Current Research in Translational Medicine 73 (2025) 103476

Contents lists available at ScienceDirect

Current Research in Translational Medicine

journal homepage: www.elsevier.com/locate/retram

Original article

Evaluation and management of hepatic dysfunction, portal hypertension and portal/splanchnic vein thrombosis in patients with myelofibrosis undergoing allogeneic haematopoietic cell transplantation: A practice based survey on behalf of the Chronic Malignancies Working Party of the EBMT

Giorgia Battipaglia [a,1,*], Nicola Polverelli [b,1], Joe Tuffnell [c], Patrizia Chiusolo [d], Marie Robin [e], Massimiliano Gambella [f], Annoek Broers [g], Elisa Sala [h], Jakob Passweg [i], Sabine Furst [j], Lone Smidtrup Friis [k], Remy Dulery [l], Moniek de Witte [m], Micha Srour [n], Maria Chiara Finazzi [o], Claudia Wehr [p], Arnon Nagler [q], Deborah Richardson [r], Wolfgang Bethge [s], Andrew Clark [t], Joanna Drozd-Sokolowska [u], Kavita Raj [v], Tomasz Czerw [w], Juan Carlos Hernández-Boluda [x], Donal P. McLornan [v]

[a] Department of Clinical Medicine and Surgery, Hematology and Bone Marrow Transplant Division, University of Naples Federico II, Naples, Italy
[b] Unit of Bone Marrow Transplantation, Division of Hematology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[c] EBMT Leiden Study Unit, Leiden, the Netherlands
[d] Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Sezione di Ematologia, Dipartimento di Scienze Radiologiche ed Ematologiche, Università Cattolica del Sacro Cuore, Roma, Italy
[e] Saint-Louis Hospital, BMT Unit, Paris, France
[f] IRCCS Ospedale Policlinico San Martino, Genova, Italy
[g] Erasmus MC Cancer Institute, Rotterdam, the Netherlands
[h] Klinik fuer Innere Medzin III, Ulm, Germany
[i] University Hospital of Basel, Basel, Switzerland
[j] Programme de Transplantation et Therapie cellulaire de Marseille, Marseille, France
[k] Rigshospitalet, Copenaghen, Denmark
[l] Sorbonne University, Department of Clinical Hematology and Cellular Therapy, Saint-Antoine Hospital, Assistance Publique – Hôpitaux de Paris, Paris, France
[m] University Medical Center of Utrecht, Utrecht, the Netherlands
[n] CHU de Lille, Lille, France
[o] ASST Papa Giovanni XXIII, Bergamo, Italy
[p] Department of Medicine I/ Hematology, Oncology and Stem Cell Transplantation, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Germany
[q] Chaim Sheba Medical Center, Tel-Hashomer, Israel
[r] Southampton General Hospital, Southampton, United Kingdom
[s] Universitaet Tuebingen, Tuebingen, Germany
[t] Glasgow Royal Infirmary, Glasgow, United Kingdom
[u] Central Clinical Hospital, The Medical University of Warsaw, Warsaw, Poland
[v] University College London Hospital NHS Trust, London, United Kingdom
[w] Maria-Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Poland
[x] Department of Hematology, Hospital Clinico Universitario, Valencia, Spain

ARTICLE INFO

Keywords:
Myelofibrosis
Transplantation

ABSTRACT

Heterogeneous approaches exist in regard to the management of disease-related co-morbidities in potential allogeneic haematopoietic cell transplantation (allo-HCT) candidates with myelofibrosis (MF). The EBMT Chronic Malignancies Working Party launched an electronic survey to evaluate how MF-specific comorbidities

* Corresponding author at: Department of Clinical Medicine and Surgery, Federico II University of Naples, Italy.
E-mail address: giorgia.battipaglia@unina.it (G. Battipaglia).
[1] Shared first authorship.

https://doi.org/10.1016/j.retram.2024.103476
Received 16 February 2024; Accepted 16 October 2024
Available online 29 October 2024

Portal hypertension
Hepatic dysfunction
Splanchnic vein thrombosis
Portal thrombosis
Gastroesophageal varices

are approached and whether they ultimately affect the decision to transplant. A total of 41/63 (65%) Centers, all of whom were experienced in the management of MF allo-HCT, responded. Responses were aggregated and reported in a comparative fashion. Screening for portal hypertension (PH) was routinely performed in 54% centers, never in 12% and guided by clinical manifestations in the remaining. Involvement of hepatologists/gastroenterologists was always/very often considered in patients with signs of PH prior to transplant. Centers reported that radiological evidence of PH did not routinely represent a formal contraindication for allo-HCT in most cases (78%). Of note, most centers (61%) did not perform routine screening for gastroesophageal varices; this was systematically considered or guided by clinical manifestations in only 7% and 32% centers, respectively. Presence of gastroesophageal varices was always (15%) or occasionally (19%) considered a formal contraindication to allo-HCT. A prior history of portal vein thrombosis never (78%) or occasionally (15%) represented a formal contraindication. Three Centers would not proceed to transplant in such cases. Less importance was assigned to non-portal splanchnic vein thrombosis (SVT), with all but one centre proceeding to transplant regardless of prior SVT. This survey highlights a considerable heterogeneity across responding centers in approaching MF-related comorbidities prior to transplant, suggesting that harmonisation guidelines are needed to address these issues in this patient population.

