

Safety and efficacy of laparoscopic cornuotomy in the surgical management of complete interstitial ectopic pregnancy

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ABSTRACT

Background: Laparoscopic cornuotomy is a relatively novel surgical approach to manage interstitial ectopic pregnancy (IEP) and there is little information regarding its safety and efficacy.

Objectives: To describe the success, complications and long-term outcomes of women undergoing laparoscopic cornuotomy for IEP.

Methods: Retrospective observational study carried out in a tertiary early pregnancy unit from June 2009 to April 2024.

Main Outcome Measures: The main outcome measure was a complete resolution of the IEP without the need for any additional medical or surgical treatment.

Results: There were 102 cases of complete IEP, of which 71 were managed surgically. The majority of operations were performed laparoscopically (70/71), including 62/70 who underwent a laparoscopic cornuotomy, and 8/70 who underwent an Endoloop-assisted salpingectomy. The remaining patient underwent a planned open procedure. A total of 60/62 [97%, 95% confidence interval (CI), 92-100] laparoscopic cornuotomies were successful, whilst the remaining two patients required further intervention for persistent trophoblast. The median total estimated blood loss for patients undergoing laparoscopic cornuotomy was 50 mLs (interquartile range: 50-150). There were 2/62 (3%, 95% CI, 0-8) intraoperative and 3/62 (5%, 95% CI, 0-10) postoperative complications. Twenty-seven patients (27/62, 44%) subsequently conceived, resulting in a total of 52 pregnancies. There were 25 pregnancies resulting in live birth, 13 of which were vaginal with no cases of uterine rupture.

Conclusions: Laparoscopic cornuotomy is an effective treatment for complete IEP with only a small proportion of patients requiring interventions for retained pregnancy tissue.

What is New? This is the largest study of laparoscopic cornuotomy so far which showed that the procedure is effective with a low-risk of future pregnancy complications.

Keywords: Pregnancy, interstitial, ectopic pregnancy, laparoscopy, intraoperative complications

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Received: 08.01.2026 **Accepted:** 26.07.2026 **Publication Date:** 15.09.2026

Cite this article as: Davies D, Helm B, Moatti Z, Eagles N, Naftalin J, Jurkovic D. Safety and efficacy of laparoscopic cornuotomy in the surgical management of complete interstitial ectopic pregnancy. Facts Views Vis Obgyn. 2026;18(3):184-194



Introduction

Interstitial ectopic pregnancies (IEPs) occur when a pregnancy implants in the interstitial portion of the Fallopian tube, defined as the tubal segment traversing the myometrium.¹⁻³ The increased vascularity of the surrounding myometrium, relative to that of the Fallopian tube, increases the risk of rapid blood loss if rupture occurs.^{3,4} These features likely account for the increased mortality rate of IEPs compared to ectopic pregnancies implanted in the more distal aspects of the Fallopian tube.⁵

IEPs can be diagnostically challenging. Their proximity to the uterine cavity means they can be mistaken for normally sited (eutopic) pregnancies which have implanted in the upper lateral aspect of the uterine cavity, previously termed angular pregnancies.^{1,6} This differentiation can be even more difficult in cases of partial IEPs (pIEPs), where the pregnancy implants in the interstitial portion of the Fallopian tube but expands medially, resulting in some of the pregnancy protruding into the uterine cavity.¹

The “interstitial line” sign describes visualisation of the proximal part of the interstitial tube between the lateral aspect of the uterine cavity and the medial aspect of the gestational sac, as a means of accurately diagnosing complete interstitial pregnancies. This has been reported to be 80% sensitive and 98% specific for the diagnosis of IEP and has been included in international guidelines for the diagnosis of ectopic pregnancy.^{1,7}

Historically, management of IEPs involved either hysterectomy or cornual resection, where the pregnancy and surrounding healthy myometrium of the uterine cornu were resected en bloc. Cornual resections are associated with short and long-term morbidity including increased intraoperative blood loss, and increased risk of both pre-term labour and scar rupture in future pregnancies due to the removal of healthy myometrium.⁸⁻¹¹

The development of high-resolution ultrasound and improved access for women to attend early pregnancy units (EPUs) has enabled earlier and more accurate detection of IEP. This has facilitated the use of more conservative management options including expectant management,^{12,13} medical management,^{4,14-16} and laparoscopic cornuotomy.^{4,17} A recent consensus statement on the diagnosis of ectopic pregnancies reclassified IEPs as tubal pregnancies in part to “discourage surgeons from performing uterine wedge

resection which is associated with an increased risk of both intra- and post-operative complications”.¹

The aim of this study is to examine the efficacy and safety of laparoscopic cornuotomy for the surgical management of complete IEP.

Methods

This was a retrospective cohort study conducted at the tertiary referral Early Pregnancy Unit (EPU) at University College London Hospital (UCLH), London, UK. The unit accepts self-referrals from women in addition to referrals from primary care and other EPUs. All women who received a diagnosis of IEP between June 2009 and April 2024 were included in the study. Clinical data was retrieved from electronic patient records on Viewpoint (GE HealthCare, Chicago, Illinois) and EPIC (Epic Systems Corporation, Verona, Wisconsin), including ultrasound images and reports, operative notes, discharge summaries, biochemistry results and histopathology results.

