Review

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# Placenta Accreta Spectrum Part I: anesthesia considerations based on an extended review of the literature

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**Abstract:** "Placenta Accreta Spectrum" (PAS) describes abnormal placental adherence to the uterine wall without spontaneous separation at delivery. Though relatively rare, PAS presents a particular challenge to anesthesiologists, as it is associated with massive peripartum hemorrhage and high maternal morbidity and mortality. Standardized evidence-based PAS management strategies are currently evolving and emphasize: "PAS centers of excellence", multidisciplinary teams, novel diagnostics/pharmaceuticals (especially regarding hemostasis, hemostatic agents, point-of-care diagnostics), and novel operative/interventional approaches (expectant management, balloon occlusion, embolization). Though available data are heterogeneous, these developments affect anesthetic management and must be considered in planed anesthetic approaches. This two-part review provides a critical overview of the current evidence and offers structured evidence-based recommendations to help anesthesiologists improve outcomes for women with PAS. This first part discusses PAS management in centers of excellence, multidisciplinary care team, anesthetic approach and monitoring, surgical approaches, patient safety checklists, temperature management, interventional radiology, postoperative care and pain therapy. The diagnosis and treatment of hemostatic disturbances and preoperative prepartum anemia, blood loss, transfusion management and postpartum venous thromboembolism will be addressed in the second part of this series.

**Keywords:** abnormally invasive placenta; anesthesia; anesthetic management; interventional radiology; placenta accreta spectrum; placenta percreta.

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## Introduction

"Placenta Accreta Spectrum" (PAS), or "Abnormally Invasive Placenta" (AIP), are umbrella terms that describe the abnormal adherence of the placenta to the uterine wall without spontaneous separation at delivery [1]. PAS encompasses a range of invasively growing placental villi—including, placenta accreta, increta, and percreta. In placenta percreta, the most severe form of PAS, the placental villi penetrate through the decidua, myometrium, and uterine serosa (often into the bladder and pelvis), which makes it difficult to surgically remove the placenta without causing a massive peripartum hemorrhage (PPH) [1–3]. Because pregnancy following caesarean section (C-section) is one of the leading causes of PAS, it is anticipated that PAS rates, estimated between

0.8 and 3.1 per 1,000 births after previous cesarean section, will continue to increase in the coming years as rates of C-sections continue to rise worldwide [1, 4, 5].

Most PAS diagnoses occur well before childbirth (and C-section), so an individually tailored PAS treatment regime in a center of excellence using a multidisciplinary care team approach is feasible and recommended [6–14]. Although those trials propose the superiority of a treatment in centers of excellence, a universally accepted definition of exactly what a "center of excellence" is mostly missing. The International Society for Placenta Accreta Spectrum (IS-PAS; former International Society for Abnormally Invasive Placenta; IS-AIP) defines a center of excellence by the "any-time-availability" of a multidisciplinary care team with the corresponding personal and technical infrastructure [1]. These multidisciplinary care teams include an expert obstetrician, obstetric anesthesiology specialist, a surgeon experienced with complex pelvic surgery—often a gynecological oncologist, an urologist (e.g., for ureteric re-implantation), a neonatologist, and a radiologist experienced with PAS diagnostics and interventional management. There should be rapid onsite access to colorectal and vascular surgeons, hematologists, adult intensive care facilities, (gestational age appropriate) neonatal intensive care facilities, massive transfusion facilities, and intraoperative autotransfusion (cell salvage) services. After initial medical assessment, an interdisciplinary presentation and case review should be performed (involving every attending discipline) to work up the planned approach as well as necessary technical and staff preparations. The planned delivery date and interdisciplinary approach should be written in the patient's chart. A multidisciplinary PAS team should be available 24 h a day, 7 days a week to ensure that expertise is available for emergency situations. This systematic multidisciplinary approach reduces the need for massive transfusion, the incidence of coagulopathy, the duration of surgery, the incidence of hypotension, the length of intensive care unit (ICU) stay, the incidence of ureteral injuries, and the need for early reoperation [15–19].

There are different surgical procedures and therapeutic options to manage PAS — namely, (1) cesarean hysterectomy, (2) local uterine resection/uterus conserving surgery, and (3) conservative therapy — i.e., leaving the placenta *in situ*, depending on placental localization, invasion (e.g., into the cervix or parametrium), and the extent of adherence [1]. To a lesser extent, patients are additionally stratified based on factors like overall pregnancy risk, number of prior preterm deliveries, individual patient wishes, family planning considerations, comorbidities, and history of bleeding. Women with PAS generally undergo planned C-section at between 34 and 36 weeks gestation [1]. Caesarean hysterectomy is the most commonly accepted approach [20]. Here, the placenta is left *in situ* after delivery of the fetus, since forced placental removal attempts are associated with significant risk of hemorrhage [20]. In the conservative approach, the entire placenta remains untouched (*in situ*) until it is either completely resorbed or the adherent/invasive interface is significantly reduced. This area can then be locally resected in the postpartum period [1]. Though initial blood loss and transfusion requirements during delivery seem to be reduced, obstetricians and anesthesiologists should be aware that there is still an increased risk of (1) secondary bleeding, (2) hemostatic consumption and/or disseminated intravascular coagulation (DIC), and (3) postpartum infection in the following weeks [1]. Surgical removal of part of the myometrium where the placenta is abnormally adherent (local surgical resection) has been proposed as a technique for managing PAS while conserving the uterus [20]. It is reasonably successful and may have both slightly less blood loss and maternal morbidity than hysterectomy [1]. Nevertheless, hysterectomy can be indicated for primary, secondary, or emergency procedures [1].

In regard to tailored PAS treatment regimes, interventional radiology techniques are being increasingly used in PAS management (Supplementary Table S2).

