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Portuguese Consensus and Recommendations for Acquired Coagulopathic Bleeding Management (CCBM)

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Abstract

We aimed to determine how Portuguese physicians handle major bleeding. We also aim to establish global diagnostic and therapeutic recommendations to be followed in clinical practice by using a step-wise approach of evidence generation. This study followed a three-step process: a steering committee desk review, a Delphi technique, an expert panel meeting. A modified 3-round Delphi including 31 statements was performed. Questions were answered in a five-point Likert-type scale. Consensus threshold was established as a percentage of agreement among participants $\geq$90% in the first round, and $\geq$85% in the second and third rounds. The level of consensus achieved by panelists was discussed with the scientific committee (January-2020). Fifty-one physicians participated in the study (compliance rate >90%). Analyzing the three rounds, consensus was reached on 20 items (64.5%) in the first, 4/11 items (36.4%) in the second and 6/7 items (85.7%) in the third. One statement about administration of clotting factor concentrates for bleeding control did not reach consensus. A high level of consensus was reached toward the need for implementing Patient Blood Management strategies in Portuguese hospitals, reduce exposure to allogeneic blood components, to use goal directed therapies for acquired bleeding management, and the need for evaluating blood transfusion indirect costs. A final version with 12 recommendations was built, according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE). Our results provide critically appraised and updated evidence on bleeding coagulopathies management in Portugal. Additional studies, mainly about indirect costs of blood transfusion, are needed.

Keywords

acquired blood coagulation disorders, bleeding management, consensus, delphi technique, grade approach

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Introduction

In the past decades, the early diagnosis and treatment of acquired coagulopathy associated with different clinical scenarios including perioperative hemorrhage, trauma and obstetric complications has evolved. A more accurate scientific knowledge of the pathophysiological mechanisms underlying these situations, together with a better understanding of clot characteristics (formation, stability and lysis in real time) provided by accurate and dynamic monitoring, and the availability of different hemostatic agents, used alone or in combination, supported better clinical decisions.[1-3]

The therapeutic strategy for acute bleeding is mainly based on two approaches: (i) the use of predefined transfused ratios with variable combination of red cell concentrate, fresh frozen plasma and platelet concentrate (the ratio of 1:1:1 is usually

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associated with better outcomes) or (ii) the use of individualized goal-directed therapy, where different clusters of coagulation factors and pharmacological agents can be employed.[4-8] This last approach usually relies on close monitoring on clot formation and lyses by viscoelastic tests.

Blood transfusion is a sparse resource and is associated with several risks including human error and potential harmful effects that are recognized by most physicians. These are the main reasons why there is an increasing concern for the development of a quick and effective diagnostic and treatment approach to control severe bleeding in any clinical setting.

In schedule surgery, which in many cases depends on blood transfusion, there is a broader concept of strategies to save patient's blood, known as "patient blood management" (PBM). PBM seeks to systematically organize patients' multiple clinical characteristics with the ultimate goal of optimizing erythropoiesis, minimizing bleeding and managing anemia tolerance, both in the pre-, intra- and post-operative periods.[9]

Broad concepts like PBM, but also others like viscoelastic testing, use of predefined ratios or goal directed therapy for the control of coagulopathic bleeding in different clinical scenarios are commonly discussed and have been the subject of several studies.

Having this complex context in mind and given the possible diagnostic and therapeutic options and the diverse healthcare scenarios among institutions and geographic regions in Portugal (e.g. therapeutic access, know-how, diagnostic framework), we aimed to determine how Portuguese physicians handle major bleeding management. We also aim to establish global diagnostic and therapeutic recommendations to be followed in clinical practice by using a step-wise approach of evidence generation.

Methods

To produce a list of recommendations, a three-step process was created: (1) a steering committee desk review, (2) Delphi technique, and (3) an expert panel meeting.

First, an ad hoc created steering committee constituted by five portuguese physicians, specialists in immunohemotherapy (3) and anesthesiology (2) with national responsibility and expertise in bleeding control, met on May 2019 to elaborate an initial list of statements based on an unstructured desk review performed by these practitioners. In this review, recommendations and guidelines from several international societies were taken in consideration.

Second, a modified Delphi technique was designed as a 3-round exercise to obtained possible agreement on bleeding coagulopathies management with a broad panel of medical experts. The expert panel consisted of 51 physicians (including immunohemotherapy, anesthesiology, and critical care specialists) with clinical expertise in major bleeding management, from public and private portuguese hospitals, geographically distributed to capture any regional specificities (North, Center and South Portugal). This panel of physicians where chosen based on their established scientific or academic activities, participation on government working parties, alongside with clinical practice. To each one the goal of the study was fully explained in a personal interview, and they all gave their written consent.

Because the Delphi rounds were completed anonymously and no personal data were collected, institutional review board approval was not necessary under Portuguese legislation. The list of statements created by the steering committee during the first stage was used for the Delphi exercise. The panel of experts should answer to each statement their degree of agreement, using a five-point, ordinal, Likert-type scale. The scale was rated as "strongly disagree," "disagree," "neither agree nor disagree," "agree," and "strongly agree." Additionally, panel members during rounds 1 and 2 had the opportunity to add comments to each statement in free-text boxes. The modified Delphi study run between October 2019 and December 2019. Panel members answered via online survey platform at each round (Welphi Platform; https://www.welphi.com). In rounds 2 and 3, panel members contrasted their previous round personal opinion with other participants' opinions. Participants were allowed to reconsider their initial opinion when they intended to, after the first round of Delphi panel. In the second round, relevant comments from first round could originate modifications in the description of statements, or addition of new statements. For the purpose of the analysis, the answers given to categories "strongly agree" and "agree," or on the categories "strongly disagree" and "disagree" were aggregated into "positive consensus" and "negative consensus," respectively. Consensus threshold was established as a percentage of agreement among the participants equal or greater to 90% in the first round; and equal or greater to 85% in the second and third rounds. A statement that did not reach consensus on the first round followed for the next round and so on. As convergence indicators, the percentage variation of the concordance ratio between rounds was used. Stability analyses were assessed by the proportion of experts who varied their inter-round response.

