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Survival outcomes and treatment patterns in myelofibrosis in the JAK inhibitor era

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Summary

Data on real-world survival and treatment patterns in large, unselected myelofibrosis (MF) cohorts remain limited. We analysed 1649 patients with MF diagnosed from 2010 onwards and included in the Spanish Myelofibrosis Registry across 64 centres. Janus kinase (JAK) inhibitors were administered to approximately half of the patients. Among those aged ≤70 years with intermediate-2/high-risk International Prognostic Scoring System (IPSS), only 25% ultimately underwent transplantation. Median survival was 6.6 years, with no significant differences between primary and secondary MF; acute leukaemia was the most frequent cause of death, accounting for 20% of cases. Compared with a matched general population, relative survival at 5 and 10 years was 68% and 44% respectively. The reduction in relative survival was more pronounced in patients aged >65 years and in male patients, two subgroups that also exhibited a higher burden of comorbidities and a greater frequency of high molecular risk mutations. Remarkably, patients in the high-risk IPSS category had a 10-year relative survival of only 12%; however, survival reduction was not confined to high-risk disease, with divergence from expected survival emerging early among lower-risk categories. These findings highlight the persistent impact of MF on life expectancy in the contemporary JAK inhibitor era and the need for improvement in its overall management.

KEYWORDS
IPSS, JAK inhibitor, myelofibrosis, ruxolitinib, survival, transplantation, treatment

For affiliations refer to page 1722.

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INTRODUCTION

Myelofibrosis (MF) is a chronic myeloproliferative neoplasm (MPN) that may arise de novo (primary MF, PMF) or evolve from prior essential thrombocythaemia (ET) or polycythaemia vera (PV) (secondary MF, SMF). The disease is characterized by clonal proliferation of haematopoietic progenitors associated with bone marrow fibrosis and extramedullary haematopoiesis.[1] Constitutive signalling through the Janus kinase (JAK)–Signal Transducer and Activator of Transcription (STAT) pathway via activating mutations in *JAK2*, calreticulin (*CALR*) and thrombopoietin receptor (*MPL*) (the so-called MPN driver genes) plays a central role in its pathogenesis,[2,3] while concomitant somatic mutations, mostly affecting epigenetic modifiers or spliceosome components, contribute to phenotypic variability and may promote disease progression.[4,5] Although the clinical course of MF is highly heterogeneous, it is typically a debilitating disease associated with a substantially reduced life expectancy.[6–9]

The introduction of JAK inhibitors into clinical practice has been associated with a marked improvement in the control of MF-related symptoms.[10,11] Whether these agents confer a survival benefit remains to be demonstrated through adequately design prospective studies, although this perception is widespread.[12–14] This potential advantage is unlikely to result from a decreased risk of progression to acute myeloid leukaemia (AML), but rather from improved clinical status and reduced patient vulnerability. Additional factors may have influenced survival estimates over the last decade, including a "lead time bias" driven by the increased recognition of prefibrotic MF,[15] as well as the broader use of allogeneic haematopoietic stem cell transplantation (allo-HSCT) and novel therapeutic agents.[16,17]

In the present study, we aimed to estimate the relative survival of patients with MF in the JAK inhibitor era using a large, real-world, multicentre series from the Spanish MF Registry. In addition, we assessed the impact of the disease across different population subsets and described current treatment patterns.

METHODS

Patients

The Spanish Myelofibrosis Registry is a nationwide registry contributed to by centres affiliated with the *Grupo Español de Enfermedades Mieloproliferativas Filadelfia Negativas* (GEMFIN). Written informed consent for inclusion in the registry is obtained from all patients. MF diagnosis was made according to the World Health Organization criteria applicable at the time of first observation in each patient. The registry was established in 2011 and includes patients with MF, both PMF and SMF, diagnosed from January 2000 onwards. Data collection was initially retrospective; patients identified from 2011 onwards have been enrolled prospectively.

As of March 2026, the registry comprised 2130 patients diagnosed with MF between January 2000 and December 2025 across 64 participating centres. The present study was restricted to the 1649 patients diagnosed from 2010 onwards, corresponding to the period during which JAK inhibitor therapy first became available. The study was approved by the GEMFIN scientific board.

