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Second-line treatment of postpartum haemorrhage (PPH)

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Abstract

Introduction Postpartum haemorrhage (PPH) remains to be the most common cause of maternal mortality and is responsible for 25 % of the maternal deaths worldwide. Although the absolute risk of maternal death is much lower, a recent increase of PPH and related maternal adverse outcomes has been noted in high-income countries as well. Generally, PPH requires early recognition of its cause, immediate control of the bleeding source by medical, mechanical, invasive-non-surgical and surgical procedures, rapid stabilization of the mother's condition, and a multidisciplinary approach. Second-line treatment of PPH remains challenging, since there is a lack of univocal recommendations from current guidelines and sufficient data from randomized controlled trials.

Materials For this review, electronic searches were performed in PubMed, Embase, and the Cochrane Central Register of Controlled Trials using the keywords "postpartum haemorrhage" in combination with 'uterine tamponade' and, especially with 'arterial embolisation', 'uterine compression sutures', and 'post(peri)partum hysterectomy' (from January 2000 to November 2011).

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Reference lists of identified articles were searched and article references to the keywords selected.

Results Treatment options such as uterine compression sutures, embolisation, arterial ligation and hysterectomy were evaluated with regard to their prerequisites, benefits, drawbacks and respective success rate. In addition, a treatment algorithm for the second-line treatment of PPH is presented.

Keywords Postpartum haemorrhage · Treatment algorithm · Compression sutures · Embolisation · Arterial ligation · Hysterectomy

Introduction

Postpartum haemorrhage (PPH) remains to be the most common cause of maternal mortality and is responsible for 25 % of the maternal deaths worldwide [1]. The absolute risk of death is much lower in high-income countries with a rate of 1:100,000 deliveries as compared to low-income countries with an estimated rate of 1:1,000 [2]. Severe PPH is also the most common cause of serious maternal morbidity worldwide. Annually, approximately 20 million women worldwide suffer from acute or chronic disability following immediate PPH [3]. Severe maternal morbidity due to PPH has been estimated 4.5-6.7/1,000 deliveries [4]. Interestingly, recently published population-based studies of severe maternal morbidity demonstrate that the incidence of PPH and related maternal adverse outcomes have significantly increased during the past 5 years in some high-income countries [5, 6].

Primary PPH is 'traditionally' defined as any blood loss from the genital tract \geq 500 ml within 24 h after birth, while severe PPH is blood loss \geq 1,000 ml within 24 h [7];

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however, the definition of PPH is still a matter of debate [8], and there is currently no single, satisfactory definition of primary PPH [9]. The prevalence of PPH and severe PPH was estimated approximately 6 and 1.9 % of all deliveries, with a wide variation across regions of the world [10]. The majority of maternal deaths due to haemorrhage must be considered preventable, with 60–80 % of cases judged to have received 'major substandard care' [11, 12].

The major problems in risk management of PPH are

- 1. Delay in diagnosis and treatment failures resulting from underestimation of blood loss
- 2. Lack of easy-to use local protocols
- 3. Lack of adequate education and training
- 4. Poor communication and
- 5. Deficiencies in organization [8, 13].

PPH requires early recognition of its cause, immediate control of the bleeding source by multiple interventions (medical, mechanical, invasive-non-surgical and surgical procedures), rapid stabilization of the mother's condition, and, most importantly, a multidisciplinary approach.

Anticipation of risk factors and active management of the third stage of labor, including the prophylactic application of uterotonics, are considered to be among the keypoints in the prevention of PPH [11]. Further steps in the first-line treatment of PPH include the exclusion of retained placental tissue and of severe bleeding from vaginal or cervical lacerations, mechanical expression of the uterus or its bimanual compression, emptying the bladder, the continuous intravenous application of oxytocin (or sulprostone in case of oxytocin failure) and volume replacement. Tranexamic acid, calcium, fibrinogen concentrate and recombinant factor VII may be the medications of choice in cases of coagulopathy.

Second-line treatment of PPH remains challenging, since there is a lack of univocal recommendations from current guidelines, and sufficient data from randomized controlled trials related to second-line treatment of PPH are not available.

Materials and methods

Electronic searches were performed in PubMed, Embase, and the Cochrane Central Register of Controlled Trials using the keywords "postpartum haemorrhage" in combination with 'uterine tamponade' and, especially with 'arterial embolisation', 'uterine compression sutures', and 'post(peri)partum hysterectomy' (from January 2000 to November 2011). Reference lists of articles identified by this strategy were also searched and article references to the keywords were selected. In addition, relevant chapters of textbooks and current guidelines were examined to capture any further information or additional reports not identified in the electronic search.

