Anesthetic Management of Postpartum Hemorrhage

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Maternal Mortality

Global, regional, and national levels of maternal mortality, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015

*GBD 2015 Maternal Mortality Collaborators**

Summary

Background In transitioning from the Millennium Development Goal to the Sustainable Development Goal era, it is imperative to comprehensively assess progress toward reducing maternal mortality to identify areas of success, remaining challenges, and frame policy discussions. We aimed to quantify maternal mortality throughout the world by underlying cause and age from 1990 to 2015.

Methods We estimated maternal mortality at the global, regional, and national levels from 1990 to 2015 for ages 10–54 years by systematically compiling and processing all available data sources from 186 of 195 countries and territories, 11 of which were analysed at the subnational level. We quantified eight underlying causes of maternal death and four timing categories, improving estimation methods since GBD 2013 for adult all-cause mortality, HIV-related maternal mortality, and late maternal death. Secondary analyses then allowed systematic examination of drivers of trends, including the relation between maternal mortality and coverage of specific reproductive health-care services as well as assessment of observed versus expected maternal mortality as a function of Socio-demographic Index (SDI), a summary indicator derived from measures of income per capita, educational attainment, and fertility.

Findings Only ten countries achieved MDG 5, but 122 of 195 countries have already met SDG 3.1. Geographical disparities widened between 1990 and 2015 and, in 2015, 24 countries still had a maternal mortality ratio greater than 400. The proportion of all maternal deaths occurring in the bottom two SDI quintiles, where haemorrhage is the dominant cause of maternal death, increased from roughly 68% in 1990 to more than 80% in 2015. The middle SDI quintile improved the most from 1990 to 2015, but also has the most complicated causal profile. Maternal mortality in the highest SDI quintile is mostly due to other direct maternal disorders, indirect maternal disorders, and abortion,

Lancet 2016; 388: 1775–812

This online publication has been corrected. The corrected version first appeared at thelancet.com on January 5, 2017

See Editorial page 1447

See Comment pages 1448 and 1450

*Collaborators listed at the end of the Article

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GBD 2015 Maternal Mortality Collaborators, Lancet 2015; 388: 1775-812

Maternal Mortality

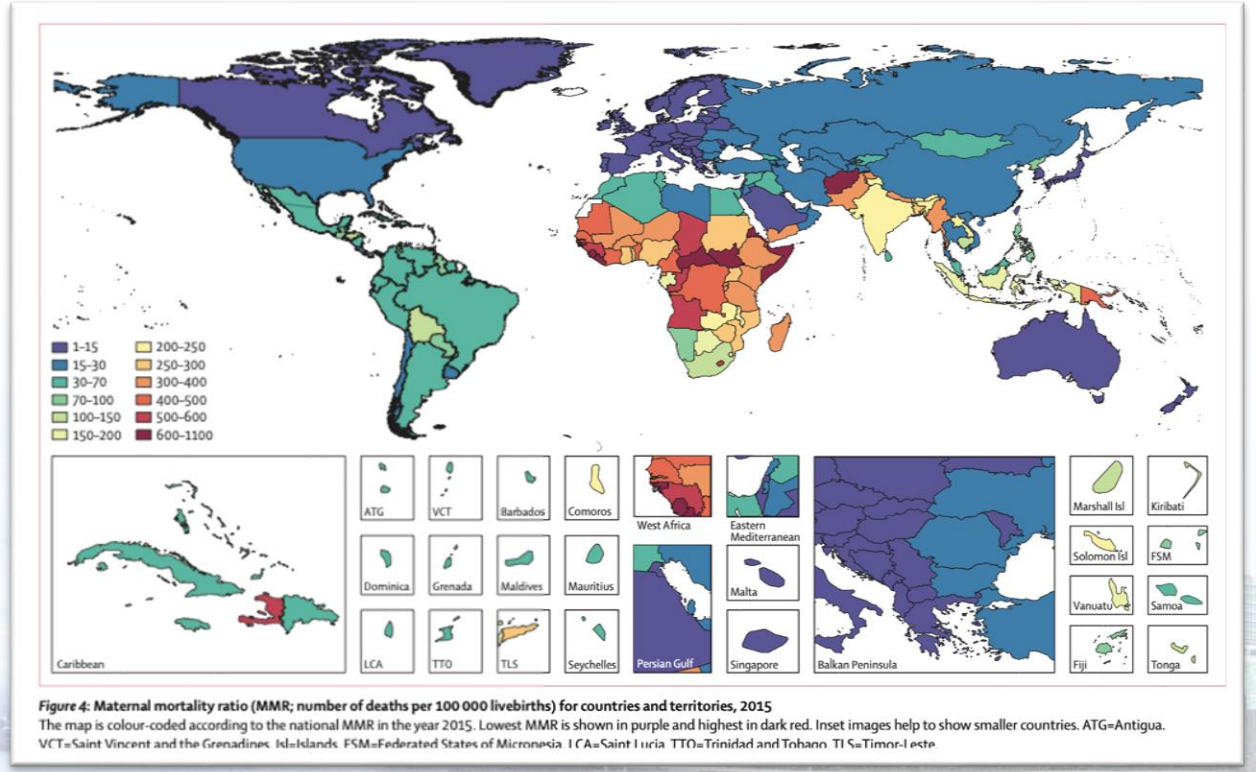


Figure 4: **Maternal mortality ratio (MMR; number of deaths per 100 000 livebirths) for countries and territories, 2015**
The map is colour-coded according to the national MMR in the year 2015. Lowest MMR is shown in purple and highest in dark red. Inset images help to show smaller countries. ATG=Antigua. VCT=Saint Vincent and the Grenadines. Isl=Islands. FSM=Federated States of Micronesia. LCA=Saint Lucia. TTO=Trinidad and Tobago. TLS=Timor-Leste

