Thieme

Peripartum Haemorrhage, Diagnosis and Therapy. Guideline of the DGGG, OEGGG and SGGG (S2k Level, AWMF Registry No. 015/063, March 2016)

Peripartale Blutungen, Diagnose und Therapie. Leitlinie der DGGG, OEGGG und SGGG (S2k-Level, AWMF-Registernummer 015/063, März 2016)

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Key words

peri-/postpartum haemorrhage, abnormally invasive placenta, uterine atony, surgical therapy, medical therapy, embolisation

Schlüsselwörter

peripartale Blutung, Plazentaimplantationsstörung, Uterusatonie, chirurgische Therapie, medikamentöse Therapie, Embolisation

received 24. 1. 2018
revised 8. 2. 2018
accepted 26. 2. 2018

Bibliography

DOI https://doi.org/10.1055/a-0582-0122
Geburtsh Frauenheilk 2018; 78: 382–399 © Georg Thieme Verlag KG Stuttgart · New York | ISSN 0016-5751

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Deutsche Version unter:
https://doi.org/10.1055/a-0582-0122

ABSTRACT

Purpose This is an official interdisciplinary guideline, published and coordinated by the German Society of Gynaecology and Obstetrics (DGGG), the Austrian Society of Gynaecology and Obstetrics (OEGGG) and the Swiss Society of Gynaecology and Obstetrics (SGGG). The guideline was developed for use in German-speaking countries and is backed by the German Society of Anaesthesiology and Intensive Medicine (DGAI), the Society of Thrombosis and Haemostasis Research (GTH) and the German Association of Midwives. The aim is to provide a consensus-based overview of the diagnosis and management of peripartum bleeding obtained from an evaluation of the relevant literature.

Methods This S2k guideline was developed from the structured consensus of representative members of the various

professional associations and professions commissioned by the Guideline Commission of the DGGG.
Recommendations The guideline encompasses recommendations on definitions, risk stratification, prevention and management.

ZUSAMMENFASSUNG

Ziel Erstellung einer offiziellen interdisziplinären Leitlinie, publiziert und koordiniert von der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe (DGGG), der Österreichischen Gesellschaft für Gynäkologie und Geburtshilfe (OEGGG) und der Schweizerischen Gesellschaft für Gynäkologie und Geburtshilfe (SGGG). Die Leitlinie wurde für den deutschsprachigen Raum entwickelt und wird von der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin (DGAI), der Gesellschaft für Thrombose- und Hämostaseforschung (GTH) und dem Deutschen Hebammenverband mitgetragen. Das Ziel dieser Leitlinie ist es, durch die Evaluation der relevanten Literatur einen konsensbasierten Überblick über die Diagnostik und das Management der peripartalen Blutung zu geben.
Methoden Diese S2k-Leitlinie wurde durch einen strukturierten Konsens von repräsentativen Mitgliedern verschiedener Fachgesellschaften und Professionen im Auftrag der Leitlinienkommission der DGGG entwickelt.
Empfehlungen Es werden Empfehlungen zur Definition, Risikostratifizierung, Prävention und Management gegeben.

I Guideline Information

Guidelines programme of the DGGG, OEGGG and SGGG

Information on the guidelines programme is available at the end of the guideline.

Citation format

Peripartum haemorrhage, diagnosis and therapy. Guideline of the DGGG, OEGGG and SGGG (S2k Level, AWMF Registry No. 015/063, March 2016). Geburtsh Frauenheilk 2018; 78: 382–399

Guideline documents

The complete long version (in German), a PDF slideshow for PowerPoint presentations and a summary of the conflicts of interest of all the authors is available on the AWMF homepage under: http://www.awmf.org/leitlinien/detail/ll/015-063.html

Guideline authors

The following professional and scientific societies/working groups/organisations/associations have stated their interest in contributing to the compilation of the guideline text and participating in the consensus conference and nominated representatives to attend the consensus conference (▶ **Table 1**).

▶ **Table 1** Authors and representativity of the guideline group: participation of the target user group.

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Abbreviations

AAGBI	Association of Anaesthetists of Great Britain and Ireland
AFE	amniotic fluid embolism
AMSTL	active management of third stage of labour
aPTT	activated partial thromboplastin time
AT/AT III	antithrombin/antithrombin III
BGA	blood gas analysis
BMI	body mass index
BL	blood loss
BW	body weight
CMACE	Centre for Maternal and Child Enquiries
DDAVP	desmopressin
DIC	disseminated intravascular coagulation
ESA	European Society of Anaesthesiology
FFP	fresh frozen plasma
Hb	haemoglobin
HR	heart rate
Hct	haematocrit
IM	intramuscular
INR	international normalized ratio
IU	international unit
IUFD	intrauterine fetal death
IV	intravenous
MAP	mean arterial pressure
MRI	magnetic resonance imaging
NICE	National Institute for Health and Care Excellence
OAA	Obstetric Anaesthetists Association
OR	odds ratio
PCC	prothrombin complex concentrate
POC	point of care
PPH	postpartum haemorrhage
rFVIIa	recombinant factor VII a
RBC	red blood cell concentrate
ROTEM	rotational thromboelastometry
RR_{sys}/RR_{dia}	RR systolic/RR diastolic
s/p	status post
TEG	thromboelastography
US	ultrasound
VET	viscoelastic test
WHO	World Health Organisation

II Guideline Application

Purpose and objectives

This aim of this guideline is to create an interdisciplinary (including anaesthesiologists and intensive care physicians, obstetricians, midwives, puerperal care nursing staff) management and treatment algorithm for the management of peripartum haemorrhage (diagnosis, risk selection, therapy).

The guideline was compiled to improve the knowledge of all persons involved in the care of pregnant women and women in childbed who experience or have an increased risk of haemorrhage.

The aim was to improve the care of affected patients and reduce problems in the management of PPH.