All women underwent pre-operative transvaginal ultrasound using high-end equipment (Voluson E8 or E10; GE HealthCare, Chicago, Illinois). The majority of the examinations were initially performed by clinical fellows in early pregnancy and gynaecology (Level-II operators) under the supervision of expert (Level-III) operators who confirmed the diagnosis in all cases.^{18,19} The diagnosis of IEP was made when pregnancy was seen implanted within the interstitial portion of the Fallopian tube, with morphological features varying from a solid homogeneous swelling to a gestational sac containing

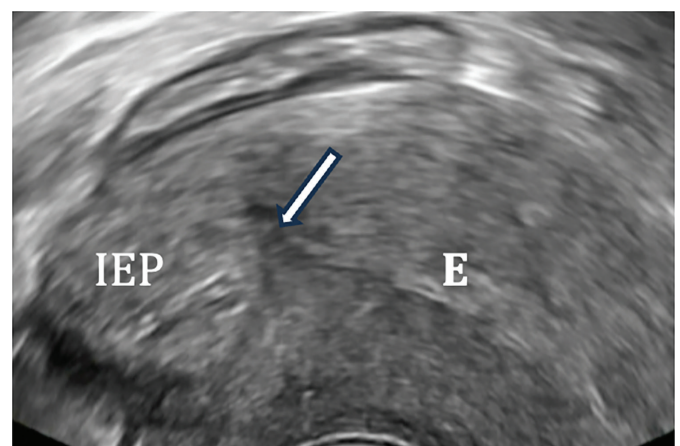


Figure 1. A B-mode ultrasound image of the uterus in the transverse plane. A thin interstitial tube (arrow) is seen adjoining the endometrial cavity (E) and a right interstitial ectopic pregnancy (IEP).

a live embryo.¹⁸ Crucial to the diagnosis of complete IEP was the presence of the “interstitial line sign”, as described above (Figure 1). In addition, the pregnancy had to be at least partially enveloped by myometrium.¹⁹ The diagnosis was supported in many cases by three-dimensional ultrasound scanning (Figure 2). Serum human chorionic gonadotrophin (hCG) and progesterone levels were measured in all clinically stable women diagnosed with complete IEP.

Active surgical management was recommended if patients were experiencing moderate to severe pelvic pain; there was a live embryo; the pregnancy measured >30 mm in the mean diameter, or if there was significant haemoperitoneum defined by the presence of blood clots within the lesser pelvis. All other patients were assessed for suitability of non-surgical management, with consideration given to symptoms, serum hCG and patient preference. The protocols used for expectant and medical management have been described previously.²⁰ Surgery was performed by gynaecologists with expertise in minimally invasive surgery. None of the patients who had surgery for complete IEP underwent cornual resection. pIEPs were surgically treated by transcervical

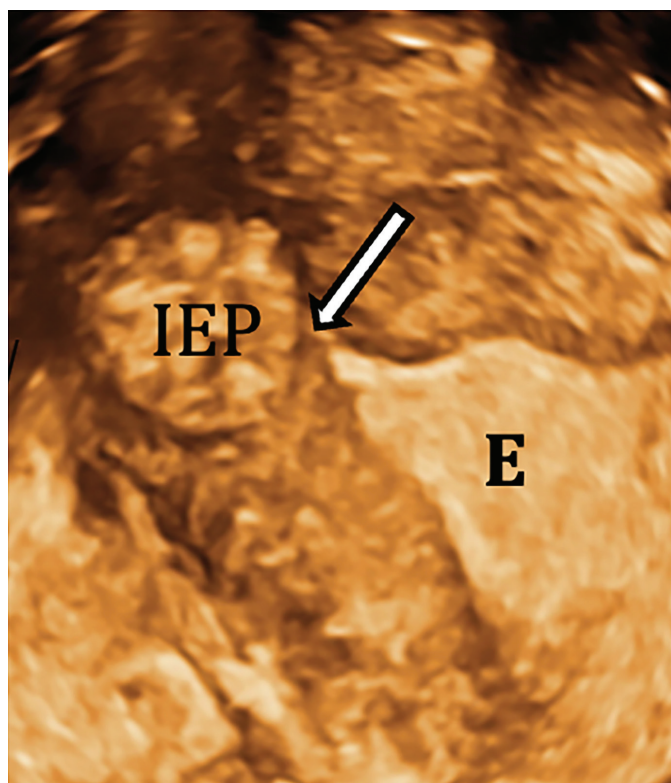


Figure 2. A three-dimensional ultrasound image of the uterus in the coronal plane. The interstitial tube (arrow) is clearly seen adjoining the endometrial cavity (E) and a right interstitial ectopic pregnancy (IEP).

evacuation under continuous transabdominal or transrectal ultrasound guidance.

