European Journal of Obstetrics & Gynecology and Reproductive Biology 198 (2016) 12–21

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Postpartum hemorrhage: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF) in collaboration with the French Society of Anesthesiology and Intensive Care (SFAR)

Loïc Sentilhes [a,*], Christophe Vayssière [b,c], Catherine Deneux-Tharaux [d], Antoine Guy Aya [e,f], Françoise Bayoumeu [g], Marie-Pierre Bonnet [d,h], Rachid Djoudi [i], Patricia Dolley [j], Michel Dreyfus [j,k], Chantal Ducroux-Schouwey [l], Corinne Dupont [m,n], Anne François [o], Denis Gallot [p,q], Jean-Baptiste Haumonté [r], Cyril Huissoud [m,s], Gilles Kayem [t], Hawa Keita [u,v], Bruno Langer [w], Alexandre Mignon [g], Olivier Morel [x], Olivier Parant [y,z,A], Jean-Pierre Pelage [B], Emmanuelle Phan [l], Mathias Rossignol [C], Véronique Tessier [D,E], Frédéric J. Mercier [F,G,H], François Goffinet [d,E,I]

[a] Service de Gynécologie-Obstétrique, CHU Bordeaux, 33076 Bordeaux, France
[b] Service de Gynécologie-Obstétrique, Hôpital Paule de Viguier, CHU Toulouse, 31059 Toulouse, France
[c] UMR 1027 Inserm Université Toulouse III « Epidémiologie Périnatale et handicap de l'enfant, Santé des adolescents », 31000 Toulouse, France
[d] INSERM U1153, Equipe de recherche en Epidémiologie Obstétricale, Périnatale et Pédiatrique (EPOPé), Paris, France
[e] Département Anesthésie-Douleur, Groupe Hospitalo-Universitaire Caremeau, Place du Pr Debré, 30029 Nîmes Cedex 09, France
[f] EA2992 – Faculté de médecine Montpellier-Nîmes, 186, chemin du carreau-de-Lanes, 30029 Nîmes Cedex 2, France
[g] CHU de Toulouse, Pole d'anesthésie Réanimation, Hôpital Paule de Viguier, Toulouse F-31059, France
[h] Département d'anesthésie-réanimation, Hôpital Cochin, APHP, université Paris-Descartes, Paris, France
[i] Etablissement Français du Sang, 20, Avenue du Stade de France, 93218 La Plaine Saint-Denis Cedex, France
[j] Service de Gynécologie-Obstétrique, CHU Caen et UFR de Médecine Caen, 14033 Caen, France
[k] UFR de Médecine Caen, 14033 Caen, France
[l] Association d'usagers, Collectif interassociatif autour de la naissance (CIANE), Paris, France
[m] Réseau périnatal Aurore – Hôpital de la Croix Rousse, université Lyon 1, Lyon, France
[n] EA 4129, laboratoire « Santé, individu, société », faculté de médecine Laennec, 69372 Lyon, France
[o] Etablissement Français du Sang Ile de France, site de l'Hôpital Européen Georges-Pompidou, APHP, Paris, France
[p] Service de Gynécologie-Obstétrique, CHU Estaing, 63003 Clermont-Ferrand, France
[q] R2D2-EA7281, Université d'Auvergne, 63000 Clermont-Ferrand, France
[r] Service de Gynécologie-Obstétrique, CHU Marseille, Hôpital Nord, AP-HM, 13015 Marseille, France
[s] INSERM U846, Stem Cell and Brain Research Institute, Lyon, France
[t] Service de Gynécologie-Obstétrique, Hôpital Louis-Mourier, AP-HP, 92701 Colombes, France
[u] Service d'Anesthésie, CHU Louis-Mourier, AP—HP/Université Paris-7, 178, rue des Renouilliers, 92700 Colombes, France
[v] Université Paris-Diderot, Sorbonne Paris Cité, EA recherche clinique coordonnée ville-hôpital, méthodologies et société (REMES), 75010 Paris, France
[w] Département de Gynécologie-Obstétrique, Hôpital de Hautepierre, Avenue Molière, 67098 Strasbourg, France
[x] Service d'Obstétrique et de Médecine fœtale, Pôle de Gynécologie-Obstétrique, CHU de Nancy, Université de Lorraine, 10 rue Heydenreich, 54000 Nancy, France
[y] Inserm, UMR1027, Toulouse F-31073, France
[z] Université de Toulouse III, UMR1027, Toulouse F-31073, France
[A] CHU Toulouse, Pole de Gynécologie Obstétrique, Hôpital Paule de Viguier, Toulouse F-31059, France
[B] Département de Radiologie, CHU Caen, 14033 Caen, France
[C] Département d'Anesthésie Réanimation SMUR, Hôpital Lariboisière, Assistance Publique Hôpitaux de Paris, France
[D] Collège National des Sages-Femmes, France
[E] DHU Risques et Grossesse, 53 avenue de l'observatoire, Paris, France
[F] Société Française d'Anesthésie et de Réanimation, France
[G] Département d'Anesthésie, Hôpital Antoine Béclère, APHP, Clamart, France
[H] Faculté de Médecine de K. Bicêtre, Université Paris-Sud, France
[I] Maternité Port-Royal, Université Paris Descartes, Groupe hospitalier Cochin Broca Hôtel-Dieu, Assistance Publique-Hôpitaux de Paris, Paris, France

* Corresponding author at: Department of Obstetrics and Gynecology, Bordeaux University Hospital, Place Amélie Raba Léon, 33076 Bordeaux, France. Tel.: +33 2 41 35 77 44; fax: +33 2 41 35 57 89.
E-mail address: loicsentilhes@hotmail.com (L. Sentilhes).

http://dx.doi.org/10.1016/j.ejogrb.2015.12.012
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ARTICLE INFO

Article history:
Received 10 July 2015
Received in revised form 27 October 2015
Accepted 10 December 2015

Keywords:
Postpartum hemorrhage
Oxytocin
Transfusion
Peripartum hysterectomy
Placenta accreta

ABSTRACT

Postpartum haemorrhage (PPH) is defined as blood loss ≥500 mL after delivery and severe PPH as blood loss ≥1000 mL, regardless of the route of delivery (professional consensus). The preventive administration of uterotonic agents just after delivery is effective in reducing the incidence of PPH and its systematic use is recommended, regardless of the route of delivery (Grade A). Oxytocin is the first-line prophylactic drug, regardless of the route of delivery (Grade A); a slowly dose of 5 or 10 IU can be administered (Grade A) either IV or IM (professional consensus).After vaginal delivery, routine cord drainage (Grade B), controlled cord traction (Grade A), uterine massage (Grade A), and routine bladder voiding (professional consensus) are not systematically recommended for PPH prevention. After caesarean delivery, placental delivery by controlled cord traction is recommended (grade B). The routine use of a collector bag to assess postpartum blood loss at vaginal delivery is not systematically recommended (Grade B), since the incidence of severe PPH is not affected by this intervention. In cases of overt PPH after vaginal delivery, placement of a blood collection bag is recommended (professional consensus). The initial treatment of PPH consists in a manual uterine examination, together with antibiotic prophylaxis, careful visual assessment of the lower genital tract, a uterine massage, and the administration of 5–10 IU oxytocin injected slowly IV or IM, followed by a maintenance infusion not to exceed a cumulative dose of 40 IU (professional consensus). If oxytocin fails to control the bleeding, the administration of sulprostone is recommended within 30 minutes of the PPH diagnosis (Grade C). Intrauterine balloon tamponade can be performed if sulprostone fails and before recourse to either surgery or interventional radiology (professional consensus). Fluid resuscitation is recommended for PPH persistent after first line uterotonics, or if clinical signs of severity (Grade B). The objective of RBC transfusion is to maintain a haemoglobin concentration (Hb) >8 g/dL. During active haemorrhaging, it is desirable to maintain a fibrinogen level ≥2 g/L (professional consensus). RBC, fibrinogen and fresh frozen plasma (FFP) may be administered without awaiting laboratory results (professional consensus). Tranexamic acid may be used at a dose of 1 g, renewable once if ineffective the first time in the treatment of PPH when bleeding persists after sulprostone administration (professional consensus), even though its clinical value has not yet been demonstrated in obstetric settings. It is recommended to prevent and treat hypothermia in women with PPH by warming infusion solutions and blood products and by active skin warming (Grade C). Oxygen administration is recommended in women with severe PPH (professional consensus). If PPH is not controlled by pharmacological treatments and possibly intra-uterine balloon, invasive treatments by arterial embolization or surgery are recommended (Grade C). No technique for conservative surgery is favoured over any other (professional consensus). Hospital-to-hospital transfer of a woman with a PPH for embolization is possible once hemoperitoneum is ruled out and if the patient's hemodynamic condition so allows (professional consensus).