Third, on January 2020, the steering committee together with experts in the Delphi technique, constituted a focus group to analyze the results of the Delphi exercise. The aim of this final meeting was to critically appraise the agreed statements that in theory put in evidence the real-life clinical reality in our country. The steering committee also intended to obtain practice based recommendations for the management of major bleeding, that were graded according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group, based on the Oxford Centre for Evidence-based Medicine.[10]

Results

During the initial steering committee meeting, a list of global statements, including topics on, blood transfusion, implementation of PBM in Portuguese hospitals, major bleeding management in surgery, trauma and obstetrics, use of viscoelastic testing, goal directed therapy versus fixed ratios and

therapeutic associated direct and indirect costs associated with major bleeding was created. The final Delphi questionnaire developed by the committee initially included 31 statements (items) (Table 1). These statements aim at reflecting global aspects in the approach of coagulopathy, and were based on recommendations from international societies or issues that are presently under discussion among the scientific community. They do not pretend to enter in deep particular clinical situations.

In the Delphi first round, all 51 experts completed the Delphi exercise, while in the following second and third rounds, 48 (94.11% response rate) and 47 (97.91% response rate) experts completed the task, respectively. No new items were proposed during the exercise. One item (statement n. 11) had its text reformulated after the first round by the scientific committee to improve interpretability.

In the first round, consensus was reached on 20 of the 31 items (64.5%), all of them with positive agreement. Eleven remaining items were returned for reconsideration in the second round, where four of them (36.4%) reached consensus (three in agreement and one in disagreement). During the third round with the remaining seven non-consensual statements, six (85.7%) obtained consensus (two in positive agreement and four in disagreement) (Figure 1). One final statement did not reach consensus (item n. 29). Table 1 presents the global results for all the evaluated statements. Supplemental material (Tables S1, S2, and S3) provides complete details of the Delphi technique analysis in the original language (Portuguese). The comments provided by the expert panel members during the Delphi exercise considered the need of aligning recommendations with different clinical situations.

Some variations in the responses between rounds were observed. The median variation in agreement rates between first and second rounds was of 3.06% [IQR −1.41, 7.23], while between second and third rounds of −4.08% [IQR −7.14, 8.07]. Median variation in disagreement rates between first and second rounds was 1.99% [IQR −1.84, 3.62]; between second and third rounds of 8.02% [IQR −2.04, 10.20]). Statements n. 15 and 29 presented the highest changes in agreement rates: 16.5% and 9.68% between first and second rounds, and 8.1% and 14.2% between second and third rounds, respectively. Statement n. 27 showed more variation in the disagreement rates: 4.78% between first and second rounds and 10.24% between second and third rounds (see Supplemental Material Table S4).

In the final meeting, the focus group elaborated 12 recommendations that were built grounded on the consensual opinion of the 51 Portuguese physicians who participated in the Delphi exercise, and were simultaneously supported by the current scientific best evidence. Table 2 presents these 12 recommendations, as well as the scientific references supporting them. Recommendations were mainly graded as A-B, as originated from systematic reviews and primary studies (e.g. randomized controlled trials, cohort studies).

Discussion

We were able to perform a nationwide, multidisciplinary-based study that generated agreement endpoints to reinforce clinical practice, or supplement existing guidance on bleeding coagulopathies management. With the results of this study we developed critically appraised evidence-based recommendations to manage major bleeding clinical settings in our country.

The Delphi approach we used has the advantage of avoiding the dominant personality effect due to the anonymous responses, and allows for the re-evaluation of panelists opinions in the light of group answers, without losing the gains from face-to-face discussions.[41-43] Studies also state the added value of comments allowed in the Delphi exercise along with personal interaction as a way of supporting the change on the level of agreement between rounds or to detail the reasons behind a lack of consensus.[44,45]

Globally the participation of the panelists in the three rounds of the Delphi panel was over 90% and this fact highlights the interest and importance of this field and reinforces the value of these statements.

From the 31 statements enrolled in the Delphi questionnaire, only one (3.2%) (statement 29—"*In the face of active bleeding with coagulation changes, the first therapeutic option is to use clotting factor concentrates*") did not reach consensus by the end of the exercise. In our opinion this reflects a particular and important issue that is not consensual among the international scientific community.

Therapeutic approaches for improving hemostasis in cases of bleeding depends on its severity, and include allogeneic blood product administration, pharmacologic agents (ie, tranexamic acid), with an increasing use of clotting factor concentrates like fibrinogen and prothrombin complex concentrate.[46] Clotting factor concentrates may be administered in different regimens depending on the patient's level of severity, anatomical bleeding localization, comorbidities, and treating recommendations. However, the available evidence on the benefit/risk ratio of using clotting factor concentrates for decreasing bleeding and related complications, in different clinical situations, is still not widely accepted.[47-49]

Most physicians recognize the potential harmful effects of transfusion therapy and try to avoid exposure to allogeneic blood. We found a high level of consensus for the use of transfusion strategy to reduce exposure to allogeneic blood products (recommendation 1).