Anesthesiologists should be aware of the implications associated with PAS: including prepartum lab workup, patient blood and anemia management, cell salvage, prewarming, special patient safety checklists and team time out, anesthesiology approach, monitoring, hemostatic management, access to interventional radiology, point-of-care testing, PPH algorithms, and postoperative care, e.g., ICU, pain therapy, and venous thromboembolism (VTE) prophylaxis.

In this two-part literature review, we survey the current literature and recommend a multimodal step-by-step approach to perioperative PAS management in an effort to optimize patient safety. This first part of the two-part review focuses on general therapeutic and anesthesiology management approaches to PAS. The second part of this series addresses hemostatic changes, blood loss, and transfusion management in PAS patients.

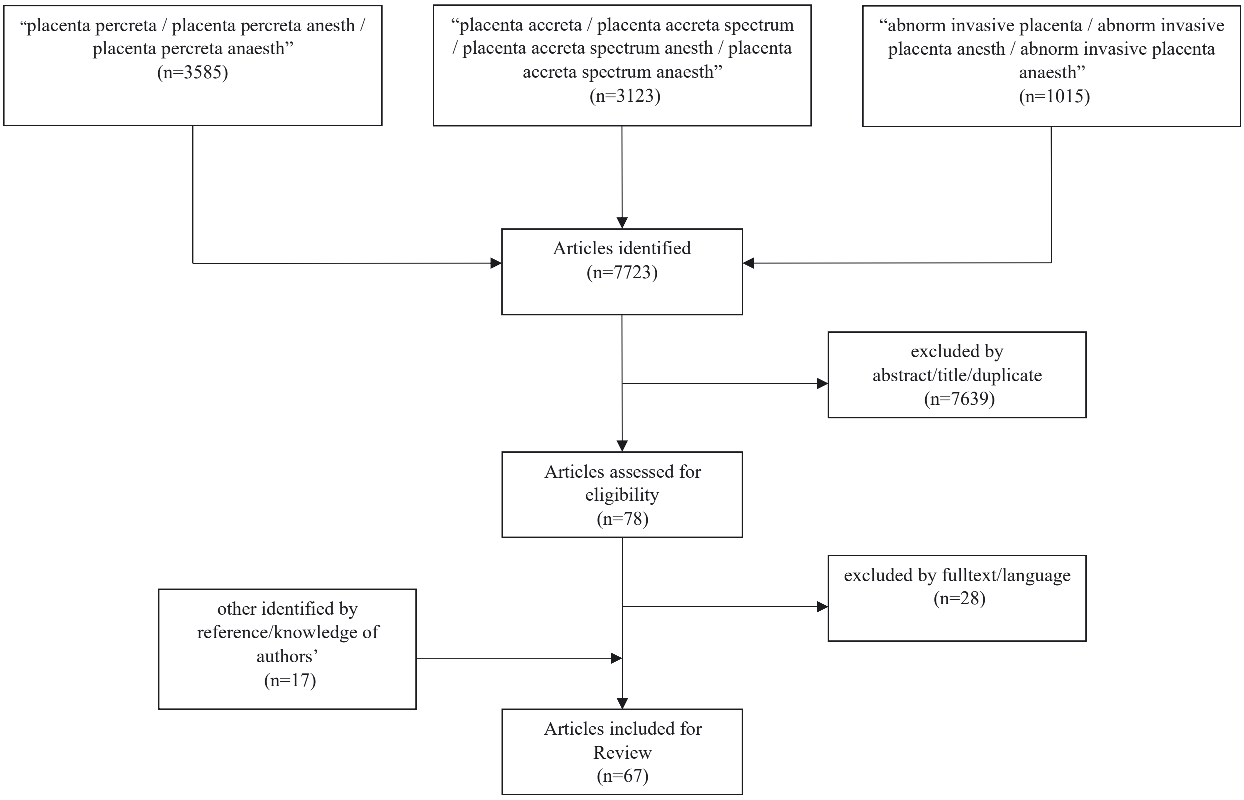


**Figure 1:** Flowchart: trial inclusion in anesthesia and hemostatic considerations analysis.

# Literature findings: placenta accreta spectrum part I and II: anesthesia and hemostatic considerations based on an extended review of the literature

We conducted a computerized literature review of the Medline database using the following search queries "((abnorm invasive placenta OR placenta percreta OR placenta accreta OR placenta accreta spectrum)) AND (anaesth OR anesth)" to identify studies, case reports, series and reviews that investigated the impact of anesthesia management on PAS outcome. We then screened publications for inclusion based on the following criteria: (1) anesthetic approach, (2) monitoring, (3) anesthetic medication and uterotonics, (4) post-operative care, (5) cell salvage, (6) hemostatic products — e.g., tranexamic acid (TXA), fibrinogen or prothrombin complex concentrate (PCC), (7) estimated blood loss (EBL) and transfusion and (8) laboratory work-up. We included publications that reported information concerning anesthesiology approach, anesthetic drugs, or data from at least two of the six other criteria in the primary analysis. We additionally noted the (1) type of placental abnormally and the (2) surgical approach used.

Additionally, we extracted data from publications that presented results from PAS patients who underwent interventional radiology procedures for a separate radiological analysis and analyzed blood loss, transfusion/hemodynamics, hysterectomy rate, ICU admission rates, operative approach, and procedure duration. We also performed hand searching of references for all included publications.

