CSL Behring

# Controversies 1

Moderator: Dr. Juan Vicente Llau

Thursday, May 11, 2023 4pm – 5.30pm | Sevilla Room 3 + 4

## 1. CHRONIC LIVER DISEASE—HOW SHOULD I PERFORM BLEEDING AND THROMBOSIS PROPHYLAXIS?

Dr. Annabel Blasi

Cirrhosis patients present a "hemostatic rebalance" that provides them with hemostatic competence, which is translated into the same thrombin generation time, yet with a decrease in lysis. However, such hemostatic balance is fragile, and a small alteration may trigger both bleeding and thrombotic states.

**Bleeding risk in cirrhosis patients** basically depends on **three factors:**

### 1 PROCEDURE APPLIED

The most commonly observed bleeding is that related to portal hypertension, and not so much surgery or other invasive procedures[1,2]. However, there is currently no consensus between scientific societies on what procedures are high or low risk.

### 2 CHARACTERISTICS OF THE PATIENT

Fibrinogen and platelet levels have to be taken into account, although no cutoff points are currently defined. Other factors influencing hemostasis are the presence of kidney failure or infections.

### 3 OPERATOR SKILLS

Currently, there are no tools to properly assess the risk of bleeding and thrombosis in liver disease patients[3-5]. Nevertheless, the use of viscoelastics has been associated to a decrease in the use of blood products.

✕ PT/APTT: do not reflect the actual hemostatic competence of the patient
✕ Platelet count: only useful if levels are extremely low and with no established cutoff points
✕ Platelet function test: low value, since patients generally suffer from thrombocytopenia
✕ Fibrinogen: no set thresholds
✕ Fibrinolysis: not available in usual practice
✕ Bleeding time: does not predict risk
✕ Thrombin generation or thromboelastography: no set thresholds

### RECOMENDATIONS FOUND IN EASL GUIDELINES, 2022:

**Prophylaxis of bleeding**

- Traditional or viscoelastic tests (VET) are not indicated to predict risk, but they may be used to assess severity or the hemostatic state, and guide management in case bleeding occurs during the procedure.
- Prophylactic plasma transfusion or using prothrombin complex concentrate to correct INR is not recommended. It must be noted that in patients with portal hypertension, each 100 ml of administered volume increase portal pressure by 1 mmHg, which in turn increases bleeding.
- Using platelet concentrate is not recommended if the count is > 50 x $10^9$ or if it can be treated with local hemostasis. Platelet transfusion may be considered in high risk procedures in which local hemostasis is not possible, or if the count is < 20 x $10^9$.
- Fibrinogen correction or routine use of tranexamic acid is not recommended.

**Active bleeding**

- VETs may prove useful to save on blood products, and they can be used when available.
- If hemostasis is achieved by decreasing portal hypertension in variceal bleeding, correcting hemostatic imbalances is not indicated.
- Routine use of tranexamic acid is not recommended, due to the higher risk of thrombotic events in cirrhosis patients.

### ANTICOAGULATION IN CIRRHOSIS PATIENTS

**Even though no evidence is available, standard thromboprophylaxis seems safe in cirrhosis patients:**

✓ Direct Oral Anticoagulants (DOACs) in Child-Pugh A & B.

**Treatment of deep vein thrombosis and pulmonary embolism:**

✓ DOACs in Child-Pugh A and with caution in patients Child-Pugh B or CrCl < 30 ml/min. Antivitamin K & HBPM in Child-
✓ Pugh A & B
✓ HBPM in Child-Pugh C

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## 2. USE AND AVAILABILITY OF VISCOELASTIC TESTS. ARE THEY INDISPENSABLE? MULTIDISCIPLINARY CONSENSUS DOCUMENT

Dr. Sonia Mª Veiras del Río and Dr. Gabriel José Yanes

The use of VETs is part of the therapeutic arsenal in Spanish hospitals, both when caring for bleeding patients and in risk of thrombosis, more recently.