A high level of consensus was also achieved regarding the need for implementation of PBM strategies in Portuguese hospitals (recommendation 2). Worldwide, PBM is emerging as a multidisciplinary, multimodality strategy to address anemia and decrease bleeding, with the goal of reducing transfusions and improving patient outcomes.[9,50,11] This approach includes early preoperative recognition and treatment of anemic patients, surgical efforts to minimize blood loss, early management of coagulopathy among other strategies.[5,9]

PBM programs, which are recommended by the World Health Organization since 2010, can minimize healthcare risks

Table 1. Results of the Delphi Exercise.

Order	Statements*	Positive agreement %	Negative agreement %	Number answers	Round of consensus
1	The implementation of Patient Blood Management strategies promotes the reduction in the use of allogeneic components (fresh frozen plasma, platelet concentrate, and erythrocyte concentrate)	100.00	0.00	51	First
2	The implementation of Patient Blood Management strategies promotes a reduction in complications associated with transfusion	98.04	0.00	51	First
3	Patient Blood Management strategies ensure the best clinical outcomes for patients (lowest rates of morbidity and mortality)	98.04	0.00	51	First
4	Patient Blood Management strategies reduce the total associated costs with bleeding management	100.00	0.00	51	First
5	The implementation of Patient Blood Management strategies is necessary	100.00	0.00	51	First
6	In Portuguese hospitals, the implementation of Patient Blood Management strategies is feasible	98.04	1.96	51	First
7	Massive hemorrhage and transfusion of fibrinogen concentrate, fresh frozen plasma and platelet concentrate are associated with increased morbidity and mortality	98.04	1.96	51	First
8	The cost/effectiveness of using predefined transfusion ratios (fresh frozen plasma + platelet concentrate + erythrocyte concentrate) has not yet been demonstrated	85.11	4.26	48	Third
9	Transfusions of allogeneic components increase morbidity and mortality	90.20	1.96	51	First
10	Transfusions of allogeneic components increase total costs	92.16	0.00	51	First
11	CRITERION FIRST ROUND: Indirect costs associated with adverse events of the transfusion have minimal impact on hospital costs. REFORMULATED CRITERION: Indirect costs associated with adverse events of the transfusion have a reduced impact on hospital costs.	4.26	89.36	48	Third
12	It is also acceptable and effective to use predefined transfusion ratios compared to the targeted administration of clotting factor concentrates	8.51	89.36	48	Third
13	The use of goal-directed therapy strategies, using concentrated clotting factors, reduces the costs associated with transfusion, trauma, heart surgery and liver transplantation	92.16	0.00	51	First
14	The use of strategies based on the administration of clotting factor concentrates reduces transfusions of allogeneic components.	96.08	0.00	51	First
15	The use of strategies based on the administration of clotting factor concentrates reduces costs.	89.36	0.00	48	Third
16	Viscoelastic tests used to guide targeted therapy increase global hospital costs.	4.17	89.58	48	Second
17	The use of coagulation factors concentrates based on goal-directed therapy, although increasing direct costs, decreases total costs	89.58	2.08	48	Second
18	One of the great advantages of viscoelastic tests is to provide quickly understanding of the coagulation process and guide early actions, depending on the results of the tests	98.04	0.00	51	First
19	In the context of elective surgery, the control of coagulopathy guided by viscoelastic tests reduces the need for transfusions	90.20	1.96	51	First
20	Administration of tranexamic acid reduces perioperative bleeding	90.20	1.96	51	First
21	In trauma, the administration of tranexamic acid is cost-effective	94.12	1.96	51	First
22	Administration of tranexamic acid reduces postpartum hemorrhage	96.08	1.96	51	First
23	The use of fibrinogen concentrate is important for the rapid and effective control of bleeding	90.20	0.00	51	First
24	The administration of fibrinogen concentrate reduces the need for transfusion of allogeneic components, minimizing the risks of this procedure	94.12	0.00	51	First
25	The administration of fibrinogen concentrate reduces the need for transfusion of allogeneic components and reduces the total costs of bleeding management	89.58	0.00	48	Second
26	The administration of fibrinogen concentrate is permissible, even if laboratory results are not available	85.42	4.17	48	Second
27	Fresh frozen plasma can be used to effectively restore fibrinogen levels	2.13	91.49	47	Third
28	In the face of active bleeding with coagulation changes, the first therapeutic option is fresh frozen plasma	6.38	85.11	47	Third
29	In the face of active bleeding with coagulation changes, the first therapeutic option is to use clotting factor concentrates	78.72	12.77	47	Not reached

(continued)

Table 1. (continued)

Order	Statements*	Positive agreement %	Negative agreement %	Number answers	Round of consensus
30	I recognize the fundamental role of early administration of fibrinogen concentrate in situations of bleeding	92.16	0.00	51	First
31	I recognize the importance of the availability of viscoelastic tests in Portuguese hospitals	96.08	0.00	51	First

*The original version of the Delphi exercise (Portuguese language) is available in supplemental material.

