

**The aftermath of conservative management of placenta accreta: Can these women
and their uteri handle another pregnancy?**

Julia Knypinski

DISSERTATION

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ABSTRACT

The aftermath of conservative management of placenta accreta: Can these women and their uteri handle another pregnancy?

Julia Knypinski

The University of Texas Southwestern Medical Center, 2015

Supervising Professor: C. Edward Wells, M.D.

Background: Placenta accreta, an invasion of the placenta into the myometrium of the uterus, is one of the leading causes of postpartum hysterectomies. The American Congress of Obstetrics and Gynecology (ACOG) recommends that when placenta accreta is suspected, a hysterectomy should be performed without attempting to remove the placenta. Several methods exist for the conservative management of placenta accreta, which leaves women capable of subsequent pregnancies.

Objective: The purpose of this literature review is to evaluate the fertility and pregnancy outcomes of women who undergo conservative management of placenta accreta.

Methods: An online literature search was performed looking for key works. Retrieved articles, their references, and past literature reviews on the subject were screened for relevance.

Results: Several studies assessing the fertility outcomes of women after conservative management of placenta accreta were found. 345 subsequent live births were documented with a recurrence rate of placenta accreta of 21%. It was found that previous C-sections and placenta previa pose the greatest statistical risk for placenta accreta. Relatively few women desired another pregnancy and postpartum hemorrhage can have a significant negative psychological impact on women.

Conclusion: Women who undergo conservative management of placenta accreta can successfully carry pregnancies to term. Children born of these pregnancies have no neonatal morbidity. The rate of recurrence of placenta accreta and postpartum hemorrhage remains high.

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INTRODUCTION

My Experience:

The International Medical Exchange Program (IMEP) is a wonderful opportunity for UT Southwestern students to explore the world of medicine abroad. Every year it allows a few brave souls to step out of the realm of comfort that comes with the four-year plan and set off on a journey to discover the world, their careers and especially, themselves. Throughout this year students are exposed to four three-month long rotations of their choice. The first two are completed in Paris through our relationship with the University of Paris Descartes in some of Paris's most prestigious and historic hospitals. The following two rotations are chosen from an array of countries and programs around the world in an effort to foster a better understanding of the challenges of medicine in underdeveloped countries. As someone who comes from a diverse background and has always felt a citizen of the world, this program felt like the perfect supplement to my medical education. Thanks to the efforts of countless people I was given the opportunity of spending one year of my life doing the work I love and learning from the patients I love in three languages, across three continents. Opportunities like IMEP allow students to gain a different perspective on the medicine we deal with every day and foster in students a sense of curiosity and creativity in problem solving.

My first rotation in Paris was in obstetrics at the Port-Royal maternity ward. I was taking a 24-hour call and was paged into the operating room for an emergency C-section. All I knew about the patient was that we were delivering a 25-weeker due to severe pre-eclampsia and that this was going to be a repeat C-section. Upon entering the abdominal cavity and exposing the uterus I saw a large mass of oddly shaped purple tissue over the uterus and the resident started very urgently and quickly speaking with the attending on call. I caught the words placenta accreta and understood the apprehension and stress in the room. What we were facing was an anteriorly positioned, placenta accreta, and complete previa. The resident swiftly decided to deliver through a high classical uterine incision and passed off the tiny preemie to the midwife. Focusing back on the mother and the bulging purple mass in front of us I automatically assumed we would proceed with a hysterectomy. Although this woman was young, in her mid-20s, she had 3 children now,

two of which were born very pre-maturely due to severe pre-eclampsia, now was status post two C/sections, and the likelihood of her and her uterus being capable of carrying a subsequent pregnancy to term, to me, were slim and risky. However, in the discussion between the resident and attending, the option of hysterectomy was never mentioned. First they discussed uterine embolization, which was rejected as an option after they realized it was the middle of the night on a weekend and the interventional radiologist was not available. Next, they discussed hypogastric ligation and decided that it was the best option. I spent the next three hours holding up the uterus while an OBGYN resident performed vascular surgery in the middle of the night, as if this was a completely common practice.

The patient made it through surgery without a major hemorrhage and was placed on the high-risk post-partum floor where our team followed her care. The hope was that after devascularizing her uterus the placenta's blood flow would be cut off, it would separate from the myometrial layer and eventually be passed or reabsorbed. Unfortunately for this woman, this was not the case. Her uterus had a very strong collateral arterial supply and the ligation did not devascularize the placenta as anticipated. Daily uterine Dopplers continued to show that the placental had a strong blood supply. Furthermore, because her placenta was also a complete previa there was no exit for her placenta as the os was covered. Thirdly, her hypertension and severe preeclampsia did not resolved as her placenta was still in situ and she continued to need multiple IV anti-hypertensive medications to keep her blood pressure within normal range. In addition to all of these medical issues, this woman was undocumented, homeless and now the parents of a 25-week preemie in addition to her other children. When I asked why we had not done a hysterectomy following the C-section, I was told that it was due to her young age and that at the time it had been medically unnecessary as she was hemodynamically stable. Eventually, when the patient became medically stable and controlled on oral anti-hypertensives, we were forced into discharging her. My resident agreed that she would likely re-present to the emergency room in septic shock and need a hysterectomy at that time. In the end, the efforts of the team to preserve her uterus and her fertility had failed. This woman would never carry a child to term again and, because of the conservative management she received, would need additional medical care, additional surgery, and the additional risks that come with it.

Fast-forward half a year and I am finishing up my obstetrics and gynecology rotation in Lima, Peru at the National Maternal and Perinatal Institute. A urogynecologist approaches me with the case of a 29-year-old G2P1 at 34 weeks with a history of 1 previous C-section, a complete placenta previa with premature rupture of membranes who had a diagnosis of placenta accreta. During the C-section a partial hysterectomy was performed when it was discovered that she had placenta percreta with invasion into the bladder and cervix. The patient went on to develop hematuria with hydroureter and hydronephrosis and spent an extended period of time in the hospital. Since it was obvious that conservative management of this issue might have benefitted this patient I decided to dedicate this paper to learning about the options for conservative management of placenta accreta and its implications for future pregnancies.