GBD 2015 Maternal Mortality Collaborators, Lancet 2015; 388: 1775-812

Maternal mortality - PPH

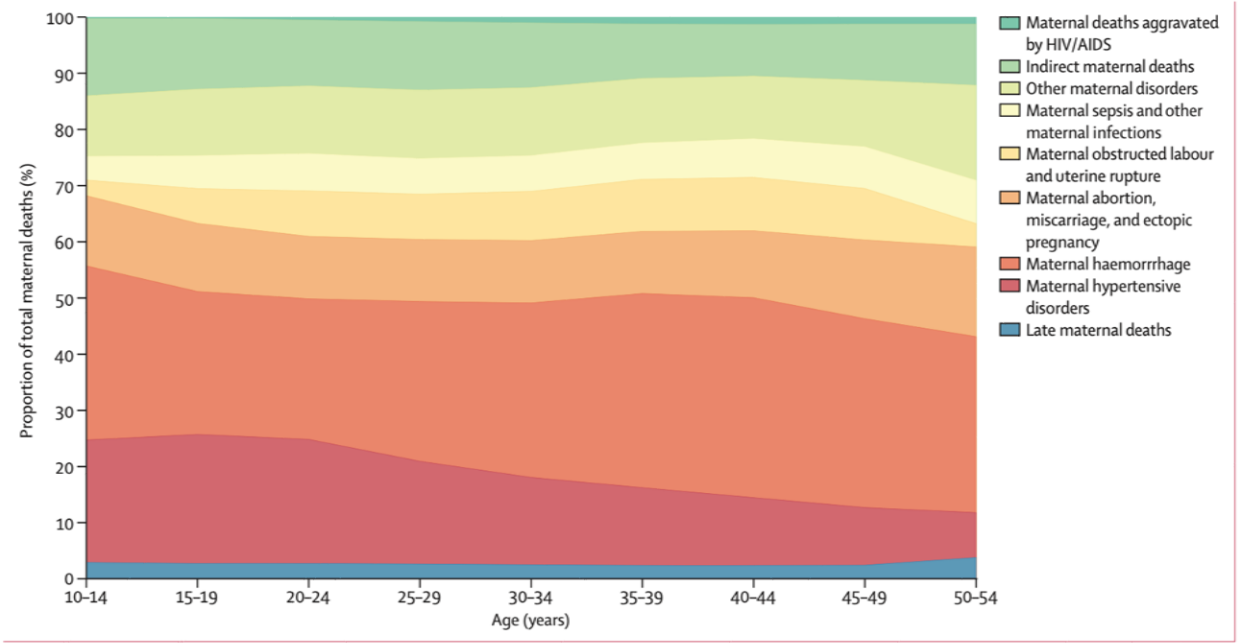


Figure 7: **Global proportion of total maternal deaths by underlying cause and age, 2015**
The stacked area graph shows the proportion of total maternal deaths due to each cause globally in 2015 as a function of female age group.

GBD 2015 Maternal Mortality Collaborators, Lancet 2015; 388: 1775-812

Causes of maternal death

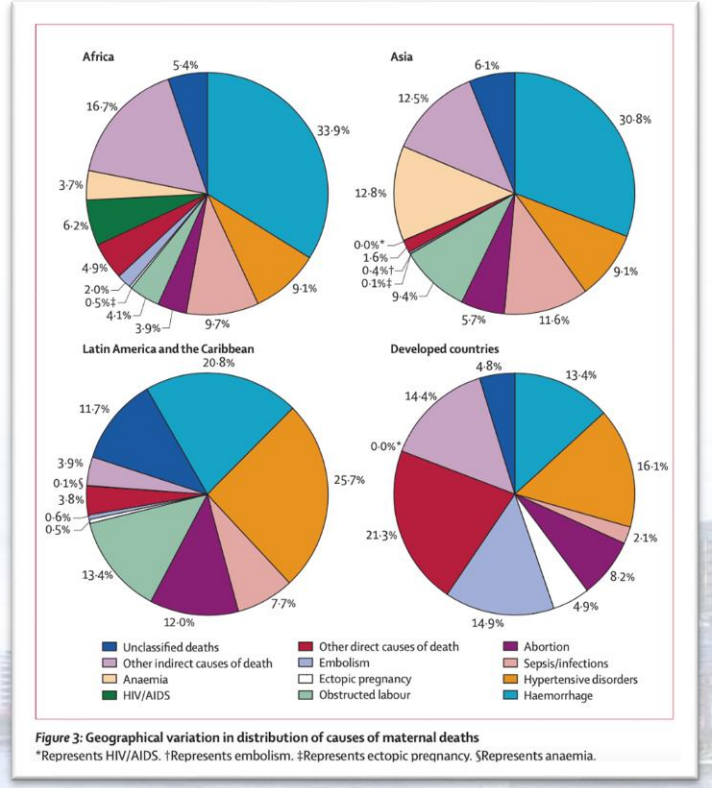


Figure 3: Geographical variation in distribution of causes of maternal deaths
*Represents HIV/AIDS. †Represents embolism. ‡Represents ectopic pregnancy. §Represents anaemia.

Khan et al. *Lancet* 2006; 367: 1066–74

Maternal Cardiac Arrest

AHA Scientific Statement

Cardiac Arrest in Pregnancy

A Scientific Statement From the American Heart Association

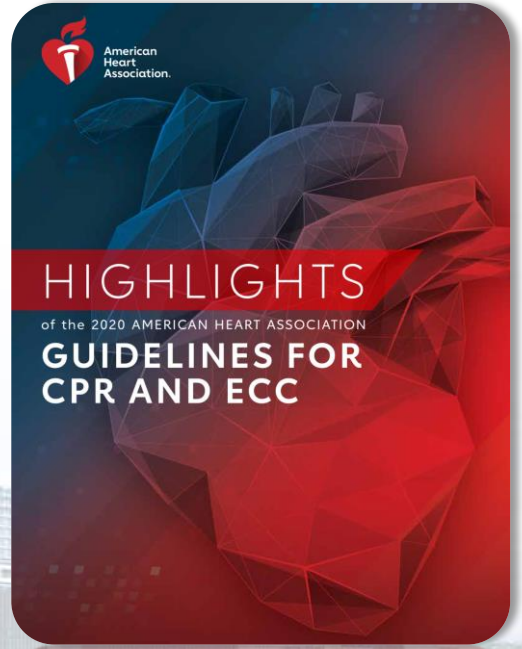
Farida M. Jeejeebhoy, MD, Chair; Carolyn M. Zelop, MD; Steve Lipman, MD; Brendan Carvalho, MD; Jose Joglar, MD; Jill M. Mhyre, MD; Vern L. Katz, MD; Stephen E. Lapinsky, MB BCh, MSc; Sharon Einav, MD; Carole A. Warnes, MD; Richard L. Page, MD; Russell E. Griffin, LP, FP-C; Amish Jain, MD; Katie N. Dainty, PhD; Julie Arafeh, RN, MS; Rory Windrim, MD; Gideon Koren, MD; Clifton W. Callaway, MD, PhD; on behalf of the American Heart Association Emergency Cardiovascular Care Committee, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Diseases in the Young, and Council on Clinical Cardiology

