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Review Article

Surgical and Reproductive Outcomes after Hysteroscopic Removal of Retained Products of Conception: A Systematic Review and Meta-analysis

Salvatore Giovanni Vitale, MD, PhD, John Preston Parry, MD, MPH, Jose Carugno, MD, PhD, Aarathi Cholkeri-Singh, MD, Luigi Della Corte, MD, Stefano Cianci, MD, PhD, Antonio Schiattarella, MD, Gaetano Riemma, MD, and Pasquale De Franciscis, MD, PhD

From the Obstetrics and Gynecology Unit, Department of General Surgery and Medical Surgical Specialties, University of Catania (Dr. Vitale), Catania, Italy, Parryscope and Positive Steps Fertility, Madison, Mississippi; Department of Obstetrics and Gynecology, University of Mississippi Medical Center (Dr. John Preston Parry), Jackson, Mississippi, Obstetrics, Gynecology and Reproductive Sciences Department, Minimally Invasive Gynecology Unit, Miller School of Medicine, University of Miami (Dr. Jose Carugno's), Miami, FL, USA, Department of Minimally Invasive Gynecology, Advocate Lutheran General Hospital, Park Ridge, IL, USA (Dr. Aarathi Cholkeri-Singh's), Department of Neuroscience, Reproductive Sciences and Dentistry, School of Medicine, University of Naples Federico II (Dr. Luigi Della Corte's), Naples, Italy, and Department of Woman, Child and General and Specialized Surgery, Obstetrics and Gynecology Unit, University of Campania, Luigi Vanvitelli, Naples, Italy (Drs. Stefano Cianci, Antonio Schiattarella, Gaetano Riemma, Pasquale De Franciscis)

ABSTRACT **Objective:** To evaluate the impact of hysteroscopy for retained products of conception (RPOC) removal on surgical and reproductive outcomes.

Data Sources: Electronic databases (MEDLINE, Scopus, ClinicalTrials.gov, SciELO, EMBASE, and the Cochrane Central Register of Controlled Trials at the Cochrane Library) were searched from inception to March 2020.

Methods of Study Selection: Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Meta-analysis of Observational Studies in Epidemiology guidelines were followed. Medical Subject Headings terms and text words such as "retained products of conception," "placental remnants," "placenta," and "hysteroscopy" were used for the identification of relevant studies. We included observational and randomized studies that analyzed surgical and/or reproductive outcomes of women who underwent hysteroscopic removal of RPOC. The primary outcome was the complete resection rate after 1 procedure.

Tabulation, Integration, and Results: Twenty out of 245 studies were applicable, with data provided for 2112 women. The pooled complete resection rate was 91% (95% confidence interval [CI], 0.83−0.96). The incomplete resection rate evaluated was 7% (95% CI, 0.03−0.14), with a complication rate of 2% (95% CI, 0.00−0.04). Out of 1478 procedures, only 12 cases (0.8%) of postsurgical intrauterine adhesions were reported. Regarding post-therapy fecundity, women attempting postoperative conception had a clinical pregnancy rate of 87% (95% CI, 0.75−0.95), with a live birth rate of 71% (95% CI, 0.60−0.81) and a pregnancy loss rate of 9% (95% CI, 0.06−0.12).

Conclusion: Hysteroscopy has a high rate of completely removing RPOC in a single surgical step, with low complication rates. Subsequent fecundity seems reassuring, with appropriate clinical pregnancy and live birth rates. However, standardization of approach and comparative trials of different hysteroscopic approaches are needed. Journal of Minimally Invasive Gynecology (2021) 28, 204−217. © 2020 AAGL. All rights reserved.

Keywords: Intrauterine adhesions; Fertility; Surgical complications

"Retained products of conception" (RPOC) is defined as the persistence of trophoblastic tissue or retained placenta inside the uterine cavity after a pregnancy [1]. It can be present after a vaginal or cesarean delivery of a newborn, pregnancy loss, or medical or surgical voluntary pregnancy termination. Approximately 6% of the pregnancies are complicated by RPOC-related conditions, including infections and postpartum hemorrhage [2]. Most of the patients with RPOC are symptomatic. Common symptoms include

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Corresponding author: Salvatore Giovanni Vitale, MD, PhD, Obstetrics and Gynecology Unit, Department of General Surgery and Medical Surgical Specialties, University of Catania, Via Santa Sofia 78, Catania 95123, Italy.
E-mail: vitalesalvatore@hotmail.com

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abnormal uterine bleeding, pelvic pain, and fever. If left untreated, RPOC can have a negative impact on fertility [3,4].

For almost a century, dilatation and blind removal through sharp, blunt, or suction curettage (D&C) has been used to surgically treat RPOC. However, blind techniques are associated with complications such as heavy bleeding, infections (endometritis and pelvic inflammatory disease), and uterine perforation [5]. Moreover, persistent RPOC can occur after a blind D&C. The incomplete removal of RPOC can be evaluated by ultrasound. If, after the blind D&C, the residual endometrial thickness is greater than 20-mm, an unsuccessful or incomplete removal of RPOC is more likely to have occurred [1].

In addition, a common adverse outcome associated with D&C is intrauterine adhesion (IUA) formation. The incidence of post-D&C IUA formation is estimated to be between 15% and 40% [6]. The pathogenesis of IUA formation after D&C is related to damage of the basalis layer of the endometrium, with the generation of intracavitary granulation tissue at the margins that fuse to form fibrous tissue bridges. In the most severe cases, the uterine cavity may be obliterated from synechiae without evidence of a functional endometrium [7−9]. IUAs, also referred to as Asherman's syndrome, negatively affect reproductive outcomes, with pregnancy loss of up to 90% and with subfertility superimposed on recurrent early pregnancy loss. Obstetric complications such as placenta accreta and other placentation abnormalities and preterm delivery are common sequelae of pregnancy experienced by women with IUAs [10,11].

Hysteroscopy is considered the gold standard for the diagnosis and treatment of intrauterine disorders. Goldenberg [12] in 1996 was the first to report the use of hysteroscopy for RPOC, facilitating directed identification and treatment. Over the last 10 years, several studies have been conducted to evaluate the efficacy of hysteroscopy for the treatment of RPOC. A variety of approaches to RPOC has been reported. The aim of this systematic review and meta-analysis was to summarize the literature on hysteroscopic management of RPOC and analyze its effect on surgical and reproductive outcomes.

Materials and Methods

Our meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Supplemental Appendix 1) [13] and Meta-analysis of Observational Studies in Epidemiology guidelines (Supplemental Appendix 2) [14]. The research protocol was registered in the International Prospective Register of Systematic Reviews database (number: CRD42020180768).

Study Search

The research protocol was defined a priori. It addressed methods for searching the literature, including examining articles, as well as data extraction and analysis. Electronic databases (MEDLINE, Scopus, ClinicalTrials.gov, SciELO, EMBASE, and the Cochrane Central Register of Controlled Trials at the Cochrane Library) were searched from the inception of each database to March 2020. The search terms used were the following text words and Medical Subject Headings (MeSH) terms: "retained products of conception" or "placental remnants" or "placenta (MeSH)" and "hysteroscopy (MeSH)." No restrictions for geographic location were applied. Moreover, the reference lists of all identified research articles were examined to identify studies not captured by electronic searches. The electronic search as well as the eligibility of the identified studies were independently assessed by 2 authors (G.R. and S.C.). Disagreement was resolved by discussion with a third reviewer (P.D.F.).

