

# Hysteroscopy and Retained Products of Conception: An Update

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## Abstract

Retained products of conception (RPOC) can occur after early or mid-trimester pregnancy termination and also following vaginal or cesarean delivery. It is frequently associated with continuous vaginal bleeding, pelvic pain, and infection. Late complications include intrauterine adhesions formation and infertility. Conventionally, the management of RPOC has been with blind dilation and suction curettage (D and C); however, hysteroscopic resection of RPOC is a safe and efficient alternative. In this review, we analyze the current available evidence regarding the use of hysteroscopic surgery for the treatment of RPOC comparing outcomes and complications of both traditional curettage and hysteroscopic technique. Data search has been conducted using the following databases MEDLINE, EMBASE, Web of Sciences, Scopus, Clinical Trial. Gov., OVID, and Cochrane Library interrogate all articles related to hysteroscopy and the preserved product of conception, updated through September 2020.

**Keywords:** Hysteroscopic morcellation, office hysteroscopy, resectoscopy, retained products of conception

## INTRODUCTION

Retained products of conception (RPOC) is defined by retention of trophoblastic tissue inside the uterine cavity. It is a complication that involves about 1% of full-term pregnancies,<sup>[1]</sup> whether delivered by vaginal or cesarean section, and it is more common after miscarriage or voluntary termination of pregnancy, in the first or second trimester, with a reported prevalence of up to 6%.<sup>[2]</sup> RPOC is even more frequent after medical abortions with a prevalence up to 15%.<sup>[2]</sup> Even though RPOC can be incidentally diagnosed during an ultrasound examination, it is frequently associated with several clinical signs such as abnormal bleeding, abdominal pain and/or fever, a persisting dilated cervix, and it may cause severe long-term complications, such as endometritis and intrauterine adhesions formation (IUAs) potentially leading to secondary infertility.<sup>[2]</sup>

The diagnosis and management of RPOC are challenging because there are no defined diagnostic criteria or treatment protocols.<sup>[3]</sup> The diagnosis is usually made in the presence of ultrasound findings of a heterogeneous intracavitary hyperechoic focal mass, with poorly defined endometrium-myometrium interface, a fluid layer, and/or increased and irregular endometrial thickness. A color Doppler examination should also be used to improve the diagnostic accuracy: Demonstrating blood flow in the mass can help distinguish between RPOC and a hematoma, as well as to classify RPOC on the basis of its vascularity.<sup>[4]</sup>

Kamaya *et al.* first tried to categorize them on the basis of Doppler vascularity, from Type 0 (avascular) to type 3 (marked vascularity),<sup>[4]</sup> whereas the Gutenberg Classification represents the evolution of this characterization; it incorporates both vascularity and echogenicity of ultrasound findings.<sup>[5]</sup> Used as preoperative evaluation, the Gutenberg

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Classification is very useful in surgical planning as it allows to predict the risk of bleeding during hysteroscopic removal of RPOC and so to determine the safest environment in which to safely perform the procedure (in office vs. operating room setting).<sup>[6]</sup> In the study conducted by Alonso Pacheco *et al.*,<sup>[6]</sup> a comparison between the hysteroscopic management of RPOC in Gutenberg type 0–1 versus type 2–3 RPOC was made, demonstrating that patients classified as Gutenberg type 2 or 3 RPOC required the use of monopolar energy during the procedure, compared to none of the patients classified as Type 0–1, in order to reduce the risk uncontrollable massive bleeding.

Highly vascular RPOC can be confused with acquired uterine arteriovenous malformation (AVM), a rare cause of postpartum vaginal bleeding. Recognizing the two different entities is mandatory because the treatment modality for RPOC (i.e., dilation and curettage) can worsen vaginal bleeding and lead to shock or death and is therefore contraindicated for uterine AVM. For this reason, a correct ultrasound diagnosis is needed.<sup>[7]</sup> It is important to look at certain findings on ultrasound (US) that increase the likelihood for AVM, such as hypoechoic areas in the myometrium and high velocity and multidirectional blood flow. If there is a vascular component seen in RPOC, it will be located in the endometrium, whereas the vascular component in AVM is primarily situated in the myometrium.<sup>[8]</sup> In case of suspect, the patient should undergo a computed tomography angiography and finally arteriography for confirmation of the diagnosis and possible embolization.<sup>[9]</sup>

Office hysteroscopy allows direct visualization of the retained tissue as well as to obtain biopsy for pathology evaluation. During hysteroscopy, the residual trophoblastic tissue mimics a polypoid lesion showing a smooth surface and/or a friable micro-papillary texture, with an overall hypotrophic appearance, with well-circumscribed boundaries and friable necrotic foci that bleeds readily.<sup>[1]</sup> The advantage of hysteroscopy in the management of RPOC is double: It is not only effective for the diagnosis but, above all, allows treating the RPOC.<sup>[1]</sup>

The purpose of the present review is to provide to provide an overview of different approaches to the removal of RPOC, associated complications, advantages, and disadvantages of the different procedures.