Statistical methods

The main study outcome was the relative survival after MF diagnosis. Actuarial survival curves were estimated by the Kaplan–Meier method and compared by the log rank test. Relative survival was calculated according to the cohort method proposed by Dickman et al.[18] Relative survival is defined as the ratio between the actuarial survival observed in the group of patients studied and the expected survival derived from a subset of the general population matched to the patients by age, sex and calendar year of diagnosis. Relative survival allows comparing patient's survival across distant time periods after discounting changes in the general population life expectancy and other demographic effects. Estimates of expected survival were calculated by the Ederer II method[19] from Spanish life tables stratified by age, sex and calendar year that were obtained from the Human Mortality Database (www.mortality.org).

Disease-specific incidence mortality represents the excess mortality observed in MF patients over the expected mortality derived from the general population. It can be regarded as the MF-attributable mortality and is usually expressed in terms of incidence rate per person-years of follow-up. Disease-specific mortality rates and relative survival curves were compared by Poisson regression[18] with correction for overdispersion when needed. All tests were two-sided, and p values less than 0.05 were considered significant.

Median follow-up was estimated using the reverse Kaplan–Meier method. Cumulative incidence was used to estimate risk of AML in the framework of competing events (death, transplant). Sub-distribution hazard ratios (SHRs) and their 95% confidence intervals (CIs) were estimated using the Fine and Gray competing risks model.[20] The primary cause of death was initially assigned by the attending physician at each participating centre and subsequently centrally reviewed. In cases where leukaemic transformation had occurred, AML was systematically classified as the primary cause of death, regardless of the immediate terminal event (e.g. infection or bleeding).

All the statistical analyses were performed with IBM SPSS, version 26 and Stata, version 17 (www.stata.com).

RESULTS

Baseline patient characteristics

The main clinical characteristics of the 1649 patients at MF diagnosis are shown in Table 1. Median age was 69 years

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(interquartile range [IQR]: 60–76), 1064 patients (65%) were aged >65 years and 962 (58%) were male. A total of 888 patients (54%) had PMF and 761 had SMF (post-PV, $n=297$; post-ET, $n=464$). Most patients (85.5%) had grade 2–3 bone marrow fibrosis at diagnosis. Symptomatic splenomegaly, constitutional symptoms and moderate-to-severe anaemia were present in 298 (19%), 631 (38.5%) and 439 (30%) patients respectively. Anaemia with Haemoglobin (Hb) < 10 g/dL was significantly more frequent in patients aged >65 years (35% vs. 23%; $p<0.001$), but did not differ according to patient sex. Patients >65 years had a significantly higher frequency of hypercholesterolaemia (38% vs. 17.5%; $p<0.001$), arterial hypertension (61% vs. 31%; $p<0.001$), diabetes mellitus (25% vs. 11%; $p<0.001$), cardiac failure (9.5% vs. 2%; $p<0.001$), atrial fibrillation (16.5% vs. 6%; $p<0.001$), renal insufficiency (14.5% vs. 5%; $p<0.001$), chronic obstructive pulmonary disease (8.5% vs. 3%; $p<0.001$), prior history of malignancy (21% vs. 6%; $p<0.001$) and prior thrombosis before MF diagnosis (24% vs. 15%; $p<0.001$). By contrast, smoking was less frequent in this age group (22.5% vs. 30%; $p=0.002$). Male patients had a significantly higher frequency of smoking (34% vs. 13%; $p<0.001$), arterial hypertension (52% vs. 46%; $p=0.027$), diabetes mellitus (22.5% vs. 15%; $p<0.001$), atrial fibrillation (14.5% vs. 9%; $p=0.003$), renal insufficiency (14% vs. 6%; $p<0.001$), chronic obstructive pulmonary disease (9% vs. 2%; $p<0.001$) and prior thrombosis before MF diagnosis (23% vs. 17%; $p=0.011$).