Surgical Technique for Laparoscopic Cornuotomy (Figure 3) and Video 1

At diagnostic laparoscopy, prior to starting the cornuotomy, the surgeon would confirm visibility and laterality of the IEP. This would typically appear as a hypervascular purple bulge over the fundo-lateral aspect of the uterus, often partially involving some of the isthmic portion of the Fallopian tube. Visualisation of complete IEP can be challenging at surgery when it is small, relatively medial or in the presence of concurrent uterine pathology such as large or subserous fibroids, or severe adenomyosis. Where the surgeon was uncertain of the location of the IEP, intraoperative transvaginal or transrectal ultrasound would be performed to guide the site of incision. Techniques used to reduce blood loss included the intramyometrial injection of Argipressin (20IU in 20 mLs of normal saline) directly over the IEP prior to the first incision. An incision would then be made in the myometrium or proximal section of the interstitial tube overlying the IEP using laparoscopic scissors, monopolar hook (Karl Storz, Tuttlingen, Germany) or an advanced energy device such as Thunderbeat® (Olympus Medical Systems Corp., Tokyo, Japan) or Harmonic Scalpel® (Ethicon, Johnson & Johnson Med Tech., Raritan, New Jersey, USA). The incision would be large enough to facilitate the introduction of laparoscopic grasping instruments (Johann or Maryland grasper,

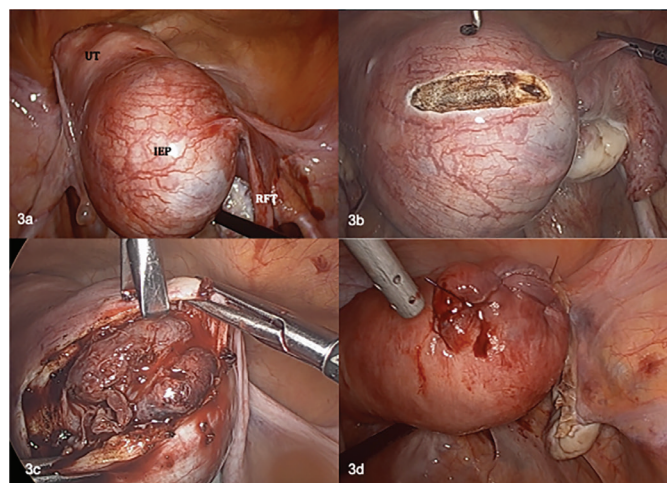


Figure 3. (a) Laparoscopic view of a large right interstitial pregnancy (IEP) (UT, uterus; RFT, distal segment of the right fallopian tube). (b) Initial cornual myometrial incision performed using monopolar diathermy. (c) Evacuation of interstitial pregnancy through the cornuotomy incision. (d) Incision closed using interrupted sutures, with haemostasis achieved.

Karl Storz, Tuttlingen, Germany) which were used to remove the trophoblastic tissue. Hydro-dissection and aspiration were also used as a method to separate and retrieve trophoblast tissue. All retrieved trophoblastic tissue was sent for histological analysis to confirm the diagnosis. In cases where it was uncertain if all of the trophoblastic tissue had been removed, intraoperative ultrasound was used to clarify. Once all the visible trophoblastic tissue had been removed, the incision was then closed laparoscopically using Vicryl, Monocryl, or PDS suture material (Ethicon, Johnson & Johnson Med Tech., Raritan, New Jersey, USA) or V-Loc™ (Medtronic, Minneapolis, Minnesota). An ipsilateral salpingectomy would be performed if the sutures were felt to occlude the Fallopian tube, in order to reduce the risk of recurrent ipsilateral tubal ectopic pregnancy. Blood in the abdomen or pelvis would be aspirated and its volume measured to establish the blood loss. All patients stayed in hospital until they met routine discharge criteria and were followed up as outpatients with repeat serum hCG measurements, usually starting one week post-surgery. If hCG clearance was slower than expected given a half-life of 24 hours,^{21,22} this was diagnosed as residual trophoblast.

The use of Endoloop ligatures (Ethicon, Johnson & Johnson Med Tech., Raritan, New Jersey, USA) can be used as an alternative to cornuotomy in cases where rapid haemostasis is required, or in large interstitial pregnancies that protrude laterally into the fallopian tube. They can be used as a tourniquet to encircle the IEP²³ prior to salpingectomy of the affected fallopian tube. Figure 4 illustrates a proposed decision-making algorithm to guide selection between techniques.

Statistical Analysis

Data was summarised using the mean and standard deviation for normally distributed continuous variables and the median and inter-quartile range for those not following a normal distribution. Logistic regression was used to examine factors associated with residual trophoblast in women undergoing planned laparoscopic cornuotomy. The analysis was performed in two stages.

The first stage examined the separate association between each factor and residual trophoblast in a series of univariable analyses. For some categorical variables, there were no occurrences of residual trophoblast in some categories, therefore logistic regression was unable to be performed and Fisher's exact test was used.

