

## GUIDELINE AND CONSENSUS

# Comprehensive scheme to manage pregnancy with scarred uterus at advanced maternal age: Interpretation of Chinese expert consensus

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## Abstract

Deferral of marriage and child-bearing age as well as high occurrence of uterine surgery history such as cesarean section and myomectomy in women who are about to have babies are challenging obstetrical health care worldwide, since pregnancy at advanced maternal age and pregnancy with scarred uterus are both high-risk pregnancy. In China, one-child policy had been implemented for three decades and contributes to high cesarean section rates. With family planning policy turning to two and three-child, there are rising pregnancy at advanced maternal age with scarred uterus. A clinical management scheme can help obstetricians a lot to assess risks, prevent pregnancy complications and manage pregnancy in an organized manner. However, there are insufficient studies on relevant clinical issues for the specific population, and there is no consensus or practice guidelines until now. We have developed Chinese expert consensus based on our pioneering research findings on the prevention and treatment strategy for major pregnancy complications in women of advanced maternal age. We formulate the consensus comprising general management scheme to standardize clinical care, practical risk scoring systems to early warn major pregnancy complications, and nationwide expert recommendations to be in accordance with evidence-based appraisal method. Consecutive supervision along with stratified management are highly emphasized. We interpret the consensus containing up-to-date literature review, research findings interpretation and most concerned questions discussion. This consensus interpretation helps standardize how to manage pregnant women of advanced maternal age with scarred uterus and improve the maternal-fetal outcomes.

**Key words:** pregnancy with scarred uterus, advanced maternal age, clinical management scheme, expert consensus interpretation, risk scoring system

## INTRODUCTION

Increasing pregnant women of advanced maternal age with scarred uterus across the world has been a major challenge for global obstetric health care. Such pregnant women are of high risk of pregnancy-related complications, mostly critical and severe including cesarean section pregnancy (CSP), placenta previa, placenta accreta spectrum (PAS)


disorders, uterine rupture, postpartum hemorrhage (PPH), etc., which pose serious threats to mothers and babies' health. In order to standardize clinical management process, early warn and treat high-risk patients to improve maternal and fetal outcomes, Chinese experts have explored on relevant clinical issues for the specific population, especially on how to prevent and treat major pregnancy complications. In 2021, an expert consensus on

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how to manage pregnant women of advanced maternal age with scarred uterus was developed, which was published on *Chinese Journal of Practical Gynecology and Obstetrics*.<sup>[1]</sup> To promote the popularization of this practical expert consensus among hospitals at all levels worldwide, we have translated it into English along with exhaustive consensus interpretation.

## PRE-PREGNANCY ASSESSMENT AND PREGNANCY PREPARATION GUIDANCE

### Question 1: How to evaluate scarred uterus in women of advanced maternal age before pregnancy?

#### Recommendations and consensus

(1) The general assessment for women of advanced maternal age before pregnancy can be found in *A Comprehensive Approach to Care of Women of Advanced Maternal Age* (hereinafter referred to as “2019 Approach”).<sup>[2]</sup>

(2) A detailed inquiry about the history of uterine surgery, detailed surgical records, pathological results, and postoperative recovery can provide important information for evaluation.

(3) Perform vaginal ultrasound examination before pregnancy, and if necessary, perform hysteroscopy, contrast examination, or pelvic magnetic resonance imaging (MRI) to promptly detect and evaluate uterine scar diverticulum.

(4) For women with a history of poor pregnancy and childbirth or a risk of genetic diseases in their offspring, carry out etiological screening and genetic counseling to assess the risk of recurrent adverse pregnancy outcomes or genetic diseases in their offspring during the second pregnancy, give suggestions on appropriate prenatal testing methods.

(5) Conduct multidisciplinary consultations for women of advanced maternal age who suffer from basic diseases and require assisted reproductive technology to determine whether they can conceive again.

(6) Women of advanced maternal age with a high risk of pregnancy related venous thromboembolism (VTE) should have a detailed risk assessment before pregnancy and personalized management with informed selection.

#### Interpretation

The consultation results of scarred uterus in women of advanced maternal age should not be as simple as whether pregnancy is possible or not, but should provide specific evaluation opinions based on pregnancy risk, and the patient and their family members should make a decision on whether to conceive again.

(1) It is very important for women of advanced maternal age to be clear about their past history, childbearing history and family history before pregnancy, and to carry out physical examination, routine gynecological examination and necessary auxiliary examinations to assess the pregnancy risks related to advanced maternal age. See *2019 Approach* for details.<sup>[2]</sup>

(2) The history of uterine surgery includes cesarean section (CS), myomectomy, mediastinotomy, cornual hysterectomy, and uteroplasty. Ask for a detailed history of uterine surgery, preferably by reviewing previous surgical records and pathological results, and inquire about postoperative recovery. Clarify the hospital's level, doctor's level, surgical site, involvement of myometrium and endometrium, surgical suture method, postoperative fever, infection, and incision healing can help in pre-pregnancy evaluation of scarred uterus in women of advanced maternal age.

