OBSTETRICS

Prevention and management of postpartum hemorrhage: a comparison of 4 national guidelines

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OBJECTIVE: The purpose of this study was to compare 4 national guidelines for the prevention and management of postpartum hemorrhage (PPH).

STUDY DESIGN: We performed a descriptive analysis of guidelines from the American College of Obstetrician and Gynecologists practice bulletin, the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, the Royal College of Obstetrician and Gynaecologists (RCOG), and the Society of Obstetricians and Gynaecologists of Canada on PPH to determine differences, if any, with regard to definitions, risk factors, prevention, treatment, and resuscitation.

RESULTS: PPH was defined differently in all 4 guidelines. Risk factors that were emphasized in the guidelines conferred a high risk of catastrophic bleeding (eg, previous cesarean delivery and placenta previa). All organizations, except the American College of Obstetrician and Gynecologists, recommended active management of the third stage of labor for primary prevention of PPH in all vaginal deliveries. Oxytocin was recommended universally as the medication of choice for PPH prevention in vaginal deliveries. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists and RCOG recommended development of a massive transfusion protocol to manage PPH resuscitation. Recommendations for nonsurgical treatment strategies such as uterine packing and balloon tamponade varied across all guidelines. All organizations recommended transfer to a tertiary care facility for suspicion of abnormal placentation. Specific indications for hysterectomy were not available in any guideline, with RCOG recommending hysterectomy "sooner rather than later" with the assistance of a second consultant.

CONCLUSION: Substantial variation exists in PPH prevention and management guidelines among 4 national organizations that highlights the need for better evidence and more consistent synthesis of the available evidence with regard to a leading cause of maternal death.

Key words: guideline, management, postpartum hemorrhage, prevention

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Postpartum hemorrhage (PPH) is the most common cause of maternal death and is responsible for one-quarter of maternal deaths globally, totaling approximately 140,000 deaths annually.[1,2] Although PPH is common, with an incidence of 5-15% of births,[3,4] life-threatening bleeding, defined by the Royal College of Obstetrician and Gynaecologists (RCOG) as an estimated blood loss >2.5 L or receipt of >5 units of blood products or treatment for coagulopathy, which is estimated to occur in 3.7 per 1000 pregnancies.[5]

An important component of patient safety and the reduction of adverse outcomes includes the development of unambiguous guidelines.[6] Previous comparisons of national guidelines on topics such as vaginal birth after cesarean delivery,[7] intrapartum fetal surveillance,[8] fetal growth restriction,[9] and shoulder dystocia[10] have highlighted differences in definitions, causes, and recommendations. Because PPH is a leading cause of maternal morbidity and death, synthesis of national guidelines could inform schema to optimize peripartum outcomes. The purpose of this descriptive review is to compare 4 national guidelines and recommendations for 5 aspects of PPH: definition, risk factors, prevention, resuscitation, and treatment (nonsurgical and surgical).

Materials and Methods

The American College of Obstetrician and Gynecologists (ACOG) practice bulletin on PPH, guidelines from the

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TABLE 1
Summary of definitions, risk factors, prevention, and resuscitation recommendations among 4 national guidelines

Variable	American College of Obstetricians and Gynecologists (reaffirmed 2013)	Royal Australian and New Zealand College of Obstetricians and Gynaecologists (reviewed 2014)	Royal College of Obstetrician and Gynaecologists (2011)	Society of Obstetricians and Gynaecologists of Canada (2009)
Definition	>500 mL (vaginal)	>500 mL during puerperium	Minor (500 mL-1 L)	Any amount threatening hemodynamic stability
	>1000 mL (cesarean)	Severe postpartum hemorrhage >1000 mL	Moderate major (1-2 L)	
			Severe major (>2 L)	
Incidence	4-6% of pregnancies	5-15% in Australia	3.7/1000 (>5 units packed red blood cells)	5% of all deliveries
Prevention	Not discussed	Active management of third-stage labor	Active management of third-stage labor	Active management of third-stage labor
		Determine placental location	Determine placental location	Carbetocin 100 μg over 1 minute intravenously (cesarean or vaginal + 1 risk factor)
		Oxytocin, dose not specified	Oxytocin, 5 IU intravenous (cesarean delivery)	
			Ergometrine 0.5 mg/oxytocin 5 IU intramuscularly 2nd line	
Resuscitation	Ample intravenous access	"Massive hemorrhage protocol" activation	Intravenous access × 2	Intravenous access × 2
	Crystalloid	Venous thromboembolism prophylaxis	Crystalloid, rapid, and warmed	Crystalloid solution
	Blood as needed			
	Blood bank notification			Postpartum hemorrhage tray
Medical management				
Oxytocin-Syntocinon	10-40 units intravenous or 10 units intramuscularly	Dose not specified, intravenous/intramuscularly	5 units intravenous, may repeat, or 40 units intravenous in 500 mL at 125 mL/hr	10 units intramuscularly/ 5 units intravenous or 20-40 units intravenous at 500 to 1000 mL/hr
Carbetocin				100 μg intravenous over 1 minute
Ergots	Methyl-ergonovine 0.2 mg intramuscularly every 2-4 hr	Ergometrine, dose not specified	Ergometrine 0.5 mg intravenous or intramuscularly	Ergonovine 0.25 mg intramuscularly or intravenously every 2 hr
Prostaglandins F_{2a}-carboprost	0.25 mg intramuscularly every 15-90 minutes, 8 dose maximum	500 μg intramuscularly incrementally up to 3 mg	0.25 mg intramuscularly every 15, 8 dose maximum or 0.5 mg intramyometrial	0.25 mg intramuscularly every 15, 8 dose maximum
Prostaglandins E_2-dinoprostone	20 mg PV or PR every 2 hr			
Prostaglandins E_1-misoprostol	800-1000 μg rectal	1000 μg rectal	1000 μg rectal	400-1000 μg oral or rectal
Factor VIIa	50-100 μg/kg every 2 hr		Base on coagulation results	Not recommended
Tranexamic acid			Not recommended	Not recommended