Introduction

Myelofibrosis (MF) is a heterogeneous disorder, characterised by varying degrees of splenomegaly, constitutional symptoms, frequent cytopenias and an inherent risk of vascular complications and transformation to blast phase disease [1]. Despite marked therapeutic advances in the field following the advent of JAK inhibitors, alongside an increasing list of other novel compounds, none are curative and patients ultimately display both poor quality of life and shortened survival [2,3]. Allogeneic hematopoietic cell transplantation (allo-HCT) remains the only curative option but success is still hampered by high rates of non-relapse mortality (NRM), ranging from 20 to 35% at 1-year, and a relapse risk of around 20–25% [1,4–6]. The risk of post- transplant complications can be elevated by the concomitant presence of MF-related co-morbidities, which of note may initially be asymptomatic and clinically 'silent' [7]. These include significant hepatic dysfunction, portal hypertension (PH), oesophageal and/or gastric varices, hepatic-dysfunction associated coagulopathy, pulmonary hypertension, splanchnic venous thrombosis (SVT) and potential cavernoma formation [8–11]. Careful evaluation based on multidisciplinary approaches is frequently essential in guiding the final allo-HCT decision for such patients, estimating the perceived individualised risk-benefit ratio [12].

To date, there is limited real world data on how best to approach potential allo-HCT candidates with MF-specific comorbidities (such as established PH or SVT) and transplant centers specific practice in this regard. Moreover, the potential influence of these MF related co-morbidities on NRM rates remains of concern in the decision making process. Previously our group, in an international consensus paper, highlighted a lack of data on how the presence of SVT affected allo-HCT outcomes, the complexity of the decision making process and an agreement that a history of SVT *per se* was not an unequivocal barrier to proceeding with transplant, in the context of no other significant co-morbidities, an adequate performance status and adequate hepatic function [13]. Recent work from our group has also highlighted that a high hematopoietic cell transplantation comorbidity index (HCT-CI) in MF allo-HCT associated with high NRM rates and decreased overall survival [14]. Given these issues, we launched an electronic survey to evaluate current 'real world' European clinical practice in approaching such disease-specific comorbidities in MF allo-HCT candidates and whether their presence truly affected the transplant decision process.

Methodology

The Myeloproliferative Neoplasms (MPN) subcommittee of the Chronic Malignancies Working Party (CMWP) of the European Blood and Marrow Transplantation (EBMT) generated an electronic survey proposal to investigate approaches to a number of MF-allo-HCT specific issues such as splenic/ hepatic imaging prior to allo-HCT, PH or pulmonary hypertension assessment, screening for occult oesophageal/gastric varices, involvement of additional specialists in MF transplant candidate assessment (e.g. hepatologists or haemostasis specialists for SVT etc.), and also included specific clinical vignettes addressing these aspects to understand in detail any variations in practice. As per EBMT studies policy, patients provided informed consent authorizing the use of their personal information for research purposes. The survey was sent to a total of 63 Centers starting in February 2023, with multiple rounds of reminders to ensure wide survey completion. By time of survey closure, a total of 41 Centers (65%) had responded. Descriptive statistics were utilized to analyse the answers submitted by participating centers and the distribution of responses.

Results

Centre activity regarding number of allo-HCT performed for MF per annum and city/ country

Among respondents, 23 (56%) performed on average 6–10 allo-HCT for MF per year, 13 (32%) performed 1–5 allo-HCT per year and only 5 (12%) performed >10 allo-HCT per year. The distribution of responding Centers by city and country is listed in Table 1 while main results of the survey are summarized in Table 2.

Pre- and peri-transplant assessment

Centers were first surveyed on radiological assessment of hepato-splenomegaly prior to allo-HCT. Briefly, except for two, most Centers routinely evaluate spleen (n = 36, 88%) and liver (n = 32; 78%) dimensions prior to allo-HCT, mainly relying on the use of computerised tomography (CT) scan (n = 21; 51%) alone or with the addition of concomitant ultrasound (US) imaging (n = 12, 29%). Use of US imaging alone was reported by 17 (41%) Centers. Use of pre-transplant FibroScan (transient elastography) or two-dimensional shear wave elastography (2D-SWE) was less common. FibroScan was routinely performed for both spleen and liver in only 8 (19%) Centers and liver only in 2 (5%) and 2D-SWE was routinely used in 8 (19%) Centers, only if clinically indicated in 4 (10%) Centers and never used in 29 (71%) Centers. Of note, in the peri-transplant setting, elastography evaluation of the liver alone or coupled with spleen assessment was reported by 5 (12%) and 3 (7%) Centers, respectively, on a weekly basis or when clinically indicated.