(3) In recent years, the incidence rate of scar diverticulum after CS has greatly increased, which can increase the risk of scar pregnancy, scar rupture during pregnancy, uterine rupture and placental implantation after CS.<sup>[3]</sup> The standardized method of ultrasonic evaluation of scar after CS are referred to the review published by *Ultrasound in Obstetrics and Gynecology* (OBGYN).<sup>[4]</sup> The diagnosis and treatment of scar diverticulum can be found in a management scheme published by Fertil Steril,<sup>[5]</sup> which provides detailed diagnosis and treatment ideas. At present, there is no evidence-based medical research from China or abroad on whether the patients with scar diverticulum should be operated before pregnancy and the risk of subsequent pregnancy. It is recommended that women of advanced maternal age with scar diverticulum detected by ultrasound and MRI should be consulted by gynecological experts to assess the risk of subsequent pregnancy so that patients and their families could make informed choices.

(4) For women of advanced maternal age, those with a history of recurrent miscarriage, preterm birth, pre-eclampsia, fetal growth restriction, intrauterine fetal death or other adverse pregnancy outcomes, those have given birth to children with genetic diseases, and those suffer from genetic diseases or have a related family history, it is recommended to carry out etiological screening and genetic counseling. If necessary, take preimplantation genetic screening/diagnosis.

(5) Women of advanced maternal age often have underlying medical conditions such as medical diseases, operation history, and gynecological history. Multidisciplinary consultation is suggested to evaluate whether a subsequent pregnancy is appropriate. For women after adenomyomectomy or myomectomy, the feasibility of assisted reproductive technology should also be evaluated by a multidisciplinary team including obstetrics, reproductive medicine, gynecology and other necessary

disciplines.

(6) Advanced maternal age (> 35 years) is a high risk factor for women to develop VTE during pregnancy and postpartum. Other risk factors include personal history of VTE, thrombophilia, body mass index > 30 kg/m<sup>2</sup>, immobility, nulliparity, smoking, pregnancy complications including multiple gestation, gestational diabetes, pre (eclampsia), CS, antepartum hemorrhage, postpartum infection, medical diseases like hypertension, diabetes, sickle cell disease, systemic lupus erythematosus.<sup>[5]</sup> It is recommended to conduct detailed risk assessment, health education, and individuation management for those with high risk factors. Refer to 2018 American College of Obstetricians and Gynecologists (ACOG) guideline for specific methods.<sup>[6]</sup>

### **Question 2: What is the optimal interpregnancy interval (IPI) for women with scarred uterus?**

#### **Recommendations and consensus**

(1) It is advisable for women of advanced maternal age with scarred uterus to conceive between 12 to 24 months after CS.

(2) There is no consensus on the timing of conception after myomectomy. It is recommended to provide individuation guidance based on comprehensive evaluation of the location, pathological type, size and number of myomas, and surgical suture method when operates.

(3) Timing of conception after other uterine surgeries requires individuation guidance.

#### **Interpretation**

(1) IPI refers to the time interval between the previous delivery and the current conception. The 13th Five Year Plan Key Research and Development Project in China conducted a single-center analysis of the relationship between IPI and adverse pregnancy outcomes for puerpera who was pregnant again after CS. We found that a long IPI (more than 60 months) would increase risks of premature delivery, premature rupture of fetal membranes and hypertension in pregnancy (HIP), while a short IPI (less than 12 months) would increase the risk of premature delivery, and there was no significant difference when it comes to the risk of any adverse pregnancy outcomes between IPI for 13–24 months and 25–60 months. Most studies in China and other countries found that the risk of uterine rupture and blood transfusion was increased in patients with IPI less than 6 months,<sup>[7]</sup> and the risk of uterine rupture, placenta previa, and placental abruption was the lowest in patients with IPI of 18 to 24 months.<sup>[8,9]</sup> A retrospective cohort study carried out by Martimucci *et al.* shows that the risk of PAS disorders may not increase for those who are pregnant again in a short interval after CS.<sup>[10]</sup> Considering fertility, women of advanced maternal age can conceive as early as 12 months after CS,<sup>[11]</sup> but related

risk is higher than that of 18 to 24 months. To sum up, we suggests that women of advanced maternal age with scarred uterus after CS conceive again 12 to 24 months after the operation.

