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Postpartum Hemorrhage

Maternal hemorrhage, defined as a cumulative blood loss of greater than or equal to 1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process, remains

the leading cause of maternal mortality worldwide (1). Additional important secondary sequelae from hemorrhage exist and include adult respiratory distress syndrome, shock, disseminated intravascular coagulation, acute renal failure, loss of fertility, and pituitary necrosis (Sheehan syndrome).

Hemorrhage that leads to blood transfusion is the leading cause of severe maternal morbidity in the United States closely followed by disseminated intravascular coagulation (2). In the United States, the rate of postpartum hemorrhage increased 26% between 1994 and 2006 primarily because of increased rates of atony (3). In contrast, maternal mortality from postpartum obstetric hemorrhage has decreased since the late 1980s and accounted for slightly more than 10% of maternal mortalities (approximately 1.7 deaths per 100,000 live births) in 2009 (2, (4). This observed decrease in mortality is associated with increasing rates of transfusion and peripartum hysterectomy (2–4).

The purpose of this Practice Bulletin is to discuss the risk factors for postpartum hemorrhage as well as its evaluation, prevention, and management. In addition, this document will encourage obstetrician–gynecologists and other obstetric care providers to play key roles in implementing standardized bundles of care (eg, policies, guidelines, and algorithms) for the management of postpartum hemorrhage.

Background

The American College of Obstetricians and Gynecologists' (ACOG) reVITALize program defines postpartum hemorrhage as cumulative blood loss greater than or equal to 1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process (includes intrapartum loss) regardless of route of delivery (5). This is in contrast to the more traditional definitions of postpartum hemorrhage as an estimated blood loss in excess of 500 mL after a vaginal birth or a loss of greater than 1,000 mL after a cesarean birth (6). This new classification is likely to reduce the number of individuals labeled with postpartum hemorrhage. However, despite this new characterization, a blood loss greater than 500 mL in a vaginal delivery should be considered abnormal and should serve as an indication for the health care provider to investigate the increased blood deficit. Although visually estimated blood loss is considered inaccurate, use of an educational process, with limited instruction on estimating blood loss, has been shown to improve the accuracy of such estimates (7). Historically, a decrease in hematocrit of 10% had been proposed as an alternative marker to define postpartum hemorrhage; however, determinations of hemoglobin or hematocrit concentrations are often delayed, may not reflect current hematologic status, and are not clinically useful in the setting of acute postpartum hemorrhage (8).

In postpartum women, it is important to recognize that the signs or symptoms of considerable blood loss (eg, tachycardia and hypotension) often do not present or do not present until blood loss is

substantial (9). Therefore, in a patient with tachycardia and hypotension, the obstetrician–gynecologist or other obstetric care provider should be concerned that considerable blood loss, usually representing 25% of the woman’s total blood volume (or approximately 1,500 mL or more), has occurred (10). Thus, earlier recognition of postpartum hemorrhage (eg, before deterioration in vital signs) should be the goal in order to improve outcomes.

Differential Diagnosis

The initial management of any patient with obstetric hemorrhage requires that the obstetrician–gynecologist or other obstetric care provider first identify the source of bleeding (uterine, cervical, vaginal, periurethral, periclitoral, perineal, perianal, or rectal). This can be quickly done with a careful physical examination. After the anatomic site is identified, it is important to identify the cause because treatment may vary. The most common etiologies (see Box 1) are broken into primary or secondary causes. Primary postpartum hemorrhage occurs within the first 24 hours of birth, whereas secondary postpartum hemorrhage is defined as excessive bleeding that occurs more than 24 hours after delivery and up to 12 weeks postpartum (11, 12).

Box 1. Etiology of Postpartum Hemorrhage ↻

Primary:

- Uterine atony
- Lacerations
- Retained placenta
- Abnormally adherent placenta (accreta)
- Defects of coagulation (eg, disseminated intravascular coagulation)*
- Uterine inversion

Secondary:

- Subinvolution of the placental site
- Retained products of conception
- Infection
- Inherited coagulation defects (eg, factor deficiency such as von Willebrand)

*These include inherited coagulation defects as well as acute coagulopathies that may develop from events such as amniotic fluid embolism, placental abruption, or severe preeclampsia.

When evaluating a patient who is bleeding, it may be helpful to consider “the 4 Ts” mnemonic device—tone, trauma, tissue, and thrombin (13). Abnormal uterine tone (uterine atony) is estimated to cause 70–80% of postpartum hemorrhage and usually should be suspected first as the etiology of postpartum hemorrhage (14). Recommended interventions for uterine atony include uterine massage, bimanual compression, and uterotonic drugs (15). Maternal trauma is indicated by lacerations, expanding hematomas, or uterine rupture. Retention of placental tissue can be readily diagnosed with manual

examination or bedside ultrasonography of the uterine cavity and is addressed with manual removal or uterine curettage. Thrombin is a reminder to evaluate the patient's coagulation status and if abnormal to correct with replacement of clotting factors, fibrinogen, or other factor replacement sources (see sections on Transfusion Therapy and Massive Transfusion). It is important to identify the most likely diagnosis or diagnoses to initiate appropriate interventions. These diagnoses are outlined individually in the Clinical Considerations and Recommendations section.

Risk Factors

Because obstetric hemorrhage is unpredictable, relatively common, and leads to severe morbidity and mortality, all obstetric unit members, including the physicians, midwives, and nurses who provide obstetric care, should be prepared to manage women who experience it. A number of well-established risk factors such as prolonged labor or chorioamnionitis are associated with postpartum hemorrhage (Table 1). However, many women without these risk factors can experience a postpartum hemorrhage (16). State and national organizations have suggested that a maternal risk assessment should be conducted antenatally and at the time of admission and continuously modified as other risk factors develop during labor or the postpartum period (17).

Risk assessment tools are readily available (18, 19) and have been shown to identify 60–85% of patients who will experience a significant obstetric hemorrhage (17, 20, 21). An example of this type of assessment tool is outlined in Table 2. However, a validation study of this tool among a retrospective cohort of more than 10,000 women showed that although the tool correctly identified more than 80% of patients with severe postpartum hemorrhage, more than 40% of women who did not experience hemorrhage were placed into the high-risk group giving the tool a specificity of just below 60% (20). Additionally, approximately 1% of women in the low-risk group experienced a severe postpartum hemorrhage, which indicates that the clinical value for identifying patients through risk assessment is low. These findings reinforce the need for diligent surveillance in all patients, including those initially thought to be at low risk.