A total of 666 patients (40%) underwent NGS profiling, of whom 263 (39.5%) harboured at least one high molecular risk (HMR) mutation as defined in Mutation-enhanced International Prognostic Scoring System (MIPSS70)+ Version 2.0,[21] and 86 (13%) had two or more. Patients >65 years (45% vs. 33%; $p=0.002$) and male patients (45% vs. 31%; $p<0.001$) had a significantly higher frequency of HMR mutations. Among the 579 (35%) patients with available cytogenetic data, 59 (10%) and 58 (10%) patients were classified as having unfavourable and very high-risk cytogenetics respectively.[22] The proportion of patients with adverse cytogenetics did not vary according to patient age or sex.

Treatments during follow-up

Table 2 summarizes the main treatments administered to the study cohort. Hydroxycarbamide was given to 728 patients (44% of the series), while 45 patients (3%) received interferon. Anaemia-directed therapies included erythropoiesis-stimulating agents ($n=565$; 34%), danazol ($n=135$; 8%), prednisone ($n=159$; 10%) and immunomodulatory drugs ($n=34$; 2%). JAK inhibitors were given to 850 patients (51.5%), predominantly ruxolitinib ($n=801$), followed by momelotinib ($n=84$) and fedratinib ($n=37$). Of these, 764, 78 and 8 patients received one, two or three lines of JAK inhibitor therapy respectively. Spleen irradiation (outside of allo-HSCT conditioning) and splenectomy were performed in 10 (0.6%) and 14 (0.8%) patients respectively.

A total of 167 patients (10%) underwent allo-HSCT after a median time of 541 days (range: 51–4554) from MF diagnosis. Among patients aged ≤70 years with intermediate-2 or high-risk IPSS at diagnosis ($n=351$), 88 (25%) underwent allo-HSCT during the observation period. The estimated 3-year survival rate after transplantation was 49% (95% CI: 41–57).

Survival and follow-up events

After a median follow-up of 5.4 years (95% CI: 5.0–5.7), 131 patients (8%) had progressed to AML, and 665 patients (40%) had died. Median overall survival of the series was 6.6 years (95% CI: 6.1–7.4; Figure 1); this was 6.0 years (95% CI: 5.3–6.7) in PMF and 7.3 years (95% CI: 6.6–8.1) in SMF ($p=0.078$). Among patients for whom the cause of death was known ($n=597$, 90% of those who died), the most common cause was AML ($n=119$; 20%), followed by disease progression without acute transformation ($n=110$; 18%), infection ($n=107$; 18%), transplant-related mortality ($n=57$; 10%), second malignancies ($n=54$; 9%), cardiorespiratory failure ($n=53$; 9%), bleeding ($n=36$; 6%), thrombosis ($n=19$; 3%) and other causes ($n=42$; 7%). As shown in Figure S1, the IPSS[23] discriminated four risk groups with significantly different survival ($p<0.001$). The projected median survival for patients in the low-risk ($n=193$, 14% of the cohort), intermediate-1 ($n=419$, 30%), intermediate-2 ($n=446$, 32%) and high-risk ($n=344$, 24%) IPSS categories was not reached, 9.3 years (95% CI: 7.7–10.7), 6.1 years (95% CI: 5.3–6.7) and 2.9 years (95% CI: 2.4–3.5) respectively. Of note, only patients in the high-risk category had a predicted median survival below 5 years.

The cumulative incidence of AML at 5 and 10 years from MF diagnosis was 9% and 11% (Figure S2). When stratified by IPSS, only the high-risk category showed a significantly higher risk of leukaemic transformation (SHR for high-risk vs. intermediate-2: 3.0; 95% CI: 1.42–6.33; $p=0.004$). In contrast, the IPSS failed to show significant differences in AML risk between the intermediate-2 and intermediate-1 categories (SHR: 0.83; 95% CI: 0.42–1.64) and between the intermediate-1 and low-risk categories (SHR: 1.60; 95% CI: 0.96–2.70). Neither male sex nor age >65 years was associated with higher incidence of AML (SHR: 1.15, 95% CI: 0.81–1.64; $p=0.42$ for male sex and SHR: 1.36, 95% CI: 0.95–1.45; $p=0.09$ for age >65 years).