## MATERIALS AND METHODS

The data research was conducted using the following databases: MEDLINE, EMBASE, Web of Sciences, Scopus, Clinical Trial. Government, OVID and Cochrane Library querying for all articles related to Hysteroscopy and RPOC. The final literature search was performed in September

2020. Two authors (VF and AG) independently screened titles and abstracts of studies obtained in the search. The studies were identified with the use of a combination of the following text words: “*Retained products of conception;*” or “*office hysteroscopy*” or “*resectoscopy*” or “*hysteroscopic morcellation.*” The selection criteria of this narrative review included randomized clinical trials, nonrandomized controlled studies (observational prospective, retrospective cohort studies, case–control studies, case series) and review articles on the role of hysteroscopy in RPOC. Articles were excluded according to the following criteria: (a) Articles were not written in English, (b) articles were published as conference papers or abstract only, and (c) studies including information that overlapped other publications. Sixty articles were evaluated for this manuscript, but according to the inclusion and exclusion criteria, only 46 were considered eligible.

## Management

The management options for RPOC consists of expectant management, medical treatment, and surgical intervention<sup>[2]</sup> based on the patient’s severity of the bleeding, the presence of intrauterine infection, and ultrasonographic characteristic of the retained material. The rate of complete evacuation of the retained products when treated with expectant management has been reported between 47% and 81%,<sup>[10,11]</sup> compared to 95%–97% with surgical treatment.<sup>[12]</sup> Medical treatment involves the administration of uterotonic agents such as misoprostol; if this fails, surgical treatment is required.<sup>[13,14]</sup>

In patients undergoing surgical intervention, hysteroscopic resection or dilation and curettage are usually performed. Historically, D and C has been the first choice; however, considering that it is a “blind” procedure that could potentially damage the basal layer of the endometrium, exposing the uterus to unnecessary trauma, with risks of bleeding, uterine perforation, and IUA formation,<sup>[11]</sup> hysteroscopic management, a procedure performed under direct visualization, is now favored.<sup>[15–17]</sup>

Operative hysteroscopy is a safe and effective alternative to D and C with the advantage of providing direct visualization, leading to higher level of complete treatment,<sup>[3]</sup> a reduction of need for a second procedure and a decrease of postoperative intra-uterine adhesion formation.<sup>[18,19]</sup>

The Gutenberg Classification can be very useful in surgical planning as it predicts the risk of bleeding during hysteroscopic removal of RPOC allowing to determine the safest environment in which to safely perform the procedure (in office vs operating room setting).<sup>[5]</sup>

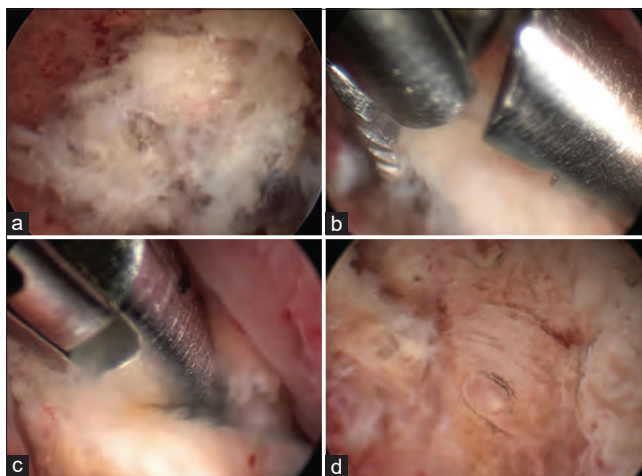
## Office hysteroscopy

Few data on the role of office hysteroscopy in the management of RPOC are available in the literature. The first papers describing