We identified 7,723 publications published between 1973 and February 28 2021. Of those, 7,639 publications were excluded based on initial screening criteria (abstract, title duplicates). Of the remaining 78 publications, 28 were excluded following full-text screening. We identified 17 additional articles following hand searching of references from the retrieved full-texts, making 67 publications eligible for inclusion (Figure 1). We included 55 case reports/trials for anesthetic management analysis, which contained data of 3,459 women (Supplementary Table S1) [6–9, 12, 14, 21–69]. For the analysis of interventional radiology in PAS 37 trials/reports met the criteria for inclusion, containing the data of 4,507 women

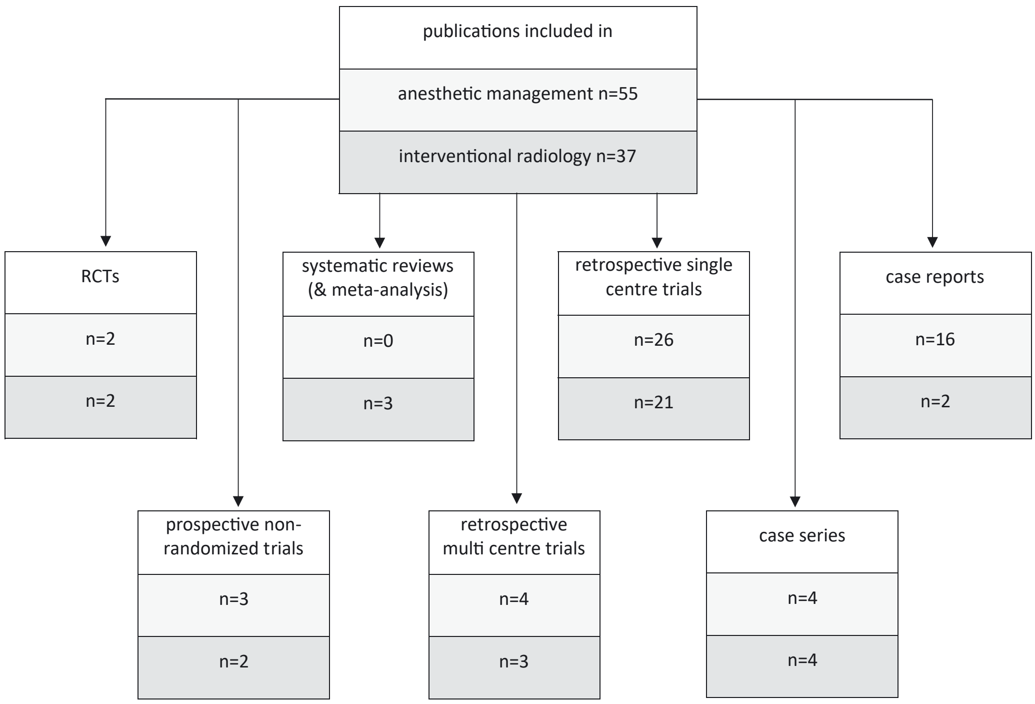


**Figure 2:** Type of included trials in anesthesia and hemostatic considerations analysis and interventional radiology analysis.

(Supplementary Table S2) [12, 23–26, 29, 36–51, 64, 66, 68, 70–81]. 25 studies were included in both analyses.

Of the 55 publications included in the primary analysis, we identified two randomized-controlled trials (RCTs) and no meta-analysis or systematic reviews (Figure 2, Supplementary Table S1).

This first part of the two-part review only the presents the results of this literature review with regard to anesthetic approach, surgical approach, monitoring, temperature management, interventional radiology, post-operative care and pain therapy. The results regarding hemostatic considerations, coagulopathy, anemia, laboratory work-up, blood loss, transfusion, use of hemostatic agents and postpartum venous thromboembolism prophylaxis will be addressed in the second part of this review.

## Patient (surgical) safety checklist and team time-out

World Health Organization (WHO) initiatives have shown that surgical safety checklists and team time-outs prior to surgical incision help improve patient safety [82, 83]. None of the trials identified in this review reported the routine use of either checklists or team time-outs in PAS patients. Both checklists and team time-outs can be performed quickly and easily adapted to various clinical settings, to improve the treatment team's understanding of the clinical situation prior to surgery and synchronize the team members involved [82, 84]. We recommend that checklists and team time-outs for PAS-surgery are used both preoperatively and intraoperatively. We advise that immediately prior to skin incision a pause be made for the first team time-out, where the entire team introduces themselves and their functions. In this team time-out the scheduled interdisciplinary approach, as discussed in the initial interdisciplinary case review, should be present briefly, including the intended operating procedure, expected surgical difficulties, and special operating room and anesthesia considerations (e.g., expected blood loss estimate, cell salvage system preparation, blood product availability, etc.). A second short team time-out during PAS-surgery should be performed following delivery of the placenta immediately after intraoperative PAS evaluation by the obstetrician/surgeon. The following information is of particular relevance to the healthcare team and should be explicitly stated in the second team time-out:

- PAS confirmed, intraoperative staging, spontaneous or manual removal of the placenta [85]?
- Planed operating procedure: Placenta *in situ*, local surgical resection or hysterectomy?

- Uterotonics: Yes/No (which?)?
- Bleeding?
- Cardio-pulmonary state?
- Conversion from neuraxial to general anesthesia?

Recent screening, diagnosis, and management guidelines of PAS disorders from the Society of Obstetricians and Gynaecologists of Canada (SOGC) highly recommend surgical safety checklists when all members of the health care team and their resources are assembled in the operating room (OR) [86].

> **Anesthetic considerations**
> - A patient safety checklist and team time-out should be performed prior to surgery. A second team time-out following delivery and surgical PAS evaluation should be performed and focus specifically on the intended management, expected complications, and the current state of bleeding.

## Anesthesia (general vs. neuraxial) in PAS operative procedures

None of the trials that we identified in this review specifically assessed the difference between neuraxial vs. general anesthesia in PAS patients (Supplementary Table S1).