Primary and Secondary Outcomes

The primary outcome of this meta-analysis was the complete resection rate (CRR). It was defined as the complete removal of the visualized RPOC in 1 hysteroscopic procedure, without the need for reintervention. The CRR was evaluated in accordance with the absence of RPOC at follow-up, including ultrasonography or diagnostic hysteroscopy (depending on the methodology of the study). The secondary outcomes were the following: incomplete resection rate (IRR), defined as incomplete removal of RPOC that required at least 2 operative hysteroscopies; complication rate (CR), defined as surgical complications developed during or after the procedure; and time between diagnosis and treatment (TDT), defined as the time interval between the RPOC diagnosis and complete resection of the disease. Moreover, we evaluated the negative findings rate, defined as histopathologic examination of the specimens retrieved during hysteroscopy in which RPOC were not found.

The reproductive outcomes assessed after the resection of RPOC were the following: live-birth rate (LBR), defined as the birth of a living fetus after 24 weeks of gestational age; clinical pregnancy rate (CPR), defined as ultrasonographic visualization of 1 or more intrauterine gestational sacs; and pregnancy loss rate (PLR), defined as a spontaneous pregnancy loss occurring before 24 weeks of gestation.

Risk of Bias

For observational studies suitable for this review, the risk of bias in each included study was assessed using the Newcastle-Ottawa Scale (NOS) criteria. According to the NOS, each study is judged on 3 broad elements: the selection of study groups, the comparability of these groups, and the ascertainment of the outcome of interest. Assessment of the selection of a study includes the following criteria: evaluation of the representativeness of the exposed cohort, selection of the nonexposed cohort, ascertainment of exposure, and demonstration that the outcome of interest was not likely to occur spontaneously at study initiation. The

comparability of studies is assessed, including the evaluation of the comparability of the cohorts on the basis of the design or analysis. Moreover, the ascertainment of the outcome of interest is evaluated, including the method of determining the outcome of interest, duration, and adequacy of follow-up. According to the NOS, a study can be awarded a maximum of 1 star for each numbered item within the selection and outcome categories. A maximum of 2 stars can be given for comparability. For randomized clinical trials, the risk of bias in each included study was assessed by using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* [15]. Seven domains related to risk of bias were assessed in each included trial because there is evidence that these issues are associated with biased estimates of treatment effect: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; and (7) other bias. Reviews of authors' judgments were categorized as "low risk," "high risk," or "unclear risk" of bias [14]. Risk of bias assessment was independently assessed by 3 authors (J.C., A.S., and C.S. A.). Disagreement was resolved by discussion with a fourth reviewer (S.C.). The potential for publication bias was evaluated graphically using the funnel plot.

Statistical Analysis

Two authors conducted the data analysis in an independent manner using Review Manager 5.3 (The Nordic Cochrane Centre 2014, Copenhagen, Denmark) and Stata 14.1 (StataCorp LLC, College Station, TX).

In a conservative approach, we considered the "main results" the random effect estimates of event proportion, allowing for variation of true proportion across studies. This was calculated by means of the method of DerSimonian and Laird. After application of the Freeman-Tukey double arcsine transformation to stabilize variances, the pooled estimate was calculated. The confidence interval (CI) was calculated using the exact method. Using the Higgins I^2 index, heterogeneity was quantified to depict the percentage of total variation across the studies that could be related to heterogeneity itself rather than by chance. In our meta-analysis, I^2 values of 25%, 50%, and 75% were used as cutoff points for low, moderate, and high degrees of heterogeneity. All the other proportions, with a relative CI, were analyzed using the same approach or as relative risk (RR).

Results

Study Characteristics

Two-hundred forty-five studies were originally identified through the database search. Of these, 32 were removed as duplicates. After title and abstract screening, 192 studies were removed as case reports (53 records), review articles (28 records), or out-of-topic research articles (133 records). The excluded articles, with reasons for their exclusion, are described in Supplemental Appendix 3. Twenty-one studies were selected, of which 1 was removed for being a study protocol without published results. Twenty studies [2,5,16−33], with a total of 2112 participants, were included in quantitative synthesis and meta-analysis (Fig. 1). Seventeen studies (85%) were retrospective analyses of women who had undergone hysteroscopic treatment of RPOC. One trial [24] had a randomized controlled design and compared hysteroscopic morcellation of RPOC with resectoscopic loop resection. Two studies [5,20] were retrospective cohort studies comparing hysteroscopy and D&C for the removal of RPOC. The results of quality assessment for the 19 non−randomized controlled trial studies are shown in Supplemental Table 1, whereas the risk of bias for the randomized trial is depicted in Supplemental Table 2. Publication bias was not apparent by means of funnel plot analysis (Supplemental Fig. 1). Eight studies reported both surgical and postsurgical reproductive outcomes. Eight studies [2,16,17,19,22,24,26,33] reported surgical outcomes only, whereas 4 [5,25,29,30] evaluated only reproductive outcomes. Three studies included only RPOC after vaginal delivery (VD) or cesarean section (CS) [20,22,27]. Seventeen out of 20 studies evaluated RPOC identified after pregnancy loss or term deliveries. Nine hundred sixty-six women (46%) experienced RPOC after a VD or CS, whereas 1136 patients (54%) experienced RPOC after having a pregnancy loss (Table 1).

Regarding hysteroscopic resection, 20% (4/20) of the studies were conducted in an outpatient setting (the patients were discharged the same day of the procedure) under general or local anesthesia; 20% (4/20) were carried out in the office without anesthesia; whereas 60% (12/20) were performed in the operating room (OR) (Table 1). Regarding instrumentation used for the removal of RPOC, 10 studies (50%) used a 26 Fr resectoscope with the "cold loop" technique (avoiding the use of energy); 6 (30%) used hysteroscopic morcellators; and in 4 (20%) studies, a 5-mm hysteroscope with bipolar electrodes and 5 Fr polyp forceps and scissors were used (Table 1).

