

Spanish expert agreement with the 2023 EBMT framework for adult sinusoidal obstruction syndrome/veno-occlusive disease management: a Delphi study

Consenso de expertos españoles sobre el marco de la EBMT de 2023 para el manejo del síndrome de obstrucción sinusoidal/enfermedad venooclusiva en adultos: estudio Delphi

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Abstract

Introduction: Sinusoidal obstruction syndrome/veno-occlusive disease (SOS/VOD) represents a serious complication of hematopoietic stem cell transplant (HSCT), manifesting as both classical and late-onset presentations. Diagnosis and management remain challenging due to diverse diagnostic and severity criteria, persistent uncertainties around defibrotide use, and difficulties in identifying high-risk patients. **Objective:** The aim of the study was to assess national agreement with the 2023 European Society for Blood and Marrow Transplantation (EBMT) adult framework for SOS/VOD management and to identify areas of consensus, residual uncertainty, and potential implementation challenges in Spanish HSCT practice. **Materials and methods:** A Delphi consensus study based on the RAND/UCLA methodology was conducted. Spanish hematologists with expertise in HSCT evaluated 33 statements covering key aspects of adult SOS/VOD management in a 2-round online Delphi process. **Results:** After 2 Delphi rounds, consensus was reached on 30 out of 33 statements (90.9%). Thirty-one statements were deemed appropriate, including 1 with neutral agreement, while 2 were considered doubtful with disagreement among panelists. **Conclusion:** Spanish hematologists involved in HSCT demonstrated strong agreement with most of the components of the 2023 EBMT adult framework for SOS/VOD management. These findings identified residual uncertainties that may inform future implementation and educational initiatives in Spanish HSCT practice.

Keywords: Adult. Defibrotide. Delphi consensus. Hematopoietic cell transplantation. Sinusoidal obstruction syndrome. Veno-occlusive disease.

Resumen

Introducción: El síndrome de obstrucción sinusoidal/enfermedad venooclusiva hepática (SOS/EVOH) es una complicación grave del trasplante de progenitores hematopoyéticos (TPH), cuyo diagnóstico y manejo siguen siendo complejos debido a la variabilidad de los criterios diagnósticos y de gravedad, a la identificación de pacientes de alto riesgo y a las incertidumbres terapéuticas. **Objetivo:** Evaluar el grado de acuerdo de los hematólogos españoles con el marco de la EBMT de

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2023 para el manejo del SOS/EVOH en adultos e identificar áreas de consenso, incertidumbre residual y posibles retos para su implementación. **Material y métodos:** Se realizó un estudio Delphi basado en la metodología RAND/UCLA. Expertos españoles en TPH evaluaron 33 enunciados sobre aspectos clave del manejo del SOS/EVOH en 2 rondas online. **Resultados:** 30 de 33 enunciados alcanzaron consenso (90,9%). Se consideraron apropiados 31 enunciados, incluido 1 con acuerdo neutro, mientras que 2 fueron considerados dudosos debido a un desacuerdo entre los panelistas. **Conclusiones:** Los expertos mostraron un alto grado de acuerdo con la mayoría de los componentes del marco EBMT de 2023, y se identificaron áreas de incertidumbre que pueden orientar futuras iniciativas de implementación y formación.

Palabras clave: Adulto. Consenso Delphi. Defibrotide. Enfermedad venooclusiva. Síndrome de obstrucción sinusoidal. Trasplante de progenitores hematopoyéticos

Introduction

Sinusoidal obstruction syndrome (SOS), formerly veno-occlusive disease (VOD), is a serious complication following hematopoietic stem cell transplant (HSCT).¹ In HSCT patients, conditioning chemotherapy frequently causes endothelial cell injury, compromising sinusoidal wall integrity and potentially leading to sinusoidal obstruction and post-sinusoidal portal hypertension.² SOS/VOD affects 5-15% of HSCT recipients, although its incidence varies based on patient risk factors and conditioning regimen intensity.³