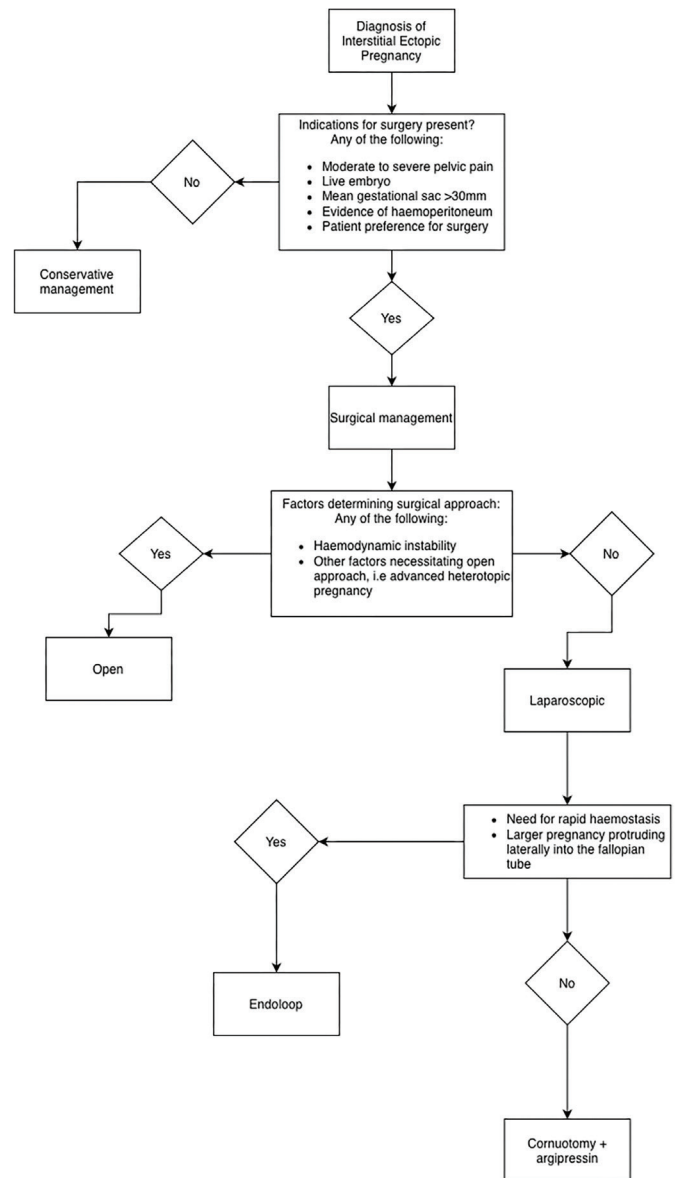


Figure 4. Decision tree to guide management of interstitial ectopic pregnancies.

The second stage examined the joint association between the factors and the outcome in a multivariable analysis. To limit the number of variables, only factors with a *P* value of <0.2 from the univariable analyses were included. A backwards selection procedure was used to retain only the important predictor variables; this involves removing non-significant variables until only the important variables remain.

Results

In the study period between June 2009 and April 2024, 104 patients attending our unit were diagnosed with a total of 106 IEPs, as two women presented with recurrent IEPs.

There were 102 complete and 4 pIEPs. The 102 complete IEPs included four cases of heterotopic pregnancy, where the concomitant normally sited pregnancy was live in all cases. Approximately half of all cases were external referrals from other EPU (56/106, 53%), with the remainder (50/106, 47%) from our clinic population. Several women had undergone some form of medical or surgical intervention (often without a conclusive pre-treatment diagnosis of IEP) at their local hospital prior to being referred to our unit, but for the purpose of this study the primary management was taken to be that following ultrasound diagnosis at our unit.

Patient demographic data are shown in Table 1. The majority of patients were nulliparous, with nearly 40% (39/104) having experienced previous miscarriage. One fifth of patients (21/104) had a previous history of at least one tubal ectopic pregnancy. For these women, the IEP was ipsilateral to the site of a previous tubal ectopic pregnancy in 17/19 [89%, 95% confidence interval (CI): 76-100] cases where the previous site was known (including 2 cases where there had been an ectopic on each side).

The most common presenting symptoms were concurrent vaginal bleeding and pain (43/106, 41%), although one fifth of patients were asymptomatic (22/106, 21%). Of the 106 cases of IEP (complete and partial), 88 (83%) were diagnosed on the initial ultrasound scan and the remaining 18 (17%) during follow up visits. The median gestational age at diagnosis was 7 weeks and 2 days. A conclusive ultrasound diagnosis of IEP was made in all cases prior to a decision regarding management. IEPs were classified into morphological types, where 19/106 (18%) showed evidence of cardiac activity (type 1), whilst the remaining 87/106 (82%) did not (type II-V).¹⁸

A summary of the management of IEPs during the study period is shown in the study flowchart (Figure 5).

Surgical Management of Complete IEP

A total of 71/102 (70%) pregnancies were treated surgically. 70/71 (99%) had planned laparoscopic surgery, including 62/70 (89%) who underwent a laparoscopic cornuotomy, and 8/70 (11%) who underwent an Endoloop assisted salpingectomy. Of the 62 laparoscopic cornuotomies, 54 were the primary management, and the remaining 8 were following unsuccessful expectant or medical treatment (Figure 5). One patient with a heterotopic pregnancy (live eutopic and complete interstitial at 14 weeks') had a planned open cornuotomy to maximise the chance of preserving the normally sited twin. In 69/70 (99%) cases,

Table 1. Demographic information for patients diagnosed with an interstitial pregnancy.

