

Hysteroscopic removal of retained products of conception in the outpatient setting*

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Abstract

This article presents an overview of the diagnosis and classification of retained products of conception (RPOC) as well as removal techniques and discusses the associated complications, advantages and disadvantages of these procedures. RPOC occur when tissue from the placenta or the fetus remain in the uterus after all types of termination of pregnancy and deliveries, including vaginal or cesarean delivery, spontaneous miscarriage, or induced medical or surgical abortion. The diagnosis is based on the combination of clinical findings and ultrasound (US) evaluation (gray-scale and Doppler flow). Hysteroscopy has emerged as the preferred treatment for women with RPOC largely due to its demonstrated safety, feasibility, low incidence of postoperative intrauterine adhesions (IUAs) and high rates of subsequent fertility. Furthermore, thanks to the availability of hysteroscopic tissue removal systems (HTRs) and the miniresectoscope, many hysteroscopic procedures can now be performed without anaesthesia or cervical dilation in an ambulatory setting. Further studies are required to provide a more comprehensive understanding of the reproductive outcomes in patients with pregnancies complicated by RPOC.

Keywords: Retained products of conception, hysteroscopy, intrauterine adhesions, hysteroscopic tissue removal system, reproductive outcomes.

Introduction

Retained products of conception (RPOC) occur when tissue from the placenta or the fetus remain in the uterus after all types of termination of pregnancy and deliveries, including vaginal or cesarean delivery, spontaneous miscarriage, or induced medical or surgical abortion. This complication is also termed “placental polyp,” “retained placental fragment” or “residual trophoblastic tissue.”

The incidence of RPOC varies as a function of the type of pregnancy; i.e., full-term delivery, miscarriage, or induced abortion. The incidence of RPOC following full-term vaginal or cesarean delivery is low, around 1% (Weissbach et al., 2015; Capmas et al., 2019). The rate is significantly higher for miscarriages and for medical abortions, with a prevalence of 6% and 15% respectively (Smorgick et al., 2014). However, these figures are likely to vary widely depending on the population

and the definition of RPOC used in the study.

The signs and symptoms of RPOC include abnormal uterine bleeding, abdominal pain, fever and signs of infection, and a persisting dilated cervix. However, RPOC are also frequently diagnosed incidentally during an ultrasound (US) examination. In the long term, RPOC can cause severe complications, such as endometritis and intrauterine adhesions formation (IUAs), and may potentially lead to secondary infertility (Smorgick et al., 2014). A number of risk factors are associated with RPOC, including second trimester demise, morbidly adherent placenta, history of RPOC in a previous pregnancy, presence of IUAs, and uterine anomalies such as uterine septum. More recent works have suggested that ART-related pregnancies may be a risk factor for RPOC (Baba et al., 2013).

The diagnosis and management of RPOC is challenging because there are no universally accepted diagnostic criteria or treatment protocols

(Hooker et al., 2016). The diagnosis is usually based on ultrasound findings indicative of a heterogeneous intracavitary hyperechoic focal mass, with a poorly defined endometrium-myometrium interface, a fluid layer, and/or increased and irregular endometrial thickness. A color Doppler examination can improve diagnostic accuracy and help differentiate between different types of RPOC (Kamaya et al., 2009).

In outpatient settings today, several strategies are used to manage RPOC, ranging from expectant or medical management to surgical evacuation of the uterine cavity. Goldenberg was the first to report the use of hysteroscopy for the removal of residual trophoblastic tissue using a cutting loop as a curette for selective removal (Goldenberg et al., 1997). Since then, additional hysteroscopic techniques such as the tissue removal devices have been introduced to deal with this pathology.

This article presents an overview of the diagnosis and classification of RPOC as well as hysteroscopic removal techniques and discusses the associated complications, advantages and disadvantages of these procedures.

Diagnosis and classification

The diagnosis of RPOC presents a major clinical challenge, since overdiagnosis may lead to unnecessary interventions and possible complications, while underdiagnosis may cause long term sequela such as IUAs. Since the first report by Robinson in 1972, US has been used as the first-line diagnostic tool for suspected RPOC, thanks to its wide availability, high reproducibility and non-invasiveness (Robinson, 1972). Older studies did report high rates of false positive results for the diagnosis of RPOC by US, reaching 17-51% (Shen et al., 2003; DeVries et al., 2000; Malvern et al., 1973; Sadan et al., 2004). However, these findings have been attributed to the incorrect interpretation of the variable appearance of the normal post-pregnancy uterus, and more recent studies found significantly higher rates of accurate diagnosis.