Prevention

Many organizations have recommended active management of the third stage of labor as a method to reduce the incidence of postpartum hemorrhage (22–24). The three components of active management are as follows: 1) oxytocin administration, 2) uterine massage, and 3) umbilical cord traction (25). Prophylactic oxytocin, by dilute intravenous infusion (bolus dose of 10 units), or intramuscular injection (10 units), remains the most effective medication with the fewest adverse effects (26). Oxytocin plus methylergonovine or oxytocin in combination with misoprostol appears to be no more effective than oxytocin used alone for prophylaxis (26, 27). The timing of oxytocin administration—after delayed umbilical cord clamping, with delivery of the anterior shoulder, or with placental delivery—has not been adequately studied or found to be associated with a difference in the risk of hemorrhage (28). Specifically, delaying oxytocin until after delayed umbilical cord clamping has not been found to increase the risk of hemorrhage (29). The World Health Organization, ACOG, American Academy of Family Physicians, and Association of Women's Health, Obstetric and Neonatal Nurses recommend

administering uterotonics (usually oxytocin) after all births for the prevention of postpartum hemorrhage (13, 22, 24). Therefore, all obstetric care facilities should have guidelines for the routine administration of uterotonics in the immediate postpartum period.

Table 1. Antenatal and Intrapartum Risk Factors for Postpartum Hemorrhage ↩

Etiology	Primary Problem	Risk Factors, Signs
Abnormalities of uterine contraction—atony	Atonic uterus	Prolonged use of oxytocin High parity Chorioamnionitis General anesthesia
	Over-distended uterus	Twins or multiple gestation Polyhydramnios Macrosomia
	Fibroid uterus	Multiple uterine fibroids
	Uterine inversion	Excessive umbilical cord traction Short umbilical cord Fundal implantation of the placenta
Genital tract trauma	Episiotomy Cervical, vaginal, and perineal lacerations Uterine rupture	Operative vaginal delivery Precipitous delivery
Retained placental tissue	Retained placenta Placenta accreta	Succenturiate placenta Previous uterine surgery Incomplete placenta at delivery
Abnormalities of coagulation	Preeclampsia Inherited clotting factor deficiency (von Willebrand, hemophilia) Severe infection Amniotic fluid embolism Excessive crystalloid replacement Therapeutic anticoagulation	Abnormal bruising Petechia Fetal death Placental abruption Fever, sepsis Hemorrhage Current thromboembolism treatment

Modified from New South Wales Ministry of Health. Maternity—prevention, early recognition and management of postpartum haemorrhage (PPH). Policy Directive. North Sydney: NSW Ministry of Health; 2010. Available at: http://www1.health.nsw.gov.au/pds/ActivePDSDocuments/PD2010_064.pdf. Retrieved July 24, 2017. Copyright 2017.

Table 2. Example of Risk Assessment Tool

Low Risk	Medium Risk	High Risk
Singleton pregnancy	Prior cesarean or uterine surgery	Placenta previa, accreta, increta, percreta
Less than four previous deliveries	More than four previous deliveries	HCT <30
Unscarred uterus	Multiple gestation	Bleeding at admission
Absence of postpartum hemorrhage history	Large uterine fibroids	Known coagulation defect
	Chorioamnionitis	History of postpartum hemorrhage
	Magnesium sulfate use	Abnormal vital signs (tachycardia and hypotension)
	Prolonged use of oxytocin	

Abbreviation: HCT, hematocrit.

Modified from Lyndon A, Lagrew D, Shields L, Main E, Cape V, editors. Improving health care response to obstetric hemorrhage version 2.0. A California quality improvement toolkit. [Stamford \(CA\): California Maternal Quality Care Collaborative; Sacramento \(CA\): California Department of Public Health; 2015.](#)

Although the number of well-conducted studies is limited, one small study found that the use of uterine massage was associated with reduced postpartum blood loss and reduced need for additional uterotonic agents (30); however, a Cochrane review found no statistical differences and found the evidence inconclusive (31). Furthermore, neither early umbilical cord clamping nor umbilical cord traction have been shown to have a significant effect on the incidence or volume of postpartum hemorrhage (32). Additionally, in a Cochrane review, two trials examining nipple stimulation or breastfeeding did not demonstrate a difference in postpartum hemorrhage (33, 34).

Techniques for Management

Management may vary greatly among patients and depends on the etiology and available treatment options. In general, management of postpartum hemorrhage should use a multidisciplinary and multifaceted approach that involves maintaining hemodynamic stability while simultaneously identifying and treating the cause of blood loss. Treatment options for postpartum hemorrhage because of uterine atony include administration of uterotonics or pharmacologic agents, tamponade of the uterus (eg, intrauterine balloons), surgical techniques to control the bleeding (eg, the B-Lynch procedure), embolization of pelvic arteries or, ultimately, hysterectomy. Generally, less invasive methods should be tried initially if possible; however, if unsuccessful, more invasive measures may be required. More specific guidance for these management approaches is delineated later in the document.

Systematic approaches to postpartum hemorrhage based on algorithms have been created, and these approaches have been used more widely at individual hospitals and in health systems (19, 35, 36). These approaches employ a multidisciplinary (eg, obstetrics, nursing, anesthesia, transfusion medicine), multifaceted, stepwise approach to the detection and management of postpartum hemorrhage. The approaches are aimed at treating cases early and consistently to reduce severe maternal morbidity and mortality as well as to identify the need for more aggressive interventions (such as hysterectomy or

other surgeries) and intensive care unit admissions. Although it does appear that hemorrhage is treated earlier with such approaches, evidence regarding maternal outcomes, such as severe maternal morbidity or intensive care unit admission, is inconsistent (12).

Facilities With Limited Resources

Many hospitals that provide maternal services are located in rural or small communities. In the United States, obstetric services are provided in 50% of critical access hospitals and 92% of rural hospitals (37). Because these centers typically do not have the same resources as most urban centers, developing a comprehensive plan for dealing with obstetric emergencies such as postpartum hemorrhage is important. In particular, these small centers should consider establishing guidelines regarding appropriate case selection to triage or transfer patients to higher-level centers. Additionally, assessing available resources and developing a comprehensive plan for evaluating and managing obstetric hemorrhage are important for reducing morbidity. For more information see Obstetric Care Consensus No. 2, Levels of Maternal Care (38).