Dahlke. Postpartum hemorrhage guidelines. Am J Obstet Gynecol 2015. *(continued)*

TABLE 1
Summary of definitions, risk factors, prevention, and resuscitation recommendations among 4 national guidelines *(continued)*

Variable	American College of Obstetricians and Gynecologists (reaffirmed 2013)	Royal Australian and New Zealand College of Obstetricians and Gynaecologists (reviewed 2014)	Royal College of Obstetrician and Gynaecologists (2011)	Society of Obstetricians and Gynaecologists of Canada (2009)
Surgical management				
Uterine packing	4-inch gauze, 5000 units thrombin in 5 mL saline solution			
Balloon tamponade	Foley: 60-80 mL saline solution (≥1)	Type or technique not specified	First-line "surgical" intervention if caused by atony: 4-6 hr, ideally remove during daytime, deflate but leave in place	Ensure entire balloon is positioned past the cervical canal, consider antibiotic prophylaxis, 8-48 hr
	Blakemore tube: Sengstaken technique not specified			
	Bakri: 300-500 mL saline solution			
Brace suture	B-Lynch, square	B-Lynch	B-Lynch, square	B-Lynch, square
Vessel ligation	Uterine artery	Uterine artery	Uterine artery	Uterine artery
	Internal iliac artery	Internal iliac artery	Internal iliac artery	Internal iliac artery
Hysterectomy	Indication not specified	Indication not specified	"Sooner rather than later" second consultant recommended	Indication not specified
Embolization	If bleeding stable, persistent, nonexcessive	Yes, does not preclude surgical management	Yes, consider	Yes, if stable, ongoing & no surgical options

PR, per rectum; *PV*, per vagina.

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Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZOG), RCOG, and the Society of Obstetricians and Gynaecologists of Canada (SOGC) were accessed on July 1, 2014, and the data were compared. The following aspects of PPH were summarized: definition, risk factors, prevention, resuscitation, and treatment (nonsurgical and surgical). Recommendations and strength of evidence were reviewed based on each guideline's method of reporting. Finally, the references were compared with regard to the total number of randomized control trials, Cochrane reviews, and systematic reviews/metaanalyses that were cited. Institutional review board approval was exempted because of the descriptive nature of our study and analysis.

RESULTS

Definition

All of the guidelines used different definitions of primary PPH. The ACOG practice bulletin defines PPH as blood loss of >500 mL for vaginal deliveries and >1000 mL for cesarean delivery. The RANZOG guideline defines PPH as >500 mL during puerperium and classifies severe PPH as blood loss of >1000 mL. The RCOG guideline divides PPH into 3 categories: minor (500 mL to 1 L), moderate major (>1 L to 2 L), or severe major (>2 L). Finally, the SOGC guideline is the only organization that defines PPH qualitatively: any amount of bleeding that threatens hemodynamic stability (Table 1).

Three guidelines (ACOG, RCOG, and SOGC) comment on the unreliability of estimated blood loss, such as using a visible estimate or through the use of blood collection drapes. None of the guidelines, however, recommended a preferred method to estimate blood loss. Despite the noted unreliability, estimates of blood loss nonetheless are used to initiate levels of treatment in RCOG guidelines. For example, minor PPH (500 mL to 1 L) should prompt basic measures such as intravenous access, indwelling bladder catheterization, full blood count and type, and screen; major PPH (estimated blood loss, >1 L) prompts a treatment protocol to achieve full resuscitation.