During the postpartum period 6-8 weeks after delivery, the uterus undergoes involution and returns to its original state and the endometrium resumes its normal thickness (Mulic-Lutvica et al., 2001; Steinkeler et al., 2012). RPOC can only be successfully diagnosed if the clinician has a clear understanding of what to expect in a normal, uncomplicated recovery. Uterine cavity contents such as fluid, debris, and blood clots appear as echogenic findings on US. In most cases, these findings are a normal part of the postpartum recovery process, should not be diagnosed as

RPOC per se and usually disappear by the end of the puerperal period (Mulic-Lutvica et al., 2001; Steinkeler et al., 2012; Edwards and Ellwood, 2000). The patient's history should always be elicited and related to the clinical symptoms.

The timing of the examination during puerperium is crucial. Sokol et al. (2004) conducted a prospective observational study on normal transabdominal US findings after uncomplicated vaginal delivery in 40 women within 48h after delivery (Sokol et al., 2004). In 40% of these women, there was echogenic material in the endometrial cavity. No association with heavier or prolonged bleeding was found and none of the women needed medical care. Edwards and Ellwood (2000) performed transabdominal US in 40 women at days 7, 14 and 21 after a normal vaginal delivery. The mean duration of postpartum bleeding was 24.5 days. They showed that 51% had an echogenic mass within the uterine cavity at seven days postpartum, which then dropped sharply to 6% at day 21. This US finding was likely blood clots, which raises questions as to the significance of finding an echogenic mass when diagnosing RPOC, which has a positive predictive value (PPV) of 59% (Edwards and Ellwood, 2000). This suggests that it may be worthwhile postponing the US evaluation until the end of the puerperal period.

The key finding of RPOC on a gray-scale US is a thickened endometrial echo complex (EEC), with a cut-off value of 10 mm (ranging from 8 to 13 mm) or an intracavitary mass with a thickened EEC (Sellmyer et al., 2013). By contrast, specificity is rather low. If no endometrial mass is detected or the endometrium thickness is less than 10 mm, RPOC are rare. In clinical settings, however, the diagnosis of RPOC is not made solely on the basis of gray-scale US findings.

Recent studies have shown that colour Doppler US enhances RPOC diagnostic accuracy. For example, detection of vascularity in a thickened endometrium or endometrial mass was reported to increase the PPV for the diagnosis of RPOC to 65% or even 100% (Van den Bosch et al., 2008; Atri et al., 2011). However, even if there is no hypervascularity in the intracavitary mass or thickened EEC, this does not exclude RPOC (Durfee et al., 2005; Sellmyer et al., 2013). The presence of intrinsic vascularity helps distinguish simple clots which may resemble RPOC on gray-scale imaging from true RPOC. When utilising Doppler sonography, signals arising from tissue within the endometrial cavity need to be differentiated from signals within the adjacent myometrium, which may represent the implantation site, as in

cases of subinvolution. Other potential pitfalls in this diagnosis are rare but can include enhanced myometrial vascularity (EMV), preexisting endometrial polyps, submucosal fibroid and invasive moles.

One possible explanation for the wide range of percentage margin for the diagnosis of RPOC on colour Doppler US is when retained products expelled spontaneously during the period of time between the US scan and the surgical procedure or follow-up examination. Another possibility is the subinvolution of the placental site. Specifically, if a blood clot is adjacent to the involution site, the colour Doppler flow may appear to be within the endometrium. Thus Doppler signals arising from tissue within the endometrial cavity need to be differentiated from signals occurring within the adjacent myometrium.

The degree of vascularisation into the thickened EEC or mass is also important. Kamaya et al. (2009) were the first to categorise suspected RPOC on the basis of Doppler vascularity (Kamaya et al., 2009). They divided them into four types ranging from Type 0 (avascular) to type 3 (marked vascularity).

This Doppler characterisation was later adapted to create the Gutenberg RPOC classification which incorporates the vascularity and the echogenicity of ultrasound findings (Figure 1) (Tinelli and Haimovich, 2017). This classification is designed to predict the risk of intraoperative bleeding during the hysteroscopic removal of RPOC (Figure 2) (Alonso Pacheco et al., 2019).

Studies over the last 30 years have explored the relationship between RPOC and clinical and sonographic parameters (Ben-Ami et al., 2005; Neill et al., 2002). The results suggest that combining ultrasound and clinical assessment improves diagnostic accuracy when they are both positive or negative, but provides little clarification when the clinical and ultrasound findings do not coincide. Thus a combination of clinical and sonographic evaluations should be carried out before the decision to proceed with surgery, to help avoid unnecessary invasive procedures.