Severe SOS/VOD, particularly when associated with multi-organ dysfunction (MOD) or multi-organ failure (MOF),⁴ has historically been associated with mortality exceeding 80%.⁵ The heterogeneous manifestations of SOS/VOD also complicate early diagnosis, and outcomes in severe forms may remain poor once MOD/MOF or overt organ damage develops, despite appropriate treatment.^{3,6}

Several attempts have been made to improve SOS/VOD management by developing recommendations covering pre-transplant risk stratification, diagnosis, severity grading, and treatment.^{1,7-10} The available frameworks include the classical Baltimore and Seattle criteria, the adult EBMT criteria, age-agnostic criteria, and pediatric- or adolescent/young adult-specific recommendations, which differ in their time restrictions, the role of bilirubin, the incorporation of refractory thrombocytopenia, imaging findings, and their approach to severity grading.^{1,3,9-13} These differences have a measurable effect on disease classification: a meta-analysis reported SOS/VOD incidences ranging from 17.3% with the Seattle criteria to 9.6% with the Baltimore criteria.⁵ Additional findings, including increased serum alanine aminotransferase, thrombocytopenia with rapid platelet consumption, altered hepatic venous flow on ultrasound, and liver stiffness measurements (LSM), may support earlier recognition.¹⁴

Despite these developments, relevant challenges remain, including identifying high-risk patients, early diagnosis and severity assessment, and uncertainty regarding the optimal timing and scope of defibrotide treatment.^{8,15} The 2023 EBMT update introduced probable, clinical, and proven SOS/VOD categories applicable to both classical and late-onset disease, with the aim of facilitating earlier recognition and severity assessment.¹ In addition, it also provides a common basis for assessing severity and guiding management, although its applicability may vary according to available resources, local organization, and clinical practice.

Recent national initiatives have addressed complementary aspects of adult SOS/VOD management. The Italian Delphi sought to standardize diagnostic and therapeutic pathways across centers; the UK Delphi focused on practical risk assessment and patient monitoring for prompt diagnosis; and the Australian and New Zealand practice statement summarized evidence and provided recommendations adapted to the Australasian setting.¹⁶⁻¹⁸

In contrast, the present study was not intended to generate an alternative set of recommendations, but to assess the acceptance and applicability of the 2023 EBMT adult framework among Spanish hematologists. Its specific contribution is to identify areas of national agreement and residual uncertainty that may affect implementation in Spain. These may reflect differences in healthcare organization, access to diagnostic and monitoring resources. Thus, the Delphi approach was used to assess acceptance of the updated EBMT framework and identify areas in which local practice conditions may still generate uncertainty.

We hypothesized that the updated EBMT adult framework would be broadly accepted by Spanish hematologists involved in HSCT. However, we expected residual uncertainty in areas with limited evidence, variable access to diagnostic resources, or differences across clinical practice settings. This study aimed to assess

national agreement with the 2023 EBMT adult framework for SOS/VOD management, and to identify areas of consensus, residual uncertainty, and potential implementation challenges in Spanish HSCT practice.

Materials and methods

Expert panel and study design

This consensus was designed to address SOS/VOD management in adults and included both classical SOS/VOD and late-onset SOS/VOD after HSCT. This study was conducted following the Delphi methodology developed by RAND/UCLA.¹⁹ The recommendation preparation group (RPG) comprised 5 hematology experts in SOS/VOD. The study coordinator oversaw the project's scientific direction and final selection of statements, while the remaining RPG members contributed topic-specific expertise, literature appraisal, statement development, and interpretation of the Delphi results. This consensus was developed as an independent Spanish expert Delphi initiative and was not formally endorsed by, or conducted on behalf of, a scientific society.

Of the 39 invited panelists, all were hematologists with recognized expertise in SOS/VOD management from different autonomous regions of Spain (Supplementary Fig. S1). Thirty-eight participated in round 1 and 37 completed round 2, corresponding to response rates of 97.4% and 94.9%, respectively. Panelists were selected based on their clinical experience in HSCT and SOS/VOD management, participation in transplant programs, and geographical representation across the Spanish autonomous regions. Expertise was further characterized through specific questions on transplant activity included in the questionnaire (Supplementary Figs. S2 and S3).