Clinical Considerations and Recommendations

What should be considered in the initial evaluation and management of a patient with excessive bleeding in the immediate postpartum period?

When postpartum bleeding exceeds expected volumes (500 mL in a vaginal delivery or 1,000 mL in a cesarean delivery), a careful and thorough evaluation should be undertaken. A rapid physical examination of the uterus, cervix, vagina, vulva, and perineum can often identify the etiology (sometimes multiple sources) of the postpartum hemorrhage. Obstetrician–gynecologists and other obstetric care providers should be familiar with algorithms for the diagnosis and management of postpartum hemorrhage (18, 39) and, ideally, these should be posted on labor and delivery units (see For More Information). The most common etiologies include uterine atony, genital tract lacerations, retained placental tissue and, less commonly, placental abruption, coagulopathy (acquired or inherited), amniotic fluid embolism, placenta accreta, or uterine inversion.

Uterine Atony

Because uterine atony causes 70–80% of cases of postpartum hemorrhage, it remains the single most common cause, and its incidence appears to be increasing (14, 21, 40). At the time of delivery, risk factors include, but are not limited to, prolonged labor, induction of labor, prolonged use of oxytocin, chorioamnionitis, multiple gestation, polyhydramnios, and uterine leiomyomas (see Table 1 and Table 2).

In the setting of postpartum hemorrhage, identification of a soft, poorly contracted (boggy) uterus suggests atony as a causative factor. When atony is suspected, the bladder should be emptied and a bimanual pelvic examination conducted, any intrauterine clots should be removed, and uterine massage should be performed. In addition to oxytocin, a second uterotonic agent is required in 3–25% of cases of postpartum hemorrhage (15). Supplemental uterotonics that are most commonly administered include

methylergonovine, 15-methyl prostaglandin F_{2α}, or misoprostol. As discussed in a 2015 systematic review, there is a lack of evidence that suggests which specific additional uterotonics are the most effective (12). Treatment of refractory atony may require the use of secondary methods such as uterine tamponade with an intrauterine tamponade balloon or compression sutures (41, 42).

Occasionally, the fundus is firm and contracted down, but the lower uterine segment is dilated and atonic. In this setting, the usual approach is to manually remove any clots and to use bimanual compression to reduce the blood loss while waiting for the uterotonic agents to work. Treatment with the intrauterine tamponade balloon can be considered if there is persistent lower uterine segment atony.

Obstetric Trauma

Genital tract lacerations are the most common complications of obstetric trauma. Although such lacerations are predominantly venous bleeding, they can be the primary source of a postpartum hemorrhage. Rapid identification and repair of cervical lacerations, lacerations complicated by arterial bleeding, and high vaginal lacerations should be performed. Similarly, distal vaginal, vulvar, periclitoral, and perineal lacerations should be repaired if contributing significantly to blood loss. If a uterine artery laceration is suspected, interventional radiology or surgical exploration and ligation should be considered. Repair may require assistance from anesthesia and transfer to a well-equipped operating room.

Genital tract hematomas (labial, vaginal, broad ligament, or retroperitoneal) also can lead to significant blood loss and should be suspected in the setting of a precipitous uncontrolled delivery or an operative vaginal delivery. Labial, rectal, pelvic pressure or pain, or vital sign deterioration may be the only symptoms of genital tract hematomas and may not be recognized until hours after delivery. Once identified, most genital tract hematomas can be managed conservatively. However, rapid progressive enlargement of the hematoma, particularly in the setting of abnormal vital signs, indicates a need for incision and drainage. One reason that opening a hematoma is reserved for only the most severe cases is that often a single bleeding source is not identified when a hematoma is incised. Exploration with suturing or packing may be needed to achieve hemostasis. Arterial embolization is another option for management of a hematoma and should be considered as a possibility before opening the hematoma.

Deterioration of maternal vital signs without obvious bleeding should alert the obstetric team that there may be intraperitoneal or retroperitoneal bleeding. In this setting, resuscitative measures, diagnostic imaging, and surgical intervention or an interventional radiology procedure should not be delayed.

Retained Placenta

Detailed visual inspection of the placenta for completeness should be conducted after all deliveries. Even when the placenta appears intact, there may be additional remaining products of conception (eg, succenturiate lobe) within the uterine cavity. Manual removal of the placenta, prior uterine surgery, or other risk factors for morbidly adherent placenta should raise suspicion for retained placental tissue or placenta accreta. Ultrasonography or intrauterine manual examination is usually used to diagnose

retained placental tissue. Retained placental tissue is unlikely when ultrasonography reveals a normal endometrial stripe. However, although ultrasonographic images of retained placental tissue can be inconsistent, detection of an echogenic mass within the uterus is highly suspicious. When a retained placenta is identified, the first step is to attempt manual removal of the tissue. If a woman has adequate regional analgesia, assessment of the uterine cavity may be performed. If manual extraction fails, either a “banjo” curette or large oval forceps (Sopher or Bierer) can be used for removal. Because of the concern for uterine perforation in the postpartum uterus and to ensure removal of all tissue, ultrasound guidance may be used. If the placental tissue is adherent to the uterine wall, there should be increased suspicion for placenta accreta, particularly in the presence of risk factors for placenta accreta. Management of placenta accreta is discussed later in the document.

Acute Coagulopathy

An acute coagulopathy can complicate postpartum hemorrhage and, in such a setting, two specific etiologies beyond massive blood loss alone should be considered: 1) placental abruption and 2) amniotic fluid embolism. Placental abruption often is associated with uterine atony secondary to extravasation of blood into the myometrium (Couvelaire uterus), and disseminated intravascular coagulation and hypofibrinogenemia are known complications. Placental abruption usually presents as a combination of vaginal bleeding, frequent uterine contractions (tachysystole), and pain (43). The classic contraction pattern includes high-frequency, low-amplitude contractions. Placental abruption is responsible for 17% of cases that require massive transfusion (44).

Amniotic fluid embolism is a rare, unpredictable, unpreventable, and devastating obstetric emergency signaled by a triad of hemodynamic and respiratory compromise in addition to strictly defined disseminated intravascular coagulation (45). Given the profound coagulopathy, postpartum hemorrhage is almost always seen with amniotic fluid embolism. Coagulopathy and the resultant hemorrhage should be managed with aggressive volume replacement and initiation of a massive transfusion protocol (discussed later in this document).