Targeted areas of patient care

- Outpatient care
- Primary/specialised care
- Inpatient care

Target user groups/target audience

This guideline is aimed at the following groups of people:

- gynaecologists/obstetricians in private practice (non-hospital based)
- hospital-based gynaecologists/obstetricians
- anaesthesiologists and intensive care physicians
- haemostasis specialists and lab clinicians
- interventional radiologists
- midwives
- nursing staff (surgery, anaesthesiology, intensive care unit, obstetrics/postpartum care)

Adoption of the guideline and period of validity

The validity of this guideline was confirmed in September 2015 by the respective boards/representatives of the participating professional societies/working groups/organisations/associations, by the board of the DGGG and the DGGG Guideline Commission and by the SGGG and the OEGGG, which constitutes approval of the entire contents of the guideline. This guideline is valid from May 1, 2016 through to March 31, 2019. Because of the contents of this guideline, the above-mentioned period of validity is only an estimate. The guideline can be updated earlier if urgently required. Should the guideline continue to reflect the current level of scientific knowledge, then the guideline's period of validity can be extended.

III Methodology

Basic principles

The methodology used to compile this guideline is determined by the class assigned to the guideline. The AWMF Guidance Manual (version 1.0) has set out the respective rules and requirements. Guidelines are differentiated into lowest (S1), intermediate (S2) and highest (S3) class. The lowest class consists of a set of recommendations for action compiled by a non-representative group of experts. In 2004 the S2 class was divided into two subclasses: a systematic evidence-based (S2e) subclass and a structural consensus-based subclass (S2k). The highest S3 class combines both approaches.

This guideline is classified as: **S2k**

Grading of recommendations

The grading of evidence and the grading of recommendations was not envisaged for S2k class guidelines. Individual statements and recommendations are differentiated by syntax, not by symbols (▶ **Table 2**).

▶ **Table 2** Grading of recommendations.

Description of grade of recommendation	Syntax
Strong recommendation, highly binding	must/must not
Recommendation, moderately binding	should/should not
Open recommendation, not binding	may/may not

The above classification of **recommendations** reflects the evaluated evidence and the clinical relevance of the studies on which the recommendations are based and various measures/factors which did not appear in the grading of evidence, such as the choice of patient population, intention-to-treat or per-protocol-outcome analyses, medical or ethical behaviour towards patients, country-specific application, etc.

Statements

Expert statements included in this guideline which are not recommendations for action but simple statements of fact are referred to as **statements**. It is not possible to provide a level of evidence for these statements.

Achieving consensus and level of consensus

During structured consensus-based decision-making (S2k/S3 level), the authorised representatives present at the respective session vote on draft Statements and Recommendations. Discussions during the session may lead to significant changes in the wording of Statements and Recommendations. At the end of the session, the extent of agreement (level of consensus) is determined based on the number of participants (▶ **Table 3**).

▶ **Table 3** Classification of extent of agreement in consensus decision-making.

Symbol	Level of consensus	Extent of agreement in percent
+++	Strong consensus	> 95 % of participants agree
++	Consensus	> 75–95 % of participants agree
+	Majority agreement	> 50–75 % of participants agree
–	No consensus	< 50 % of participants agree

Expert consensus

As the name implies, this refers to consensus decisions taken with regard to specific Recommendations/Statements without a previous systematic search of the literature (S2k) or when evidence is lacking (S2e/S3). The term “Expert Consensus” (EC) used here is synonymous with the terms “Good Clinical Practice” (GCP) and “Clinical Consensus Point” (CCP) used in other guidelines. The level of recommendation is graded as previously described in the Chapter Grading of recommendations but only semantically (“must”/“must not” or “should”/“should not” or “may”/“may not”) and without using symbols.

IV Guideline

1 Introduction

The incidence of postpartum haemorrhage (PPH) is continually increasing [1 – 5], mostly because of the increase in uterine atony and disorders of placental implantation and increased rates of surgical vaginal delivery and Caesarean sections and the consequent increase in primary blood loss and, in the case of Caesarean section, the increased PPH rates in subsequent pregnancies [2, 6 – 11].

In the western world, life-threatening postpartum haemorrhage occurs in approximately 2 of 1000 births and severe maternal morbidity occurs in around 3 of 1000 births [12 – 22]. PPH is

▶ **Table 4** The 4 Ts: causes of PPH [6, 16, 30 – 32].

Tone (uterine atony)	**Uterine distension** (multiparity, polyhydramnios, fetal macrosomia) Tocolytics Precipitate labour or prolonged labour (Prolonged) oxytocin augmentation Chorioamnionitis Uterine fibroids
Tissue (placenta)	Retained placenta **Abnormally invasive placenta** (morbidly adherent placenta, placenta accreta/increta/percreta) Placental remnants
Trauma	Vulvovaginal injury Cervical tear Episiotomy/perineal tear Uterine rupture Uterine inversion
Thrombin (coagulopathy)	**Pregnancy-induced:** Thrombocytopenia (HELLP syndrome, disseminated intravascular coagulation [DIC]) (e.g. in pre-eclampsia, intrauterine fetal death [IUFD], placental abruption, amniotic fluid embolism) **Other:** von Willebrand disease, plasmatic coagulopathies, thrombopathy, coagulation factor deficiencies (loss, consumption, dilution)

the cause of approximately 30 % of all maternal deaths in the Third World and 13 % of maternal deaths in industrialised countries [21].

The majority of maternal deaths from PPH could be avoided; major substandard care was present in 60–80 % of all cases [1, 20, 21, 23 – 25]. What is especially alarming is that a visual estimation of blood loss during delivery results in the extent of bleeding being underestimated by 30–50 % [26 – 29].

In Britain and America, the causes of PPH have been summarized as the "4 Ts". (Combinations of these causes are the rule.) (▶ **Table 4**).

The main risk management problems in the management of PPH are [1, 24, 33, 34]:

- Delayed diagnosis and/or therapy due to underestimation of the actual amount of blood lost
- Delayed provision of blood or coagulation products
- Lack of or failure to follow simple instructions
- Lack of adequate training or advanced training
- Poor communication within the interdisciplinary team
- Deficits in the organisational structure
- Delay in initiating treatment standards

2 Definitions

Consensus-based Recommendation 2.E1	
Expert consensus	**Level of consensus +++**
The following **definition of PPH** is proposed (for German-speaking areas): ▪ Blood loss of ≥ 500 ml following vaginal delivery ▪ Blood loss of ≥ 1000 ml following Caesarean section	

3 Risk Stratification and Prevention

A complete and detailed patient history, ultrasound examination during antenatal appointments, assessment of the patient's risk of bleeding, presentation to the maternity hospital, and preparations for increased blood loss could reduce patients' risk of PPH [35].

