Diagnosis and therapy of life-threatening peripartum haemorrhage: Czech-Slovak interdisciplinary guidelines

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Czech Republic – Consensus interdisciplinary guidelines for the prevention and treatment of postpartum haemorrhage

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Introduction

This document presents the updated Czech-Slovak guidelines for diagnostic and therapeutic procedures in patients who develop life-threatening haemorrhage related to pregnancy and/or delivery, focussing on life-threatening peripartum haemorrhage (LTPPH). Guidance and recommendations are based on available published literature in the given field and on opinions of the workgroup members, including external opponents. Implementation of these guidelines should be considered with regards to the current clinical context and in terms of the risk–benefit profile of individual specific procedures. The guidelines are not intended to replace essential specialised literature in the given field and do not describe the duties of healthcare professionals as determined by legal standards.

Terminology

The term 'peripartum haemorrhage' is widely used in international literature (including World Health Organization guidelines) to describe bleeding conditions related to delivery, and comprises bleeding conditions before, during and after delivery. Postpartum haemorrhage, i.e. bleeding after delivery, is the most common form of peripartum haemorrhage (Tunçalp *et al*. 2013). Based on the consensus of the guidelines workgroup, the abbreviation 'PPH' may be used for both 'peripartum haemorrhage' and 'postpartum haemorrhage'. Bleeding conditions during pregnancy and delivery that are life-threatening for the mother are described as 'life-threatening peripartum haemorrhage' (LTPPH).

Methodology and principles of formulating individual guidelines

Considering that the available Czech-Slovak literature is insufficient to formulate guidelines using *de novo* methods that are used to design international guidelines (such as GRADE), the following inputs were used to formulate the current guidelines: (a) Published guidelines related to the topic; (b) Systematic/critical analysis of selected specialised literature related to the issues of individual guidelines; (c) Other citable sources; and (d) Opinions of the authors at the time of formulating the document (Abdul-Kadir *et al*. 2014, Bohlmann and Rath 2014, Carvalho *et al*. 2016, Clark 2016, Collins *et al*. 2016, Committee on Practice Bulletins-Obstetrics 2017, Dahlke *et al*. 2015, Evensen *et al*. 2017, John M. Eisenberg Center for Clinical Decisions and Communications Science 2007, Jones *et al*. 2016, Kassebaum *et al*. 2015, Lier *et al*. 2016, Lockhart 2015, Main *et al*. 2015, Mousa *et al*. 2008, Schlembach *et al*. 2014, Sentilhes *et al*. 2014, Sentilhes *et al*. 2016a, Sentilhes *et al*. 2016b, Shaylor *et al*. 2017, Solomon *et al*. 2012, Su and Chong 2012, Vaught 2016, Vendittelli *et al*. 2016, Wattar *et al*. 2017, Wise 2016, Woiski *et al*. 2015, Woiski *et al*. 2016).

Power/urgency and conclusiveness of evidence are not provided for the individual guidelines and opinions presented here. The guidelines workgroup agreed that these guidelines should be regarded as equivalent to 'good therapeutic practice' or a 'description of the proper procedure', reflecting the professional understanding of the given issue and the authors' opinion at the time of formulating the document.

The following terms are thus used in the document:

- **Recommend** (equivalent of a 'strong' guideline)
- **Suggest** (equivalent of a 'weak' guideline)
- **Not recommended**

The consensus of ≥80% of workgroup members was required to formulate each guideline/opinion, i.e. at least 10 of the 12 members had to vote 'yes' for a guideline to be accepted.

General considerations

Epidemiology

Haemorrhage related to pregnancy and/or delivery still represents one of the major causes of maternal deaths worldwide, and is the most common cause of direct maternal deaths in the Czech Republic. Approximately 80 peripartum hysterectomies are performed annually in the Czech Republic, and up to 90% of these procedures are estimated to be performed for the indication of LTPPH based on primary uterine atony or uterine atony associated with myomatous uterus, or haemorrhage caused by a placentation disorder (Kassebaum *et al*. 2016, Ústav zdravotnických informací a statistiky ČR 2017).