What are the medical and surgical approaches for the management of postpartum hemorrhage?

When treating postpartum hemorrhage, it is necessary to balance the use of less invasive management techniques with the need to control the bleeding and achieve hemostasis. Treatment is based upon the etiology for the postpartum hemorrhage. Although hemorrhage etiologies such as lacerations and accreta have specific treatment approaches, the evidence evaluating these approaches is almost nonexistent. However, there is a wide range of approaches to treat postpartum hemorrhage in the setting of atony, which is the most common cause. Thus, this section will focus on the evidence underlying the different approaches to treat postpartum hemorrhage. Generally, in the treatment of postpartum hemorrhage, less invasive methods should be used initially if possible, but if unsuccessful, preservation of life may require more aggressive interventions, including hysterectomy. Few randomized controlled trials that examine the management of postpartum hemorrhage have been conducted, so management decisions usually are based on observational studies and clinical judgment.

Medical Management

Uterotonic agents should be the first-line treatment for postpartum hemorrhage caused by uterine atony. The specific agent selected, outside of recognized contraindications, is at the health care provider's discretion because none has been shown to have greater efficacy than others for the treatment of uterine atony (12). Common medical agents (eg, oxytocin, methylergonovine, 15-methyl prostaglandin F_{2α}, and misoprostol) and their doses are outlined in Table 3. It is common for multiple uterotonic agents to be used, assuming there are no contraindications, and without adequate uterine response and ongoing hemorrhage, they should be used in rapid succession (15). When uterotonics fail to adequately control postpartum hemorrhage, prompt escalation to other interventions (such as tamponade or surgical techniques) and escalation of intensity of care and support personnel are indicated.

Tranexamic Acid

Tranexamic acid is an antifibrinolytic agent that can be given intravenously or orally. A large, randomized, international trial, the WOMAN trial, compared 1 g of intravenous tranexamic acid to placebo in the setting of postpartum hemorrhage (46). Although the composite primary endpoint of hysterectomy or death from all causes was not reduced with tranexamic acid treatment, a significant reduction of mortality in the subgroup of death from obstetric hemorrhage was noted (1.5% versus 1.9%, $P=.045$ for tranexamic acid compared to placebo, respectively). When the treatment was given within 3 hours of birth, the mortality rates from obstetric hemorrhage were 1.2% versus 1.7% comparing tranexamic acid to placebo ($P=.008$). Tranexamic acid has been shown in a number of small studies to modestly reduce obstetric blood loss when given prophylactically and as part of treatment for postpartum hemorrhage (47, 48). Additionally, the risk of thrombosis appears to not be different from controls when used in surgeries (49, 50), and the risk of thrombosis was not higher in women who received tranexamic acid as part of the WOMAN trial. At this time, data are insufficient to recommend the use of tranexamic acid as prophylaxis against postpartum hemorrhage outside of the context of research. Although the generalizability of the WOMAN trial and the degree of effect in the United States is uncertain, given the mortality reduction findings, tranexamic acid should be considered in the setting of obstetric hemorrhage when initial medical therapy fails. Earlier use is likely to be superior to delayed treatment, given that in the stratified analysis it appeared that the benefit was primarily in women treated sooner than 3 hours from the time of delivery. For those clinicians unfamiliar with tranexamic acid, it should be used in consultation with a local or regional expert in massive hemorrhage and specifically incorporated into management guidelines.

Table 3. Acute Medical Management of Postpartum Hemorrhage

Drug*	Dose and Route	Frequency	Contraindications	Adverse Effects
Oxytocin	IV: 10–40 units per 500–1,000 mL as continuous infusion or IM: 10 units	Continuous	Rare, hypersensitivity to medication	Usually none. Nausea, vomiting, hyponatremia with prolonged dosing. Hypotension can result from IV push, which is not recommended.
Methylergonovine	IM: 0.2 mg	Every 2–4 h	Hypertension, preeclampsia, cardiovascular disease, hypersensitivity to drug	Nausea, vomiting, severe hypertension particularly when given IV, which is not recommended
15-methyl PGF _{2α}	IM: 0.25 mg Intramyometrial: 0.25 mg	Every 15–90 min, eight doses maximum	Asthma. Relative contraindication for hypertension, active hepatic, pulmonary, or cardiac disease	Nausea, vomiting, diarrhea, fever (transient), headache, chills, shivering hypertension, bronchospasm
Misoprostol	600–1,000 micrograms oral, sublingual, or rectal	One time	Rare, hypersensitivity to medication or to prostaglandins	Nausea, vomiting, diarrhea shivering, fever (transient), headache

Abbreviations: IV, intravenously; IM, intramuscularly; PG, prostaglandin.

*All agents can cause nausea and vomiting.

Modified from Lyndon A, Lagrew D, Shields L, Main E, Cape V, editors. Improving health care response to obstetric hemorrhage version 2.0. A California quality improvement toolkit. Stamford (CA): California Maternal Quality Care Collaborative; Sacramento (CA): California Department of Public Health; 2015.

Tamponade Techniques

When uterotonics and bimanual uterine massage fail to sustain uterine contractions and satisfactorily control hemorrhage, the use of compression (including manual compression), intrauterine tamponade or packing can be effective in decreasing hemorrhage secondary to uterine atony (Table 4). Although the evidence that compares these approaches is poor or absent, it is important for institutions to adopt an approach and train personnel in this approach. For example, the California Maternal Quality Care Collaborative recommends the use of an intrauterine balloon for tamponade after uterotonics have failed.

Evidence for the benefits of use of intrauterine balloon tamponade is limited; however, in one study, 86% of women who had balloon tamponade did not require further procedures or surgeries (12, 51). Similarly, a summary of studies showed that 75% of patients did not need further treatment after intrauterine balloon tamponade (12). In some refractory cases, intrauterine tamponade and uterine compression sutures (described later) may be used together (52).

Table 4. Tamponade Techniques for Postpartum Hemorrhage

Technique	Comment
Commercially available intrauterine balloon tamponade devices	Inserted transcervically or through cesarean incision; has an exit port for blood drainage
- Bakri Balloon	Inflated with 300–500 mL of saline
- ebb uterine tamponade system	Double Balloon: maximum recommended fill volumes are 750 mL for the uterine balloon and 300 mL for the vaginal balloon.
Foley catheter	Insert one or more 60 mL bulbs and fill with 60 mL of saline.
Uterine packing	4-inch gauze, can be soaked with 5,000 units of thrombin in 5 mL of saline then insert from one cornua to the other with ring forceps.