Characteristic	n=104
Age, mean (SD)	34.3 (SD: 5.0)
*BMI, mean (SD)	27.4 (SD: 7.8)
Ethnicity, n (%)	
White	36 (34.6)
Asian or British Asian	11 (10.6)
Black, Black British, Caribbean or African	14 (13.5)
Mixed or multiple ethnic groups	2 (1.9)
Other ethnic group	7 (6.7)
Unknown	34 (32.7)
Gravidity, n (%)	
1	25 (24.0)
2	25 (24.0)
≥3	54 (51.9)
Parity, n (%)	
0	60 (57.7)
1	27 (26.0)
≥2	17 (16.3)
Gynaecology history, n (%)	
Miscarriage	39 (37.5)
Recurrent miscarriage	7 (6.7)
Termination of pregnancy	28 (26.9)
Ectopic pregnancy	21 (20.2)
In vitro fertilization	13 (12.1)
Endometriosis	10 (9.6)
Pelvic infection	4 (3.8)
Adenomyosis	2 (1.9)
Subfertility	14 (13.5)
Fibroids	11 (10.6)
Ovarian cyst	4 (3.8)
Polycystic ovarian syndrome	6 (5.8)
Other (cervical pathology, uterine septum, endometrial hyperplasia)	6 (5.8)
Surgical history, n (%)	
Previous laparoscopic abdominal surgery	32 (30.8)
Previous open abdominal surgery (excluding caesarean section)	8 (7.7)
*Previous surgical management of pregnancy tissue	30 (28.8)
Previous hysteroscopic procedure	7 (6.7)
Obstetric history, n (%)	
Previous caesarean section	15 (14.4)

*n=25, missing data. *Includes surgical management of miscarriage or retained products of conception, and surgical termination of pregnancy. SD: Standard deviation, BMI: Body mass index.

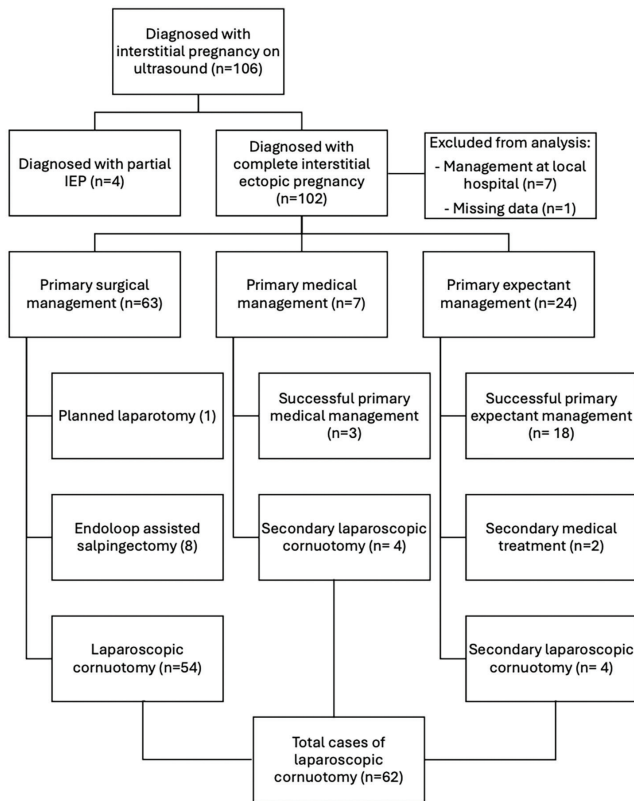


Figure 5. Flowchart showing the management of interstitial pregnancies.

the operation was completed laparoscopically, but in one case the procedure was converted to open surgery due to the presence of extensive bowel adhesions involving the uterine cornu at the site of the interstitial pregnancy.

Laparoscopic Cornuotomy

The median total estimated blood loss (EBL) for cases managed with laparoscopic cornuotomy was 50 mL [$n=53^*$, interquartile range (IQR) 50-150]. An EBL of ≥ 1000 mL was recorded in 3/53 (6%) cases, although in two of these, the blood loss was almost entirely attributed to pre-operative haemoperitoneum. There were no other instances of blood transfusion recorded. Argipressin was used in 71% (42/59^{*}) of cornuotomies, as a measure to further reduce blood loss. Out of 62 cases undergoing planned laparoscopic cornuotomy, 36/62 (58%) had excision of the IEP and ipsilateral salpingectomy (or excision of stump, if previous salpingectomy), whereas the remaining cases had excision of the IEP only.

The mean number of days until discharge from hospital was 1.2 ($n=62$, standard deviation 0.8). Follow-up after laparoscopic cornuotomy involved serial hCG

measurements until levels dropped such that the patient could be discharged, typically <10 IU/L. The median time for hCG resolution following surgery was 20 days ($n=48^*$, IQR: 14-35).

*Patients with missing data were excluded from the analysis.

Residual Trophoblast

Of the 62 interstitial pregnancies managed with planned laparoscopic cornuotomy, there were 9/62 (15%, 95% CI, 6-23) cases of residual trophoblast tissue. Further intervention was required in only 2/62 (3%, 95% CI, 0-8) cases: one case resolved with methotrexate and one case underwent emergency laparotomy, discussed below. The remaining 7 cases were all managed expectantly with serial hCG monitoring and in some cases confirmed with a resolution scan. In total, 60/62 (97%, 95% CI, 92-100) of interstitial pregnancies resolved completely following laparoscopic cornuotomy.