Figure 2 illustrates the actuarial survival estimated for the patients, the expected survival in the matched general population and the calculated relative survival. When compared to the general population matched for age, sex and year of diagnosis, a marked effect of the disease on patients' life expectancy was observed. Specifically, relative survival at 5 and 10 years from diagnosis was 68% and 44%, respectively, relative to that expected in the general population. Relative survival of MF according to sex and age is shown in Figure 3. The decrease in relative survival was more pronounced in patients aged >65 years (incidence rate ratio [IRR]: 2.5, 95% CI: 2.0–3.1; $p<0.001$) and in male patients (IRR: 1.66; 95% CI: 1.34–2.06; $p<0.001$).

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TABLE 1 Main clinical characteristics at diagnosis of 1649 patients diagnosed with myelofibrosis after 2010.

Variables	Evaluable cases	
Age (years)[a]	1649	69 (60–76)
Sex, males/females	1649	962 (58%)/687 (42%)
Myelofibrosis type	1649	
Primary myelofibrosis		888 (53.9%)
Post-essential thrombocythaemia		464 (28.1%)
Post-polycythaemia vera		297 (18%)
Symptomatic splenomegaly	1605	298 (18.6%)
Constitutional symptoms	1638	631 (38.5%)
Splenomegaly by palpation or ultrasound	1572	1141 (72.8%)
Palpable splenomegaly ≥10 cm below costal margin	1224	213 (17.4%)
Palpable hepatomegaly	1444	190 (13.2%)
Hb, g/dL[a]	1453	11.1 (9.6–13.0)
<10 g/dL		439 (30.1%)
<8 g/dL		94 (6.5%)
Leukocytes, $\times 10^9$/L[a]	1563	10.0 (6.3–16.4)
>25		162 (10.4)
Platelets, $\times 10^9$/L[a]	1546	334 (183–561)
<100		167 (10.8%)
<50		58 (3.4%)
Blasts, %[a]	1358	0 (0–1)
≥1%		549 (40.4%)
Bone marrow fibrosis	1649	
Grade 0–1		239 (14.5%)
Grade 2–3		1410 (85.5%)
Genotype	1446	
JAK2		1014 (70.1%)
CALR		264 (18.3%)
MPL		80 (5.5%)
Triple negative		80 (5.5%)
Other[b]		8 (0.6%)
Cytogenetic risk group	579	
Favourable		462 (79.8)
Unfavourable		59 (10.2)
Very high risk		58 (10.0)
High molecular risk (HMR)[c]	666	263 (39.5)
IPSS category	1402	
Low risk		193 (14%)
Intermediate-1		419 (30%)
Intermediate-2		446 (32%)
High risk		344 (24%)

Note: All percentages are calculated from the total number of cases with available data.

[a]Median (interquartile range).

[b]JAK2+/MPL+: $n = 2$; JAK2+/CALR+: $n = 6$.

[c]HMR: pathogenic/likely pathogenic mutations in ASXL1, SRSF2, EZH2, IDH1, IDH2, U2AF1Q157 genes.

Figure 4 shows relative survival by IPSS risk category at diagnosis. Relative survival for patients in the low and intermediate-1 IPSS categories did not significantly diverge from the expected survival in the general population until approximately 2 years after diagnosis and remained at 72% and 57% of the expected survival at 10 years respectively. In

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TABLE 2 Main treatments given to 1649 myelofibrosis patients diagnosed after 2010.

Variables	n (%)
Hydroxycarbamide	728 (44.1)
Interferon	45 (2.7)
Erythropoiesis-stimulating agents	565 (34.3)
Danazol	135 (8.2)
Prednisone	159 (9.6)
Immunomodulatory drugs	34 (2.1)
Thalidomide	16 (1)
Lenalidomide	18 (1.1)
JAK inhibitors	850 (51.5)
Ruxolitinib	801 (48.6)
Fedratinib	37 (2.2)
Momelotinib	84 (5.1)
Pacritinib	7 (0.4)
Gandotinib	1 (0.1)
Spleen irradiation	10 (0.6)
Splenectomy	14 (0.8)
Haematopoietic cell transplantation	167 (10.1)