(2) For those are pregnant after myomectomy, the risk of uterine rupture may be related to operations (incision and suture methods for myometrium, destruction of local tissue, infection or hematoma of myometrium, laparoscopic electrocoagulation for hemostasis, and *etc.*), the number, size and location of myomas, and the time interval between surgery and following conception.<sup>[12]</sup> If the interval is too short, uterine rupture is likely to occur, and if it is too long, myoma is likely to relapse. There is yet no recommendations from international guidelines about the optimal interval.<sup>[13]</sup> A retrospective cohort study in South Korea found that those conceive within 12 months after transabdominal or laparoscopic myomectomy had a higher risk of PAS disorders than those after 12 months or more.<sup>[14]</sup> Determine the interval based on information in every surgery report about size and localization of myomas, use of energy, entering the uterine activity, how many layers of stitches, post-operation infection.<sup>[13]</sup> Refer to *Chinese Expert Consensus on the Diagnosis and Treatment of Uterine Fibroid* for detailed guidance of contraception duration after myomectomy of 3 or 6 months to 12 months according to myoma's category.<sup>[15]</sup> If it is adenomyoma by pathology, the risk of uterine rupture will be high in following pregnancy, for which preparation of pregnancy should be at least 12 months after adenomyomectomy with risk of uterine rupture been adequately understood.

(3) The American Society for Reproductive Medicine released *Uterine Septum: a Guideline* in 2016, which mentions that the uterine cavity heals 2 months after septum incision but evidence of when to conceive after the surgery is insufficient.<sup>[16]</sup> Pregnancy after cornua uteri resection or uteroplasty is of relatively high risk of uterine rupture with poor maternal and fetal outcomes, for which evidence-based medical research for appropriate IPI is currently absent. Consultants should fully inform the risks and give personalized recommendations.

## **FIRST TRIMESTER SCREENING AND MANAGEMENT**

### **Question 3: What are the key screening items for women of advanced maternal age with scarred uterus in early pregnancy?**

#### **Recommendations and consensus**

(1) First trimester screening mainly uses ultrasound to monitor the position of gestational sac with focus on CSP screening.

(2) If there are more than one gestational sacs, comprehensively evaluate advantages and disadvantages of

fetal reduction surgery, and determine the timing if needed.

(3) Observe the scar of CS by ultrasound and assess risks of some obstetric complications as early as first trimester.

(4) Pregnant women complicated with basic diseases or adverse history of pregnancy and childbirth who have missed the pre-pregnancy assessment are advised multidisciplinary consultations to formulate individuation prenatal care measures.

### Interpretation

Routine management for women of advanced maternal age at first trimester is detailed in *2019 Approach*. For women of advanced maternal age with scarred uterus, the content following needs to be emphasized.

(1) Implantation of gestational sac in the hysterotomy scar, *i.e.* CSP, is a life-threatening obstetrical complication, which could develop into PAS, leading to hemorrhage, uterine dehiscence or rupture, and premature delivery. Chinese experts formulated *Expert Consensus on the Diagnosis and Treatment of Uterine Scar Pregnancy After Cesarean Section (2016)* with standardized CSP diagnosis and treatment, in which experts proposed CSP treatment principle as “diagnose early, terminate early, and clear early”.<sup>[17]</sup> In 2016, a study by American scholars provided current standards for CSP diagnosis and introduced the sonographic method for differential diagnosis between CSP and intrauterine pregnancy at first trimester.<sup>[18]</sup> For CSP patients who strongly request to continue pregnancy, physicians need to fully explain the risks of continuing pregnancy to patients and their family members, including health threats to mothers, potential adverse outcomes for the embryo or fetus with informed consent forms signed. Refer these patients to medical units with capability of rescue and interventional therapy. For scars caused by operations other than CS, it is recommended to take operation records as references when ultrasonically monitoring gestational sacs.

(2) Getting pregnant naturally, the incidence of multiple pregnancies in women of advanced maternal age is higher than that in women of appropriate maternal age, while assisted reproductive technology leads to increasing multiple pregnancies as well.<sup>[19]</sup> Zygosity and chorionicity can mostly be determined based on ultrasound examination at first trimester. If a pregnant woman with twin or multiple pregnancies has a history of late miscarriage or premature delivery, fetal reduction could be suggested and informed to the pregnant woman and her family members to make their decision. For those who cannot have fetal reduction at first trimester because of homozygous cleavage, it is necessary to inform the patient of the risks of multiple pregnancies accompanied by scarred uterus. The patient and her family members should make an informed choice about the pregnancy. Evaluate fetal conditions according to nuchal translucency (NT) along with ultrasound examination,

and evaluate the relationship between gestational sacs and previous operation site based on operation records, so that fetal reduction individuation scheme can be set up.