the effectiveness of the hysteroscopic removal in an outpatient setting without general anesthesia or dilation of the cervical canal were published by Jimenez *et al.*<sup>[20]</sup> and Perez-Medina *et al.*<sup>[21]</sup> These studies highlight several advantages, as no need for hospitalization, and an immediate return to daily activities, clear benefits for patients, especially breastfeeding mothers. However, considering that when performed in-office only small-caliber instruments can be used, it could represent a problem when facing larger masses of tissue, tissue strongly adhered to the myometrium, or in cases of profused bleeding. Recently, a study conducted by Maček *et al.* evaluated the success and safety of office hysteroscopy in removing RPOC and identify possible preoperative predictive factors of success, such as beta-human chorionic gonadotropin (b-hCG) levels or ultrasonic features, considering, for example, that persistently high b-hCG serum levels may indicate higher vitality and thus possibly stronger vascularization and adherence of tissue.<sup>[22]</sup> The researchers reported that adequate conditions for performing in office hysteroscopy are when patients present RPOC up to 30 mm in thickness, negative or low b-hCG levels (up to 80 units/L), and absent or minimal vascularization on Doppler US.<sup>[22]</sup> According to the technique [Figure 1], in office hysteroscopy is performed with the use of miniaturized mechanical instruments, such as “alligator forceps,” able to detach the trophoblastic remnants from the myometrial bed, by repeatedly opening and closing the jaws of the forceps. If the material is more densely adherent to the uterine wall, scissors may be used or, if proceeding with great caution, a bipolar electrode, ensuring to prevent iatrogenic damage to the myometrium.<sup>[23]</sup>

### Operative hysteroscopy: Resectoscopy

The first report on the use of operative hysteroscopy for the treatment of RPOC dates back to 1997, in which the group of Goldenberg *et al.*<sup>[24]</sup> described their experience

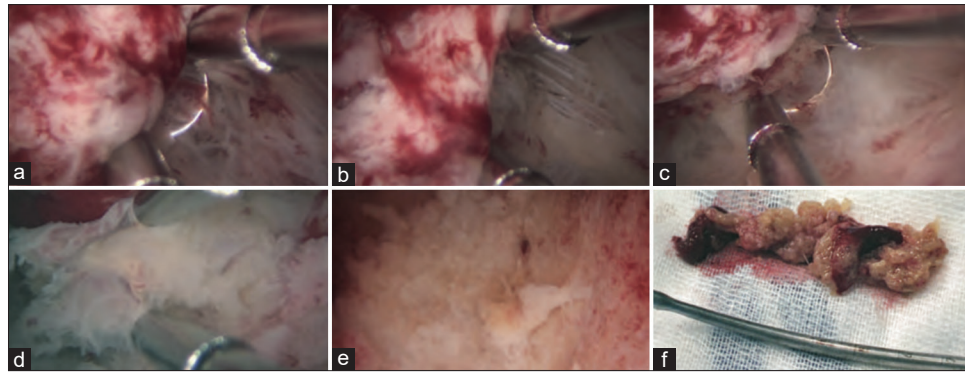


**Figure 1:** Office hysteroscopic removal of residual trophoblastic tissue with a 5-Fr alligator forceps. Identified the lesion (a), with an alligator forceps (b-c), the residual is completely removed (d)

with selective removal of residual intrauterine trophoblastic tissue through hysteroscopy, using the cutting loop of the resectoscope as a curette for selective removal of the adherent residual tissue. Since that time, additional studies have reported increasing experience with this technique and have assessed all the advantages that can derive from the use of this procedure.<sup>[18,25,26]</sup> Faivre *et al.*<sup>[25]</sup> report on the feasibility, efficiency, and reproductive outcomes of hysteroscopic resection of late residual trophoblastic tissue in 50 patients in an observational study over 6 years, evidencing that hysteroscopic resection of RPOC was a safe and efficient procedure, that could be proposed as an alternative to conventional nonselective blind curettage. In 2011, Rein *et al.*,<sup>[18]</sup> demonstrated the superiority of selective hysteroscopic resection of residual trophoblastic tissue over the D and C, both in terms of IUAs formation and pregnancy rates; later, Golan *et al.*<sup>[26]</sup> confirmed, based on a 6-year study, including 159 patients, that hysteroscopic removal of RPOC is a simple, safe, and probably, the preferred procedure for the management of patients diagnosed with RPOC. In all these studies, operative hysteroscopy is performed with the use of a resectoscope with angled loop used in a “cold way,” not activated, to reduce the risk of thermal myometrial damage. The procedure is performed as follows [Figure 2], after introducing the hysteroscope, under direct visualization, the RPOC and their location within the endometrial cavity were documented and the loop of the resectoscope was then used as a curette to extract the remains in fragments.<sup>[23]</sup> An attempt was made to avoid electrocautery in all cases; however, in situations when difficulty was encountered completing total evacuation due to firm adherence of RPOC to the uterine wall with associated excessive bleeding, monopolar electrosurgery was used to provide hemostasis allowing a complete evacuation of the uterine cavity.<sup>[18]</sup>