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Introduction and method [1–3]

The sponsor (the French College of Gynecologists and Obstetricians (CNGOF)) appointed a steering committee (Appendix) to define the exact questions to be put to the experts, to choose them,follow their work and draft the synthesis of recommendations resulting from their work [1]. The experts analyzed the scientific literature on the subject to answer the questions raised. A literature review identified the relevant articles through mid-2014 by searching the MEDLINE database and the Cochrane Library. The search was restricted to articles published in English and French [2,3]. Priority was given to articles reporting results of original research, although review articles and commentaries were also consulted. Guidelines published by organizations or institutions such as the American College of Obstetricians and Gynecologists (ACOG) [4], the Royal College of Obstetricians and Gynaecologists (RCOG) [5], the Canadian Society of Gynecology and Obstetrics (SOGC) [6], the World Health Organization [7] as well as previous guidelines published by the CNGOF [8] were reviewed, and additional studies were located by reviewing bibliographies of identified articles. For each question, each overview of validated scientific data was assigned a level of evidence based on the quality of its data, in accordance with the framework defined by the HAS (French Health Authority) [3], summarized below.

Quality of evidence assessment

LE1: very powerful randomized comparative trials, meta-analysis of randomized comparative trials.
LE2: not very powerful randomized trial, well-run non-randomized comparative studies, cohort studies.
LE3: case-control studies.
LE4: non-randomized comparative studies with large biases, retrospective studies, cross-sectional studies, and case series.

A synthesis of recommendations was drafted by the organizing committee based on the replies given by the expert authors. Each recommendation for practice was allocated a grade, defined by the HAS as follows.

Classification of recommendations

Grade A: Recommendations are based on good and consistent scientific evidence.
Grade B: Recommendations are based on limited or inconsistent scientific evidence.
Grade C: Recommendations are based primarily on consensus and expert opinion.

Professional consensus: In the absence of any conclusive scientific evidence, some practices have nevertheless been recommended on the basis of agreement between the members of the working group (professional consensus).

All texts were reviewed by persons not involved in the work, i.e., practitioners in the various specialties (Appendix) concerned and working in different situations (public, private, university or non-university establishments). Once the review was completed, changes were made, if appropriate, considering the assessment of the quality of the evidence.

The original long texts in French are cited [9–22], but their individual references are not included here in view of the enormous space they would occupy in this article intended to summarize the guidelines.

Epidemiology of postpartum hemorrhage

Regardless of mode of delivery, postpartum hemorrhage (PPH) is defined as blood loss ≥500 mL after delivery and severe PPH as blood loss ≥1000 mL (professional consensus). The threshold for clinical intervention must take the blood flow rate and clinical context into account. Thus, beginning active management before the threshold of 500 mL is reached is justified when the bleeding rate is high or clinical tolerance poor. Inversely, for cesarean deliveries, in view of the blood loss inherent in this surgical procedure, the threshold of action can be set at a level of blood loss higher than 500 mL if clinical tolerance allows (professional consensus).

In the population-based studies, the incidence of PPH is around 5% of deliveries in the absence of a precise measurement of blood loss and around 10% when it is quantified. The incidence of severe PPH is around 2%. Uterine atony is the principal cause of PPH. Lacerations of the genital tract are responsible for approximately 1 of every 5 cases of PPH and for a still higher rate of severe PPHs.

Maternal mortality due to obstetric hemorrhage has fallen in France (currently 1.6 deaths/100,000 live births), but it remains the leading cause of maternal death (16%) and the most avoidable (80%). In developed countries, PPH is the principal cause of severe maternal morbidity. Beyond the direct consequences of acute hypovolemia, it exposes women to the complications of transfusion, resuscitation, and to infertility if hysterectomy is required.

The principal risk factors of PPH are those for uterine atony, but they are globally not predictive. The risk of recurrence during a subsequent delivery is multiplied by 3 and increases still more with each PPH. Particular attention must be paid to the risk factors related to aspects of the management of labor or delivery, because these may be modifiable (professional consensus). In particular, a dose-dependent association has been reported between PPH and oxytocin administration during labor (LE3); this result must be taken into account in evaluating the benefit-risk balance of this intervention, which is intended to avoid recourse to a cesarean delivery when labor dystocia occurs (professional consensus).

Prenatal management of women at risk of postpartum hemorrhage (excluding those with abnormal placentation)

A multidisciplinary discussion of the site of delivery is necessary and must take into account the nature of the risk (including history of severe PPH and hemostatic disorders) and the speed of access to labile blood products (professional consensus).

Prevention of severe anemia relies on iron supplementation, most often oral (Grade B). Women with coagulation disorders must be followed up in close collaboration with a physician competent in hemostasis, who will plan the specific management for delivery (Grade C).

Preventive doses of anticoagulant agents do not increase the risk of PPH, and access to epidural or spinal anesthesia is most often possible, if there has been a sufficient delay (>12 h) since the last injection (Grade C). In this situation, routine induction of labor during a period without anticoagulants, sometime called a "treatment window", is not recommended (professional consensus).

Curative anticoagulant treatment by LMWH is accompanied by a modest increase in the risk of hemorrhage and requires a delay (>24 h) before use of either epidural or spinal anesthesia (professional consensus). Aspirin use does not increase either the frequency or severity of PPH (LE2) and is not a contraindication to the use of epidural or spinal anesthesia (Grade B).

Clinical and pharmacological prevention of postpartum hemorrhage during the third phase of labor

Vaginal delivery

Preventive administration of uterotonics is effective in reducing the incidence of PPH, and oxytocin is the preferred treatment (Grade A). It can be administered after delivery of the shoulders or rapidly after birth, or after placental delivery if not performed previously (Grade B). A dose of 5 or 10 IU can be administered (Grade A) either IV or IM (professional consensus). For IV administration, a slow IV injection (lasting approximately one minute) is preferable, although no data contraindicate IV bolus injections (rapid IV injection of 1 to 2 seconds) in women with no cardiovascular risk factors (professional consensus). In women at cardiovascular risk, very slow IV administration—for longer than five minutes—is recommended to limit hemodynamic effects (professional consensus). Routine maintenance infusion of oxytocin is not recommended (professional consensus).