Let's look at some numbers:

Bleeding is the most significant cause of maternal death worldwide with more than half of those occurring within the first day of delivery. About 10.5% (some estimate as high at 12-17%) of live births world-wide, or about 14 million births, are complicated by postpartum hemorrhage; a woman dies every 4 minutes from postpartum hemorrhage.¹ Uterine atony and placenta accreta are the two leading causes of postpartum hysterectomies with up to 64% of Cesarean hysterectomies done for abnormally adherent placentation.²

An abnormally or morbidly adherent placenta, sometimes simply referred to as placenta accreta, is a pathological attachment and invasion of placental tissue into the myometrium of the uterus. There are three subtypes defined by the extent of invasion, these include accreta where the chorionic villi attach to the myometrium, increta where the chorionic villi invade into the myometrium and the most severe case of percreta where the chorionic villi invade through the myometrium, often attaching to surrounding organs. (See Figure 1.) The diagnosis can be made clinically when the placenta does not detach during the third stage of labor or on histological sample, it can also be suspected to varying degrees using imaging including ultrasound and MRI.³ The incidence of morbidly adherent placenta has been increasing with recent numbers as high as 1/333-533 deliveries. In the Assessment of Perinatal Excellence study, which spanned from 2008 to 2011 across 25

institutions in the USA the overall frequency of placenta accreta was 1/731 births on average but varied from none to 1/197 depending on the hospital.⁴ In a large Canadian study the incidence of placenta accreta was 14.4/10,000 births and placenta accreta with postpartum hemorrhage was 7.2/10,000 live births.⁵

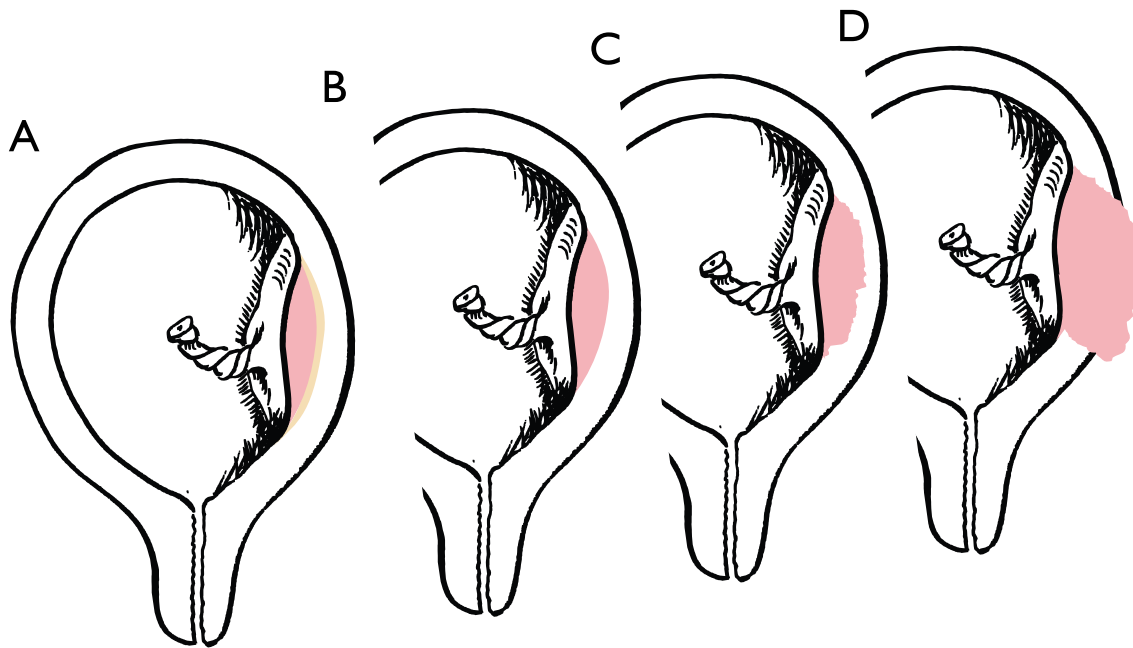


Figure 1: Abnormal placentation. A: Normal placenta with intact decidua. B: Accreta with villi attached to the myometrium. C: Increta with villi invading into the myometrium. D: Percreta with villi invading through the myometrium and serosa. Image by R. Kraszewski

Placenta previa and increasing numbers of C-sections are two independent risk factors for placenta accreta. This is due to the fact that damage from the hysterotomy causes the placenta to grow at the scar site into the myometrium since the protective barrier of the Nitabuch layer is destroyed.^{6,7} Placenta previa in the current pregnancy with a previous C-section is the most strongly associated risk factor, followed by placenta previa and then by previous C-sections. In the Canadian study, only 8.8% of patients had both risk factors.⁵ Other lesser risk factors also reported include advanced maternal age, multiparity, nulliparity, prior uterine instrumentation, surgery or radiation, fibroids and structural anomalies, pregnancy-related hypertension, and smoking.^{5,8} However, Bowman et al. showed that after controlling for both placenta previa and previous C-sections no other risk factors could be identified.⁷ However, there is evidence that increased maternal age is a risk factor for increasing numbers of C-sections and placenta previa, so its difficult to tease

out this risk factor.⁹ Silver et al. studied the maternal morbidity of increasing rates of C-sections through the Maternal-Fetal Medicine Units (MFMU) Network and reported that the rate of placenta accreta is directly correlated to the number of previous C-sections and that placenta previa increases the risk substantially as shown in Figure 2.¹⁰

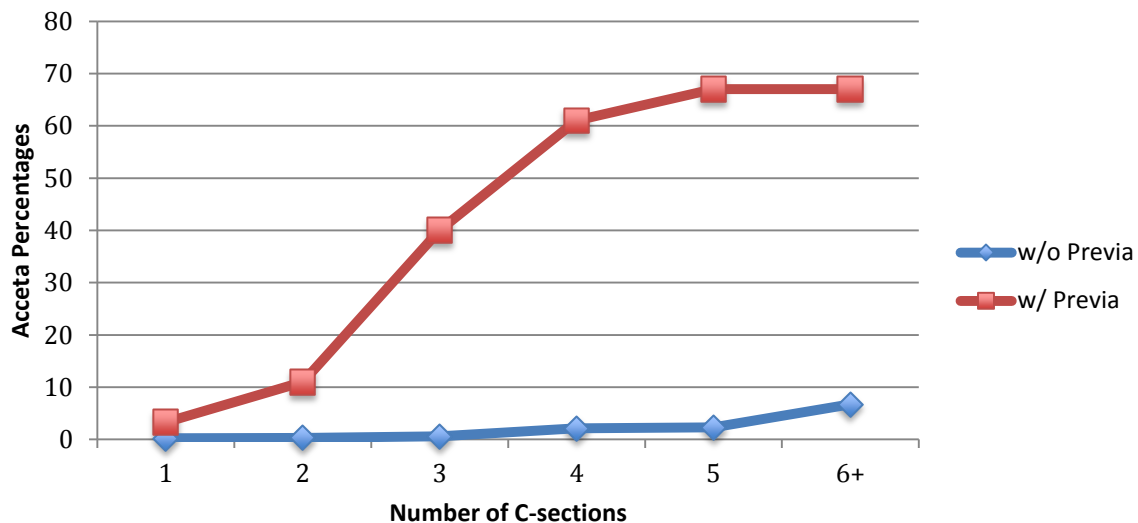


Figure 2: Placenta accreta risk with placenta previa. The percentage of pregnancies increases with each C-section and a pregnancy with a placenta previa augments the risk substantially. Adapted from: Silver, 2006.¹⁰

