

Study of the burden of blood transfusions in patients with lower-risk myelodysplastic syndromes who receive regular transfusions

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Introduction

- Myelodysplastic syndromes (MDS) are a group of myeloid neoplasms characterized by ineffective hematopoiesis and increased risk of leukemic evolution
- The annual incidence of MDS is estimated to be 4-5 per 100,000^{1,2} with a median age at diagnosis of 70 years
- Patients with higher-risk (HR) MDS, which accounts for 30% of MDS, have a poor prognosis with a median survival of 18 months and a high risk of progression to acute myeloid leukemia (AML)
- Patients with lower-risk (LR) MDS, which accounts for 70% of MDS, have a median survival of 8 years³ and have a low risk of progression to AML
- Management of LR MDS is mostly aimed at treating anemia using erythropoiesis-stimulating agents, iron chelation therapy, and repeated blood transfusions

Objectives

- To describe the clinical and economic burden of blood transfusions, their immediate complications, and associated costs in patients with transfusion-dependent LR MDS
- To describe the mortality of patients with a transfusion-dependent MDS-related diagnosis

Methods

- This retrospective, observational study used data from the French PMSI-MCO nationwide hospital discharge database

Study period

- Patients with MDS who were hospitalized as an inpatient or outpatient and received a blood transfusion between 2012 and 2013, were included in the analysis and followed until December 31, 2018
- Patient comorbidities were analyzed for up to 2 years prior to inclusion in the study
- Patients were followed until the end of the study or until death

Inclusion criteria

- Adult patients (aged ≥ 18 years) with a primary diagnosis, related diagnosis, or associated diagnosis of LR MDS between 2012 and 2013 were identified by International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code D46 and included in this analysis
- Patients with an average of 1 transfusion every 2 months relative to their duration of follow-up, and a minimum of 2 transfusions during the study period, were identified by ICD-10-CM-Z513 or Classification Commune des Actes Médicaux (CCAM) code (FELF008, FELF011, FELF001, FELP003)

Exclusion criteria

- Patients with HR MDS were identified by the following treatments and excluded from the study:
 - Stem cell transplantation (allograft) (Homogeneous Group of Patients [GHM] code 27Z02 from Diagnosis-Related Group [DRG] and CCAM code FELF009)
 - Chemotherapy (ICD-10-CM-Z511)
 - Hypomethylating agents, for example azacitidine (common dispensing unit [UCD] number 3400892747620)
 - Patients who progressed to AML (ICD-10-CM-C920)

Analyses

- Patient characteristics at inclusion were described: age, sex, comorbidities of interest (e.g. chronic obstructive pulmonary disease, heart failure, hepatic disease, kidney failure, cancer, diabetes)
- Overall survival was assessed descriptively using Kaplan-Meier analyses for the duration of follow-up

Transfusions

- Transfusion dependence was defined as a rate of ≥ 1 transfusion every 8 weeks⁴
- The number of follow-up transfusions was calculated per patient per year (PPPY)
- Length of stay in hospital and the cost of hospitalization due to transfusion were assessed

Transfusion complications

- The number of complications per patient were reported and included:
 - Pulmonary involvement: acute edema, transfusion-related acute lung injury
 - Infections: bacterial sepsis and fungal infection
 - Post-transfusion purpura
 - Anti-erythrocytic immunization
 - Post-transfusion volume overload
 - Other transfusion complications

- Length of stay in hospital; arrival and transfer via the emergency, resuscitation, intensive care, and continuous monitoring departments; and cost were assessed for hospitalizations due to transfusion complications

Costs associated with treatment

- Healthcare resource utilization (HCRU) was considered from the national health insurance (NHI) perspective
- Associated costs during the study period were enumerated
- Annual costs were extrapolated for patients with < 1 year of follow-up
- Costs were attributed from official French national tariffs expressed in 2020 EUR

Results

- 5,081 patients with LR MDS were eligible for inclusion in this study (Figure 1)
 - 55.4% of patients were male and the median age was 81 years
 - Median follow-up was 10.9 months and mean follow-up was 18.8 months

Comorbidities and mortality

- The most common comorbidities in patients at inclusion were cancer (24.1%), heart failure (18.2%), and diabetes (16.1%) (Figure 2)
 - The intrahospital mortality rate was 64.9%
- The estimated probability of survival at 17 months was 50% (Figure 3)