If a balloon tamponade system is not available, the uterus may be packed with gauze. This requires careful layering of the material back and forth from one uterine cornu to the other repeatedly using a sponge stick, and ending with extension of the gauze through the cervical os. To avoid leaving gauze in the uterus at time of removal, it can be carefully counted and tied together. Similarly, multiple large Foley catheters (which were common before the development of commercial intrauterine tamponade devices) can still be used, but the challenge is placing multiple devices and keeping careful count of them. In cases where compression, or intrauterine tamponade, or both, fail to adequately control hemorrhage, they may be used to temporize while planning to move to uterine artery embolization (UAE) or hysterectomy.

Uterine Artery Embolization

Candidates for UAE typically are hemodynamically stable, appear to have persistent slow bleeding and have failed less invasive therapy (uterotonic agents, uterine massage, uterine compression, and manual removal of any clots) (12). When successful, UAE also has the benefit of a woman retaining her uterus and, potentially, future fertility. Fluoroscopic identification of bleeding vessels allows embolization with absorbable gelatin sponges, coils, or microparticles. Studies (n=15) have shown that UAE for postpartum hemorrhage has a median success rate of 89%, ranging from 58% to 98% (12). Moreover, one of the largest series (114 UAE procedures) reported a success rate greater than 80%, with 15% requiring subsequent hysterectomy (53). The risk of significant harm (uterine necrosis, deep vein thrombosis, or peripheral neuropathy) appears to be low (less than 5%) based on reports from small case series (12). After UAE, infertility has been reported in up to 43% of women (12). Other studies have reported that in

women who have had a UAE, subsequent pregnancy complications such as preterm birth (5–15%) and fetal growth restriction (7%) appear to be similar to the general obstetric population (12, 54).

Surgical Management

Vascular Ligation

When less invasive approaches such as uterotonic agents (with or without tamponade measures) or UAE fail to control bleeding in the setting of postpartum hemorrhage, exploratory laparotomy is indicated. In the setting of a vaginal delivery, it is common to use a midline vertical abdominal incision to optimize exposure and reduce risk of surgical bleeding. In the setting of cesarean birth, the existing surgical incision may be used. Several techniques are available to control bleeding with limited evidence for each (12). The general aim of vascular ligation in the setting of atony is to diminish the pulse pressure of blood flowing to the uterus. A common first approach is bilateral uterine artery ligation (O’Leary sutures), which commonly accomplishes this goal of reducing blood flow to the uterus, and is quickly and easily performed (55, 56). Similarly, to further diminish blood flow to the uterus, sutures also can be placed across the vessels within the utero–ovarian ligaments. Reports from case series indicate that, when used as a second-line approach to postpartum hemorrhage, the median success of vascular ligation is 92% (12).

However, because these less invasive vascular techniques appear to be effective, it appears that internal iliac (hypogastric) artery ligation is performed less frequently than in the past. The procedure has been found to be considerably less successful than originally thought (57) and because practitioners have become less familiar with this technique (which requires a retroperitoneal approach) it is rarely used today.

Uterine Compression Sutures

Although there are no good-quality studies that provide evidence for the success of uterine compression sutures, the B-Lynch technique probably is the most common uterine compression technique for atony (42); however, other techniques, such as Cho and Hayman, have been described (42, 58–61). The effectiveness of uterine compression sutures as a secondary treatment for uterine atony unresponsive to medical management appears to be approximately 60–75%, with none of the techniques shown to be superior to another (12, 62, 63). B-lynch sutures are placed from the cervix to fundus and provide physical compression of the uterus. A large suture (eg, a number 1 chromic suture) should be used to prevent breaking and the suture should be rapidly absorbed to prevent risk of bowel herniation through a persistent loop of suture after uterine involution. Physicians should be familiar with the technique and it could be helpful to have diagrams available on labor and delivery for quick reference such as those available in the Alliance for Innovation on Maternal Health Obstetric Hemorrhage Bundle (64) (see For More Information). Direct comparisons between compression sutures and uterine balloons have been described in small case series and suggest they have similar effectiveness (65). Uterine necrosis after placement of compression sutures has been reported; however, the exact incidence is not clear because of the small number of patients in case reports and series.

Hysterectomy

When more conservative therapies have failed, hysterectomy is considered the definitive treatment and is not only associated with permanent sterility but also potential surgical complications. For example, six small studies have shown that bladder injuries range from 6% to 12% and ureteral injuries range from 0.4% to 41% (12). There are inadequate studies that compared hysterectomy to other management approaches. Additionally, there is inadequate evidence examining different surgical approaches to hysterectomy (eg, total hysterectomy versus supracervical hysterectomy). Therefore, in the setting of an emergent postpartum hysterectomy, the surgical approach felt to be the fastest and safest should be used.

What are the clinical considerations for placenta accreta not diagnosed before delivery?

Placenta accreta is a life-threatening condition in which either a portion of or the entire placenta invades into the myometrium and fails to separate from the uterine wall during the third stage of labor (66). The risk factors that have the most significant effect appear to be a history of prior uterine surgery, particularly prior cesarean delivery, and placenta previa (67, 68). One multicenter study of more than 30,000 patients who had cesarean deliveries without labor found that the risk of placenta accreta increased with the number of cesarean deliveries (ie, 0.2%, 0.3%, 0.6%, 2.1%, 2.3%, and 6.7% for women experiencing their first through sixth cesarean deliveries, respectively) (68). Therefore, in the presence of placenta previa and a history of cesarean delivery, the obstetrician–gynecologist should have a high clinical suspicion for placenta accreta. The risk was far higher in women with placenta previa with 3%, 11%, 40%, 61%, and 67% of such women with their first through fifth or more cesarean deliveries having a placenta accreta. When diagnosed antenatally, an organized, multidisciplinary management and delivery plan should be developed. Preparations will include establishing a delivery date and assembling an experienced team (including surgical, anesthesiology, blood bank, nursing, and neonatal intensive care unit personnel) and relevant resources (including an operating room and equipment) (66).

