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The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition.

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Sixth edition of the European Guide for the management of hemorrhage and coagulopathy in trauma patients.

Six scientific societies are on board, following a structured evidence-based consensus.

The guide includes 39 real-life recommendations, with varied degrees of evidence and literature-based arguments for each one of them.

The key messages in this guide revolve around early identification and management of coagulopathies, following a chronological approach to prevent bleeding out, placing priority on the optimization of resources, and avoiding empirical management, unless no bleeding and coagulation monitoring method is available.

- **Recommendation 1:** Direct transport of severely injured patients to a well-equipped hospital (1B). Minimizing the time between the injury and the bleeding control (1B) .

- **Recommendation 2:** Local compression of open wounds (1B). Tourniquet close to open wounds in the limbs (1B).

- **Recommendation 3:** Do not delay securing the airway in case of obstruction or GCS lower or equal to 8 (1B). Preventing hypoxia (1A). Preventing hyperoxia, except in cases of imminent exsanguination (2B). Provide normal ventilation to trauma patients (1B). Hyperventilate if signs of brain herniation are observed (2C).

- **Recommendation 4:** There are no clear recommendations in favor or against the administration of blood products outside the hospital.

- **Recommendation 5:** Assessing the severity of the trauma hemorrhage using a combination of physiological data, anatomical pattern of the injury, trauma mechanism, and initial response of the patient to resuscitation (1C). Using the shock index and/or the pulse pressure to assess the degree of hypovolemia (1C).

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- **Recommendation 6:** If there is an apparent source of bleeding, and in cases of hemorrhagic shock with suspected source of bleeding, an immediate procedure will be implemented to control it (1B).

- **Recommendation 7:** Patients with no identified source of bleeding, but with no need for immediate control, will undergo diagnostic tests to determine the source of the bleeding (CAT, ultrasound) (1C).

- **Recommendation 8:** The use of pre-hospital ultrasound is recommended to identify hemoperitoneum/hemopericardium/hemopneumothorax, provided that transportation is not delayed (2B). The use of POCUS–point of care ultrasound–is recommended in thoracoabdominal traumas (1C). Body CAT scan with contrast is recommended to identify the type of injury and the potential source of bleeding (1B).

- **Recommendation 9:** Serial hemoglobin and hematocrit measurements are recommended as a bleeding analytical marker (1B). Non-invasive measurement of hemoglobin has been recently tested, proving to be highly precise when compared to laboratory measurements.

- **Recommendation 10:** Lactate should be measured to estimate and monitor the degree of hemorrhage and tissue hypoperfusion. Alternatively, the base excess can be measured (1B).

- **Recommendation 11:** Monitoring hemostasis, using standard lab tests and/or viscoelastic tests (1C).

- **Recommendation 12:** AVOIDING routine use of platelet function tests in trauma patients receiving anti-platelet therapies or experiencing a suspected platelet dysfunction (1C).

- **Recommendation 13:** Restrictive strategies to replace the initial volume with a targeted SBP of 80-90 mmHg (average 50-60 mmHg) until the bleeding has stopped (1B). In cases of BTI with GCS<8, an average of at least 80 mmHg is recommended (1C).

- **Recommendation 14:** Administering noradrenaline associated to fluids in order to reach the target pressure (1C). In case of myocardial dysfunction, adding dobutamine (1C).

- **Recommendation 15:** Using sodium chloride 0.9% or balanced crystalloids is recommended in initial resuscitation after trauma (1B). Hypotonic solutions, such as Ringer's lactate, should be avoided in cases of severe head trauma (1B). Restricted use of colloids given their effects on hemostasis (1C).

- **Recommendation 16:** Hemoglobin target 7-9 g/dL (1C).

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- **Recommendation 17:** Blood salvaging is recommended in cases of severe bleeding in the abdominal, pelvic, or thoracic cavities (2B).

- **Recommendation 18:** Early implementation of measures aimed at reducing heat loss and recovering/maintaining normal temperature (1C).

- **Recommendation 19:** Damage control surgery is recommended in severe trauma with hemorrhagic shock, with data on active bleeding, coagulopathy and/or intra-abdominal vascular and pancreatic lesions (1B).

- **Recommendation 20:** Using a pelvic belt in pre-hospital context if a pelvic fracture is suspected (1C). Patients with pelvic ring fracture and hemorrhagic shock must undergo pelvic closure and stabilization as soon as possible (1B).