There is no consensus in the literature on a standardised postpartum US protocol or the interpretation of US findings in the uterine cavity. In a recent study (Levinsohn-Tavor et

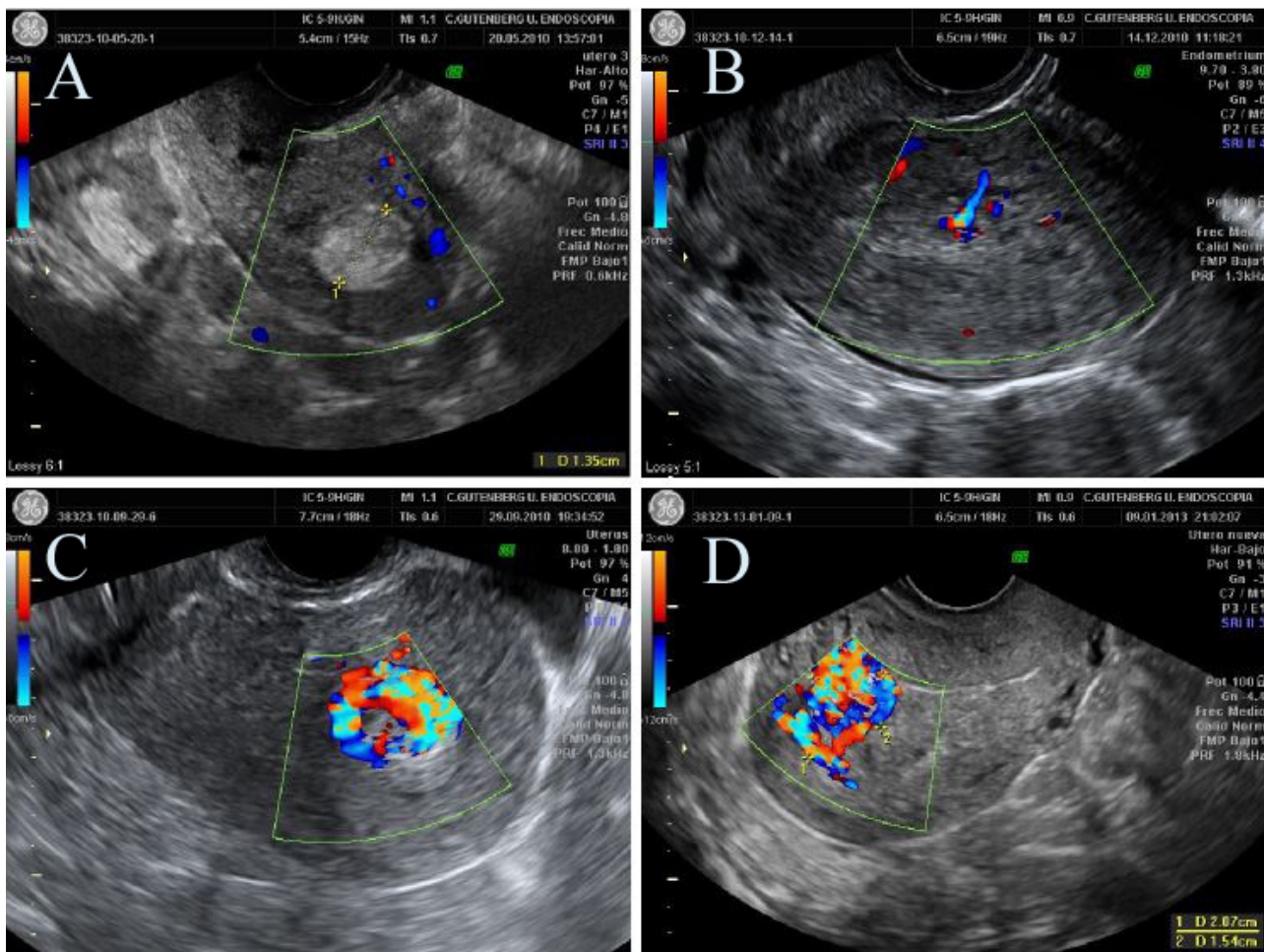


Figure 1: Ultrasonographic patterns of RPOC. Gutenberg Classification. A- Type 0: hyperechogenic avascular mass. B-Type 1: Different echoes with minimal or no vascularisation. C- Type 2: Highly vascularised mass confined to the cavity. D- Type 3: Highly vascularised mass with highly vascularised endometrium (Reproduced with permission from Alonso Pacheco et al., 2019).