Results

Uterine tamponade: intermediate step between firstand second-line treatments of PPH

Uterine tamponade can be attempted to apply pressure to the placental site; this may be an effective 'first-line surgical' treatment of PPH for most women after vaginal delivery where uterine atony is the only or main cause of haemorrhage unresponsive to the medical interventions [11]. Bleeding from vaginal and cervical lacerations and retained placental tissue should be excluded before using uterine tamponade.

In recent years, tamponade using various types of hydrostatic balloon catheters (e.g. Bakri balloon, Senkstaken-Blakemore tube, Rush catheter) has superseded uterine packing for control of atonic PPH [11], however, there have been no randomized controlled trials on their use in the treatment of PPH [7]. The resulting tamponade effect when distending a balloon in the uterine cavity may actively be caused by a number of mechanisms, including uterine shape changes, secondary uterine activity, balloonendometrial interactions and distal effects on the flow within the uterine arteries [14, 15]. Balloon tamponade can be a life-saving intervention, especially in low resource settings where blood transfusion and surgical facilities may not be available [16]. The method has the advantages that (1) insertion is easy and rapid with minimal anaesthesia; (2) it can be performed by relatively inexperienced personnel; (3) removal is painless, and (4) failed cases can be identified rapidly. No immediate problems or long-term complications have been reported [17, 18], however, concerns remain, if the procedure is associated with an increased risk of infection [7]. The administration of broad spectrum antibiotic prophylaxis has been suggested as long as the balloon is in place [16].

Case series have reported success rates (i.e. no need for hysterectomy or other invasive procedures) ranging from 71 to 100 % [7]. According to a recent systematic review, the average success rate of uterine balloon tamponade was 84.0 % (95 % CI 77.5–88.8, 17). Ultrasound, if available, is useful to confirm correct placement in the uterine cavity and to evaluate for significant residual placental tissue [18]. Use of balloon tamponade has been described as a prognostic test in PPH [19]. The 'tamponade test' has shown to be positive (bleeding ceases) in 87–91 % of cases [18, 19] and allows the obstetrician to rapidly identify women requiring laparotomy or arterial embolisation (negative 'tamponade test', 19) if bleeding continues.

There is no clear evidence how long the balloon tamponade should be left in place (commonly up to 24 h). In most cases, 4–6 h of tamponade may be appropriate to achieve haemostasis [11]. Balloon tamponade is also used as a temporizing procedure to stabilize the mother's condition while preparing her for laparotomy or arterial embolisation, or while the patient is being transferred to a tertiary care centre with greater facilities [16].

After adequate placement of the balloon catheter, the following situations may occur: (1) the bleeding stops or is significantly reduced, then continue high-dose oxytocin or sulprostone infusion to maintain uterine tone. Before its complete removal the balloon can be gradually deflated as the bleeding subsides but left in place to ensure the bleeding does not reoccur [11, 20]; (2) the bleeding continues but is not excessive, and the mother is haemodynamically stable, then consider arterial embolisation, if available; (3) balloon tamponade fails ('negative tamponade test'), excessive bleeding continues and the mother's condition threatens to become unstable, then immediate laparotomy for controlling of haemorrhage is required.

To stabilize the mother's condition by prompt resuscitation and restoration of the circulating blood volume and timely administration of tranexamic acid and coagulation factors (fibrinogen, fresh frozen plasma) is mandatory [21, 22] before transferring her to either the operating theatre or the interventional radiology unit.

Recommendations from current guidelines

The recent RCOG guideline [11] recommended that obstetricians must consider all available interventions to stop haemorrhage including haemostasis brace suturing, bilateral ligation of uterine arteries or internal iliac arteries, selective arterial embolisation, and finally hysterectomy, especially in cases of placenta accreta or uterine rupture (Grade C).

According to the RCOG guideline, each obstetric unit should have the capacity to provide at least one brace technique and a laminated diagram of the brace technique should be kept in theatre.

The American College of Obstetricians and Gynecologists (ACOG) suggests that the failure of uterotonic agents with or without tamponade measures following vaginal delivery requires exploratory laparotomy. Surgical techniques recommended to control uterine bleeding are bilateral uterine ligation or stepwise uterine devascularization, the B-Lynch technique for stopping excessive bleeding caused by uterine atony and haemostatic multiple square suturing for PPH caused by uterine atony, placenta praevia, or placenta accreta. Candidates for arterial embolisation may be the patients with stabile vital signs and persistent bleeding, if the rate of loss is not excessive [9].

The recently published Canadian Guideline (SGOC) recommended surgical techniques such as ligation of the internal iliac arteries, compression sutures and hysterectomy for the management of intractable PPH unresponsive to medical therapy (EL III-B) [20]. Arterial embolisation should be considered when there is active bleeding in a haemodynamically stable woman and before surgical intervention.