Risk factors

Risk factors described in the guidelines are summarized in Table 2. All guidelines

TABLE 2
Risk factors associated with postpartum hemorrhage in 4 national guidelines

Risk factor	National guideline
Preexisting factors	
History of postpartum hemorrhage	ACOG, SOGC, RCOG
Preeclampsia	ACOG, SOGC, RCOG
Overdistended uterus (macrosomia, twins, hydramnios)	ACOG, SOGC, RCOG
Obesity	RCOG
Anemia	RCOG
Asian or Hispanic ethnicity	ACOG, RCOG
Uterine anomalies (fibroid tumors) or previous uterine surgery	SOGC
Hereditary coagulopathies	SOGC
High parity	SOGC
Fetal death	SOGC
Placental factors	
Placental abruption	RCOG
Placenta previa	SOGC, RCOG
Fundal placenta	SOGC
Retained placenta	RCOG
Abnormal placentation	SOGC, RCOG, RANZOG
Intrapartum factors	
Prolonged labor	ACOG, SOGC, RCOG
Augmented labor	ACOG, SOGC
Rapid labor	ACOG, SOGC
Episiotomy	ACOG, RCOG
Operative delivery	ACOG, SOGC, RCOG
Infection (chorioamnionitis, pyrexia)	ACOG, SOGC, RCOG
Prolonged rupture of membranes	SOGC
Anesthetics, nitroglycerin	SOGC
Malposition	SOGC
Deep engagement	SOGC
Excessive cord traction	SOGC
Amniotic fluid embolism	SOGC
Induction of labor (oxytocin use)	RCOG, SOGC
Cesarean delivery	RCOG

ACOG, American College of Obstetrician and Gynecologists; *RANZOG*, Royal Australian and New Zealand College of Obstetricians and Gynaecologists; *RCOG*, Royal College of Obstetrician and Gynaecologists; *SOGC*, Society of Obstetricians and Gynaecologists of Canada.

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note that most women who experience PPH do not have any known risk factors; none of the guidelines provide an estimate of what proportion of women with PPH are without risk factors. The RCOG guideline is the only 1 that provides approximate odds ratios (OR) for various risk factors. Those identified as highest risk include women with suspected or proven placental abruption (OR, 13; 99% CI, 7.6–12.9), known placenta previa (OR, 12; 99% CI, 7.2–23), multiple pregnancy (OR, 5; 99% CI, 3.0–6.6), and preeclampsia/gestational hypertension (OR, 4; 99% CI, not specified), with delivery in a consultant-led maternity unit advised for women with these risk factors.

Women at risk for abnormal placentation and subsequent hemorrhage (such as those with a history of cesarean delivery and placenta previa) are discussed specifically in all 4 guidelines. RANZOG and SOGC guidelines recommend antenatal assessment of placentation and location in these high-risk women to prompt transfer to a tertiary care center or unit with rapid access to blood products or an intensive care unit. In addition, ACOG and RCOG guidelines recommend patient counseling about the likelihood of hysterectomy and blood transfusion, the availability of blood products, and cell-saver technology and encourage planned delivery with preoperative anesthesia assessment. None of the guidelines specify the preferred modality for evaluation of abnormal placentation (eg, ultrasound vs magnetic resonance imaging).

Prevention

There are no specific recommendations discussed in any of the guidelines with regard to PPH prevention strategies before the onset of the third stage of labor. All guidelines, with the exception of ACOG, discuss active management of the third stage of labor (AMTSL) with strong recommendations for its use in primary prevention of PPH. AMTSL traditionally involves 3 interventions that are designed to assist in placenta expulsion: uterotonics, immediate umbilical cord clamping, and controlled cord traction. Despite strong recommendation of this practice, RCOG and SOGC guidelines separate and stratify these interventions and recommend delayed cord clamping for neonatal benefit when feasible.

Oxytocin is recommended universally as the first-line uterotonic of choice for prevention of uterine atony. ACOG and RANZOG guidelines do not specify dosing or route of administration. The RCOG guideline recommends 10 units intramuscularly for uncomplicated vaginal deliveries and 5 IU intravenous slow infusion after cesarean delivery. Finally, the SOGC guideline recommends different uterotonic medications depending on the clinical scenario. For example, oxytocin 10 units intramuscularly or 5-10 units intravenously over 1-2 minutes is recommended for low-risk vaginal deliveries; carbetocin 100 μg intravenously over 1 minute is recommended for cesarean delivery or vaginal delivery in women with 1 risk factor for PPH. Carbetocin, a oxytocin analogue with a significantly longer half-life than endogenous or synthetic oxytocin, is available in the United Kingdom, Ireland, Canada, Australia, and New Zealand, but not the United States.[11] Misoprostol is recommended by the RANZOG guideline as a second-line preventive medication or when oxytocin is not available for PPH prevention; SOGC guidelines recommends ergonovine as a second-line agent or when oxytocin is not available. Syntometrine at a fixed dose combination of 5 IU oxytocin and 0.5 mg ergometrine is recommended by the RCOG guideline as second-line prophylactic agents if available and emphasizes the higher side-effect profile of this medication.