Abstract—This is the first scientific statement from the American Heart Association on maternal resuscitation. This document will provide readers with up-to-date and comprehensive information, guidelines, and recommendations for all aspects of maternal resuscitation. Maternal resuscitation is an acute event that involves many subspecialties and allied health providers; this document will be relevant to all healthcare providers who are involved in resuscitation and specifically maternal resuscitation. **(*Circulation*. 2015;132:1747-1773. DOI: 10.1161/CIR.0000000000000300.)**

Key Words: AHA Scientific Statements ■ cardiopulmonary resuscitation ■ heart arrest ■ pregnancy

Cardiac arrest in pregnancy is one of the most challenging clinical scenarios. Although most features of resuscitating per 100 000 live births in 1987 to 17.8 deaths per 100 000 live births in 2009.[4] However, maternal mortality rates are just

Jeejeebhoy et al. Circulation 2015; 132:1747-73



American Heart Association 2020

Causes of Maternal Cardiac arrest – B: bleeding

Table 5. Most Common Etiologies of Maternal Arrest and Mortality

Letter	Cause	Etiology
A	Anesthetic complications	High neuraxial block
		Hypotension
		Loss of airway
		Aspiration
		Respiratory depression
		Local anesthetic systemic toxicity
	Accidents/trauma	Trauma
		Suicide
B	Bleeding	Coagulopathy
		Uterine atony
		Placenta accreta
		Placental abruption
		Placenta previa
		Retained products of conception
		Uterine rupture
		Surgical
		Transfusion reaction
C	Cardiovascular causes	Myocardial infarction
		Aortic dissection
		Cardiomyopathy
		Arrhythmias
		Valve disease
		Congenital heart disease
D	Drugs	Oxytocin
		Magnesium
		Drug error
		Illicit drugs
		Opioids
		Insulin
		Anaphylaxis
E	Embolic causes	Amniotic fluid embolus
		Pulmonary embolus
		Cerebrovascular event
		Venous air embolism
F	Fever	Sepsis
		Infection
G	General	H's and T's
H	Hypertension	Preeclampsia
		Eclampsia
		HELLP syndrome, intracranial bleed

HELLP indicates hemolysis, elevated liver enzymes, and low platelet count.

Jeejeebhoy et al. Circulation 2015; 132:1747-73

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 183, OCTOBER 2017 *(Replaces Practice Bulletin Number 76, October 2006)*

Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins–Obstetrics in collaboration with Laurence E. Shields, MD; Dena Goffman, MD; and Aaron B. Caughey, MD, PhD.

Postpartum Hemorrhage

Maternal hemorrhage, *defined as a cumulative blood loss of greater than or equal to 1,000 panied by signs or symptoms of hypovolemia within 24 hours after the birth process, rem maternal mortality worldwide (1). Additional important secondary sequelae from hemorrha respiratory distress syndrome, shock, disseminated intravascular coagulation, acute renal fa pituitary necrosis (Sheehan syndrome).*

Hemorrhage that leads to blood transfusion is the leading cause of severe maternal mor closely followed by disseminated intravascular coagulation (2). In the United States, the r rhage increased 26% between 1994 and 2006 primarily because of increased rates of atony 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.

Definition of PPH

: Bleeding
> 500 ml Normal labor
>1,000 ml Cesarean delivery

Obstetrics & Gynecology 2017;130(4):e168–86

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.

4Ts

- Tone
- Trauma
- Tissue
- Thrombin

Obstetrics & Gynecology 2017;130(4):e168–86

ACOG Practice Bulletin No.183

Table 2. Example of Risk Assessment Tool

Low Risk	Medium Risk	High Risk
Singleton pregnancy	Prior cesarean or uterine surgery	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.

Obstetrics & Gynecology 2017;130(4):e168–86

Incidence of PPH

- Any route of delivery : 2.9 - 3.2%
- Cesarean delivery : 0.6 - 3.1%

Anesth Analg 2010; 110(5): 1368-73
J Obstet Gynaecol Can 2008; 30(11): 1002-7
Am J Obstet Genecol 2011; 205(5): 462 e1-7
Am J Obstet Gynecol 2009; 201(3): 273 e1-9

Incidence of PPH – Siriraj hospital Cesarean delivery

Year	Cesarean delivery ราย	PPH ราย	%
2563	2,682	135	5.0
2562	3,214	162	5.0
2561	3,517	148	4.2
2560	3,804	128	3.4
2559	3,790	96	2.6

Siriraj Hospital data, by coding ICD-10

Choice of Anesthesia

	General Anesthesia	Regional Anesthesia (Spinal, Epidural, CSE)
Maternal Advantages	- Maternal unawareness - Secure airway - Hemodynamics	- No airway involvement - Better postoperative analgesia
Maternal Drawbacks	- Risk of pulmonary aspiration - Failed intubation (Higher mortality) - More meds used - Uterine relaxation	- Hypotension - Relative hypovolemia
Fetal effects	Lower Apgar score* Lower umbilical pH*	Less effect to fetus except hypotension

*Int J Obstet Anesth 2019;37:5-15

Sum: choice of anesthesia

- Depends on several factors
- Patient: preoperative hypovolemic
- Surgical: massive bleeding is expected