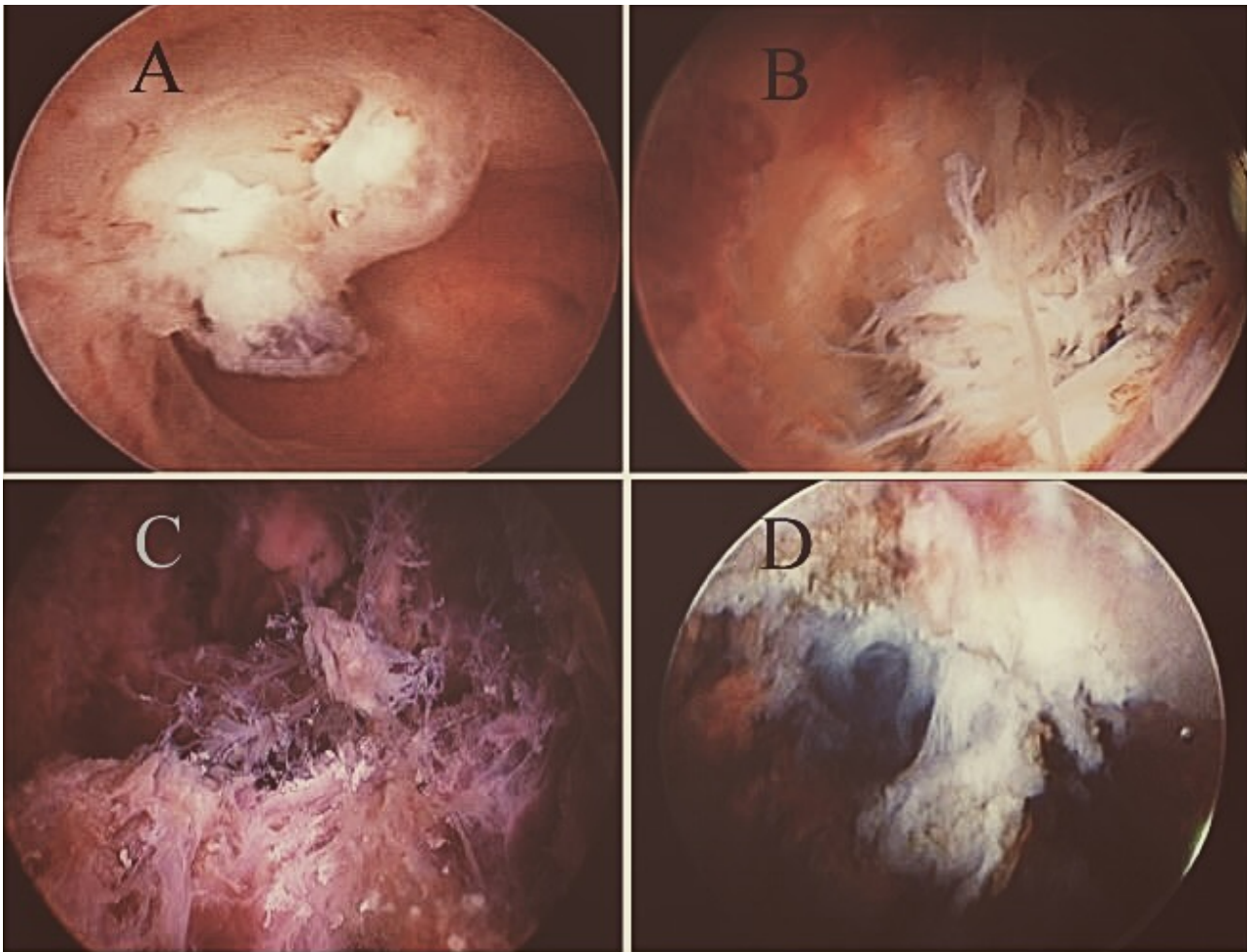


Figure 2: Hysteroscopic patterns of RPOC. Gutenberg classification. A- Type 0: white mass in with no clear structures. B- Type 1: well-defined avascular chorionic villi. C- Type 2: Well vascularised chorionic villi. D- Fig 4: Aneurism over myometrium in the implantation area (Reproduced with permission from Alonso Pacheco et al., 2019).