Respondents were then surveyed on their approach to portal hypertension (PH) in candidates to allo-HCT for MF. Screening for PH is routinely performed in 22 (54%) Centers, never in 5 (12%), and guided by clinical manifestations (i.e. presence of massive splenomegaly, positive history of portal vein or splanchnic vein thrombosis and /or presence of abnormal liver function tests (LFTs) in the remaining (Fig. 1). Involvement of hepatologists/gastroenterologists is always/very often considered in patients with signs of PH prior to transplant, while their

Table 1
Distribution of centers answering the survey.

Country	Number of Centers	City
Austria	**1**	**Linz**
Belgium	**1**	**Brussels**
Denmark	**1**	**Copenhagen**
France	**10**	**Vandœuvre-lès-Nancy**
		Lille
		Nice
		Marseille
		Paris
		Nantes
		Paris
		Pessac
		Pierre Benite
		Montpellier
Germany	**7**	**Frankfurt**
		Dresden
		Regensburg
		Tuebingen
		Munich
		Ulm
		Freiburg
Israel	**1**	**Tel Aviv**
Italy	**7**	**Rome (University Tor Vergata)**
		Genova
		Udine
		Bergamo
		Pavia
		Rome (University La Sapienza)
		Rome (University Cattolica Sacro Cuore)
Netherlands	**3**	**Utrecht**
		Nijmegen
		Rotterdam
Poland	**1**	**Orzesze**
Portugal	**1**	**Gdansk**
Russian Federation	**1**	**Saint Petersburg**
Spain	**1**	**Valencia**
Switzerland	**1**	**Basel**
United Kingdom	**5**	**Nottingham**
		Glasgow
		Cardiff
		London (University College London Hospital NHS Trust)
		Southampton

consultative advice was rarely considered in the absence of documented evidence of PH manifestations. Only 3 (7%) Centers tended to involve hepatologists in all cases, while pre-existing LFT abnormalities ($n = 7$; 17%), imaging abnormalities ($n = 8$; 20%), or signs of PH ($n = 9$; 22%) are indications for hepatology referral in the remaining Centers. Of note, most Centers ($n = 25$; 61%) do not routinely perform oesophago-gastroduodenoscopy (OGD) screening for gastroesophageal varices; this is systematically considered or guided by clinical manifestations (i.e. prior history of gastrointestinal bleeding, documented PH) in 3 (7%) and 13 (32%) Centers, respectively.

Transplant decision process: is this influenced by MF-specific co-morbidities?

Distribution of answers for transplant decision process in the presence of comorbidities is summarized in Fig. 2. Radiological evidence of PH does not routinely represent a formal contraindication for allo-HCT in most Centers (n=32; 78%). Documented presence of gastroesophageal varices is not considered a contraindication to allo-HCT for 27 (66%) Centers (including 23 Centers highlighting the importance of pre allo-HCT treatment with variceal banding/sclerotherapy), while in 14 (34%) Centers this is always ($n = 6$) or occasionally ($n = 8$, depending on clinical manifestations and eventually specialists' advice) a formal contraindication to allo-HCT. Regarding thrombosis, a prior history of portal vein thrombosis (PVT) never (78%) or occasionally (15%) represents a formal contraindication. Three (7%) Centers would not actually proceed to transplant in such cases. However, in PVT cases complicated by the formation of a cavernoma, only 18 (44%) Centers would proceed with transplant, 13 (32%) would consider it a formal contraindication and 8 (20%) would prioritize assessment of the clinical consequences of prior thrombosis and cavernoma formation to guide allo-HCT decisions. Of note, 2 (5%) Centers had yet to face that clinical dilemma to date. Need for transjugular intrahepatic portosystemic shunt (TIPS) represents a formal contraindication to transplant for 7 (17%) Centers while 8 (20%) would balance disease severity and clinical sequelae of thrombosis. The remaining 26 (63%) Centers would proceed to allo-HCT regardless of a prior TIPS.

Table 2
Main results of the survey.