Literature review and statement development

A targeted PubMed literature review covering 2019–July 2023 was conducted on adult SOS/VOD after HSCT, including diagnosis, severity grading, risk assessment, differential diagnosis, prophylaxis, supportive care, defibrotide treatment, imaging, elastography, and hemodynamic assessment. The RPG reviewed the retrieved literature and included additional relevant literature where applicable. The main published diagnostic and severity grading frameworks were also considered,^{1,3,9–13} although the final statements were

anchored in the 2023 EBMT adult criteria according to the scope of the study.

Each member of the RPG was assigned 1 topic and tasked with critically reviewing the related literature, synthesizing the evidence, and proposing appropriate evidence-based statements. The proposed statements were subsequently reviewed by the entire RPG to ensure clinical relevance, minimize overlap, and harmonize terminology before the final set was submitted to the Delphi panel.

Delphi process and consensus analysis

In round 1, 33 unique statements were evaluated by the panelists. One additional statement on serial elastography was introduced in round 2 following review by the RPG. Seven statements from round 1 were re-evaluated in round 2 together with this additional statement. The baseline pre-transplant elastography statement reached agreement in round 2 but was not retained in the final reported set because the evidence supporting baseline LSM for pre-transplant risk prediction was considered insufficient at the time of the RPG review.

Each panelist rated their level of agreement with each statement using a 9-point Likert scale ranging from 1 (totally disagree) to 9 (totally agree). Panelists voted independently through an online questionnaire and were blinded to the individual ratings of the other participants. No free-text qualitative rationale was systematically collected from panelists. After the first round, the RPG reviewed the voting results and identified statements requiring re-evaluation. Only minor wording clarifications were introduced between rounds when needed, without changing the intended meaning of the statements.

According to the RAND/UCLA framework, appropriateness was determined by the median score, and the level of agreement was established according to the distribution of ratings across the 3-point regions of the 9-point scale.¹⁹ Agreement was reached when more than two-thirds of panelists rated a statement within the same 3-point region (either 1–3 or 7–9). Disagreement was defined according to the predefined RAND/UCLA distribution criteria, and a neutral result was defined when the median was 4–6 and fewer than one-third of ratings fell within either extreme region. Statements that did not reach consensus were interpreted based on voting distribution, available evidence, feasibility considerations, and discussion within the RPG.

The final wording, median scores, appropriateness classifications, and agreement levels are reported in

Table 1. Detailed voting distributions for statements reaching agreement are provided in Supplementary Table S1, and complete results for the 8 statements evaluated in round 2 are in Supplementary Table S2.

Results

Of the 33 statements included in the final analysis, 30 reached agreement (90.9%). Thirty-one statements were considered appropriate, including 1 with a neutral level of agreement, whereas 2 were rated as doubtful with disagreement among panelists. Five statements reached agreement in round 2; 4 were retained in the final set, whereas the baseline pre-transplant elastography statement was excluded because the evidence supporting its use for pre-transplant risk prediction was considered insufficient at the time of the RPG review.

The 3 statements without agreement concerned early hepatic venous pressure gradient (HVPG) measurement, busulfan-level monitoring, and the comparison between newer elastography techniques and classical Lassa radiological criteria. **Table 1** summarizes the 33 statements included in the final analysis; detailed voting distributions are provided in Supplementary Table S1, and complete round 2 results are in Supplementary Table S2.

Suspected SOS/VOD

Agreement was reached on 7 of the 8 statements addressing suspected SOS/VOD, including daily clinical and laboratory evaluations, clinical features raising suspicion, abdominal ultrasound, and consideration of therapeutic measures while diagnostic investigations are undertaken. Although panelists did not disagree with the potential usefulness of HVPG in selected situations, no consensus was achieved regarding its routine use at the earliest stage of clinical suspicion (**Table 1**, statements 1-8).