al., 2020), we presented our clinical approach to managing patients with suspected RPOC based on a classification of US findings in the uterine cavity into high, moderate, and low probability of RPOC (Figure 3A-C). The findings confirmed the presence of RPOC in 62%, 32%, and 0% of the high, moderate, and low probability groups, respectively. In the low probability group with normal sonographic findings, no surgical intervention is recommended. In the high probability group, surgical evacuation of the uterine content is indicated and we recommend operative hysteroscopy. When sonographic findings are within the moderate probability category, and the patient is clinically stable, expectant management with a follow-up scan at the end of the puerperal period is recommended. This approach may increase the positive predictive value of the US examination and avoid unnecessary interventions. Very recently, we conducted a larger prospective study that confirmed our results (Levinsohn-Tavor et al., 2022). This 3-group approach is now included in the Israeli professional guidelines for the diagnosis and treatment of RPOC

(Israeli Society of Obstetrics and Gynecology, position paper 122, <https://www.ima.org.il/main/EditClinicalInstruction.aspx?ClinicalInstructionId=2499>).

Hysteroscopy for removal of retained products of conception

The surgical management of retained products of conception (RPOC) by hysteroscopy was first proposed by Goldenberg et al. in 1997 using the 10 mm resectoscope as an outpatient procedure under general anesthesia (Goldenberg et al., 1997). Subsequently, multiple studies have described the surgical technique and its short and long-term outcomes using different types of hysteroscopes, with and without general anesthesia (Smorgick et al., 2014; Hooker et al., 2016; Cohen et al., 2001; Golan et al., 2011; Barel et al., 2015). All hysteroscopic techniques rely on the direct visualisation of the uterine cavity, which enables targeted, focused removal of the RPOC rather than blind, global curettage, avoiding unnecessary trauma to the unaffected parts of the cavity. In addition,

