*P*	Infection led to death	*P**	*P***
Red blood cell transfusions, N (%) of patients						
Yes	770 (30.2)	89 (46.1)	<0.01	45 (61.6)	<0.01	<0.01
No	1773 (69.5)	103 (53.4)		28 (38.4)		
Unknown	9 (0.4)	1 (0.5)		0 (0)		
Units transfused, median (IQR)	2 (2-5)	3 (2-6)	0.05	4 (2-9)	0.041	0.40

*Univariable analysis included all patients. **Univariable analysis included only patients who had an infection. IPSS: International Prognostic Scoring System; IPSS-R: Revised IPSS; MDS-CI: Myelodysplastic syndrome-specific comorbidity index; ANC: absolute neutrophil count; SD: standard deviation; IQR: interquartile range.

Table 2. Multivariable logistic regression risk factor analysis for risk factors for all infections and infection-related death in the full cohort.

Covariates	All infections		Infection-related death	
	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
Age at diagnosis in years	1.01 (0.99-1.03)	0.19	1.05 (1.02-1.08)	<0.01
Male sex (Ref female)	0.91 (0.65-1.26)	0.57	1.25 (0.76-2.05)	0.37
Hemoglobin <8 g/dL (Ref ≥8 g/dL)	1.78 (1.14-2.78)	0.01	2.54 (1.41-4.56)	<0.01
Platelets <50x10^9/L (Ref ≥50x10^9/L)	1.64 (1.03-2.62)	0.04	2.92 (1.60-5.34)	<0.01
ANC <0.8x10^9/L (Ref ≥0.8x10^9/L)	2.34 (1.58-3.48)	<0.01	1.80 (0.97-3.33)	0.06
Cytogenetics intermediate/poor/very poor (Ref very good/good)	2.39 (1.08-5.30)	0.03	3.07 (1.02-9.30)	0.05
Red blood cell transfusion (Ref no)	1.66 (1.19-2.32)	<0.01	2.52 (1.50-4.24)	<0.01
Monocytes, %	0.97 (0.95-1.00)	0.05	-	-
MDS-CI intermediate/high (Ref low)	1.33 (0.97-1.84)	0.08	-	-

95% CI: 95% confidence interval; Ref: reference; ANC: absolute neutrophil count; MDS-CI: myelodysplastic syndrome-specific comorbidity index.

100 days after diagnosis. One third of all infectious episodes resulted in death. In total, 297 patients died within the first year of follow-up, and infection, accounting for 73 (24.6%) deaths, was the most common cause of death. In the group of patients who had an infection, more patients died in the first year of follow-up, compared to the group of patients without an infectious episode (49.2% *vs*. 8.6%). Among patients without an infectious episode, acute myeloid leukemia was the most common cause of death (1.1% *vs*. 19.3%).

Risk factor analysis

The multivariable model analyzing risk factors for infections (including infectious episodes resulting in death) (Table 2) showed an independent association of increased risk for infectious episodes among patients with hemoglobin level <8 g/dL (odds ratio [OR]=1.78, 95% confidence interval [95% CI]: 1.14-2.78), platelet count <50x10^9/L (OR=1.64, 95% CI: 1.03-2.62), absolute neutrophil count <0.8x10^9/L (OR=2.34, 95% CI: 1.58-3.48), intermediate/poor/very poor cytogenetics (OR=2.39, 95% CI: 1.08-5.30), and having received red blood cell transfusions at baseline (OR=1.66, 95% CI: 1.19-2.32).

In the multivariable model for infection-related death (Table 2), an independent association for increased risk was found with older age at initial LR-MDS diagnosis (OR=1.05, 95% CI: 1.02-1.08), hemoglobin level <8 g/dL (OR=2.54, 95% CI: 1.41-4.56), platelet count <50x10^9/L (OR=2.92, 95% CI: 1.60-5.34), intermediate/poor/very poor cytogenetics (OR=3.07, 95% CI: 1.02-9.30), and having received red blood cell transfusions at baseline (OR=2.52, 95% CI: 1.50-4.24). A trend towards an increased risk of infection-related death was observed for absolute neutrophil count <0.8x10^9/L. However, this association did not reach statistical significance.

Outcomes of the multivariable analysis analyzing risk factors for infections and infection-related death including the IPSS-R risk groups are shown in *Online Supplementary Table S2*. The IPSS-R risk groups intermediate, high, and very high were associated with an increased risk of infectious episodes as well as infection-related death. The risk was the highest in the high- and very high-risk groups.