Consensus-based Recommendation 3.E2	
Expert consensus	**Level of consensus +++**
Location and structure of the placenta must be documented during ultrasound examination in the 2nd trimester. If necessary, patients with low-lying placenta should undergo an additional ultrasound scan to screen for vasa praevia and the findings should be documented [36].	

Consensus-based Recommendation 3.E3	
Expert consensus	**Level of consensus +++**
An implantation disorder should be considered in women with a high-risk history (previous operations) or findings (placenta praevia) which indicate high risk.	

3.1 Risk stratification and risk factors which facilitate peripartum/postpartum haemorrhage (▶ **Table 5**)

▶ **Table 5** Risk factors for PPH [16, 23, 37 – 39].

	Odds ratio or range	
Blood loss	> 500 ml	> 1000 ml
Sociodemographic risk factors		
▪ obesity (BMI > 35)	1.6	
▪ maternal age (≥ 30 years)	1.3–1.4	1.5
Obstetric risk factors		
▪ placenta praevia	4–13.1	15.9
▪ premature placental separation	2.9–12.6	2.6
▪ retained placenta	4.1–7.8	11.7–16.0
▪ prolonged expulsion of the placenta	7.6	
▪ pre-eclampsia	5.0	
▪ grand multiparity	2.3–4.5	2.6
▪ s/p PPH	3.0–3.6	
▪ fetal macrosomia	1.9–2.4	
▪ HELLP syndrome	1.9	
▪ Polyhydramnios	1.9	
▪ (prolonged) oxytocin augmentation	1.8	
▪ labour induction	1.3–2	2.1–2.4
▪ protracted labour	1.1–2	
Surgical risk factors		
▪ emergency Caesarean section	3.6	
▪ elective Caesarean section	2.5	
▪ operative vaginal delivery	1.8–1.9	
▪ episiotomy	1.7–2.21	2.07
▪ perineal tear	1.7	2.5
Other risk factors		
▪ antepartum haemorrhage	3.8	
▪ von Willebrand disease	3.3	
▪ anaemia (< 9 g/dl)	2.2	
▪ fever during delivery	2	

Other risk factors include precipitous birth, high maternal parity, fibroids and uterine malformations [39].

Caution: The majority of patients who develop PPH do not have identifiable risk factors [39].

3.2 Sonographic risk stratification (placentation disorders)

Consensus-based Recommendation 3.E4	
Expert consensus	**Level of consensus +++**
Patients with suspected abnormally invasive placenta must present early to a suitable maternity hospital where they must be treated by a multidisciplinary team ("by the best team at an optimal point in time") [20, 40].	

The diagnostic value of MRI has not yet been convincingly demonstrated in these cases [41, 42], but MRI examination could provide additional information when findings are ambiguous [42, 43].

3.3 Prevention

3.3.1 Active management of third stage of labour

3.3.1.1 Active management after vaginal delivery

Consensus-based Recommendation 3.E5	
Expert consensus	**Level of consensus +++**
After the infant has been born and commenced breathing, oxytocin (Syntocinon® 3–5 IU slow IV infusion) must be administered for PPH prevention [44].	

Consensus-based Recommendation 3.E6	
Expert consensus	**Level of consensus ++**
Immediate clamping of the umbilical cord at birth and controlled cord traction have no impact on reducing postpartum haemorrhage and should not be carried out.	

3.3.1.2 Prevention of PPH during Caesarean section

Consensus-based Recommendation 3.E7	
Expert consensus	**Level of consensus +++**
PPH prophylaxis must be administered as in vaginal delivery.	

Prophylaxis can consist of administering either oxytocin (Syntocinon® 3–5 IU by short infusion [or slow IV infusion]) or carbetocin (Pabal® 100 µg) by short infusion or slow IV infusion.

3.3.2 If risk factors are present

Consensus-based Recommendation 3.E8	
Expert consensus	**Level of consensus +++**
If risk factors are present, the following measures must be taken: ▪ Adequate venous access for every woman in labour, adequate intravenous access in case of complications of bleeding ▪ Uterotonics must be available (oxytocin, e.g. Syntocinon®), prostaglandins (e.g. sulprostone: Nalador®), misoprostol (Cytotec®, off-label use) ▪ Check logistics: – Check availability of emergency laboratory tests (complete blood count, blood gas analysis [BGA], aPTT, prothrombin time [PT] or INR, antithrombin [AT], fibrinogen, possibly thromboelastography or thromboelastometry [ROTEM]) – Obstetrician and anaesthesiologist must be on site, experienced obstetrician and experienced anaesthesiologist on call – Check availability of blood products: cross-matching, ordering of packed red blood cells, fresh frozen plasma and platelets – Check availability of haemostatic agents (tranexamic acid [Cyclokapron®], fibrinogen [Haemocomplettan®], factor XIII [Fibrogammin®], recombinant activated factor VII a [rFVIIa, NovoSeven®, off-label use]).	

4 Management of PPH

Consensus-based Statement 4.S1	
Expert consensus	**Strength of consensus +++**
Alongside general interventions (such as stabilising the patient's haemodynamic status), causal treatment of PPH includes medical therapy and/or surgical procedures that must be performed quickly, in a coordianted and often simultaneous manner [45 – 47].	

