NAC ENDORSEMENT WITH CAVEATS:

The European Guideline on Management of Major Bleeding and Coagulopathy Following Trauma: Sixth Edition

A Joint Endorsement with the Trauma Association of Canada & Canadian Prehospital and Transport Transfusion Blood Program Network

ENDORSEMENT SUBCOMMITTEE

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Hemorrhagic shock from post-traumatic bleeding is still the leading cause of potentially preventable deaths among injured patients. One third of these patients have coagulopathies at hospital admission requiring aggressive resuscitation, including massive transfusion to correct these coagulopathies and maintain end-organ function. To inform best practice on massive transfusion, the National Advisory Committee on Blood and Blood Products (NAC) held a Massive Transfusion Consensus Conference with a subsequent publication of proceedings. Multiple studies have been published to advance the treatment strategies of these severely injured patients since then. In November 2019, NAC agreed that endorsement of the fifth edition of the *European guideline on management of major bleeding and coagulopathy following trauma* (hereby referred to as the European guideline) could serve as a complementary document. This European guideline was originally published in 2007; the current sixth edition was updated in 2023.

A Review Working Group (RWG) was formed to independently utilize the AGREEII (Appraisal of Guidelines for Research and Evaluation) tool to assess the methodological rigour and quality in which the European guideline was developed, in accordance with the process detailed in the *NAC Guideline Endorsement Framework*. The RWG membership includes three transfusion medicine experts from NAC, two trauma experts from the Trauma Association of Canada, and one member of the Canadian Prehospital and Transport Transfusion Network. The European guideline achieved scores deemed acceptable by NAC, achieving at least 50% in all Domains and a minimum score of 70% in the Domain of Rigour of Development (Domain 3).

NAC thus endorses the European guideline with the caveats below to reflect Canadian practice and other recommendations made by NAC. NAC has also engaged the Trauma Association of Canada Board of Directors, who have provided a joint endorsement. This statement has also been reviewed and endorsed by the current Chair, Past Chair, and the Research Chair of Canadian Prehospital and Transport Transfusion Network.

Caveats regarding testing:

- The RWG continues to agree on the strategy of early and repeated monitoring of hemostasis. Evidence is evolving for use of viscoelastic hemostatic assays; its superiority over conventional laboratory testing has not been established. When developing local protocols, the monitoring strategy should consider local resources, availability, and expertise.
- Transfusion targets may vary, and this reflects a lack of evidence. The RWG endorses the suggested hemoglobin targets of 70-90 g/L, plasma transfusion with prothrombin time/activated partial thromboplastin time >1.5x normal and/or viscoelastic evidence of coagulation factor deficiency, and platelet transfusion to maintain >50 x 10^9/L.
- The RWG felt that the value and evidence for benefit in using platelet function testing to guide platelet transfusion management continues to be unclear.
- Measurement of factor XIII is still not standard of care in Canada; limited testing capability makes the European guideline recommendations infeasible in bleeding patients.

Caveats regarding product practice and use of adjuncts:

- Evidence is growing regarding plasma therapy versus clotting factor concentrate resuscitation (prothrombin complex and fibrinogen concentrates) strategies.[1]
- Initial empiric resuscitation with fibrinogen replacement in addition to a ratio-based strategy is not specifically supported by the current randomized controlled trial evidence, though research is ongoing.[2] Empiric fibrinogen replacement may be a reasonable approach in select settings, including rural settings and/or settings where fibrinogen testing is limited. Empiric prothrombin complex concentrates may be considered with fibrinogen concentrates in accordance to a clotting factor concentrate resuscitation strategy.
- Treatment using factor XIII is not standard of care in any Canadian centres or broadly across North America. Readers should be aware that NAC recommends that Canadian Blood Services issue factor XIII concentrate for patients with factor XIII deficiency.
- Dosing strategies have not been compared for tranexamic acid, but the use of bolus strategies is an acceptable alternative to traditional bolus and infusion dosing strategies.

Statements regarding prehospital transfusion in Canada:

- The European guideline is equivocal on recommending prehospital transfusion, as the evidence base is derived from urban trauma systems in Europe and the United States, where prehospital transport times are short with rapid access to trauma hospitals. This does not reflect broad Canadian needs given low population densities and geographic barriers limiting access to timely care. Additionally, our smaller centres may lack timely access to and volume of blood products, limiting damage control resuscitation prior to transfer.
- Several Canadian critical care transport programs have demonstrated that prehospital transfusion is safe, operationally feasible, and fiscally sustainable. These prehospital blood programs play a critical role in addressing health equity, ensuring that patients in geographically isolated regions have timely access to blood products.
- Therefore, any Canadian adaptation of this guideline should include a context-specific recommendation endorsing the availability and use of prehospital blood products given the extended transport times and limited in-hospital transfusion capacity.

Limitations noted by the review working group:

- Recommendations for some patient cohorts continue not to be well defined in this guideline nor the literature, notably for pediatric massive hemorrhage, where it is unclear if the practices in this guideline can be extrapolated.
- Future editions may appropriately address implied and/or alternative consent models often seen in trauma with limited patient/public consultation as well as considerations of providing Rh-incompatible red blood cells to persons of childbearing potential.
- Key partner involvement that could be included in future editions of the European guideline could include: transfusion medicine/blood suppliers, pediatricians, interventionalists (such as interventional radiology), and patients. Large sections of these guidelines are based on expert opinion due to lack of evidence, with noted industry support of guideline authors.

- Feasibility of implementation/cost-benefit is still not explored and may not be applicable to Canada.

The RWG encourages the use of local consultation and/or resources, where examples below demonstrate the adoption of many recommendations in these guidelines:

- Alberta Precision Laboratories, Transfusion Medicine –Massive Hemorrhage Protocol: https://www.albertahealthservices.ca/lab/Page17976.aspx
- SaskBlood Massive Hemorrhage Protocol Resources: https://saskblood.ca/mhp/
- Ontario Regional Blood Coordinating Network Provincial Massive Hemorrhage Toolkit: https://transfusionontario.org/en/category/massive-hemorrhage-protocol/toolkit/
- Canadian Blood Services' Clinical Guide to Transfusion: https://professionaleducation.blood.ca/en/transfusion/clinical-guide-transfusion

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