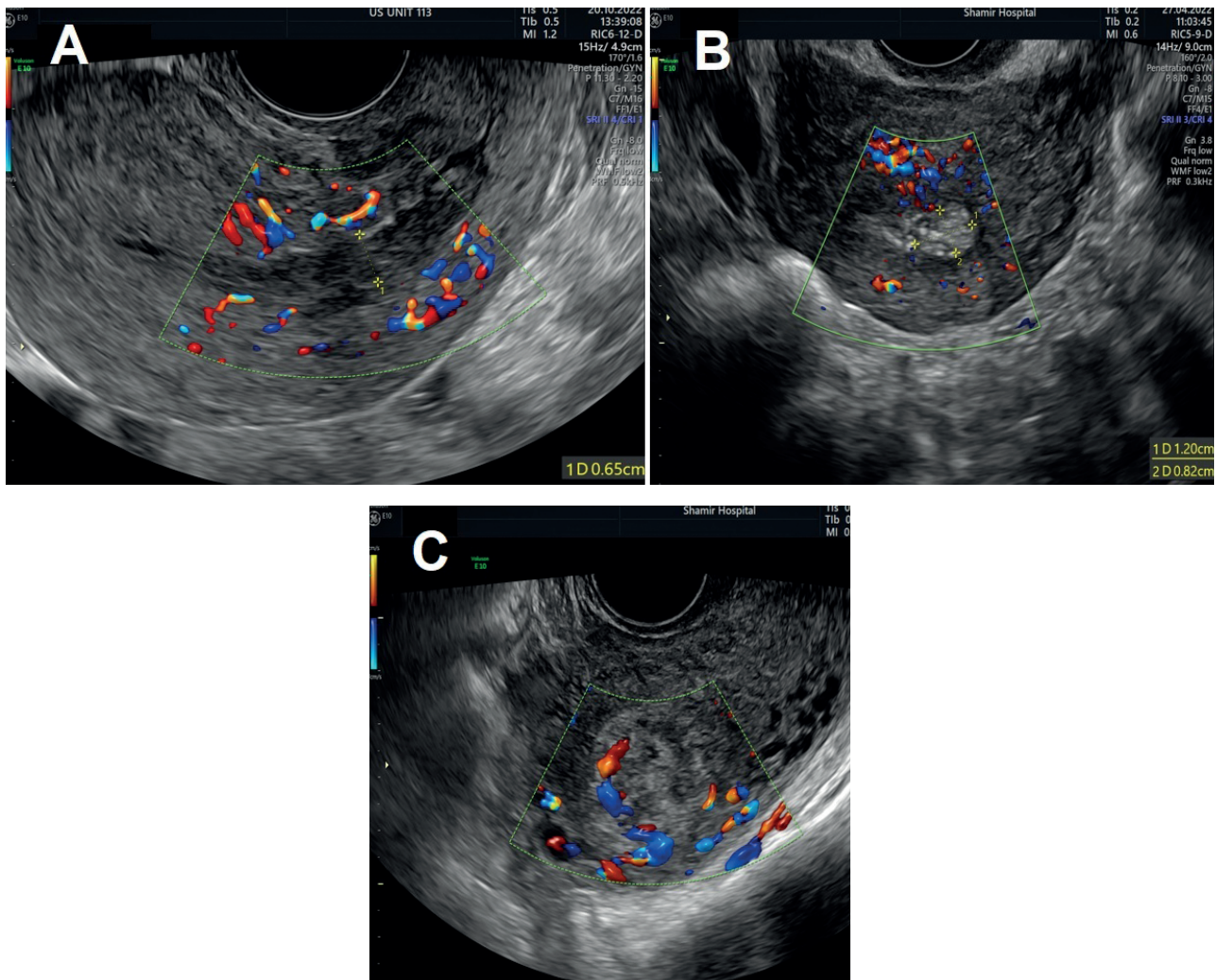


Figure 3: Images of the uterine cavity in patients with suspected retained products of conception after delivery. (A) Low probability: no echogenic mass, endometrial thickness < 10 mm, no vascularity. (B) Moderate probability: endometrial thickness > 10 mm without vascularity; (C) High probability: an echogenic mass or endometrial thickness > 10 mm with vascularity.

hysteroscopy has the advantage of complete visualisation of the uterine cavity, which makes it possible to confirm that all the retained products have been removed, in addition to the identification and treatment of uterine anomalies. To minimise the risk of postoperative intrauterine adhesions and their fertility sequelae, the hysteroscopic procedure is performed using a non-traumatic technique with limited or no electrosurgery. Other strategies for the prevention of intrauterine adhesions include the use of barrier intrauterine gel, oral oestrogen, and diagnostic office hysteroscopy performed about 6 weeks after surgery (AAGL/ESGE guidelines) (AAGL/ESGE guidelines, 2017).

1. Resectoscopy

In this technique, the loop of the resectoscope is used for blunt separation of the RPOC from the uterine walls along the surgical plane between the endometrium and the RPOC. In cases of large, vascular RPOC when the surgical plane cannot be clearly observed, the resectoscope loop may be

used to resect the superficial areas of the RPOC, followed by blunt separation of the deeper areas adjacent to the endometrium. When a large bore resectoscope is used (e.g., 10 mm), cervical dilation is performed, which requires general anaesthesia or sedation. However, unless heavy bleeding has occurred, most of these procedures are performed in the outpatient setting. The recent development of a small diameter “mini-resectoscope” (5-6 mm) now permits some procedures without anaesthesia. Because of its smaller loop, the mini resectoscope is typically used to remove smaller RPOC (< 2 cm).

2. Mechanical instruments (hysteroscopic shears and graspers)

Mechanical instruments can be introduced through the working channel of the small diameter (4-5 mm) hysteroscope using a vaginoscopic approach without cervical dilation or anaesthesia (Raz et al., 2022). The grasper and/or scissors are used to separate the RPOC from the uterine wall, and the subsequent grasping and removal of the RPOC mass. These

instruments are appropriate for the removal of small non-vascular RPOC, usually <2 cm (Mohr-Sasson et al., 2022).

Overall, favourable outcomes have been reported for hysteroscopic removal of RPOC, with low rates of complications and postoperative adhesions and high rates of subsequent pregnancies (Smorgick et al., 2014; Hooker et al., 2016). The rare reported intra- and postoperative complications include uterine perforation, bleeding requiring transfusion, and re-admission for fever (all in less than 1% of the cases). Postoperative adhesions were reported in 5% to 20% and were classified as mild in most cases (Smorgick et al., 2014; Hooker et al., 2016). The postoperative fertility rate was >80%, although subsequent pregnancies were complicated by adherent placenta and recurrent RPOC (Capmas et al., 2019; Smorgick et al., 2018).