In the multivariable model for infection-related death that only included patients who experienced an infectious episode (Table 3), an independent association was found between increased risk of infectious episodes resulting in death and older age at diagnosis (OR=1.06, 95% CI: 1.02-1.10), hemoglobin level <8 g/dL (OR=3.47, 95% CI: 1.44-8.34), as well as platelet count <50x10^9/L (OR=2.46, 95% CI: 1.01-5.96).

Discussion

In this multicenter cohort study, we aimed to identify risk factors for infections and infection-related death in patients

Table 3. Multivariable logistic regression risk factor analysis for risk factors for infection-related death in patients who had an infection.

Covariates	Odds ratio (95% CI)	*P*
Age at diagnosis in years	1.06 (1.02-1.10)	<0.01
Male sex (Ref female)	1.54 (0.78-3.03)	0.21
Hemoglobin <8 g/dL (Ref ≥8 g/dL)	3.47 (1.44-8.34)	<0.01
Platelets <50x10^9/L (Ref ≥50x10^9/L)	2.46 (1.01-5.96)	0.05
Red blood cell transfusion (Ref no)	1.84 (0.95-3.57)	0.07

95% CI: 95% confidence interval; Ref: reference.

diagnosed with LR-MDS registered in the EUMDS Registry. The prevalence of infections in this LR-MDS cohort was 7.6%. In addition, we found that infection was the main cause of death, accounting for 24.6% of all deaths within 1 year of the diagnosis of LR-MDS. Intermediate or higher IPSS-R risk group, and specifically the components severe anemia, severe thrombocytopenia, poorer cytogenetics, as well as having received a red blood cell transfusion at diagnosis were associated with both an increased risk of infections and infection-related death in the first year of follow-up. Severe neutropenia was significantly associated with an increased risk of infection in general, and there was also a trend towards an increased risk of infection-related death which did not reach statistical significance. However, neutropenia was not associated with infection-related death in patients who experienced at least one infectious episode. Older age at initial diagnosis was associated with infection-related death in general and also with infection-related death in patients who experienced an infectious episode. Previous studies evaluating the risk of infections or infection-related mortality were not focused on patients with LR-MDS specifically. Most studies included patients diagnosed with HR-MDS, or patients who received treatment with azacitidine. Neutropenia is considered to be an important risk factor for infections, although the association between neutropenia and risk of infections has not been demonstrated consistently.[11,14,15,17,20,21] Neutrophil dysfunction with normal neutrophil counts might also be present in patients with MDS.[11,22] In the current study, low absolute neutrophil count at baseline was associated with infections in general, but not with infection-related death. However, it could still be possible that the patients who died from infection had more neutrophil dysfunction, which we could not evaluate in this study. Furthermore, patients with severe neutropenia might be more closely monitored, and receive more urgent management if they present with infectious symptoms. Recently, low platelet count was found to be associated with infections in studies that mostly included patients diagnosed with HR-MDS who were treated with azacitidine, although results were not consistent.[14,16,17,21,23] Two studies found that low platelet count was the most important risk factor for infection in patients treated with azacitidine.[14,17] This is consistent with the findings in the current study. It is increasingly known that platelets contribute greatly to host defenses by multiple mechanisms such as enhancing leukocyte and neutrophil recruitment, activation of monocytes, and promoting effector functions of immune cells.[24,25] This might also play a role in MDS patients. Future research should focus on these effects in patients with MDS. Anemia and having received red blood cell transfusions were significantly associated with infections in the current study. Patients with these conditions might have been transfusion-dependent or might have had iron overload due to receiving multiple red blood cell transfusions or ineffective erythropoiesis. Data were insufficient to analyze this hypothesis thoroughly, as we were not able to evaluate the need for transfusions or the presence of iron overload over time. However, we did find that patients with an infection and patients who died from infections were significantly more often treated with red blood cell transfusions at LR-MDS diagnosis, and received slightly more units than those without an infection. Frequent transfusions induce immune modulation and immune tolerance, resulting from massive antigenic stimulation, and these effects might have consequences in LR-MDS patients who have an already altered immune status.[26,27] Furthermore, ferritin levels ≥1,000 μg/dL at LR-MDS diagnosis were more often seen in patients who had an infectious episode, although these data were incomplete. Thus, both transfusion dependency and iron overload have been associated with an increased infection risk.[11,14,28] This could also be seen as a reflection of more severe bone marrow suppression; however, iron overload situated in the bone marrow is known to adversely affect hematopoiesis. Whether this plays a role in LR-MDS needs to be evaluated in future research. Older age was only associated with infection-related death. This might be explained by a decline in immune response to infections, frailty, and also by differences in decision-making surrounding treatment in older patients.[29] It is well-known that advanced age, *per se*, and lower-risk MDS are independently associated with impairment in both arms of immunity and patients with these conditions present both quantitative and quantitative defects in various immunological parameters and indices. The potentially contributing role of these factors in the frequency and severity of infections has not been thoroughly investigated; however,