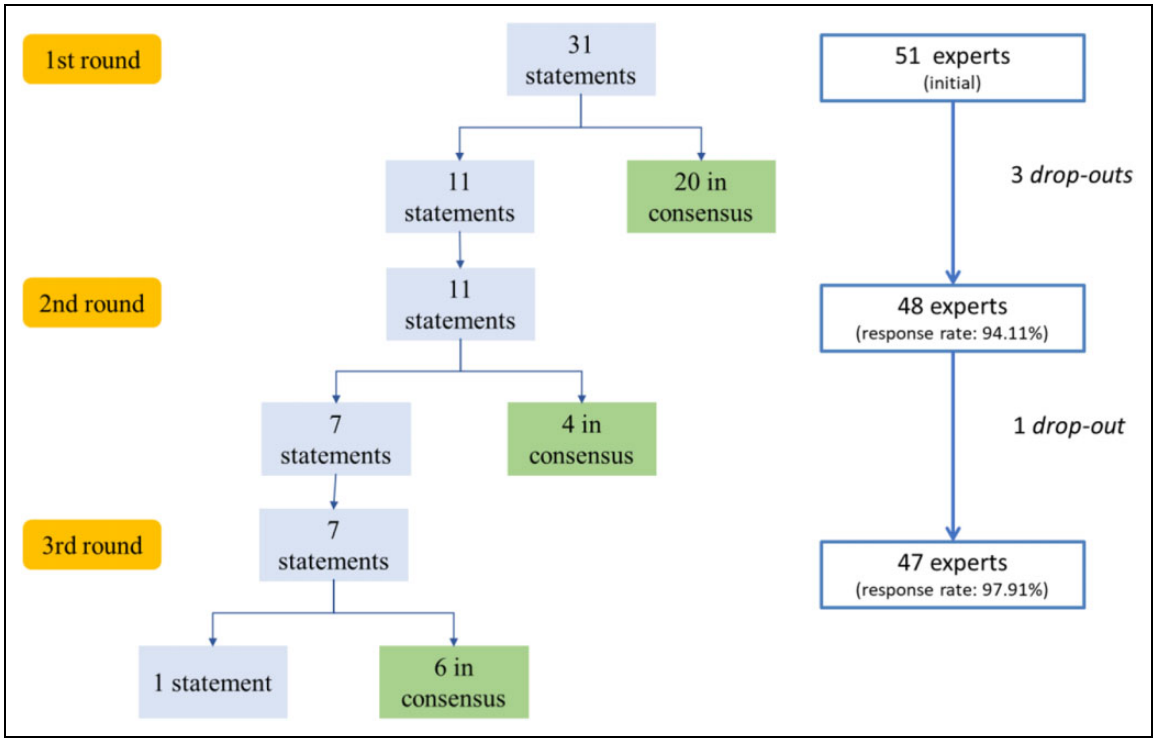

Figure 1. Flowchart of the consensus obtained in the Delphi study.

and reduce hospital costs.[51,52] Studies show that the implementation of a transfusion strategy program can reduce the use of all allogeneic blood components by around 30%, decrease death rate by 40 to 50% and post-surgical hospital costs to upon 50%.[53,54,12] Portugal is trying to implement, at a national level, a PBM program. The first normative for elective surgeries was published in 2018, aiming to reduce costs for our national health service (SNS). However, further efforts are still needed, including audit of hospitals transfusion practices, educational programs, reformulation of the computerized systems for the prescription of blood components and clinical protocols, both promoted by hospital administration, clinical committees, and scientific organizations. Nevertheless, some hospitals have already developed PBM programs.

During our exercise, there was a clear consensus on the early use of tranexamic acid in post-partum hemorrhage (PPH), coagulopathy of trauma, and in perioperative bleeding (recommendations 3, 4 and 5). Tranexamic acid is an antifibrinolytic drug which reduces the breakdown of blood clot and is known to reduce serious bleeding.[4,18,19,20] A recent meta-analysis of individual patient-level data showed that the administration of tranexamic acid significantly increases overall survival from bleeding (OR 1.20 [95% CI 1.08-1.33]; $P = 0.001$) in cases of trauma or PPH. However, treatment delay reduced tranexamic clinical benefit ($P < 0.0001$), whereas immediate treatment improved survival by more than 70%. Thereafter, in PPH the survival benefit decreased by 10% for every 15 min of treatment delay until 3 hours, after which there was no evident benefit,[21] thus, the need for clear protocols for prompt treatment is obvious.

We also found that more than 85% of panelists supported the use of fibrinogen concentrate in severe bleeding scenarios with acquired coagulopathy, even if laboratory results are not available as quickly as needed. The use of fresh frozen plasma (FFP) as a source of fibrinogen supplementation was not recommended (recommendations 6, 7, 8 and 9). Among the hemostatic

Table 2. Recommendations for the Management of Bleeding Coagulopathies.

N	Recommendations	GRADE	References
1	We recommend a transfusion strategy that reduces exposure to allogeneic blood products	1A	9,11,12,13-17
2	We recommend the implementation of Patient Blood Management strategies in Portuguese hospitals	1A	9,11,12,13-17
3	We recommend the early use of tranexamic acid in post-partum hemorrhage	1A	18-21,22,23
4	We recommend the early use of tranexamic acid in trauma coagulopathy	1A	18-21,22,23
5	We recommend the early use of tranexamic acid in perioperative bleeding	1B	18-21,22,23
6	We recommend the supplementation of fibrinogen with fibrinogen concentrate in acquired bleeding settings	1B	24,25,26,27-32
7	We recommend administration of fibrinogen concentrate early in the process of controlling acquired coagulopathy associated with bleeding clinical settings	1C	24,25,26,27-32
8	We recommend the administration of fibrinogen concentrate in severe bleeding even if laboratory results are not available at the time of its administration	2C	24,25,26,27-32
9	We recommend against the use of fresh frozen plasma as a source of fibrinogen supplementation	1A	24,25,26,27-32
10	We recommend the widespread use of viscoelastic tests in Portuguese hospitals, to allow goal-directed therapy	1B	4,22,28,33-36
11	We recommend the use of goal-directed therapeutic strategies using viscoelastic tests and coagulation factor concentrates in any clinical situation associated with severe bleeding	1B	4,22,28,33-36
12	We recommend that in the evaluation of costs associated with blood transfusion, indirect costs should be taken in consideration	2C	2,37,29,35,38-40