The WHO Guideline [7] concluded that uterine artery embolisation; if available, may be offered as a second-line treatment of PPH due to uterine atony pointing out that the quantity of evidence is very low and the strength of recommendation is weak. Considering surgical interventions, compression sutures may be attempted first and, if that intervention fails, uterine, utero-ovarian and hypogastric vessel ligation may be tried. If life-threatening bleeding continues even after ligation, subtotal or total hysterectomy should be performed (Quality of evidence: no formed scientific evidence of benefit or harm, strength of recommendation: strong).

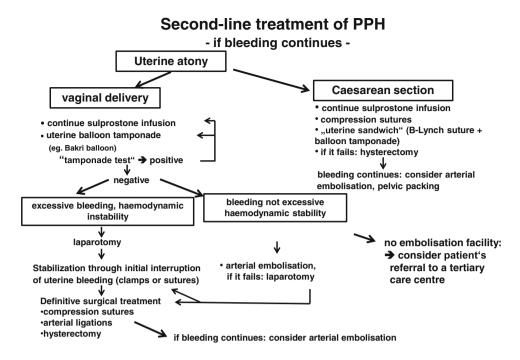
French authorities [12, 23] recommended arterial embolisation in patients with persistent PPH refractory to sulprostone treatment after vaginal delivery. If there is no embolisation facility, or haemodynamic instability occurs or embolisation fails, surgical intervention is required. If delivery was by caesarean section, the most appropriate first-line surgery is vessel ligation; if this fails, or occasionally immediately, hysterectomy should be performed (EL IV).

Finally, the German Guideline [24] recommended surgical measures preserving the woman's fertility, if medical treatment of PPH (including "tamponade test") fails. Hysterectomy is required in patients unresponsive to conservative surgical interventions or arterial embolisation. Figure 1 shows a flow chart of the different steps for the second-line treatment of PPH.

Selective arterial embolisation

According to a recent national cohort study, one woman in every 4,300 giving birth in the UK is managed with surgical or radiological therapies for PPH [25].

Selective arterial embolisation has become a mainstay second-line intervention for uncontrolled PPH that is strongly recommended by various authorities worldwide, but should only be applied when the patient is haemodynamically stable and the embolisation unit is located close to the delivery ward [26]. There is currently no clear consensus as to which point it should be considered in the management algorithm [27]. The choice of selective embolisation of the internal iliac arteries or subselective Fig. 1 Treatment algorithm if bleeding continues due to uterine atony after delivery (after exclusion of placental remnants)



embolisation of the uterine arteries is a consideration usually determined at the time of the procedure [26].

Since the first report of transcatheter arterial embolisation for intractable PPH in 1979 [28], more than 40 case series and case reports have been published [7, 26, 29], however, no randomized controlled trial evaluating embolisation for PPH exists likely due to the emergent, multifactorial nature surrounding the intervention and the difficulty performing randomization because of ethical considerations [26]. The techniques and strategies of selective arterial embolisation have been described recently [26, 29–31].

In a recent nationwide cohort study from the Netherlands [32], the incidence of arterial embolisation for obstetric haemorrhage was estimated 3.2/10.000 deliveries with a case fatality rate of 2 %; however, great differences exist in the use of arterial embolisation among European countries. As recently highlighted by Kayem et al. [25], embolisation is used significantly more frequently in the Netherlands than in the UK (p < 0.05). Conversely, the use of uterine compression sutures is more frequent in the UK. If angiographic embolisation is not available in a hospital, then elective referral of patients at increased risk of PPH to a centre where it is available should be considered [27].

A recently published study from France has shown that hospital-to-hospital transfer was not associated with an increased risk of embolisation failures [33]. However, it should be emphasized that patient's transfer can only be justified, if the woman is haemodynamically stable and haemorrhage is not excessive.

Taking into consideration the dramatically rising incidence of placental implantation abnormalities [34] due to rising caesarean section rates, screening for abnormal placentation with ultrasound or magnetic resonance imaging (MRI) has been suggested for all women with a previous history of caesarean section [11], particularly those with a diagnosed placenta praevia [34]. Any degree of abnormal placentation carries with it the potential for massive haemorrhage when attempts are made to deliver the placenta in the usual fashion [35]. If placenta accreta or percreta is diagnosed antenatally, there should be consultant-led multidisciplinary planning for delivery [11, 26, 29].

The preventive role of interventional radiology procedures in cases of known placenta accreta or other abnormal placentation has been discussed controversially in the current literature [26, 27, 34, 36–38]. Temporary balloon occlusion with or without embolisation in the setting of placentation abnormalities has shown to reduce further blood loss and to avoid further surgery when appropriate [39–41], however, opposite results have been published [42–44]. In addition, there are reports of thromboembolic events after balloon occlusion [45, 46]. Further research is still needed to examine more closely the best management approaches in these challenging clinical situations [29].