(3) In 2011, a research from America showed that observation of scar in first trimester for those are pregnant again after CS help assess risks of obstetric complications related to the previous CS, which include low-lying placenta, placenta previa, PAS and peripartum uterine rupture.<sup>[20]</sup> A study published in 2022 from Singapore proposed that transvaginal ultrasound (TVUS) examination performed from 11 w to 13 w<sup>+6</sup> for pregnant women with previous CS to evaluate the position between scar and placenta helps to predict risks of PAS. If the scar is above cervicoisthmic canal (CIC) while placenta is low-lying, there is high risk of PAS. If the scar is within CIC and/or placenta is high-lying, there is low risk of PAS. Verified by ultrasound in second and third trimester as well as pregnancy outcomes, this method is of 100% sensitivity, 95.31% specificity, 16.7% positive predictive value, and 100% negative predictive value. First trimester detection of low-lying placenta or scar exposed above CIC effectively predicts high risk of PAS. Initiate multidisciplinary management timely for pregnant women of high risk.<sup>[21]</sup>

## SECOND AND THIRD TRIMESTER MANAGEMENT

### Question 4: How to appropriately manage pregnant women of advanced maternal age with scarred uterus in second and third trimester?

#### Recommendations and consensus

(1) Increase the frequency of examinations in second and third trimester moderately and screen for fetal cardiac abnormalities.

(2) Monitor coagulation function for pregnant women of advanced maternal age with scarred uterus, especially those undergoing fetal reduction.

#### Interpretation

(1) Increase frequency of prenatal examinations moderately according to basic diseases, pregnancy history and delivery history. Data from the European Survey of Congenital Anomalies with 51608 cases of congenital heart defects (CHD) suggest that mothers of advanced maternal age (35 to 44 years old when delivery) is linked with a higher prevalence of CHD compared to those aged 25–29 years, especially for some CHD subtypes (pulmonary valve stenosis, atrial septal defect, coarctation of aorta, and Tetralogy of Fallot).<sup>[22]</sup> We recommend to have fetal cardiac ultrasound examination from 18 w to 24 w<sup>+6</sup>.

(2) If a pregnant woman with scarred uterus misses the timing of fetal reduction in first trimester with a will to



perform it in second trimester, potassium chloride fetal reduction can be performed after evaluation. Thermal ablation fetal reduction can be performed for complex twins. Both are recommended to be conducted as early as possible from 14 w to 26 w<sup>+6</sup>, determining fetal reduction method according to chorionicity. For details, please refer to *Technical Specifications for Radio Frequency Ablation Selective Fetal Reduction (2021 Update)* from China, *Reduction of Multiple Pregnancy: Counseling and Techniques* from UK, and *Committee Opinion No. 719: Multiple Pregnancy Reduction* released by ACOG in 2017.<sup>[23–25]</sup> Combining national and local guidelines along with legal requirements, OBGYN should make sure patients counselled and guided as they choose between sustaining and reducing. The 13th Five Year Plan Key Research and Development Project conducted preliminary studies and found that we need to monitor blood coagulation function to prevent hemorrhage after reduction, no matter in first or second trimester.

### **Question 5: If pregnancy at scar site or suspect PAS is discovered in second trimester, how to manage it?**

#### **Recommendations and consensus**

Based on current experience, if we discover pregnancy at scar site or suspect PAS in second trimester, we should closely monitor patients and fully evaluate risks as well as advantages and disadvantages of alternative treatments. Make sure patients are informed.

#### **Interpretation**

There is a dilemma on how to handle CSP cases discovered late in second trimester due to missed diagnose or misdiagnose mainly for whether to choose expectant treatment or pregnancy termination. A systematic review pointed out that if the late-discovered CSP is lack of detectable fetal heart activity, expectant treatment is feasible as the likelihood of major maternal complications in such cases is relatively low. Conversely, failure to treat CSP with positive embryonic/fetal heart activity will result in high burdens of second trimester complications, and there is no confirmed optimal management currently.<sup>[26]</sup> A Chinese study suggests that if there are no signs of miscarriage or premature birth when CSP is discovered or PAS is suspected in second trimester, there is a high possibility of massive hemorrhage and inviable fetus during induced labor. Weighing advantages and disadvantages, induced labor is of no significant benefits for both mother and fetus, while damages are obvious. Terminating pregnancy until the fetus can survive may be of more benefits.<sup>[27]</sup> If these patients request pregnancy termination in the second trimester, it should be covered in a tertiary medical institution with experienced multi-disciplinary treatment (MDT) collaboration and rescue capabilities to optimize patients' outcomes.<sup>[28]</sup> CSP and PAS can lead to uterine rupture which may cause severe and insidious intraperitoneal hemorrhage. Therefore, thorough

evaluation and communication with patients are necessary.

### **Question 6: How to predict the potential risks of pregnancy with scarred uterus?**

#### **Recommendations and consensus**

- (1) It is recommended to predict the risk of PAS with a combination of medical history and imaging, and take serological examination if necessary.
- (2) It is recommended to assess the risk of uterine rupture with a combination of medical history and imaging.
- (3) We suggest a risk scoring table to predict the risk of iatrogenic premature birth and conduct timely referrals according to the score.

#### **Interpretation**

Placenta previa, PAS and uterine rupture are common complications of pregnancy with scarred uterus.