Factors associated with residual trophoblast were examined. Univariable analysis demonstrated that the majority of variables examined were not significantly associated with residual trophoblast (Table 2), however a significant association with previous surgical removal of pregnancy tissue from the uterine cavity (including surgical management of miscarriage or retained products of conception, and surgical termination of pregnancy) was observed.

Multivariable analysis (Table 3) showed that both previous laparoscopic abdominal surgery and surgical management of pregnancy tissue were independently associated with residual trophoblast. After adjusting for the other factors in the analysis, previous laparoscopic abdominal surgery was associated with a 5-fold increase in the odds of residual trophoblast, whilst surgical management of pregnancy tissue was associated with a 6-fold increase (Table 3).

Surgical Complications

Patient records were reviewed up until the time of data collection to capture delayed post-operative complications. Of the 62 cases of IEP managed with planned laparoscopic cornuotomy, 2/62 (3%, 95% CI: 0-8) intraoperative complications and 3/62 (5%, 95% CI: 0-10) postoperative complications were recorded. The intraoperative complications included the case requiring conversion to laparotomy due to adhesions, which resulted in a total blood loss of 1,300 mL, and another

Table 2. Univariable associations with residual trophoblast following laparoscopic cornuotomy.

Variable	Category	Trophoblast n/N (%)	Odds ratio (95% CI)	P value
Age*	-	-	1.10 (0.53, 2.28)	0.80
Ethnicity	White	4/24 (17%)	(+)	0.92
	Asian	1/7 (14%)		
	Black	0/7 (0%)		
	Mixed/other	1/7 (14%)		
Previous	No	7/42 (17%)	1	0.49
Miscarriage	Yes	2/20 (10%)	0.56 (0.10, 2.95)	
Previous TOP	No	4/44 (9%)	1	0.07
	Yes	5/18 (28%)	3.84 (0.90, 16.5)	
Previous ectopic	No	6/46 (13%)	1	0.58
	Yes	3/16 (19%)	1.54 (0.34, 7.04)	
Previous caesarean	No	7/51 (14%)	1	0.71
	Yes	2/11 (18%)	1.40 (0.25, 7.86)	
IVF	No	9/56 (16%)	(+)	0.58
	Yes	0/6 (0%)		
Previous laparoscopic	No	4/44 (9%)	1	0.07
abdominal surgery	Yes	5/18 (28%)	3.85 (0.90, 16.5)	
Previous open	No	8/56 (14%)	1	0.88
abdominal surgery	Yes	1/6 (17%)	1.20 (0.12, 11.7)	
**Previous surgical management of pregnancy tissue	No	4/46 (9%)	1	0.04
	Yes	5/16 (31%)	4.77 (1.09, 20.8)	
Previous transcervical	No	9/60 (15%)	(+)	1.00
Procedure	Yes	0/2 (0%)		
Gestational age (wk)	-	-	0.84 (0.52, 1.36)	0.48
Mean diameter (cm)	-	-	0.69 (0.33, 1.45)	0.33
Appearance	Type I	3/16 (19%)	1	0.58
	Type II-IV	6/46 (13%)	0.65 (0.14, 2.97)	
Type of surgery	Excision of pregnancy only	5/26 (19%)	1	0.38
	Additional salpingectomy/stump excision	4/36 (11%)	0.53 (0.13, 2.18)	

*Odds Ratio given for a 5-year increase in age.
+Unable to calculate odds ratios due to no occurrences of residual trophoblast in one category. Analysis using Fisher's exact test.
**Includes surgical management of miscarriage or retained products of conception, and surgical termination of pregnancy.
CI: Confidence interval, IVF: *In vitro* fertilisation, TOP: Termination of pregnancy.

Table 3. Multivariable associations with residual trophoblast following laparoscopic cornuotomy.

Variable	Category	Odds ratio (95% CI)	P value
Previous laparoscopic	No	1	0.05
abdominal surgery	Yes	5.18 (1.03, 26.1)	
Previous surgical management of pregnancy tissue*	No	1	0.03
	Yes	6.28 (1.24, 31.7)	

*Includes surgical management of miscarriage or retained products of conception, and surgical termination of pregnancy. CI: Confidence interval.

patient requiring blood transfusion (2 units) for an EBL of 2500 mLs, although the large majority of this was attributed to pre-operative haemoperitoneum.

All three post-operative complications occurred in patients with residual trophoblast. Two cases, with suspected persistent trophoblast based on slowly declining hCG levels, developed acute haemoperitoneum and underwent emergency surgery at their local hospital, at 24 and 43 days post cornuotomy respectively. The first had a laparoscopy and washout; however, the haemoperitoneum was unexplained as no source of bleeding was identified. The second case underwent a laparotomy where bleeding was noted from the right ovary. In both cases, the hCG declined to pre-pregnancy levels following the second surgery. A third patient with residual trophoblast presented with pain 33 days following her primary surgery and underwent a diagnostic laparoscopy and washout of an infected pelvic collection.