Definitions

Peripartum haemorrhage can be defined and classified according to estimated blood loss:

- **'Moderate blood loss'** (blood loss ≤1000 mL)
- **'Severe blood loss'** (blood loss >1000 mL)
- **'Life-threatening blood loss'**, defined as rapidly increasing blood loss clinically estimated as >1500 mL or any blood loss associated with the development of clinical and/or laboratory signs of shock/tissue hypoperfusion

Clinical note: during pregnancy, blood volume increases by up to 40% of the original volume. Initial symptoms of haemorrhagic shock are, therefore, less apparent in pregnancy. Tachycardia and tachypnoea, together with a slight decrease in blood pressure, occur with blood loss between 1000 and 1500 mL. With blood loss >1500 mL, systolic blood pressure falls below 80 mmHg, and is associated with tachycardia, tachypnoea and changes in consciousness. The first hours of bleeding are usually not associated with decreased haemoglobin levels (Carvalho Pacagnella *et al*. 2013). The obstetrician should be alerted to the possibility of severe blood loss by a significant rise in leukocyte levels and by the aforementioned clinical symptoms, especially in cases where obstetric haemorrhage is hidden (for example, in the retroperitoneum).

Risk factors and causes

Although patients with PPH may not have any risk factors, studies have defined risk factors for PPH that are already present in the prenatal period and risk factors that occur during parturition (Kramer *et al*. 2013). LTPPH occurs when at least one of 4 potential causes, known as the '4 Ts' (tone, tissue, trauma and thrombin), is disturbed. Risk factors taking account of the 4 Ts are shown in **Table 1**. In most cases, PPH occurs due to non-surgical causes (uterine hypotony/atony in 80% of cases), while a small number of cases may be due to surgical causes, such as placental detachment disorders and obstetric injuries (Mousa *et al*. 2008, Arulkumaran 2012).

[Table 1 near here]

Guidelines

Preventive measures

The purpose of preventive measures is to minimise the risks of PPH/LTPPH. Preventive procedures are implemented both in the antepartum and intrapartum periods and are aimed at preventing fertility loss or death in connection with LTPPH.

Guideline 1
*It is **recommended** that women with risk factors for LTPPH deliver their baby in a healthcare institution where appropriate personnel and materials are available for LTPPH management.*

Guideline 2
*In women with a high risk of LTPPH (abnormal placentation) it is **recommended** that the management plan is formulated with the participation of a multidisciplinary team sufficiently in advance of the birth.*

Guideline 3
*Antepartum treatment of anaemia is **recommended**. Iron products should be administered to pregnant women if their haemoglobin levels decrease below 110 g/L in the first trimester or below 105 g/L in week 28 of pregnancy.*

Guideline 4
*Parenteral administration of iron is **suggested** in women with sideropenic anaemia who do not respond to oral iron supplementation. The cause of anaemia should be assessed, at the latest after the end of pregnancy.*

Guideline 5
*Uterine massage after delivery of the child and before delivery of the placenta to prevent LTPPH is **not recommended**.*

Guideline 6
*If the child adapts well, umbilical cord ligation before 1 minute has elapsed is **not recommended**.*

Guideline 7
*Prophylactic administration of uterotonics in the third stage of labour immediately after delivery of the child and before umbilical cord ligation, is **recommended** in all vaginal births to decrease the risk of PPH and LTPPH. Oxytocin should be considered for first-line treatment.*

Guideline 8
*After delivery by caesarean section, it is **recommended** that uterotonics are administered to prevent LTPPH.*

Guideline 9
*Carbetocin administration is **suggested** in women with an increased risk of LTPPH.*

Guideline 10
*Carbetocin administration, including single administration of tranexamic acid (TXA), is **suggested** in women with an increased risk of LTPPH undergoing caesarean section.*

Organisation of care management

- Moderate blood loss: an obstetrician should be called in all cases
- Severe blood loss: an anaesthesiologist should also be called in all cases
- Life-threatening blood loss: a multidisciplinary crisis team should be activated in all cases

Guideline 11
*It is **recommended** that every healthcare institution with a Gynaecology and Obstetrics department has a controlled document of an institution-specific standard organisational crisis plan for LTPPH situations.*

Guideline 12
*It is **recommended** that the crisis plan clearly defines organisational and specialised roles of individual crisis team members if an LTPPH situation occurs (e.g. non-medical personnel, obstetricians, anaesthesiologists, haematologists, etc.) and that it also defines the minimum required equipment for sites where patients with LTPPH are managed.*