General anesthesia:
more hemodynamic stability

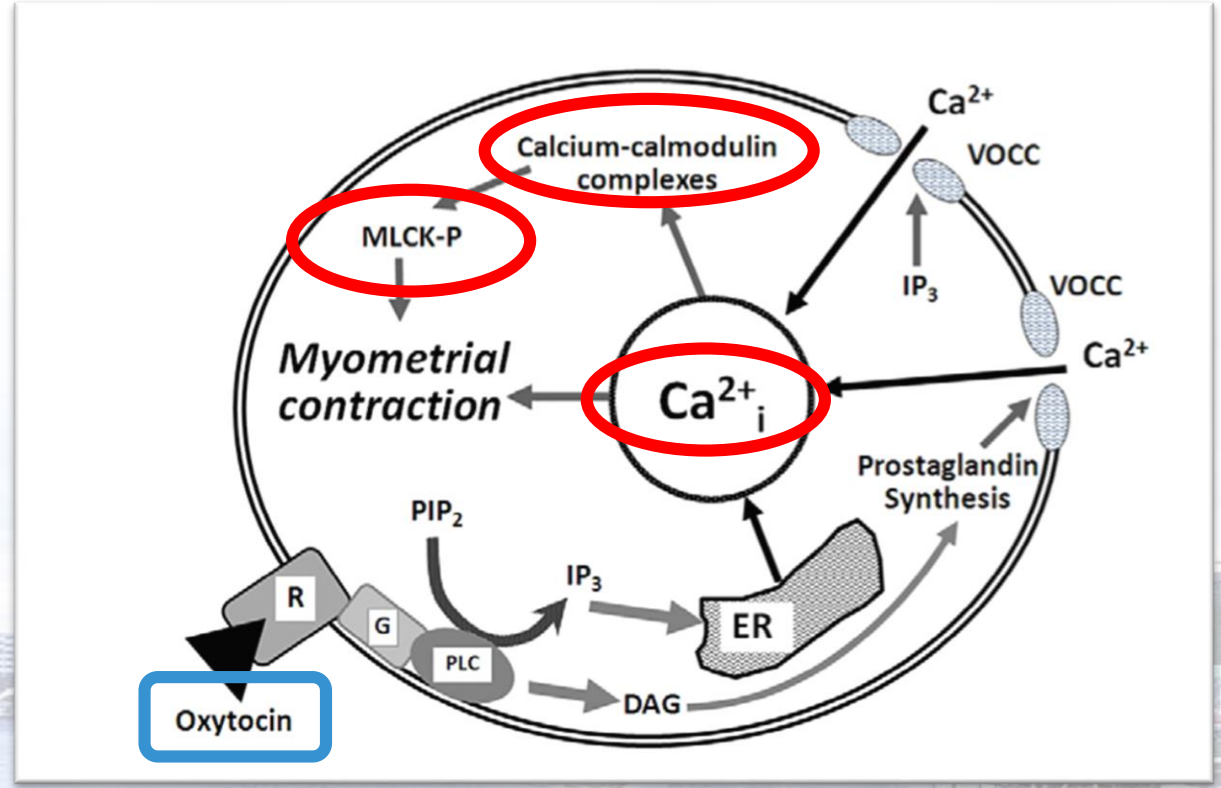
Anesthetic Management of postpartum hemorrhage

- Resuscitation
- IV 2 large-bore at least
- Close monitoring : Invasive (Art-line)
- Keep warm
- PRC, FFP , Platelets, cryoprecipitate
- Follow lab : Hb, platelets, PT, PTT, Thromboelastogram
- If massive transfusion : E'lyte, Ca^{++},
- Arterial blood gas
- Correct the cause

Uterotonic Agents

- Aim: prevention and treatment of PPH
- Most common cause of PPH- Uterine atony
- Bleeding from:
  - Increased blood flow : uterine artery 100 - **350 ml/min**
  - Vessels do not have a thick elastic layer
  - Inability to undergo vasospasm
  - Torn during delivery → uncontrolled hemorrhage

Oxytocin = first line drug



Int J Obstet Anesth 2010;19:313-9

The usage of Oxytocin

1. Low-risk elective cesarean section

2. Intrapartum cesarean section
High-risk cesarean section

1. Low risk elective cesarean section

Oxytocin Requirements at Elective Cesarean Delivery: A Dose-Finding Study

José C. A. Carvalho, MD, PhD, Mrinalini Balki, MD, John Kingdom, MD, and Ror

OBJECTIVE: Oxytocin is frequently used by intravenous bolus and infusion to minimize blood loss and prevent postpartum hemorrhage at cesarean delivery. Current dosing regimens are arbitrary whereas large doses may pose a serious risk to the mother. The purpose of this study was to estimate the minimum effective intravenous bolus dose of oxytocin (ED_{90}) required for adequate uterine contraction at elective cesarean in nonlaboring women.

METHODS: A randomized, single-blinded study was undertaken in 40 healthy term pregnant women presenting for elective cesarean under spinal anesthesia. Oxytocin was administered by bolus according to a biased coin up-and-down sequential allocation scheme with increments or decrements of 0.5 IU. Uterine contraction was assessed by the obstetrician, who was blinded to the dose of oxytocin, as either satisfactory or unsatisfactory. After achieving sustained uterine contraction, an infusion of 40 mU/min of oxytocin was started. Oxytocin-induced adverse effects and

cental site. However, when given in
rapid bolus, oxytocin is associated
effects, including hypotension, nau
pain, headache, flushing, and myo
For these reasons, the manufacturer
recommend bolus administration.

A variety of regimens for admini
have been described previously but
ical.[3–6] Furthermore, the minimu
oxytocin at cesarean delivery has
lished. The purpose of our study w
mate the minimum effective dose
required to produce adequate uterin
tive cesarean delivery in nonlaborin

MATERIALS AND METHODS

- The ED90 of oxytocin 0.35 IU

(95% CI 0.18 – 0.52 U)

- 97.1% response rate at 0.5 U
- 100% response rate at 1.0 U

Obstet Gynecol. 2004;104:1005-10

2. Intrapartum cesarean section

Minimum Oxytocin Dose Requirement After Cesarean Delivery for Labor Arrest

Mrinalini Balki, MD, Michael Ronayne, MD, Sharon Davies, MD, Shafagh Fallah, PhD, John Kingdom, MD, Rory Windrim, MD, and José C. A. Carvalho, MD, PhD

OBJECTIVE: To estimate the minimum effective intravenous dose of oxytocin required for adequate uterine contraction after cesarean delivery for labor arrest.

METHODS: A randomized single-blinded study was undertaken in 30 parturients undergoing cesarean deliveries under epidural anesthesia for labor arrest despite intravenous oxytocin augmentation. Oxytocin was administered as a slow intravenous bolus immediately after delivery of the infant, according to a biased coin up-down sequential allocation scheme. After assisted spontaneous delivery of the placenta, the obstetrician, blinded to the oxytocin dose, assessed uterine contraction as either satisfactory or unsatisfactory. Additional boluses of oxytocin were administered as required, followed by a maintenance infusion. Data were interpreted and analyzed by a logistic regression model at 95% confidence intervals.