treatments available, fibrinogen replacement has become the standard-of-care in several major surgical centers in Europe and is recommended in current trauma treatment guidelines, and others European Guidelines.[5,55,24,56,25,26] Fibrinogen is the first coagulation factor to reach a critically low concentration during bleeding and subsequent activation of coagulation, and this reduction is associated with a worse outcome in injured patients.[46,24]

The expert panel also agreed on recommending the use of goal-directed therapeutic strategies based on viscoelastic testing (VET) and coagulation factor concentrates in Portuguese hospitals (recommendations 10 and 11). VET are point-of-care tests commonly used to provide prompt diagnosis of coagulopathy and allow quick and targeted treatments in bleeding patients. These tests have also been shown to be cost effective in both cardiac surgery and trauma.[57] A recent meta-analysis demonstrated that the use of thromboelastography (TEG®) or thromboelastometry (ROTEM®) guided treatment algorithm resulting in reductions of red blood cells (RR 0.88 [95% CI 0.79-0.97]) and platelets transfusions (RR 0.78 [95 CI 0.66-0.93]).[58] So the implementation of point-of-care coagulation management algorithms is strongly suggested.

Finally, costs evaluations of blood transfusion should take into consideration indirect costs (recommendation 12). Economic evaluation in health care generally classifies costs as direct, indirect, and intangible. Direct costs include resources associated with the provision of a treatment. Indirect costs refer to productivity, loss incurred by a clinical condition, and intangible costs like pain and sufferings by patients, which are usually difficult to quantify in economic terms.[59,60] In a study published in 2011, the weighted average cost of transfusion (two-unit red blood cells transfusion) was EUR 877.69 (data from the United Kingdom, Sweden, Switzerland, Austria, and France).[61] However, the important methodological variations between studies may have influenced the magnitude and precision of our cost calculation, potentially underestimating the true (both direct and indirect) cost of transfusions. Future cost-effectiveness studies should consider costs with hospital stay, nursing, medication, related adverse events treatment, access and transport of blood components, and evaluate patients' experiences.

However, given the difficulties of performing interventional studies across the world in this field (e.g. rare conditions, few available patients, need of critical clinical care), different approaches should be considered. Real-world data from national registries can provide credible evidence (e.g. disease prevalence, clinical and treatments scenarios) to medical experts and healthcare providers on acquired bleeding coagulopathies. Some countries[62-65] have already national registries for inherited bleeding disorders, allowing easy and permanent access to patients' data which favors prompt treatment, improves quality of care and facilitates administrative, statistical, economic and research activities. It could be beneficial to develop an informative tool implemented at a nationwide level to guide better healthcare decisions for the management of acquired hemorrhagic coagulopathies.

Our study has some limitations. The exercise is based on expert opinion rather than patient level data; however, the Delphi technique is a widely used and accepted method for achieving convergence and is well recognized as a qualitative technique for data elicitation.

Additionally, the 31 statements developed by the steering committee covered a wide and global spectrum of issues related with the diagnose and treatment of major bleeding in three different scenarios (perioperative, obstetric and trauma coagulopathy).We did not enter in detail in each one of these situations, and the 12 recommendations follow the same

rational idea, so we think that this work should be continued and complemented.

Conclusions

The results of this study are a first step toward providing updated estimates for bleeding coagulopathies management. We highly recommend the implementation of PBM, use of viscoelastic tests to monitor hemostasis, administration of tranexamic acid, fibrinogen concentrates, to be able to use a goal-directed algorithm for bleeding patient's management in Portuguese hospitals. The expert committee also highlighted the need of a national registry including these patients. Our results should be supplemented by additional studies, exploring treatment algorithms, therapy access, patient's adherence, and direct and indirect costs.

Informed consent for patient information to be published in this article was not obtained because no clinical data on any patient was collected. However informed consent was obtained from the physicians who participated in this study.