Obstetrics teams may choose to use blood collection bags routinely, or not (professional consensus).

Routine cord drainage (LE2), controlled cord traction (LE1), uterine massage (LE1), and routine voiding after delivery (expert opinion) do not affect the incidence of PPH. Moreover, no scientific evidence justifies a recommendation that any of the following will prevent PPH: early or late cord clamping (professional consensus), any particular maternal position during labor (professional consensus), or very early breastfeeding (professional consensus). Tranexamic acid must not be used routinely for PPH prevention (professional consensus).

In cases of placental retention, oxytocin administration is not effective, whether administered by an intrafunicular (LE1), IV, or IM (LE2) route. Should placental delivery not occur, its manual removal is recommended between 30 and 60 min after delivery, in the absence of bleeding (professional consensus). Routine manual uterine examination is not recommended after vaginal delivery for women with previous cesareans (professional consensus).

Cesarean delivery

No evidence justifies preferring one cesarean technique to another because it prevents PPH more effectively (professional consensus). Placental delivery by controlled cord traction is associated with less blood loss than manual removal is (Grade B). A slow (at least one-minute) IV injection of 5–10 IU of oxytocin is recommended (Grade A) except for women with overt cardiovascular risks, when the injection must last at least 5 min to limit its hemodynamic effects (professional consensus). Routine maintenance treatment by an IV oxytocin infusion can be performed as long as it does not exceed 10 IU/h (professional consensus). The treatment can be stopped at the end of two hours if

uterine tone is satisfactory and there is no abnormal bleeding (professional consensus).

Carbetocin reduces the risk of PPH, but in the absence of a non-inferiority trial, oxytocin remains the preventive treatment of reference for preventing PPH after cesarean deliveries (professional consensus). Tranexamic acid must not be used routinely for PPH prevention (professional consensus).

Estimation of blood loss is essential for cesareans and must appear in the surgical report (professional consensus).

Initial management for postpartum hemorrhage after vaginal delivery (Fig. 1)

All relevant staff (midwife, obstetrician, and anesthesiology/critical care team) must be called simultaneously when any PPH is diagnosed (professional consensus). In the case of overt PPH, placement of a blood collection bag is recommended (professional consensus). Once the diagnosis is made, the anesthesiologist-intensivist shall immediately begin appropriate resuscitation based on noninvasive monitoring (heart rate, blood pressure, pulse oximetry), establish or secure venous access, take initial blood samples if none are available (irregular antibody screening, complete blood count, platelets, hemostasis), plasma expansion by crystalloids, oxygen therapy, and protection against hypothermia (professional consensus). Finally, this physician ensures that the patient is anesthetized in optimal safety conditions to enable the obstetrician to perform diagnostic and most often treatment procedures (professional consensus).

If PPH occurs before placental delivery, its manual removal is the first obstetric procedure to perform; otherwise, if the placenta has been expelled, a manual uterine examination will be performed (professional consensus). This procedure should be followed by a uterine massage (professional consensus). Pharmaceutical treatment consists of a slow IV or IM injection of 5–10 IU oxytocin followed by a maintenance infusion of 5–10 IU/h for 2 h (professional consensus). The cumulative dose must not exceed 40 IU, especially in that a second-line treatment must begin immediately if the treatment is ineffective for a maximum period of 30 min (professional consensus). In some at-risk situations or if the PPH persists after the manual exploration of the uterus, careful visual assessment of the lower genital tract must be performed with adequate analgesia (professional consensus). Antibiotic prophylaxis is recommended after manual exploration of the uterus (professional consensus). The management and monitoring steps for PPH must be recorded on a special monitoring form (professional consensus).

The essential elements of a system that guarantees the speed and effectiveness essential to controlling PPH are a department protocol that is regularly updated and trained staff who communicate correctly (professional consensus). Each department is responsible for training all professionals likely to deal with patients with PPH to manage this situation (professional consensus). Critical retrospective study of PPH files should be encouraged (professional consensus).

Management after vaginal delivery of postpartum hemorrhage, persisting despite initial measures or severe from the outset (Fig. 1)

Additional steps must be taken if hemorrhaging persists for 15–30 min after diagnosis and correct initial management (Grade C). This time limit should be reduced if the hemorrhage is very strong from the outset or if maternal hemodynamic tolerance is poor (professional consensus). Help should be requested when a hemorrhage worsens (professional consensus). Clinical monitoring must focus on the heart rate, blood pressure, color of mucosa and integument, a search for bleeding at puncture points, diuresis, and the hemorrhage volume (Grade B).

A search for the cause of the hemorrhage (manual uterine examination and careful visual assessment of the genital tract) must already have been performed (Grade C). Sulprostone and carboprost are effective drugs in the treatment of severe or persistent PPH (LE4). Sulprostone is recommended (Grade C) and must be administered within 30 min of the PPH diagnosis, should oxytocin be ineffective; this time limit can be shortened as a function of the severity of the bleeding (Grade C). Misoprotol is not recommended as a second-line treatment (Grade A). Intrauterine balloon tamponade appears to be effective (LE4). It can be proposed if sulprostone treatment fails and before recourse to surgical or interventional radiology management (professional consensus). Its use is left to the clinician's discretion. It must not delay the implementation of invasive procedures (professional consensus).

The sometimes rapid course of coagulation disorders during PPH justifies laboratory monitoring of coagulation (professional consensus). Recommendations for the prevention and treatment of hypothermia (professional consensus) including the heating of infusion solutions and of blood products, active skin warming (Grade C), and oxygen treatment (professional consensus).

Fluid resuscitation is recommended should PPH worsen (Grade B). The prescription of units of packed red blood cells is based principally on clinical signs of PPH severity, without necessarily awaiting blood test results (professional consensus). The objective of transfusion is to maintain a hemoglobin concentration (Hb) $>$ 8 g/dL. During an active hemorrhage, it is desirable to maintain a fibrinogen level $\geq$2 g/L (professional consensus). Depending on the severity of the hemorrhage or coagulopathy, fibrinogen and fresh frozen plasma (FFP) can be administered without awaiting blood test results (professional consensus). It is desirable to anticipate an order (i.e., order early) so that concentrated platelets can maintain a platelet count $>$50,000/mm^3 (professional consensus).

Tranexamic acid may be useful in the management of PPH, although its clinical value has not yet been demonstrated in obstetrics (professional consensus). Its use is left to the clinician's discretion (professional consensus). The expert advisory group suggests that any use be limited to cases of sulprostone-resistant PPH, at a dose of 1 g, renewable once if ineffective the first time (professional consensus).

No evidence supports a recommendation for the routine use of rFVIIa for either of prevention or early treatment of severe PPH (professional consensus). For the moment, its prescription must therefore be envisioned only for an uncontrolled hemorrhage after the failure of conventional treatment (professional consensus), and after having attempted to correct platelet levels and other hemostasis indicators (Grade C).

Use of general anesthesia with intubation is recommended when the woman's hemodynamic condition is unstable, even when an epidural catheter has been placed, to protect the airways and control ventilation (professional consensus).

Women who received multiple transfusions after a vaginal delivery may receive LMWH for prophylaxis against thrombotic events for 7–14 days postpartum (professional consensus). This period can be extended if additional thromboembolic risk factors are present (professional consensus).