RESULTS: All patients received oxytocin infusions at a mean ± standard deviation of 9.8 ± 6.3 hours before cesarean delivery (maximum infusion dose 10.3 ± 8.2

dose is 9 times more than p
cesarean delivery in nonlab
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tocin administration durin
uterotonic agents, rather
achieve superior uterine co
loss during cesarean delive
(Obstet Gynecol 2006;107:45–

LEVEL OF EVIDENCE: I

Oxytocin is the drug of choice both for induction and augmentation of labor, as well as for achieving uterine contraction after delivery, whether spontaneous or operative. Prophylactic oxytocin is commonly administered after delivery of the infant or placenta and has been shown to reduce the incidence of postpartum hemorrhage by up to 40 %.[1,2]

Several empirical regimens have been proposed for oxytocin administration during cesarean delivery,

Women with arrested labour, the ED90 was found to be 3.0 U

Obstet Gynecol 2006;107:45–50

Pregnancy with arrested labor

- The phenomenon of receptor desensitization
- Explained by receptor down-regulation.
- Loss of oxytocin receptors during oxytocin-induced and oxytocin-augmented labor (> 3-fold)

ED90	Elective cases	Labor arrested	* times
Oxytocin (U)	0.35	3	8.6
Carbetocin (mcg)	14.8	121	8.1

Obstet Gynecol 2006;107:45–50.

Carbetocin

- The newly developed synthetic analogue of oxytocin
- 1-desamino-1-monocarbo-[2-O-methyltyrosine]-oxytocin
- A half-life 4–10 times the duration of oxytocin
- IV 8–30 mcg, IM 10-70 mcg → tetanic contraction
- Persists ~ 11 min
- Rhythmic uterine contractions persist for

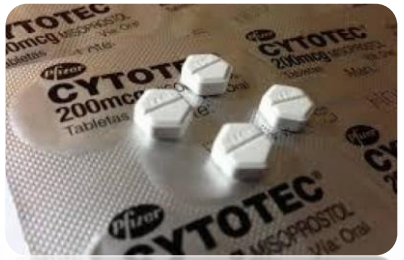
ED90	Elective cases	Labor arrested	* times
Oxytocin (U)	0.35	3	8.6
Carbetocin (mcg)	14.8	121	8.1

Ergot alkaloid

- IV (optional, not recommended in some country,) 0.2 mg slowly
  - Repeated 15 minutely not exceed 0.8 mg/day
  - Duration of action 3-6 hr
- IM 0.2 mg
  - Action within 10 min
  - Repeated 2-4 hourly

Prostaglandins

- PGF_{2alpha} (Carboprost, Hemabate®)
- PGE_1 (Misoprostol, Cytotec®)
- PGE_2 (Sulprostone, Nalador®)



Anaesthesia 2019, 74, 1305–1319 doi:10.1111/anae.14757

Guidelines

International consensus statement on the use of uterotonic agents during caesarean section

Box 1 Suggested dose regimens for uterotonic administration at low-risk elective caesarean section, and caesarean section in labouring women. N.B. take account of national drug license restrictions. See text for further information.

First-line drugs

Oxytocin

Elective caesarean section	Intrapartum caesarean section
Bolus 1 IU oxytocin; start oxytocin infusion at 2.5–7.5 $IU.h^{-1}$ (0.04–0.125 $IU.min^{-1}$).	3 IU oxytocin over ≥ 30 s; start oxytocin infusion at 7.5–15 $IU.h^{-1}$ (0.125–0.25 $IU.min^{-1}$).
If required after 2 min, give a further dose of 3 IU over ≥ 30 s.	
Consider second-line agent early in the event of failure of this regimen to produce sustained uterine tone.	
Review the patient's clinical condition before discontinuing the infusion; this will usually be between 2 h and 4 h after commencement.	

Alternative – carbetocin

Elective caesarean section	Intrapartum caesarean section
100 μg over ≥ 30 s.	100 μg over ≥ 30 s.
Smaller doses (as low as 20 μg) may be sufficient; in this case, doses can be repeated if required, up to 100 μg.	Do not exceed 100 μg – if required move to second-line drug.
Do not exceed 100 μg – if required move to second-line drug.	

Anaesthesia 2019; 74: 1305-19

Second-line drugs

These drugs should be considered for both prophylaxis and treatment of postpartum haemorrhage.
Consider early use in the event of failure of first-line drugs to produce sustained uterine tone.
Depending on local availability, the following drugs can be used:

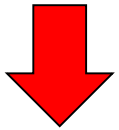
1. Ergometrine (ergonovine) 200–500 μg/methylergometrine (methylergonovine) 200 μg: i.m., or slow i.v. in exceptional circumstances; may be repeated after 2 h.
2. Misoprostol 400–600 μg: sublingual, rectal, vaginal, oral; repeat after 15 min if required, maximum dose 800 μg.
3. Carboprost 250 μg: i.m. or intramyometrial (contraindicated i.v.); up to every 15 min if required, maximum eight doses.
4. Sulprostone 500 μg: i.v. at 100 $\mu g.h^{-1}$; maximum dose 1500 μg.

Consider early use of adjunctive medication to counter adverse effects, for example, antiemetics.
Further uterotonic administration (third-line drugs) should be considered within a multimodal postpartum haemorrhage regimen (pharmacology/haematology and antifibrinolysis/surgery/interventional radiology).