Pre-hematopoietic cell transplant risk assessment

Agreement was reached on assessment of previous potentially hepatotoxic treatments and liver involvement, the current limitations of serum biomarkers and thomboelastography as pre-transplant risk indicators, and use of the Center for International Blood and Marrow Transplant Research risk score. The statement on busulfan-level monitoring did not reach agreement and was classified as doubtful because of disagreement among the participants (**Table 1**, statements 9-14).

Differential diagnosis

The panel agreed on serial elastography or FibroScan during transplantation, the clinical utility of the 2023 EBMT probable SOS/VOD category, and the role of liver biopsy in selected differential diagnoses. In contrast, no agreement was reached on the statement comparing newer elastography techniques with classical Lassa radiological criteria (**Table 1**, statements 15-18). The baseline pre-transplant elastography statement reached agreement in round 2 but was not retained in the final reported set because the evidence supporting baseline LSM for pre-transplant SOS/VOD risk prediction was considered insufficient at the time of the RPG review, resulting in 33 statements in the final analysis (Supplementary Table S2).

SOS/VOD severity assessment

All 6 statements addressing SOS/VOD severity were considered appropriate and reached agreement, including use of the EBMT criteria at diagnosis and during disease progression, assignment of the appropriate severity category, consideration of additional risk factors, and assessment of MOD using the SOFA score (**Table 1**, statements 19-24).

SOS/VOD treatment

All 9 statements in the SOS/VOD treatment section were considered appropriate and fulfilled the criteria for agreement. These addressed timely initiation of defibrotide according to disease severity, intensified supportive care and monitoring in mild disease, bleeding-related precautions and temporary treatment interruption, treatment duration and follow-up, and avoidance of delaying SOS/VOD-specific treatment while awaiting biopsy or HVPG results (**Table 1**, statements 25-33).

Discussion

This study assessed national agreement with the 2023 EBMT adult framework and identified areas of residual uncertainty relevant to its implementation in Spanish HSCT practice. Thirty of the 33 statements included in the final analysis reached agreement, indicating broad alignment between the framework and the views of Spanish hematologists involved in HSCT. The findings were also broadly consistent with recent international consensus efforts and practice statements in adult SOS/VOD.¹⁵⁻¹⁸

Table 1. Final Delphi statements on adult SOS/VOD management and voting results included in the final analysis