	N (%)
Number of allo-HCT/year in answering centers	
<5	13 (32)
6–10	23 (56)
>10	5 (12)
Pre- and peri-transplant assessment	
Assessment of organ dimensions prior to allo-HCT	
Spleen	36 (88)
Liver	32 (78)
Radiological technique used for organ dimensions assessment	
CT scan alone	21 (51)
US imaging alone	17 (41)
CT scan + US imaging	12 (29)
Screening for PH prior to allo-HCT	
Always	22 (54)
Never	5 (12)
Only if clinical manifestations	14 (34)
Screening of oesophageal varices through OGD	
Always	3 (7)
Only if clinical manifestations	13 (32)
Not routinely performed	25 (61)
Post-transplant monitoring	
Radiological assessment of hepato-splenomegaly	29 (71)
Monitoring of SVT	32 (78)
Routine monitoring of PH	14 (34)
Monitoring of PH only if clinically indicated	25 (61)

Abbreviations: allo-HCT, allogeneic hematopoietic cell transplantation; CT, computed tomography; US, ultrasound; PH, portal hypertension; OGD, oesophago-gastroduodenoscopy; SVT, splanchnic vein thrombosis

Less emphasis is placed upon a prior history of a non-portal SVT, with all but one centre proceeding to allo-HCT regardless of a prior SVT (including 3 (7%) stating the importance of balancing the perceived risk-benefit ratio according to disease severity and clinical sequelae to guide the allo-HCT decision. For management of ongoing anticoagulation prior to and following allo-HCT, the transplant team alone regularly manages treatment monitoring in 23 (56%) Centers while in the remaining cases a multidisciplinary approach with the involvement of hepatologists or of a dedicated haemostasis team is preferred. Three Centers declined to answer. Lastly, detection of pulmonary hypertension prior to allo-HCT represents a formal contraindication to allo-HCT in 7 (17%) Centers while 30 (73%) would proceed to allo-HCT but most of them ($n = 26$; 63%) would do so only after pulmonogist evaluation. The remaining Centers ($n = 4$;10%) consider disease severity and the benefit-risk ratio in the decision process.

Post-transplant monitoring

Radiological assessment of hepato-splenomegaly is generally performed after transplant ($n = 29$ (71%) of Centers), but at highly heterogeneous intervals. In general, assessment was performed once ($n = 10$) or twice ($n = 10$) per annum. Other centers reported more frequent evaluation (three times per year, $n = 4$ (10%); four times a year, $n = 2$ (5%); monthly evaluation during the first 3 months, followed by an

evaluation every 3–6 months, $n = 1$ (2%)). Two centers (5%) consider post-transplant radiological assessment only if clinically indicated or according to pre-transplant results or a history of prior splenectomy. Post-transplant monitoring of SVT is performed through US doppler assessment in 78% of cases ($n = 32$, alone [$n = 11$], coupled with CT scan [$n = 16$] or with magnetic resonance imaging [$n = 3$], or with both [$n = 3$]). It was only performed based on prior CT imaging ($n = 3$) or on hepatology advice ($n = 1$). It was not routinely considered in 3 cases and one centre declared to have not had such as case. Lastly, post-transplant monitoring in patients with PH is routinely considered ($n = 14$; 34%) or based on the presence of overt symptoms ($n = 25$; 61%), respectively.

Clinical cases

Three anecdotal clinical cases were submitted to answering Centers to check their attitude in clinical practice.

Case summary 1

A 45-year-old male patient with MIPSS70v2.0 high risk MF is losing response to ruxolitinib and has a sibling donor available. He is planned for transplant. Routine pre-transplant investigations 4 weeks prior to admission reveal mildly elevated bilirubin (29 μmol/L) and transaminases < 2 ULN. Virology is all negative and abdominal doppler ultrasound study reveals a previously undetected chronic portal vein thrombosis with no cavernoma formation detected on CT-scan imaging. Grade 1–2 gastric varices were found on OGD.

Distribution of answers to case summary 1

Only one centre would consider this case as a formal contraindication for transplant while 31 centers (76%) would proceed to transplantation. Among these, only two Centers would directly proceed to transplant in the subsequent 4 weeks (including one detailing the preference for a treosulfan-based regimen) while sixteen would rather delay transplant, ideally after 8–12 weeks in order to become established on anticoagulation and beta-blockers and thirteen would proceed only after a fibroscan followed by hepatology review. Interestingly, 7 (17%) Centers reveal not knowing how to proceed in such a difficult case, with six guiding transplant-decision according to hepatologists and thrombosis team evaluation. Two Centers declined to answer.

Case summary 2

A 57-years female patient with a MIPSS70 v2.0 high risk with large splenomegaly has been intolerant to ruxolitinib and second-line JAK inhibitors (cytopenias and transfusion dependence, resolved after ruxolitinib withdrawal) and has no access to other JAK inhibitors. She has an HLA-identical brother. Her previous history includes a splenic vein thrombosis with residual cavernoma for which she has been thereafter under LMWH. A concomitant PH with grade 3 and recent evolution to bone marrow fibrosis grade 3. Karnofsky performance status is 100%.