In the setting of postpartum hemorrhage and a vaginal delivery, accreta should be strongly suspected if the placenta does not detach easily, and there should be no further attempt to manually remove the placenta in the delivery room. The patient should be moved to an operating room, if not already there, for further assessment. The patient should be counseled about the likely need for hysterectomy and blood transfusion. In the operating room, the extent (eg, area and depth) of the abnormal attachment can be assessed to determine the plan (eg, curettage, wedge resection, medical management, or hysterectomy). If there is ongoing hemorrhage and likely accreta is diagnosed, plans for a prompt hysterectomy should be underway. Adequate intravenous access with at least two large bore intravenous lines should be obtained. Blood products (including red blood cells, fresh frozen plasma, platelets, and cryoprecipitate) should be made readily available while the local blood bank is alerted that additional blood products may be needed. Once the diagnosis of suspected accreta is made, other specialties such as urology, surgery, or interventional radiology should be notified in case additional support is needed.

Uterine conserving options may work in the setting of a small focal accreta; however, in most cases with ongoing bleeding, abdominal hysterectomy will be needed. Attempts at uterine conservation have been recently reviewed (69) and were associated with a 40% risk of emergency hysterectomy, and 42% of women in this setting suffered major morbidity. The risk of an abnormally adherent placenta in a subsequent pregnancy appears to be approximately 20% in a review of 407 patients (70). Thus, an attempt to conserve the uterus in the presence of a focal accreta may be considered for women with a strong desire to retain fertility and a clear understanding of the significant risks of this approach; however, without control of ongoing bleeding, hysterectomy should be the surgical plan.

What is the management approach for hemorrhage caused by a ruptured uterus?

Uterine rupture can occur at the site of a previous cesarean delivery or other surgical procedure that involves the uterine wall, from intrauterine manipulation or trauma, from congenital malformation (small uterine horn), or it can occur spontaneously, particularly in the setting of abnormal labor (71–73). Surgical repair is required, with the specific approach tailored to reconstruct the uterus, if possible. Care depends on the extent and site of rupture, the patient's current clinical condition, and her desire for future childbearing. For example, rupture of a previous cesarean delivery scar often can be managed by revision of the edges of the prior incision followed by primary closure. In addition to the myometrial disruption, consideration should be given to neighboring structures, such as the broad ligament, parametrial vessels, ureters, and bladder. Although the patient may wish to avoid hysterectomy, this procedure may be necessary in a life-threatening situation. Supportive care with intravenous fluids, uterotonic medications, and blood transfusion will depend on the degree of blood loss and the patient's hemodynamic status.

What is the management approach for an inverted uterus?

Uterine inversion (when the uterine corpus descends to, and sometimes completely through, the uterine cervix) can be associated with marked hemorrhage and cardiovascular collapse. It is relatively rare with an incidence of 1 in 3,700 to 20,000 at vaginal delivery and 1 in 1,860 at cesarean delivery (74, 75). Uterine inversion in a prior pregnancy leads to an increased risk in a subsequent pregnancy (1 per 26 subsequent deliveries) although it is still relatively uncommon (74). Upon bimanual examination, the finding of a firm mass at or below the cervix, coupled with the absence of identification of the uterine corpus on abdominal examination, suggests inversion. If the inversion occurs before placental separation, detachment or removal of the placenta is generally not undertaken before replacement of the uterus because, presumably, this could lead to additional hemorrhage (76).

Manual replacement of the uterine corpus involves placing the palm of the hand or a closed fist against the fundus (now inverted and lowermost at or through the cervix), as if holding a tennis ball, with the fingertips exerting upward pressure circumferentially (77). To restore normal anatomy, relaxation of the uterus may be necessary. Terbutaline, magnesium sulfate, halogenated general anesthetics, and nitroglycerin have all been used for uterine relaxation without clear evidence supporting any one approach as superior to the others (78). Manual replacement with or without uterine relaxants usually is successful with the large majority being successfully replaced in one small series (76). In the unusual

circumstance in which it is not, laparotomy is required. Two procedures have been reported to return the uterine corpus to the abdominal cavity. The Huntington procedure involves progressive upward traction on the inverted corpus using Babcock or Allis forceps (79). The Haultain procedure involves incising the cervix posteriorly, which allows for digital repositioning of the inverted corpus, with subsequent repair of the incision (80).

Supportive measures and treatment of the associated hemorrhage should be employed while the inversion is corrected. In the setting of recurrent uterine inversion, the use of intrauterine tamponade balloons has been reported to prevent recurrent uterine inversion as well as the accompanying hemorrhage in a number of case reports (81–84). The use of uterine compression sutures for prevention of acute recurrence also has been successful in a limited number of case reports (59, 85).

What is the management approach for secondary or delayed postpartum hemorrhage?

Secondary postpartum hemorrhage, defined as excessive bleeding that occurs more than 24 hours after delivery and up to 12 weeks postpartum, occurs in approximately 1% of pregnancies (11). In the event of secondary hemorrhage, a number of specific etiologies should be considered. Uterine atony (perhaps secondary to retained products of conception) with or without infection contributes to secondary hemorrhage. Ultrasound evaluation can help identify intrauterine tissue. Endometritis should be strongly suspected in the presence of uterine tenderness and a low grade fever. Secondary postpartum hemorrhage also may be the first indication of bleeding disorders such as von Willebrand disease.

Treatment should be focused on the etiology of the hemorrhage and may include uterotonic agents and antibiotics, but if these fail to resolve the problem or if retained products of conception are suspected, uterine curettage may be necessary. If treating endometritis, broad antibiotic coverage with clindamycin and gentamicin is a common choice, although other combinations also are used (86). Often the volume of tissue removed by curettage is relatively small, yet bleeding usually subsides promptly. Concurrent ultrasound assessment at the time of curettage can help prevent uterine perforation. Patients should be counseled about the possibility of hysterectomy before initiating any operative procedure.

What is best practice for blood product replacement during and after a postpartum hemorrhage?

The Timing of Transfusion Therapy ⇐

Initiation of transfusion therapy generally is based on estimated blood deficit and ongoing blood loss. However, in the setting of postpartum hemorrhage, acute changes in hemoglobin or hematocrit will not accurately reflect blood loss. As noted previously, maternal vital signs typically do not change drastically until significant blood loss has occurred (10). Inadequate early resuscitation and hypoperfusion may lead to lactic acidosis, systemic inflammatory response syndrome with accompanying multiorgan dysfunction, and coagulopathy (87). In women with ongoing bleeding that equates to the blood loss of 1,500 mL or more or in women with abnormal vital signs (tachycardia and hypotension), immediate preparation for transfusion should be made (18, 19, 39). Because such a large blood loss includes depletion of coagulation factors, it is common for such patients to develop a consumptive coagulopathy,

commonly labeled as disseminated intravascular coagulation, and the patients will require platelets and coagulation factors in addition to packed red blood cells.