Placenta accreta is an ever-feared obstetric complication as the forcible removal of the placenta can, and often does, lead to massive hemorrhage from the exposed spiral arteries.¹¹ Although reports vary on the incidence of maternal mortality due to placenta accreta and its sequelae, it has been estimated as high as 6-7%.⁸ However, some studies show that there has been an alarming increase of maternal morbidity that can likely be attributed to an increase in the number of C-sections, which leads to higher rates of placenta accreta and thus higher risks of massive postpartum hemorrhage.¹⁰ Both C-sections and placenta accreta have been increasing at a fast rate, as shown in figure 3.⁶ In a retrospective look by Breen, it was found that 1/7000 deliveries was complicated by placenta accreta between 1871-1972.¹² In the 70s, that rate increased to 1/4027 and then up to 1/533 in a study looking at the twenty years between 1982-2002.¹³ This was mirrored by the increased C-section rate from 5% in the 70s to almost 33% in 2010.¹⁴

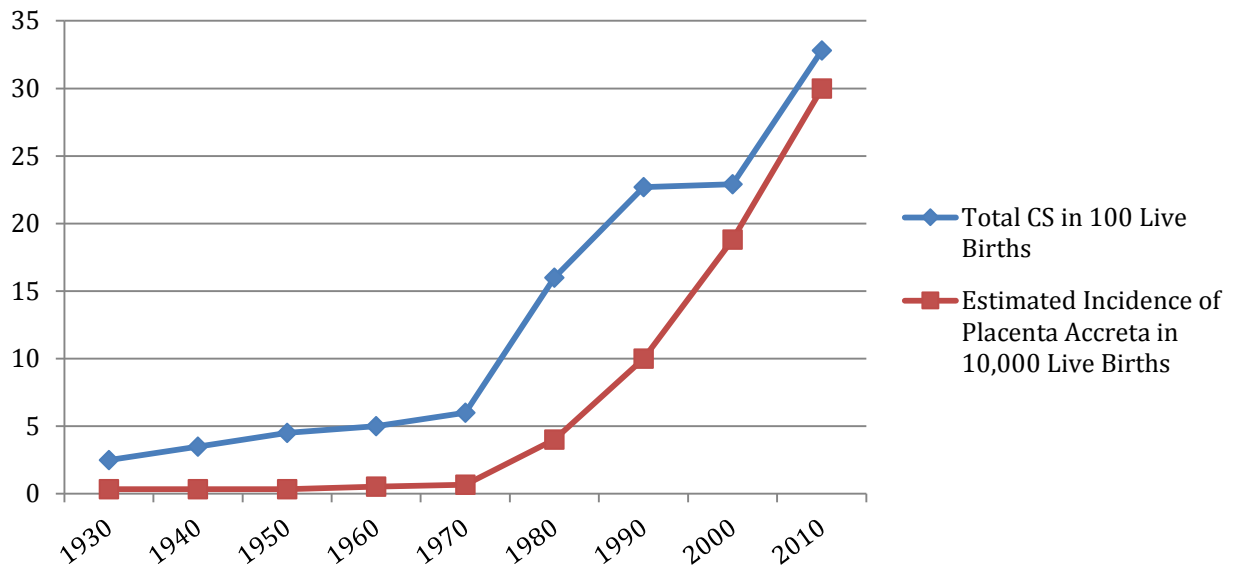


Figure 3: Paralleled increasing rates of placenta accreta and C-sections. Over the last decade the increasing number of C-sections has been paralleled with an increasing rate of placenta accreta. Adapted from Wortman, 2013.⁶ Total CS in 100 live births.^{6,14,15} Estimated incidence of Placenta Accreta in 10,000 live births. ^{6,8,16,17}

Management: What are the options?

Throughout time and in different countries there have been several methods used to manage placenta accreta. Two questions arise in the treatment of placenta accreta; one related to the placenta and one related to the uterus. First, do you leave the placenta in situ or forcibly remove it (referred to as extirpative management)? And secondly, do you leave the uterus in (referred to as conservative treatment) or perform a hysterectomy. Additionally, many different methods have been attempted to control bleeding, both after a hysterectomy and in an attempt to prevent a hysterectomy and conserve the uterus. The first documented case of conservative treatment was in 1986 when the placenta was left in situ and methotrexate was administered postnatally. The patient spontaneously passed the placenta and had no further complications.¹⁸ Since then, other forms of adjuvant therapy have been used in an effort to control bleeding and preserve the uterus including embolization, ligation of pelvic arteries, balloon occlusion and different forms of suturing of the uterus or placental bed. Case series have shown that conservative management is successful in up to 78-80% of cases with a 6% rate of severe maternal morbidity.^{19,20} Of the women who failed conservative management and required a hysterectomy, half were primary (within 24 hours of delivery) and half were delayed over 24 hours. Very close

follow up is required when managing a patient conservatively as it may take up to 6 months to fully resorb the placenta and sometimes hysteroscopy and resection of retained tissue is needed.²⁰ This paper will focus on the fertility and subsequent pregnancies of women who have had conservative treatment for placenta accreta around the world.

MATERIALS AND METHODS:

Ovid MEDLINE and PubMed were searched for studies published in English or French. Search terms included; placenta accreta, morbidly adherent placenta, placenta percreta, placenta increta, fertility, pregnancy outcomes, conservative management. Reference lists of retrieved articles were screened. Articles incorporated into past literature reviews on the subject were screened.

RESULTS:

Allons-y: the French approach:

Since my original experience with this subject matter was in Paris, France at Port-Royal I decided to start my search there. I discovered that Port-Royal is the institution that originally introduced conservative management of placenta accreta to the French hospital system. There are a series of studies that come out of the French public hospital system that have evaluated different methods of controlling post-partum hemorrhage, both in the context of placenta accreta as well as other pathologies and the future fertility and pregnancy outcomes of these women.

It all began with a case study published in 2002 from the Maternity Ward at Port-Royal in Paris describing the successful conservative management of a patient with placenta accreta who went on to have a successful pregnancy. Treated in 1997, she was a G4P2 with a past obstetric history of a C-section for failure to progress, a subsequent normal vaginal delivery, and a dilation & curettage for a spontaneous first-trimester abortion. Placenta accreta was not suspected prenatally and when it came time to deliver, she had an uneventful vaginal delivery. However, the placenta did not deliver spontaneously after the allotted 30 minutes. When attempts were made to remove it, only fragments broke off at which point the team clinically diagnosed her with placenta accreta. Because the woman was hemodynamically stable, not actively bleeding, and desired future

fertility it was decided to leave the placenta in situ and embolize her uterine arteries prophylactically in order to prevent delayed bleeding. The patient was closely monitored and had no complications. Pathology did confirm a placenta accreta with placental vili invading into the myometrium. Serum progesterone and hCG levels were serially followed and normalized 85 days after delivery. The placenta left in situ was resorbed in 6 months with sonography showing a normal uterus. The woman went on to have a 5th pregnancy with no complications, the baby was delivered vaginally, the placenta was extracted manually, pathology showed a normal placenta. This was the first reported case of a pregnancy with normal delivery and placentation after conservative treatment of placenta accreta.²¹ Because of this case and a growing number of case reports showing good results with conservative management, a decision was made to change protocols at the Maternity Ward at Port-Royal.