The majority of PPH is unpredictable and is typically secondary to uterine atony (emergency intervention, 37). Table 1 shows the main indications of arterial embolisation. Selective arterial embolisation is a reasonable option in patients with uterine atony resistant to conservative treatment after vaginal delivery [23, 30, 33, 37, 47] (Table 2).

As recently highlighted by Jacobs [48], the need for laparotomy is rare, as the combination of balloon tamponade and uterine artery embolisation controls bleeding in virtually all cases of uterine atony at vaginal delivery,

Table 1 Main indications for selective arterial embolisation

| 1. | Elective and prophylactic intervention: | | | |
|----|--|--|--|--|
| | Occlusive balloon catheter \pm embolisation | | | |
| | \rightarrow antenatally diagnosed abnormalities of placental implantation | | | |
| 2. | Emergency intervention: | | | |
| | Uterine atony after vaginal delivery resistent to conservative treatment | | | |
| | Genital tract injuries | | | |
| | Placental implantation abnormalities (e.g. placenta previa, accreta) retained placental tissue | | | |

Failure of conservative surgical procedures or persistent bleeding after hysterectomy

Others: e.g. pseudoaneurysma

Table 2 Prerequisites for selective arterial embolisation

| Logistics | | | | |
|--|--|--|--|--|
| Interventional radiology unit | | | | |
| Specialized equipment | | | | |
| Experienced trained radiologist | | | | |
| Availibility of a 24-h service | | | | |
| Rapid and safe transfer of the patient from the delivery ward to the radiology unit | | | | |
| Constant monitoring of the patient (anaesthetist, obstetrician) | | | | |
| Clinical | | | | |
| No severe (life-threatening) bleeding | | | | |
| Haemodynamic stability of the mother | | | | |
| If possible, no coagulopathy present (coagulopathy does not contraindicate embolisation, 23) | | | | |
| | | | | |

however, arterial embolisation should be considered early in the treatment plan to avoid the morbidity from multiple transfusions and surgical procedures, which are often the cause of ongoing haemorrhage [28, 47, 49].

If uterine tamponade fails and the bleeding is not excessive, arterial embolisation is recommended before laparotomy in the haemodynamically stable patient [30, 37, 50]. For persistent uterine atony, the success rate of emergency arterial embolisation varies from 70 to 100 % [37, 51].

Genital tract injury may be a valuable indication of arterial embolisation, especially in cases, where the bleeding site is difficult to expose and access or has already been sutured (e.g. upper vaginal lacerations, large midline paravaginal haematomas, or cervical tears after vaginal delivery) [21, 30, 48].

If the exact bleeding site cannot be identified, a subselective embolisation of the uterine or vaginal arteries should be performed because each of these has been separately reported as the most common source of haemorrhage [37].

Severe PPH related to abnormal placentation remains challenging. In the management of placenta accreta, uterine

artery ligation or ligation of the internal iliac arteries may often be insufficient to block uteroplacental circulation because low intervillous resistance helps maintain persistent uteroplacental blood flow via physiological anastomoses and neoarteries. Selective and repeated embolisation is probably more effective in reducing uteroplacental blood flow to further induce thrombosis of the intervillous space and to achieve necrosis of retained placental tissue [52]. Moreover, angiography allows objective evaluation of the degree of devascularisation of retained placental tissue [52].

Several authors have reported successful embolisation after ligation of the internal iliac arteries and uterine arteries, and after hysterectomy (review by 30). A recent case-series could demonstrate that the failure of ligation is due to newly developed collateral pathways in most cases, or, less frequently, to incomplete ligation [52].

The use of particles allows rapid and more distal vessel occlusion, thereby decreasing collateral inflow to the uterus and pelvis and thus providing more effective haemostasis. Sources of bleeding other than the internal iliac arteries may be identified and embolised [27]. However, after failed internal iliac artery ligation, embolisation of the anastomotic routes that contribute to the bleeding may result in ischaemic complications [52].

The prerequisites for arterial embolisation are shown in Tab. 2. There are no specific contraindications to arterial embolisation; however, uterine rupture and erosion should be treated surgically [30]. Transfer duration from the delivery ward to the radiology unit plus speed and capacity of the intervening radiologist plus the time needed for the procedure should be taken into account before attempting embolisation [53].

Resuscitation equipment and constant monitoring of the patient both by an anaesthetist and an obstetrician should be available in the angiography unit [23]. It is important to note that the embolisation should not be performed if haemorrhage is excessive and/or if the mother is haemo-dynamically unstable.

If the patient's haemodynamic status becomes unstable, arterial embolisation—even if initially indicated—should not be performed, because facilities equipment to handle major bleeding are mostly much better in the operating room [53]. If coagulopathy is present, it should be corrected before the procedure, although many radiologists will go ahead while the coagulopathy is being treated, since the haemorrhage is generally the cause of the coagulopathy [48].