#### **Predict risk of pas**

PAS is a severe complication with adverse outcomes ranging from excessive hemorrhage, necessary for hysterectomy, disseminated intravascular coagulation (DIC), massive transfusion, ureteral/bladder/bowel injury, and even death.<sup>[29]</sup> With prenatal diagnosis as well as prediction of severity and related adverse outcomes, it will contribute to timely referral for high-risk patients. Care approach arrangement and necessary resources preparation by MDT in advance help improve prognosis of patients. Obstetric expert organizations across the world have developed clinical practice guidelines for PAS: *Diagnosis and Treatment Guidelines for Placenta Implantation (2015)* released by the Chinese Medical Association has introduced a flowchart for diagnosis and treatment of PAS.<sup>[30]</sup> The International Federation of Gynecology and Obstetrics (FIGO) has collaborated with maternal and fetal medicine experts from various countries or regions worldwide and developed a comprehensive PAS guideline.<sup>[31]</sup> The Society of Obstetricians and Gynaecologists of Canada (SOGC) released a clinical guideline for screening, diagnosis, and management of PAS in 2019.<sup>[32]</sup> The Society for Maternal-Fetal Medicine (SMFM) released a consensus in 2021 to standardize methods and biomarkers for ultrasound diagnosis of PAS.<sup>[33]</sup> Adhering to the three levels of prevention idea, how to predict risk of PAS at early stage is our focus.

- (1) Medical history: A cohort study from the Nordic population found that placenta previa, prior cesarean section (CS) and the number of CS, previous PPH, high body mass index (BMI), parous women, previous uterine surgery, women older than 35 years old, and *in vitro* fertilization (IVF) pregnancies are high risk factors for PAS.<sup>[34]</sup> A single-center case-control study of the IVF/intracytoplasmic sperm injection (ICSI) population in

USA found that cryopreserved embryo transfer is a strong independent risk factor for placenta accreta.<sup>[35]</sup> We are currently lack of a comprehensive medical history scoring system for PAS.

(2) Imaging: Ultrasound signs as “loss of low echo area behind placenta” and “excessive proliferation of sub-placental blood vessels” indicate highly suspicious PAS.<sup>[36]</sup> For placenta previa patients with scarred uterus, Chinese scholars recently developed a method that can effectively predict hysterectomy possibility before operation according to scoring of ultrasonic signs.<sup>[37]</sup> The ultrasound scoring scale from the 13th Five Year Plan Key Research and Development Project predicts PAS category, risk of intraoperative hemorrhage, and risk of hysterectomy based on imaging characteristics before delivery along with medical history.<sup>[38]</sup> Furthermore, in addition to previous research, the project team introduced prenatal three-dimensional (3D) power Doppler for patients with pernicious placenta previa to quantitatively evaluate vessel index of blood vessels around placenta in the lower segment of the uterus, which help predict PAS and serve as a supplement for the aforementioned ultrasound scoring scale.<sup>[39]</sup> The complete ultrasound scoring system developed by the project team shows in Table 1. In addition, the project team also found that MRI can further evaluate the depth and extent of implantation, on which is of certain value to predict invasive placental implantation and adverse pregnancy outcomes.<sup>[40]</sup>

(3) Serum biomarkers: Researchers from Turkey discovered that elevated serum YKL-40 level was correlated with diagnosis and severity of PAS.<sup>[41]</sup> To date, PAS-associated predictive biomarkers comprise alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), pregnancy-associated plasma protein A (PAPP-A), cell-free fetal DNA (cffDNA), angiogenic-related factors including placental growth factor (PLGF), vascular endothelial growth factor

(VEGF) and soluble fms-like tyrosine kinase-1 (sFlt-1), placenta-specific mRNA, microRNA, NanoVelcro chips *etc.* The existing research is not clear yet on how to predict PAS severity through these biomarkers and not applicable in clinical practice.<sup>[29]</sup> PAS diagnosis by imaging combined with serology is a promising research hotspot, and there is an urgent need for a comprehensive PAS scoring system applicable in clinical practice. Project team tested serum from ten patients who were pregnant with placenta previa and scarred uterus. We found that the expression levels of S100A9 in serum from six patients were significantly upregulated compared to the other four patients. The six with upregulated S100A9 developed PAS eventually, while the other four did not. The actual predictive value of serum S100A9 level for PAS in pregnant women with both placenta previa and scarred uterus calls for prospective experiments as further validation.<sup>[42]</sup>

Predict risk of uterine rupture

Pregnant women with scarred uterus should be highly aware of uterine rupture. Key improvements for maternal and fetal outcomes are risk prediction and early-stage signs identification of uterine rupture. We should notice that symptoms of uterine rupture are atypical and non-specific, which is difficult to identify. So it is necessary to inform pregnant women of advanced maternal age with scarred uterus of contingent uterine rupture.