3. Hysteroscopic tissue removal systems and retained products of conception

In 1999, Dr. Mark Hans Emanuel, a Dutch gynaecologist, designed the first generation of hysteroscopic mechanical shavers with the support of Smith and Nephew Ltd. (Andover, MA, USA). Since then, several hysteroscopic tissue removal systems (HTRS) have become available (Emanuel and Wamsteker, 2005). TruClear® (Medtronic, Dublin, Ireland) was the first to receive FDA approval in 2005, followed by MyoSure® (Hologic, Marlborough, MA, USA) and the Integrated Bigatti Shaver® (Karl Storz, Tuttlingen, Germany). The innovative hybrid Symphion™ (Minerva Surgical Inc, Santa Clara, CA, USA) system enables automatic aspiration of tissue fragments resected with a bipolar radiofrequency through a self-contained, recirculating fluid management system. Aveta® (Meditrina, Inc., San José, CA, USA) is a disposable system with high-speed mechanical oscillation mechanism.

When using HTRS for the management of RPOC, the blade of the device is introduced into the uterine cavity through the working channel of a rigid hysteroscope. For optimal uterine cavity distension, irrigation, and visibility, a continuous flow system is used (Georgiou et al., 2018; Hamerlynck et al., 2013). At the tip of the device, through a lateral window opening, the cutting blades cut the target tissue and the sample is aspirated by a vacuum source. Aspiration of blood clots and direct removal of intrauterine pathology result in good visualization, which permits satisfactory imaging throughout the procedure. The tissue can also be approached laterally, so that it can be scooped out of the myometrium when necessary.

HTRS are becoming an increasingly popular choice for the management of polyps and fibroids. They are also attracting interest for RPOC, given their precision, safety, and effectiveness (Georgiou et al., 2018). Hamerlynck et al. first described the use of hysteroscopic morcellation in the management of placental remnants in 2013 (Hamerlynck et al., 2013). This retrospective case series covered 105 procedures performed between January 2005 and May 2013. The RPOCs had a mean diameter of 26 mm and the success rate of removal for a single approach of 94%.

When using manual HTRS, the operator is able to selectively remove products of conception under direct visualisation, thus causing minimal damage to the endometrium and reducing the risk of post-operative adhesion formation. Ansari et al. conducted a 5-year retrospective series that reported on 52 cases of RPOC treated by a HTRS, which were confirmed histologically. They found that the shaver technique enabled a faster procedure with minimal damage to the healthy endometrium. They also found that the later the surgical procedure was performed after a miscarriage, the less bleeding was observed as a consequence of the devascularisation of the placental remnants. The authors did not report any complications (Ansari et al., 2018).

The advantages of manual HTRS with complete and fast removal of RPOC have been confirmed in several case series (Georgiou et al., 2018; Mallick and Middleton, 2017; Sutherland and Rajesh, 2018; Capote et al., 2018; Arnold et al., 2016). Hamerlynck et al. (2016) conducted a randomised controlled trial which showed that HTRS constitute a faster alternative to loop resection (Hamerlynck et al., 2016). She compared 37 cases treated by HTRS to 36 cases treated by loop resection. Both techniques are considered safe and show high rates of complete removal and tissue availability with 3% de novo intrauterine adhesion formation. In the HTRS group, the procedure was significantly faster (median operating time, 10.0 minutes [interquartile range (IQR), 5.8 – 16.4 minutes] vs. 6.2 minutes [IQR, 4–11.2 minutes]; $p = 0.023$).

Van Wessel et al. (2020) recently reported findings on reproductive and obstetric outcomes after HTRS and resection. In this cohort study, the authors randomised 46 patients with RPOC in the morcellation group and compared the outcomes to 40 patients in the loop resection group. The mean time from procedure to conception after removal of RPOC was similar, at 14 weeks with HTRS and 15 weeks with loop resection. The live birth rate was higher in HTRS (88.9%) than for resection (68.2%), although the difference was not statistically significant (Van Wessel et al., 2020).

Another comparative analysis of clinical efficacy and reproductive outcome was recently published by Yong et al. (Yong et al., 2023). This cohort retrospective comparative study included 361 patients diagnosed with RPOC in the morcellation group who were compared to 261 patients in the hysteroscopy electrosurgery group. Bipolar energy was used in the hysteroscopy group. The operative time was shorter in the HTRS group (21 vs. 31 min., $p=0.039$), whereas in terms of efficacy, in HTRS group a complete resection rate of 94% was achieved compared to 93% in the hysteroscopy group. In 24 of the 25 failures in the morcellator group, placenta accreta was found. The mean follow-up was 3 years, and the conception rate was higher in the mechanical removal group. Postpartum placenta abnormalities were found in 3.8% of the cases in the HTRS group compared to 10.5% in the other ($p=0.017$), probably due to the energy damage caused to the uterine wall. Although these data are promising, it is clear that more randomised comparative studies are needed to assess the relative value of HTRS in the treatment of RPOC.