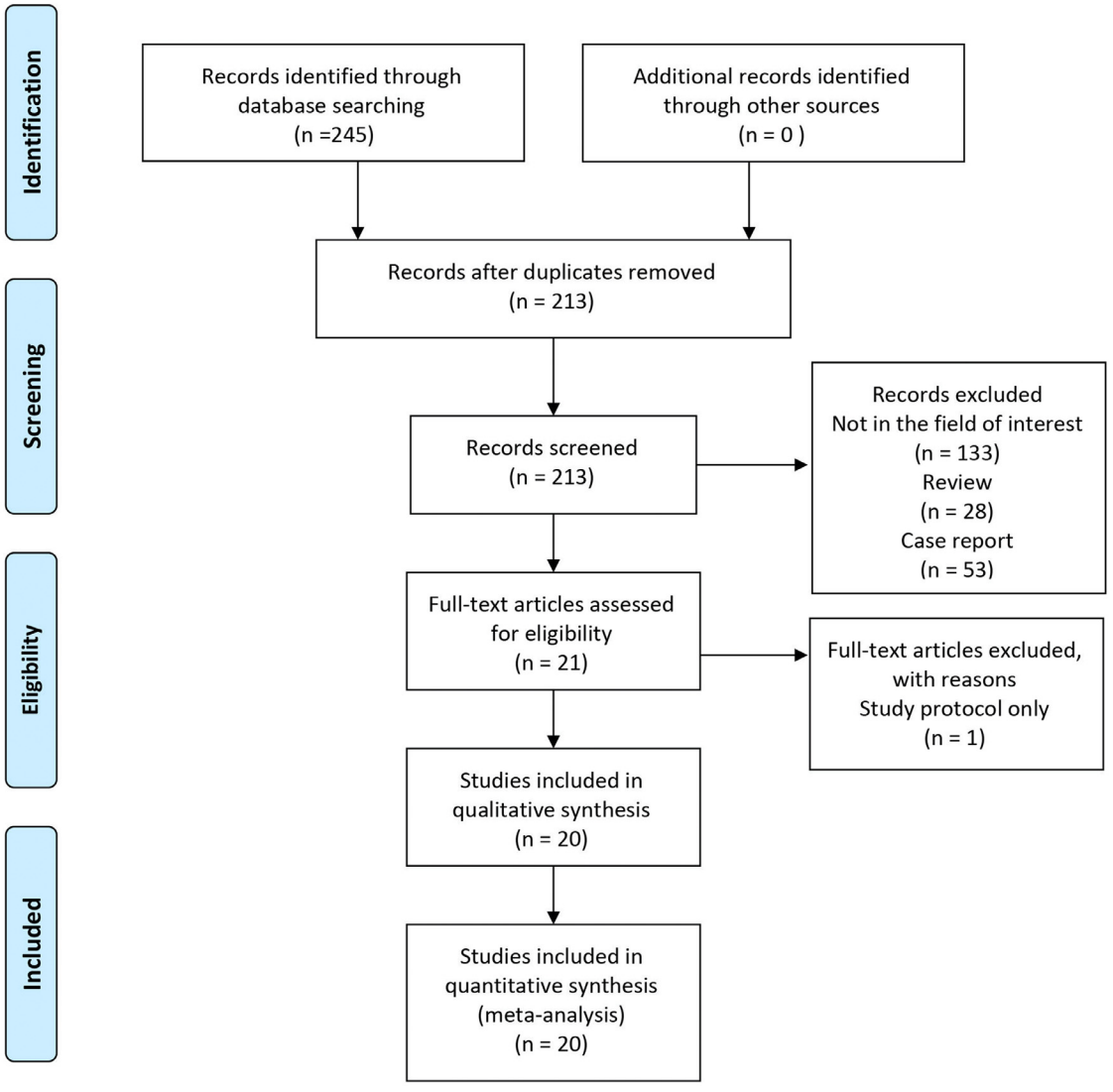
Regarding postsurgical follow-up, in most of the cases, which account for 68% (1438/2112) of the procedures, RPOC identification was through second-look hysteroscopy, whereas in the other 32% (674/2112), the presence or absence of residual retained tissue was evaluated using ultrasonography or other diagnostic techniques.

Surgical Outcomes

The CRR of RPOC in a single hysteroscopic procedure was 91% (95% CI, 0.83−0.96; $I^2 = 94\%$) (Fig. 2). The pooled IRR evaluated was 7% (95% CI, 0.03−0.14; $I^2 = 92\%$) (Fig. 3). Concerning intra- and postoperative complications, the pooled CR was 2% (95% CI, 0.00−0.04; $I^2 = 78\%$) (Fig. 4).

Fig. 1

Flow diagram of studies included in the systematic review and meta-analysis.



Regarding the 16 studies that reported surgical outcomes, 9 did not report any complications. Macek et al [26] reported 12 cases of mild to moderate bleeding (50 mL −200 mL) and 2 vasovagal reactions that had no consequences on the CRR. Sonnier et al [32] observed 10 cases of heavy uterine bleeding (more than 200 mL) and 7 uterine perforations that needed subsequent laparoscopic management, for a total of 17 cases with complications out of 22 of the incomplete interventions. Six procedures were complicated by perforation, fluid overload, or cervical laceration in the series reported by Smorgick et al [2] and were part of the 11 incomplete procedures. Hamerlynck et al [33] reported 6 uterine perforations, 1 hemorrhage, 1 postoperative fever, and 1 case of abdominal pain. Of these, only 5 procedures were declared as incomplete. In summary, 17.5% (28/160) of the incomplete procedures and 2% (28/1478) of the overall operations were related to complications. There were no significant differences between complications in the studies that compared different instrumentations and techniques [5,20,24].

Only 12 cases (0.8%; 12/1478 procedures) of Asherman's syndrome were reported. Evaluation of the pooled negative findings rate showed that subsequent histopathologic examination did not find any trophoblastic tissue in 11% of the cases (95% CI, 0.05−0.20; $I^2 = 95\%$) (Fig. 5). Mean TDT was reported by 11 studies [5,16−18,23,24,26,28,30,32,34]. It ranged from 37 days [5] to 109.2 days [18] (Table 1).

Table 1

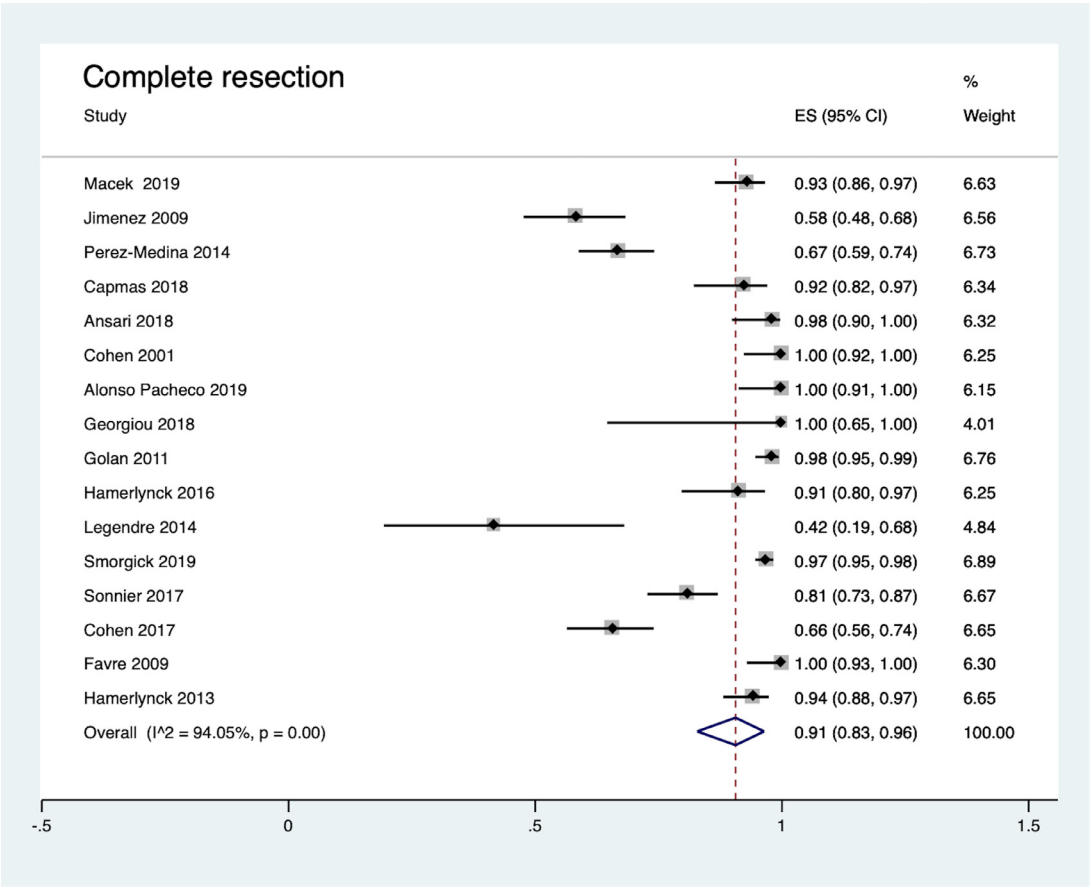
Main characteristics of the studies included in quantitative analysis