Role of arterial embolization in postpartum hemorrhage (Fig. 1)

The selective embolization of both uterine arteries is recommended, or, if that is not possible, of the anterior trunks of the internal iliac (hypogastric) arteries, without a microcatheter (professional consensus). Arterial embolization must be preferentially practiced

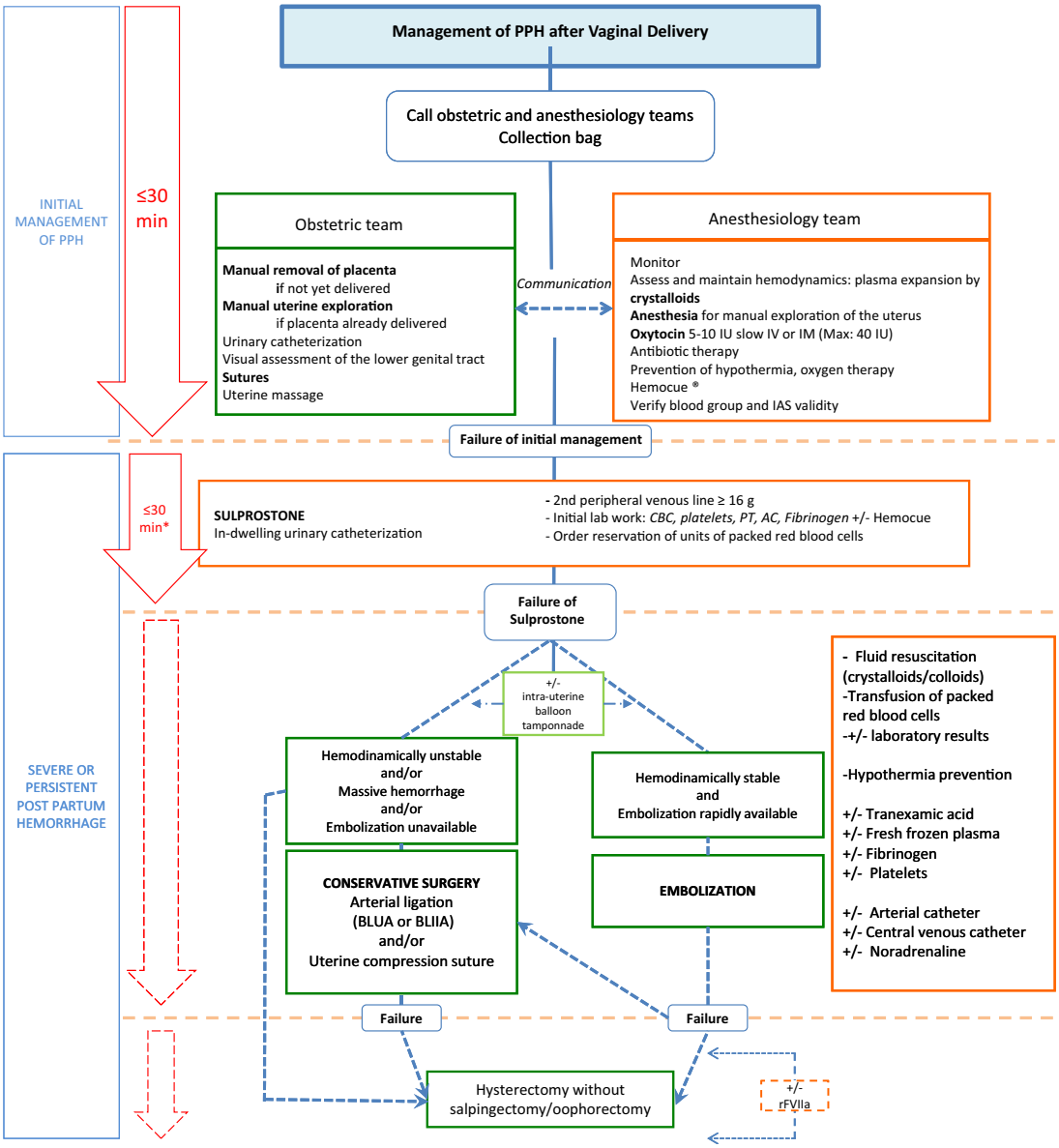

Fig. 1. Algorithm for management of PPH after vaginal delivery. *For general guidance, to be adapted according to the quantity of bleeding. PPH, postpartum hemorrhage; Min, minute; slow IV, slow intravenous; IM, intramuscular; IU, international unit; IAS, irregular antibody screening; BLUA, bilateral ligation of the uterine arteries; BLIIA, bilateral ligation of the internal iliac arteries; CBC, complete blood count; PT, prothrombin time; ACT, activated clotting time; rFVIIa, recombinant activated Factor VII.

with resorbable gelatin pledgets rather than slurry or powder (Grade C). A single session of arterial embolization stops PPH in 73% to 100% (LE3) of cases. A second embolization session stops it in 85% to 100% of cases (LE3). Arterial embolization is indicated preferentially for uterine atony resistant to uterotonics, especially after vaginal delivery, in cases of cervico-uterine hemorrhage, vaginal thrombus, or cervicovaginal lacerationseither sutured or inaccessible to any surgical procedure (Grade C). The serious complication rate attributable to embolization is approximately 5% (LE4). The existence of a coagulation disorder is not a contraindication to embolization (professional consensus). Embolization remains possible after the failure of arterial ligation (selective or proximal) or after a hysterectomy, although these events increase its technical difficulty (professional consensus). Embolization preserves a woman's childbearing potential (LE3). There is no significant difference in the PPH recurrence rate after arterial ligation or embolization (LE3).

Surgical management of postpartum hemorrhage (Figs. 1 and 2)

In the absence of comparative studies of the effectiveness of different surgical techniques, no technique for conservative surgery should be favored over any other (professional consensus).

The techniques of vessel ligation (bilateral ligation of the uterine arteries (BLUA) or bilateral ligation of the internal iliac arteries (BLIIA)) as first-line conservative surgical treatment of PPH appear to have an effectiveness rate of 60–70% (LE4) in halting bleeding. BLUA is a simple surgical technique with a low risk of serious immediate complications (professional consensus). Neither BLUA nor BLIIA appear to affect fertility or subsequent obstetric outcome (LE4).

The effectiveness of techniques of uterine compression sutures in stopping bleeding in cases of PPH resistant to pharmacological treatment appear to be on the order of 75% (LE3). No technique of uterine compression has been demonstrated to be superior to any

another in the treatment of PPH. Pregnancies after uterine compression sutures do not seem to produce an excess rate of complications in subsequent pregnancies (LE4).

The effectiveness of a second conservative surgical technique for stopping PPH after the failure of vessel ligation or uterine compression sutures ranges from 44% to 100% (LE4). It is therefore possible, after discussion with the anesthesiologist, but it must not delay the performance of an emergency hysterectomy (professional consensus).

The type of hysterectomy (total or subtotal) is left to the operator's discretion (professional consensus).

Specificities of obstetric and anesthetic management of postpartum hemorrhage associated with cesarean delivery (Figs. 2 and 3)

The intervention threshold for beginning active management depends on the bleeding rate, its cause, and its clinical context. It may be higher than 500 mL after a cesarean (professional consensus). The principal risk factor for a hemorrhage during a cesarean is its performance during labor (LE3). Blood loss during cesareans can be difficult to assess. The most practical method of estimating blood loss is by measuring the aspirated volume, subtracting the volume of the amniotic fluid, and then adding the weight of the soaked pads (professional consensus). The blood evacuated by the genital tract must also be taken into account (professional consensus).

The causes of PPH associated with cesarean delivery include causes associated with placental delivery (mainly, uterine atony) and complications of intraoperative trauma (especially uterine lacerations and wounds to a uterine pedicle).