In June of 1997 the protocol shifted from one of systematic manual removal of the placenta in order to leave the uterine cavity empty (extirpative management) to the newer protocol that treated placenta accreta conservatively and left it in situ. Thus researchers have information from 1993-1997 using traditional extirpative methods and from 1997 on using conservative management. Since implementing a conservative management approach the rate of hysterectomies has greatly decreased. From 1993 to 1996, 8 of 9 cases of placenta accreta were managed with a hysterectomy while from 1997 to 2001, the number of cases did not change at 9, but there were 0 hysterectomies.²¹

In a study published in 2004 researchers at Port-Royal looked at these two groups of women, one before and one after the change in practice. There were 33 cases of abnormal placentation (including placenta accreta, increta, and percreta) and the two groups consisted of women from Jan 1993- June 1997 (Group A) and women from July 1997- Dec 2002 (group B). In this study placenta accreta was defined in four different ways, both clinically and histologically. The criteria for diagnosis included:

1. Difficulty manually removing the placenta with no cleavage plane.
2. Heavy bleeding from implantation site after forced removal during a C-section.
3. Histological confirmation.
4. Prenatal diagnosis with failure to remove at time of delivery.

Conservative treatment depended on whether the diagnosis was suspected before delivery. If the discovery was made when gentle removal was unsuccessful and the patient was stable then the placenta was left in situ, as in the earlier case report from 1997. If the diagnosis was suspected prenatally the case was discussed on departmental rounds and the following plan went into effect:

1. The exact placental position was determined using imaging techniques.
2. A C-section was planned with a midline skin incision and vertical uterine incision away from the placental bed.
3. Delivery of the placenta was attempted with oxytocin and moderate cord traction.
4. If extraction failed the placenta was left in situ.

Maternal morbidity was determined by need for transfusion (the transfusion protocol did not change between these two periods), hysterectomy, ICU admission and length of stay, DIC and endometritis with or without sepsis.²²

Results showed that the two groups did not differ significantly on any demographics or risk factors. Of note, the average gestational age for the groups was low (33-35 weeks) as 17/33 (51%) went into spontaneous preterm labor or had vaginal bleeding and delivered early. In terms of risk factors, all but one woman had a previously known risk factor for placenta accreta with placenta previa being present in 20/33 patients (60.6%).²² This is similar to the follow up study done in 2010 that showed that 95.8% of women with placenta accreta had at least one risk factor with placenta previa (52.1%) and a previous c-section (53.8%) being the highest risk factors and with 31.7% (53/167) having both.²⁰ In group A, who was treated with forcible removal of the placenta, 11/13 (84.6%) patients had a hysterectomy and in group B, who were treated conservatively, only 3/20 (15%) had a hysterectomy. Of the three hysterectomies that were performed, one was diagnosed prenatally and the patient desired surgical management, the second was due to massive hemorrhage when the surgeon forcibly removed the placenta not realizing it was an accreta, and the third was a delayed hysterectomy on post-partum day 26 due to severe endometritis and recurrence of hemorrhage. In period A only 2 artery ligation were performed compared to 6 in period B, however this was not statistically significant. Other complications in group B included 6 cases of postpartum endometritis, 3 of which were

confirmed sepsis and treated successfully with antibiotics. However, group B had fewer transfusions and DIC, meaning that even if future fertility is not desired, conservative management could reduce the risk of bleeding. The time to resorption of the placenta was 3-12 months (averaging 6 months) and one patient came in with contractions and cervical dilation on postpartum day 15 and expelled the placenta.²² Not much data was available at the time of the study about future fertility and pregnancy outcomes. However 6 years later, the researchers went back and telephoned this same cohort of women to ask about their pregnancy outcomes as part of a national multicenter study. This multicenter study is discussed in detail in the next section.²³

Multicenter French Study:

In 2010, two new studies were published using the French public hospital system, which includes Port-Royal. This was a much larger study as it included more women (Jan 1993 to Dec 2007) and 40 (out of 45 = 88.9%) tertiary university hospitals across the country. Of the 40 hospitals that agreed to participate, 25 (62.5%) had used a form of conservative management for a placenta accreta during these years. Since earlier studies were smaller and only involved one tertiary care institution the results were less capable of being extrapolated. One of these articles examined the maternal morbidity outcomes and the other fertility and pregnancy outcomes for women who had undergone conservative management of placenta accreta.^{20,23} It's important to note that this study cannot truly be compared to the Port-Royal study of 2004 considering those women with conservative management were among the 167 of this study. This is also true of two studies out of two University hospitals in Marseilles. One article in 2005 and one in 2010 looked at the fertility and pregnancy outcomes of women treated conservatively for placenta accreta during 1993-2007.^{24,25} Both of these hospitals are included in the multicenter study as are some cases studies from Port-Royal on placenta percreta and successful subsequent pregnancies.²⁶

Due to the longer time frame, more hospitals performing conservative management, and increasing C-section rates the number of women who were eligible for this study was substantially higher at 167 (out of 311 with placenta accreta – 62.5%). Unlike the other smaller studies that compared women with placenta accreta who were treated with

extirpative management vs conservative management, this study focused only on the results of women treated with conservative management. In this study the primary outcome was uterine preservation and the secondary outcome was maternal morbidity defined as a composite of the following: sepsis, septic shock, peritonitis, uterine necrosis, postpartum uterine rupture, fistula, injury to adjacent organs, acute pulmonary edema, acute renal failure, deep vein thrombophlebitis, pulmonary embolism or maternal death.

Results of this larger study showed that, of the 311 women who were diagnosed with placenta accreta, 53.7% were treated using conservative management. It was interesting to see the trend in conservative management of placenta accreta as well as the increasing numbers of women with placenta accreta. For example, the first case managed conservatively was in 1993 and was the only case that year, the cases per year steadily increased as the number of hospital willing to do conservative management increased. In 1997, when Port-Royal changed its protocol, many hospitals following its lead and by 2007 there were 25 cases in 13 hospitals around France. (See Figure 4.)