One of the projects promoted by the Hemostasis, Transfusion Medicine and Fluid Therapy section at SEDAR was a survey to get to know the degree of implementation of VETs in national hospitals, which reports a wide variability in the implementation and adherence to current guidelines[6].

The current census of these tools indicates they are available in 88 hospitals throughout the country; 78 hospitals are represented in the survey, which means that this effort covers over 90% of hospitals

### RESULTS FOUND:

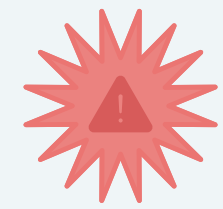
- ✓ Only a small percentage of Spanish hospitals have VETs available. In most cases, these are ROTEM.
- ✓ Most VETs are found in four Spanish regions (Catalonia, Madrid, Andalusia and Valencian Community), with a lower number in the remaining regions, probably due to a lower density of high complexity hospitals, among other causes.
- ✓ In a high percentage of cases, using VETs is not associated to the use of a treatment algorithm. These are the main.
- ✓ Scenarios in which they are used:

**Cardiac surgery**

- On demand (in most cases)
- Pre-exit from ECC
- Post-ECC

**Liver transplant**

- Baseline
- In anhepatic phase
- Post-reperfusion
- End of surgery



**Trauma / Ortophedics**

- On demand (in most cases) (guidelines recommend baseline determination)

- ✓ In all three scenarios, a VET-based follow-up is reported after surgery.
- ✓ Maximum firmness or maximum amplitude are the most commonly used parameters to assess the amplitude/firmness of the clot (although the literature backs the use of earlier indexes –A5 or A10-).
- ✓ In almost 20% of cases, VET parameters are corrected to normal ranges, even if there is no bleeding.

### THE FOLLOWING ACTIONS MAY EMERGE FROM THE RESULTS FOUND:

**Improving accessibility to VETs**

**Applying earlier indexes**

**Eradicating inadequate uses**

**Generating evidence in terms of cutoff points and determination time**

In order to cover these objectives, a multidisciplinary document is being drafted (anesthesiology, laboratory, hematology) on the use of VET in clinical practice, aimed at physicians in any specialty who are involved in the management of VETs.

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## 3. PCC, FIBRINOGEN AND FXIII IN A MASSIVE BLEEDING-SEQUENTIAL OR SIMULTANEOUS?

Dr. Marta Barquero

It is important to pose **three key questions** when determining whether the administration of fibrinogen, prothrombin complex concentrate (PCC), and factor XIII should be performed simultaneously or sequentially:


The specific pathophysiology behind each scenario must be known, because the endothelial injury, hemostatic conditions, and mechanisms of coagulopathy will be different, even if the bleeding volume is the same. The administration of factors should be performed sequentially in case of bleeding and coagulopathy. At any rate, the first factor to fall will be fibrinogen, and then more slowly, platelets and coagulation factors.

Unlike the initial proposal of the hemostatic pyramid by K. Görglinger, in most recent algorithms, the order of administration of coagulation factors and platelets is inverted, or else left to the physician's judgment[7,8].

Currently, there are specific protocols to monitor coagulopathy in bleeding patients. Most of them are based on VETs, but also on more generally accessible and early parameters, such as gasometry, which may prove useful if access to other tools is limited[9].

### Controversies associated to the administration of factor XIII:

- Doubts in pathophysiology
- Lack of relevant information
- Non-defined threshold
- Specific lab monitoring, not generally available 24/7
- Acute or more sustained administration: is one dose enough?

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## 4. MANAGEMENT OF ANTI-THROMBOSIS DRUGS IN ESAIC/ESRA GUIDELINE-SHOULD WE CHANGE OUR CLINICAL PRACTICE?

Dr. Raquel Ferrandis

The management of anti-thrombosis drugs to perform regional blocks is included in numerous clinical practice guidelines[10-14]. At a national level, there is a multidisciplinary consensus document on the perioperative management and anti-thrombosis treatment periprocedure[15].