Authors' Note

The CCBM project group members are José Aguiar, Hospital Geral Santo António; Maria João Aguiar, Hospital Curry Cabral; Claudia Almeida, Centro Hospitalar São João, Porto; Ângela Alves, Hospital de Santa Maria; Daniel Alves, Hospital de Santarém; Sofia Appleton, Centro Hospitalar do Oeste; Teresa Araujo, Hospital Curry Cabral; Carla Bentes, Centro Hospitalar Vila Nova de Gaia/Espinho; Carlos Bento, Centro Hospitalar de Coimbra, Coimbra; André Caiado, Hospital de São José; Cristina Carmona, Hospital Fernando da Fonseca; Alexandre Carrilho, Hospital de São José; Joana Carvalhas, Centro Hospitalar de Coimbra, Coimbra; Manuela Carvalho, Centro Hospitalar São João, Porto; Manuela Castro, Hospital Fernando da Fonseca; Cristina Catarino, Hospital de Santa Maria; Patrícia Conde, Hospital de Santa Maria; Sandra Dias, Hospital Curry Cabral; José Luís Ferreira, Hospital da Estefânia; Susana Fevereiro, Hospital de Santa Cruz; Isabel Fragata, Hospital de Santa Marta; Ana Garção, Hospital de Santa Maria; Miguel Ghira, Hospital Beatriz Ângelo; Manuela Gomes, Hospital da Luz; Pedro Gomes, Hospital da Luz; Helena Gomes, Centro Hospitalar Vila Nova de Gaia/Espinho; Luciana Gonçalves, Centro Hospitalar São João, Porto; Miguel Jorreto, Hospital Viana do castelo; Filipa Lança, Hospital de Santa Maria; Muriel Lérias, Hospital de Santa Maria; Alexandre Marques, Hospital da Luz; Ana Mascarenhas, Hospital Curry Cabral; Francisco Matos, Hospital de São José; Carla Monteiro, Centro Hospitalar São João, Porto; Zélia Moreira, Hospital Geral Santo António; Rosario Orfão, Centro Hospitalar de Coimbra, Coimbra; António Pais Martins, Hospital São Francisco Xavier; Suzana Parente, Hospital São Francisco Xavier; Francelina Peixoto, Hospital de Santarém; Carla Pereira, Hospital de Santa Maria; Luciane Pereira, Centro Hospitalar de Coimbra, Coimbra; Nuno Pereira, Hospital do Litoral Alentejano; Isabel Pimentel, Hospital da Luz; Cristina Ramos, Hospital de Santa Marta; André Rato, Hospital de Santa Cruz; António Robalo Nunes, Base do Lumiar; Anabela Rodrigues, Hospital de Santa Maria; Graça Rodrigues, Hospital Beatriz Ângelo; Paula Sá, Hospital Geral Santo António; Carlos Seco, Centro Hospitalar de Coimbra, Coimbra; Vânia Simões, Hospital de Santarém; Joaquim Varandas, Hospital de Santa Cruz; José Paulo Vasconcelos, Hospital Lusíadas; Elisa Vedes, Hospital da Luz; Manuela Vieira, Centro Hospitalar Vila Nova de Gaia/Espinho; Hugo Vilela, Hospital de Santa Cruz; João Viterbo, Centro Hospitalar São João, Porto.

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Supplemental Material

Supplemental material for this article is available online.

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Table S1. Delhpi exercise – round 1

Ordem	Statements	CONCORDO COMPLETAMENTE		CONCORDO		NÃO CONCORDO NEM DISCORDO		DISCORDO		DISCORDO COMPLETAMENTE		TOTAL RESP.
		n	%	n	%	n	%	n	%	n	%	
1	A implementação de estratégias de Patient Blood Management (PBM) traduz- se numa redução da utilização de componentes alogénicos (Plasma Fresco Congelado (PFC), Concentrado de Plaquetas (CP) e Concentrado de Eritrócitos, (CE)).	37	72.55	14	27.45	0	0.00	0	0.00	0	0.00	51
2	A Implementação de estratégias de PBM traduz-se numa redução das complicações associadas à transfusão.	31	60.78	19	37.25	1	1.96	0	0.00	0	0.00	51
3	As estratégias de PBM asseguram os melhores resultados clínicos para os doentes (menores taxas de morbilidade e de mortalidade).	32	62.75	18	35.29	1	1.96	0	0.00	0	0.00	51
4	As estratégias de PBM reduzem os CUSTOS totais associados.	31	60.78	20	39.22	0	0.00	0	0.00	0	0.00	51
5	É necessária a implementação de estrategias de PBM.	44	86.27	7	13.73	0	0.00	0	0.00	0	0.00	51
6	Nos hospitais portugueses, a implementação de estratégias de PBM é exequível.	24	47.06	26	50.98	0	0.00	1	1.96	0	0.00	51
7	A hemorragia massiva e a transfusão de CEs, PFC e CP estão associados a um aumento de morbilidade e de mortalidade.	43	84.31	7	13.73	0	0.00	1	1.96	0	0.00	51
8	O custo/efetividade da utilização de rácios transfusionais pré-definidos (PFC + plaquetas + CEs) ainda não foi demonstrado.	12	23.53	24	47.06	9	17.65	5	9.80	1	1.96	51
9	As transfusões de componentes alogénicos aumentam a morbilidade e a mortalidade.	30	58.82	16	31.37	4	7.84	1	1.96	0	0.00	51
10	As transfusões de componentes alogénicos aumentam os CUSTOS.	25	49.02	22	43.14	4	7.84	0	0.00	0	0.00	51
11	Os CUSTOS indiretos relacionados com os eventos adversos associados à transfusão têm um impacto mínimo nos custos hospitalares.	0	0.00	2	3.92	4	7.84	29	56.86	16	31.37	51
12	É igualmente aceitável e eficaz a utilização de rácios transfusionais pré-definidos comparativamente à administração dirigida de concentrados de fatores da coagulação.	1	1.96	8	15.69	4	7.84	22	43.14	16	31.37	51
13	A utilização de estratégias de terapêutica dirigida (goal-directed), utilizando concentrados de fatores da coagulação reduz os CUSTOS associados à transfusão, no trauma, cirurgia cardíaca e transplante hepático.	23	45.10	24	47.06	4	7.84	0	0.00	0	0.00	51
14	A utilização de estratégias baseadas na administração de concentrados de fatores da coagulação reduz as transfusões de componentes alogénicos.	28	54.90	21	41.18	2	3.92	0	0.00	0	0.00	51
15	A utilização de estratégias baseadas na administração de concentrados de fatores da coagulação reduz CUSTOS.	7	13.73	26	50.98	16	31.37	2	3.92	0	0.00	51