TABLE 3
Summary of recommendations with level A or B classification (strong strength) of evidence in 4 national guidelines

Variable	Classification (strength) of recommendation (A or B [strong])
Definition	Clinical markers preferred over estimated blood loss quantification measures (SOGC-B)
Risk factors	None
Prevention	
Active management of third-stage of labor	Recommended to all women (SOGC-A and RCOG-A)
Oxytocin	5-10 IU intramuscularly for management of third-stage labor without risk factors (RCOG-A, SOGC-A)
	20-40 IU in 1 L, 150 mL/hr acceptable alternative to active management of third-stage labor (SOGC-B)
	10 units intravenously over 1-2 minutes for vaginal delivery (SOGC-B)
Other	Misoprostol, if oxytocin not available (RCOG-A, SOGC-B)
	Ergonovine 0.2 mg intramuscularly second line, more maternal side-effects (SOGC-A)
	Carbetocin 100 μg intravenously over 1 minute for cesarean delivery (SOGC-B)
	Carbetocin 100 μg intramuscularly decreases need for uterine massage in vaginal delivery (SOGC-B)
Treatment	Internal iliac artery ligation, compression sutures, hysterectomy for intractable postpartum hemorrhage unresponsive to medical therapy (SOGC-B)
Resuscitation	All obstetric units should have emergency postpartum hemorrhage equipment tray (SOGC-B)
Other	Prophylactic pelvic artery occlusion for accreta is equivocal (RCOG-B)

RCOG, Royal College of Obstetrician and Gynaecologists; *SOGC*, Society of Obstetricians and Gynaecologists of Canada

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Resuscitation

All 4 guidelines discuss resuscitative measures during PPH with emphasis on fluid management and indications for blood products. A multidisciplinary approach with strong communication with anesthesia is recommended strongly. Although the SOGC guideline suggests that institutions develop and make available specific PPH trays, RANZOG advocates institutional development of a massive transfusion protocol in cases of severe PPH, and that guideline is the only one that provides a massive transfusion protocol algorithm template. Cell-saver technology or autologous transfusion is discussed briefly in ACOG and RCOG guidelines to assist in resuscitative efforts.

Treatment

Treatment modalities, when PPH is identified, can be categorized as nonsurgical or surgical. In general, there is large variation among guidelines with regard to PPH treatment. Notably, all guidelines, except RANZOG, recommend instituting a policy or establishing a protocol when PPH is identified, yet the specifics to the protocol vary or are not established. Regarding unique nonsurgical management options, the RCOG guideline discusses pneumatic antishock gear as a temporizing measure if available, although does not specify when, in the management schema, it should be used.

Tranexamic acid, an antifibrinolytic amino acid derivative of lysine, is discussed only in RCOG guidelines. Although shown to decrease bleeding significantly in nonobstetric procedures, particularly in trauma, RCOG recommends against its use. Similarly, another antifibrinolytic medication, recombinant factor VIIa, is mentioned in ACOG, RCOG, and SOGC guidelines. It is discussed extensively in the ACOG guideline; however, indications for its use are not specified. In contrast, recombinant factor VIIa is not recommended in

TABLE 4
Summary of recommendations with level C or L classification (weak strength) of evidence in 4 national guidelines

Variable	Classification (strength) of recommendation (C or L [weak])
Diagnosis	None
Risk factors	High clinical suspicion for conditions associated with placenta accreta (ACOG-C)
	All women with previous cesarean delivery must rule out placenta accreta/ increta (RCOG-C)
	Deliver accreta/increta in facility with intensive care unit blood consultants (RCOG-C)
	Accelerating placenta delivery before 30-45 minutes will not reduce postpartum hemorrhage (SOGC-C)
Prevention	
Oxytocin	5 units intravenously for cesarean delivery (RCOG-C)
Other	Postpartum hemorrhage of 500-1000 mL should prompt basic resuscitation (RCOG-C)
	Postpartum hemorrhage of >1000 mL should prompt full resuscitation protocol (RCOG-C)
	Syntometrine (Alliance) may be used in the absence of hypertension (RCOG-C)
	Intraumbilical misoprostol (800 μg) or oxytocin (10-30 IU) for manual placenta removal (SOGC-C)
Treatment	Uterotonic agents should be first-line treatment for postpartum hemorrhage because of atony (ACOG-C)
	Exploratory laparotomy is next step if uterotonics fail (ACOG-C)
	Mild or severe postpartum hemorrhage protocols should be initiated when identified (RCOG-C)
	Four components of postpartum hemorrhage management: communication/resuscitation/ monitoring/investigation (RCOG-C)
	Recombinant activated factor VII cannot be recommended (SOGC-L)
	Balloon tamponade controls postpartum hemorrhage from uterine atony not responsive to medication (SOGC-L)
Resuscitation	None
Other	Postpartum hemorrhage management requires a multidisciplinary approach (ACOG-C and SOGC-C)

ACOG, American College of Obstetrician and Gynecologists; *RCOG*, Royal College of Obstetrician and Gynaecologists; *SOGC*, Society of Obstetricians and Gynaecologists of Canada.

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SOGC and RCOG guidelines as a medical treatment option for PPH.