### General anesthesia

Several studies reported findings from PAS patients who underwent general anesthesia (Supplementary Table S1). In one prospective observational trial, for instance, all women at high risk for placenta accreta received general anesthesia [32]. A wide variety of anesthetics were used to induce and maintain general anesthesia, which may simply reflect local standard operating procedures (Supplementary Table S1). Because incision-to-cord-clamping times can be much longer in PAS patients than in standard C-sections, anesthesia-related new-born distress and/or anesthesia of the new-born can occur if PAS patients undergoing general anesthesia for the entire operative procedure. Therefore, in our opinion, it is important to alert neonatology prior to surgery and discuss this as part of the initial team time-out.

### Neuraxial anesthesia

Case reports, small retrospective, and prospective series have demonstrated the safety of neuraxial anesthesia for PAS management [33, 87]. However, the likelihood of conversion from neuraxial to general anesthesia increases (more than 50%) as bleeding increases [33, 88].

Each anesthetic approach has several benefits and detriments (Table 1). Therefore, a combination of neuraxial and planned secondary general anesthesia seems reasonable to maximize both patient comfort and safety. Initial neuraxial anesthesia enables women to take part in childbirth. It remains unclear which neuraxial anesthetic approach is superior. Proponents of spinal anesthesia, either as a single-shot spinal anesthesia (SPA) or as a combined spinal and epidural anesthesia (CSE), argue that this approach offers improved analgesia and patient comfort. However, neuraxial anesthesia may induce hypotension and therefore secondary fetal bradycardia or fetal distress. There are two systematic Cochrane Database reviews—one comparing SPA and epidural anesthesia (EDA) for C-section, another comparing CSE to EDA for analgesia for women in labor. Both found this effect, also known as spinal anesthesia induced hypotension (SAIH), to be more distinctive in SPA than in EDA [89, 90]. Furthermore, both failed to show any superiority of SPA or CSE in relation to analgesia or patient comfort. Whether this SAIH leads to otherwise preventable emergency situations related to C-sections or PAS in particular or has relevant effect on neonatal outcome is currently unclear. Nevertheless, SPA cannot be generally recommended for these reasons. Given the minor hemodynamic changes an EDA with e.g., ropivacaine 0.75% at a slow rate and 5–10 µg sufentanil appears to be favorable. This grants the opportunity to slowly "titrate" the EDA to an optimal level. With this slow rate hemodynamic changes can be easily countered with norepinephrine. The epidural catheter can also be used for postoperative (see below) and intraoperative analgesia in cases of prolonged surgery.

If PAS is confirmed following childbirth, a planned conversion to general anesthesia before resection of the placenta minimizes stress and possible complications intraoperatively. Once PAS has been confirmed intraoperatively or if massive bleeding after birth is anticipated (second team time-out) switching from neuraxial to general anesthesia should be strongly considered in order to avoid emergency conversion under difficult conditions [33, 88].

**Table 1:** Anesthetic approach – considerations of (dis-advantages).

| Approach | GA | SPA | EDA | CSE | EDA + sec.planned GA |
|---|---|---|---|---|---|
| Advantage | – No conversion of anesthesia during operation<br>– Certain analgesia<br>– Controlled setting and safe Hemodynamic stability<br>– CVL + AL (if necessary) can be placed under GA before operation | – Fast onset of anesthesia, probably better analgesia than EDA<br>– Birth experience, possible mother-child-bonding | – Titration and mantainance of anesthesia<br>– No SAIH, more hemodynamic stability<br>– Postoperative analgesia via PCEA possible<br>– Birth experience, possible mother-child-bonding | – Fast onset of anesthesia, titration for mantainance of anesthesia if needed<br>– PCEA for postoperative analgesia<br>– Birth experience, possible mother-child-bonding<br>– Probable better analgesia than EDA alone | – Advantage of EDA<br>– No discomfort from long procedure time<br>– CVL + AL (if necessary) can be placed under GA<br>– Possebility to pass on GA if PAS is unincisive (second team time out after birth)<br>– Controlled setting if hemodynamic instability occurs during further operation |
| Disadvantage | – No mother-child-bonding possible, no birth experience<br>– Possible anesthetic drug exposure of the fetus and neonatal intervention<br>– No EDA for postoperative pain therapy | – Hemodynamic instability due to SAIH<br>– Discomfort from declining analgesia in long lasting procedures<br>– Possible need for secondary conversion to GA in hemodynamic instability<br>– Analgesia before incision, but no further availability for postoperative therapy<br>– CVL placement (if necessary) with out GA | – Discomfort in long lasting procedures<br>– Possible need for secondary conversion to GA in hemodynamic instability<br>– CVL placement (if necessary) without GA | – Discomfort in long lasting procedures<br>– Hemodynamic instability due to SAIH<br>– Possible need for secondary conversion to GA in hemodynamic instability<br>– CVL placement (if necessary) without GA | – Probably already hemodynamic instability before conversion into GA and/or CVL setup<br>– Short interruption of operation for e.g. intubation |

AL, arterial line; CSE, combined spinal and epidural anesthesia; CVL, central venous line; EDA, epidural anesthesia; GA, general anesthesia; PCEA, patient controlled epidural analgesia; SAIH, spinal anesthesia induced hypotension; sec., secondary; SPA, spinal anesthesia.