The European guideline (signed by ESAIC and ESRA) to perform regional blocks in patients treated with anti-thrombosis drugs[16] has been published recently. It is a pragmatic consensus evidence-based document, aimed at reducing as much as possible the risk of bleeding (the risk of thrombosis is not assessed in this guideline).

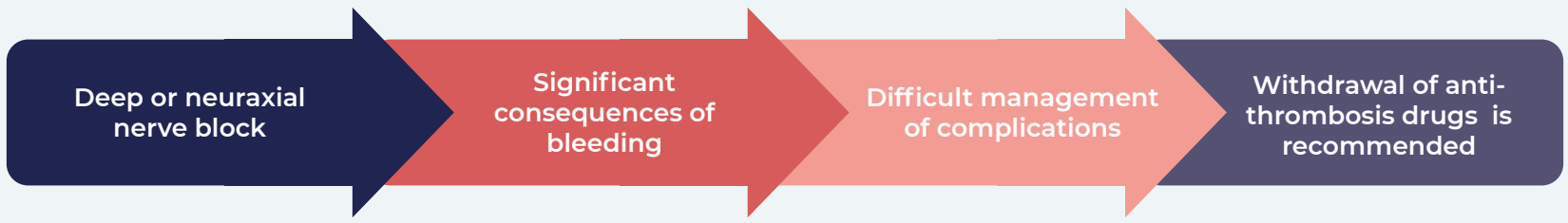
- **45 claims:**

**57,5% with consensus > 90%**

**42,5% with consensus 75-90%**

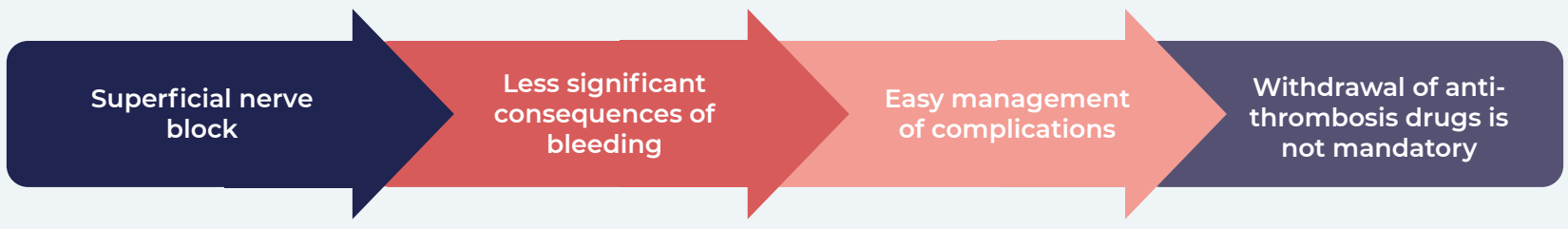
- **Many of the recommendations correspond to specific clinical situations. The evidence level in all of them is C, because this guideline covers situations with no evidence available.**
- **Categorization of blocks in two categories[16]:**

**High risk:**




- Acenocumarol: suspension time about 3 days for acenocumarol and search of normal INR (< 1.2).
- DOAC: low doses are considered for postoperative thromboprophylaxis. In patients with DOACs at high doses, a 72-hour is recommended, with no bridge therapy with HBPM. In patients with renal dysfunction (ClCr<30 ml/min for apixaban, rivaroxaban, edoxaban; ClCr<50 ml/min for dabigatran), a suspension time cannot be recommended, therefore specific monitoring is advised.
- Aspirin: does not require suspension in doses < 200 mg, which are considered low doses because there is no evidence with 300-400 mg.

**Low risk:**




- Currently, it is necessary to create local multidisciplinary protocols adapted to different scenarios.
- A thorough assessment of risks and the search for strategies to minimize them must be recorded in the clinical history of patients.