All guidelines discuss 8 surgical techniques: (1) uterine packing, (2) balloon tamponade, (3) uterine curettage, (4) uterine artery ligation, (5) brace suture, (6) hypogastric artery ligation, (7) arterial embolization, and (8) hysterectomy. In general, less invasive fertility-sparing interventions are promoted. The SOGC guideline is the only 1 that provides figures of both B-Lynch and Cho compression suture techniques. The ACOG guideline is the only guideline that discusses the management of hemorrhage because of a ruptured uterus or inverted uterus. With regard to hysterectomy, the RCOG guideline emphasizes early recourse to hysterectomy and not delaying this decision until the woman is in extremis and further recommends subtotal hysterectomy, unless trauma to the lower uterine segment or cervix is noted. Additionally, the SOGC guideline notes that indications for hysterectomy include massive hemorrhage that is not responsive to previous interventions and that the surgical intervention chosen should be familiar to surgeons.

Tables 3 and 4 summarize all recommendations by each respective national guideline with regard to the classification or strength of evidence. Notably, none of the recommendations with either strong or weak strength of evidence are endorsed by >2 of the national guidelines that were reviewed.

References

The number of references cited in each guideline ranges from 12 (RANZOG) to 110 (RCOG) with publication years between 1901 through 2010. Table 5 summarizes the randomized controlled trials referenced with regard to PPH prevention or treatment in the setting of vaginal or cesarean delivery.[12-23] Finally, Table 6 summarizes the number of randomized controlled trials, Cochrane reviews, and systematic reviews referenced in the guidelines. Notably, the ACOG practice bulletin does not cite a single randomized controlled trial or Cochrane review in its guideline.

Comment

Recent epidemiologic studies note that PPH, particularly because of uterine atony, is increasing in the United States and abroad and that it is the major cause of obstetric morbidity and death in the world.[24-26] Recommendations in the 4 national guidelines reviewed herein suggest significant differences in how this common complication is defined, anticipated, prevented, and treated. Also notable is the types of studies that have been used to make recommendations, which suggests variation in the methods

TABLE 5
Summary of randomized controlled trials for prevention and management of postpartum hemorrhage cited in 4 national guidelines

Study	N[a]	Intervention: postpartum hemorrhage prevention	Results
Boucher et al[12] (Canada, 2004) RCOG, SOGC	160	100 μg carbetocin intramuscularly vs 10 units oxytocin infusion	No difference in need postpartum hemorrhage indicators; oxytocin group required additional uterine massage ($P < .02$)
Gülmezoglu et al[13] (Switzerland, 2001) SOGC	18,459	600 μg oral misoprostol vs 10 units oxytocin intravenously or intramuscularly	Oxytocin group lower incidence of estimated blood loss >1000 mL, need for additional oxytocics; misoprostol with higher shivering and raised body temperature
Jackson et al[14] (United States, 2001) SOGC	1486	20 units oxytocin intravenous bolus before or after placenta delivery	No difference in need for additional oxytocics, postpartum hemorrhage incidence, third-stage duration, incidence of retained placenta
Leung et al[15] (Hong Kong, 2006) RCOG, SOGC	329	100 μg carbetocin intramuscularly vs 1 mL Syntometrine (5 units oxytocin + 0.5 mg ergometrine)	No difference in hemoglobin concentration, need for additional oxytocics, postpartum hemorrhage, or retained placenta; carbetocin had lower nausea, vomiting, hypertension but higher maternal tachycardia
Nordström et al[16] (Sweden, 1997) SOGC	1000	Intravenous oxytocin vs saline solution	Oxytocin reduced mean total blood loss, postpartum hemorrhage frequency, need for additional oxytocics, and postpartum hemoglobin <10 g/dL
Parsons et al[17] (Netherlands, 2007) SOGC	450	800 μg rectal misoprostol vs 10 units oxytocin intramuscularly	No difference in hemoglobin; shivering more common in misoprostol group
Boucher et al[18] (Canada, 1998) RCOG	114	100 μg carbetocin vs oxytocin infusion	Carbetocin mean blood loss 41 mL less, increased uterine involution, decreased need for additional oxytocics
Dansereau et al[19] (Canada, 1999) RCOG, SOGC	694	100 μg carbetocin vs oxytocin infusion	Carbetocin reduced need for additional oxytocic intervention
Chou and MacKenzie[20] (Taiwan, 1994) RCOG	60	0.125 mg prostaglandin F_2 alpha vs oxytocin 20 units intravenously	No difference in estimated blood loss, hemoglobin, side-effects
Lokugamage et al[21] (United Kingdom, 2001) RCOG	40	500 μg oral misoprostol vs 10 units oxytocin	No difference in estimated blood loss, need for additional oxytocics, need for transfusion, degree of shivering
Munn et al[22] (United States, 2001) RCOG	321	10 U/500 mL vs 80 U/500 mL oxytocin intravenous infusion over 30 min	Additional uterotonics required in low dose group, similar rate of hypotension
Postpartum hemorrhage treatment			
Blum et al[23] (multiple countries, 2010) RANZOG	809	800 μg misoprostol vs 40 units intravenous oxytocin	No difference in bleeding parameters, shivering; fever more common in misoprostol arm

RANZOG, Royal Australian and New Zealand College of Obstetricians and Gynaecologists; *RCOG*, Royal College of Obstetrician and Gynaecologists; *SOGC*, Society of Obstetricians and Gynaecologists of Canada.