**Anesthetic considerations**
- EDA enables women to take part in childbirth; EDA can be used for postoperative pain therapy
- Fetal distress due to SAIH in following single shot spinal anesthesia should be avoided
- Scheduled intraoperative conversion to general anesthesia after childbirth and second team time out should be planned and explained to patients in advance

## Monitoring

We did not identify any studies that reported advanced monitoring during anesthesia in PAS patients (Supplementary Table S1). Standard monitoring included electrocardiogram (ECG), pulse oximetry, and non-invasive blood pressure (NIBP) and, in most cases, an arterial line (AL) was placed (invasive blood pressure; IBP) (Supplementary Table S1) [32, 69]. In addition to continuous IBP, advanced hemodynamic monitoring might be useful to detect hypovolemic changes, though none was reported in trials/case reports included in this review. Because massive bleeding with high volume resuscitation and transfusion rates frequently occurs in PAS, pulse pressure variation (PPV), stroke volume variation (SVV), stroke volume (SV) and cardiac output (CO) for targeted volume management should be considered, especially in women with placental invasion of the surrounding organs who are at a high risk of bleeding. A central venous line (CVL) was placed in most cases where general anesthesia was induced prior to surgery (Supplementary Table S1) and might be beneficial when high doses of vasopressors are required or in patients where peripheral intravenous cannulation is difficult (requiring small bore needles). Repetitive central venous or arterial blood gas analysis to determine lactate, hemoglobin (Hb), electrolyte levels including potassium and calcium and gas exchange parameters (e.g., pH value, carbon dioxide, bicarbonate) should be taken before birth and during the PAS management.

Additionally, body temperature, neuromuscular monitoring, and brain function monitoring (electroencephalogram) might be indicated in general anesthesia.

**Anesthetic considerations**
- Standard monitoring (ECG, pulse oximetry, NIBP) has to be considered as minimum
- Arterial line with IBP-measurement appears to be reasonable in most cases
  - Advanced monitoring as PPV, SVV, SV and CO should be considered in cases with expected high blood loss
- Central venous lines are justified if higher doses of vasopressors are needed or peripheral venous catheters are difficult to be placed
- If general anesthesia is applied, temperature, muscle relaxation, and brain function should be monitored

## Temperature management and prewarming

We did not identify any studies in this review that reported data regarding preoperative or intraoperative warming or temperature management. Inadvertent perioperative hypothermia, defined as a body core temperature below 36 °C, is mainly caused by a shift in vasoconstriction and shivering thresholds, and sympathicolysis related vasodilatation (during neuraxial anesthesia) [91, 92]. Induction of general anesthesia aggravates the redistribution of warm blood from the body core to the periphery [93] with a decrease of the body core temperature from 0.8 to 1.5 °C [94]. In PAS patients with PPH, massive bleeding, and volume shifts, perioperative hypothermia may affect coagulation by altering platelet function [95, 96] and thereby perpetuating intraoperative blood loss [97]. A brief forced-air warming at 43 °C (prewarming) during epidural catheter placement and/or 10–20 min before induction of general anesthesia is effective for maintaining intra- and postoperative normothermia [94]. National and international guidelines recommend active warming before and during anesthesia induction in general [92, 98]. In addition to maintenance of normothermia, using a forced-air warming gown during neuraxial anesthesia placement or before general anesthesia induction may reduce patient agitation and improve preoperative well-being. This forced-air warming should be continued during the entire surgical procedure. Due to expected large in- and transfusion-volumes a fluid warmer should be used.

**Anesthetic considerations**
- A brief forced-air prewarming at 43 °C during neuraxial anesthesia and/or 10 min before and during general anesthesia induction is effective to maintain intra- and postoperative normothermia
- The intraoperative use of forced-air warming and a fluid warmer can reasonable prevent a secondary hypothermia

## Interventional radiology: balloon occlusion and/or embolization, hybrid-OR

Our literature search yielded 37 relevant publications where interventional radiology performed either (1) balloon occlusion of the infrarenal abdominal aorta (IAABO), the internal iliac arteries (IIABO), common iliac arteries (CIABO) or (2) embolization of the uterine arteries (UAE)

(Supplementary Table S2). The type of trials included here is shown in Figure 2.

Studies reported balloon occlusion interventions used in both emergency procedures and routine elective procedures. Usually, the epidural catheter was placed before the patients were transferred to the radiology suite where the balloon occlusion catheter was positioned under X-ray imaging [26, 36, 37]. Patients were then transferred to the OR for C-section where balloon catheter position was either reconfirmed or in some cases the catheter used without confirmation [38]. Meller et al. and Yamada et al. demonstrated the possibility of performing the entire procedure in a hybrid-OR [39, 74]. In general, the balloons were inflated routinely during C-section (1) after the umbilical cord had been clamped and (2) before any attempt of a surgical separation of the placenta or begin of hysterectomy [40, 41]. In some studies, balloons were only inflated if deemed necessary intraoperatively [75].

The regime of inflation and removal of the catheters and sheaths was not always reported but if varied widely. The duration of inflation and deflation till next inflation varied according to position of catheter and approach between several minutes up to an hour [25, 37, 41, 42, 76]. Generally, estimated blood loss (EBL), transfusion rate, operation time, hysterectomy rates, and ICU admission were analyzed. The two RCTs as well as Peng et al. did not identify any advantage for the use of IIABO compared to standard care [23, 43, 68]. In contrast, Cali et al. showed a significant reduction of EBL and RBC transfusion for the IIABO group in a non-randomized prospective trial in PAS [26]. These findings dovetail with the retrospective data presented by Zhou et al. [38]. Mei et al. compared IIABO with IAABO and found less EBL and shorter operating times for the IAABO group [40].

In a meta-analysis of 1811 women with PAS, Shahin et al. found a significant reduction in EBL and red blood cell concentrates (RBCs) transfusion for all endovascular procedures except UAE [70]. Moreover, they found that IAABO was associated with lower hysterectomy rates and blood loss than other endovascular methods [70]. Due to anastomosis from the ovarian or renal arteries, Matsubara et al. concluded that occlusion of the aorta may be beneficial to other locations [99]. Liu et al. found that aorta occlusion at the level of the renal arteries was associated with less blood loss in 57 retrospective analyzed PAS patients [44]. The postoperative levels of creatinine and lactate dehydrogenase were not affected [44].