Author, year	Study period	Location	Study design	Case number	Median age	Setting	Anesthesia	OR/In office	Treatment	RPOC after VD or CS	RPOC after PL	Mean TDT (d)
Macek et al [29], 2019	2012–2015	Slovenia	Retrospective	101	31.8	Outpatient	None	In office	TruClear 5-mm (15 Fr) mechanical morcellator (Medtronic, Minnesota, MN)	75	26	57
Jimenez et al [31], 2009	2001–2008	Spain	Retrospective	84	32	Outpatient	None	In office	5-mm (15 Fr) hysteroscope + instruments	37	47	NA
Pérez-Medina et al [28], 2014	2004–2014	Spain	Retrospective	185	32	Outpatient	None	In office	5-mm (15 Fr) hysteroscope + instruments	28	157	40
Herman et al [30], 2018	2011–2015	Israel	Retrospective	178	30.5	Inpatient	General	OR	8-mm (24 Fr) resectoscope	85	93	52
Ben-Ami et al [5], 2014	2000–2010	Israel	Retrospective	83	30.5	Inpatient	General	OR	8-mm (24 Fr) resectoscope vs D&C	50	33	37
Capmas et al [18], 2018	2012–2014	France	Retrospective	114	33.5	Inpatient	Local	OR	8-mm (24 Fr) resectoscope	30	84	109.2
Ansari et al [17], 2018	2013–2018	Iran, Italy	Retrospective	52	36	Inpatient	General	OR	8-mm (24 Fr) intrauterine Bigatti shaver (Karl Storz, Tuttlingen, Germany)	5	47	54.2
Cohen et al [20], 2001	1997–2000	United States	Retrospective	70	NA	Inpatient	General	OR	8-mm (24 Fr) resectoscope vs D&C	19	51	NA
Alonso Pacheco et al, 2019 [16]	2008–2017	Spain	Retrospective	40	35.92	Inpatient	General	OR	8-mm (24 Fr) resectoscope	11	29	69
Georgiou et al [22], 2018	2017–2018	UK	Retrospective	7	30	Outpatient	Local	OR	8-mm (24 Fr) MyoSure hysteroscopic morcellator (Hologic, Inc., Marlborough, MA)	7	0	NA
Golan et al [23], 2011	2001–2007	Israel	Retrospective	159	NA	Inpatient	General	OR	8-mm (24 Fr) resectoscope	51	108	60.2
Hamerlynck et al [24], 2016	2011–2015	Belgium, Netherlands	RCT	84	NA	Outpatient	General or local	OR	8-mm (24 Fr) TruClear 8.0 mechanical morcellator vs 8-mm (26 Fr) resectoscope	48	36	70
Ikhena et al [25], 2016	2004–2014	United States	Retrospective	111	35	Inpatient	General	OR	8-mm (24 Fr) resectoscope	40	71	NA
Legendre et al [27], 2014	2001–2011	France	Retrospective	12	37.3	Outpatient	General	OR	8-mm (24 Fr) resectoscope	12	0	NA
Smorgick et al, 2019 [2]	2013–2018	Israel	Retrospective	358	35.9	Inpatient	General	OR	8-mm (24 Fr) resectoscope	216	142	54
Sonnier et al [32] 2017	2008–2011	France	Retrospective	115	32.9	Inpatient	General	OR	8-mm (24 Fr) resectoscope	30	85	49
van Wessel et al [29], 2019	2018–2018	Belgium, Netherlands	Retrospective	86	33	Outpatient	General or local	OR	8-mm (24 Fr) TruClear 8.0 vs 8-mm (26 Fr) resectoscope	49	37	NA
Cohen et al [19], 2017	2011–2014	Israel	Retrospective	108	32.6	Outpatient	None	In office	5-mm (15 Fr) hysteroscope + instruments	108	0	NA
Faivre et al [21], 2009	1999–2006	France	Retrospective	50	32.5	Inpatient	General or local	OR	8-mm (26 Fr) resectoscope	8	42	NA
Hamerlynck et al, 2013 [33]	2005–2010	Belgium, Netherlands	Retrospective	105	34	Inpatient	General or local	OR	8-mm (24 Fr) TruClear 8.0 mechanical morcellator	57	48	NA

CS = cesarean section; D&C = dilatation and curettage; NA = not available; OR = operating room; PL = pregnancy loss; RCT = randomized controlled trial; RPOC = retained products of conception; TDT = time between diagnosis and treatment; VD = vaginal delivery.

Fig. 2

Forest plot for complete resection rate. CI = confidence interval; ES = effect size.



Reproductive Outcomes

Women who tried to conceive after surgery had a CPR of 87% (95% CI, 0.75−0.95; $I^2 = 92\%$) (Fig. 6). From these pregnancies, the resulting LBR was 71% (95% CI, 0.60−0.81; $I^2 = 84\%$) (Fig. 7), and the pooled PLR was 9% (95% CI, 0.06−0.12; $I^2 = 17\%$) (Fig. 8).

Hysteroscopy vs D&C

Regarding the 2 studies comparing hysteroscopy with blind D&C, [5,20], the IRR was reported only by Cohen et al [20], showing 0% (0/46) for inpatient hysteroscopy compared with 12.5% (3/24) for D&C that required reintervention. Therefore, the CRR was 100% for hysteroscopy vs 77.5% for D&C. The operators' skills were comparable. Complications were absent in both groups.

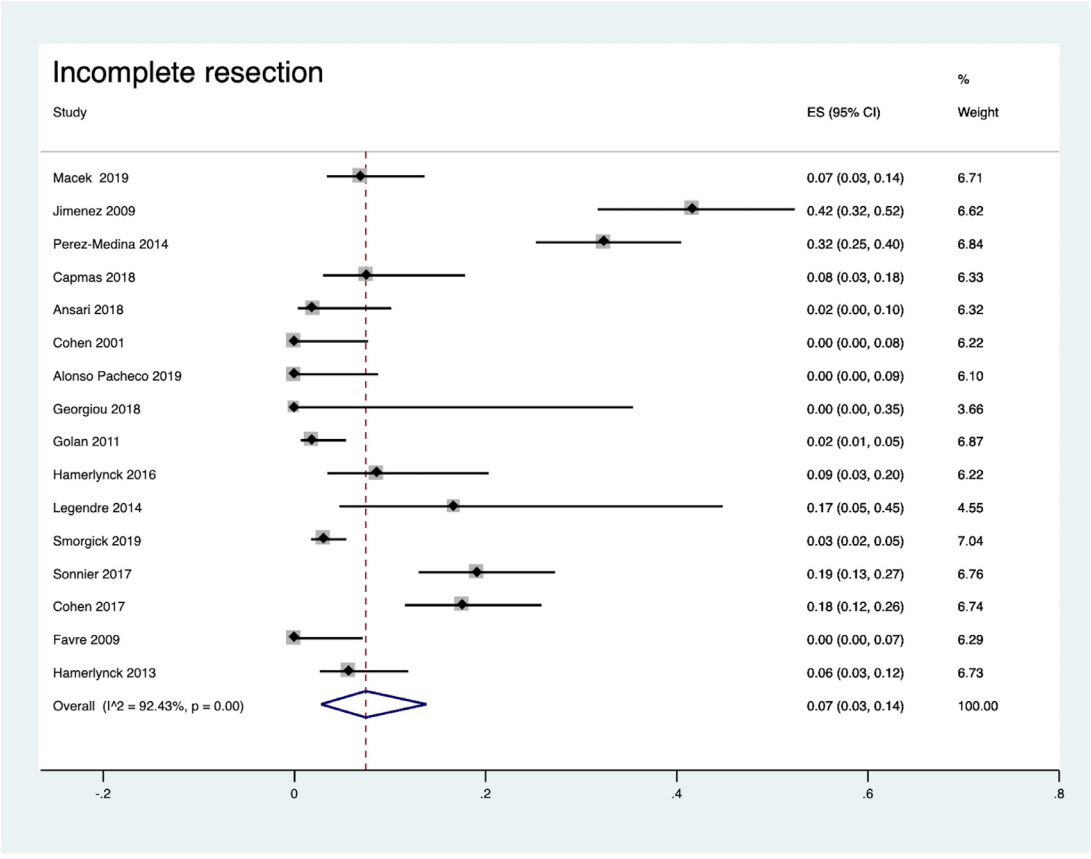
Concerning fertility issues, the PLR for hysteroscopic resection did not significantly differ from that for D&C (17/97 vs 14/113; RR 1.31; 95% CI, 0.49−3.46), as well as that for CPR (97/100 vs 104/110; RR 1.13; 95% CI, 0.58−2.22) and LBR (77/97 vs 90/104; RR 0.92; 95% CI, 0.81−1.04).