(1) Predict uterine rupture by medical history: According to study results of the Royal College of Obstetricians & Gynaecologists (RCOG), ACOG, SOGC and the 13th Five Year Plan Key Research and Development Project, high-risk factors of uterine rupture in pregnant women of advanced maternal age with previous CS include: age older than 40, the number of previous CS or other uterine operations, history of uterine rupture, type of CS, continuity of myometrium monitored by ultrasound, estimated fetal weight > 4000 g, overdue pregnancy, obesity, history of CSP and CSP rupture.<sup>[43–48]</sup>

Table 1: Ultrasound scoring system predicts placenta accreta spectrum disorders in second trimester

Item	0	1	2
Placenta location	Normal	Low-lying (less than 2 cm from the cervical opening)	Placenta previa
Placenta thickness (cm)	< 3	≥ 3 and ≤ 5	> 5
Bladder line	Continuous	Discontinuous	Disappeared
Hypoechoic band behind placenta	Continuous	Discontinuous partly	Disappeared
Placental lacunae	Absent	Present	Fused into a piece, accompanied by the “boiling water sign”
Placenta basal blood flow	Basal blood flow is regular	Basal blood flow is increasing and clustering	Emergence of “cross-border” blood vessels
Placenta VFI	< 10	≥ 10 and ≤ 20	> 20
Cervical sinuses	Absent	Present	Fused into a piece, accompanied by the “boiling water sign”
Cervical morphology	Intact	Incomplete	Disappearing
History of CS	No	Once	More than once

VFI: vascularization flow index; CS: cesarean section.

(2) Predict uterine rupture by imaging: How to conduct imaging prediction is still a controversy and we should focus on monitoring myometrium continuity of the lower uterine segment. Our experts recommend that patients of PAS with previous CS are more likely to develop into uterine rupture if they have following signs: placenta locates at the anterior wall of uterus, blood sinus of the implanted placenta extends from the chorionic plate to serous layer of uterus, missing myometrium, and turbulence seen by ultrasound. MRI detects the depth of myometrium defect due to scar with certain reference value.

In order to prevent severe complications at delivery such as uterine rupture and severe hemorrhage, doctors often consider selective termination of pregnancy with scarred uterus, leading to an increase in iatrogenic premature delivery. The 13th Five Year Plan Key Research and Development Project established a scoring table for risk prediction of iatrogenic premature delivery in target population based on a single-center study (see Table 2). A comprehensive score less than 2 indicates low risk of iatrogenic premature delivery, score of 2 to 5 indicates medium risk, 6 to 8 indicates high risk, and more than 8 indicates extremely high risk.<sup>[49]</sup> When scores indicate a medium or high risk of iatrogenic premature delivery, we should inform patients and their family members, conduct timely referral to maternal-fetal medical center with rescue capabilities as well as neonatal intensive care unit (NICU), and continue prenatal examinations there. Table 2 is accessible with to be-collected-information easily obtained, convenient for basic-level hospitals, and applicable to clinical practice for reference. Nevertheless, its predictive value remains to be verified by a multicenter prospective cohort study.

## TERMINATION OF PREGNANCY AND DELIVERY MANAGEMENT

### **Question 7: How to determine appropriate timing of pregnancy termination for pregnant women of advanced maternal age with scarred uterus?**

#### **Recommendations and consensus**

(1) Individualize and determine the timing of pregnancy

termination based on history of scarred uterus.

(2) For patients suspected of PAS, evaluate and determine termination timing based on their second to third trimester situation.

#### **Interpretation**

(1) Pregnant women aged  $\geq 40$  with scarred uterus can terminate pregnancy from 39 w to 40 w<sup>+6</sup>. For those with history of uterine rupture, 34 w to 35 w<sup>+6</sup> may be the best termination timing by CS.<sup>[50]</sup> In cases with history of previous delivery by classical CS, termination from 37 w to 37 w<sup>+6</sup> is beneficial for newborns.<sup>[51]</sup> For those with history of myomectomy, selective CS is feasible after 38 w.<sup>[52]</sup>

(2) Patients suspected of PAS should have ultrasound examination at 28 w, 32 w, and 34 w and predict severity of PAS based on the aforementioned PAS ultrasound scoring system (Table 1) combining MRI examination and clinical manifestations, to decide individuation delivery timing.<sup>[53]</sup> FIGO guidelines recommend that pregnant women with a lower risk of antepartum hemorrhage can deliver at 37 w.<sup>[54]</sup> If there are situations including preterm premature rupture of fetal membranes (PPROM), uterine contractions, vaginal bleeding, and suspected placenta percreta, terminate pregnancy from 34 w to 36 w<sup>+6</sup>.<sup>[55]</sup>

### **Question 8: How to choose the appropriate method to terminate pregnancy?**

#### **Recommendations and consensus**

(1) Assess indications and contraindications before trial of labor after cesarean (TOLAC), and carefully manage puerpera at delivery.

(2) Know well operation history, conduct ultrasonic monitor and evaluation, analyze advantages and disadvantages of trial of labor versus CS, and help pregnant women and their family members make informed choices.