Balloon occlusion-related complications occur frequently and were reported in 28 studies/case reports (Supplementary Table S2). The prevalence of arterial thrombosis, reported in 10 trials, varies from 1 to 14% (Supplementary Table S2) [42, 81]. Arterial dissection, rupture, aneurysm, and AV-fistula were reported in five trials, and single trials observed neurological symptoms of the lower limb, fever, vasospasm, gastrointestinal symptoms (requiring a conversion from neuraxial to general anesthesia), arterial wall hematoma and a vascular injury with need of a iliofemoral bypass [24, 29, 36, 37, 42, 43, 45, 70, 76, 78]. Further complications are associated with the procedure itself, like balloon rupture, misplacement, catheter migration, or failure to provide adequate intraoperative hemostasis for other reasons [36, 46, 70, 77]. On the other hand, six trials reported that no catheter-related (major) complications occurred [12, 26, 47, 48, 68, 75]. In a systematic review, catheter-associated complications were found in 7.5% of total cases (4.5% minor and 3% major complications) [71]. The fewest complications occurred with the use of IAABO [71].

Various approaches were used for uterine artery embolization. Either UAE was used routinely to prevent PPH, or as a therapy if PPH occurs [29, 49–51]. The two largest trials assessing the use of UAE found divergent results. While Shahin et al. reported no significant benefit for UAE, Labarta et al. found it effective in 89.4% (1739 patients) with PPH due to uterine atony [70, 72]. However, it remains unclear if these results are transferrable to PAS patients. The prevalence of UAE related complications differed as well. While Yuan et al. and Meller et al. had no serious vascular complications, Kim et al. pointed to a high incidence of severe complications, namely: uterine necrosis, intra-abdominal hematoma, paralytic ileus, and late complications (two patients had total uterine necrosis and subsequent hysterectomies) [49, 51, 74]. In a meta-analysis, 43 of 263 women with abnormal placental implantation had a self-limiting post-embolization syndrome after UAE, whereas two women suffered uterine necrosis with subsequent hysterectomy and 10 women developed groin hematoma [70].

Additionally, cross-clamping of the aorta or surgical ligation of arteries, especially the uterine artery, were reported as alternative surgical approaches [25, 36, 46, 50, 73, 77]. Further, an intraarterial infusion of pituitrin (a formerly in obstetrics used extract of bovine posterior hormones by now replaced by other drugs with oxytocic activity) in the internal iliac arteries in addition to an IIABO was proposed [25]. Though not mentioned in any of the reviewed studies, manual compression of the aorta is another possible approach [100]. Aortic compression may be situational conducted either open or closed. Given that mostly used as an emergency maneuver if massive bleeding occurs, no standardized approach can be proposed.

In conclusion, endovascular interventions seem beneficial for women with PAS undergoing cesarean section, especially regarding EBL, transfusion rate, and uterus preservation.

Abdominal aorta balloon occlusion appears to be more beneficial than more distal occlusions for three reasons. First, the procedure is easier to perform with a single catheter and does not require a cross-over approach. Blood loss may be reduced due to occlusion of possible anastomoses from ovarian (and renal) arteries. Moreover, this procedure is advantageous as it is becoming more routinely performed in the clinical setting among both obstetric and trauma patients. For these reasons we, as well as the new SCOG guideline, recommend the IAABO as a promising approach [86]. The localization of the occlusion, whether at the level of the renal arteries or below, is currently being discussed and warrants further investigation. Because results even across IAABO studies vary widely, there may be an underlying effect of the inflation regimes which have yet to be assessed.

Still, balloon occlusion may not be indicated in every woman with PAS. The circulatory disturbances caused by occlusion and re-opening may lead to a decompensation in women with cardiac diseases. Women with contusion or intracranial hemorrhage could be threatened by the presumable increased intracranial pressure due to elevated blood pressure following the occlusion [101]. Finally, the blood pressure decreases following balloon deflation and a reperfusion-syndrome with severe metabolic derangements may occur [102, 103]. These adverse effects have to be anticipated to avoid potentially lethal complications and may limit the use of vascular occlusions.

UAE can lead to serious complications, like post-embolization syndrome, uterine necrosis, and vascular complications. Given the risks, it seems that the prophylactic use of UAE to prevent PPH in PAS is unjustifiable. Conversely, in women with ongoing PPH, the current American College of Obstetricians and Gynecologists, the Royal College of Obstetricians and Gynaecologists, and the Society of Obstetricians and Gynaecologists of Canada recommend UAE only if patients are (1) actively bleeding, and (2) stable enough to transfer [13, 104, 105]. Using a hybrid-OR decreases risks associated with patient transport and UAE or balloon occlusion may help stabilize PAS patients with active bleeding during C-section [39, 74].

The frequency with which methodological failures associated with endovascular techniques have been reported (balloon rupture, catheter displacement, or other causes), indicates that interventional radiologist experience may be a deciding factor in success/failure rates [36, 46, 70, 74, 77]. On account of the risks of severe complications like thrombosis, dissection, or hemodynamic disturbances, anesthesiologists should familiarize with these procedures and be prepared to respond accordingly if a severe complication arises.

Finally, endovascular techniques expose the fetus to radiation, though the dosage is normally below the maximal recommended fetal radiation dose (100 mGy) [106].