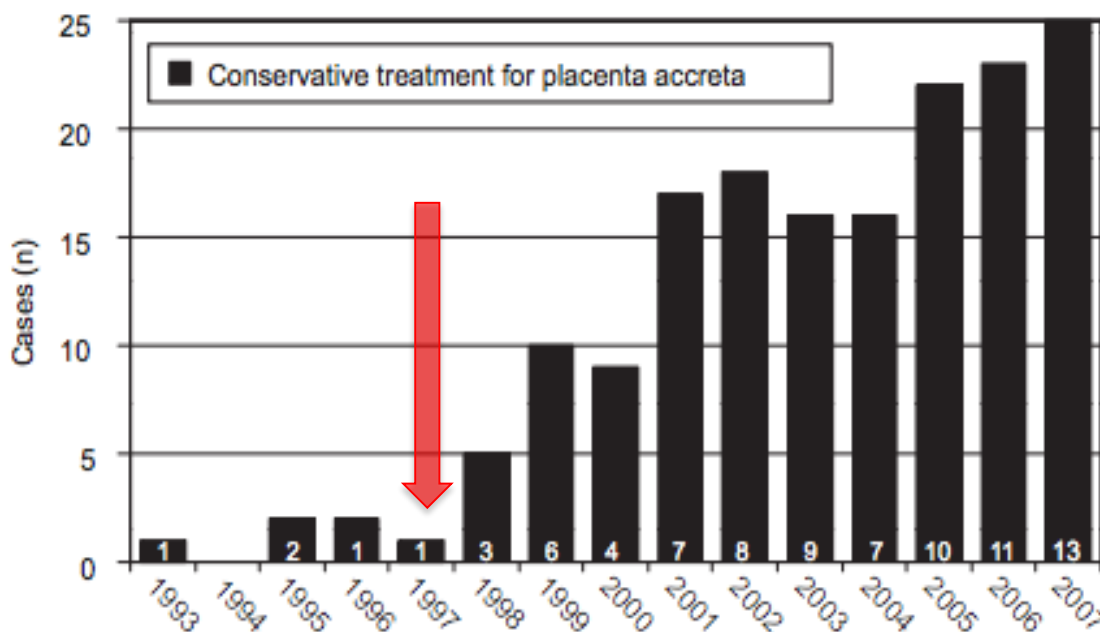


Figure 4: Rates of conservative management of placenta accreta in France. The annual number of cases of placenta accreta treated with conservative management during 1993-2007 in hospitals across France. The number in the bars indicates the number of hospitals performing conservative management and the height indicates the number of total cases. The red arrow points to 1997 when the Port-Royal protocol was changed. From: Sentilhes, 2010. ²⁰

As in the smaller Port-Royal study,²² most women (95.8%) had at least one risk factor for placenta accreta with placenta previa (52.1%) and a previous C-section (53.8%) being the most common - 31.7% of women had both risk factors. The same protocol for diagnosis and management of placenta accreta was used in these institutions as the one established by Port-Royal in 1997. Since the protocol states that if the diagnosis is made prenatally a planned C-section is scheduled, and due to the likely increasing use of imaging for diagnostic purposes, 74 cases were diagnosed prenatally and had planned C-sections. Additionally, other women had C-sections, bringing the total to 113/167 (67.7%). About half, 86, of women with placenta accreta had primary postpartum hemorrhage, of these 15 (17.4%) were managed with uterotonics only, 57 required uterine devascularization of some kind and 18 required a hysterectomy, some needing both. Only 10.8% of women needed a primary hysterectomy, all due to primary postpartum hemorrhage. However, an additional 10.8% needed a delayed hysterectomy, for a variety of reasons, of which secondary postpartum hemorrhage accounted for 44.4%. In the end, 131 women (78.4%) were treated successfully with conservative management. Ten (6.0%) women suffered severe maternal morbidity including 1 maternal death. Of those 10 women, 8 (80%) needed delayed hysterectomies due to severe, and often multiple complications. One woman had a bladder injury during a primary hysterectomy and 1 had a pulmonary embolism without a hysterectomy. Of the 109 women who underwent a uterine devascularization, about half (52.3%) had it due to primary postpartum hemorrhage and the other half (47.7%) was prophylactic. In this study the median time to spontaneous placental resorption was 13.5 weeks with a wide range, and 25% of women needed to have a hysteroscopic resection, curettage or both to remove retained placenta. Placenta percreta was diagnosed in 18 women and all had the placenta left in situ. In this sub set of patients, 4 (22%) had primary hysterectomies for postpartum hemorrhage and 4 (22%) had delayed hysterectomies. Meaning, that 10/18, or 55.56% were successfully treated with conservative management. For the 8 cases of placenta percreta with bladder involvement, 6 (75%) were successfully treated with conservative management. Of the ten women who suffered severe maternal morbidity, 3 (30%) had placenta percreta of which 2 had bladder involvement.²⁰

Another study was conducted to determine if these 131 women who were successfully treated (no hysterectomy) were capable of becoming pregnant, and the results of those pregnancies.²³ In 2008, a researcher successfully contacted 96 (73.3%) of the women, of those 85 (88.5%) patients had preserved fertility. There were 9 patients who underwent a bilateral tubal ligation and 2 patients with synechiae that were either untreated or failed treatment. Of the 85 women with retained fertility, only 27 (31.8%) desired a pregnancy. Interestingly, the other 58 (68.3%) of women stated fear of recurrence of placenta accreta as the primary reason for not pursuing another pregnancy. Of the 27 who desired pregnancy, 3 were trying to become pregnancy at the time of the study, and 25 had cumulatively had 34 spontaneous pregnancies; none of these 34 pregnancies were through assisted reproduction. Twenty-one (61.8%) of the pregnancies ended in third-trimester deliveries, occurring to 18 women. Placenta accreta recurred in 6/21 (28.6%) of the pregnancies carried to term and was treated successfully with conservative management in 4/6 cases (66.7%). The other two cases were managed with a C-section/hysterectomy and a hysterectomy after unsuccessful extirpative treatment. Of all 21 deliveries, postpartum hemorrhage occurred in 4 (19%) and was due to placenta accreta in 3/4 of those cases. Importantly no adverse neonatal outcomes were noted for women who had had embolization or vessel ligation. Of the 21 infants born, only one infant was born small for gestational age, however his mother had current and past history of pre-eclampsia. This study concludes that conservative management for placenta accreta does not negatively affect a woman's fertility and pregnancy outcomes, however, the risk of recurrence of placenta accreta and postpartum hemorrhage is substantial.²³

Comparing placenta accreta to postpartum hemorrhage:

Another series of articles was published out of France on the fertility and pregnancy outcomes following different conservative management for severe postpartum hemorrhage. Although our interest in this review is the effects of conservative management of placenta accreta on future fertility and pregnancy, placenta accreta is a cause of postpartum hemorrhage. Although placenta accreta only accounts for a low percentage of postpartum hemorrhage, up to 50% of placenta accreta causes postpartum hemorrhage (22.6% with severe postpartum hemorrhage) and 29% of postpartum hemorrhage with

hysterectomies is due to placenta accreta.⁵ Additionally, since placenta accreta is a rare diagnosis and conservative management is not currently the worldwide standard the studies are small. By using the fertility and pregnancy outcomes of women who underwent conservative management for all types of postpartum hemorrhage we can see more robust results. Two studies came out of the Antoine-Béclère hospital in Clamart, which is on the outskirts of Paris. Both were published in 2003, one investigates the fertility and pregnancy outcomes following hypogastric artery ligation and the other pelvic artery embolization for the indication of postpartum hemorrhage.^{27,28}