Note that although these systems are considered safe and require a short learning curve, complications have been described, as with any other surgical tool. Safety is not only based on the device itself but also on training and prior experience.

Discussion

The diagnosis and management of RPOC have evolved considerably in the last 15 years. Previously, the diagnosis was based primarily on the clinical presentation of heavy vaginal bleeding and the management primarily by curettage, which may cause severe IUAs and Asherman's syndrome in up to 40% of women (Westendorp et al., 1998). Currently, the diagnosis is based on the combination of clinical findings and US evaluation (which includes gray-scale and Doppler flow scans), and the management is preferably by hysteroscopy, with low rates of postoperative IUAs and high rates of subsequent fertility (Capmas et al., 2019; Smorgick et al., 2014; Hooker et al., 2016). Indeed, a recent study comparing the management of postpartum RPOC between two periods has showed that most cases of RPOC are currently managed by hysteroscopy rather than curettage and that the rates of postoperative IUAs have concurrently decreased (Nir et al., 2022). Furthermore, thanks to the availability of HTRS and the miniresectoscope, many hysteroscopic procedure can now be performed without anaesthesia or cervical dilation in an ambulatory setting.

The timing of surgical intervention for RPOC has remained an important clinical question. In cases of postabortion RPOC (either medical or surgical, spontaneous or induced), expectant management can be offered to asymptomatic or mildly symptomatic patients since up to 60% of cases will resolve by spontaneous expulsion of the RPOC (Takahashi et al., 2019). An expectant management period of 2 menstrual cycles is usually considered acceptable. Obviously, significant symptoms such as bleeding or infection require early surgical intervention. Interestingly, Tzur et al found that medical treatment with misoprostol does not increase the rates of spontaneous expulsion of RPOC in this setting (Tzur et al., 2022).

In cases of postpartum RPOC, menstruation can be delayed due to lactation. Thus, the timing of surgical intervention is more difficult to ascertain, and the decision is individualised according to the patient's symptoms, ultrasound findings and classification (i.e., high or medium probability for RPOC, Figure 1) and the patient's desire for prolonged lactation (Levinsohn-Tavor et al., 2020; 2022). Unless surgical intervention is urgently required because of significant symptoms, the hysteroscopy is usually offered after 6 to 8 weeks from delivery. Of note, delaying the surgical intervention for >6 weeks after delivery has also the advantage of improved visualisation of the uterine cavity during hysteroscopy, since early intervention may be hindered by blood clots, decidua and debris in the cavity, and by difficulty in maintaining the intrauterine pressure due to cervical dilation.

Several hysteroscopic instruments are currently available for removal of RPOC, including mechanical instruments (grasper/scissors), HTRS, traditional large-bore resectoscopes, and the newer mini-resectoscopes. All these instruments have the advantages provided by hysteroscopy, namely a focused and non-traumatic procedure in the cavity, and all appear to have low rates of complications and IUAs and high rates of subsequent fertility, as opposed to curettage. The reusable mechanical instruments have the advantage of low cost, require minimal or no cervical dilation, and can be used in the see and treat setting without anaesthesia (Raz et al., 2022; Mohr-Sasson et al., 2022). However, they are mostly used for small and non-vascular RPOC, and require surgical expertise and relatively longer learning curve. The HTRS can also be used in the see and treat setting with no or minimal cervical dilation, appear to have a relatively shorter learning curve, and may be used for larger, albeit non-vascular RPOC. Nevertheless, cost is higher for the non-reusable blades. The traditional large-bore resectoscope remains the most appropriate

tool for removing large and vascular RPOC in the operative room, although surgical expertise is certainly required to minimise complications such as uterine perforation, and its learning curve is probably the longest of all hysteroscopic techniques.

Conclusion

Operative hysteroscopy has emerged as the preferred treatment for women with retained products of conception (RPOC), largely due to its demonstrated safety, feasibility, and low incidence of postoperative intrauterine adhesions (IUAs). The procedure may also offer potential benefits in terms of future conception rates. However, further studies are required to provide a more comprehensive understanding of the reproductive outcomes in patients with pregnancies complicated by RPOC. This includes investigating whether different hysteroscopic approaches, such as the utilisation of HTRS, enhance future fertility rates. Existing literature indicates the superiority of hysteroscopy over traditional dilatation and curettage for the treatment of RPOC, but additional research will help solidify these findings.

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