**Anesthetic considerations**

- Balloon occlusion approaches may reduce EBL, transfusion rate, and hysterectomy rate
  - IAABO seems to be superior to other approaches
  - Inflation and deflation of the catheters may have relevant hemodynamic and homeostatic effects
- UAE may be helpful to treat active post-partum hemorrhage
- Severe complications may occur during endovascular interventions
- A hybrid-OR could simplify processes, reduce procedure time, and eliminate risks due to patient transfer

# Postoperative care

Roughly half of the trials/case reports included in this review reported information regarding postoperative care. Overall, there was a high rate of postoperative ICU admission. Because there is a high risk of massive bleeding and large volume transfusion, critical care specialists should be involved prior to surgery as part of the multidisciplinary team [7, 107]. The primary reasons cited for postoperative ICU admission were (1) the need for further fluid resuscitation, (2) further correction of coagulopathy, (3) management of perioperative hypofibrinogenemia and potential reduction of other coagulation factors (e.g., consumption of FXIII), (4) identification and management of arterial catheter complications, (5) timing of venous-thrombo-embolism-prophylaxis, and (6) pain therapy [107]. Patil et al. reported hypothermia (from large fluid infusions and prolonged surgery), hyperkalemia, hypocalcemia, acidosis, volume depletion or overload or transfusion reactions as most common reasons for ICU admission in their review [10]. Therefore, standard monitoring, respiratory rate, level of consciousness, body core temperature, blood glucose levels (every 4 h for the first 24 h), electrolytes as well as arterial blood gas analysis (hourly for the first 2 h, then every 4 h for the following 12 h), pain, bleeding, and urine output as a marker of volume depletion should be monitored for roughly 24 h postoperatively [10].

Postoperative ICU admission or maternity-based high dependency unit (HDU) admission (with the objective of allowing early mother-child-bonding) should be determined dependent on the course of the operation and subsequent homeostatic disturbances. Regardless, close observation is necessary to identify postoperative hemorrhage and potential adverse events following surgery and interventional radiology procedures.

**Anesthetic considerations**
- Critical care specialists should be involved in preoperative planning
- Maternity-based HDU or adult ICU for 24 h should be considered postoperatively
- Postoperative ICU considerations:
  - Correction of coagulopathy
  - Normalizing electrolytes and blood-glucose
  - Normalizing body-core temperature
  - Refinement of fluid status
  - Observation for postoperative hemorrhage
  - Observation for catheter-associated complications (if applicable)
  - Pain management
  - Thrombosis prophylaxis

## Postoperative pain therapy

Adequate pain control after C-section is one of patients' foremost concerns. Optimal analgesia is also a key point in the enhanced recovery after surgery (ERAS) concept. Correspondingly, maternal mobility improves the interaction with the newborn. Inadequate pain control leads to delayed consequences such as postpartum depression, chronic pain, and opioid consumption [108]. Because opiates are avoided before umbilical cord clamping in general anesthesia, ketamine and neuraxial techniques are the only options for providing analgesia starting from skin incision. Out of 179 different surgical procedures, C-section is ranked ninth most painful postoperatively [109]. Women who received general anesthesia for C-section generally require high levels of opiates (on average 27 mg morphine equivalent) to alleviate postoperative pain [109]. Even when neuraxial anesthesia was applicated, postoperative numeric rating scale (NRS) pain scores amount up to 6–7 under mobilization (e.g., caring for the newborn) and chronic post-surgical pain were detected in upwards of 11% of women after planned caesarean section without PAS [110, 111]. C-section in women with PAS is thought to be even more painful, due to the more invasive nature of the operation. For its possible side effects (e.g., addiction, obstipation, weariness) postoperative systemic opioids should be considered as a recue medication. Therefore, advanced planning of postoperative analgesia is warranted.

None of the 73 trials/case reports included in this review specifically assessed postoperative analgesia in women with PAS. According to the anesthetic technique different approaches for the postoperative analgesia can be offered. In 17 of the included trials/case reports an epidural catheter was placed (as an EDA or CSE), in 24 publications the women received a primary general anesthesia (Supplementary Table S1).

3 mg morphine epidural can alleviate postoperative pain and spare other analgesics for the first 24 h if route is available [110, 112]. A catheter left *in situ* may prolong the postoperative immobilization, but it might be reasonable to leave the catheter in place for patient controlled epidural analgesia (PCEA) in dependency on the extent of the operation, especially if early postoperative mobilization appears unattainable.

Other regional anesthetic techniques such as transversus abdominal plane (TAP) block, a quadratus lumborum (QL) block, or erector spinae block has been shown to reduce postoperative opioid requirements and pain scores if no neuraxial morphine has been administered [113–115]. These approaches seem beneficial if cesarean section was conducted under general anesthesia alone.

Though primary developed for cancer pain, the use of the WHO analgesics ladder seems advisable [116]. We recommend additional postoperative analgesia with paracetamol and non-steroidal anti-inflammatory drugs, like ibuprofen (WHO level 1).

This multimodal analgesia is the current gold standard for pain management after cesarean delivery and can effectively reduce systemic opioid administration [108, 117, 118].

If the pain relief measures described above are insufficient, rescue medication using opioids at WHO levels 2 and 3 is inevitable [116]. The oral route is as effective as the intravenous and should be preferred if available [119]. Oral opioids (morphine sulfate, hydrocodone, oxycodone and tramadol) are currently available and acceptable. Codeine is contraindicated during breastfeeding [108]. In special cases of extraordinarily severe postoperative pain, patient controlled intravenous analgesia (PCIA) can be utilized [120].

Dexamethasone, which is frequently used for prevention of postoperative nausea and vomiting, may have an additional analgesic effect [121]. Other co-analgesics like ketamine, clonidine, gabapentin, lidocaine, or magnesium have been cited as possible co-analgesic treatments, however there is currently no data regarding the efficacy of these additional approaches in PAS [107].