### Operative hysteroscopy: Hysteroscopic morcellation (hysteroscopic tissue retrieval systems)

Hysteroscopic morcellation is also a good method for the removal of placental remnants, as an alternative to the cold loop technique, with complete removal with only one procedure in 94.3% of patients,<sup>[27]</sup> with the advantage of using mechanical energy, thus avoiding potential thermal damage of the healthy endometrium. The use of mechanical hysteroscopic tissue removal for this indication also limits the risk of uterine perforation because of the instrument’s blunted tip and lateral operating opening. In the first report of the use of hysteroscopic morcellation to treat RPOC, the authors chose the hysteroscopic morcellator over the resectoscope in a case in which there was minimal myometrium separating the placental remnant from the serosa. Since Hamerlynck *et al.* have reported the use of hysteroscopic morcellation in the management of RPOC in

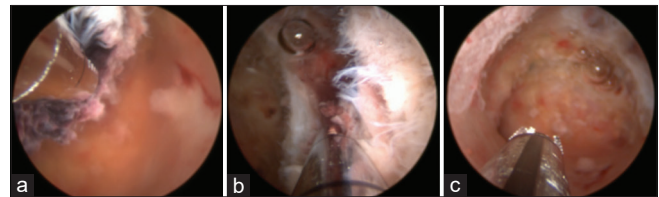


**Figure 2:** Resectoscopic removal of retained trophoblastic tissue using angled loop used in a “cold way”. Once the trophoblastic remnant has been identified, the inactivated loop is advanced repeatedly toward the uterine fundus with antegrade movements, until a cleavage plane is seen to appear between the trophoblastic tissue and the myometrium (a, b, c); subsequently, the suspect material is removed with retrograde movements of the ‘cold loop’, still not activated (d), making sure to pre-serve integrity of the myometrium (e). Macroscopic image (f) of trophoblastic remnant following removal from the uterine cavity

2013,<sup>[27]</sup> the advantages of mechanical hysteroscopic tissue removal with complete removal of RPOC were confirmed by several case series.<sup>[28-31]</sup> For instance, in 2018, Ansari *et al.* have evaluated, in a 5-year retrospective case series, the efficacy and the feasibility of operative hysteroscopy using the Intrauterine Bigatti Shaver (IBS®) for the treatment of placental remnants.<sup>[30]</sup> The researchers have demonstrated that the shaver technique allows a faster procedure with minimal damage to the healthy endometrium. They also assessed that the longer the surgical procedure was performed after a miscarriage, the less bleeding was observed, as consequences of the devascularization of the placental remnants.<sup>[30]</sup>

When using hysteroscopic morcellators for the management of RPOC, the procedure is as follows [Figure 3], the blade of the hysteroscopic morcellator is introduced into the uterine cavity through the working channel of a rigid hysteroscope. Continuous flow is used for optimal uterine cavity distension, irrigation, and visibility. At the tip of the morcellator, through a lateral window opening, the cutting blades precede removing tissue and the sample is aspirated by means of a vacuum source. Aspiration of blood clots and direct removal of intrauterine pathology result in good visualization, allowing good imaging throughout the procedure and the tissue can also be approached laterally, scooping it out of the myometrium when necessary.<sup>[32]</sup>

One of the most severe complications during hysteroscopic removal of RPOC is uncontrollable massive bleeding, potentially requiring the need to proceed with an undesired hysterectomy as the last resource to stop the bleeding, which can happen when the RPOC present rich blood flow.<sup>[15]</sup> Therefore, careful management of RPOC when present with blood flow at the Doppler preoperative evaluation is required to prevent unexpected severe complications. To prevent such bleeding, some authors have described various ways