4.1 Procedures

- Measure blood loss! (Caution: blood loss in bandages, etc.)
- Rapid diagnosis of the cause of bleeding (4 T's):
  - Estimation of uterine tone
  - Check whether placenta is complete (ultrasound, manual or instrumental examination)
  - Exclude vulvovaginal trauma by speculum examination
  - Administer uterotonics (in case of atony) and tranexamic acid to treat critical blood loss
  - Uterine compression
- Call in anaesthesiologist (multidisciplinary team) at an early stage
- Drug therapy and/or surgical procedures, depending on the cause of bleeding
- Control vital signs, consider timely invasive monitoring
- Initial volume substitution to maintain normovolaemia: cristalloids, in exceptional cases (e.g. acute haemorrhage and haemodynamic instability) colloidal solutions [48]
- Cross-matching of blood, emergency laboratory tests (incl. full blood count, coagulation)
- Order packed red blood cells and fresh frozen plasma, provide blood products if required (delivery room, operating theatre)
- Coagulation factors, especially fibrinogen
- Other haemostatic agents (e.g. desmopressin), factor XIII or rFVIIa if necessary
- Intensive monitoring of patient during hospital stay, consider invasive monitoring
- Timely surgical intervention when conservative measures fail (see below for appropriate procedures)

Measuring blood loss

One of the cardinal problems which occur not only when defining but primarily when diagnosing and treating PPH is that the extent of postpartum blood loss is rarely measured and **is known to be underestimated by 30–50 % if assessment is done on a purely visual basis** [35, 49].

Consensus-based Recommendation 4.E9	
Expert consensus	**Level of consensus +++**
Collecting all blood-soaked pads, bedding, linens and significant coagulum is strongly recommended.	

5 General (Emergency) Measures and Diagnosis to Determine Causes of PPH

5.1 Atony

- Diagnosis: increased fundal height; soft slack uterus; usually intermittent heavy bleeding.
- Void the bladder!
- Mechanical procedures: uterine massage (endogenous prostaglandin formation), bimanual uterine compression (e.g. Hamilton's manoeuvre)
- Exclude vulvovaginal trauma (by speculum examination and abdominal US if necessary)
- Exclude retained placenta (examine the placenta to ensure it is complete, sonography)

Consensus-based Recommendation 5.E10	
Expert consensus	**Level of consensus +++**

Therapy:

After vaginal delivery

- uterotonics, tranexamic acid if required
- careful curettage in the delivery room or operating theatre if retained placenta is suspected
- uterine tamponade if required
- other surgical procedures
- consider embolisation

After caesarean section

- uterotonics, tranexamic acid if required
- surgical procedures

5.2 Implantation disorders

The management of abnormally invasive placenta depends on the time of diagnosis and type of delivery.

Approach for antenatal diagnosis

If an advanced implantation disorder (placenta increta, percreta) is diagnosed in the antenatal period, delivery must always be by Caesarean section.

- Extensive findings: Caesarean section with hysterectomy; alternatively, consider expectant management (e.g. delayed delivery of placenta)
- Focal findings: partial resection of the uterine wall
- If necessary carry out interventional radiology with prophylactic occlusion of the internal iliac arteries [50, 51]

Approach for intrapartum diagnosis

- Vaginal delivery:
  - If the placenta fails to separate and bleeding is present: carry out manual separation of the placenta followed by curettage with intraoperative ultrasound monitoring, if required [52]
  - If severe bleeding from the placental bed persists: carry out surgical therapy, alternatively embolisation of the uterine arteries
- Caesarean section:
  - Do not manipulate the placenta or attempt to separate it manually
  - Perform Caesarean section with hysterectomy or alternatively consider expectant management (e.g. delayed delivery of placenta)

Consensus-based Recommendation 5.E11	
Expert consensus	**Level of consensus ++**

Therapy:

After vaginal delivery

- uterotonics, tranexamic acid if required
- if necessary, manual separation of the placenta followed by curettage
- if necessary, uterine tamponade as a bridging procedure
- laparotomy and other surgical measures
- possibly embolisation

After Caesarean section

- uterotonics, tranexamic acid if required
- surgical measures
- consider embolisation

5.3 Uterine inversion

Consensus-based Recommendation 5.E12	
Expert consensus	**Level of consensus ++**

Therapy:

The goal is the reposition of the uterus and treatment of the symptoms of haemorrhagic shock. The following procedures must be carried out immediately after making the diagnosis in the order stated below:

- Stop administration of any uterotonic drug
- Call in experienced obstetrician and anaesthesiologist
  - Ensure adequate intravenous access, volume substitution
  - Make no attempt to remove the placenta (higher blood loss); the placenta must, where possible (placenta accreta), only be removed after repositioning [53, 54]
  - Attempt to reposition the fundus (Johnson's manoeuvre)
- If attempts at repositioning are unsuccessful, administer uterine relaxants (e.g. nitroglycerin 50 µg IV, betamimetics) and repeat the attempt to reposition the uterus with Johnson's manoeuvre
- If repositioning attempts continue to be unsuccessful → perform laparotomy and Huntington's procedure, simultaneously with Johnson's manoeuvre if necessary; if attempts are still unsuccessful, perform the Haultain procedure
- Administer uterotonics (e.g. oxytocin) after successful repositioning
- Provide antibiotic protection (e.g. cephalosporin or clindamycin)

6 Medication and Surgical Measures to Treat PPH

6.1 Uterotonics

6.1.1 Oxytocin (Syntocinon®) IV (IM if necessary)

Consensus-based Recommendation 6.E13	
Expert consensus	**Level of consensus +++**

A maximum of 6 IU undiluted oxytocin can be administered slowly and intravenously:

- 3–5 IU (1 vial) in 10 ml NaCl 0.9 % as a single (slow intravenous!) bolus
- If necessary, this can be followed by 10–40 IU oxytocin in 500–1000 ml saline as a continuous infusion (dose depends on the clinical situation, particularly the impact on uterine tone) [16, 55].

The onset of action after IV administration (half-life of 4–10 min) is less than one minute or 3–5 minutes following intramuscular administration (maximum 10 IU).

6.1.2 Carbetocin (Pabal®)

The use of carbetocin to treat PPH is currently not yet been sufficiently investigated. The use of carbetocin to treat PPH has been reported in individual cases.

6.1.3 Methylergometrine (Methergin®)

Consensus-based Recommendation 6.E14	
Expert consensus	**Level of consensus +++**
Given the range of serious side effects and the fact that better alternatives are available, the utmost caution is advised when administering methylergometrine to manage postpartum haemorrhage.	