Statement	M	Level of appropriateness	Level of agreement
Suspected SOS/VOD			
1. Daily clinical and laboratory evaluations of the presence of SOS/VOD should be conducted during admission	9.0	Appropriate	Agreement
2. SOS/VOD should be suspected whenever the patient has 2 or more of the following signs: bilirubin ≥ 2 mg/dL, painful hepatomegaly, weight gain $> 5\%$ and/or ascites	9.0	Appropriate	Agreement
3. If SOS/VOD is suspected, an abdominal ultrasound should be requested	9.0	Appropriate	Agreement
4. In the event of suspected moderate SOS/VOD or higher, a hepatic venous gradient determination is recommended [†]	8.0	Appropriate	Agreement
5. In the event of suspicion of SOS/VOD, in addition to imaging and/or hemodynamic tests, the initiation of therapeutic measures should be considered	9.0	Appropriate	Agreement
6. If SOS/VOD is suspected to be of moderate severity or higher, treatment with defibrotide should be initiated [§]	9.0	Appropriate	Agreement
7. In high-risk patients if there are signs of suspected SOS/VOD, therapeutic measures should start without waiting for confirmatory tests (or confirmed diagnosis)	9.0	Appropriate	Agreement
8. At the first suspicion of SOS/VOD, a hepatic venous gradient determination should be requested [†]	7.0	Appropriate	Neutral
Pre-hematopoietic cell transplant risk assessment			
9. The risk/benefit of prior use of drugs conjugated with calicheamicin derivatives (gemtuzumab-ozogamicin and inotuzumab-ozogamicin), as well as oxaliplatin, should be assessed, as they may increase the risk of SOS/VOD after transplantation	9.0	Appropriate	Agreement
10. Patients with a history of liver involvement, regardless of the cause, are at increased risk of developing SOS/VOD	9.0	Appropriate	Agreement
11. Serum biomarkers are not currently indicated as pre-transplant risk indicators for SOS/VOD	8.0	Appropriate	Agreement
12. Thromboelastography as a technique for assessing procoagulant status is not currently indicated as a pre-transplant risk indicator for SOS/VOD	8.0	Appropriate	Agreement
13. The CIBMTR pre-transplant score evaluates the risk of SOS/VOD based on the patient's age, performance status, use of sirolimus, conditioning used, history of HCV and/or HBV infection, and primary disease, but is not adapted to the pediatric population or second transplants	8.0	Appropriate	Agreement
14. If available, monitoring of busulfan levels is recommended	6.0	Doubtful	Disagreement
Differential diagnosis			
15. Serial elastography or fibroscan throughout the transplant can predict the development of SOS/VOD	9.0	Appropriate	Agreement
16. The new category of probable diagnosis of SOS/VOD according to the European Society for Blood and Marrow Transplantation (EBMT) 2023 criteria facilitates the decision to start treatment based on the criteria of risk and severity of the complication	9.0	Appropriate	Agreement
17. Liver biopsy, particularly transjugular biopsy, remains very useful for differential diagnosis in patients with suspected SOS/VOD and other post-transplant liver complications	9.0	Appropriate	Agreement
18. New elastography techniques are better than classic Lussau radiological criteria	5.0	Doubtful	Disagreement
SOS/VOD severity assessment			
19. The severity of SOS/VOD should be evaluated according to EBMT severity criteria in all patients at diagnosis and during disease progression, considering the time of onset, bilirubin number and kinetics, transaminase number, weight gain, and renal function	9.0	Appropriate	Agreement
20. It is recommended that the severity category be assigned when the patient meets 2 or more criteria in one of those categories	9.0	Appropriate	Agreement
21. If patients meet 2 or more criteria in different categories, they should be classified into the highest risk category	9.0	Appropriate	Agreement
22. Patients with criteria for mild SOS/VOD, but with 2 or more risk factors for SOS/VOD should be directly classified as moderate-risk SOS/VOD	9.0	Appropriate	Agreement
23. Multiorgan dysfunction, which classifies SOS/VOD as very severe, should be defined using the SOFA scoring scale when ≥ 2 organs have a score of ≥ 2 or with an increase of ≥ 2 points in previously affected organs	9.0	Appropriate	Agreement
24. Since most patients have bilirubin levels ≥ 2 mg/dL, which corresponds to at least a grade 2 of liver involvement on the SOFA scale, the presence of any failure of another organ with a score of ≥ 2 on this scale leads to the diagnosis of multi-organ failure and therefore very severe SOS/VOD	8.0	Appropriate	Agreement

(Continúa)

Table 1. Final Delphi statements on adult SOS/VOD management and voting results included in the final analysis (continuación)

Statement	M	Level of appropriateness	Level of agreement
SOS/VOD treatment			
25. Treatment with defibrotide should be initiated as soon as possible after diagnostic confirmation (probable, clinical, proven) due to the high mortality associated with severe or very severe SOS/VOD	9.0	Appropriate	Agreement
26. Treatment in < 2-3 days is recommended in cases of moderate SOS/VOD	9.0	Appropriate	Agreement
27. In patients with mild SOS/VOD, supportive care should be intensified and severe criteria monitoring strictly applied to allow immediate initiation of defibrotide in case of progression to other severity criteria	9.0	Appropriate	Agreement
28. In patients treated with defibrotide, any other agents that may increase the risk of bleeding should be discontinued, keeping the threshold for platelet transfusion at $30 \times 10^9/L$	8.0	Appropriate	Agreement
29. For invasive procedures, defibrotide should be discontinued at least 2 h before and 2 h after the procedure	8.0	Appropriate	Agreement
30. In patients with life-threatening bleeding, defibrotide should be discontinued immediately, and its resumption should be assessed on a risk/benefit basis	9.0	Appropriate	Agreement
31. The recommended duration of treatment with defibrotide is at least 21 days, and until resolution of all SOS/VOD symptoms	8.0	Appropriate	Agreement
32. Close follow-up is recommended for patients in whom defibrotide treatment is discontinued before the recommended 21 days, as recurrences may rarely occur	8.5	Appropriate	Agreement
33. It is not recommended to wait for the results of biopsy and/or portal pressure gradient measurement to initiate SOS/VOD-specific treatment	9.0	Appropriate	Agreement