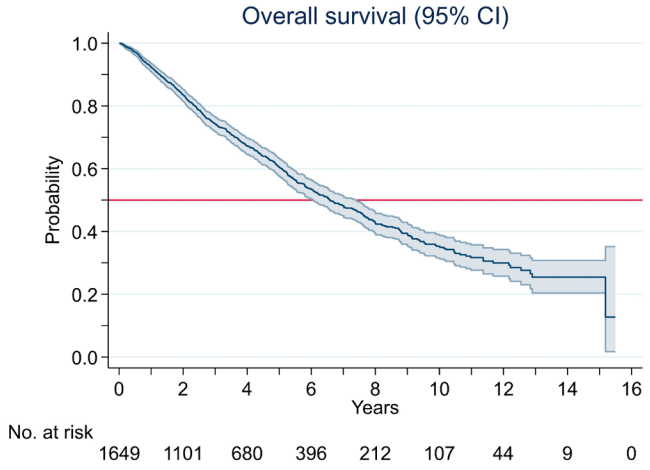

FIGURE 1 Overall survival of 1649 patients diagnosed with myelofibrosis from 2010 to 2025 across 64 GEMFIN centres.

contrast, patients in the intermediate-2 and high-risk IPSS categories had a significantly increased mortality from the first year of follow-up, with 10-year relative survival rates of 43% and 12%, respectively, relative to the general population. MF-attributable mortality increased progressively and significantly across successive IPSS risk groups (Table 3).

DISCUSSION

The present study demonstrates, in a large multicentre real-world cohort, that despite the introduction of JAK inhibitors and other recent therapeutic advances, MF remains

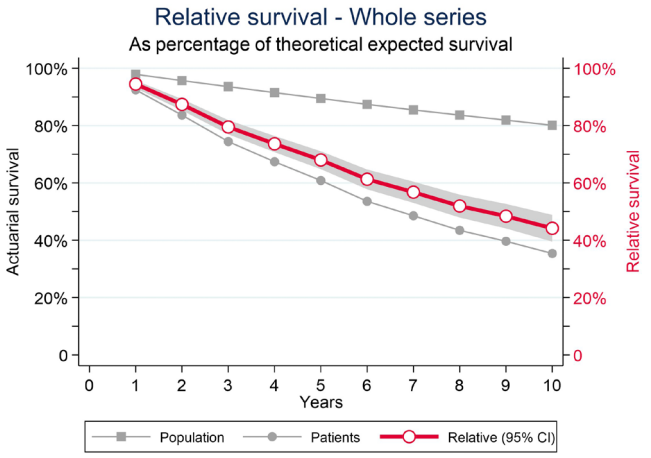

FIGURE 2 Observed survival in myelofibrosis patients compared with the expected survival of a general population subset matched by age, sex and calendar year at diagnosis.

associated with a substantial reduction in life expectancy compared with a matched general population. Relative survival at 5 and 10 years from diagnosis was 68%, and 44%, respectively, reflecting significant excess mortality attributable to the disease. Remarkably, patients in the high-risk IPSS category had reduced their 10-year life expectancy to less than 15% of that expected in their pairs of the general population. Notably, the survival reduction was not confined to patients with high-risk disease, but was also evident among those classified within lower-risk IPSS categories at diagnosis, with divergence from expected survival emerging early during follow-up. As anticipated, MF-attributable mortality increased progressively across successive IPSS risk groups. Furthermore, the reduction in relative survival was more pronounced in older patients (>65 years) and in male individuals, two subgroups that also had a higher burden of comorbidities and a greater frequency of HMR mutations at diagnosis.

Our study provides a comprehensive overview of treatment patterns in 1649 patients diagnosed from 2010 onwards across 64 centres participating in the Spanish MF Registry, reflecting contemporary real-world management of MF. JAK inhibitors were the most commonly used therapy, with more than half of patients exposed to these drugs, predominantly ruxolitinib. Despite its later approval by the European Medicine Agency (EMA), momelotinib was used more often than fedratinib in our series, likely reflecting its beneficial effect on anaemia.[24] Consistent with the efficacy of JAK inhibitors in controlling splenomegaly, spleen-directed procedures such as irradiation and splenectomy were rarely performed outside the transplantation setting. We did not compare survival outcomes between patients treated or not with JAK inhibitors, given the inherent differences in baseline clinical characteristics that would preclude any meaningful interpretation. A substantial proportion of patients received anaemia-directed therapies, mainly ESAs, used in nearly a third of the cohort, and danazol. The use of immunomodulatory drugs was minimal, with only 2% of patients