Ordem	Statements	CONCORDO COMPLETAMENTE		CONCORDO		NÃO CONCORDO NEM DISCORDO		DISCORDO		DISCORDO COMPLETAMENTE		TOTAL RESP.
		n	%	n	%	n	%	n	%	n	%	
16	Os testes viscoelásticos para orientação da terapêutica dirigida incrementam os CUSTOS hospitalares globais.	0	0.00	2	3.92	7	13.73	32	62.75	10	19.61	51
17	A utilização de concentrados de factores da coagulação baseada em terapêutica dirigida (goal-directed), ainda que aumente os custos directos, diminui os custos totais.	17	33.33	25	49.02	7	13.73	2	3.92	0	0.00	51
18	Uma das grandes vantagens dos testes viscoelásticos é perceber rapidamente o que está a acontecer na coagulação e atuar precocemente, em função dos resultados dos testes.	37	72.55	13	25.49	1	1.96	0	0.00	0	0.00	51
19	No contexto da cirurgia electiva, o controlo da coagulopatia guiada por testes viscoelásticos reduz as necessidades transfusionais.	26	50.98	20	39.22	4	7.84	1	1.96	0	0.00	51
20	A administração de ácido tranexâmico reduz a hemorragia peri-operatória.	29	56.86	17	33.33	4	7.84	1	1.96	0	0.00	51
21	A administração de ácido tranexâmico é custo-efectiva no trauma.	31	60.78	17	33.33	2	3.92	1	1.96	0	0.00	51
22	A administração de ácido tranexâmico reduz a hemorragia pós-parto.	28	54.90	21	41.18	1	1.96	1	1.96	0	0.00	51
23	A utilização de concentrado de fibrinogénio é importante para o controlo rápido e eficaz da hemorragia.	26	50.98	20	39.22	5	9.80	0	0.00	0	0.00	51
24	A administração de concentrado de fibrinogénio reduz a necessidade de transfusão de componentes alogénicos, minimizando os seus riscos.	27	52.94	21	41.18	3	5.88	0	0.00	0	0.00	51
25	A administração de concentrado de fibrinogénio reduz a necessidade de transfusão de componentes alogénicos e reduz os CUSTOS totais.	17	33.33	25	49.02	9	17.65	0	0.00	0	0.00	51
26	É admissível a administração de concentrado de fibrinogénio, ainda que os resultados laboratoriais não estejam disponíveis à data em que a administração tem que ser efetuada.	10	19.61	32	62.75	8	15.69	1	1.96	0	0.00	51
27	O PFC pode ser utilizado na reposição eficaz dos níveis de fibrinogénio.	0	0.00	8	15.69	4	7.84	29	56.86	10	19.61	51
28	Perante uma hemorragia ativa, com alterações da coagulação, a primeira opção terapêutica é o PFC.	0	0.00	6	11.76	7	13.73	27	52.94	11	21.57	51
29	Perante uma hemorragia ativa com alterações da coagulação, a primeira opção terapêutica é administrar concentrados de fator da coagulação específicos.	15	29.41	13	25.49	8	15.69	14	27.45	1	1.96	51
30	Reconheço o papel fundamental da administração precoce de concentrado de fibrinogénio, em situações de hemorragia.	24	47.06	23	45.10	4	7.84	0	0.00	0	0.00	51
31	Reconheço a importância da disponibilidade dos testes viscoelásticos nos hospitais portugueses.	38	74.51	11	21.57	2	3.92	0	0.00	0	0.00	51

Table S2. Delhpi exercise – round 2

Ordem	Statements	CONCORDO COMPLETAMENTE		CONCORDO		NÃO CONCORDO NEM DISCORDO		DISCORDO		DISCORDO COMPLETAMENTE		TOTAL RESP.
		n	%	n	%	n	%	n	%	n	%	
8	O custo/efetividade da utilização de rácios transfusionais pré-definidos (PFC + plaquetas + CEs) ainda não foi demonstrado.	12	25.00	25	52.08	8	16.67	1	2.08	2	4.17	48
11	Os CUSTOS indiretos relacionados com os eventos adversos associados à transfusão têm um impacto mínimo nos custos hospitalares.	1	2.08	3	6.25	6	12.50	23	47.92	15	31.25	48
12	É igualmente aceitável e eficaz a utilização de rácios transfusionais pré-definidos comparativamente à administração dirigida de concentrados de fatores da coagulação.	0	0.00	7	14.58	3	6.25	20	41.67	18	37.50	48
15	A utilização de estratégias baseadas na administração de concentrados de fatores da coagulação reduz CUSTOS.	11	22.92	28	58.33	8	16.67	1	2.08	0	0.00	48
16	Os testes viscoelásticos para orientação da terapêutica dirigida incrementam os CUSTOS hospitalares globais.	0	0.00	2	4.17	3	6.25	29	60.42	14	29.17	48
17	A utilização de concentrados de factores da coagulação baseada em terapêutica dirigida (goal-directed), ainda que aumente os custos directos, diminui os custos totais.	19	39.58	24	50.00	4	8.33	1	2.08	0	0.00	48
25	A administração de concentrado de fibrinogénio reduz a necessidade de transfusão de componentes alogénicos e reduz os CUSTOS totais.	12	25.00	31	64.58	5	10.42	0	0.00	0	0.00	48
26	É admissível a administração de concentrado de fibrinogénio, ainda que os resultados laboratoriais não estejam disponíveis à data em que a administração tem que ser efetuada.	9	18.75	32	66.67	5	10.42	2	4.17	0	0.00	48
27	O PFC pode ser utilizado na reposição eficaz dos níveis de fibrinogénio.	1	2.08	4	8.33	4	8.33	20	41.67	19	39.58	48
28	Perante uma hemorragia ativa, com alterações da coagulação, a primeira opção terapêutica é o PFC.	1	2.08	6	12.50	4	8.33	27	56.25	10	20.83	48
29	Perante uma hemorragia ativa com alterações da coagulação, a primeira opção terapêutica é administrar concentrados de fator da coagulação específicos.	12	25.00	19	39.58	7	14.58	9	18.75	1	2.08	48