Meta-regression and Subgroup Analyses

Statistical heterogeneity with high inconsistency ($I^2 > 75\%$) for the CRR was noted. To reduce the inconsistency and explain the differences among the trials for this primary outcome, the potential sources of heterogeneity among the studies were assessed by means of a meta-regression analyses on predefined subgroups used in the assay. Meta-regression analysis assessed setting (outpatient/inpatient), use of anesthesia (none/local or general), size of the device (24 Fr [8-mm])/smaller than 24 Fr), and type of resection (cold loop/mechanical retrieval) as potential sources. Analysis showed that setting ($p < .001$), use of anesthesia ($p = .001$), and size of the device ($p = .015$) were significant sources of heterogeneity (meta-regression $p < .05$). However, using the cold loop technique relative to mechanical tissue removal of RPOC did not result in a statistically significant shift in treatment outcomes ($p = .263$)

Fig. 3

Forest plot for incomplete resection rate. CI = confidence interval; ES = effect size.



Meta-regression analysis showed no relationship between the TDT and all the evaluated surgical outcomes, including CRR (p = .06), IRR (p = .07), and CR (p = .78). Regarding reproductive issues, the TDT did not influence subsequent fertility because no correlation to PLR (p = .86), CPR (p = .79), or LBR (p = .77) was noted.

RPOC Developed after Vaginal or Cesarean Delivery

We conducted a subgroup analysis related to the timing of RPOC (after previable pregnancy loss relative to postpartum). Three studies [20,22,27] evaluated only post-VD or -CS RPOC. Limiting the analysis to postdelivery RPOC reduced between-study heterogeneity from high (I^2 >75%) to low (I^2 = 0%). The pooled CRR was 71% (95% CI, 0.41−0.94; I^2 = 0%), with a significant decrease related to the overall CRR (RR 0.75; 95% CI, 0.66−0.85); meanwhile, the IRR was 14% (95% CI, 0.08−0.22; I^2 = 0%). Incomplete procedures were significantly higher in postdelivery procedures (RR 1.53; 95% CI, 1.01−2.32). No complications were reported by any subgroup within these 3 studies.

Discussion

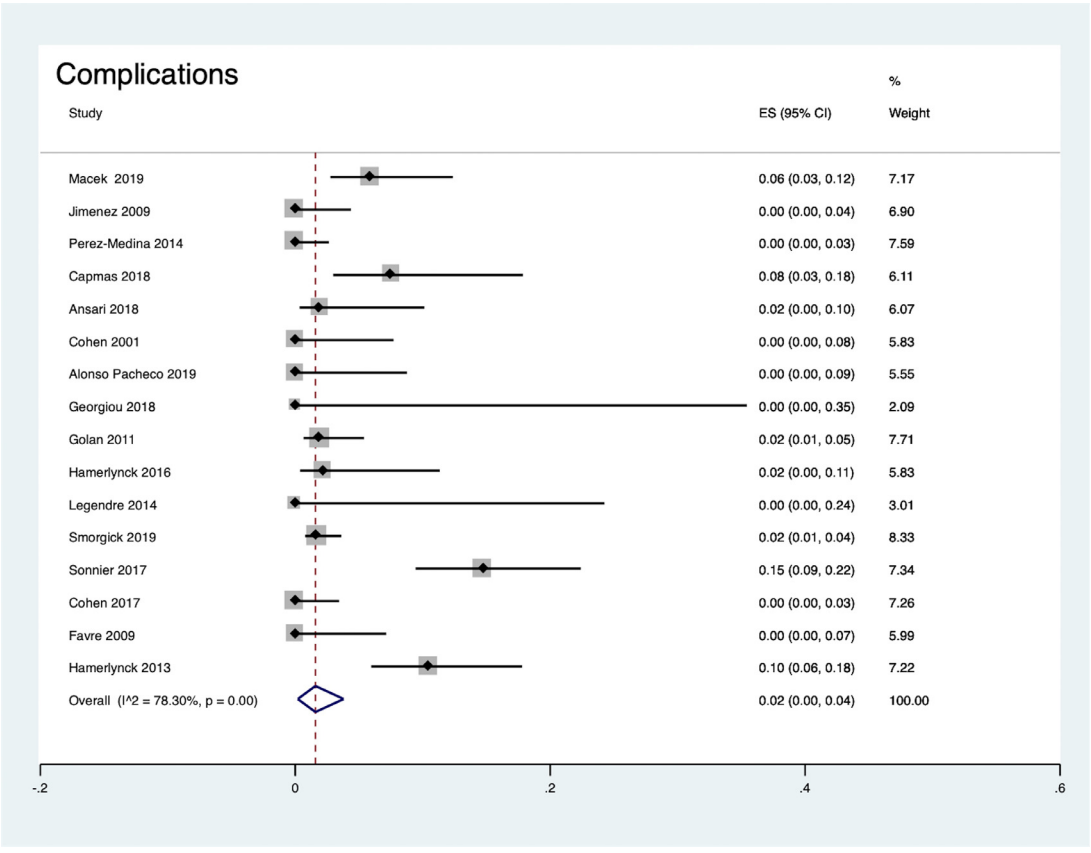
Our systematic review and meta-analysis show that the hysteroscopic approach to the patient diagnosed with RPOC is effective and safe, completely resecting the pathologic condition in a single procedure in 91% of the cases, and having low rates of complications, infection, and IUA formation. Moreover, women who tried to conceive after the procedure had a high rate of fertility and live births, with a low rate of subsequent pregnancy loss.

To date, there is no agreed-upon standard approach to RPOC. Blind D&C is still the most widely used first-line method of managing ultrasound-diagnosed RPOC. However, blind curettage in an area without RPOC can traumatize the endometrium's stratum basale without benefit, while creating risk for IUAs [35,36].

As technology has evolved, clinical practice should evolve as well. A century ago, the management of RPOC under direct visualization was not realistic (Fig. 9). However, blind D&Cs for RPOC, postpartum hemorrhage, and more may need to be reconsidered because the complications are inversely proportional to visualization. Incomplete curettage increases the risk for repeat surgery, and

Fig. 4

Forest plot for complication rate. CI = confidence interval; ES = effect size.