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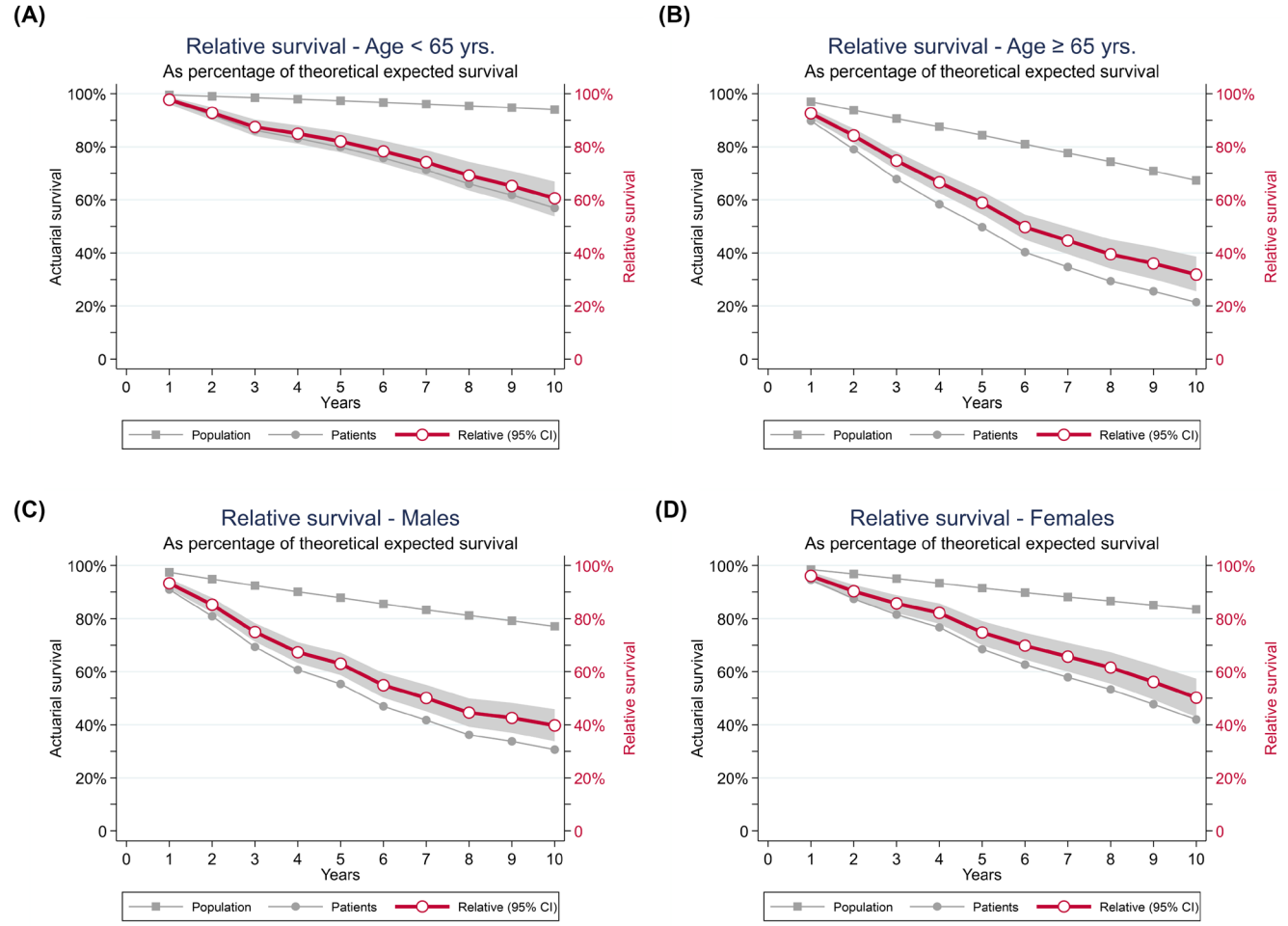

FIGURE 3 Observed survival in myelofibrosis patients compared with the expected survival of a matched general population subset, stratified by age and sex. (A) Patients aged <65 years. (B) Patients aged ≥65 years. (C) Male patients. (D) Female patients.