Guideline 13
*It is **recommended** that regular formalised training in LTPPH crisis situations is implemented for the entire crisis team, including subsequent formalised evaluation.*

Guideline 14
*It is **recommended** that a quality indicator is defined for LTPPH diagnosis and treatment, including formalised evaluation of this indicator.*

Roles and responsibilities for individual LTPPH crisis team members
The role of a midwife:

- Identify the development of haemorrhage and estimate the blood loss volume
- Inform the obstetrician
- Ensure vascular access using a peripheral venous catheter with the widest lumen possible
- Initiate infusion therapy using balanced crystalloid solutions
- Collect blood for laboratory assessments
- Ensure emptying of the urinary bladder by inserting an indwelling urinary catheter
- Initiate clinical and instrumental monitoring of physiological functions – consciousness, blood pressure, heart rate, respiratory rate, peripheral haemoglobin saturation with oxygen, diuresis and body temperature
- Record data defined by the crisis plan for LTPPH.

The role of an obstetrician:

- Identify the source of bleeding
- Assess vital physiological functions
- Prescribe monitoring of vital physiological functions
- Initiate oxygen therapy
- Check/ensure vascular access points
- Initiate fluid resuscitation
- Initiate administration of uterotonics
- Consider implementation of procedures to stop uterine bleeding (for example, uterine massage, bimanual uterine compression, external aortic compression).

The role of an anaesthesiologist:

- Assess vital physiological functions
- Check/ensure monitoring of vital physiological functions
- Initiate/continue oxygen therapy
- Check/ensure vascular access points

- Continue fluid resuscitation
- Initiate procedures to prevent hypothermia and acidemia
- Initiate/ensure procedures for pharmacological and/or instrumental support of organ functions
- Initiate coagulation support procedures and consult a haematologist as needed.

Diagnostic and therapeutic procedure in LTPPH
Early identification of developing LTPPH is the key factor for achieving the best possible clinical outcome. In cases where estimated blood loss is >1000 mL and/or signs of shock are identified, the multidisciplinary team must be activated.

Essential aims of diagnostic and therapeutic procedures for LTPPH are as follows:
- Early identification of haemorrhage and its cause
- Urgent initiation of procedures to remove the cause(s) of haemorrhage
- Early identification of tissue hypoperfusion and its early correction
- Early identification of coagulopathy and its treatment
- Organ function support/replacement
- Prevention of an LTPPH recurrence and potential complications related to the therapy of a coagulation disorder.

Uterine hypotony or atony
Uterine hypotony or atony is the most common cause of LTPPH.

Guideline 15
When uterine hypotony or atony is found, use of a structured stepwise procedure is ***recommended*** (**Table 2**).

Indications for hysterectomy:
- Continued uterine bleeding after all appropriate and available pharmacological and surgical interventions
- Invasive placenta
- Devastating uterine injury
- When the uterus is the expected source of sepsis.

[Table 2 near here]

Role of interventional radiology methods in LTPPH
Guideline 16
In all LTPPH conditions caused by uterine hypotony or atony, and where all standard surgical procedures at the site have failed (or cannot be used), use of an interventional radiology method (selective embolisation of pelvic arteries) is ***recommended*** *if available.*

Initial laboratory assessments and availability of transfusion products
Guideline 17
The following initial assessments are ***recommended*** *for cases of developing LTPPH: blood count, activated partial thromboplastin time (aPTT), prothrombin time (PT), fibrinogen level and pretransfusion testing (blood group, screening of irregular anti-erythrocyte antibodies and compatibility testing).*

Guideline 18
*In conditions of developing LTPPH, it is **recommended** to ensure availability of at least 4 units of fresh frozen plasma, 4 units of erythrocytes and 5 g of fibrinogen (either as fibrinogen concentrate or cryoprecipitate).*

Optimisation of tissue perfusion and systemic homeostasis
Guideline 19
*It is **recommended** that immediate fluid resuscitation is initiated in all patients with LTPPH, using balanced crystalloid solutions.*

Guideline 20
*It is **recommended** that synthetic colloids for fluid resuscitation of patients with LTPPH are only used in situations where crystalloid solutions are insufficient to achieve and/or maintain haemodynamic targets of fluid resuscitation.*