- **Recommendation 21:** Temporary extraperitoneal packing when there is active bleeding and/or when the angioembolization therapy is not available. Packing will be combined with open abdominal surgery whenever necessary (1C). Considering the use of REBOA–Resuscitative Endovascular Balloon Occlusion of the Aorta–in not compressible life-threatening bleeding as a pathway until hemorrhagic control (2C).

- **Recommendation 22:** Using topical hemostatic agents (based on collagen, gelatins, cellulose, or fibrin) combined with other surgical measures or with packing in moderate venous or arterial bleedings (1B).

- **Recommendation 23:** Administering tranexamic acid (TXA) within the first three hours after the injury. 1-gram iv doses followed by 1-gram infusion within 8 hours (1A). There is no need to wait for the viscoelastic test results to administer TXA (1B).

- **Recommendation 24:** Starting monitoring and coagulation correction measures upon arrival to hospital (1B).

- **Recommendation 25:** In the initial management of patients with expected massive hemorrhage, one of the following strategies is recommended: fibrinogen concentrate or cryoprecipitate + packed red blood cells (1C) plasma and red blood cells at a ratio of at least 1:2 (1C). Additionally, a high ratio between platelets and red blood cells is recommended (2B).

- **Recommendation 26:** Following goal-oriented resuscitation strategies, based on standard laboratory values or VET (1B).

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- **Recommendation 27:** In case of using plasma for hemostatic correction, PT o aPTT values above 1.5 times normal should be used as a guide, or else evidence of factor deficiency in VET (1C). Plasma should not be used to correct hypofibrinogenemia if fibrinogen concentrates or cryoprecipitate are available (1C).

- **Recommendation 28:** If we apply a correction strategy with fibrinogen concentrates, we should build on laboratory parameters or evidence of functional deficiency of the factor in VET (1C).

- **Recommendation 29:** Treatment with fibrinogen concentrate or cryoprecipitate in major bleeding together with hypofibrinogenemia (data in VET or level below 1.5 g/liter in Clauss) (1C). An initial supplementation of 3-4 g of fibrinogen is suggested. Repeated doses should be guided by VET or laboratory parameters (2C).

- **Recommendation 30:** Administering platelets to reach counts above 50,000 in bleeding trauma patients, and > 100,000 in case of TBI (2C). An initial administration of 4 concentrates from a single donor or an apheresis pool is suggested (2B).

- **Recommendation 31:** Monitoring calcium levels and keeping them within normal range in bleeding trauma, particularly during massive transfusion (1C). Using calcium chloride is recommended to correct hypocalcemia (1C).

- **Recommendation 32:** Recombinant activated factor VII is not recommended as a first-line therapy (1B). Only in cases of persistent bleeding and after proper implementation of conventional hemostatic measures (2C).

- **Recommendation 33:** Emergent reversal of vitamin K-dependent oral anticoagulants, with an early use of prothrombin complex concentrate (PCC) and 5-10 mg iv of phytomenadione (1A).

- **Recommendation 34:** Plasma measurement of anti-Xa oral agents—apixaban, edoxaban, rivaroxaban—is suggested if there is a suspicion that the patient is taking them (2C). As a reliable alternative to such specific measurement, the use of anti-Xa trials calibrated for HBPM is suggested (2C). In case of life-threatening bleeding in presence of apixaban or rivaroxaban, particularly in TBI, the use of andexanet alfa is suggested (2C). If andexanet is not available, or in patients treated with edoxaban, the use of 25-50 UI/kg of PCC is suggested (2C).

- **Recommendation 35:** Plasma levels of dabigatran should be measured, using diluted thrombin times in patients suspected of such therapy (2C). If that measurement is not available, the standard thrombin time should be measured for the qualitative estimation of the presence of

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dabigatran (2C). In life-threatening bleedings in presence of dabigatran, a reversion with idarucizumab iv 5 grams is recommended (1C).

- **Recommendation 36:** Avoiding the routine transfusion of platelets to bleeding patients treated with anti-platelet drugs (1C). Point-of-care platelet function has no clear place in the evidence, and neither does the administration of desmopressin as a potential alternative to the transfusion of platelets.

- **Recommendation 37:** Early start of mechanical thromboprophylaxis with pneumatic compression while the patient stays immobilized and in risk of bleeding (1C).

- **Recommendation 38:** Implementation in every healthcare center of evidence-based guides for the management of bleeding in trauma patients (1B).

- **Recommendation 39:** Local clinical safety and quality management systems should include parameters to assess the key measures to control bleeding and their outcomes (1B).

Finally, training to care for trauma patients is recommended, stressing the critical role of coagulation to determine the progress of such patients.