Intraoperative obstetric management of PPH depends on its clinical context and cause; it must be conducted in close collaboration with the anesthesiologist (professional consensus) (Fig. 2). Immediate surgical treatment of PPH resistant to pharmacologic and medical treatment must be favored (professional consensus); immediate embolization is not recommended (professional consensus) (Fig. 2). The specific conservative surgical technique conservative is at the discretion of the obstetric staff (professional consensus). If general anesthesia is necessary, limitation of halogenated anesthetics is recommended in cases of uterine atony (professional consensus) (Fig. 2).

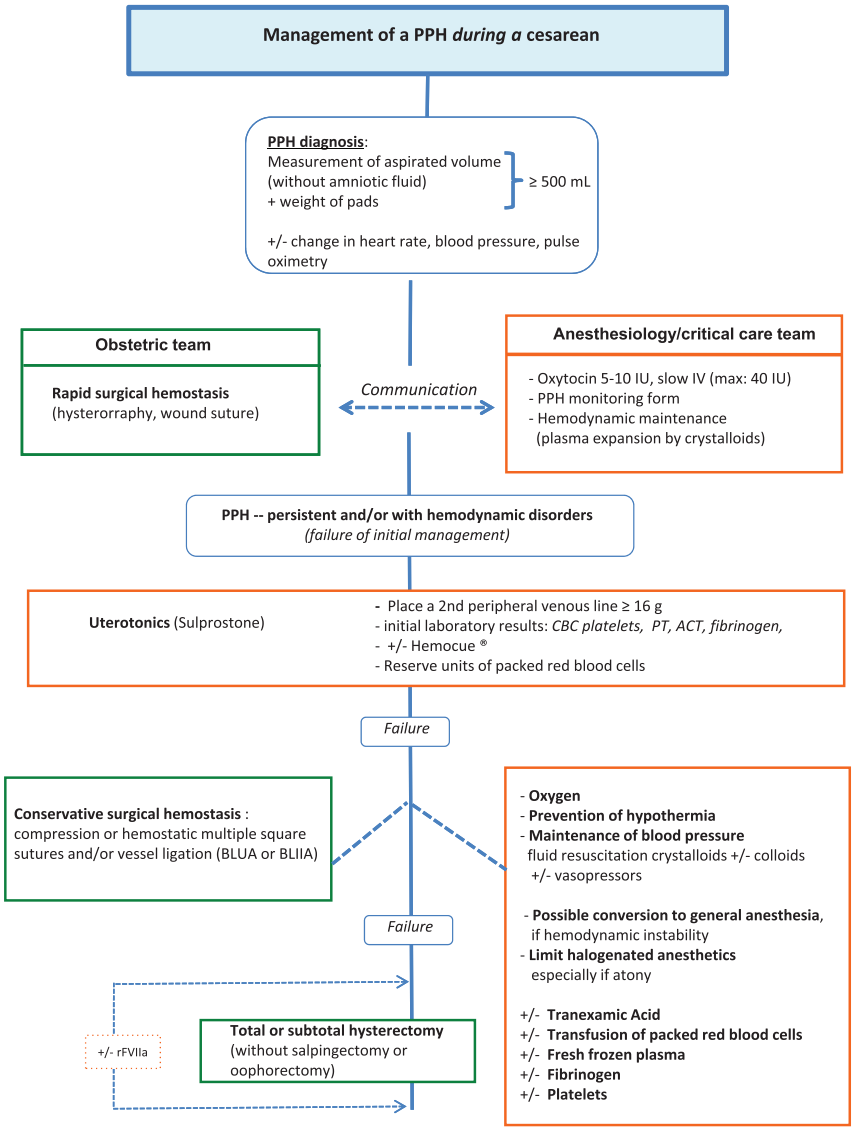

Fig. 2. Algorithm for management of PPH *during a* cesarean. PPH, postpartum hemorrhage; BLUA, bilateral ligation of uterine arteries; BLIIA, bilateral ligation of internal iliac arteries; IU, international unit; IV, intravenous; CBC, complete blood count; PT, prothrombin time; ACT, activated clotting time; rFVIIa, recombinant activated factor VII.

When hemorrhage involves a blood loss greater than 1000 mL and occurs during or soon after a cesarean, thromboprophylaxis is recommended (professional consensus). This prophylactic treatment should last for 7–14 days when there are no other risk factors for thrombosis (professional consensus). It may last as long as 6 weeks when there are persistent or multiple risk factors (professional consensus).

Each medical team must set up a procedure for specific monitoring in the recovery room, including ways that team members can be reached in an emergency (professional consensus). The specific monitoring associated with postoperative cesareans must focus on the quantity of visible vaginal bleeding and uterine tone and volume, as well as the appearance of the abdominal wall (professional consensus); recovery room nurses must be made aware of the importance of these factors (professional consensus). Uterine retraction must be verified at least every 30 min during the 2 h of postpartum monitoring in the recovery room (professional consensus). A rapid bedside abdominal-pelvic ultrasound must be possible, especially in cases of hypovolemia without any visible hemorrhage (professional consensus).

In the postoperative period, a hemoperitoneum or suspicion of a vascular wound mandates emergency laparotomy under general anesthesia (professional consensus) (Fig. 3). In the contrary case, initiation of a uterotonic agent (oxytocin or sulprostone, depending on severity) is required (professional consensus). Intrauterine balloon tamponade or embolization can be considered if the patient is hemodynamically stable (professional consensus) (Fig. 3).

Hospital-to-hospital transfer

Severe postpartum hemorrhage sometimes requires an inter-hospital transfer to continue resuscitation at a more appropriate facility or for arterial embolization unavailable at the initial maternity ward (professional consensus). This is possible under some conditions.

Direct contact is essential between staff at the (sending) maternity unit of birth and the staff at the (receiving) multidisciplinary center to which transfer is sought; this enables transmission of all the medical information and validation of the indication for and feasibility of transfer (professional consensus). The final decision about transport is multidisciplinary and involves the ambulance service's coordinating and transfer physicians and the anesthesiologists/intensivists and obstetricians at both the sending and receiving maternity units) (professional consensus). The ambulance transfer with medical accompaniment can be performed only after correction of any life-threatening failure (professional consensus).

Hospital-to-hospital transfer of a woman with a PPH for embolization is possible only after ruling out a hemoperitoneum, a condition for which laparotomy is preferred, and if her hemodynamic condition so allows (professional consensus). A thorough hemodynamic assessment must be performed again before departure (professional consensus). Any blood transfusion must be continued during the transportation with the objective of maintaining Hb >8 g/dL (professional consensus). The specific treatments for PPH (oxytocin, sulprostone, intrauterine balloon tamponade) begun in the sending maternity ward must be continued during transport (professional consensus).

If the bleeding is too great or the hemorrhagic shock uncontrollable, the transfer is dangerous, and surgery to obtain hemostasis onsite (vessel ligation, compression sutures, or hysterectomy) must be preferred (professional consensus). The emergency ambulance team can then remain to reinforce local resources, if they are inadequate. The emergency ambulance system can also organize the supply of labile blood products if they are currently otherwise unavailable (professional consensus).

Management of blood products in the maternity ward

The effectiveness of transfusion management in PPH treatment relies on a procedure for life-threatening emergencies that is widely disseminated in the facility, control of access to blood products, and coordination between the clinical and transfusion staff (professional consensus). The availability of immunology and hematology results (blood groups and phenotypes, irregular antibody screening) must be verified at admission to the labor room (professional consensus). In women with an identified hemorrhage risk, an irregular antibody screening less than 3 days old is recommended (professional consensus). Prescribers must anticipate the request for fresh frozen plasma because it must thaw before it can be used (Grade C). Complex immunological situations concerning rare blood groups must be discussed antenatally with the French Blood Agency (EFS) (professional consensus).