Guideline 21
*When synthetic colloids are used, use of balanced gelatin solutions is **recommended**.*

Guideline 22
*It is **recommended** that the target systolic blood pressure is maintained between 80–90 mmHg in patients with LTPPH, until the bleeding source is controlled.*

Guideline 23
*If the target systolic blood pressure values cannot be achieved, use of ephedrine, noradrenaline or phenylephrine is **recommended**.*

Diagnosis and therapy of coagulopathy in LTPPH
Guideline 24
*Cooperation with a haematologist, if available, is **recommended** for diagnosis and therapeutic management of coagulopathy in cases where LTPPH is not responding to standard therapeutic procedures.*

Guideline 25
*It is **recommended** to monitor coagulation and initiate measures for coagulation adjustment as soon as possible after LTPPH has been identified.*

Guideline 26
*In addition to the standard and repeated assessments (blood count, aPTT, PT, fibrinogen level), it is **recommended** that viscoelastometric methods (ROTEM, TEG) are also used, if available, to identify and monitor the type of coagulation disorder in LTPPH.*

Guideline 27
*In order to derive the most benefit from recovery of endogenous haemostatic mechanisms and therapeutic procedures for coagulation support, aiming for a maximum correction of hypothermia, acidosis and ionised calcium level is **recommended**.*

Guideline 28
*Early application of procedures to prevent hypothermia and maintain normothermia is **recommended**.*

Guideline 29
During administration of transfusion products (especially fresh frozen plasma), it is ***recommended*** *that ionised calcium levels are monitored and maintained in the normal range.*

Guideline 30
Fibrinogen replacement is ***recommended*** *in patients with LTPPH if their fibrinogen levels decrease below 2 g/L and/or if fibrinogen deficiency is found based on viscoelastometric methods, or if it is justified to assume fibrinogen deficiency without determining fibrinogen levels. A minimum initial dose of fibrinogen 4 g, or an equivalent of this dose when transfusion products enriched with fibrinogen are used, is* ***recommended****. It is also* ***recommended*** *that every obstetric site is equipped with an adequate stock of immediately available fibrinogen.*

Guideline 31
Administration of TXA is ***recommended*** *as soon as possible after the onset of LTPPH. If TXA is required, we* ***recommend*** *administering the initial dose of 1 g over 10 minutes and subsequent infusion of an additional 1 g over 8 hours. Alternatively, a dosing of 20–25 mg/kg can be used.*

Guideline 32
When bleeding has stopped, TXA administration is ***not recommended*** *in patients with LTPPH.*

Guideline 33
Administration of fresh frozen plasma is ***recommended*** *in cases of LTPPH where (a) laboratory signs of a coagulation disorder correctable by plasma administration are also present; (b) the type and/or cause of the coagulation disorder cannot be identified; (c) administration of a coagulation factor concentrate is not indicated.*

Guideline 34
Administration of prothrombin complex concentrates (PCCs) is ***recommended*** *in patients with LTPPH who are (a) treated with vitamin K antagonists or (b) in cases where a deficiency of factors provided by the PCC is expected. Routine administration of PCC in patients with LTPPH is* ***not recommended****.*

Guideline 35
The use of recombinant (r)FVIIa in patients with LTPPH is off-label. Administration of rFVIIa is ***recommended*** *in cases of LTPPH where properly implemented standard procedures fail, as a rescue procedure before indication for hysterectomy, provided that the conditions for optimal efficacy of the administered rFVIIa are achieved (fibrinogen level >1 g/L, haemoglobin concentration >60 g/L, thrombocytes >50 x* 10^9*/L, pH >7.2).*

Guideline 36
Administration of erythrocyte transfusion products is ***recommended*** *in patients with LTPPH to achieve target haemoglobin levels in the range 70–80 g/L. The target haemoglobin level should be individualised with respect to circulatory stability, medical history, comorbidities and estimated organ reserve.*

Guideline 37
*Administration of thrombocytes is **recommended** in patients with LTPPH to achieve a target platelet count of at least 50 x 10^9/L or in the case of their function disorder.*

Guideline 38
*Routine measurement of antithrombin levels is **not recommended** in patients with LTPPH.*

Guideline 39
*Routine antithrombin replacement is **not recommended** in patients with LTPPH.*

Guideline 40
*Initiation of pharmacological prophylaxis of thromboembolic disease is **recommended** at least 24 hours after achieving control of LTPPH. Mechanical thromboprophylaxis (intermittent pneumatic compression and/or elastic stockings) should be initiated immediately, as soon as allowed by the clinical condition.*

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Appendix A. Workgroup members, opponents and guidelines approval

The workgroup

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Guidelines approval

Czech Society of Anaesthesiology and Intensive Care Medicine (CSARIM) of the Czech Medical Association of J. E. Purkyně.
CSARIM, Obstetrical Anaesthesia and Analgesia Section.