Consensus-based Recommendation 6.E15	
Expert consensus	**Level of consensus ++**
Methylergometrine should not be administered as an intravenous bolus.	

6.1.4 Prostaglandins

Consensus-based Recommendation 6.E16	
Expert consensus	**Level of consensus +++**
If first-line uterotonics are not effective and patients do not respond to first-line uterotonics, prostaglandins must be administered immediately [56].	

Consensus-based Recommendation 6.E17	
Expert consensus	**Level of consensus +++**
Oxytocin receptor agonists and prostaglandins must not be administered simultaneously.	

Consensus-based Statement 6.S2	
Expert consensus	**Level of consensus ++**
Note: Postpartum uterine atony and uterine haemorrhage are life-threatening pathologies and an urgent indication for the administration of prostaglandin derivatives if no other alternatives are available or oxytocin is not effective, until patients can receive obstetric/gynaecological treatment. In this situation the side effects and contraindications must be carefully considered (benefits and drawbacks weighed up). Close haemodynamic monitoring is necessary when prostaglandin derivatives are administered.	

6.1.4.1 Sulprostone (Nalador®)

Dosage:

- 1 vial = 500 µg in 500 ml solution administered via an infusion pump
- Initial dose: 100 ml/h, up to a maximum of 500 ml/h if required
- Maintenance dose: 100 ml/h
- Maximum dose 1000 µg/10 hours (2 vials)
- Maximum daily dose 1500 µg (3 vials)

6.1.4.2 Misoprostol (Cytotec®)

Dosage: 800–1000 µg misoprostol administered rectally or 600 µg administered orally [57 – 60].

A Cochrane meta-analysis showed that oxytocin infusion was more effective as a first-line therapy than the administration of misoprostol and additionally had fewer side effects. When used after prophylactic uterotonics, misoprostol and oxytocin were equally effective [61].

Consensus-based Statement 6.S3	
Expert consensus	**Level of consensus +++**
Note: Because of its delayed onset of action and the availability of better and approved alternatives, misoprostol is not suitable to treat persistent PPH. The use of misoprostol to treat moderately persistent PPH after the administration of oxytocin may be considered (off-label use!). However, the current data is still insufficient to make a final recommendation.	

Consensus-based Statement 6.S4	
Expert consensus	**Level of consensus +++**
Note: Postpartum uterine atony and uterine haemorrhage are life-threatening pathologies and the administration of misoprostol is urgently indicated if no other alternatives are available, until patients can receive obstetric/gynaecological treatment. In this context the side effects and contraindications must be carefully considered (benefits and drawbacks weighed up). Close haemodynamic monitoring is essential when misoprostol is administered.	

6.1.4.3 Intrauterine application of prostaglandins

Consensus-based Statement 6.S5	
Expert consensus	**Level of consensus +++**
The intramyometrial application of sulprostone (e.g. to the uterine fundus in cases with caesarean section) is contra-indicated [56].	

7 Uterine Tamponade

The objective of uterine cavity tamponade is twofold: to treat PPH (i.e., to achieve definitive haemostasis) and as a "bridging" measure (i.e., to achieve temporary haemostasis and haemodynamic stabilisation and allow other measures [surgical or interventional radiology] to be put in place) [62 – 64]. In addition to other second-line treatment strategies, uterine tamponade can significantly reduce the rate of emergency hysterectomies [65, 66].

In addition to tamponade strips, there are a number of different balloon tamponade systems available for uterine tamponade; their efficacy has been described in various publications and their use has the advantage of allowing the early detection of persistent bleeding [64, 67 – 73].

Consensus-based Recommendation 7.E18	
Expert consensus	**Level of consensus ++**
▪ Parallel administration of uterotonics ▪ Vaginal examination/ultrasound (to exclude trauma, retained placenta, clot evacuation) ▪ Bladder catheter ▪ Use a liquid (0.9 % saline, body temperature if possible) to fill the balloon tamponade – NOT air ▪ Additional vaginal tamponade ▪ Intensive monitoring, antibiotic prophylaxis ▪ Can be left in utero for up to 24 hours	

There has been a recent report on the use of a special gauze (Celox®) coated with a haemostatic agent (chitosan), originally developed for emergency treatment and military combat medicine, to successfully manage PPH [74].

Consensus-based Recommendation 7.E19	
Expert consensus	**Level of consensus ++**
Uterine tamponade – in whatever form – does not preclude other necessary therapeutic options, such as compression sutures [64, 75]; the use of compression sutures is strongly recommended, particularly to treat atony [75 – 78].	

8 Surgical Measures (Compression, Devascularisation, Hysterectomy) and Embolisation

8.1 Bridging procedures

Consensus-based Recommendation 8.E20	
Expert consensus	**Level of consensus ++**
In the event of the lethal triad consisting of persistent haemorrhage, haemorrhagic shock und coagulopathy, the following three-stage approach is recommended [62]: ▪ Early surgical haemostasis carried out by the attending surgical obstetrician using a Pfannenstiel incision or median laparotomy, eventeration of the uterus with cranial traction and uterine compression, and atraumatic clamping of the uterine arteries to minimise perfusion. Placement of uterine compression sutures and application of a uterine tamponade. ▪ Parallel correction of hypovolaemia, temperature, disturbed acid-base balance and coagulopathy by the anaesthesiologist; if possible, surgery should then be paused until stabilisation. ▪ Definitive (surgical) treatment of the now haemodynamically stable patient by a surgeon with the appropriate surgical expertise. If the necessary infrastructure is available, option to perform interventional radiological embolisation of afferent uterine arteries [79, 80]. The benefit of this approach is that it can preserve fertility, as has been described for large case series [81 – 84].	

8.2 Uterine compression sutures

The aim of these sutures is to compress the uterus, reduce the placental adhesion area and tamponade the bleeding site. This approach is indicated for uterine bleeding after vaginal delivery or following Caesarean section. At present it is not possible to say anything about the optimal efficacy of specific types of sutures. All of the employed methods had high success rates in terms of preventing hysterectomy which would otherwise have been necessary. The choice of the appropriate suture method depends on the indication (atony, bleeding from the placental bed, diffuse bleeding) [85].