Subsequent Pregnancies

Out of 62 women who underwent laparoscopic cornuotomy for complete IEP, 27/62 (44%) had at least one subsequent pregnancy. The total number of subsequent pregnancies was 52. Of these, 44/52 (85%) were eutopic pregnancies, 6/52 (12%) were classified as "pregnancy of unknown location" which resolved, 1/52 (2%) was a tubal ectopic, and 1/52 (2%) was a heterotopic pregnancy including a correctly sited pregnancy and a recurrent IEP. The rate of confirmed miscarriage was 14/52 (27%).

At least one subsequent live birth was recorded for 19/27 (70%) patients who became pregnant following laparoscopic cornuotomy. Of a total of 52 pregnancies, 25 (48%) ended in live delivery of at least one child, including 23 singletons, 1 set of twins and 1 set of triplets, making a total of 28 live births. Outcomes for eutopic pregnancies were unknown for 5 patients, so this may be an underestimate of the number of live births. Of the deliveries, only 2 (8%) were preterm: one woman who delivered at 36 weeks and had previously had a preterm delivery prior to the IEP, and the other was the triplet pregnancy delivered by caesarean. Of the 25 deliveries, 12 (48%) were by caesarean section (none of which were documented to be an emergency) and 13 (52%) were by vaginal delivery, with no recorded intrapartum complications.

Discussion

Main Findings

This is the largest study looking at outcomes of laparoscopic cornuotomy, and our data suggests that it is an effective procedure associated with a short hospital stay, low intraoperative blood loss and low chance of requiring further intervention for persistent trophoblastic tissue. The benefits of laparoscopic surgery have been corroborated by other studies that directly compare laparoscopic and open techniques.^{24,25}

Several factors may have contributed to the low EBL observed in our study. Firstly, most ectopics were diagnosed prior to rupture, meaning patients were clinically stable and had no significant haemoperitoneum at the onset of surgery. Secondly, the technique of laparoscopic cornuotomy avoids transection of large terminal branches of the uterine artery, which are the main cause of excessive bleeding at cornual resection. The use of additional haemostatic measures, including Argipressin, likely also contributed to the low recorded blood loss.

The success rate of 97% compares favourably to non-surgical management. Earlier studies found typically good success rates of conservative management, ranging from around 71-90% for expectant management^{20,12} and 80-94% success for methotrexate (local or systemic).^{20,26} More recent studies have found lower rates of success, such as work by Ben-David et al.¹⁴ demonstrating 70% success with non-surgical management and a 17% risk of uterine rupture during treatment, and a recent systematic review and meta-analysis which found an estimated success rate of 69% for methotrexate treatment from a total of 124 patients.²⁷

The rate of persistent trophoblastic tissue following laparoscopic cornuotomy for IEP is not well established in the literature, with most studies consisting of small sample sizes. Furthermore, there is a lack of studies that distinguish between cases in which residual trophoblast can be managed expectantly, and those where further intervention (typically methotrexate or surgery) is required. Whilst our overall incidence of residual trophoblast was relatively high at 15%, only 3% required further intervention. Our results compare favourably to the existing literature. A study by Ng et al.,⁹ found that 9/52 (17%) of cases undergoing laparoscopic management (both wedge resection and cornuotomy techniques) of IEP required methotrexate for persistently

raised serum hCG. Tulandi and Al-Jaroudi³ found a 1/11 (9%) re-intervention rate following laparoscopic excision of IEP, whilst Moon et al.²³ found that 1 in 24 (4%) cases managed by laparoscopic cornuotomy required subsequent methotrexate.

The rate of persistent trophoblast following salpingotomy for tubal ectopic pregnancy is better established and quoted as between 3 and 20% in the literature.²⁸ A significant proportion of these patients go on to have further treatment in the form of methotrexate or further surgery, often at rates higher than the 3% found in this study.²⁹⁻³¹ Therefore, both the incidence and the risk of intervention for persistent trophoblast in IEPs undergoing laparoscopic cornuotomy appear comparable to that for salpingotomy for tubal ectopic pregnancy.

The finding of a 5-fold increase in the odds of residual trophoblast with previous laparoscopic abdominal surgery, and a 6-fold increase with previous surgical management of pregnancy tissue was interesting and unexpected, and to our knowledge has not been previously reported. However, given a total number of just 9 patients with residual trophoblast, these results lack robustness and need to be interpreted with caution.

Some papers describe performing cornual resection rather than cornuotomy for IEPs above a certain size: 35 mm³ or 40 mm,^{32,33} with the aim of minimising the risk of persistent trophoblast. However, our data did not find an association between size of the IEP and the rate of persistent trophoblast. Nor was there a link between IEPs with cardiac activity and residual trophoblast (Table 2).