#### **Interpretation**

Pregnant women of advanced maternal age with scarred uterus are suggested to deliver at medical institutions with multidisciplinary collaboration and sufficient rescue capabilities. Obstetricians should fully inform pregnant

**Table 2: Risk scoring table for iatrogenic premature delivery**

Item	0	1	2	3
Height (cm)	> 160	> 150 and $\leq 160$	> 140 and $\leq 150$	< 140
Parity	0 or 1	2	-	$\geq 3$
Number of bleeding episodes during pregnancy	0	1	2	$\geq 3$
IPI (month)	-	$\geq 13$	0–12	-
Placenta previa	No	-	Yes	-
HIP	No	-	-	Yes

IPI: interpregnancy interval; HIP: hypertension in pregnancy.

women or puerpera and their family members of any situations.

(1) Women of advanced maternal age and women with scarred uterus are more prone to have breech presentation when deliver.<sup>[56]</sup> For management scheme of TOLAC, refer to 2019 ACOG guideline for TOLAC, 2016 Chinese expert consensus, 2013 French clinical practice guideline, and 2005 Canadian clinical practice guideline.<sup>[47,57–59]</sup>

(2) For puerpera with previous myomectomy, we need to know well size and type of myomas, whether entering uterine cavity at operation, suture methods *etc.*<sup>[60]</sup> We also need to carry out individual assessment, color Doppler ultrasound along with MRI prenatally to fully analyze risks of vaginal delivery.<sup>[61]</sup> Obstetricians inform puerpera and their family members of advantages and disadvantages of labor trial and CS respectively, with informed consent well signed. Extend indications for CS when puerpera are over 40 with adverse history of pregnancy and childbirth.

### Question 9: Before termination, what preparations are necessary?

#### Recommendations and consensus

(1) For puerpera of high risk, prenatal multidisciplinary consultations are recommended to develop treatment and

emergency plans.

(2) Estimate intraoperative hemorrhage for PAS patients based on ultrasonic scoring and prepare accordingly.

#### Interpretation

(1) Risks of perinatal complications for puerpera of advanced maternal age with scarred uterus is high, involving a wide range of disciplines, which we should attach great importance to MDT consultation. For patients with complex situations or suspected PAS in uterine scar, MDT should be organized to obtain diagnosis and MDT plans. Adequately talk with puerpera and their family members, inform situations, elucidate advantages and disadvantages of alternative treatment plans, and inform them of possible emergency situations.

(2) Project team found that the ultrasound score of PAS patients positively correlates between the volume of intraoperative hemorrhage. Low score of  $\leq 6$ , medium score of 7–9, and high score of  $\geq 10$  correspond to intraoperative hemorrhage volume median value of 600 mL, 1200 mL, and 2500 mL, respectively.<sup>[62]</sup> Operation teams can prepare blood and other preparations according to the score (see Table 3 as a preparation checklist before pregnancy termination for PAS patients), or transfer timely to medical institutions with sufficient capabilities.

**Table 3: Checklist for preparation before pregnancy termination in patients with placenta accreta spectrum disorders**

Category	Items to check
Preoperative examination	<input type="checkbox"/> Blood routine Hb ____g/L; PLT ____ $\times 10^9$ /L <input type="checkbox"/> Blood coagulation FIB ____ g/L; D-Dimer ____ <input type="checkbox"/> Blood type[ ] RH[ ] <input type="checkbox"/> Thrombelastogram <input type="checkbox"/> Liver and renal function <input type="checkbox"/> CK-MB <input type="checkbox"/> AFP <input type="checkbox"/> CRP <input type="checkbox"/> Electrocardiogram <input type="checkbox"/> Echocardiogram <input type="checkbox"/> Urinary color ultrasound <input type="checkbox"/> Ultrasound of arteriovenous vessels in both lower limbs <input type="checkbox"/> PAS scoring ____points <input type="checkbox"/> Placenta MRI
Preoperative preparation	<input type="checkbox"/> Preparation of blood products: Red blood cells suspension ____IU; Plasma ____IU; Fibrinogen ____g; Platelet ____IU; Prothrombin complex ____IU <input type="checkbox"/> Drug preparation: Catecholamine ____; Carboprost tromethamine ____; Carboprost methylate suppositories ____ <input type="checkbox"/> Intraoperative antibiotics ____ groups <input type="checkbox"/> Commonly used intraoperative blood vessel extraction ____groups; Other blood collection vessels ____groups
Preoperative consultation	<input type="checkbox"/> Cystoscopy +D-J <input type="checkbox"/> Catheter <input type="checkbox"/> Imbedding Departments, persons, and contact information _____ <input type="checkbox"/> Femoral artery separation and aortic balloon implantation Departments, persons, and contact information _____ <input type="checkbox"/> Intraoperative bedside ultrasound Departments, persons, and contact information _____ <input type="checkbox"/> neonatal pediatric consultation Departments, persons, and contact information _____ <input type="checkbox"/> ICU preparation Departments, persons, and contact information _____ <input type="checkbox"/> Other consultation departments Departments, persons, and contact information _____
Operating room preparation	<input type="checkbox"/> Central venous catheterization <input type="checkbox"/> Peripheral vein <input type="checkbox"/> artery <input type="checkbox"/> Heating blood transfusion device <input type="checkbox"/> Heating blanket <input type="checkbox"/> Femoral artery separation in advance <input type="checkbox"/> Bring with ultrasound evaluation <input type="checkbox"/> Bring with MRI films
Necessary intraoperative examination	<input type="checkbox"/> Blood routine Hb ____g/L; PLT ____ $\times 10^9$ /L <input type="checkbox"/> Blood coagulation FIB ____ g/L; D-Dimer ____ <input type="checkbox"/> Thrombelastogram <input type="checkbox"/> Liver and renal function <input type="checkbox"/> Albumin <input type="checkbox"/> electrolyte