According to the French guideline [23] coagulopathy does not contraindicate arterial embolisation. Case series reported on success rates ranging from 78 to 100 % [7]. In a recent retrospective cohort study including 100 patients with PPH [33] failed arterial embolisation was significantly associated with a higher rate of estimated blood loss of more than 1,500 ml and more than 5 red blood cell units transfused reflecting severe coagulopathy. Placenta accreta was not significantly associated with failed arterial embolisation, which is in accordance with a further recent study by Park et al. [54]. Others reported that the success rate in patients with placenta accreta are lower (60–83 %) compared to the overall success rate of the procedure [31, 55]. Unfavorable artery anatomy or the inability to catheterize the uterine arteries due to vascular spasm may be the contributing factors to a failure of arterial embolisation [26, 54].

The advantages of arterial embolisation are the minimal invasive technique associated with a lower complication rate, particularly organ injuries, compared to laparotomy, a shorter hospital stay and that embolisation can be carried out under local anaesthesia [2]. The greatest advantage of arterial embolisation for PPH is the ability to preserve the uterus and woman's future fertility. Numerous follow-up studies have addressed obstetric prognosis and pregnancy outcomes following arterial embolisation for PPH [56–61]. These studies could clearly demonstrate that the arterial embolisation for PPH does not impair menstrual function and subsequent pregnancy outcomes, however, recurrence of severe PPH due to abnormal placentation is increased [56, 59]. Embolisation should be performed as selectively as possible to minimize ischaemia and other complications.

Procedure-related morbidity is in the range from 3 to 9 % [30, 36]. Postembolisation fever and pelvic pain are the most common complications which typically resolve within 2–3 days. Major complications such as buttock ischaemia, small bowel necrosis, and uterine, vaginal, cervical and bladder necrosis are considered to occur rarely as well as neurological complications (e.g. temporary neuropathy of the sciatic nerve) [62, 63].

The dose of radiation associated with arterial embolisation is unlikely to result in a measurable increase in the genetic risk to the patient's future children [64].

Surgical procedures

If embolisation is unsuccessful, surgical interventions can be attempted subsequently and have shown to be effective [33]. The need for laparotomy after second-line treatment of PPH at vaginal delivery is rare. The main reasons for surgical interventions are major haemorrhage requiring immediate control of the bleeding, haemodynamic instability, or if abdominal bleeding is suspected, especially in women who had an operative vaginal delivery associated with upper vaginal laceration or are otherwise at risk of uterine rupture, and a lack of an embolisation facility [48].

The choice and sequence of surgical measures should be based on the causes of PPH and the surgeon's experience and skills. A review of the management of PPH found no statistical difference among the outcomes of the various available surgical methods [17].

Uterine sutures

Uterine compression suturing (UCS) was recommended as the first-line measure preventing hysterectomy in patients with uterine atony who respond to bimanual compression [48, 65, 66]. Despite the lack of comparative studies, the available observational data suggest that UCS may be more effective, are easier to perform thus requiring less skill and are associated with fewer complications in comparison with IAA ligation [66–70]. The main aim of UCS is to control bleeding from the placental site, by opposing the anterior and posterior uterine walls together [71]. UCS has also been used in different modifications for controlling massive PPH due to placenta praevia or accreta at caesarean delivery [72–79].

In a recent prospective population-based study, the estimated rate of use of UCS was 18 cases per 100.000 deliveries (95 % CI; 15–20 per 100.000); UCS was mostly attempted in women delivering by caesarean section and in only 8.5 % of patients delivering vaginally [70].

The first description of a UCS was published in 1996 by Schnarwyler et al. [80]; 1 year later, the B-Lynch suture was first reported [81] and has gained the most popularity, with a number of subsequent publications attesting its efficacy (reviews by [71, 82–84]). More than 1,800 cases have been reported so far [83]. The striking feature of the B-Lynch suture is that it envelops and compresses the uterus, similar to the result achieved with manual compression [81]; it does not sew the anterior and the posterior uterus wall together, which distinguishes it from other UCS.

The B-Lynch suture involves lower uterine incision to check for emptiness of the uterine cavity and is therefore particularly suitable when the uterus has already been opened at caesarean delivery.

Concerns have been raised on the potential risk of occlusion of the uterine cavity and blood entrapment, as the uterus has to be transfixed from front to back to place the sutures [85]. Another potential problem with the B-Lynch suture is that the sutures can slip off the fundus and the lateral upper margins [75].