Distribution of answers to case summary 2

Three (8%) Centers would consider this clinical scenario as formal contraindication for transplant while 12 (29%) would proceed as soon as possible with 4 performing either splenectomy ($n = 2$) or spleen radiotherapy ($n = 2$) prior to transplant. For most Centers ($n = 23$, 56%) final decision is guided by risk assessment by thrombosis team and hepatologists, with particular focus on effective treatment for oesophageal varices and discussion for TIPS. Two Centers were not confident with such a situation and thus did not provide a final answer while one center, considering the high-risk situation, would privilege detailed discussion with the patient.

Case summary 3

A 62-years male patient with a MIPSS70 v2.0 low risk with massive splenomegaly not responsive to JAK-inhibitors is contraindicated for splenectomy. He experienced a recent portal vein thrombosis with residual cavernoma ad signs of PH now under LMWH. Karnofsky performance status is 100%. A matched unrelated donor is available.

Distribution of answers to case summary 2

Twenty Centers (49%) would not propose allo-HCT due to a low risk MIPSS70 v2.0 while six (15%) would consider to proceed to transplant. Nine Centers (22%) would consider spleen irradiation either alone ($n = 4$) or followed by allo-HCT ($n = 5$) while one would consider splenectomy. One center would look for a clinical trial, whenever available and another would balance the decision after multidisciplinary discussion with hepatologists and thrombosis team. Three Centers did not answer the question.

Discussion

Our survey highlights a considerable heterogeneity across responding Centers in approaching MF-specific comorbidities prior to transplant and how these ultimately affect the allo-HCT decision, suggesting that harmonisation guidelines are needed to optimise approaches in this frequently comorbid patient population. A recent non-transplant study elegantly highlighted that incorporation of specific comorbidity burden in established risk prediction tools for primary MF (Dynamic

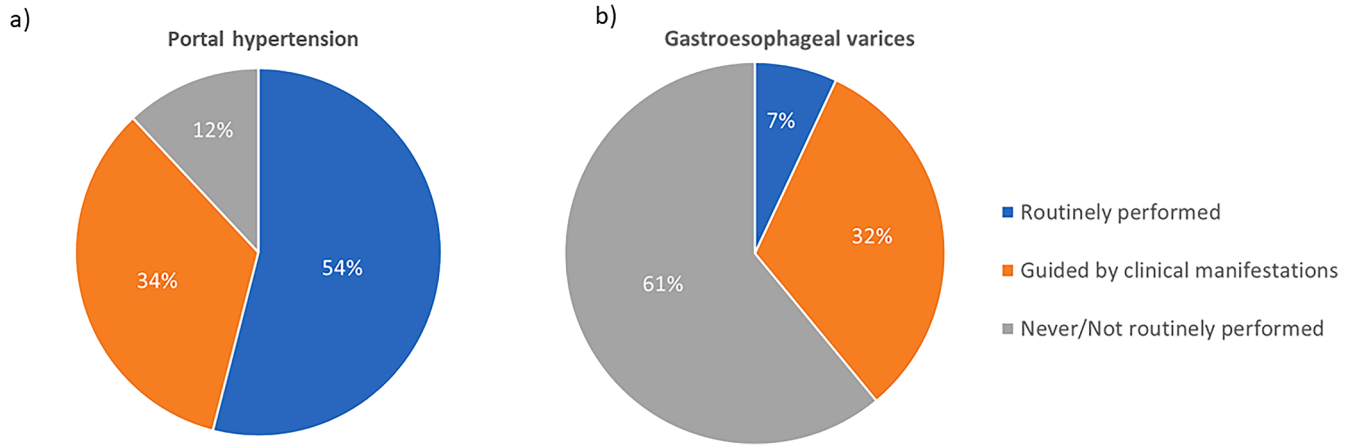

Fig. 1. Distribution of answers for pre-transplant evaluation of comorbidities: a) portal hypertension b) gastroesophageal varices.