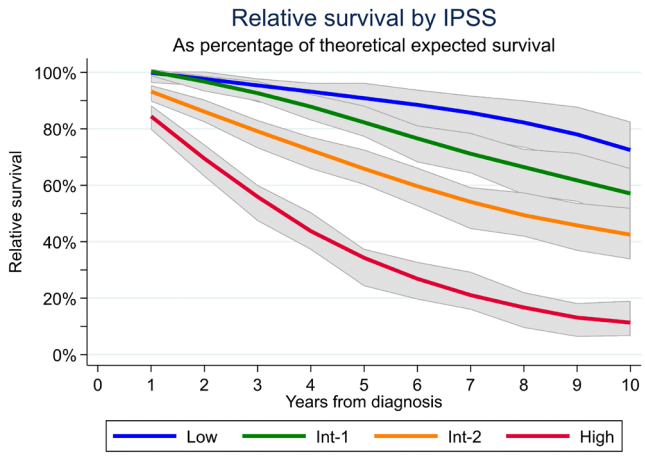

FIGURE 4 Relative survival of myelofibrosis patients stratified by IPSS risk group at diagnosis, compared with the expected survival of a matched general population subset.

receiving these agents, consistent with their limited efficacy and potential thrombotic risk, as previously reported.[25]

Allo-HSCT, the only potentially curative treatment for MF, was performed in 10% of patients overall, in line with other nationwide studies.[8,26] Among patients aged ≤70 years with intermediate-2 or high-risk IPSS at diagnosis, this proportion increased to 25%, indicating that a substantial subset of transplant-eligible patients did not ultimately undergo the procedure. Notably, only the high-risk IPSS category identified patients with a predicted median survival below 5 years, and this subgroup was also the only one significantly associated with an increased risk of AML transformation. Taken together, these findings reinforce the need to complement the IPSS with molecular and genomic data, particularly when making transplant decisions for patients in intermediate-risk categories.[21,27–30]

The median survival of the present series was 6.6 years, with no significant differences observed between PMF and

TABLE 3 Myelofibrosis-attributable mortality for the different IPSS risk categories at diagnosis.

Comparison	IRR (95% CI)	*p*-value
Intermediate-1 vs. Low risk	1.92 (1.19–3.12)	0.008
Intermediate-2 vs. Intermediate-1	1.89 (1.42–2.53)	<0.001
High vs. Intermediate-2	2.37 (1.89–2.97)	<0.001

Abbreviations: CI, confidence interval; IRR, incidence rate ratios.

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SMF. AML was the most frequent cause of death, accounting for 20% of deaths among patients with known cause of death. This finding is consistent with historical data[6] and underscores the persistent unmet need for effective therapies capable of reducing the intrinsic risk of leukaemic transformation in MF. Nevertheless, it should be noted that the majority of deaths were attributable to causes other than AML, supporting the notion that survival in MF may be improved not only through disease-modifying strategies, but also by optimizing the management of disease-related complications, such as transfusion dependency, infections, and vascular events, even in the absence of effective prevention of clonal evolution.

Another noteworthy finding was the greater reduction in relative survival observed in patients aged >65 years and in male patients, an observation previously reported in similar studies.[9,31] The underlying mechanisms driving this association remain speculative. On the one hand, these patient populations exhibited a higher prevalence of cardiovascular risk factors and comorbidities, which may interact with the MF phenotype to increase long-term mortality. In this regard, chronic anaemia, one of the most prevalent and debilitating manifestations of MF, is well recognized to worsen outcomes in patients with pre-existing cardiovascular disease, and has been shown to be an independent predictor of mortality in those with heart failure.[32] The synergistic interplay between disease-related anaemia and cardiac or renal comorbidities may thus create a vicious cycle that accelerates clinical deterioration in these vulnerable subgroups. Furthermore, baseline cardiovascular risk factors and prior history of thrombosis have been associated with increased risk of vascular events during follow-up in MF.[25,33,34] On the other hand, both older and male patients have been shown to display a more aggressive disease phenotype,[35–37] consistent with our findings of a higher frequency of anaemia and high-risk somatic mutations in these groups. Importantly, however, we did not observe a significantly increased risk of AML transformation in either of these populations, suggesting that the excess mortality in these groups is driven primarily by non-leukaemic causes.