## BIBLIOGRAPHY


1. Muciño-Bermejo J, Carrillo-Esper R, Uribe M, Méndez-Sánchez N (2013) Coagulation abnormalities in the cirrhotic patient. Ann Hepatol 12:713–724

2. Ferro D, Angelico F, Caldwell SH, Violi F (2012) Bleeding and thrombosis in cirrhotic patients: what really matters? Dig Liver Dis 44:275–279

3. Blasi A (2015) Coagulopathy in liver disease: Lack of an assessment tool. World J Gastroenterol 21:10062–10071

4. Hartmann M, Szalai C, Saner FH (2016) Hemostasis in liver transplantation: Pathophysiology, monitoring, and treatment. World J Gastroenterol 22:1541–1550

5. Kang YG, Martin DJ, Marquez J, Lewis JH, Bontempo FA, Shaw BW, Starzl TE, Winter PM (1985) Intraoperative changes in blood coagulation and thrombelastographic monitoring in liver transplantation. Anesth Analg 64:888–896

6. Barquero M, Yanes GJ, Blasi A, Colomina MJ (2023) Use of viscoelastic tests in the principle bleeding scenarios in Spanish hospitals. Rev Esp Anestesiol Reanim. https://doi.org/10.1016/J.REDARE.2022.05.004

7. Barquero López M, Martínez Cabañero J, Muñoz Valencia A, Sáez Ibarra C, De La Rosa Estadella M, Campos Serra A, Gil Velázquez A, Pujol Caballé G, Navarro Soto S, Puyana JC (2022) Dynamic use of fibrinogen under viscoelastic assessment results in reduced need for plasma and diminished overall transfusion requirements in severe trauma. J Trauma Acute Care Surg 93:166–175

8. Gorlinger K. Coagulation management during liver transplantation. Hamostaseologie. 2006; 26:S64–S76.

9. Hofer S, Schlimp CJ, Casu S, Grouzi E (2021) Management of Coagulopathy in Bleeding Patients. J Clin Med. https://doi.org/10.3390/JCM11010001

10. Halvorsen S, Mehilli J, Cassese S, et al (2022) 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgeryDeveloped by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC) Endorsed by the European Society of Anaesthesiology and Intensive Care (ESAIC). Eur Heart J 43:3826–3924

11. Douketis JD, Spyropoulos AC, Murad MH, et al (2022) Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline. Chest 162:e207–e243

12. Kietaibl S, Ahmed A, Afshari A, et al (2023) Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care: Second update 2022. Eur J Anaesthesiol 40:226–304

13. Godier A, Fontana P, Motte S, et al (2018) Management of antiplatelet therapy in patients undergoing elective invasive procedures. Proposals from the French Working Group on perioperative haemostasis (GIHP) and the French Study Group on thrombosis and haemostasis (GFHT). In collaboration with the French Society for Anaesthesia and Intensive Care Medicine (SFAR). Anaesthesia, Crit care pain Med 37:379–389

14. Keeling D, Tait RC, Watson H, British Committee of Standards for Haematology (2016) Peri-operative management of anticoagulation and antiplatelet therapy. Br J Haematol 175:602–613

15. Vivas D, Roldán I, Ferrandis R, et al (2018) Manejo perioperatorio y periprocedimiento del tratamiento antitrombótico: documento de consenso de SEC, SEDAR, SEACV, SECTCV, AEC, SECPRE, SEPD, SEGO, SEHH, SETH, SEMERGEN, SEMFYC, SEMG, SEMICYUC, SEMI, SEMES, SEPAR, SENEC, SEO, SEPA, SERVEI, SECOT y AEU. Rev Española Cardiol 71:553–564

16. Kietaibl S, Ferrandis R, Godier A, et al (2022) Regional anaesthesia in patients on antithrombotic drugs: Joint ESAIC/ESRA guidelines. Eur J Anaesthesiol 39:100–132