Transfusion and Massive Obstetric Hemorrhage↩

Massive transfusion usually is defined as a transfusion of 10 or more units of packed red blood cells within 24 hours, transfusion of 4 units of packed red blood cells within 1 hour when ongoing need for more blood is anticipated, or replacement of a complete blood volume (87). Despite the low quality of evidence regarding the benefit of massive transfusion for early postpartum hemorrhage (12), massive transfusion protocols should be part of a comprehensive management plan for treatment of postpartum hemorrhage in settings with adequate blood banking.

Recommendations for optimal blood product replacement therapy and timing of transfusion in obstetric patients have been primarily limited to consensus opinion (18), protocols adapted from trauma literature (88, 89), and a few clinical reports (19, 39, 90–92). All recommend the use of multicomponent therapy with fixed ratios of packed red blood cells, fresh or thawed plasma, platelets, and cryoprecipitate. When a massive transfusion protocol is needed, fixed ratios of packed red blood cells, fresh frozen plasma, and platelets should be used. The recommended initial transfusion ratio for packed red blood cells: fresh frozen plasma: platelets has been in the range of 1:1:1 and is designed to mimic replacement of whole blood. In a recent survey, more than 80% of institutions reported using the 1:1 red blood cell: plasma ratio (93). These recommendations are different from protocols that have previously suggested ratios such as 4:4:1 or 6:4:1 and are related to how a unit of platelets is defined (18). What is more important than the actual ratio is that there is a specific protocol for multicomponent therapy in place at each institution. In women with suspected disseminated intravascular coagulation (ie, consumptive coagulopathy, or low fibrinogen, or both) administration of cryoprecipitate also should be considered. Findings of critically low fibrinogen should be particularly anticipated in the setting of placental abruption or amniotic fluid embolism, and early use of cryoprecipitate is commonly included as part of the resuscitation.

Although smaller hospitals may not have all blood products, every obstetric unit should have a comprehensive maternal hemorrhage emergency management plan that includes protocols for accessing packed red blood cells. In emergency situations, type specific or type O Rh-negative blood also should be readily available. Physicians should be familiar with their hospitals' protocol and recommendations for use of combination blood component therapy. No specific hemorrhage protocol has been proved to be more effective than another; therefore, each hospital will need to address its specific resources and make modifications specific to its unique setting. For examples of algorithms, see For More Information.

It is also important to establish approaches to address situations in which patients decline various treatment approaches. For example, refusal of blood products is common in patients who are Jehovah's Witnesses. This subset of patients has between a 44-fold to 130-fold higher risk of maternal mortality from obstetric hemorrhage because of refusal of blood products (94, 95). Because this population may accept some blood products, a predelivery directive that can be used in the event of a severe

postpartum hemorrhage can be discussed with the patient during the prenatal period (18, 96). Greater detail on this issue is outlined in Committee Opinion No. 664, Refusal of Medically Recommended Treatment During Pregnancy.

Although transfusion is often lifesaving in obstetrics, usage of blood products, particularly in the setting of massive transfusion, is not without risk. Massive transfusion is associated with hyperkalemia from packed red blood cells and citrate (used as a preservative in stored blood products) toxicity that will typically worsen hypocalcemia. The combination of acidosis, hypocalcemia, and hypothermia all contribute to worsening coagulopathy and increased morbidity (87, 97). Overzealous resuscitation with crystalloid also can be associated with dilution-related coagulopathy and can contribute to pulmonary edema (98). Other complications include transfusion febrile nonhemolytic reactions (0.8 per 1,000 units transfused), acute hemolytic transfusion reaction (0.19 per 1,000 units transfused), and acute transfusion reactions related lung injury (TRALI, 0.1 per 1,000 units transfused) (99). Transfusion-associated infections (eg, hepatitis, human immunodeficiency virus, West Nile virus, Chagas disease, malaria, and Lyme disease) are relatively rare (less than 1/100,000–1,000,000) (100).

Other Related Therapies

Cell Salvage

Intraoperative cell salvage—also known as autologous blood transfusion—has been shown to be effective and safe in obstetric patients. Limitations are primarily related to availability of appropriate staff and equipment. In certain settings where significant blood loss is anticipated, such as placenta previa and placenta accreta, having this tool available may reduce the need for or volume of allogeneic blood transfusion. Early concerns related to amniotic fluid contamination have been dispelled with higher quality filtering techniques (101). There is some concern for anti-D isoimmunization, and appropriate testing and treatment with anti-D immunoglobulin is necessary (102, 103). However, because the large majority of postpartum hemorrhage events are unpredictable, cell salvage is rarely available or used.

Prothrombin Complex and Fibrinogen Concentrates

Prothrombin complex concentrates (PCCs) are human plasma-derived concentrates of vitamin K-dependent clotting factors. They are the first-line treatment modality for the urgent reversal of acquired coagulation factor deficiency induced by vitamin-K antagonists (eg, warfarin) (104). Different preparations of PCCs are available that contain three factors (factors II, IX, and X) or four factors (factors II, VII, IX, and X). Fibrinogen concentrates are approved for the treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency. Data regarding the use of PCC and fibrinogen concentrates in the setting of postpartum hemorrhage and disseminated intravascular coagulation are limited. Thus, these should be used only after multiple rounds of the standard massive transfusion agents and in consultation with a local or regional expert in massive hemorrhage.

Recombinant Factor VII

Factor VII is a vitamin K-dependent serine protease with a pivotal role in coagulation. The only U.S. Food and Drug Administration-approved indication for recombinant factor VII is for treatment of patients with hemophilia A and B. The role of recombinant factor VII in primary postpartum hemorrhage is controversial (105, 106). It has been reported to significantly improve hemostasis in hemorrhaging obstetric patients, but also may result in life-threatening thrombosis (107) estimated to be in the range of 2–9% (12). Use of recombinant factor VII is not considered first-line therapy and should be reserved for extenuating circumstances after multiple rounds of the standard massive transfusion agents and in consultation with a local or regional expert in massive hemorrhage.

What is the best approach to managing anemia in the nonacute postpartum period once the postpartum hemorrhage has been treated?