The guidelines were approved at the CSARIM Committee meeting held on 6 December, 2017.

Czech Gynecological and Obstetrical Society (CGOS) of the Czech Medical Association of J. E. Purkyně.
CGOS, Analgesia and Intensive Care Medicine Section.

The guidelines were approved at the CGOS Committee meeting held on 5 December, 2017.

Table 1. Risk factors for postpartum hemorrhage in relation to the '4 Ts' (Tone, Tissue, Trauma and Thrombin)

	Aetiology	Risk factors
Uterine hypotony/atony – myometrial retraction disorders (Tone)	**Excessively enlarged uterus**	Polyhydramnios Multiple pregnancy Foetal macrosomia
	Myometrial 'exhaustion'	Precipitate delivery Protracted delivery Multiparity
	Intra-amnial infection	Fever Long-term amniotic fluid outflow
	Functional or anatomical uterine alterations	Uterus myomatosus Placenta praevia Uterine anomalies
Retained gestational sac residues (Tissue)	**Retained foetal membranes** **Placental abnormalities** **Retained cotyledon or accessory placenta**	Doubts about integrity of the placenta/membranes Previous uterine surgery Multiparity Placental abnormalities based on ultrasound examination
	Retained blood coagula	Uterine hypotony/atony
Obstetric injury (Trauma)	**Laceration of the uterine cervix, vagina, perineum**	Precipitate delivery Surgical delivery
	Rupture/laceration following hysterotomy in caesarean section	Foetal malpresentation Foetus deeply engaged in the pelvis
	Uterine rupture	Previous uterine surgery
	Uterine inversion	Multiparity Placenta adherens/accreta
Blood coagulation disorders (Thrombin)	**Congenital disorders:** • Haemophilia A • von Willebrand disease	History of congenital coagulation disorders Liver disease
	Acquired disorders: • Idiopathic thrombocytopenic purpura • Thrombocytopenia associated with pre-eclampsia **Disseminated intravascular coagulation:** • Preeclampsia • Dead foetus • Severe infection • Placental abruption • Amniotic fluid embolism	Formation of haematoma, petechiae Hypertension Intrauterine foetal death Fever, leukocytosis Antepartum haemorrhage Sudden collapse condition
	Therapeutic anticoagulation	history of thromboembolic disease

Table 2. Procedure for management of uterine hypotony or atony

Step I

a) Uterine massage
b) Uterotonics
   - oxytocin or carbetocin
   - methylergometrine (unless maternal hypertension is present)
c) Prostaglandins
d) Digital or instrumental revision of the uterine cavity

If these interventions fail, proceed to Step II

Step II

a) Removal of coagula
b) Uterotonics

Alternatively:
c) Bakri balloon catheter or vaginal tamponade as appropriate

If these interventions fail, proceed to Step III

Step III

a) Selective catheter embolisation of uterine artery (if interventional radiology is available)
b) Surgical intervention (gradual devascularisation of the uterus)
   - gradual ligation of uterine artery and ovarian artery
   - B-Lynch uterine suture
   - ligation of internal iliac artery

c) Administration of recombinant activated factor VII should be considered (if interventions (a) and (b) cannot be used, administration of this factor should be considered as the first procedure under step III; an analysis of the UniSeven national registry data found that administration of recombinant activated factor VII reduced the hysterectomy rate by 74% [Blatný *et al*. 2011])

If these interventions fail, proceed to Step IV

Step IV

Hysterectomy

Indications for hysterectomy
   - continued uterine bleeding all appropriate and available options (pharmacological and surgical) have been attempted
   - invasive placenta
   - devastating uterine injury
   - the uterus is the expected source of sepsis