In a few of the procedures, hysterectomy was not averted because the sutures slid off the uterus fundus or uterine occlusion occurred after the knots were tied too tight. The tension is probably critical to success. Too tight sutures may compromise the blood supply to the uterus thus increasing the risk of uterine ischaemia and necrosis [86]. Numerous modifications of the original B-Lynch suture have been published in order to improve the technique [74, 75, 87–90]. Details of these modifications have been reviewed recently [82, 83]. The Hayman modification offers the potential advantage that it can be applied faster and easier, avoiding opening of the uterine cavity when PPH follows vaginal delivery. The technique has shown to effectively and rapidly control massive bleeding in women with placenta praevia or accreta [74]; however, it should be ensured that the uterine cavity is empty and the cervical canal remains patent.

A further modification of the B-Lynch suture described by Marasinghe and Condous [69] comprises of vertical compression sutures and is distinct from B-Lynch and Hayman's sutures by having an additional firm puncture just below the uterine fundus thus eliminating the risk of the sutures sliding off at the fundus uteri.

In order to avoid the potential risk of occlusion of the uterine cavity and blood entrapment, Zheng et al. [85] described a modification of B-Lynch sutures without entering the uterine cavity and without suturing the anterior and posterior walls of the uterus together.

The technique by Pereira et al. [90, 91] is an efficient, but more complex and time-consuming five-step procedure, in which a series of longitudinal and transverse sutures are placed around the uterus without penetrating the endometrial cavity thus decreasing the risk of infection.

Finally, the Cho multiple square sutures [87], opposing the anterior and posterior uterus walls until no space is left in the uterine cavity, is an efficient procedure, especially in case of PPH due to placenta praevia or accreta. However, the drawback of this technique is the possibility of pyometra and Asherman's syndrome [92, 93]. Success rates of UCS (i.e. no need for hysterectomy or other invasive procedure) range from 82 to 100 % [7, 94, 95].

A recent systematic review [17] reported on a success rate of 91.7 % (95 % CI 84.9–95.5 %) for various UCS, however, no prospective randomized studies that compare the efficacy and short and long term morbidity of the different types of UCS exist. In a recently published prospective population-based study, the overall risk of failure, leading to hysterectomy, was 25 % (95 % CI 19–31 %) and there were no significant differences in failure rates among B-Lynch sutures, modified B-Lynch-sutures, and other suture techniques. A prolonged delay of 2–6 h between delivery and UCS was independently associated with a fourfold increase in the odds of hysterectomy [70].

Short term and long term complications (from directly postoperatively up to 2 years) that have hitherto been reported are pyometra and uterine inflammation, ischaemic uterine necrosis, uterine suture erosion and uterine synechiae [reviews by 82, 83, 96].

Recent reports on synechiae after UCS warned of the mid- and long-term outcomes on the uterine cavity and fertility which might be underestimated [93, 97]. Since

there is a lack of sufficient data regarding the impact of UCS on future fertility and pregnancy outcomes [82, 83], long-term studies are urgently needed.

Routine follow-up, both by hysteroscopy and an imaging technique, has been recommended [96, 98]. A review of reported cases of uterine evaluation after placement of UCS has recently been published [96].

The "uterine sandwich" technique combining the B-Lynch suture with the placement of an intrauterine balloon catheter was successfully employed past caesarean delivery in patients with persistent bleeding from uterine atony refractory to both medical therapy and a B-Lynch suture and in cases of massive haemorrhage due to placenta accreta [99–101]. A recently published prospective observational study including 11 patients who had had unsuccessful medical therapy for PPH has shown that the 'uterine sandwich' technique was successful in avoiding hysterectomy in all cases, and there was no documented postpartum morbidity [102].

Combinations of UCS with additional invasive haemostatic procedures have recently been reviewed [82]. When UCS is combined with additional pelvic vessel ligation, there appears to be an increased risk of uterine ischaemic necrosis and inflammation [82].

Conservative measure to spare the uterus are reasonable as long as the woman remains haemodynamically stable and is not experiencing life-threatening haemorrhage complicated with severe coagulopathy.

Arterial ligation

Among conservative (uterus preserving) options, arterial ligation is one of the most frequently used worldwide. Bilateral uterine artery ligation as first described by O'Leary [103, 104] consists of a mass ligation of the uterine vessels (including arteries and veins) and the myometrium at the level of the lower uterine segment. Occlusion of the uterine artery reduces 90 % of the blood flow. Uterine artery ligation has become a first-line procedure for controlling uterine bleeding at laparotomy, since the technique is easy to perform, associated with minor morbidity and has shown to be successful (not requiring hysterectomy) in 80–96 % of cases [105, 106].

O'Leary sutures have mostly been used in patients with uterine atony and abnormal placentation, but in uterine trauma, when the avulsed uterine artery retracts into the broad ligament forming a haematoma it is difficult to perform uterine artery ligation and salvage the uterus [48].