In 2001 it was noted that postpartum hemorrhage was the leading cause of maternal death in France, accounting for 11.4% of maternal death between 1995 and 1997.²⁹ Although these conservative techniques had been around for some time, this study evaluated the fertility and pregnancy outcomes of 68 women who had a hypogastric artery ligation due to postpartum hemorrhage over the span of 13 years. Forty-five (66.2%) of women were available for follow up questions of which 17 (37.8%) women had 21 pregnancies with 13 (61.9%) third trimester live births. No cases of secondary infertility were noted and the women had an average time of <12 months to conception from when they decided to get pregnant. Of those 13 successful pregnancies, 3 (23%) had recurrence of postpartum hemorrhage that was treated medically. Of the 21 pregnancies that occurred after hypogastric artery ligations, 4 of those women had had their ligation due to placenta accreta. However, of those 4 only one had a successful third-trimester pregnancy. The other three ended in an abortion, an ectopic and a miscarriage. Interesting was, again, the low number of women who desired a pregnancy, stating the fear of postpartum hemorrhage in any subsequent pregnancies.²⁷

In a similar study done at the same hospital and in the same year, researchers looked at the fertility and pregnancy outcomes of women who had undergone pelvic arterial embolization for severe postpartum hemorrhage. This was a smaller study, with 28 women over 5 years, 17 (60.1%) were found on follow up and 5 (29%) women had had 6 pregnancies, 4 (66.7%) of which led to third trimester deliveries. One woman was actively trying to conceive. Of the 28 women who had the procedure done, 5 were due to placenta accreta, 1 of which went on to have a subsequent pregnancy with delivery complicated by postpartum hemorrhage due to recurrent placenta accreta. A hysterectomy was required.

All four of the successful pregnancies ended in postpartum hemorrhage and two had hysterectomies, the previously mentioned woman with recurrence of placenta accreta and another woman for placenta accreta who had had her initial postpartum hemorrhage due to uterine atony. As with the previous study, it was noted that a surprisingly small number of women wanted another pregnancy, and most stated that fear of postpartum hemorrhage and its complications was the main reason.²⁸

Two more studies out of France, this time from the University Hospital in Rouen were published in 2008 and 2009 about the fertility and pregnancy outcomes after uterine devascularization and pelvic arterial embolization for postpartum hemorrhage.^{30,31} The study on arterial embolization used a cohort of women over 13 years as opposed to 5 years and thus had a much larger sample size. The main goal of this study was to evaluate if there was a difference in pregnancy outcomes for women who had undergone embolization (of uterine or anterior trunk of hypogastric arteries) with or without a uterine-sparing surgery (defined as vessel ligation and or uterine compression). It was concluded that there was no difference. Of the 1961 women who suffered from postpartum hemorrhage in those 13 years, 86.5% were successfully treated medically; only 101 (5.3%) needed embolization or both embolization and surgery (which was only 0.3% of total deliveries). Of the 85 women with successful embolization, 68 (80%) were available for follow up and 17 (25%) women had 26 pregnancies, 19 (73.1%) of which ended in a third-trimester delivery. Ten women had their embolization due to postpartum hemorrhage for placenta accreta. All ten had at least one risk factor. Of the 66 with preserved fertility, only 45% desired another pregnancy with 61.1% of the women who did not want to become pregnant stating it was due to fear of recurrence of postpartum hemorrhage. Again, in this study, no woman needed assistance to become pregnant and the mean conception time was 11.5 months. All women who had a loss in early pregnancy and wanted another pregnancy successfully had a term delivery subsequently. There was again no neonatal morbidity and uterine and umbilical Dopplers, when available, were normal (except for one woman with a past history of uteroplacental insufficiency). The rate of recurrence of postpartum hemorrhage was high and consistent with other studies at 6/19 (31.6%). Out of the 15 women who had successful third-trimester pregnancies, 2 had embolization for postpartum hemorrhage due to placenta accreta; both went on to have normal pregnancies without recurrence. Two

women with embolization for uterine atony had recurrence of postpartum hemorrhage due to placenta accreta with one requiring a hysterectomy (no desire for future fertility).³⁰

The occurrence of severe synechiae was significantly associated with placenta accreta. Of 15 women who reported amenorrhea/decreased flow after their procedures, 8 decided to have an outpatient hysteroscopy; all 8 were found to have severe synechiae. Six were successfully treated with hysteroscopic removal. However the two women whose postpartum hemorrhage was caused by placenta accreta had unsuccessful removal of synechiae and thus remained infertile. The six women who had their synechiae successfully treated did not desire more children; their success rate was impossible to determine.³² In a study by Legendre in 2014 done in a hospital in Angers it was suggested that women who are conservatively managed for placenta accreta and have persistent bleeding or pelvic pain have a systematic hysteroscopic examination. In their study they found that of 23 women treated with conservative measures over a 10-year span 12 continued to have bleeding and these 12 women underwent a hysteroscopic resection of their retained placentas. Only one of these women had a delayed hysterectomy, 2 had persistent severe synechiae, 8 desired future fertility and four conceived with two subsequent live births. They suggest that systematic hysteroscopies could prevent the formation of synechiae and improve future fertility outcomes.³³

The second study out of the Rouen University hospital determined the fertility and pregnancy outcomes of women who had undergone uterine devascularization for postpartum hemorrhage. AbdRabbo described the uterine devascularization procedure in 1994; in his seminal paper he claimed a 100% success rate in avoiding hysterectomies in 103 cases.³⁴ His method was a response to a high failure rate in ligations, which subsequently needed hysterectomies. This approach involves normal and low bilateral uterine artery ligation followed by bilateral ovarian vessel ligation in cases of persistent bleeding. This study only included women who exclusively underwent the devascularization in accordance with AbdRabbo's method. During the time period, 58 women underwent stepwise uterine devascularizations; of those 40 had no other procedure and the hemorrhage was successfully controlled. Of these 40, 32 (80%) were available for follow up, 27 (67.5%) had preserved fertility and 16 desired a pregnancy. Of these 16 women, 4 were actively trying to conceive (with an average of 10 months), 12

women had 16 pregnancies with 13 third-trimester deliveries. Of the 5 women who were infertile, one had severe intrauterine synechiae due to persistence of a partial placenta accreta and did not desire fertility or intervention. Of the 11 women who did not want another pregnancy, 6 (55%) stated fear of recurrence of postpartum hemorrhage as their reason. Of the 16 pregnancies the average time to conception was 6 months. All 13 babies had normal growth, normal uterine and umbilical Dopplers and normal weight for gestational age except for one IUGR with normal umbilical Dopplers and a maternal history of chronic hypertension. Of the 13 third-trimester deliveries, 4 (30.8%) had recurrence of postpartum hemorrhage – 3 were during C-section and due to placenta accreta. Two women of the 12 had their original stepwise uterine devascularization for postpartum hemorrhage due to placenta accreta. Both had recurrence of placenta accreta, one underwent another stepwise uterine devascularization successfully and the other opted for a hysterectomy without desire for future fertility. One woman had placenta accreta in her subsequent pregnancy when the previous stepwise uterine devascularization was done for uterine atony; she also underwent a hysterectomy and had no desire for future fertility. The only other study to assess fertility and pregnancy outcomes after stepwise uterine devascularization was AbdRabbo himself, in which he had 13 uneventful pregnancies with eutrophic babies after a delay of less than 12 months.³⁴ Only one woman had infertility following the procedure with two years of attempt at conception, however no patient required assistance to conceive. Surprisingly no spontaneous abortions occurred in the 16 pregnancies. Two women were infertile due to ovarian failure and both of these women were in the group that underwent devascularization of the suspensory ligament of the ovary, which is suspected to have contributed to the infertility.³¹ These successful pregnancies following conservative management for placenta accreta are accounted for in the multicenter national study as Antoine-Béclère hospital and the Rouen hospitals participated.