[a] Number of patients enrolled in each study.

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of the respective organizations' development of practice guidelines.

The variation among the guidelines reviewed with regard to how PPH is defined is worth highlighting. Part of this difficulty may be due to the difficulty and inaccuracies of estimating blood loss. Efforts such as the quantification of blood loss proposed by the Association of Women's Health, Obstetric and Neonatal Nurses potentially may improve the accuracy of blood loss estimation and subsequently improve the definition of PPH.[27] Although our review compared the definition of PPH from 4 guidelines, we should also note that other definitions of PPH have been developed. For example, the ACOG

TABLE 6
Summary of references for prevention and management of postpartum hemorrhage by number, year, and citation type in 4 national guidelines

Variable	American College of Obstetricians and Gynecologists (2011)	Royal Australian and New Zealand College of Obstetricians and Gynaecologists (2014)	Royal College of Obstetrician and Gynaecologists (2011)	Society of Obstetricians and Gynaecologists of Canada (2009)
Total references, n	40	12	110	55
Years published	1901-2006	2000-2010	1986-2009	1969-2009
Randomized trials cited, n	0	1	8	7
Cochrane Reviews cited, n	0	3	8	10
Systematic reviews or metaanalyses cited, n	1	2	3	3

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reVITALize initiative has developed the following definition of early PPH in the United States: cumulative blood loss of at least 1000 mL or blood loss accompanied by sign/symptoms of hypovolemia within 24 hours after the birth process (includes intrapartum loss).[28] This contrasts with the World Health Organization definition of blood loss of ≥500 mL within 24 hours after birth.[2] Finally, a recent international expert panel defined persistent (ongoing) PPH as "active bleeding >1000 mL within 24 hours after birth that continues despite the use of initial measures that include first-line uterotonic agents and uterine massage," which highlights the clinical importance of the identification of bleeding that continues despite preventative strategies.[29]

Women at high risk for abnormal placentation understandably are emphasized in all of the national guidelines. Although most PPH cannot be predicted, this is one clinical scenario in which, at least for some women, the risk is known and can be anticipated. Appropriate planning of delivery from timing to location, with transfer to a tertiary hospital as needed, is paramount. Notably, specific PPH prevention strategies are not mentioned in the ACOG guideline, despite significant emphasis in the RANZOG, RCOG, and SOGC guidelines. All of the guidelines, however, recommend institutional drills and/or protocols to prepare for this inevitable event.

Initiatives such as the National Partnership for Maternal Safety and the California Maternal Quality Care Collaborative identified obstetric hemorrhage appropriately as a key priority in improving maternal safety and provided recommendations, resources, and education to assist in this goal.[30,31] For example, the obstetric hemorrhage core bundle proposed by D'Alton et al[30] recommends the following for all US birthing facilities: (1) a standardized obstetric hemorrhage protocol and event checklist, (2) a hemorrhage kit or cart with appropriate medication and equipment, (3) a partnership with the local blood bank for rapid and sustained availability of blood products, and (4) the universal use of AMTSL.[30] Similarly, the California Maternal Quality Care Collaborative offers an obstetric hemorrhage toolkit that consists of (1) a compendium of best practices, (2) care guidelines with checklists, flowcharts, and table charts, (3) a hospital-level implementation guide, and (4) a slide set for professional education.[31] Although it might seem self-evident that these initiatives will improve PPH outcomes, nevertheless they should be evaluated prospectively.

Despite the emphasis on patient safety and institutional quality improvement, a recent survey of academic US obstetric units demonstrated at least 20% did not have a PPH protocol.[32] Similarly, outcomes that have been associated with the implementation of massive transfusion protocols for severe PPH have been shown to be favorable, yet such protocols are explicitly recommended only by RANZOG.[33] Future studies undoubtedly will shed light on optimal resuscitation and should be reflected in updated national guidelines.

AMTSL remains a recommended and highly studied preventive strategy for PPH. Recent studies, however, suggest that the major driver of this preventive strategy's effectiveness is the administration of oxytocin. In a recent multicenter randomized controlled trial in 5 maternity units in France, Deneux-Tharaux et al[34] found that controlled cord traction made minimal contribution to overall blood loss in high resource settings in those who received oxytocin. In addition, an increasingly large body of evidence suggests that delayed cord clamping may have beneficial neonatal outcomes (improved long-term iron stores and hemoglobin concentration) without increasing the risk of maternal hemorrhage.[35] These data suggest that, of the 3 interventions classically described in AMTSL (oxytocin, immediate cord clamping, controlled cord traction), oxytocin, and oxytocin alone, remains the most important intervention for the prevention of PPH.