Anaesthesia 2019; 74: 1305-19

ACOG recommendation 2017

When uterotonics fail to adequately control PPH

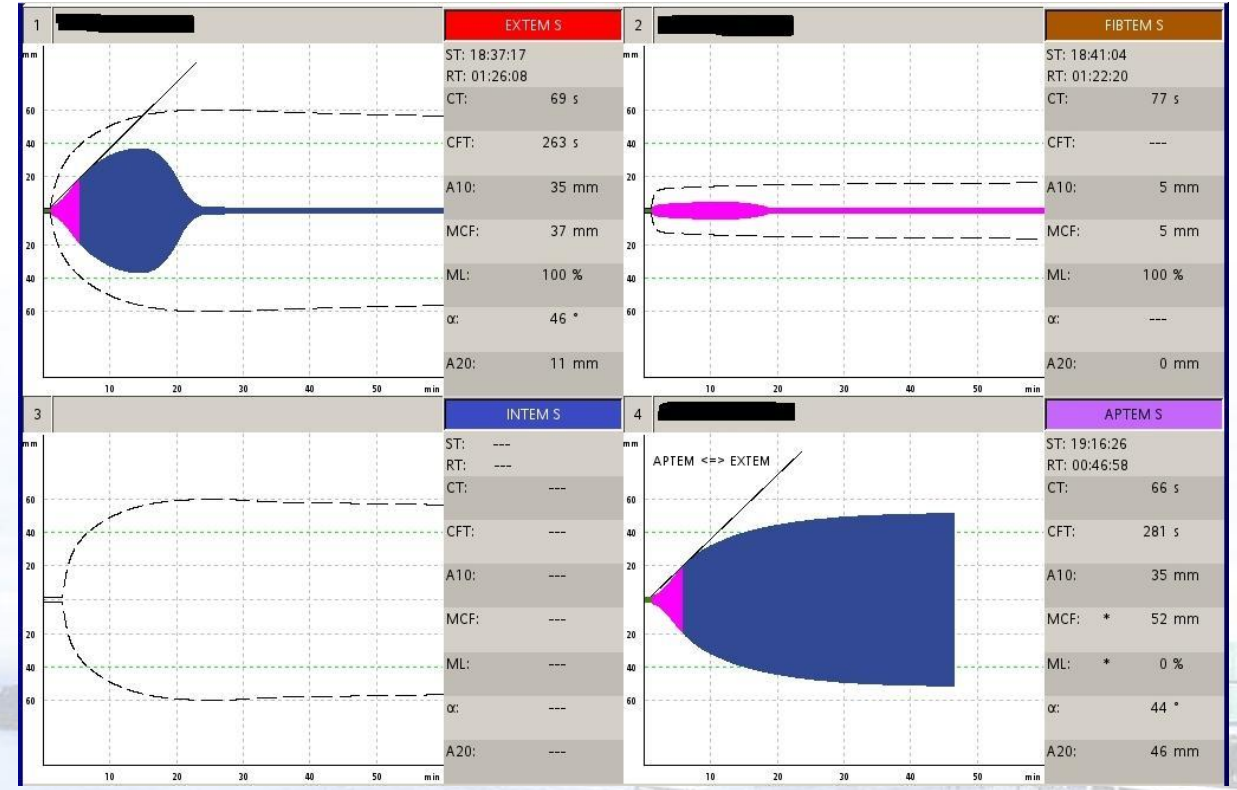


Prompt escalation to other interventions

(tamponade or surgical techniques)

Obstetrics & Gynecology 2017;130(4):e168–e186

Hyperfibrinolytic stage in PPH



Tranexamic acid

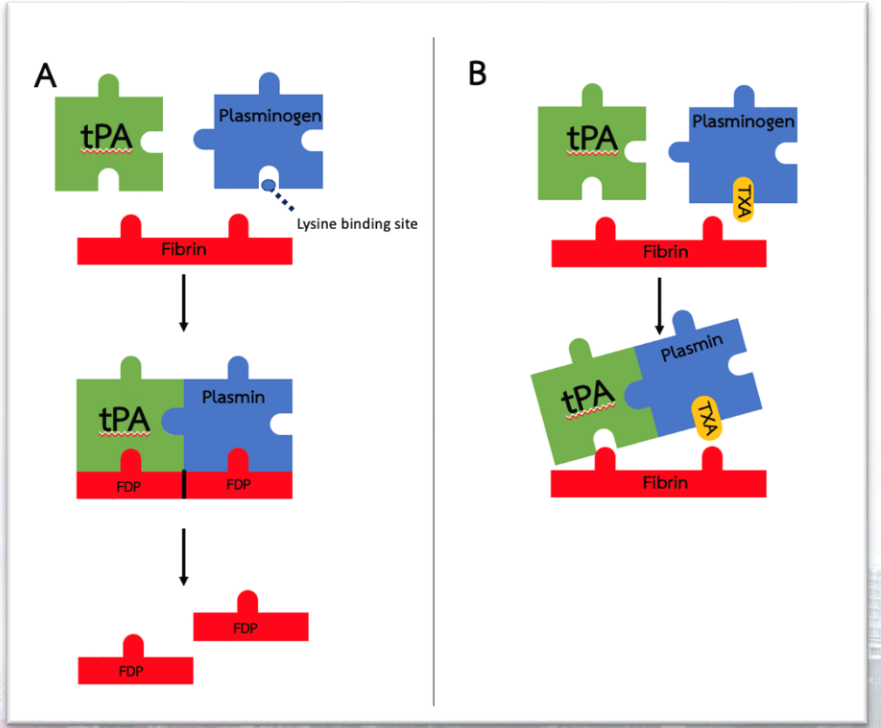


Photo by: Kriengkrai Wongdamrong

WOMAN trial – Lancet 2017

Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

WOMAN Trial Collaborators*

Summary

Background Post-partum haemorrhage is the leading cause of maternal death worldwide. Early administration of tranexamic a
of tranexami

Methods In t
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care. If bleed
tranexamic a
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increased the
death from post-partum haemorrhage. All analyses were done on an intention-to-treat basis. This trial is registered with ISRCTN76912190 (Dec 8, 2008); ClinicalTrials.gov, number NCT00872469; and PACTR201007000192283.

