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Postpartum haemorrhage in high-resource settings: Variations in clinical management and future research directions based on a comparative study of national guidelines

PLM de Vries, C Deneux-Tharaux, D Baudios, KK Chen, s donati, F Goffinet, m caballero, R D'Souzah, Suéteres M, T van den Akker

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Author of the comment: Dra. Pilar Marcos. *Intensive Care Medicine. Hospital Germans Trias i Pujol, Badalona, Barcelona.*

Introduction

Mortality due to **postpartum hemorrhage (PPH)** has decreased in countries with abundant resources, following the implementation of national clinical practice guidelines (CPG), but it is still one of the main causes of maternal death.

The **goal** of this review was to bring to light the discrepancies between these different guidelines in terms of definitions (PPH, bleeding measurement) and treatments (1st- and 2nd-line uterotonics, non-pharmacological management and fluid resuscitation, blood products and blood derivatives), thus proving the need to carry out more robust studies.

MATERIAL AND METHODS

A comparison is drawn between CPGs from 8 countries with abundant resources (France, Italy, United Kingdom, Germany, The Netherlands, Australia – New Zealand, Canada, and the US). Following the AGREE II criteria, the guidelines considered to have the highest scientific quality are those of France, Italy, and the United Kingdom.

AGREE II TOOL

DOMAINS (Score 0-100)

1. Reach and goal
2. Participation of stakeholders
3. Rigour in the preparation
4. Clarity of the presentation
5. Applicability
6. Editorial independence

Overall qualification
(0-100 score)

Would you
recommend using
this guideline?

AGREE II tool. Adapted from Brouwers MC, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ. 2010;182(18):E839–42.

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RESULTS

Definition of postpartum

- ❌ The *most* widely accepted definition of **PPH** is a blood loss > 500 mL.
- ❌ *German and Canadian PCGs* **define PPH** based on the **delivery method** → which is absurd from a pathophysiological standpoint, since the hemodynamic repercussion is secondary to the amount of blood loss, no to the way it is lost.
- ✅ *Canadian, Italian, and English PCGs* recommend assessing **clinical parameters** reflecting the maternal pathophysiological response to bleeding → highly recommended in the usual clinical practice.
- ✅ *English PCGs* are the ones that best define the **severity of PPH**, facilitating massive transfusion. Thus, **moderate PPH** is defined as bleeding > 1000-2000 mL, and **severe** PPH as bleeding > 2000 mL.

Measurement of bleeding

- ❌ *A third of PCGs* recommend **measuring blood losses** by means of collectors, weight in gauze, or both.
- ✅ *Canadian, Italian, and English PCGs* rather **measure bleeding** through clinical variables reflecting its **hemodynamic repercussion** → Highly recommended in the usual clinical practice.
- ✅ Only *French and English PCGs* recommend **measuring blood losses** right after birth.

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Prevención de la HPP

- ✓ *All guidelines* recommend as a **first choice** an **oxytocin** prophylactic bolus in case of vaginal delivery:
 - ✗ They disagree as to the route of administration. Currently, the available evidence recommends the **intramuscular route**.
 - ✗ They disagree as to the dose, ranging from 3 to 10 UI.
 - ✗ *Some PCGs* recommend a perfusion of oxytocin after the bolus, although they disagree on the dose.
- ✗ *German, Canadian, and Australian PCGs* suggest using **carbetocin** as an alternative uterotonic prophylaxis to oxytocin, in case of C-section.
- ✗ *French and German PCGs* do not recommend **performing controlled cord traction**.
- ✗ Only *half of PCGs* mention **manual extraction of the placenta**, and they recommend it 30 to 60 minutes after delivery.

2nd-line uterotonics

- ✓ *TII PCGs* recommend **several 2nd-line uterotonics** if oxytocin fails.
- ✓ All PCGs recommend **intravenous prostaglandins** (sulprostone or carboprost):
 - ✗ *All PCGs* concur on the dose and administration of sulprostone.
 - ✗ There is no uniform opinion on the doses and administration of carboprost.
 - ✗ *Half of PCGs* recommend using misoprostol (rectal or sublingual), whereas the *other half* (*French, Dutch, German, and Italian*) do not recommend it at all.
- ✓ All PCGs recommend using **ergot alkaloids** (ergometrine and methylergometrine), except for the *French and German PCGs*, which recommend them against them for their serious adverse effects.

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Non-pharmacological measures

- ✓ All PCGs recommend **uterine tamponade** when 2nd-line uterotonics fail:
 - ✗ There is no consensus on which is the best method: uterine balloon, vaginal packing with hemostatic agents.
 - ✓ Some PCGs specify it is a “bridge” measurement to a final treatment.
- ✓ All PCGs recommend **arterial embolism** when 2nd-line uterotonics fail, before resorting to more radical measures, such as hysterectomy.
- ✓ All PCGs recommend **any surgical method** that preserves the mother's fertility before resorting to hysterectomy (compression sutures or vascular ligations).
- ✓ All PCGs recommend **hysterectomy** as the last-resort therapeutic option.

Resuscitation and transfusion

- ✓ Most PCGs recommend early resuscitation with **crystalloids**, guided by hemodynamics.
- ✓ Half of PCGs recommend **PRBC and FFP transfusion** following fixed or lab test-based transfusion ratios, and the other half recommend guiding transfusion by viscoelastic tests.
- ✓ Even French and English PCGs recommend **POCT to measure hemoglobin**.
- ✓ Most PCGs recommend maintaining a **platelet** level between $50 \times 10^9/L$ and $100 \times 10^9/L$.
- ✓ All PCGs, except the American ones, recommend supplementing **fibrinogen** to maintain levels between **1.5 and 2.5 g/L**. English PCGs recommend supplementing it with cryoprecipitates, and Italian PCGs favor fibrinogen, cryoprecipitate or FFP.
- ✓ **TXA** is recommended in half of PCGs, with similar timing and dosing.
- ✓ All PCGs recommend against using **rFVIIa**, given its high cost and risk of thrombosis.
Using it would only be accepted if the hemorrhage compromises the life of the mother despite all measures.

PRBC: Packed Red Blood Cells, FFP: Frozen fresh plasma; POCT: Point of Care Testing; TXA: Tranexamic acid

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CONCLUSIONS

The review of these eight CPGs lays bare the discrepancies between them in terms of PPH management. The aspect where they most concur is resuscitation with crystalloids and the use of blood products and blood derivatives, although half of the guidelines recommend guiding the treatment through lab tests, and the other half, through viscoelastic tests. More robust studies should be carried out.