One important limitation of the Spanish Myelofibrosis Registry is that we were unable to evaluate whether relative survival improved during the JAK inhibitor era compared with the preceding decade. This limitation stems from the fact that our registry was established in 2011. Although patients diagnosed from 2000 onwards were eligible for inclusion, enrolment during the earlier period was not systematic across centres. In many cases, there was a tendency to include only patients who were still alive at the time of registry initiation, without systematically reviewing hospital records to capture patients who had already died. By contrast, patients diagnosed after 2011 were more consistently enrolled in a consecutive manner. Nevertheless, the present study represents one of the largest datasets integrating clinical and molecular information in MF, while also providing comprehensive insights into contemporary real-world treatment patterns.

In conclusion, our results demonstrate that MF remains a disease that significantly reduces life expectancy, with a more pronounced impact in elderly and male patients. JAK inhibitors are the most widely used drugs to control disease-related manifestations, while anaemia-directed therapies continue to represent a major unmet need. Novel agents capable of modifying the natural history of the disease and preventing leukaemic transformation are urgently needed. Moreover, only approximately one quarter of patients meeting criteria for allo-HSCT ultimately undergo the procedure, highlighting the need to improve referral pathways and patient selection strategies. Taken together, these findings underscore that there remains substantial room for improvement in the overall management of this disease.

AUTHOR CONTRIBUTIONS

Juan-Carlos Hernández-Boluda: Conceptualization; writing – original draft; writing – review and editing; methodology; data curation; supervision; formal analysis; investigation; project administration. **Alberto Hernández-Sánchez:** Writing – review and editing. **Eduardo Arellano-Rodrigo:** Writing – review and editing. **José-María Raya:** Writing – review and editing. **María-Teresa Gómez-Casares:** Writing – review and editing. **María-Isabel Mata-Vázquez:** Writing – review and editing. **Valentín García-Gutiérrez:** Writing – review and editing. **Rosa Ayala:** Writing – review and editing. **Manuel Pérez-Encinas:** Writing – review and editing. **Blanca Xicoy:** Writing – review and editing. **Alicia Senín:** Writing – review and editing. **Natalia de las Heras:** Writing – review and editing. **Jasson Villarreal:** Writing – review and editing. **Elvira Mora:** Writing – review and editing. **Raúl Pérez-López:** Writing – review and editing. **Paula Gómez:** Writing – review and editing. **María-Laura Fox:** Writing – review and editing. **Francisca Ferrer-Marín:** Writing – review and editing. **Clara Martínez-Valverde:** Writing – review and editing. **Anna Angona:** Writing – review and editing. **María García-Fortes:** Writing – review and editing. **Carmen García-Hernández:** Writing – review and editing. **Lucía Pérez-Lamas:** Writing – review and editing. **Mercedes Gasior:** Writing – review and editing. **Lucía Guerrero:** Writing – review and editing. **Luis-Miguel Juárez-Salcedo:** Writing – review and editing. **Beatriz Cuevas:** Writing – review and editing. **Arturo Pereira:** Conceptualization; methodology; software; investigation; formal analysis; writing – original draft; writing – review and editing. **Sonia González de Villambrosia:** Writing – review and editing. **Elena Magro:** Writing – review and editing. **María-Luisa Antelo:** Writing – review and editing. **Angel Ramírez-Payer:** Writing – review and editing. **Alberto Alvarez-Larrán:** Writing – review and editing. **María-José Ramírez:** Writing – review and editing. **Francisco Ibáñez:** Writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study was approved by the scientific board of GEMFIN. Informed consent for inclusion in the registry was obtained from all patients.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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