- Large RCT, placebo controlled
- Sample size ~ 20,000
- 21 countries
- 193 hospitals
- Tranexamic acid 1 g, Vaginal/Cesarean
- Repeat TXA 1 g in 24 hr if ongoing

Lancet 2017; 389: 2105-16
blished Online
ril 26, 2017
tp://dx.doi.org/10.1016/
140-6736(17)30638-4
is online publication has
en corrected. The corrected
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elancet.com on May 5, 2017
Editorial page 2081
ollaborators listed at end of
report

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Lancet 2017; 389: 2105-16

WOMAN trial, Lancet 2017

Findings Between March, 2010, and April, 2016, 20 060 women were enrolled and randomly assigned to receive tranexamic acid (n=10 051) or placebo (n=10 009), of whom 10 036 and 9985, respectively, were included in the analysis. Death due to bleeding was significantly reduced in women given tranexamic acid (155 [1·5%] of 10 036 patients *vs* 191 [1·9%] of 9985 in the placebo group, risk ratio [RR] 0·81, 95% CI 0·65–1·00; p=0·045), especially in women given treatment within 3 h of giving birth (89 [1·2%] in the tranexamic acid group *vs* 127 [1·7%] in the placebo group, RR 0·69, 95% CI 0·52–0·91; p=0·008). All other causes of death did not differ significantly by group. Hysterectomy was not reduced with tranexamic acid (358 [3·6%] patients in the tranexamic acid group *vs* 351 [3·5%] in the placebo group, RR 1·02, 95% CI 0·88–1·07; p=0·84). The composite primary endpoint of death from all causes or hysterectomy was not reduced with tranexamic acid (534 [5·3%] deaths or hysterectomies in the tranexamic acid group *vs* 546 [5·5%] in the placebo group, RR 0·97, 95% CI 0·87-1·09; p=0·65). Adverse events (including thromboembolic events) did not differ significantly in the tranexamic acid versus placebo group.

Interpretation Tranexamic acid reduces death due to bleeding in women with post-partum haemorrhage with no adverse effects. When used as a treatment for postpartum haemorrhage, tranexamic acid should be given as soon as possible after bleeding onset.

Lancet 2017; 389: 2105-16

Cochrane Library

Cochrane Database of Systematic Reviews

Antifibrinolytic drugs for treating primary postpartum haemorrhage (Review)

Shakur H, Beaumont D, Pavord S, Gayet-Ageron A, Ker K, Mousa HA

Cochrane Database Syst Rev. 2018 20;2(2):CD012964.

The data show that IV TXA reduces the risk of **maternal death due to bleeding** (risk ratio (RR) 0.81, 95% confidence interval (CI) 0.65 to 1.00; two trials, 20,172 women; *quality of evidence: moderate*). The quality of evidence was rated as moderate due to imprecision of effect estimate. The effect was more evident in women given treatment between one and three hours after giving birth with no apparent reduction when given after three hours (< one hour = RR 0.80, 95% CI 0.55 to 1.16; one to three hours = RR 0.60, 95% CI 0.41 to 0.88; > three hours = RR 1.07, 95% 0.76 to 1.51; test for subgroup differences: $Chi^2 = 4.90$, df = 2 (P = 0.09), $I^2 = 59.2\%$). There was no heterogeneity in the effect by mode of birth (test for subgroup differences: $Chi^2 = 0.01$, df = 1 (P = 0.91), $I^2 = 0\%$). There were fewer **deaths from all causes** in women receiving TXA, although the 95% CI for the effect estimate crosses the line of no effect (RR 0.88, 95% CI 0.74 to 1.05; two trials, 20,172 women, quality of evidence: moderate). Results from one trial with 151 women suggest that **blood loss of ≥ 500 mL** after randomisation may be reduced (RR 0.50, 95% CI 0.27 to 0.93; one trial, 151 women; *quality of evidence: low*). TXA did not reduce the risk of **serious maternal morbidity** (RR 0.99, 95% CI 0.83 to 1.19; one trial, 20,015 women; *quality of evidence: high*), **hysterectomy to control bleeding** (RR 0.95, 95% CI 0.81 to 1.12; one trial, 20,017 women; *quality of evidence: high*) receipt of **blood transfusion (any)** (RR 1.00, 95% CI 0.97 to 1.03; two trials, 20,167 women; *quality of evidence: moderate*) or maternal **vascular occlusive events** (any), although results were imprecise for this latter outcome (RR 0.88, 95% CI 0.54 to 1.43; one trial, 20,018 women; *quality of evidence: moderate)*. There was an increase in the use of brace sutures in the TXA group (RR 1.19, 95% CI 1.01, 1.41) and a reduction in the need for laparotomy for bleeding (RR 0.64, 95% CI 0.49, 0.85).

Authors' conclusions

TXA when administered intravenously reduces mortality due to bleeding in women with primary PPH, irrespective of mode of birth, and without increasing the risk of thromboembolic events. Taken together with the reliable evidence of the effect of TXA in trauma patients, the evidence suggests that TXA is effective if given as early as possible.

Facilities for IV administration may not be available in non-hospital settings therefore, alternative routes to IV administration need to be investigated.

Cochrane Database Syst Rev. 2018 20;2(2):CD012964.

Updated WHO Recommendation on Tranexamic Acid for the Treatment of Postpartum Haemorrhage

Highlights and Key Messages from the World Health Organization's 2017 Global Recommendation

October 2017

www.mcsprogram.org

Table 2. What is new about the use of tranexamic acid (TXA) to treat postpartum haemorrhage (PPH) in the 2017 WHO recommendation on TXA for PPH treatment?

	Indication	Timing	Dosing
WHO 2012 TXA Recommendation	Use of TXA is recommended for the treatment of PPH **if oxytocin and other uterotonics fail to stop the bleeding or if it is thought that the bleeding may be partly due to trauma.**	For atonic uterus, use TXA **if oxytocin and other uterotonics fail to stop the bleeding.**	**IV (slowly): 1 g** **Repeat after 30 minutes if bleeding continues.**
WHO 2017 TXA Recommendation (updated)	Use TXA **in all cases of PPH, regardless of whether the bleeding is due to genital tract trauma or other causes.**	Use TXA **within 3 hours and as early as possible after onset of PPH. Do not initiate TXA more than 3 hours after birth,** unless being used for bleeding that restarts within 24 hours of completing the first dose (see dosing).	Fixed dose of **1 g in 10 mL (100 mg/mL) IV at 1 mL per minute (i.e., administered over 10 minutes)** **Second dose** of 1 g IV **if bleeding continues after 30 minutes or if bleeding restarts within 24 hours of completing the first dose**

WHO recommendation

- IV oxytocin
- Ergometrine, oxytocin-ergometrine, PGs
- Isotonic crytalloid
- Tranexamic acid*
- Uterine massage
- Intrauterine balloon temponade

WHO recommendations for the prevention and treatment of postpartum haemorrhage 2012, *Updated in 2017 Lancet Glob Health. 2018 Jan;6(1):e18-e19.