What is striking about these numbers is how few women desired another pregnancy. In the multicenter study on placenta accreta, only 27/85 (31.8%) desired a pregnancy.²³ In the studies on postpartum hemorrhage between 18-60% of women desired another pregnancy, however these represent only the women that were available for follow up.^{27,28,30,31} In 2011, Sentilhes using data from the University in Rouen decided to

investigate the psychological effects of postpartum hemorrhage on the same cohort of women from 1994 to 2007. This included women who underwent embolization and excluded those with a peripartum hysterectomy. Ninety-one women were eligible for the study and 68 (74.7%) were found to follow up. Of these 68 women, 22 (32.4%) denied negative memories of the postpartum hemorrhage. For the 46 (67.6%) women with negative memories, the most common memory ($24/68=35.3\%$) was a fear of dying. Twenty-eight women (41.2%) said they had continuing negative effects after their deliveries and 23.5% said they thought about it at least once a month, 7.3% had a persistent fear of death and 5.9% said they could not have sexual intercourse with their partner for at least 1 year after the delivery. In terms of future pregnancies, 14 (20.6%) women did not want another pregnancy and 17 (52.9%) intentionally delayed their next pregnancy due to fear of recurrence of postpartum hemorrhage. Fifteen of these women (22%) had a subsequent full-term pregnancy and 9 (60%) had intense anxiety throughout the pregnancy. One was placed on antidepressants. Interestingly 13/68 (19%) of the women's partners said they were negatively impacted by the postpartum hemorrhage, feared the women would die, and did not want to go through another pregnancy. They stated that their main anxiety was from lack of information during the delivery.³⁵

An introspective look: the American system:

The current recommendation for the treatment of placenta accreta by the American Congress of Obstetrics and Gynecology (ACOG) is a planned preterm (34wks) C-section with a high classical incision away from the placental bed to remove the infant and then to proceed with a hysterectomy while leaving the placenta in situ with no attempt made to remove it.³⁶ This has become the standard practice at most hospitals including here at Parkland Memorial Hospital in Dallas. As such, it is impossible to compare the future fertility of these patients with those that undergo conservative management as inherent to a hysterectomy is infertility. ACOG accepts that when deciding on the treatment of postpartum hemorrhage, conservative methods should be attempted first, but that a hysterectomy should be performed to save a life. This is especially true of conservative methods that would require precious time and could potential cause more harm than good. According to ACOG, the first-line treatment should be medical; including uterotonics to

control atony. When those fail, mechanical measures can be added, with packing or tamponades of different sorts. Other surgical techniques used to control bleeding include hypogastric artery ligation, bilateral uterine artery ligation, B-lynch sutures, and square suturing. For placenta accreta specifically, ACOG states that arterial embolization can be considered when the patient is hemodynamically stable and bleeding is not excessive. It can be used as a means of controlling bleeding after a hysterectomy or in an attempt to prevent a hysterectomy.³⁷ Additionally, if the provider is confident in the diagnosis of placenta accreta, then a hysterectomy with no attempt at detaching the placenta should follow delivery of the infant.³⁸

Although most USA institutions follow these recommendations, there have been some documented cases of conservative management of placenta accreta in the USA. Earlier this year, in March 2015, a multicenter study through the Maternal-Fetal-Medicine Units (MFMU) Network reviewed the treatments and outcomes of morbidly adherent placenta. The study consisted of 158 women collected from 25 institutions over a period of three years. Half of morbidly adherent placentas were discovered prenatally and these women had worse outcomes due to more significant adherence. Other interesting results were the risk factors for placenta accreta. The study showed that a surprising number of the women did not have traditional risk factors for placenta accreta; 18.4% were nulliparous and 37.3% had never had a previous C-section. This is in contrast to the multicenter French study that showed 95.8% of women with placenta accreta had at least one risk factor.²⁰ Unfortunately, there is no mention of these other potential factors such as prior dilation/curettage or other uterine surgery in the MFMU study, possibly underestimating the risk these nulliparous women had for placenta accreta. Although ACOG currently recommends hysterectomy for placenta accreta, 48 (30%) of women were treated with other measures, including 33/48 (68.75%) treated with medications only, 14/48 (29.2%) treated with dilation and curettage, the rest (10/48, 20%) treated with artery ligation, balloon tamponade and B-Lynch suture. Unfortunately, no comparison was made between treatment with hysterectomy versus conservative management and no follow up on the fertility of these women was obtained.⁴

In 2006 a case study from the University of North Carolina described a woman with placenta increta who underwent a selective uterine artery embolization and subsequently

had a healthy, normal pregnancy. Unique to her case is that the placenta increta was discovered postpartum when she presented with irregular bleeding and an ultrasound showed a hypodense irregular mass in the uterus. After dilation and curettage the tissue proved to be placenta and the bleeding worsened. An MRI confirmed the diagnosis of placenta increta and as she desired future fertility, a selective uterine artery embolization was done. Her bleeding stopped, follow-up sonogram showed involution of the placenta and she conceived spontaneously 9 months later. The subsequent pregnancy was uncomplicated without recurrence of placental abnormalities or postpartum hemorrhage.³⁹

What about elsewhere?

A study out of Israel published in 2013 compared pregnancies with placenta accreta to those without placenta accreta from 1988 to 2011 out of a single hospital. The Soroka University Hospital is the sole tertiary care hospital in southern Israel. Since a large part of the population that delivers at this hospital is conservative Bedouin Arabs who place a high value on preserving fertility they have adopted a protocol of conservative management for placenta accreta and only perform hysterectomies in life-threatening situations. In this study, the researchers chose to only include women who had C-sections. Elective C-sections were planned for women who had risk factors for placenta accreta (previous C-sections and placenta previa) or who had strong sonographic evidence. Over the 23-year period, 139 women were diagnosed with placenta accreta and underwent a C-section. Of these women 20.1% (28/139) had hysterectomies meaning that 111 (79.9%) were successfully treated with conservative management. During these 23 years, 30 deliveries occurred to women who had a previous pregnancy with placenta accreta and four (13%) of these were complicated by recurrence of placenta accreta and one had a hysterectomy. Although the authors do not report on women's desire for another pregnancy after their first placenta accreta the number of live births is consistent with other studies. Also of note here is the age of women, advanced maternal age has been cited as a risk factor for placenta accreta and also as a reason that some of these women were not pursuing another pregnancy. Although Bowman et al. found that advanced maternal age is not an independent risk factor for placenta accreta, but it is for multiple C-sections and placenta

previa, which are themselves independent risk factors for placenta accreta.⁷ In this Israeli study, 59.7% of women were 30-34 years old and 7.9% were 35 years old or above. As with previous studies, all neonates born in subsequent pregnancies after conservative management of placenta accreta had good outcomes.¹⁹