Incomplete ligation is the most common cause of persistent bleeding and failure of the method [33, 52]. Fears regarding uterine compromise with subsequent pregnancies have been dispelled as a number of women have become pregnant after undergoing uterine ligation [107]. If bleeding persists after uterine artery ligation, the surgeon has to decide, if proceeding to stepwise uterine devascularization as first described by AbdRabbo [108] may be a valuable option. Stepwise uterine devascularization is a more complex and time-consuming five-step procedure including ligation of the tubo-ovarian and the ascendant and descendant uterine arteries. The reported success rate ranges from 84 to 100 % [17, 72, 108, 109]. Uterine necrosis and placental insufficiency in a subsequent pregnancy have not been described as complications of stepwise uterine devascularization [108, 110]. However, a single case of ovarian failure and development of intrauterine synechiae has been reported [111].

Systematic pelvic devascularization including additional ligation of the internal iliac arteries may be a further step for controlling haemorrhage due to PPH [18, 71]; however, in patients with an excessive bleeding, it is the surgeon's decision to better proceed to hysterectomy. Internal iliac artery ligation (IIAL) has been advocated as an effective measure of controlling intractable PPH and preventing maternal death [67].

The rationale for this is based on the haemodynamic studies of Burchell [112] which showed that IIAL reduces pelvic blood flow by 49 % and pulse pressure by 85 %, resulting in venous pressures in the arterial circuit thus promoting haemostasis; however, IIAL does not result in complete blockage of blood supply to the female pelvic organs but contributes to a significant decrease [72]. The technique has been used in patients with uterine atony and abnormal placentation [113], however, failures were more evident in atonic PPH than in other causes of PPH [67].

Ligation was successful in preventing hysterectomy in up to 50 % of these patients [114–118]. In selected cases, IIAL has been combined with other procedures including uterine brace sutures [119] or ovarian artery ligation [120]. IIAL has shown to be also an effective surgical method in patients with uterine lacerations at the time of caesarean delivery [114, 115, 117]. Overall success rates reported varies from 42 to 93 % [17, 52, 72].

A single-institution series of 117 patients who underwent IIAL for intractable pelvic haemorrhage over a 15-year period noted a 100 % success rate in controlling haemorrhage in obstetric cases, although uterine preservation was possible in only 11 % (13 cases, 83).

In a case-series including 88 patients with a therapeutic IIAL mainly due to uterine atony, genital tract injury and placenta praevia IIAL failed to arrest haemorrhage in nearly 40 % of cases requiring subsequent hysterectomy [67].

Joshi et al. [67] pointed out that IIAL not only contributes to the prevention of hysterectomy but also in cases where hysterectomy cannot be prevented, it facilitates hysterectomy as in case of uterine trauma; they believe that the life-saving technique of IIAL is underutilized in the management of PPH, probably due to fear of injury to iliac veins or to other neighbouring structures. IIAL may be ineffective, if ligation is incomplete or failed due to newly developed arterial anastomoses and collateral pathways, which contribute to uterine blood flow [52, 65].

Possible complications after IIAL include direct injury of the iliac vessels and the surrounding anatomic groups [113], however, in a large case-series with massive pelvic haemorrhage, only one of 117 patients had injury to the internal iliac vein [117]. As shown by numerous case reports and small case series, IIAL has no adverse effect on subsequent fertility or pregnancy outcome [113].

Nevertheless, IIAL is more difficult to perform and not more effective compared to other conservative operative procedures for controlling PPH, requires advanced surgical skill and carries an increased risk of venous, ureteral and nervous damage. For these reasons, uterine artery ligation and uterine brace techniques have largely replaced this procedure [48].

Peripartum hysterectomy

One of the most difficult decisions in obstetrics, which should be made by an experienced obstetrician in close cooperation with an experienced anaesthetist, is to determine if and when conservative fertility preserving approaches make no longer sense and immediate peripartum hysterectomy (pH) is required to save live [11, 71].

In clinical practice, this decision is frequently made too late. The 'vitious cycle' deriving from uncontrollable severe haemorrhage associated with haemodynamic instability and followed by significant coagulopathy may result in further massive blood loss thus worsening the mother's condition.

This vitious cycle should be interrupted at the earliest possible stage or it should better be primarily avoided. The cutoff point at which hysterectomy is considered a life-saving intervention is subjective [121]. There is a lack of standard guidelines for the use of conservative methods before proceeding to emergency pH [121].

The incidence of emergency pH widely ranges from 0.2 to 5 per 1,000 births [107, 121–123]. In a recent populationbased, matched case–control study from UK the incidence of pH was 4.1 cases per 10.000 births (95 % CI 3.6–4.5, 125). pH is strongly associated with previous caesarean delivery, and the risk rises with increasing number of previous caesarean deliveries, maternal age over 35 and parity >3 [124]. The risk for emergency pH increases 9.5 to 20-fold among women delivered by caesarean section as compared with women delivered vaginally [107, 121, 123].