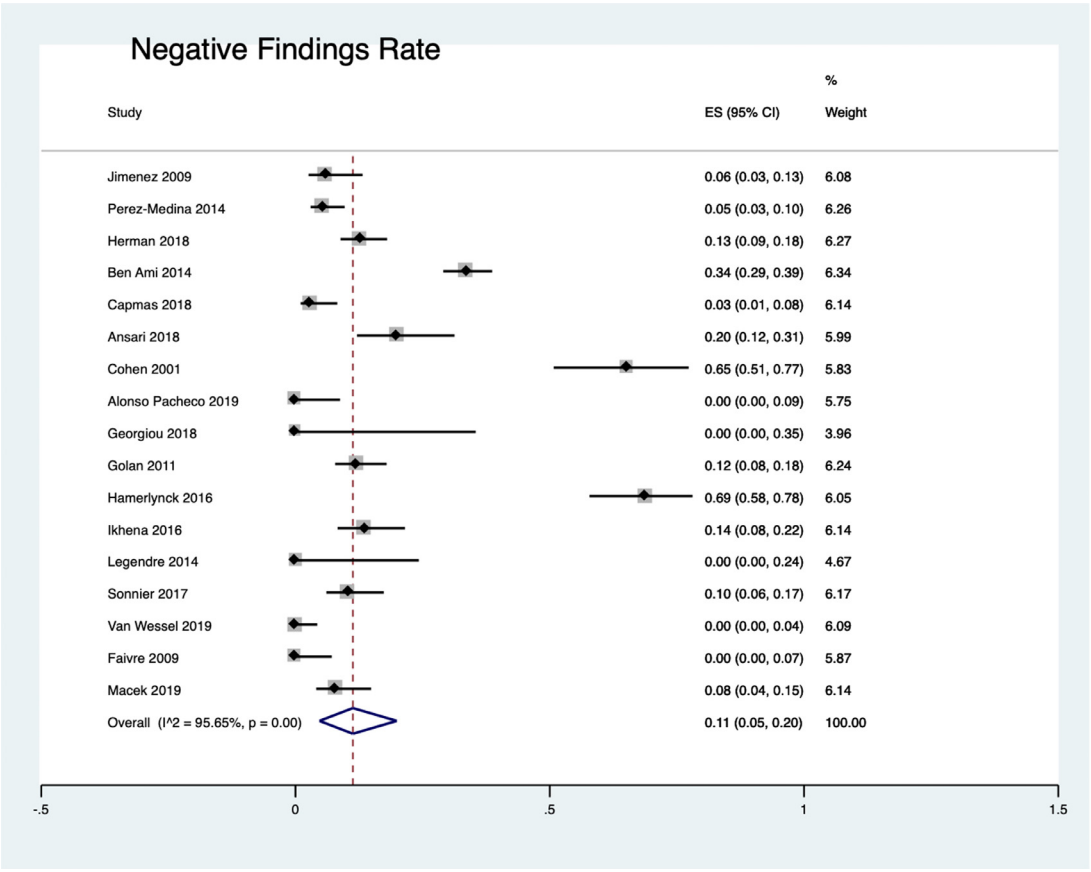
excessive curettage increases the risk for both IUA formation and endometrial and myometrial trauma, leading to increased bleeding. Both complications derive from generalized and blind curettage rather than focused and visualized approaches [37]. The hysteroscopic technique, with targeted removal of the pathologic condition, minimizes trauma to the healthy endometrium, with both short- and long-term potential benefits [5,20,37]. The safety and feasibility of hysteroscopic resection, relative to blind D&C, are increasingly accepted for most forms of intrauterine pathologic conditions. However, RPOC remain an exception, where directed resection is often an alternative approach rather than common practice.

There are several advantages in choosing hysteroscopy over blind curettage for RPOC. As previously noted, intuition and data support visualized removal relative to blind removal of the pathologic condition to reduce intraoperative and postoperative complications [38,39]. This principle extends to RPOC, where the risk for complications was significantly lower with hysteroscopy. Moreover, costs can be reduced through office hysteroscopic management relative to D&C in the OR through reduced facility- and anesthesia-associated costs [40–42]. Supporting this view, this meta-analysis found RPOC leading to IUA formation after hysteroscopic management in only 9 cases out of 1323 procedures (0.07%). According to a recent review, the true incidence of IUAs after blind D&C may be as high as 15% to 40% [6]. However, it should be noted that D&C is often performed in an emergency setting, where the predisposition to IUAs is higher because the endometrium is more damage-prone and the chance of infection might be higher. It is remarkable that a possible 150- to 400-fold reduction of IUA incidence could be achieved by choosing a targeted hysteroscopic removal over blind techniques [39]. These findings suggest the rarity of creating adhesions after hysteroscopic cold loop resection or mechanical removal of RPOC. In fact, the method of pathologic condition removal may influence the risk of de novo adhesions. The latest American Association of Gynecologic Laparoscopists Practice Report on IUAs states that the incidence of IUAs is higher for blind techniques (i.e., D&C) relative to surgery under direct visualization (i.e., hysteroscopy) for the removal of pregnancy-related pathologic conditions [39].

The extent of RPOC, ranked using the Gutenberg classification, was reported by 1 study [16]. Regarding the treatment of moderate and severe pathologic conditions,

Fig. 5

Forest plot for negative findings rate. CI = confidence interval; ES = effect size.



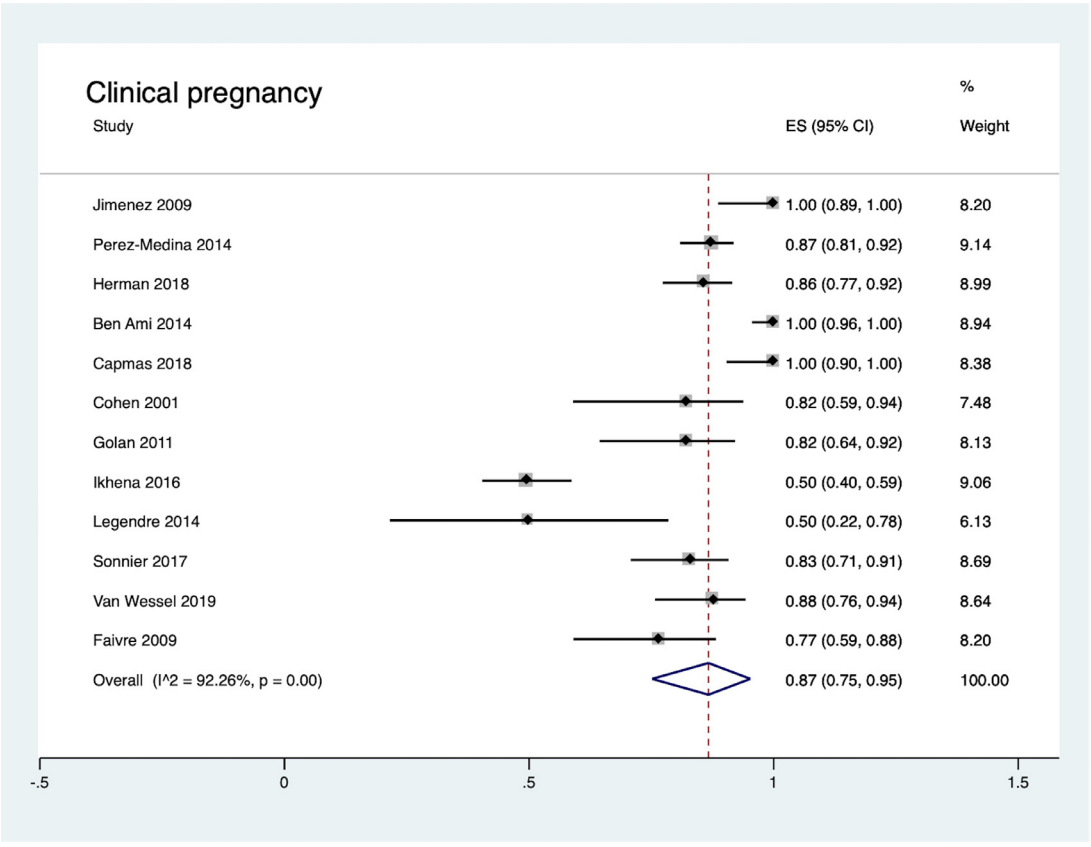
hysteroscopic resection showed high efficacy. However, severe RPOC required the use of monopolar energy during surgery to achieve hemostasis, but monopolar energy was not used for cutting and resecting the pathologic conditions and was not associated with subsequent IUAs [16].