In another study out of Israel in 2014, researchers at the Hadassah-Hebrew University Medical Center in Jerusalem compared two cohorts of patients on the outcomes of subsequent pregnancies. Of note, conservative management in this study was defined as removal of the placenta and conservation of the uterus, unlike in other studies where the placenta is left in situ to prevent postpartum hemorrhage. Over 10 years, from 1990 – 2000, 260 women were treated conservatively for placenta accreta. Of those, 134 (51.5%) were available for follow up and matched to controls. The two groups were well matched without any significant difference in demographics other than a previous pregnancy with placenta accreta. Interestingly, the group of women who were conservatively treated for placenta accreta included 23 (17.2%) women who had already had a previous pregnancy with placenta accreta. What was even more surprising was that the control cohort had 4 women (3%) who had a previous placenta accreta as well. There were no differences in the groups when it came to number of previous C-sections or placenta previas. Out of the 134, 107 attempted conception and 99 (74%) women were successful in delivering a term infant. To these 99 women, 280 live term infants were born and data was available for 272 (97%) of these pregnancies. Unlike previous studies out of France, women who had suffered a postpartum hemorrhage were not less likely to want a future pregnancy and there was no difference when comparing the placenta accreta group to the control group where 94 women had 271 live full term births. The only significant difference between the two groups was the increased risk for recurrence of placenta accreta and postpartum hemorrhage in the study group with 62/272 (22.8%) deliveries having recurrence of placenta accreta and 23/272 (8.5%) with postpartum hemorrhage. Of note, there was no difference in the two groups in neonatal outcomes, mode of delivery and maternal complications. It's interesting to note that no child of either group (total of 562) spent any time in the NICU and all were born at term with normal birth weights.⁴⁰

Large studies are not available considering placenta accreta is in and of itself a rare diagnosis, conservative management is often not the standard, and women with a history of postpartum hemorrhage often do not desire another pregnancy.

However, several case studies have been published such as one from India in 2009. The woman is a 33-year-old G3P2. After delivering a baby at home it was noted that removal of the placenta was not possible and she started profusely bleeding. After transfer to a hospital placenta accreta was diagnosed based on sonographic findings. Since she desired future fertility and had become hemodynamically stable the decision was made to treat her with IM methotrexate. The treatment was well tolerated and the placenta showed full resorption after 12 weeks. Eight months postpartum a spontaneous pregnancy was achieved which progressed normally, had no recurrence of placenta accreta, and no neonatal morbidity.⁴¹

A group from the Netherlands reported two successful cases of placenta accreta managed conservatively as well as a literature review in 2007. One of the cases was a placenta percreta in which they left the placenta in situ, however after over a year of dysmenorrhea they removed a mass from the cornea of the uterus that was necrotic, but not identified as placenta on histological inspection. The second case was one of a nulliparous woman who had no prior pregnancies, abortions or uterine instrumentation. The placenta was left partially in situ and was eventually resorbed. Subsequent pregnancies of neither patient were reported, but in a literature review the researchers found 91 women with conservative management of placenta accreta over a 20-year span. Of these 91, 60 of them were reported in case studies and 31 in 2 case series. Out of the 91 women they found 12 had subsequent pregnancies, however its possible that the others were not followed up and investigated for subsequent pregnancy outcomes.⁴²

Table 1: Summary of studies found who report fertility outcomes after conservative management of placenta accreta

Author	Year	Country	Attempts at CM of PA	Successful CM of PA	Found to f/u	Desire FF	Women w/ preg	Live births	Recur. of PA
Alanis*	2006	USA	12	10				8	1
Timmermans*	2007	Netherlands						5	
Mahendru	2009	India	1	1	1	1	1	1	0
Sentilhes	2010	France	167	131	96	27	24	21	6
Eshkoli	2013	Israel	139	111				30	4
Kabiri	2014	Israel	260		134	107	99	280	62
TOTAL			579					345	73
*These are literature reviews. All studies in these reviews from France between 1997 and 2010 were not included in the totals reflected in this chart so as to not count these women twice. - CM: Conservative management, PA: Placenta accreta, f/u: follow up, FF: future fertility, preg: pregnancies, recur: recurrence									

DISCUSSION:

In conclusion, some points can be taken away from these studies on the conservative management of postpartum hemorrhage and placenta accreta and the subsequent effects on fertility for these women. Firstly, women who undergo conservative management for postpartum hemorrhage, including placenta accreta, do not have altered fertility and can have normal pregnancies that they carry to term. Some women go on to have multiple normal pregnancies without complications. These women do not have secondary infertility, need about 12 months to conceive and no neonatal morbidity has been documented. Children are typically born at term, have normal umbilical Dopplers, normal rate of growth and normal birth weights barring any other maternal complications. Although ACOG states that subsequent successful pregnancies after conservative management are rare,³⁶ this review found 345 live full term births to women treated with conservative management specifically for placenta accreta that had relatively few complications and a 21% recurrence of placenta accreta. (See Table 1.)

Secondly, recurrence of postpartum hemorrhage – whether originally due to placenta accreta or another cause is high and women need to be well counseled on this statistic. Additionally, recurrence of placenta accreta is high as well, but can be treated conservatively on multiple occasions. It is suspected that devascularizing the uterus can lead to future abnormalities in placentation. These studies also show that when well informed, many women choose not to try for another pregnancy, most stating that it is out

of fear of another postpartum hemorrhage. However, this is dependent on personal and cultural differences. Interestingly, the cause of the postpartum hemorrhage is not always the same. Studies also show that women can be successfully treated for postpartum hemorrhage with multiple conservative measures, as well as multiple times without the need for a hysterectomy.

In terms of placenta accreta specifically, these women have a high rate of recurrence of postpartum hemorrhage due to placenta accreta. Almost all women with placenta accreta had at least one major risk factor with placenta previa with a past history of C-section being the most statistically significant. These pregnancies tend to end before full term due to preterm labor and bleeding. After conservative management for postpartum hemorrhage due to placenta accreta women are at a high risk of synechiae and the infertility that follows them.

In conclusion, although conservative management of placenta accreta comes with a multitude of risks of maternal morbidity, for women who choose to have another pregnancy the methods used to control bleeding while leaving the placenta in situ do not impede the health of future pregnancies. Placenta accreta and postpartum hemorrhage can have a serious psychological impact on women and affect whether or not they want to go through another pregnancy when the risk of recurrence is high. As in any other aspect of clinical care, it is important to inform our patients of all of their options and all of the risks attributed with their options.

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