Tranexamic acid for PPH

TABLE

Established indications for tranexamic acid

PPH: 1-g tranexamic acid as soon as possible after PPH onset (but no later than 3 h from birth) reduces PPH deaths by a third and reduces the need for laparotomy for bleeding.
Surgery: 1-g tranexamic acid just before incision reduces surgical bleeding and the need for blood transfusion by between one-quarter and one-third.
Trauma: 1-g tranexamic acid as soon as possible after injury (but no later than 3 hours) reduces deaths from bleeding by about one-third.

PPH, postpartum hemorrhage.

Roberts. Tranexamic acid to reduce bleeding. Am J Obstet Gynecol MFM 2022.

Am J Obstet Gynecol MFM 2022;00:100722. Article In Press

Reduction in crystalloid load

→ Minimizes side effects

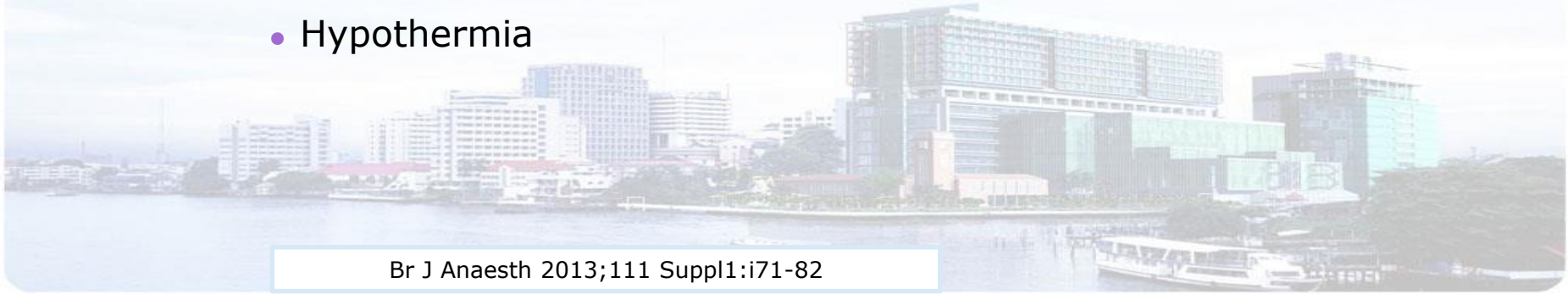
- Reperfusion injury
- Leukocyte adhesion and inflammation
- Associated acidosis
- Acute respiratory distress syndrome
- Systemic inflammatory response syndrome
- Multiorgan failure

Can J Surg 2014;57:55-60

Dealing with Massive blood transfusion

Metabolic derangement

- Acidosis
- Alkalosis
- **Hypocalcemia***, HypoMg^{2+}, HyperK^{+}
- Dilutional coagulopathy
- Low fibrinogen level and platelets
- Hypothermia



Br J Anaesth 2013;111 Suppl1:i71-82

Review Article

A systematic review of massive transfusion protocol in obstetrics

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PRC : FFP : platelets
6:4:1 or 1:1:1

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ABSTRACT

Post-partum obstetric haemorrhage is a leading cause of mortality among Japanese women, generally treated with haemostatic measures followed by supplementary transfusion. Commonly used in the setting of severe trauma, massive transfusion protocols (MTPs), preparations of red blood cell concentrate (RBC) and fresh frozen plasma (FFP) with additional supplements, have proved effective in decreasing patient mortality following major obstetric bleeding events. Although promising, the optimal configuration of RBC and FFP utilized for obstetric bleeding needs to be verified. Here, we conducted a systematic literature review to define the optimal ratio of RBC to FFP for transfusion therapy during instances of obstetric bleeding. Our analysis extracted four retrospective, observational studies, all demonstrating that an FFP/RBC ratio of $\geq$1 was associated with improved patient outcomes following obstetric haemorrhage. We therefore conclude that, from the standpoint of haemostatic resuscitation, an FFP/RBC ratio of $\geq$1 is a necessary condition for optimal clinical management during MTP administration in the field of obstetrics. Hence, we further propose an optimized MTP strategy to be utilized in the setting of severe obstetric bleeding.

Taiwan J Obstet Gynecol 2017;56(6):715-8

Table 1
Identified studies detailing massive transfusion protocols during obstetric haemorrhage.

	Year	Cases	Protocol
Bonnet MP et al. [9]	2011	38	FFP/RBC ratio exceeds 1 at 12 h following the onset of obstetric haemorrhage.
Matsunaga S et al. [10]	2012	196	Medically necessary FFP/RCC ratio is 1.3 in obstetric haemorrhage.
Gutierrez MC et al. [12]	2012	26	MTP was defined as a combination of 6 units of O-negative RBC, 4 units of FFP (liquid AB plasma or thawed type-specific plasma), and 1 apheresis platelet (PLT) unit.
Green L et al. [11]	2016	181	FFP/RBC ratio $\geq$ 1 required during massive obstetrics haemorrhage.
Tanaka H et al. [13]	2016	52	Transfusion of FFP/RBC ratio $\geq$ 1 reduces mortality during amniotic fluid embolism with coagulopathy.

FFP; fresh frozen plasma, RBC; red blood cell concentrate, RCC; red cell concentrate, MTP; massive transfusion protocol.

High FFP : RBC ratio > 1:1

Taiwan J Obstet Gynecol 2017;56(6):715-8

FIGO
International Federation of Gynecology and Obstetrics

the global voice for women's health

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SUPPLEMENT ARTICLE

International Journal of Gynecology & Obstetrics FIGO WILEY

FIGO recommendations on the management of postpartum hemorrhage 2022

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FIGO recommendation for PPH 2022

- Uterotonic agents
- Early use of Tranexamic acid
- Uterine massage
- Balloon tamponade/ other surgical intervention
- Damage control resuscitation
- IV fluid prefer RLS
- Massive transfusion protocol

Int J Gynaecol Obstet. 2022 Mar;157 Suppl 1:3-50.

KEY

- Multidisciplinary team *communication*
- Correct the cause of PPH
- Receptor desensitization of oxytocin
- Tranexamic acid 1 gm within 3 hr
- Well-prepared for massive blood loss in high-risk patients
- Massive transfusion protocol: high plasma : RBC ratio