As hysteroscopic procedures continue to move to the office setting, with higher-quality and smaller-diameter operative hysteroscopes available, this has lowered the threshold for offering a hysteroscopic approach over a blind procedure for the management of patients with RPOC. Given that office hysteroscopy can be safely performed without anesthesia, with 91% of the patients reporting mild to no discomfort, we are likely to see a more widespread use of this approach in the future for the management of patients with RPOC [43−45]. Four [19,26,28,31] of the 20 studies included in this review looked at office hysteroscopy for RPOC. Their findings demonstrated that 95.7% of the procedures could be completed in the office, with only 19 of 435 procedures needing to be performed in the OR to safely complete the procedure. Although office hysteroscopy was associated with a higher rate of 2-step removal of RPOC—24.6% (107/435) vs 5.1% (53/1043) for cases performed in the OR—this is to be expected for the context with typically smaller−caliber instruments and not having anesthesia. Moreover, patients needing a second hysteroscopy had few complications (23/435, 5.3%) and a low postsurgical IUA rate (3/435, 0.7%).

Despite this meta-analysis showing that most of the RPOC resections were effectively managed in a single step, 9% of the procedures still remained incomplete. The reasons driving these findings can be found through analyzing the IRR. In fact, 2 studies [28,31] with the highest rates of incomplete procedures accounted for 51% (81/160) of the incomplete resections. These 2 trials were both performed in the office setting without anesthesia. Pérez-Medina et al [28] reported that when procedures lasted longer than 30 minutes, they were suspended and completed in a second surgical step owing to decreased patient tolerance of the procedure or owing to the excessive size of RPOC. In fact, in the case of larger placental remnants, it might be difficult to perform a satisfying resection in 1 step, similar to hysteroscopic resection of large grade 1 or grade 2 uterine myomas. Concerning Jimenez et al [31], the study was carried out between 2001 and 2008. In the subsequent decade, hysteroscopic instrumentation for in-office treatment has been meaningfully improved, with clearer visualization, greater equipment durability, and additional approaches to removal, including morcellation [44]. However, it is

Fig. 6

Forest plot for clinical pregnancy rate. CI = confidence interval; ES = effect size.



important to emphasize that the 9% IRR does not seem to relate to missed pathologic conditions, but instead to deliberate choices that related to patient safety and satisfaction.

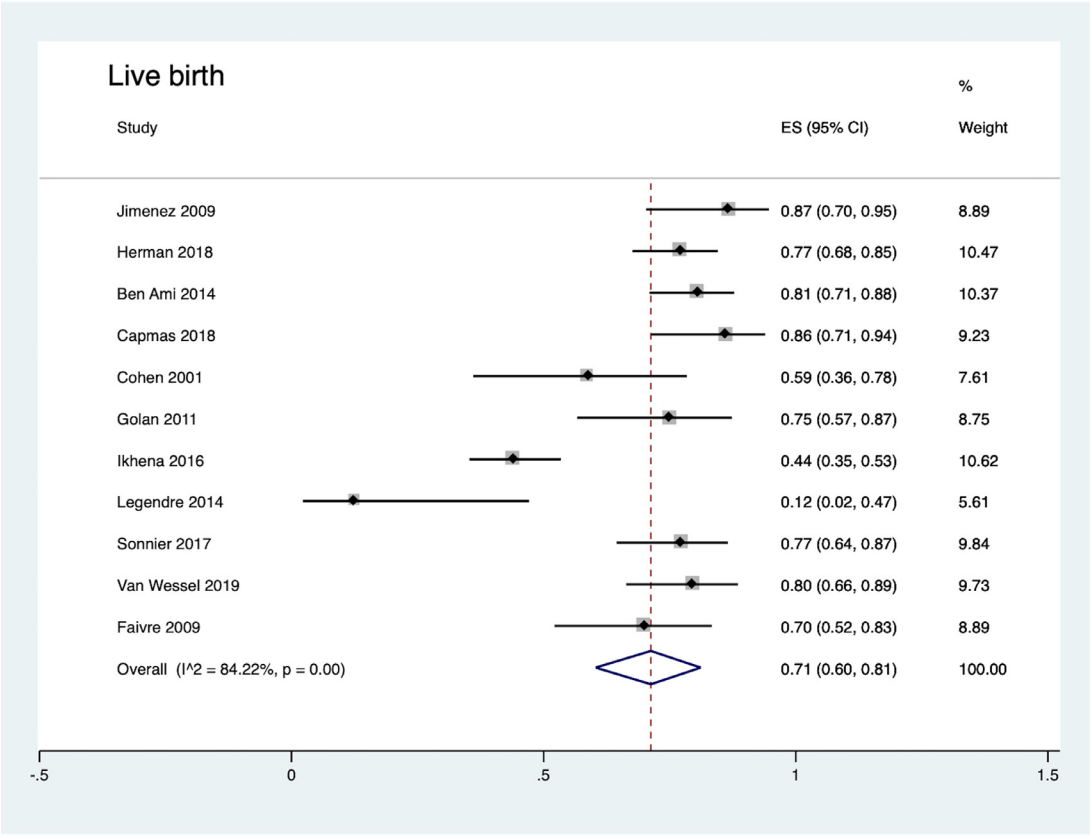
If patient tolerance, clinical circumstances, and technologic constraints were the driving forces behind incomplete resection, this raises several issues. First, there are important differences between incomplete resection with hysteroscopy and D&C, where one is more likely to know of incomplete resection with visualization relative to a blind procedure. Choosing to terminate a procedure because of safety and patient discomfort is appropriate in the office, particularly when a hysteroscopy was not planned as operative but converted from diagnostic under a see-and-treat approach. Prompt follow-up for completion in these circumstances has very different implications for progression of the pathologic condition relative to incomplete procedures with D&C, where a missed diagnosis can lead to prolonged bleeding as well as infection of RPOC [37,46]. Second, as understanding improves for what drives incomplete procedures after operative hysteroscopy, clinicians will have a better sense of what can be achieved in the office relative to the OR and will turn to approaches and technology better suited for patient conditions. If hysteroscopic management of RPOC is relatively new, whereas curettage has been used for more than a century, there is often greater opportunity to refine relatively new approaches than established ones, suggesting that incomplete procedure rates will likely improve with more widespread use and greater data availability.

A critical issue of RPOC is related to the true presence of trophoblastic tissue in the uterine cavity. Neither clinical nor sonographic parameters have been associated with histopathologic confirmation of trophoblastic tissue [1]. Our meta-analysis found that in 11% of the procedures, there was no trophoblastic material at histopathologic examination. However, Herman et al [1] reported that the surgeon's impression of the kind of tissue and its size are the 2 most important factors for confirming intracavitary RPOC, showing the need of performing at least a diagnostic hysteroscopy.