**Figure 3:** Removal of retained trophoblastic tissue using hysteroscopic morcellator. Once the blade is brought in close contact with the lesion (a), the latter is removed (b) by activating the rotating blade and the suction mechanism, until complete removal is achieved (c)

to control bleeding before the hysteroscopic resection as temporary internal iliac balloon artery occlusion, as suggested by Marques *et al.*<sup>[33]</sup> and uterine artery embolization, as proposed by Takeda *et al.*<sup>[34]</sup> A major risk of bleeding can be detected in cases of retained placenta accreta: For this situation, uterine artery embolization combined with hysteroscopic removal of the residual placental tissue can be considered.<sup>[27]</sup>

### *New proposal technique: Hysteroscopic two-step management*

The two-step hysteroscopic procedure was originally described for the treatment of large submucosal fibroids.<sup>[35,36]</sup> In 2019 Smorgick *et al.*,<sup>[37]</sup> based on that rationale, proposed a two-step hysteroscopic procedure for women with large RPOC mass and/or residual placenta accreta. The authors investigated the two-step surgical approach for the hysteroscopic management of complex RPOC cases (identified by preoperative Doppler flow measurements for the highly vascular RPOC) and assessed surgical outcomes in terms of complications and postoperative IUAs.<sup>[37]</sup> They observed that, when the RPOC removal could not be completed by hysteroscopy in a single procedure, performing a second procedure scheduled 3–4 weeks after, they were able to completely remove the RPOC in all cases

without increased intraoperative complications. Nevertheless, a higher rate of postoperative fever and postoperative IUAs was detected.<sup>[37]</sup>

## RESULTS AND DISCUSSION

RPOC may complicate any type of pregnancy and delivery, including surgical and medical abortion. Their exact incidence is unknown; it goes from 1% after pregnancy carried to term, to 15% after medical termination of early missed abortions.<sup>[2]</sup>

We reviewed the literature aiming to provide an overview of different approaches to removal of RPOC, analyzing associated complications, advantages and disadvantages of the different procedures.

Since 1997, when Goldenberg *et al.*<sup>[24]</sup> first reported on the use of hysteroscopy for the treatment of RPOC, several other studies have demonstrated that hysteroscopic removal of RPOC is the best method of surgical intervention, and reported increasing experience with this technique.<sup>[18,19,38,39]</sup> Nevertheless, traditional D and C remains the most common procedure for the management of placental remnants.<sup>[40]</sup>

To improve safety and accuracy during the procedure, D and C can be performed under US guidance; however, no direct intrauterine visualization of the cavity is possible. That is why the procedure is considered “blind” and is associated with increased risks of uterine perforation, pelvic infection, and incomplete evacuation with persistence of RPOC, with the need for repeated procedures.<sup>[6]</sup> Since RPOC occur in reproductive age women who may desire future pregnancies, an important long-term complication of RPOC and its management is infertility, which is mostly related to the formation of IUA. D and C is reported to be associated with an up to 30% chance of generating IUA formation.<sup>[41]</sup>

Operative hysteroscopy for the management of RPOC has showed to reduce risks associated with traditional D and C, with similar results. Capmas *et al.* reported a success rate around 95%,<sup>[1]</sup> Hamerlynck *et al.* described RPOC successfully removed in 94.3% with only one procedure;<sup>[42]</sup> Pacheco *et al.* found hysteroscopy to be even more effective at achieving complete evacuation on the first attempt, with persistence of RPOC seen in only 1.4% of cases compared to 28.8% of cases treated with D and C.<sup>[6]</sup> Goldenberg *et al.* also published a 100% success rate of office hysteroscopy for RPOC in 18 women.<sup>[41]</sup> There is only one study reporting conflicting results. Hrazdировá *et al.* found that a second operative procedure was necessary for 64.4% of the 45 women included in their study.<sup>[43]</sup> It is unknown why such a high failure rate was reported; however, the authors also concluded that hysteroscopic resection is a safe and efficient operative technique for the management of patients with RPOC.

Several reasons favoring operative hysteroscopy in the management of RPOC are reported in the literature.