Consensus-based Recommendation 8.E21	
Expert consensus	**Level of consensus +++**
Suitable suture materials (large needles, long suture threads) must be kept in readiness in the operating theatre.	

8.3 Vascular ligatures

In addition to simple ligature of the uterine artery [86] stepwise uterine devascularisation can also be used for haemostasis. The technique consists of 5 consecutive steps to ligate the ascending and descending branches of the uterine arteries and the ovarian arterial collaterals [87, 88].

Consensus-based Recommendation 8.E22	
Expert consensus	**Level of consensus +++**
Ligature of the internal iliac artery must only be carried out as a last resort and only by a surgeon with extensive experience of pelvic surgery.	

8.4 Postpartum hysterectomy

Consensus-based Recommendation 8.E23	
Expert consensus	**Level of consensus +++**
Conservative measures to preserve the uterus are only useful if the patient is haemodynamically stable and does not have life-threatening bleeding [89, 90]. The decision that hysterectomy is indicated must not be delayed or left too late.	

Consensus-based Recommendation 8.E24	
Expert consensus	**Level of consensus +++**
Supracervical hysterectomy is the procedure of choice for atony, as the operating time is significantly shorter and the operation does not lead to unintended vaginal shortening. Total hysterectomy should be considered for placental implantation disorders of the lower uterine segment; visualisation of the ureters during this procedure is recommended.	

Relative contraindications for uterus-preserving measures are:

- Extensive abnormally invasive placenta (placenta increta/percreta) where the placental implantation bed is open, bleeding from the placental implantation bed is resistant to treatment or the implantation bed covers large areas of the uterine wall.
- Non-reconstructable uterine injury
- Septic uterus

Consensus-based Recommendation 8.E25	
Expert consensus	**Level of consensus ++**
During the bridging time to definitive treatment, (bimanual) compression of the aorta for up to 20 minutes may be carried out to avoid unnecessary blood loss [91, 92]. If it is clear that the haemorrhage cannot be controlled by hysterectomy or is continuing even though hysterectomy has been carried out, the lesser pelvis and abdomen should be packed with sufficient moistened abdominal cloths.	

8.5 Arterial catheter embolisation

Consensus-based Recommendation 8.E26	
Expert consensus	**Level of consensus +++**
Every obstetric department should ascertain whether arterial catheter embolisation can be performed in their facility and the time it takes for this method to be available and then create the organisational structure which will determine at what point the patient should be transferred to the interventional radiology department. The precondition for transfer is that the patient is haemodynamically stable and does not have massive bleeding.	

Consensus-based Recommendation 8.E27	
Expert consensus	**Level of consensus ++**
If catheter embolisation is available on site, the radiologist should be notified early (e.g. when an attempt at haemostasis using uterine compression sutures is unsuccessful). Because of the range of side effects, medical and surgical treatment options should be largely exhausted. The time of transfer to the radiology department is also determined by how important it is to preserve the uterus.	

Consensus-based Recommendation 8.E28	
Expert consensus	**Level of consensus +++**
Before the patient is transferred, intra-abdominal packing should be considered as a bridging procedure if the patient has just undergone a hysterectomy procedure to prevent a critical loss of blood during transportation and contain the bleeding during the sometimes protracted intervention.	

Consensus-based Recommendation 8.E29	
Expert consensus	**Level of consensus ++**
If the intervention can be planned ahead (e.g., placenta increta/percreta), endovascular catheters can already be placed preoperatively into the internal iliac artery on both sides.	

Catheter embolisation may be used as a last resort to treat persistent diffuse bleeding in the lesser pelvis after postpartum hysterectomy [93].

9 Haemostasis and Coagulation Management – Intensive Medical Procedures

9.1 Background

Understanding and recognising the most probable pathophysiology of the bleeding is important, as this will offer pointers for different therapeutic approaches. The problem associated with haemostatic management is the difficulty in differentiating between increased bleeding caused by a major injury and protracted bleeding where the composition of blood has changed (i.e., the normal capacity of the system to compensate for smaller injuries has been reversed; this equates to an impairment of the coagulation system = coagulopathy). It is therefore necessary to distinguish between:

- trauma-induced coagulopathy with shock and massive tissue trauma
- initial "traumatic" haemorrhage caused by tissue trauma, and
- initial coagulopathic bleeding.

Impaired coagulation (= coagulopathy) is often an early pathology of PPH which can occur before dilutional coagulopathy occurs [39, 94].

Consensus-based Recommendation 9.E30	
Expert consensus	**Level of consensus +++**
The length of time needed to obtain diagnostic findings means that it is not possible to await the results of diagnostic procedures which differentiate between different coagulopathies (e.g. congenital vs. acquired) before making treatment decisions. As a rule (if the patient's medical history does not indicate any congenital coagulopathy), it should be assumed that patients with peripartum or postpartum haemorrhage have an acquired coagulopathy, unless a surgical cause of haemorrhage can be clearly identified.	

It is also important to take account of the fact that, because of the associated dilution effect and the use of coagulation factors, every primary mechanical bleeding treated with volume replacement and fresh frozen plasma (FFP) will become coagulopathic if volume substitution and FFP administration is continued over a lengthy period [95 – 97].

Consensus-based Statement 9.S6	
Expert consensus	**Level of consensus +++**
It is therefore essential that all hospitals with obstetric departments develop a treatment algorithm for peri-/postpartum haemorrhage which is adapted to the specific conditions in the respective hospital [46, 98 – 101]. The aim must be to identify haemorrhaging patients early on and describe the appropriate interdisciplinary surgical, interventional and haemostatic treatment to manage the bleeding. This algorithm should define the approach for the treatment process based on the clinical situation and take account of all available treatment options (pharmacological therapies, interventional procedures, surgical interventions).	

9.2 Options to treat peri-/postpartum coagulopathic haemorrhage

Consensus-based Statement 9.S7	
Expert consensus	**Level of consensus +++**
During active bleeding, any iatrogenic aggravation of the tendency to bleed (e.g. by administering artificial colloids for volume replacement which has a strong dilution-related coagulopathic effect, or attempt to achieve high-normal blood pressure) should be avoided, where possible.	