The choice of phenotypes of packed red blood cell units stored in blood banks and the prescribers' understanding of simple compatibility rules are important aspects of transfusion safety (professional consensus). All French maternity units must be associated with one of the 800 EFS blood banks, for availability (ideally) within 30 min (professional consensus). Prescribers must be aware of the conditions of procurement, logistic channels, and availability, sometimes limited in some banks, of blood products so that they can optimize the management of severe hemorrhage situations (professional consensus). All prescribers must know the different procedures, in particular those for life-threatening emergencies; these procedures must be written out and implemented in each hospital. These procedures must be regularly updated (professional consensus).

Management of placenta previa and accreta

Placenta previa

Placenta previa should be characterized by transvaginal ultrasound, especially in cases with a posterior site, to measure the distance between the internal os of the cervix and the lower edge of the placenta (Grade C). Transvaginal ultrasound does not increase the risk of hemorrhage (LE4). In women with placenta previa, a trial of vaginal delivery is possible when the distance between the cervical internal os and the lower edge of the placenta is greater than 20 mm (professional consensus). When the distance is less than 20 mm, a trial of vaginal delivery is possible, depending on the extent and control of bleeding (professional consensus). In the case of asymptomatic complete placenta previa, a cesarean delivery between 38^{+0} and 38^{+6} weeks should be planned (professional consensus). Partial manual cleavage of the placenta followed by rupture of the membranes seems preferable to transplacental incision to deliver the neonate (Grade C).

Placenta accreta

The risk factors for placenta accreta are maternal age, in vitro fertilization, and a history of uterine surgery, cesarean delivery, placenta previa, or placenta accreta (LE2). The risk of placenta accreta increases with the number of previous cesareans (LE2). Antenatal screening for placenta accreta should make it possible to improve its management (LE3). Its diagnosis can be suggested by a combination of 2D and Doppler color ultrasound imaging (LE3). Magnetic resonance imaging (MRI) is also helpful for diagnosis (LE3). Because of the possibility of false positives and false negatives on imaging, the opinion of a specialist is advised when

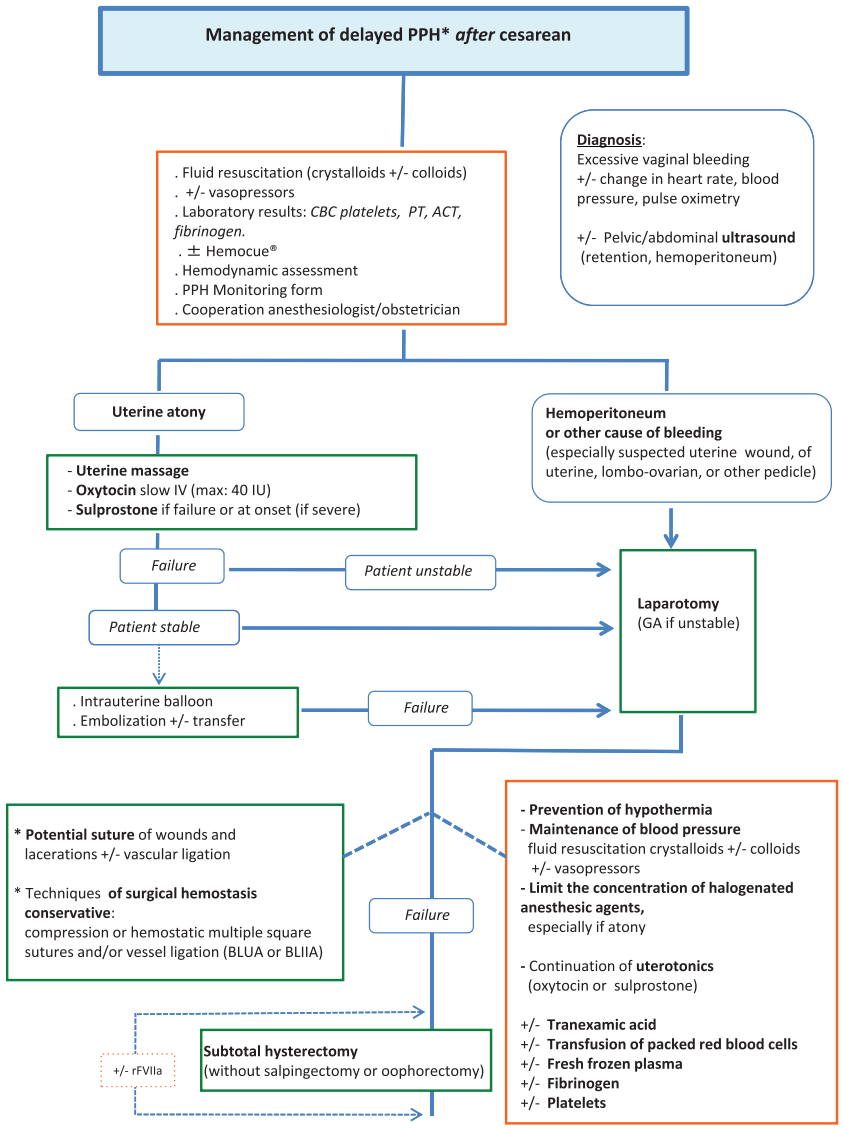

Fig. 3. Algorithm for management of delayed PPH* *after* Cesarean. PPH, postpartum hemorrhage; CBC, complete blood count; PT, prothrombin time; ACT, activated clotting time; IV, intravenous; IU, international unit; GA, general anesthesia; BLUA, bilateral ligation of uterine arteries; BLIIA, bilateral ligation of internal iliac arteries; rFVIIa, recombinant activated Factor VII.

placenta accreta is suspected (professional consensus). The delivery of a pregnancy involving antenatally suspected placenta accreta must take place in a facility with the appropriate human and technical resources (professional consensus).

The decision to deliver the child should be made together with the parents (professional consensus) and must be assessed on a case-by-case basis, taking into account gestational age, the hospital's organization, and the risk of hemorrhage (professional consensus). Delivery should be planned after 34^{+0} weeks and before 38^{+0} weeks (professional consensus).

In women with placenta accreta, extirpative techniques are recommended against (Grade C). When placenta accreta is suspected and a cesarean hysterectomy has been decided upon, the intervention must be performed with adequate human and technical resources: a gynecologic surgeon, anesthesiologist, availability of a urological or gastrointestinal surgeon, a blood bank, and an intensive care unit (professional consensus). Conservative treatment is possible for placenta accreta in women who want such treatment after information about the risk of recurrence and the potential complications associated with it (Grade C). In this case, the use of methotrexate is not recommended (professional consensus).

When placenta accreta is discovered at delivery, forcible placental delivery must be avoided (Grade C). Conservative treatment is possible, as is a cesarean hysterectomy (Grade C).

For women with abnormal placentation and a high risk of hemorrhage, the rapid availability of blood products must be verified with the local blood bank (professional consensus). When a major hemorrhagic risk is identified, general anesthesia can be chosen from the outset to avoid emergency conversions in difficult conditions (professional consensus). Epidural or combined spinal anesthesia are also possible (professional consensus).