Hb: hemoglobin; PLT: platelet; FIB: fibrinogen; CK-MB: creatine kinase-MB; AFP: alpha-fetoprotein; CRP: c-reactive protein; PAS: placenta accreta spectrum disorders; MRI: magnetic resonance imaging; ICU: intensive care unit.



**Table 4: Risk scoring table for postpartum hemorrhage**

Item	0	1	2	3	4	5
Maternal age (years)	< 34	≥ 34	-	-	-	
Placenta location	Posterior wall of uterus	Anterior wall of uterus	Lateral wall or fundus of uterus	-	-	
Placenta previa	No	-	-	Partial placenta previa	Complete placenta previa	
HIP	No	-	Yes	-	-	
Fetal position	Longitudinal-head presentation	Longitudinal-breech presentation	Transverse	-	-	
PAS disorders	No	-	-	Adherent placenta or placenta accreta	-	Placenta increta or placenta percreta

HIP: hypertension in pregnancy; PAS: placenta accreta spectrum.

## POSTPARTUM MANAGEMENT

### Question 10: How to manage in postpartum period?

#### Recommendations and consensus

(1) Puerperal management focus on PPH, puerperal infection and thrombosis. We recommend to predict and prevent related risks.

(2) Educate about the importance and measures of postpartum contraception to puerpera and their husbands.

#### Interpretation

(1) Twenty-four hours after delivery is a high-risk duration for PPH, indispensable of close observations. As for patients indwelling abdominal drainage tubes, obstetricians should be aware of whether the tube is unobstructed, and changes in amount and properties of drainage fluid when changing body position. When needed, monitor vital signs, Hb decline, transabdominal ultrasound or CT examination to indicate PPH. For details, please refer to ACOG 2017 practice bulletin for PPH, recommendations from the National Athletic Trainers Association (NATA) (the Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis), FIGO recommendations, and SOGC 2022 PPH clinical practice guideline, Chinese 2014 PPH guideline<sup>[63–67]</sup>. The Project team has established a scoring table to predict PPH risks after CS in target population (see Table 4 for details). Score of < 4 is classified as low risk, 4–8 medium risk, 8–12 high risk, and > 12 is extremely high risk.<sup>[68]</sup> The scoring table is accessible with to be-collected-information easily obtained, convenient for basic-level hospitals, and applicable to clinical practice for reference. Nevertheless, its predictive value remains to be verified by multicenter prospective cohort study.

(2) According to a systematic review, episiotomy, delivery by assisted vaginal birth and CS, prolonged delivery duration, as well as unnecessary intrapartum interventions and manipulations, would increase postpartum infections.<sup>[69]</sup>

For groups of high risks, antibiotic usage duration can be extended appropriately, with antibiotics upgrade if necessary.

(3) Re-assess risks of VTE immediately after childbirth, and inform puerpera of risks and countermeasures. Postpartum VTE risk factors evaluation and thrombosis prevention methods are detailed in RCOG 2015 guideline as well as consensus on obstetric VTE prevention and treatment from Shanghai experts in China.<sup>[70,71]</sup>

(4) For women who have a second CS or those have uterus retained with PAS, we recommend to perform tubal ligation simultaneously at CS with informed consent.

## CONCLUSION

Covering all the most clinically concerned questions ranging from pre-pregnancy assessments to pregnancy management and postpartum care with expert recommendations along with exhaustive interpretation, this consensus interpretation can serve as practical guidance for clinicians on how to manage women of advanced maternal age with scarred uterus to have newborn babies.

## DECLARATION

### Author contributions

Xiong Z: Investigation, Investigation, Writing and Editing – Original manuscript. Abdelrahim MF: Reviewing and Editing. Huang L: Supervision and Reviewing the manuscript.

### Ethics approval

Not applicable.

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### Conflict of interest

Authors have no competing interests to declare.

### Data availability statement

Not applicable.

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