in our analysis, the percentage lymphocyte count was not found to be associated with infections.[30,31] We also did not find an association between higher MDS-CI score and infections or infection-related death. The absence of an association between MDS-CI and infection-related death is likely explained by the conditions that form the MDS-CI components, which were also more often the cause of death in the group of patients with a higher MDS-CI score (*data not shown*). Since thrombocytopenia, anemia, and neutropenia all increased the risk of infections, it is likely that the patients at risk of infection have more severe bone marrow failure or a failing immune defense system. These patients might benefit from preventive measures. One of these measures is the use of antimicrobial prophylaxis. However, research regarding the use of antibacterial and antifungal therapy is limited to MDS patients on active treatment and their benefit in patients with LR-MDS receiving supportive therapy is unknown.[11] Furthermore, the types of infections found in patients with LR-MDS have not been clarified, thus it is unclear what type of antimicrobial prophylaxis could be used. Another preventive measure is granulocyte colony-stimulating factor, as this can improve cytopenias. However, previous research found contradicting results regarding its effect on the incidence of infections and did not show a benefit in the survival rate of patients with MDS.[11]

Strengths of this study are the use of a large multicenter cohort, which included LR-MDS patients from several countries. This makes the study cohort representative of the broader LR-MDS population.

This paper has several limitations. First, data regarding the type, site and severity of the infections are lacking. Furthermore, there were no criteria as to what type of infections should be reported. This might have led to an underestimation of the prevalence of infectious episodes, and an overestimation of infection-related mortality, because it is more likely that infections requiring hospitalization or death were reported compared to less severe infections that did not require hospitalization. However, with regard to prevention, the more severe infections are most clinically relevant. Treatments other than red blood cell transfusions were not included in the analyses. However, as only associations with baseline characteristics were tested, and the number of patients on treatment was limited (0.8% of patients received hypomethylating agents, 0.6% received lenalidomide, and 1.7% received granulocyte colony-stimulating factor), we do not expect that this affected the outcomes. Since the incidence date of infections was unknown, we were unable to evaluate data over time, and we could not extend the follow-up duration, as associations with covariates at baseline would become more uncertain. This was also a limitation in analyzing the effect of treatments over time during the first year of follow-up.

Future research should focus on the type of infections and causative pathogens in patients with LR-MDS, as these are crucial data for preventive strategies, such as prophylactic antibiotics, in patients at the highest risk of infections. Certain criteria for the definition of infections could be used to generate more generalizable results, and to give a better estimate of the incidence or prevalence of infections.[32,33] Furthermore, evaluation of the evolution of dynamic risk factors in relation to developing infections, such as cytopenias, iron overload and transfusion dependency, is of importance to better estimate the risk of infections and infection-related mortality over time. This could improve preventive strategies, monitoring and treatment for patients at risk of infections.

In conclusion, the prevalence of infections in patients with LR-MDS in the first year of follow-up after inclusion in the EUMDS Registry was 7.6%, and infections were associated with high mortality, accounting for approximately a quarter of all deaths. More severe bone marrow failure, as reflected by severe anemia, thrombocytopenia or neutropenia, and poor cytogenetics, or having received red blood cell transfusions at the time of diagnosis of LR-MDS were associated with an increased risk of infections within the first year of follow-up. The risk of infection-related death was highest in older patients and patients with severe anemia, thrombocytopenia, poor cytogenetics or red blood cell transfusions. These patients could benefit from close monitoring for infections, especially in the first months after diagnosis, and vigilance is warranted when these patients present with infectious symptoms.

Disclosures

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Contributions

BH, AT, CvM, ASm, TdW, SL, NB and MH designed the study. PF, CC, ASy, MM, RS, JC, GS, EH-L, LM, LA, TC, DC, IK, NB and SL provided patients and assembled data. BH, AT, CvM, ASm, NB, TdW, SL and MH analyzed and interpreted the data. All authors contributed to writing the manuscript and approved its final version.

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Data-sharing agreement

This article is based on data from the European MDS Registry (www.EUMDS.org). The data are not publicly available due to privacy or ethical restrictions. Access to data that support the findings of this study can be obtained from the EUMDS project management office upon reasonable request. A fee might be required.

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