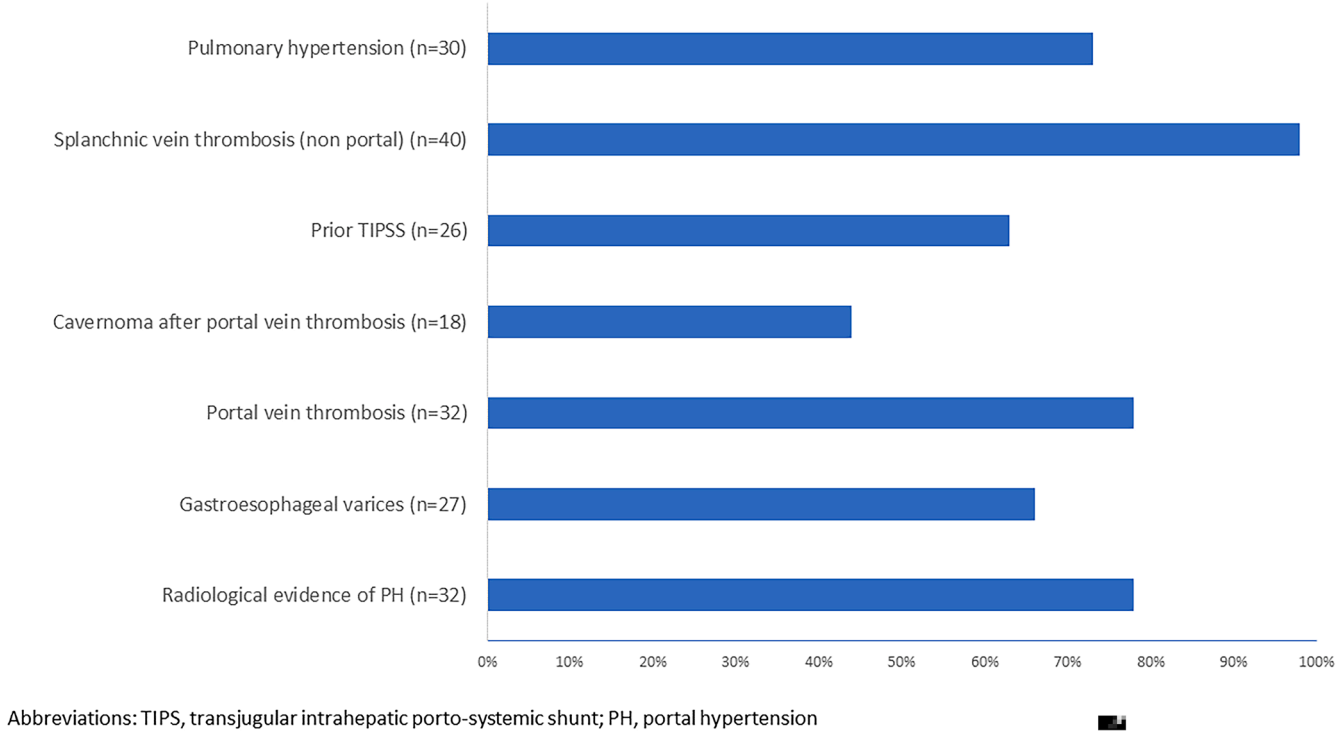

Fig. 2. Centers proceeding with transplantation regardless the presence of specific comorbidities.

International Prognostic Scoring System [DIPSS]) could significantly enhance discriminatory power for survival assessment compared to the original model [15].

Survey results highlight heterogeneous approaches to pre- and post-transplant assessment of liver and spleen dimensions, with utilisation of variable imaging techniques and widely varying intervals for pre and post-transplant monitoring.

Of interest, in alignment with the EBMT position paper [13], the vast majority of Centers assessed splenic and hepatic parenchyma using instrumental imaging before transplantation. However, the use of transient elastography via FibroScan or 2D-SWE for assessment of hepatic or splenic 'stiffness' were less commonly performed in responding Centers. Dynamic spleen stiffness measurement has been shown to correlate with survival in the non-transplant MF population and could be helpful in defining patients at higher risk of progression and hence may guide intervention [16]. How such pre-transplant assessments may correlate with post allo-HCT outcomes and the need for specific intervention remains an unanswered question that requires comprehensive evaluation. Interestingly, a number of Centers were performing elastography assessment via Fibroscan or 2D-SWE peri-transplant whilst an inpatient. A recent study has highlighted the utility of 2D-SWE in evaluation of sequential hepatic stiffness measurement to aid the recognition of early hepatic complications post allo-HCT; here, early prediction of sinusoidal obstructive syndrome at day +14 was improved [17].

In MF, the presence of PH can be multi-factorial e.g. due to splenic and hepatic extramedullary haematopoiesis, increased spleno-portal blood flow and in some cases sinusoidal microvascular thrombi or even macrovascular portal venous thrombosis. The majority of responding Centers screened for PH either routinely or as guided by the clinical situation (massive splenomegaly, history of SVT or abnormal LFTs) and in the presence of established PH, the allo-HCT team involved expert assessments by hepatology. Of note, 61% of Centers did not routinely perform OGD for primary variceal screening prior to allo-HCT with only 3 (7%) Centers systematically performing screening in all candidates. Previous small studies have suggested that up to 7–8% of MF patients can have endoscopically visualised varices [18,19]. Guidance is required on the utility of routine variceal screening prior to allo-HCT.