*Statements approved in the second Delphi round.

†Statements not approved.

‡Hepatic venous gradient determination refers to hepatic venous pressure gradient (HVPG) measurement, an invasive transjugular hemodynamic assessment.

§Treatment-related statements should be interpreted within the EBMT adult framework and the Spanish/European clinical and regulatory context.

¶The platelet threshold should be interpreted as a precautionary target and applied whenever clinically feasible. Detailed voting distributions for statements reaching agreement in the final analysis are reported in Supplementary Table S1, while the complete results of the eight statements evaluated in round 2 are provided in Supplementary Table S2.

CIBMTR: center for International Blood and Marrow Transplant Research; EBMT: European Society for Blood and Marrow Transplantation; HBV: hepatitis B virus; HCV: hepatitis C virus; M: median; SOFA: sequential Organ Failure Assessment; SOS/VOD: sinusoidal obstruction syndrome/veno-occlusive disease.

Notably, this Delphi was not designed to generate new clinical recommendations, compare or validate competing diagnostic criteria, assess adherence in routine care, or establish clinical effectiveness. Accordingly, the findings of this Delphi should be interpreted as structured expert agreement rather than as high-level clinical evidence or validation of the endorsed diagnostic or therapeutic strategies.

Regarding diagnostic suspicion, the panel supported daily clinical and laboratory assessment, maintenance of a high level of suspicion, and abdominal ultrasound when SOS/VOD is suspected. The panel also supported early consideration of therapeutic measures when SOS/VOD is suspected. The term “suspected SOS/VOD” should be understood as a dynamic clinical alert state that can precede fulfillment of probable or clinical diagnostic criteria, especially in high-risk patients.

HVPG measurement represented one area of residual uncertainty. Although its use in suspected moderate or more severe SOS/VOD reached agreement, requesting HVPG at first suspicion of disease did not. This may reflect its invasive nature, limited availability outside specialized centers, and the limitations of HVPG as a

stand-alone diagnostic test, particularly at the earliest stage of clinical suspicion.^{1,20}

The level of agreement on pre-transplantation risk assessment was also very high. Interestingly, the only statement that generated disagreement concerned busulfan-level monitoring. Higher systemic busulfan exposure has been associated with an increased risk of SOS/VOD, providing a rationale for pharmacokinetic-guided dosing.^{21,22} Differences in access to therapeutic drug monitoring and the organizational requirements needed for its implementation may therefore have influenced panelists’ assessment. Thus, this disagreement may partly reflect heterogeneity among Spanish HSCT centers rather than purely scientific disagreement about its potential value.

The panel also agreed on assessment of previous potentially hepatotoxic treatments and pre-existing liver involvement, whereas serum biomarkers and thromboelastography were not considered established pre-transplant risk indicators.

Regarding the diagnostic role of elastography, the Delphi supported serial elastography or FibroScan during transplantation as a potential aid to early

SOS/VOD detection. Available evidence predominantly supports dynamic changes in liver stiffness during the transplant period as an adjunct to clinical and ultrasound assessment rather than as a stand-alone diagnostic test.²³⁻²⁵ However, the panel did not reach agreement on the statement comparing newer elastography techniques with classical Lassau radiological criteria, which may partially reflect that these approaches provide different types of information and are not necessarily intended as directly interchangeable diagnostic tools.