Figure 1. Study participants

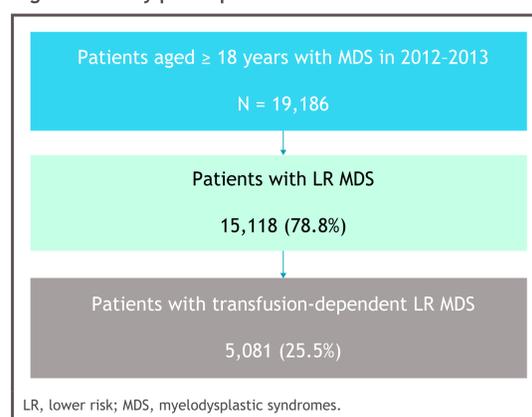


Figure 2. Proportion of patients by comorbidities at inclusion^a

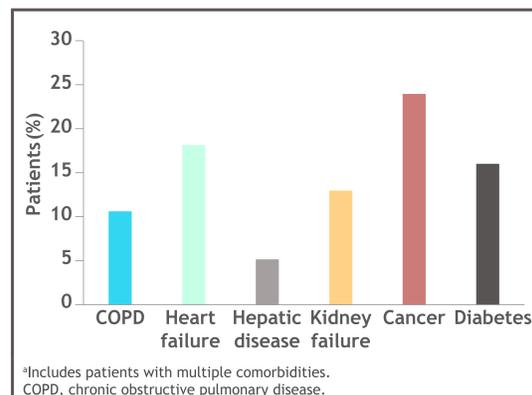
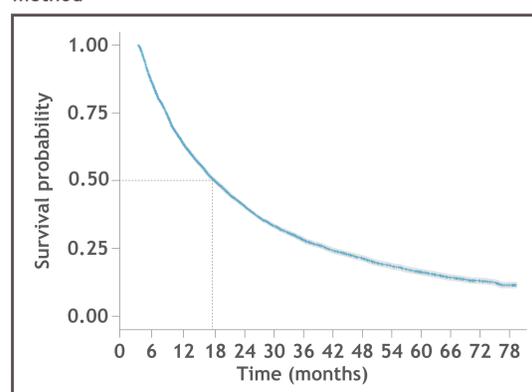


Figure 3. Global overall survival with the Kaplan-Meier method



Transfusions

- 87.6% of transfusions were performed in an outpatient setting, of which 91.2% were performed in public hospitals
- Patients received an average (standard deviation [SD]) of 20 (28) transfusions over the follow-up period and a median of 15 transfusions per year
 - The mean (SD) time between transfusions was 22 (43) days (median 15 days)

Transfusion complications

- Of 5,081 patients, 1,628 (32.0%) had ≥ 1 hospital stay related to transfusion complications, representing 2.8% of 135,939 hospital stays
 - 48.5% of hospital stays for transfusion complications were for post-transfusion purpura

- The average length of a hospital stay was 8 days
- 27.7% of patients who were hospitalized arrived through the emergency department
- 13.4% of patients with > 1 hospitalization were moved to intensive care or continuous monitoring during a hospital stay

Costs associated with transfusions

- The median cost of a hospital stay associated with transfusion was EUR 643 (Table 1)
 - The median cost of transfusion stays PPPY of follow-up was EUR 19,789
- The median cost of a hospital stay associated with transfusion complications was EUR 2,796 (Table 2)
 - The median cost of complication stays PPPY of follow-up was EUR 6,645

Table 1. Distribution of transfusion stay costs and annual cost per patient

Costs, EUR	Cost of transfusion stays ^a (N = 5,081)	Cost of transfusion stays PPPY of follow-up (N = 5,081)
Mean (SD)	1,125 (2,169)	35,914 (58,606)
Median	643	19,789
IQR	640-645	11,448-37,406
Range	263-186,489	114-1,017,412

^aNumber of hospital stays = 119,133. IQR, interquartile range; PPPY, per patient per year; SD, standard deviation.

Table 2. Distribution of complication stay costs and annual cost per patient

Costs, EUR	Cost of complication stays (N = 1,628) ^a	Cost of complication stays PPPY of follow-up (> 1 hospitalization) (N = 1,628)
Mean (SD)	4,271 (7,123)	9,839 (12,374)
Median	2,796	6,645
IQR	645-5,425	3,862-11,591
Range	333-186,489	377-232,417

^aNumber of hospital stays = 3,750. IQR, interquartile range; PPPY, per patient per year; SD, standard deviation.

Limitations

- This analysis only includes costs incurred in the context of hospital care
 - Pre- or post-operative care or consultations performed outside of hospital settings are therefore not included
 - Non-transfusion-related direct and indirect medical costs were not considered, suggesting that the economic burden of transfusion-dependent MDS may be higher than reported here
- Out-of-hospital deaths were not observed in the PMSI-MCO
- The causality between transfusion and hospitalization related to transfusion complications cannot be established fully with PMSI-MCO data

Conclusions

- This retrospective, observational study using data from the French PMSI-MCO nationwide hospital discharge database demonstrates the major economic and clinical burden of transfusions in patients with LR MDS, both in terms of public health and the economic impact for health insurance in France
- HCRU assessed from a NHI perspective illustrates the economic and clinical burden caused by transfusions and associated complications

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Disclosures

- G.J.: BMS - former employment, equity ownership
- Q.R., A.S., B.J., R.J.: HEVA - employment