Secondary postpartum hemorrhage

Secondary or late postpartum hemorrhages (0.5% to 2% of deliveries) are defined as hemorrhages occurring from 24 h to 6 weeks after delivery and requiring therapeutic action of any type (professional consensus). Their most frequent cause is retention of placental fragments and/or endometritis, more or less associated with incomplete uterine involution (professional consensus). Other causes include false-aneurysms of the uterine artery, arteriovenous fistulae (vascular abnormalities), choriocarcinoma,

and coagulation disorders. Management depends on the cause and severity of the hemorrhage: antibiotic therapy (Grade A) and uterotonic agents (professional consensus). Most often, the patient is admitted for this management (professional consensus). Should the hemorrhage persistent and retention of placental fragments be found, aspiration-curettage under ultrasound control or operative hysteroscopy is recommended (professional consensus). In cases of vascular abnormalities, selective embolization is the treatment of choice (professional consensus).

Conflicts of interest

LS was a board member and carried out consultancy work and lectured for Ferring. CV lectured for Ferring. CH was a scientific consultant for LFB Biomédicaments. GK declares a conflict of interest with LFB Biomédicaments (FIDEL clinical study of postpartum hemorrhage) and with Ferring (consultancy work). FB lectured for Ferring and declares a conflict of interest with LFB Biomédicaments (FIDEL clinical study of postpartum hemorrhage). HK declares a conflict of interest with LFB Biomédicaments (FIDEL clinical study of postpartum hemorrhage. BL declares a conflict of interest with the LFB Biomédicaments (FIDEL clinical study of postpartum hemorrhage) and with Procter & Gamble (consultancy work). AM carried out consultancy work and lectured for LFB Biomédicaments (in particular, for the FIDEL clinical study of postpartum hemorrhage. OP carried out consultancy work and lectured for Ferring. JPP was a member of the board of directors of Keocyt, carried out consultancy work and lectured for Terumo, Merit Medical, Boston Scientific, Cook, ALN, and received research grants from Terumo, Merit Medical, Cook, ALN, and BTG. FJM carried out consultancy work and lectured for LFB Biomédicaments. AF, AGA, CD, CDS, CDT, DG, FG, JBH, MPB, MR, RD, and VT had no conflicts of interest.

Appendix

A.1. Steering committee

F. Goffinet, president and methodologist (gynecologist/obstetrician, Maternité de Port-Royal, Paris, France), L. Sentilhes, co-coordinator and methodologist (gynecologist/obstetrician, CHU, Angers, France), C. Vayssière, co-coordinator (gynecologist/obstetrician, CHU, Toulouse, France), F.J. Mercier (anesthesiologist/intensivist, Société Française d'Anesthésie et de Réanimation, Clamart, France), A. François (Établissement Français du Sang, HEGP, Paris France), V. Tessier (midwife, Collège National des Sages-Femmes, Paris, France), Chantal Ducroux-Schouwey (Collectif Interassociatif Autour de la Naissance, Villeneuve), Emmanuelle Phan (Collectif Interassociatif Autour de la Naissance, Paris).

A.2. Working group

A.G. Aya (anesthesiologist/intensivist, CHU, Nîmes, France), C. Deneux-Tharaux (epidemiologist, INSERM U953, Paris, France), R. Djoudi (Établissement Français du Sang, La Plaine Saint Denis, France), P. Dolley (gynecologist/obstetrician, CHU, Caen, France), M. Dreyfus (gynecologist/obstetrician, CHU, Caen, France), C. Dupont (midwife, CHU, Lyon, France), D. Gallot (gynecologist/obstetrician, CHU, Clermont-Ferrand, France), J.B. Haumonte (gynecologist/obstetrician, CHU, Marseille, France), C. Huissoud (gynecologist/obstetrician, CHU, Lyon, France), G. Kayem (gynecologist/obstetrician, CHU, Colombes, France), H. Keïta-Meyer (anesthesiologist/intensivist, CHU, Colombes, France), B. Langer (gynecologist/obstetrician, CHU, Strasbourg, France), A. Mignon (anesthesiologist/intensivist, Hôpital Cochin, Paris), O. Morel (gynecologist/obstetrician, CHU, Nancy), O. Parant (gynecologist/obstetrician, CHU, Toulouse), J.P. Pelage (radiologist, CHU, Caen), M. Rossignol (anesthesiologist/intensivist, CHU, Paris).

A.3. Peer reviewers

J.P. Agher (gynecologist/obstetrician, Clinique Saint Jean, Toulon, France), X. Aireau (gynecologist/obstetrician, CHG, Cholet, France), M. Akrich (CIANE), F. Audibert (gynecologist/obstetrician, CHU, Montréal, Canada), E. Azria (gynecologist/obstetrician, Hopital Bichat, Paris, France), G. Bagou (anesthesiologist/intensivist, CHU, Lyon, France), G. Benoist (gynecologist/obstetrician, CHU, Caen, France), A. Bertrand (gynecologist/obstetrician, CHG, Salon de Provence, France), F. Bolandard (anesthesiologist/intensivist, CH, Narbonne, France), M. Bonnin (anesthesiologist/intensivist, CHU, Clermont-Ferrand, France), B. Bougeois (anesthesiologist/intensivist, CHU, Clichy, France), M. Boukerrou (gynecologist/obstetrician, CHU, La Réunion, France), P. Boulot (gynecologist/obstetrician, CHU, Montpellier, France), F. Broisin (anesthesiologist/intensivist, CHU, Lyon, France), S. Brunet (anesthesiologist/intensivist,Clinique Saint Louis, Ganges, France), X. Carcopino (gynecologist/obstetrician, Hôpital Nord, Marseille, France), A. Chantry (midwife, INSERM U953, Paris, France) N. Chenni (gynecologist/obstetrician, CH, Aubagne, France), F. Coatleven (gynecologist/obstetrician, CHU, Bordeaux, France), L. Cravello (gynecologist/obstetrician, CHU, Marseille, France), X. DEFFIEUX (gynecologist/obstetrician, Hôpital Antoine Béclère, Clamart, France), P. Deruelle (gynecologist/obstetrician, CHU, Lille, France), P. Diemunsch (anesthesiologist/intensivist, CHU, Strasbourg, France), G. DUCARME (gynecologist/obstetrician, CHG, La Roche sur Yon, France), L. Ducros (anesthesiologist/intensivist, CHI, Toulon, France), S. Favrin (gynecologist/obstetrician, NouvelleClinique de L'Union, Saint Jean France), C. FOULHY (midwife, CHU, Clermont-Ferrand, France), A. Fournet-Fayard (anesthesiologist/intensivist, CHU, Clermont-Ferrand, France), F. Franchi (gynecologist/obstetrician, Polyclinique du Dr R. Maymard, Bastia), L. Gaucher (midwife, CHU, Lyon, France), P. Gillard (gynecologist/obstetrician, CHU, Angers, France), C. Gomez (midwife, CHG, Arras, France), J. Guglielminotti (anesthesiologist/intensivist, Hôpital Bichat Claude Bernard, Paris, France), T. Harvey (gynecologist/obstetrician, ESPIC, Paris), N. Houi (anesthesiologist/intensivist, CHU, Angers, France), C. Huot-Thebaud (Midwife Hôpital Privé d'Antony, Antony), P. Incagnoli (anesthesiologist/intensivist, CHU, Grenoble, France), N. Kermarrec (anesthesiologist/intensivist, Hôpital Privé d'Antony, Antony), R. Kutnahorsky (gynecologist/obstetrician, CHG, Colmar, France), A. Le Gouez-Divisia (anesthesiologist/intensivist, Hôpital Antoine Béclère, Paris), C. Le Ray (gynecologist/obstetrician, Maternité de Port-Royal, Paris, France), P. Lefevre (gynecologist/obstetrician, CHG, Bayeux, France), G. Legendre (gynecologist/obstetrician, CHU, Angers, France), G. Lévy (gynecologist/obstetrician, Paris), A. Lerebours-Barbier (gynecologist/obstetrician, Clinique Océane, Vannes, France), G. Magnin (gynecologist/obstetrician, Poitiers), P. Mahiou (anesthesiologist/intensivist, Maison médicale des cèdres, Echirolles), M. Makosso (gynecologist/obstetrician, CHG, Bagnols sur Cèze), L. Mandelbrot (gynecologist/obstetrician, Hôpital Louis-Mourier, Colombes, France), L. Marpeau (gynecologist/obstetrician, CHU Rouen, France), O. Marpeau (gynecologist/obstetrician, Cabinet Privé, Aix-en- Provence, France), F. Mauviel (gynecologist/obstetrician, CHG, Toulon, France), P.Y. Mercier (gynecologist/obstetrician, CHG, Avranches, France), C. Morin (midwife, CHU, Bordeaux, France), A. Paumier (gynecologist/obstetrician, Polyclinique Atlantique, Nantes, France), M. Perineau (gynecologist/obstetrician, Clinique Sarrus Teinturiers, Toulouse), E. Peynaud Debayle (Hematologist and biologist, CHU, Colombes, France), D. Provost (anesthesiologist/intensivist, CHU, Rouen, France), C. Racinet (anesthesiologist/intensivist, Brie et Argonnes), A. Ricbourg (gynecologist/obstetrician,