Consensus-based Statement 9.S8	
Expert consensus	**Level of consensus ++**
Blood component therapy is currently the standard therapy for haemostasis, either using labile (cellular components, FFP) or stable (lyophilised factor concentrates) blood products, and should be administered early to prevent dilutional coagulopathy occurring in addition to the already existing loss of blood.	

Based on the current state of knowledge, f**ibrinogen** plays a key role. In patients with a history of peri-/postpartum haemorrhage and patients with peripartum bleeding, plasma fibrinogen concentrations should be determined (irrespective of treatment), as concentrations < 2 g/l could help identify those patients at increased risk of severe PPH [39, 46].

Consensus-based Recommendation 9.E31	
Expert consensus	**Level of consensus ++**
In any case, potentially increased fibrinolytic activity should be treated by the administration of **tranexamic acid** (an antifibrinolytic) before the substitution of fibrinogen (factor concentrate or FFP) is considered [39].	

Consensus-based Statement 9.S9	
Expert consensus	**Level of consensus +++**
The beneficial effects (lower loss of blood, reduced blood transfusion, increased Hb, lower number of invasive procedures) of administering tranexamic acid to treat PPH have since been shown in randomised, controlled studies of around 2000 patients [102 – 110]. In 2013 the ESA issued a strong recommendation based on moderate evidence for the administration of tranexamic acid to treat obstetric bleeding to reduce blood loss, bleeding duration and the number of transfusions [46]. There are no reliable data on the use of **DDAVP** (Minirin®) in obstetrics which would permit an evidence-based recommendation [111], although there have been repeated reports of observational studies with positive outcomes [112]. According to the ESA, DDAVP may be useful to treat platelet function disorders resulting from acquired von Willebrand syndrome (from drugs, acidosis, hypothermia) [46].	

Consensus-based Recommendation 9.E32	
Expert consensus	**Level of consensus +++**
Although the data is controversial and prospective randomised studies are lacking, one or two attempts at treatment with rFVIIa at a dose of 90 µg/kg BW can be undertaken as a last resort in carefully selected cases if 1. the patient has previously received adequate and appropriate treatment with other blood products, 2. the other methods used for haemostasis were not sufficiently effective, and 3. the patient still wants to have other children before undergoing a hysterectomy [39, 113 – 116]. Because of the risk of thromboembolism, recombinant FVIIa (NovoSeven®) should only be given as a last resort [117]. Plasmatic factor concentrations and platelet numbers should be optimised before rFVIIa is administered [46].	

Consensus-based Statement 9.S10	
Expert consensus	**Level of consensus ++**
In summary, the conclusions to be drawn from the currently available data on haemostatic management recommend ▪ an escalating concept (i.e., a successive step-by-step range of treatment options) adapted to the respective conditions in each hospital [46, 99, 100], ▪ early administration of tranexamic acid, preferably immediately after making the diagnosis, ▪ stabilisation of physiological preconditions for coagulation (i.e. pH, temperature, calcium level) [46, 95], ▪ if bleeding persists, viscoelastic test or conventional diagnostic tests to diagnose the cause of bleeding, ▪ if bleeding persists and substitution is required (if need be, in parallel to other mechanical forms of treatment), early replacement of coagulation factors with factor concentrates and/or FFP (fibrinogen should be considered if dilutional coagulopathy is present, otherwise PCC and F XIII may be used), ▪ if necessary (i.e. when other approaches are not effective), optimisation of platelet numbers (target > 100,000/µl for patients with active bleeding requiring transfusion) [46].	

Consensus-based Recommendation 9.E33	
Expert consensus	**Level of consensus +++**
After the underlying cause of bleeding has been treated, thromboprophylaxis must be administered within 24 hours [39]. Because of the reduced antithrombin activity (absolute activity may even be less than 0.5 kIU/l) in the majority of women with PPH, an increased risk of thromboembolism is expected **after the bleeding has stopped** [118]. After the administration of individual coagulation factor concentrates or complex preparations (e.g. PCC), antithrombin activity can be determined on the intensive care unit and substituted if necessary [119]. The target value is ≥ 80 % or ≥ 0.8 kIU/l [119 – 121].	

9.3 Anaesthesia-related aspects of managing PPH

Consensus-based Recommendation 9.E34	
Expert consensus	**Level of consensus +++**

- Maintain or achieve haemodynamic stability and normovolaemia: **myocardiac ischaemia** with reduced contractility is often present when Hb values ≤ 6 g/dl (3.726 mmol/l) with or without haemodynamic abnormality (RR_{sys} < 90 mmHg and/or RR_{dia} < 50 mmHg and/or HR ≥ 115/min) [122, 123].
- **Timely call for expert assistance** is recommended for uncontrolled blood loss of more than 500 ml following vaginal delivery or more than 1000 ml following Caesarean section and is essential if blood loss is more than 1500 ml [29, 89, 95, 124].
- For patients receiving **regional anaesthesia** (spinal anaesthesia, epidural anaesthesia): if blood loss is ≥ 1500–2000 ml and there are signs of persistent bleeding: **secure the airway and ensure sufficient oxygen supply**; if necessary, perform early intubation after consultation with the surgeon [125]. If there is a loss of protective reflexes, endotracheal intubation to secure the airway and ensure sufficient oxygenation must take priority.
- Place **wide-diameter** access points (2× ≥ 16 G) followed by arterial blood pressure measurement, if necessary even before intubation. A wide-diameter central access (≥ 9 Fr) is recommended [125 – 128].
- **Cell saver** blood (official recommendations of CMACE, NICE, OAA/AAGBI, ESA): use of mechanical autotransfusion in patients undergoing elective Caesarean section (e.g. in cases with placenta increta/percreta) can reduce the administration of allogenic blood postoperatively and the duration of hospital stay [129, 130]. In the emergency setting of PPH the following **caveats** must be taken into consideration: should only be used, after amniotic fluid removal and delivery of the neonate.
  - Cell-saver blood does not contain clotting factors or platelets. Coagulation factors should be substituted to prevent coagulopathy when administering high transfusion volumes [131].
  - Cases of hypotension have been reported following the re-transfusion of cell-saver blood with a leukocyte depletion filter [132].
- **Target values in haemodynamic therapy**
  for "healthy" pregnant women and strong bleeding:
  - **After cord clamping, hypotensive resuscitation** until surgical haemostasis is achieved with **restrictive fluid therapy** [133, 134].
  - "Normal recapillarisation time" or "palpable radial pulse" are the target values for volume replacement therapy [135, 136]
  - **Goal:** MAP > 65 mmHg or lower [137] or RR_{sys} ~ 90 mmHg [138].
  - **Target Hb:** indication for blood transfusion until surgical haemostasis: **7 g/dl** (4.347 mmol/l); after surgical haemostasis and successful treatment of the underlying pathology: **7–9 g/dl** (4.347–5.589 mmol/l) [23, 134, 138].
    Note: ensure sufficient additional iron supplementation on the ward postoperatively.
- **Pharmacological thromboprophylaxis** within 24 hours after the pathology causing the bleeding has been treated [134].