One of the most concerning problems for RPOC management is the TDT, which may lead to harmful reproductive outcomes and increased chance of infection. Two recent studies conducted by Tarasov et al [46] and Melcer et al [47] found that the TDT for RPOC did not influence subsequent fertility, with similar pregnancy rates between late and early resection [46,47]. These conclusions are in accordance with our meta-analysis findings, in which

Fig. 7

Forest plot for live-birth rate. CI = confidence interval; ES = effect size.

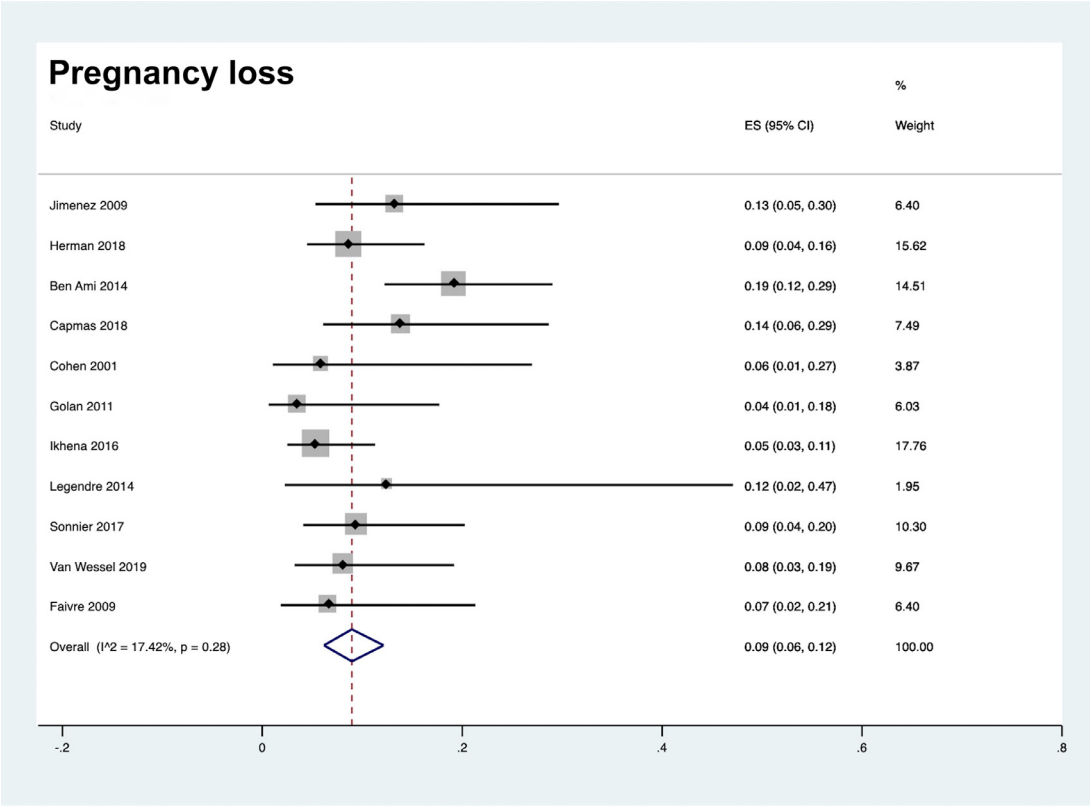


changes in the TDT were not significantly related to the CPR, LBR, and PLR. Moreover, the TDT was not significantly related to surgical outcomes. Although not statistically significant, it should be noted that the 2 studies with the highest TDT also had the highest number of postoperative complications [18,33], suggesting the importance of a timely intervention.

We recognize several limitations of this systematic review and meta-analysis. First, there is 1 systematic review and meta-analysis previously published in 2014 [48]. However, this 2014 publication included only 5 studies and 326 cases, whereas between 2014 and 2020 15 studies on hysteroscopic resection of RPOC were published, greatly increasing the data available for this topic and enhancing the value of an up-to-date systematic review and meta-analysis. The second limitation concerns the study heterogeneity for defining complete RPOC resection because in most of the included papers a follow-up hysteroscopy was performed routinely, but a smaller subset used sonography for confirmation. Third, it was not feasible to distinguish between early and late pregnancy losses because only 2 of the included studies reported such a difference, with no differences between the 2 groups [21,25]. Moreover, the research articles selected for this review did not report any subcategorization regarding women with other fertility issues in addition to RPOC. This limitation should be accounted for in future research because reproductive outcomes might be different in patients with superimposed subfertility or recurrent pregnancy loss. In addition, most of the analyzed studies did not separate RPOC of the first trimester pregnancy loss from RPOC that occurred after VD or CS. Subgroup analysis of postdelivery RPOC studies showed reduced CRR and IRR related to overall data, showing that RPOC occurring after birth could represent a separate issue with different outcomes. Finally, additional potential limitations of this systematic review and meta-analysis should be noted. One is the continued scarcity of randomized studies or prospective studies because only 1 RCT was eligible, as well as the lack of information regarding OR time, operator skills, and procedure costs in studies that compared different procedures (D&C vs hysteroscopy) or instrumentations (morcellators vs cold loop). In addition, heterogeneity in follow-up as well as lack of standardized protocols for preoperative diagnosis, operative procedures, and postsurgical

Fig. 8

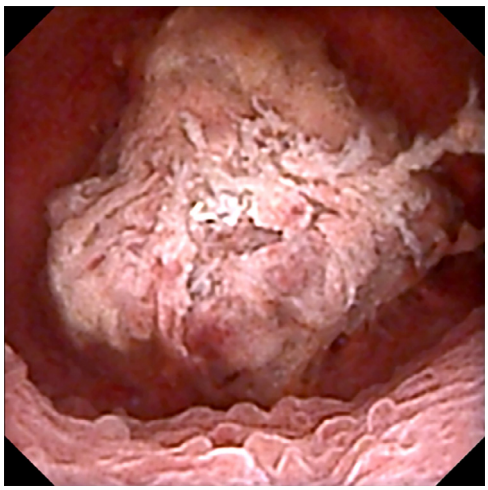
Forest plot for pregnancy loss rate. CI = confidence interval; ES = effect size.



management of women can be a limitation, although such variability is inherent to many meta-analyses. Despite these issues, this systematic review and meta-analysis incorporated an approximately 4-fold increase in available studies (from 5−18) and a 6-fold increase in the number of participants (from 326−2112) relative to the existing literature, providing clearer data-based insight into the surgical and reproductive outcomes for hysteroscopic management of RPOC.

Fig. 9

Hysteroscopic view of retained products of conception.



Conclusion

Hysteroscopic management of RPOC is effective and safe. More than 90% of the cases require only a single procedure. Postsurgical complications are uncommon, and IUAs occur only after 0.8% of the procedures. Of the patients who desired future fertility, 90% achieved a subsequent pregnancy after having RPOC treated with hysteroscopy, and only 9% had early or late pregnancy loss. However, to achieve satisfying outcomes, a short TTD is necessary. Future research will benefit from directly comparing different hysteroscopic instrumentations, as well as better characterizing variations in setting and technique. Nevertheless, the preponderance of existing evidence shows that despite heterogeneous management, patients undergoing hysteroscopic treatment of RPOC are likely to have complete resolution, a low rate of complications, and a reassuring rate of future fertility.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.jmig.2020.10.028.

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