Research is ongoing to determine the optimal dose, route, and timing of the administration of oxytocin, but it remains the first-line medication for PPH prevention.[36] Randomized trials of newer medications such as carbetocin or ranexamic acid have been conducted,[37,38] but additional studies are

necessary to determine what role, if any, these medications should play in PPH prevention or management.

As evidenced by the paucity of randomized controlled trials that compare different medical treatment strategies for PPH or optimal surgical interventions, the order for which these management options are to be used remain vastly understudied. Although interventions such has balloon tamponade have made their way into management protocols and guidelines, there has yet to be a randomized clinical trial performed to compare it with any other treatment strategy.[39]

The strengths of our analysis include synthesizing the major guideline recommendations on all aspects of PPH including definitions, risk factors, resuscitation, and medical and surgical management. In addition, we believe a critical evaluation of how the available evidence from randomized controlled trials, systematic reviews, and meta-analyses is used to develop these guidelines may improve future guidelines and recommendations. We also recognize weaknesses in our descriptive analysis. First, we limited our review to 4 English language national guidelines, despite other countries and organizations such as the World Health Organization producing similar guidelines for the prevention and management of PPH.[2] Our goal in doing this was to compare and contrast recommendations whose guidelines have been previously compared[7-10] and are germane to similarly resourced settings with similar intended audiences concerning this important topic. We also acknowledge that the authors or committees who developed the guidelines that we reviewed may be subject to differing methods for establishing recommendations within each national organization.

In summary, PPH universally remains a major cause of maternal morbidity and death in both developed and developing countries. As the evidence-base for PPH and management improves, a convergence of national guidelines ought to occur to reflect best available practices. ■

REFERENCES

1. American College of Obstetricians and Gynecologists. Clinical management guidelines for obstetrician-gynecologists: postpartum hemorrhage. ACOG Practice bulletin no. 76. Obstet Gynecol 2006;108:1039-47.
2. World Health Organization. WHO recommendations for the prevention and treatment of postpartum haemorrhage. Geneva: World Health Organization. 2012. WHO Guidelines Approved by the Guidelines Review Committee. Available at: http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548502/en/. Accessed Nov. 1, 2013.
3. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Management of postpartum hemorrhage. March 2011. Available at: http://www.ranzcog.edu.au/college-statements-guidelines.html. Accessed Nov. 1, 2013.
4. Leduc D, Senikas V, Lalonde AB, et al. Active management of the third stage of labour: prevention and treatment of postpartum hemorrhage. J Obstet Gynaecol Can 2009;31:980-93.
5. Royal College of Obstetrician and Gynaecologists. Postpartum hemorrhage: prevention and management. April 2011. Available at: http://www.rcog.org.uk/womens-health/clinical-guidance/prevention-and-management-postpartum-haemorrhage-green-top-52. Accessed Nov. 1, 2013.
6. Clark SL, Belfort MA, Byrum SL, Meyers JA, Perlin JB. Improved outcomes, fewer cesarean deliveries, and reduced litigation: results of a new paradigm in patient safety. Am J Obstet Gynecol 2008;199:105.e1-7.
7. Hill JB, Ammons A, Chauhan SP. Vaginal birth after cesarean delivery: comparison of ACOG practice bulletin with other national guidelines. Clin Obstet Gynecol 2012;55:969-77.
8. Hill JB, Chauhan SP, Magann EF, Morrison JC, Abuhamad AZ. Intrapartum fetal surveillance: review of three national guidelines. Am J Perinatol 2012;29:539-50.
9. Chauhan SP, Gupta LM, Hendrix NW, Berghella V; American College of Obstetricians and Gynecologists. Intrauterine growth restriction: comparison of American College of Obstetricians and Gynecologists practice bulletin with other national guidelines. Am J Obstet Gynecol 2009;200:409.e1-6.
10. Chauhan SP, Gherman R, Hendrix NW, Bingham JM, Hayes E. Shoulder dystocia: comparison of the ACOG practice bulletin with another national guideline. Am J Perinatol 2010;27:129-36.
11. Ferring Pharmaceuticals. Products. Available at: http://www.ferringusa.com/products. Accessed Dec. 14, 2013.
12. Boucher M, Nimrod CA, Tawagi GF, et al. Comparison of carbetocin and oxytocin for the prevention of postpartum hemorrhage following vaginal delivery: a double-blind randomized trial. J Obstet Gynaecol Can 2004;26:481-8.
13. Gülmezoglu AM, Villar J, Ngoc NT, et al. WHO multicentre randomised trial of misoprostol in the management of the third stage of labour. Lancet 2001;358:689-95.
14. Jackson KW Jr, Allbert JR, Schemmer GK, Elliot M, Humphrey A, Taylor J. A randomized controlled trial comparing oxytocin administration before and after placental delivery in the prevention of postpartum hemorrhage. Am J Obstet Gynecol 2001;185:873-7.
15. Leung SW, Ng PS, Wong WY, Cheung TH. A randomised trial of carbetocin versus syntometrine in the management of the third stage of labour. BJOG 2006;113:1459-64.
16. Nordström L, Fogelstam K, Fridman G, Larsson A, Rydhstroem H. Routine oxytocin in the third stage of labour: a placebo controlled randomised trial. BJOG 1997;104:781-6.
17. Parsons SM, Walley RL, Crane JM, Matthews K, Hutchens D. Rectal misoprostol versus oxytocin in the management of the third stage of labour. J Obstet Gynaecol Can 2007;29:711-8.
18. Boucher M, Horbay GL, Griffin P, et al. Double-blind, randomized comparison of the effect of carbetocin and oxytocin on intraoperative blood loss and uterine tone of patients undergoing cesarean section. J Perinatol 1998;18:202-7.
19. Dansereau J, Joshi AK, Helewa ME, et al. Double-blind comparison of carbetocin versus oxytocin in prevention of uterine atony after cesarean section. Am J Obstet Gynecol 1999;180:670-6.
20. Chou MM, MacKenzie IZ. A prospective, double-blind, randomized comparison of prophylactic intramyometrial 15-methyl prostaglandin F2 alpha, 125 micrograms,and intravenous oxytocin, 20 units, for the control of blood loss at elective cesarean section. Am J Obstet Gynecol 1994;171:1356-60.
21. Lokugamage AU, Paine M, Bassaw-Balroop K, Sullivan KR, Refaey HE, Rodeck CH. Active management of the third stage at caesarean section: a randomised controlled trial of misoprostol versus syntocinon. Aust N Z J Obstet Gynaecol 2001;41:411-4.
22. Munn MB, Owen J, Vincent R, Wakefield M, Chestnut DH, Hauth JC. Comparison of two oxytocin regimens to prevent uterine atony at cesarean delivery: a randomized controlled trial. Obstet Gynecol 2001;98:386-90.
23. Blum J, Winikoff B, Raghavan S, et al. Treatment of post-partum haemorrhage with sublingual misoprostol versus oxytocin in women receiving prophylactic oxytocin: a double-blind, randomised, non-inferiority trial. Lancet 2010;375:217-23.
24. Kramer MS, Berg C, Abenhaim H, et al. Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. Am J Obstet Gynecol 2013;209:449.e1-7.
25. Mehrabadi A, Liu S, Bartholomew S, et al. Temporal trends in postpartum hemorrhage and severe postpartum hemorrhage in Canada from 2003 to 2010. J Obstet Gynaecol Can 2014;36:21-33.
26. Lutomski JE, Byrne BM, Devane D, Greene RA. Increasing trends in atonic