Importantly, in most cases the presence of disease-specific comorbidities does not appear to represent truly formal contraindication to allo-HCT in the majority of experienced centers, even in symptomatic patients, where the importance of post-transplant monitoring, with active involvement of other specialists, is recognized. In contrast, a significant proportion of centers recognized that post-PVT cavernoma presents a potential concern for transplantation, as it may indicate patients at a high risk of vascular complications [20]. In this context, most recognise the need for seeking expert advice from hepatology and careful assessment of the risk-benefit ratio. Overall, multidisciplinary approaches can be extremely useful in guiding clinicians in comprehensive pre-transplant risk-assessment and in guiding transplant decisions and, indeed, periodicity and type of tailored post-transplant follow monitoring.

Despite post-transplant monitoring through radiological assessment for hepato-splenomegaly is performed in most Centers, highly heterogeneous intervals were reported. Similarly, different radiological techniques are used by different Centers for post-transplant monitoring of prior SVT, these mainly being represented by US doppler. These results reflect the lack of consensus on the timing for post-transplant organomegaly evaluation and on the best technique to be used. While several studies have shown that splenomegaly may significantly impact on post-transplant outcomes [21], data on the impact and on the results of post-transplant monitoring are scarce.

Use of a section of clinical vignette-based questions in our survey shows the absence of concordance in the choice for allo-HCT in difficult cases of MF with associated comorbidities, highlighting once again that despite recommendations for guiding transplant choice in patients with MF, these do not adequately balance the importance of comorbidities that in clinical practice may finally impact on the decision to propose allo-HCT.

Study limitations

This survey, addressed to hematopoietic stem cell transplant physicians, provides an overview of center policies in approaching disease-specific comorbidities guiding the decision to proceed or not with allo-HCT. Intrinsic biases of a survey method are present and we recognise the limitations inherent to such a report, namely the relatively low number of respondents, the bias of picking Centers who perform a specific minimum number of MF allo-HCT and a collective response rather than balanced and individualised patient level detail. Furthermore, addressing the survey only to hematologists makes it difficult to extrapolate recommendations without taking into account the opinion of other involved specialists, i.e. hepatologists, pulmonogist, etc. A multicenter prospective study with all the involved specialists would ideally be the best manner to shed light on many unanswered questions.

Conclusions

Our survey may represent a first step towards a better comprehension of how to manage difficult situations in patients with MF-related comorbidities, helping in guiding and inspiring further studies, considering the lack of specific literature on the subject. Our findings are important given the paucity of data on this issue and highlight the need for harmonisation guidelines.

Data availability

The final analysis dataset will be available upon specific request to the Working Party chair.

Ethics approval and consent to participate

Patients provided informed consent authorizing the use of their personal information for research purposes.

Acknowledgements

The CMWP of the EBMT is extremely grateful to clinicians and their teams for timely completion of this survey. The authors thank the data management unit and the clinical staff and investigators involved in this research.