**Anesthetic considerations**
- Use a multimodal non-opioid analgesia strategy to reduce systemic opioid use
- Use epidural (intrathecal) morphine if route is available
- Consider PCEA in cases of anticipated severe postoperative pain, if epidural catheter is *in situ*
- Consider TAP or QL block after primary general anesthesia
- Use systemic opioids as rescue medication, preferably via oral route (if available)

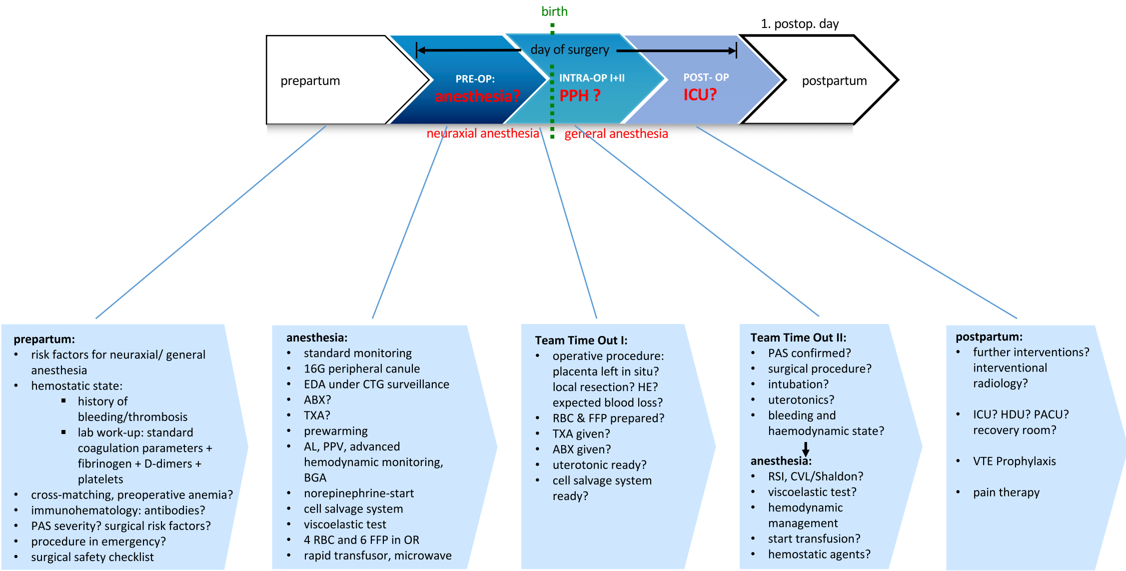


**Figure 3:** PAS-algorithm. AL, arterial line; ABX, antibiosis; BGA, blood gas analysis; CVL, central venous line; EDA, epidural anesthesia; FFP, fresh frozen plasma; HE, hysterectomy; ICU, intensive care unit; INTRA-OP, intraoperative; OR, operating room; PACU, post-anesthesia care unit; PAS, placenta accreta spectrum; PCEA, patient-controlled epidural anesthesia; POST-OP, postoperative; PPH, peripartum hemorrhage; PPV, pulse pressure variation; PRE-OP, preoperative; RBC, red blood cell concentrates; RSI, rapid sequence induction; TTO, team time out; TXA, tranexamic acid.

# PAS-algorithm

None of the trials/case reports included in this review reported a multidisciplinary PAS(-PPH) algorithm including detailed anesthetic considerations. Although, anesthetic PAS management is challenging due to requirements, such as preoperative planning, pre- and postpartum anesthetic approach and postoperative monitoring, possible further interventions or structural considerations of the hospital and department (Figure 3). Scheduled and structured team time outs may help improving multidisciplinary communication and matching current anesthetic/hemodynamic/hemostatic state with EBL, ongoing surgical procedures and excepted complications or additional interventions (Figure 3). Therefore, we propose this PAS-algorithm as a possible approach regarding the most challenging aspects in PAS management. This algorithm includes considerations concerning hemostatic and anemia management, which will be discussed detailed in the second part of this review.

**Anesthetic considerations**

– A multidisciplinary algorithm of PAS management including anesthetic considerations and PPH treatment should be adjusted to structural conditions on site

## Limitations

PAS is a rare and heterogeneous condition. As such, PAS definitions and terms vary, it is therefore possible that the presented research was incomplete due to terminology variation (e.g., suspected “morbidly adherent placenta”). Moreover, though many publications were included in this review, few were specifically designed to primarily assess anesthesiology PAS management. Anesthesiology parameters were frequently reported as either secondary outcome measures or basic characteristics. In addition, the quality of the included studies is heterogenous. Currently, there are very few meta-analyses, systematic reviews, or randomized-controlled trials available. Most PAS data are retrospective and are frequently presented as case reports or case series. A few topics of interest for this review—for example temperature management and postoperative pain therapy in PAS patients—were not addressed at all in the available literature. Therefore, recommendations have to be generated from general therapeutic approaches and reasonable adaption according to PAS circumstances.

Furthermore, it has to be assumed, that especially precarious PAS cases are those to be published. Due to the large ratio of case reports and series in the available data, this may cause a serious bias.

## Conclusions

Women presenting with PAS are at high risk of PPH, extensive surgical, anesthetic and/or interventional procedures and might be threatened by e.g., potential massive transfusion, hysterectomy, neonatal impairment, surgical complications and/or pain.

This part of the two-part review summarized current anesthesiology approaches, considering different PAS management strategies including interventional radiology. The importance of preoperative scheduling including e.g., modified surgical safety checklists and team time outs was highlighted. The anesthetic approach, monitoring, and preparation of potential massive transfusion as well as postoperative ICU-admission and pain therapy should be adjusted to structural conditions on site. A multidisciplinary algorithm of PAS management including anesthetic considerations and PPH management might be helpful to improve patient outcome. Due to the complexity of PAS and the personal and technical infrastructure needed to ensure the best possible outcome for women suffering from PAS, it seems reasonable to postulate a treatment of these women in centers of excellence providing the required recourses.

The level of evidence appears to be better for radiological interventions than for anesthesia considerations in PAS patients. Further high-quality trials are needed.

In the second part of this review, we will discuss possible hemostatic changes (e.g., a "DIC-like" hemostatic state) in PAS cases and their management. Moreover, we will address pre- and intrapartum anemia, transfusion management and the use of autologous blood transfusion systems.

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