First, residual trophoblastic tissue is usually located in a small area of the uterine cavity; hysteroscopic direct visualization allows selective tissue removal, preserving surrounding healthy endometrium from injury that a blind curettage could potentially cause; it also permits the complete removal of RPOC without the need of a second procedure, which is often required when a D and C is performed.<sup>[11]</sup> Moreover, the described hysteroscopic technique that limits the use of energy, as well as hysteroscopic morcellation, minimizes thermal damage and subsequent adhesions formation, and reduces the risk of uterine perforation.<sup>[3,11,25]</sup>

Second, direct visualization of the uterine cavity offers the opportunity of identifying and treat other pathologies and uterine anomalies, which are sometimes the underlying cause of RPOC.<sup>[3,7,19]</sup> Faivre *et al.* reported a 10% uterine malformation rate discovered during the procedure in their series of RPOC.<sup>[25]</sup>

Another potential complication of vigorous curettage is abnormal embryonic implantation in future gestations, predisposing to abnormal placental development favoring placenta accreta with its potentially devastating obstetrical consequences.<sup>[44]</sup>

We found a general agreement between authors about the low likelihood of developing IUAs associated with the use of operative hysteroscopy for the management of RPOC. Hooker *et al.* published an incidence of 12.8% after hysteroscopic resection vs. 29.6% after D and C.<sup>[3]</sup> Capmas *et al.* reported the rate of IUA after D and C from 17% to 30%, and this rate increases with the number of previous curettages, up to 32% after three procedures (including more than 50% of complex synechiae).<sup>[1]</sup> It has been hypothesized that, in addition to the above-mentioned reasons, continuous flushing of the uterus with sterile distention media solution used during hysteroscopy may reduce the risk of local inflammation that could contribute to adhesion formation.<sup>[7]</sup>

According to Hamerlynck *et al.*, from the comparison of the hysteroscopic morcellation and the hysteroscopic loop resection for the removal of RPOC, even if the hysteroscopic morcellation procedures took significantly less time, the rates of complications and postoperative adhesions were similar between the two groups: Both techniques are safe and show high rates of complete removal and tissue availability with 3% of de novo IUAs formation.<sup>[42]</sup>

A previous published literature review about intrauterine postsurgical adhesions formation after hysteroscopy explains how to prevent IUA after the hysteroscopic treatment of RPOC. First, favoring a less invasive surgical strategy (cold

loop technique), and then by performing an early (1–3 weeks after surgery) second-look hysteroscopy, alone or associated with other preventive strategies; such as the use of anti-adhesive, auto-cross-linked hyaluronic acid polysaccharide (ACP) gel.<sup>[45]</sup> We would like to highlight several interesting recommendations to minimize risks of complications related to treatment of RPOC: In case of paucity of symptoms, it might be possible to delay the procedure up to 4 weeks, after the end of any type of pregnancy, of the RPOC removal; thus, the possibility of a spontaneous resolution is considered, and any risks of uterine perforation, infection and larger spillage of distension medium, because of the uterus enlargement and cervical dilation, that is present soon after delivery, especially of full-term pregnancies, is avoided.<sup>[10]</sup> Regarding subsequent fertility, we found that hysteroscopic removal of RPOC led to higher spontaneous conception rate, mostly in terms of shorter mean time of conception.<sup>[6]</sup> Rein *et al.* reported a conception rate of 68.8% after operative hysteroscopy versus 59.9% after D and C, and a shorter mean time to conceive (11.5 months vs. 14.5 months).<sup>[18]</sup> Cohen *et al.* reported similar overall pregnancy rates in women who underwent selective hysteroscopic curettage compared with women who underwent blind D and C, but a tendency to conceive earlier for the first group.<sup>[19]</sup> However, it is not clear whether hysteroscopic morcellation or loop resection of RPOC leads to better reproductive outcomes or lower risk of IUAs.<sup>[22]</sup>

In 2020, the research group of van Wessel *et al.*, published their data on reproductive and obstetric outcomes after hysteroscopic morcellation and resection, demonstrating that the mean time to conception after removal of RPOC is similar at 14 weeks with mechanical hysteroscopic tissue removal and 15 weeks with loop resection. The live birth rate was higher in mechanical hysteroscopic tissue removal (88.9%) compared to resection (68.2%), although the difference was not statistically significant.<sup>[46]</sup>

## CONCLUSIONS

Operative hysteroscopy should be considered the treatment of choice in women with RPOC, as it is described as a safe and feasible procedure, with low rates of postoperative IUAs formation, and possible advantages in terms of future conception rates. Further studies are needed to better assess the future reproductive outcomes of patients after having pregnancies complicated with RPOC, mostly clarifying if different hysteroscopic approaches, such as the use of intrauterine morcellators, improve future fertility rates; since the current literature support superiority of hysteroscopy over traditional dilatation and curettage for treatment of RPOC.

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## Conflicts of interest

There are no conflicts of interest.

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