Surgical complications are not well established in the context of laparoscopic cornuotomy for IEP. In two of the studies reviewed that looked at surgical outcomes, no major intraoperative or postoperative complications were encountered.^{34,25} However, these sample sizes were relatively small and the time frame over which cases were followed up to assess for complications not always defined. Surgical complications have been better studied in cases of tubal ectopic pregnancy. These are varied, but studies have reported intraoperative complication rates ranging from 0-8% and postoperative complication rates of 0-15% for laparoscopic salpingectomy or salpingotomy.^{35,36} Our intraoperative complication rate of 3% and postoperative complication rate of 5% fall within these reported ranges. Postoperative complications only occurred in women with residual trophoblast. These patients therefore require particularly close monitoring.

Subsequent Pregnancy Outcomes

The true rate of subsequent pregnancy following laparoscopic cornuotomy in our study is uncertain, as our data was limited to the forty-four percent of women who presented at our unit for future early pregnancy or antenatal care. However, our data suggests that pregnancy following laparoscopic cornuotomy is generally safe. Most pregnancies were correctly sited, with a 4% recurrent ectopic pregnancy rate. There were no recorded late second trimester miscarriages, and the rate of preterm birth was low, with neither case likely to be secondary to treatment of the IEP. Half of the deliveries were vaginal, with no reported cases of uterine dehiscence or rupture. Other published studies examining subsequent pregnancy outcome after laparoscopic cornuotomy were small, but they also showed low rates of recurrent ectopic pregnancies and no cases of uterine rupture in late pregnancy or labour.^{23,34}

This data appears favourable compared to a study by Tang et al. who reported a 9.1% rate of recurrent ectopic pregnancy and a 4.5% rate of uterine rupture in women undergoing assisted conception following wedge resection for IEP.¹¹ The reported risk of uterine rupture following cornual resection varies.^{8,11}

Strengths and Limitations

This study is the largest study to our knowledge looking at outcomes from laparoscopic cornuotomy, increasing the reliability of our data. This also means we are likely to pick up less common outcomes (i.e., major complications) that smaller studies may fail to detect. Close post-operative follow-up and the retrospective nature of the study enabled longer term complications to be picked up, including those occurring at other trusts.

Limitations of a single centre retrospective study include selection bias: cases for surgical management were selected based on symptoms and morphology or size, therefore the success rate reported may not apply to other cohorts. There was also significant incomplete data regarding future pregnancies. Data were limited to pregnancies for which the patient had sought early pregnancy or antenatal care at our unit, therefore may not be an accurate reflection of actual subsequent pregnancy outcomes where these were not captured by our data collection, i.e., the patient presented elsewhere. Incomplete or missing data across other outcomes also makes the results vulnerable to selection or loss to follow up bias in these areas.

The multivariable analysis demonstrating a 5-fold increase in the odds of residual trophoblast with previous laparoscopic abdominal surgery, and 6-fold increase with previous surgical management of retained pregnancy tissue was based on a small cohort of patients and this finding has not been corroborated by other studies. Caution is therefore required when interpreting this data. The nature of an observational study means that we are unable to prove causation due to the presence of confounding, although this was considered in the statistical analysis.

Clinical and Policy Implications

Protocols for picking up patients with residual trophoblast (i.e., monitoring serum hCG) should be comprehensive to ensure they are not missed, given this cohort appears to be at higher risk of complications. The association between previous laparoscopic abdominal surgery and surgical management of pregnancy tissue with residual trophoblast has implications for clinical practice. There should be a particularly high index of suspicion when following these women up post-operatively, and meticulous surgical technique should be used, with the aid of intraoperative ultrasound to minimise the chance of residual trophoblast in the first instance.

Unanswered Questions and Future Research

Future research is required on postoperative complications following laparoscopic cornuotomy, particularly looking at complications in women with persistent trophoblast versus those without. Further large multicentre studies are recommended to obtain more robust data regarding the risk of preterm birth and intrapartum uterine rupture.

Conclusion

Laparoscopic cornuotomy is an effective treatment for complete IEP, associated with a low-risk of major intraoperative haemorrhage and short hospital stay. Although residual trophoblast is relatively common, further treatment is required only in a small proportion of patients. The future pregnancy outcomes were good, with a low-risk of recurrent ectopic pregnancy and adverse obstetric outcomes.



Video 1. A video record of a laparoscopic cornuotomy for a left interstitial pregnancy showing key surgical steps

during the procedure. (We are grateful to Mr Martin Hirsh, Consultant Gynaecologist, for providing this video): <https://www.youtube.com/watch?v=ZeSuMmZEJ-s>

Acknowledgements: None.

Contributors: Surgical and Medical Practices: J.N., D.J., Concept: D.D., B.H., J.N., D.J., Design: D.D., B.H., J.N., D.J., Data Collection or Processing: D.D., B.H., Z.M., N.E., Analysis or Interpretation: D.D., N.E., J.N., D.J., Literature Search: D.D., B.H., N.E., Writing: D.D., B.H., D.J.

Funding: The authors declared that this study received no financial support.

Competing interests: No conflict of interest was declared by the authors.

Ethics Committee Approval: According to the NHS Health Research Authority a formal ethical review was not required for this study.

Informed consent: Written informed consent was not required due to the retrospective nature of this analysis.

Data sharing: The datasets used for this study are not available publicly due to legal and confidentiality reasons, although the data analysis can be requested from the author if required.

Transparency: We affirm that this text is an honest, accurate and transparent account of the study and no important aspects have been omitted.

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