Table S3. Delhpi exercise – round 3

Ordem	Statements	CONCORDO COMPLETAMENTE		CONCORDO		NÃO CONCORDO NEM DISCORDO		DISCORDO		DISCORDO COMPLETAMENTE		TOTAL RESP.
		n	%	n	%	n	%	n	%	n	%	
8	O custo/efetividade da utilização de rácios transfusionais pré-definidos (PFC + plaquetas + CEs) ainda não foi demonstrado.	10	21.28	30	63.83	5	10.64	0	0.00	2	4.26	47
11	Os CUSTOS indiretos relacionados com os eventos adversos associados à transfusão têm um impacto mínimo nos custos hospitalares.	0	0.00	2	4.26	3	6.38	30	63.83	12	25.53	47
12	É igualmente aceitável e eficaz a utilização de rácios transfusionais pré-definidos comparativamente à administração dirigida de concentrados de fatores da coagulação.	0	0.00	4	8.51	1	2.13	27	57.45	15	31.91	47
15	A utilização de estratégias baseadas na administração de concentrados de fatores da coagulação reduz CUSTOS.	6	12.77	36	76.60	5	10.64	0	0.00	0	0.00	47
27	O PFC pode ser utilizado na reposição eficaz dos níveis de fibrinogénio.	0	0.00	1	2.13	3	6.38	24	51.06	19	40.43	47
28	Perante uma hemorragia ativa, com alterações da coagulação, a primeira opção terapêutica é o PFC.	0	0.00	3	6.38	4	8.51	31	65.96	9	19.15	47
29	Perante uma hemorragia ativa com alterações da coagulação, a primeira opção terapêutica é administrar concentrados de fator da coagulação específicos.	11	23.40	26	55.32	4	8.51	6	12.77	0	0.00	47

Table S4. Variation in responses between rounds

Statement	1st round - agreement	1st round - disagreement	2nd round - agreement	2nd round - disagreement	3rd round - agreement	3rd round - disagreement	Variation 1st - 2nd agreement	Variation 1st - 2nd disagreement	Variation 2nd - 3rd agreement	Variation 2nd - 3rd disagreement
1	100.00	0.00	-	-	-	-	-	-	-	-
2	98.04	0.00	-	-	-	-	-	-	-	-
3	98.04	0.00	-	-	-	-	-	-	-	-
4	100.00	0.00	-	-	-	-	-	-	-	-
5	100.00	0.00	-	-	-	-	-	-	-	-
6	98.04	1.96	-	-	-	-	-	-	-	-
7	98.04	1.96	-	-	-	-	-	-	-	-
8	85.11	4.26	77.08	6.25	85.11	4.26	-8.02	1.99	8.02	-1.99
9	90.20	1.96	-	-	-	-	-	-	-	-
10	92.16	0.00	-	-	-	-	-	-	-	-
11	3.92	88.24	8.33	79.17	4.26	89.36	4.41	-9.07	-4.08	10.20
12	17.65	74.51	14.58	79.17	8.51	89.36	-3.06	4.66	-6.07	10.20
13	92.16	0.00	-	-	-	-	-	-	-	-
14	96.08	0.00	-	-	-	-	-	-	-	-
15	64.71	3.92	81.25	2.08	89.36	0.00	16.54	-1.84	8.11	-2.08
16	3.92	82.35	4.17	89.58	-	-	0.25	7.23	-	-
17	82.35	3.92	89.58	2.08	-	-	7.23	-1.84	-	-
18	98.04	0.00	-	-	-	-	-	-	-	-
19	90.20	1.96	-	-	-	-	-	-	-	-
20	90.20	1.96	-	-	-	-	-	-	-	-
21	94.12	1.96	-	-	-	-	-	-	-	-

22	96.08	1.96	-	-	-	-	-	-	-	-
23	90.20	0.00	-	-	-	-	-	-	-	-
24	94.12	0.00	-	-	-	-	-	-	-	-
25	82.35	0.00	89.58	0.00	-	-	7.23	0.00	-	-
26	82.35	1.96	85.42	4.17	-	-	3.06	2.21	-	-
27	15.69	76.47	10.42	81.25	2.13	91.49	-5.27	4.78	-8.29	10.24
28	11.76	74.51	14.58	77.08	6.38	85.11	2.82	2.57	-8.20	8.02
29	54.90	29.41	64.58	20.83	78.72	12.77	9.68	-8.58	14.14	-8.07
30	92.16	0.00	-	-	-	-	-	-	-	-
31	96.08	0.00	-	-	-	-	-	-	-	-