Escalating regimen of haemostatic therapeutic options to treat PPH (based on recommendations of the S3-guideline 012/019 "Polytrauma/Schwerverletztenbehandlung" [Multitrauma/Treatment of Severely Injured Persons], DGAI recommendations on treating severe bleeding and ESA recommendations on treating perioperative haemorrhage) [100, 136].

1.	Stabilise general conditions (prophylaxis and therapy!)	Core temperature ≥ 34 °C (preferably normothermia) pH ≥ 7.2 ionised Ca^{++} concentration > 0.9 mmol/l (preferably normocalcaemia)
2.	Prevent potential (hyper-) fibrinolysis (always PRIOR to the administration of fibrinogen and/or FFP!)	Tranexamic acid (Cyklokapron®) initially 1–2 g (15–30 mg/kg BW), repeat as needed
3.	Substitution of oxygen carriers	RBC administration Haemostatic target in patients with severe bleeding: Hb ~ 7–9 g/dl (4.3–5.5 mmol/l) or Hct ~ 30 %
4.	Substitution of clotting factors (if severe haemorrhage persists) depending on availability in hospital	FFP ≥ 20 (preferably 30) ml/kg BW or/and fibrinogen (Haemocomplettan®) (2–)4(–8) g (30–60 mg/kg BW) Target: ≥ 200 mg/dl or ≥ 2.0 g/l
	Patients who require (or are anticipated to require) massive transfusion or suffer life-threatening haemorrhagic shock may benefit from high FFP : RBC ratio of ≥1 : 2 or from combined administration of FFP and factor concentrates.	If required, PCC initially 1000–2500 IU (25 IU/kg BW) If required, 1–2× FXIII (Fibrogammin® P)E; 1250 IU (15–20 IU/kg BW)
	and (if thrombocytopenia is suspected) increased platelet adhesion to endothelium + release of von Willebrand factor and FVIII from endothelium/liver sinusoids (→ agonist for vasopressin type 2 receptor)	DDAVP = desmopressin (Minirin®) 0.3 µg/kg BW over a period of 30 minutes (1 vial per 10 kg BW over a period of 30 min)
5.	Platelet substitution for primary haemostasis	Platelet concentrate (target for haemorrhage requiring transfusion: 100 000/µl)
6.	If necessary, thrombin burst with platelet and coagulation activation (consider general haemostatic conditions!)	In individual cases and when all other treatment options have been unsuccessful rFVIIa (NovoSeven®) if required, initially 90 µg/kg BW
	During ongoing bleeding	No antithrombin (ATIII) during haemorrhage, may be considered after administration of PCC and cessation of bleeding No heparin during haemorrhage
	CAUTION: Thrombosis prophylaxis is mandatory within 24 hours after cessation of the pathology causing the bleeding!	

9.4 Rotational thromboelastometry (ROTEM)/ thromboelastography (TEG)

The mean time until the results of standard laboratory parameters are available in the operating room is at least 45 minutes [139]. Coagulation disturbances can be detected significantly faster with the viscoelastic test (VET) [139, 140].

Currently, two procedures are used for point-of-care (POC) diagnostics offering prompt, bedside recognition of clotting disorders based on VET: rotational thromboelastometry (ROTEM, Tem International GmbH, Munich, Germany) and thromboelastography (TEG, Haemonetics, Braintree, MA, USA) [141].

At present there are no class 1 recommendations on the use of these procedures [46].

10 Transportation

Consensus-based Recommendation 10.E35	
Expert consensus	**Level of consensus +++**
As transporting a haemodynamically instable patient is a serious risk, any transportation of such patients as part of the management of PPH must be carefully weighed up, quite apart from the organisational conditions at the facility caring for the patient (or transportation should only be considered after haemodynamic stabilisation). It is important that the facility transferring the patient and the facility accepting the patient agree about timing and staff coverage during transportation of the patient in the run-up to the patient transfer and record what the two facilities have agreed upon in writing [142].	

11 Monitoring after PPH

Consensus-based Recommendation 11.E36	
Expert consensus	**Level of consensus +++**
Following PPH, individually adapted active monitoring must be carried out for at least 24 hours.	

12 Documentation

Consensus-based Recommendation 12.E37	
Expert consensus	**Level of consensus +++**
Every event defined as an emergency must be carefully documented. It is recommended to use the special forms developed for the respective organisational unit for documentation.	

13 Debriefing

Consensus-based Recommendation 13.E38	
Expert consensus	**Level of consensus +++**
Interdisciplinary team debriefing is recommended.	

14 Training

Consensus-based Recommendation 14.E39	
Expert consensus	**Level of consensus +++**
Simulations of haemorrhagic situations must be carried out by an interdisciplinary team at regular intervals; studies have shown that this leads to an improvement in the management of peri-/postpartum haemorrhage [35, 143].	

Conflict of Interest

Almost all of the authors give talks on the topic of PPH at conferences and company-sponsored meetings.

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