A recent retrospective cohort study [125] has shown that the indications for pH have changed significantly during the 2 past decades with uterine rupture as the indication for pH decreasing from 40.5 to 9.3 % (p < 0.0001) and placenta accreta as the indication increasing significantly from 5.4 to 46.5 % (p < 0.00001). The association between previous caesarean delivery and abnormal placentation in subsequent pregnancies has clearly been demonstrated [121, 123].

In a recent systematic review [121] the main indications leading to pH were abnormal placentation (38 %), uterine atony (29 %), and uterine rupture (12 %). Candidates for pH are (1) patients with abnormalities of placental implantation, (2) uterine damage or rupture, (3) patients with a septic uterus, frequently occurring after chorioamnionitis, (4) if bleeding continues after all other interventions have failed. Hysterectomy should also be considered in case of a life-threatening PPH, if the obstetrician has no or little experience with haemostatic brace techniques, and if arterial embolisation is not available [11]. However, the training skills of a senior obstetrician should include haemostatic brace techniques, which are usually easier to perform than peripartum hysterectomy.

In women without wish of further childbearing, the decision in favour of hysterectomy is easier to make. Multiparous women may benefit from earlier hysterectomy to avoid severe morbidity [121]. Ideally, a subtotal hysterectomy should be performed, since it is simpler, faster and easier to perform than total hysterectomy except for situations as placenta praevia accreta, complex lower segment rupture or severe concomitant cervical laceration [18, 23, 71].

A further advantage of subtotal hysterectomy over total hysterectomy may be a decreased risk of visceral injuries

| Table 3 Benefits and drawbacks of second-line | Prerequisites | Benefits | Drawbacks | Success rates | |
|---|--|---|---|--|--|
| treatment options | Arterial embolisation | | | | |
| | Sufficient radiology unit with facility for arterial | No intraabdominal surgery | Non-surgical and undefined trauma to uterine tissue | 70–100 % [7, 37, 51] | |
| | embolisation Necessity for early | Treatment option under local anesthesia | Time loss for patient | 60–83 % in placenta accreta [31, 55] | |
| | referral (stable patient) | Short hospital stay | Referral and preparation of radiological intervention | | |
| | | | High cost and facility requirements | | |
| | | | Irridation to patient | | |
| | | | Gynecologist or obstetrician do not cope with complication | | |
| | | | Ischaemic complications possible, especially when performed unselectively | | |
| | Uterine compression sutures | | | | |
| | Laparotomy | Easy to perform | Laparotomy required | 82–100 % [7, 94, 95] | |
| | | Small trauma | Possible impairment of uterine | | |
| | | Excellent results for patient and subsequent pregnancies | cavity integrity | | |
| | Arterial ligation | | | | |
| | Laparotomy | Established method | Difficult to perform | Bilateral uterine ligation: | |
| | Advanced and | Uterus saving method | High complication rate | | |
| | experienced surgeon | | Possible impairment on | 80–96 % [105, 106] | |
| | | | subsequent pregnancy | Internal iliac artery: 42–93 % [17, 52, 72] | |
| | Emergent hysterectomy | | | , 1 | |
| | Laparotomy | Ultima ratio | Difficult to perform as total | 94–99 % [<mark>32</mark> , | |
| | Advanced and experienced surgeon | | Psychological impact on patient | 107, 126, 129] | |
| | | | Definitive end of family planning | | |
| | | | High need for secondary surgery | | |

and blood loss, shorter operating time and hospital stay, however, five studies found no significant differences in complications, operating time, blood loss, or transfusion requirements between both procedures [121, 123, 126– 128]. It is often difficult to identify the level of the cervix, particularly in cases where caesarean hysterectomy is performed at full cervical dilatation [121, 123].

In a recently published systematic review [121] including 981 cases of emergency pH the maternal mortality rate was 2.6 %, which corresponds to the mortality rates reported from the literature ranging from 1 to 6 % [32, 107, 126, 129]. The maternal morbidity rate was 56.0 %, and 44 % of women required blood transfusion [121].

Additional surgery was required in 10.5 % of cases, which is comparable with the 11 % by Smith and Mousa [123], the 8 % by Baskett [130] and the 13 % by Lau et al. [131] but lower than the 33–36 % reported by others [122, 132]. The management of these cases represents a challenge for any obstetrician, and the intervention which may be appropriate to arrest haemorrhage depends on the availability of methods (e.g. arterial embolisation) and the surgeon's experience and skill (e.g. artery ligation, pelvic packing).

Subtotal or total hysterectomy should be performed sooner rather than later [11], in any case before the catastrophe deriving from massive blood loss, haemodynamic instability and significant coagulopathy is inevitable. Table 3 shows a summary of benefits and drawbacks of the respective secondary treatment options.

Conflict of interest None.

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