postpartum haemorrhage in Ireland: an 11-year population-based cohort study. BJOG 2012;119:306-14.

27. Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN). Practice brief number 1: quantification of blood loss. Available at: http://www.pphproject.org/downloads/awhonn_qbl.pdf. Accessed: December 27, 2014.

28. American Congress of Obstetricians and Gynecologists. reVITALize obstetric data definitions. Available at: http://www.acog.org/-/media/Departments/Patient-Safety-and-Quality-Improvement/2014reVITALizeObstetricDataDefinitionsV10.pdf. Accessed Dec. 27, 2014.

29. Abdul-Kadir R, McLintock C, Ducloy AS, et al. Evaluation and management of postpartum hemorrhage: consensus from an international expert panel. Transfusion 2014;54:1756-68.

30. D'Alton ME, Main EK, Menard MK, Levy BS. The National Partnership for Maternal Safety. Obstet Gynecol 2014;123:973-7.

31. California Maternal Quality Care Collaborative. OB hemorrhage toolkit. Available at: https://cmqcc.org/ob_hemorrhage. Accessed Dec. 27, 2014.

32. Kacmar RM, Mhyre JM, Scavone BM, Fuller AJ, Toledo P. The use of postpartum hemorrhage protocols in United States academic obstetric anesthesia units. Anesth Analg 2014;119:906-10.

33. Gutierrez MC, Goodnough LT, Druzin M, Butwick AJ. Postpartum hemorrhage treated with a massive transfusion protocol at a tertiary obstetric center: a retrospective study. Int J Obstet Anesth 2012;21:230-5.

34. Deneux-Tharaux C, Sentilhes L, Maillard F, et al. Effect of routine controlled cord traction as part of the active management of the third stage of labour on postpartum haemorrhage: multicentre randomised controlled trial (TRACOR). BMJ 2013;346:f1541.

35. McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. Cochrane Database Syst Rev 2013;7:CD004074.

36. Westhoff G, Cotter AM, Tolosa JE. Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. Cochrane Database Syst Rev 2013;10:CD001808.

37. Su LL, Chong YS, Samuel M. Carbetocin for preventing postpartum haemorrhage. Cochrane Database Syst Rev 2012;4:CD005457.

38. Novikova N, Hofmeyr GJ. Tranexamic acid for preventing postpartum haemorrhage. Cochrane Database Syst Rev 2010;7:CD007872.

39. Wright CE, Chauhan SP, Abuhamad AZ. Bakri balloon in the management of postpartum hemorrhage: a review. Am J Perinatol 2014;31:957-64.