References

[1] McLornan DP, Yakoub-Agha I, Robin M, Chalandon Y, Harrison CN, Kroger N. State-of-the-art review: allogeneic stem cell transplantation for myelofibrosis in 2019. Haematologica 2019. https://doi.org/10.3324/haematol.2018.206151.
[2] McLornan DP, Harrison CN. Guidance on changing therapy choice in myelofibrosis. Blood Adv 2020;4:607–10. https://doi.org/10.1182/bloodadvances.2019001426.
[3] McLornan DP, Pope JE, Gotlib J, Harrison CN. Current and future status of JAK inhibitors. Lancet Lond Engl 2021;398:803–16. https://doi.org/10.1016/S0140-6736(21)00438-4.
[4] Rondelli D, Goldberg JD, Isola L, Price LS, Shore TB, Boyer M, et al. MPD-RC 101 prospective study of reduced-intensity allogeneic hematopoietic stem cell transplantation in patients with myelofibrosis. Blood 2014;124:1183–91. https://doi.org/10.1182/blood-2014-04-572545.
[5] Robin M, Tabrizi R, Mohty M, Furst S, Michallet M, Bay J-O, et al. Allogeneic haematopoietic stem cell transplantation for myelofibrosis: a report of the Société Française de Greffe de Moelle et de Thérapie Cellulaire (SFGM-TC): allogeneic HSCT for myelofibrosis. Br J Haematol 2011;152:331–9. https://doi.org/10.1111/j.1365-2141.2010.08417.x.
[6] Hernández-Boluda JC, Pereira A, Kröger N, Beelen D, Robin M, Bornhäuser M, et al. Determinants of survival in myelofibrosis patients undergoing allogeneic hematopoietic cell transplantation. Leukemia 2021;35:215–24. https://doi.org/10.1038/s41375-020-0815-z.
[7] Verstovsek S, Mughal T, Vaddi K, Sarlis N. Myelofibrosis-associated complications: pathogenesis, clinical manifestations, and effects on outcomes. Int J Gen Med 2014:89. https://doi.org/10.2147/IJGM.S51800.
[8] Yan M, Geyer H, Mesa R, Atallah E, Callum J, Bartoszko J, et al. Clinical features of patients with philadelphia-negative myeloproliferative neoplasms complicated by portal hypertension. Clin Lymphoma Myeloma Leuk 2015;15:e1–5. https://doi.org/10.1016/j.clml.2014.04.004.
[9] Gupta R, Jamal F, Yang D, Chendri C, Aldoss I, Malki MA, et al. Pulmonary hypertension is associated with increased nonrelapse mortality after allogeneic hematopoietic cell transplantation for myelofibrosis. Bone Marrow Transplant 2020;55:877–83. https://doi.org/10.1038/s41409-019-0741-8.
[10] Liu A, Naymagon L, Tremblay D. Splanchnic vein thrombosis in myeloproliferative neoplasms: treatment considerations and unmet needs. Cancers 2022;15:11. https://doi.org/10.3390/cancers15010011.
[11] Robin M, Gras L, Gagelmann N, Koster L, Peffault De Latour R, Van Gorkom G, et al. Early hepatotoxicity in patients with myelofibrosis after Allogeneic Hematopoietic Cell Transplantation (Allo-HCT). Blood 2022;140:7585–6. https://doi.org/10.1182/blood-2022-156076.
[12] Perram J, Ross DM, McLornan D, Gowin K, Kröger N, Gupta V, et al. Innovative strategies to improve hematopoietic stem cell transplant outcomes in myelofibrosis. Am J Hematol 2022;97:1464–77. https://doi.org/10.1002/ajh.26654.
[13] Polverelli N, Hernández-Boluda JC, Czerw T, Barbui T, D'Adda M, Deeg HJ, et al. Splenomegaly in patients with primary or secondary myelofibrosis who are candidates for allogeneic hematopoietic cell transplantation: a position paper on behalf of the Chronic Malignancies Working Party of the EBMT. Lancet Haematol 2023;10:e59–70. https://doi.org/10.1016/S2352-3026(22)00330-1.
[14] Polverelli N, Bonneville EF, de Wreede LC, Koster L, Kröger NM, Schroeder T, et al. Impact of comorbidities and body mass index on the outcomes of allogeneic hematopoietic cell transplantation in myelofibrosis: A study on behalf of the Chronic Malignancies Working Party of EBMT. Am J Hematol 2024;99(5):993–6. https://doi.org/10.1002/ajh.27262.
[15] Sochacki AL, Bejan CA, Zhao S, Patel A, Kishtagari A, Spaulding TP, et al. Patient-specific comorbidities as prognostic variables for survival in myelofibrosis. Blood Adv 2023;7:756–67. https://doi.org/10.1182/bloodadvances.2021006318.
[16] Benedetti E, Tavarozzi R, Morganti R, Bruno B, Bramanti E, Baratè C, et al. Organ stiffness in the work-up of myelofibrosis and Philadelphia-negative chronic myeloproliferative neoplasms. J Clin Med 2020;9:2149. https://doi.org/10.3390/jcm9072149.
[17] Debureaux Pierre-Edouard, Bourrier Pierre, Rautou Pierre-Emmanuel, Zagdanski Anne-Marie, De Boutiny Morgane, Pagliuca Simona, et al. Elastography improves accuracy of early hepato-biliary complications diagnosis after allogeneic stem cell transplantation. Haematologica 2020;106:2374–83. https://doi.org/10.3324/haematol.2019.245407.
[18] Toros AB, Gokcay S, Cetin G, Ar MC, Karagoz Y, Kesici B. Portal hypertension and myeloproliferative neoplasms: a relationship revealed. ISRN Hematol 2013;2013:1–5. https://doi.org/10.1155/2013/673781.
[19] Wanless IR, Peterson P, Das A, Boitnott JK, Moore GW, Bernier V. Hepatic vascular disease and portal hypertension in polycythemia vera and agnogenic myeloid metaplasia: a clinicopathological study of 145 patients examined at autopsy. Hepatology 1990;12:1166–74. https://doi.org/10.1002/hep.1840120515.
[20] Wei B, Huang Z, Tang C. Optimal treatment for patients with cavernous transformation of the portal vein. Front Med 2022;9:853138. https://doi.org/10.3389/fmed.2022.853138. Mar 24PMID: 35402447; PMCID: PMC8987530.
[21] Polverelli N, Mauff K, Kroger N, Robin M, Beelen D, Beauvais D, et al. Impact of spleen size and splenectomy on outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis: a retrospective analysis by the chronic malignancies working party on behalf of European Society for Blood and Marrow Transplantation (EBMT). Am J Hematol 2021;96:69–79.