Hopital de Lariboisière, Paris, France), D. Riethmuller (gynecologist/obstetrician, CHU de Besançon, France), C. Rouillard (midwife, CHU Angers, France), P. Rozenberg (gynecologist/obstetrician, CHI, Poissy France), RC Rudigoz (gynecologist/obstetrician, Hôpital de la Croix-Rousse, Lyon, France), M. Samama (anesthesiologist/intensivist, CHU Hôtel Dieu, Paris, France), T. Schmitz (gynecologist/obstetrician, Hôpital de Robert-Debré, Paris, France), M.V. Senat (gynecologist/obstetrician, CHU, Le Kremlin-Bicêtre, France), F. Sergent (gynecologist/obstetrician, CHU, Grenoble, France), J. Séror (gynecologist/obstetrician, Cabinet d'Echographie, Paris, France), T. Simonet (anesthesiologist/intensivist, CHU, Caen, France), B. Storme (anesthesiologist/intensivist, CHU, Clermont-Ferrand, France), J. Tourres (anesthesiologist/intensivist, Polyclinique de l'Atlantique, Saint Herblain, France), C. Ventré (anesthesiologist/intensivist, Hôpital Lariboisière, France), E. Verspyck (gynecologist/obstetrician, CHU, Rouen, France), B. Vivien (anesthesiologist/intensivist, Clinique de l'Etoile, Puyricard), N. Winer (gynecologist/obstetrician, CHU, Nantes, France), L. Zieleskiewicz (anesthesiologist/intensivist, CHU, Marseille, France).

References

[1] Goffinet F, Sentilhes L, Vayssière C. Guidelines for clinical practice: postpartum haemorrhage. Introduction. J Gynecol Obstet Biol Reprod 2014;43:931–2.

[2] Sentilhes L, Goffinet F, Vayssière C. Post-partum hemorrhage: guidelines for clinical practice – method and organization. J Gynecol Obstet Biol Reprod 2014;43:933–5.

[3] HAS. Les recommandations pour la pratique clinique. Base méthodologique pour la réalisation en France. Available: http://www.has-sante.fr/portail/jcms/c_431294/les-recommandations-pour-la-pratique-clinique-base-methodologique-pour-leur-realisation-en-france.

[4] American College of Obstetricians and Gynecologists. Post-partum hemorrhage. ACOG Practice Bulletin No. 76. Obstet Gynecol 2006;108:1039–47.

[5] Society of Obstetricians, Gynecologists of Canada, SOGC Clinical Practice Guidelines, 2009.

[6] Royal College of Obstetricians and Gynecologists. Prevention and management of post-partum haemorrhage. Green Top Guideline 2009;52:1–24.

[7] World Health Organization. Recommendations for the prevention and treatment of postpartum haemorrhage. WHO; 2012, http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548502/en/.

[8] Goffinet F, Mercier F, Teyssier V, et al. Postpartum haemorrhage: recommendations for clinical practice by the French College of Obstetricians and Gynecologists (December 2004). Gynecol Obstet Fertil 2005;33:268–74.

[9] Deneux-Tharaux C, Bonnet MP, Tort J. Epidemiology of postpartum haemorrhage. J Gynecol Obstet Biol Reprod 2014;43:936–50.

[10] Fournet-Fayard A, Lebreton A, Ruivard M, et al. Antenatal management for patients with increased risk of post-partum hemorrhage (excluding abnormal placentation). J Gynecol Obstet Biol Reprod 2014;43:951–65.

[11] Dupont C, Ducloy-Bouthors AS, Huissoud C. Clinical and pharmacological procedures for the prevention of postpartum haemorrhage in the third stage of labor. J Gynecol Obstet Biol Reprod 2014;43:966–97.

[12] Dolley P, Beucher G, Dreyfus M. Initial obstetrical management of post-partum hemorrhage following vaginal delivery. J Gynecol Obstet Biol Reprod 2014;43:998–1008.

[13] Rackelboom T, Marcellin L, Benchetrit D, Mignon A. Anesthesiologists at the initial stage of postpartum hemorrhage. J Gynecol Obstet Biol Reprod 2014;43:1009–18.

[14] Morel O, Perdriolle-Galet E, Mézan de Malartic C, et al. Management of severe or persistent postpartum hemorrhage after vaginal delivery. J Gynecol Obstet Biol Reprod 2014;43:1019–29.

[15] Aya AG, Ducloy-Bouthors AS, Rugeric L, Gris JC. Anesthetic management of severe or worsening PPH. J Gynecol Obstet Biol Reprod 2014;43:1030–62.

[16] Pelage JP, Fohlen A, Le Pennec V. Role of arterial embolization in the management of postpartum hemorrhage. J Gynecol Obstet Biol Reprod 2014;43:1063–82.

[17] Haumonté JB, Sentilhes L, Macé P, Cravello L, Boubli L, d'Ercole C. Surgical treatment of postpartum hemorrhage. J Gynecol Obstet Biol Reprod 2014;43:1083–103.

[18] Parant O, Guerby P, Bayoumeu F. Obstetric and anesthetic specificities in the management of a postpartum hemorrhage (PPH) associated with cesarean section. J Gynecol Obstet Biol Reprod 2014;43:1104–22.

[19] Rossignol M, Rozenberg A. Inter-hospital transfer for severe postpartum hemorrhage. J Gynecol Obstet Biol Reprod 2014;43:1123–32.

[20] Djoudi R. Management of blood products in obstetric services. J Gynecol Obstet Biol Reprod 2014;43:1133–41.

[21] Kayem G, Keita-Meyer H. Management of placenta previa and accreta. J Gynecol Obstet Biol Reprod 2014;43:1142–60.

[22] Akladios CY, Sananes N, Gaudineau A, Boudier E, Langer B. Secondary postpartum hemorrhage. J Gynecol Obstet Biol Reprod 2014;43:1161–9.