After a patient has been stabilized posthemorrhage, the degree of anemia is sometimes not apparent until the patient receives her routine postpartum laboratory results the following day or has symptoms of dizziness or lightheadedness when she begins to ambulate. At this point a decision to treat using a transfusion of packed red blood cells (PRBCs), supplement oral iron, or intravenous iron will need to be made. The degree of ongoing blood loss (lochia), risk of subsequent blood loss, and patient symptoms should all be considered when deciding on the best approach to treatment. It is common practice to offer a transfusion of PRBCs to symptomatic women with a hemoglobin value less than 7 g/dL (hematocrit less than 20%) (108). Alternatively, the management of women with hemoglobin values less than 7 g/dL who are asymptomatic and hemodynamically stable should be individualized between transfusion, oral iron supplementation, or intravenous iron therapy. Each is designed to replace red cell mass, but at differing rates. Although transfusions historically were initiated with 2 units of PRBCs, the most recent recommendation from the American Association of Blood Banks for a stable patient is to begin with 1 unit and reassess (108).

When a blood transfusion is not necessary, but supplemental iron is indicated, the use of intravenous iron (ferrous sucrose) has been compared to oral iron for postpartum anemia in a few small randomized controlled trials. (109–112). Two of these studies have shown significant improvement in hemoglobin levels on posttreatment day 14 from intravenous iron, but these differences were modest. In absolute terms, there was a smaller increase in hemoglobin of 1.4–1.5 g/dL in those receiving oral iron as compared with 2.0–3.8 g/dL in those receiving intravenous iron (109, 111). At posttreatment day 40–42 none of the studies demonstrated a difference in hemoglobin level or any other clinical outcomes between oral or intravenous iron.

Which systems-level interventions are effective in improving the management of postpartum hemorrhage?

Using a standardized, multistage evaluation and response protocol has been associated with earlier intervention and resolution of maternal hemorrhage at an earlier stage of hemorrhage (19, 35). However, studies have not consistently demonstrated improvement in maternal outcomes, including severe morbidity or mortality (19, 35, 36). In the 2015 Agency for Health Research and Quality systematic review, there was no consistent evidence for benefit in severe postpartum hemorrhage,

transfusion, hysterectomy, intensive care unit admission, or mortality from standardized protocols (12). Despite this lack of consistent evidence, numerous organizations recommend that an organized, multidisciplinary approach be taken in order to reduce the morbidity and mortality from postpartum hemorrhage, and a quality improvement approach to this leading cause of maternal morbidity and mortality appears appropriate. Thus, all obstetric facilities should have a standardized hospital-wide process in place for management of obstetric hemorrhage. Obstetrician–gynecologists and other obstetric care providers should work with their institutions to ensure the existence of a designated multidisciplinary response team, a staged postpartum hemorrhage protocol that includes guidelines for escalation of care, and a functioning massive transfusion protocol.

Every obstetric unit should have an organized, systematic obstetric hemorrhage response that coordinates care among all critical personnel. Hospitals should consider adopting a system to implement key elements in four categories: 1) readiness to respond to a maternal hemorrhage, 2) recognition and prevention measures in place for all patients, 3) a multidisciplinary response to excessive maternal bleeding, and 4) a systems-based quality improvement process to improve responsiveness through reporting and system learning. The Council on Patient Safety in Women’s Healthcare has endorsed a system and further details can be found on the For More Information web page. Education, drills, and review of team protocol compliance are needed to ensure everyone remains proficient with the treatment algorithm and tools at each facility.

Multidisciplinary simulation-based team training, including postpartum hemorrhage scenarios, have been associated with improved safety culture and outcomes in obstetrics (113–115). Hemorrhage drills have been used for multiple purposes, including the following: identify management pitfalls (116), improve confidence and competence in skills (117), pilot and modify checklists (118), identify and correct systems issues (119, 120), familiarize staff with management algorithms, and ensure timely management of hemorrhage (19). Although one standardized approach for drills, simulation, and team training has not been established, there are several recommended tools and techniques that can be incorporated into unit-based improvement strategies (121, 122).

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based on good and consistent scientific evidence (Level A):

All obstetric care facilities should have guidelines for the routine administration of uterotonics in the immediate postpartum period.

Uterotonic agents should be the first-line treatment for postpartum hemorrhage caused by uterine atony. The specific agent selected, outside of recognized contraindications, is at the health care provider’s discretion because none has been shown to have greater efficacy than others for the treatment of uterine atony.

The following recommendations and conclusions are based on limited or inconsistent scientific evidence (Level B):

When uterotonics fail to adequately control post-partum hemorrhage, prompt escalation to other interventions (such as tamponade or surgical techniques) and escalation of intensity of care and support personnel are indicated.

Given the mortality reduction findings, tranexamic acid should be considered in the setting of obstetric hemorrhage when initial medical therapy fails.

Obstetrician–gynecologists and other obstetric care providers should work with their institutions to ensure the existence of a designated multidisciplinary response team, a staged postpartum hemorrhage protocol that includes guidelines for escalation of care, and a functioning massive transfusion protocol.

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C):

Management of postpartum hemorrhage should use a multidisciplinary and multifaceted approach that involves maintaining hemodynamic stability while simultaneously identifying and treating the cause of blood loss.

Generally, in the treatment of postpartum hemorrhage, less invasive methods should be used initially if possible, but if unsuccessful, preservation of life may require more aggressive interventions including hysterectomy.

When a massive transfusion protocol is needed, fixed ratios of packed red blood cells, fresh frozen plasma, and platelets should be used.

Hospitals should consider adopting a system to implement key elements in four categories: 1) readiness to respond to a maternal hemorrhage, 2) recognition and prevention measures in place for all patients, 3) a multidisciplinary response to excessive maternal bleeding, and 4) a systems-based quality improvement process to improve responsiveness through reporting and system learning.

For More Information↔

The American College of Obstetricians and Gynecologists has identified additional resources on topics related to this document that may be helpful for ob-gyns, other health care providers, and patients. You may view these resources at www.acog.org/More-Info/PostpartumHemorrhage.

These resources are for information only and are not meant to be comprehensive. Referral to these resources does not imply the American College of Obstetricians and Gynecologists' endorsement of the organization, the organization's website, or the content of the resource. These resources may change without notice.

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The MEDLINE database, the Cochrane Library, and ACOG's own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and June 2017. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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