Baseline pre-transplant elastography requires a different interpretation. Although the corresponding statement reached agreement in round 2, evidence supporting baseline LSM as a pre-transplant predictor of SOS/VOD was limited at the time of the RPG review, and the statement was therefore not retained in the final reported set. Early studies suggested a potential predictive role for pre-HSCT LSM,²⁶ and more recent data have provided additional support for baseline liver stiffness as a marker of SOS/VOD risk.^{27,28} However, these findings should be interpreted cautiously because evidence for pre-transplant risk prediction remains less established than that supporting dynamic post-transplant LSM changes for early diagnosis and monitoring.^{24,25} This discrepancy illustrates an inherent limitation of Delphi-based consensus processes: expert agreement may reflect the evidence and clinical perceptions available at the time of voting and may require reinterpretation as new prospective evidence becomes available.

Further investigation is warranted to clarify the comparative performance of elastography and conventional imaging, the value of serial LSM changes, and their optimal integration into diagnostic pathways. Moreover, differences in access to elastography platforms, operator expertise, and standardized monitoring protocols across centers may further contribute to variability in clinical practice and expert opinion.

Other diagnostic and severity-related findings were more consistent. The probable SOS/VOD category introduced by the 2023 EBMT criteria was favorably assessed, liver biopsy was considered useful in selected cases when alternative post-transplant liver complications are suspected, and all severity assessment statements reached agreement.

Finally, all the statements related to the treatment reached agreement among panelists, particularly those addressing early recognition, timely initiation of defibrotide according to disease severity, intensified supportive care and surveillance in milder disease, and

avoidance of delaying SOS/VOD-specific treatment while awaiting invasive diagnostic procedures. Observational evidence has associated earlier defibrotide initiation after diagnosis with improved outcomes;⁶ however, the present Delphi does not provide comparative evidence of treatment effectiveness and cannot establish that the endorsed treatment strategies improve clinical outcomes.

Safety-related statements included discontinuation of concomitant agents that may increase bleeding risk, temporary interruption of defibrotide around invasive procedures²⁹ or in life-threatening bleeding, and maintenance of a platelet transfusion threshold of $30 \times 10^9/L$ whenever clinically feasible. These should be interpreted as precautionary safety measures within the Spanish and European clinical context rather than as evidence that a particular platelet threshold has been proven to reduce bleeding risk. Experts agreed on treatment for at least 21 days and until resolution of SOS/VOD manifestations, with close monitoring recommended when treatment is discontinued earlier.

The main finding of this study has been the high degree of acceptance and consensus regarding the management of adult SOS/VOD, which supports the expected alignment between the updated EBMT framework and the views of Spanish hematologists involved in HSCT. The Delphi identified areas of strong agreement and residual uncertainty across SOS/VOD management.

Overall, the areas without agreement – early HVP measurement, busulfan-level monitoring, and the relative performance of newer elastography techniques – concentrated around interventions for which evidence, availability, or implementation may vary across centers. These findings help distinguish areas of broad national agreement with the EBMT framework from residual uncertainties that may warrant further evidence generation and implementation work in Spanish HSCT practice.

Conclusion

This study shows a high degree of agreement among hematologists actively involved in transplantation on most components of the 2023 EBMT adult framework for SOS/VOD management. This research also underscores the value of Delphi studies for pinpointing areas of consensus and persistent disagreements that may influence implementation in clinical practice. By mapping where consensus is strong and where uncertainty persists, this work lays the groundwork for

strengthening the implementation of adult SOS/VOD recommendations in Spain, with the ultimate goal of promoting earlier recognition and timely management of this potentially life-threatening complication.

Author contributions

D. Valcarcel was coordinator of the project, and he and M.J. Pascual-Cascón, R.F. Duarte, J. Sanz, and L. Yáñez San-Segundo were members of the RPG. All the authors contributed according to ICMJE guidelines for the authorship of the manuscript.

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Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

Supplementary data

Supplementary data are available at 10.24875/SANGREE.26000010. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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