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Comparison of management regimens following ultrasound diagnosis of nontubal ectopic pregnancies: a retrospective cohort study

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Objective To review management options for nontubal ectopic pregnancies.

Design Retrospective cohort study.

Setting Tertiary hospital in Melbourne, Australia.

Population A total of 100 nontubal pregnancies: 1 abdominal, 32 caesarean scar, 14 cervical, 41 cornual–interstitial, 12 ovarian.

Methods Cases were classified according to ectopic site. Management categories were medical, surgical, combination or expectant. Use of minimally invasive approaches (ultrasound-guided intra-sac injections or selective surgical techniques) was identified. Primary management was considered to be successful if no further unplanned interventions were required.

Main outcome measures Success of primary management and frequency of unplanned interventions.

Results A high rate of success (82%) was demonstrated for all management regimens, with minimal morbidity and no deaths occurring. A high success rate was shown when the primary management regimen was systemic methotrexate or ultrasound-guided intra-sac injection (88%). The success rate for primary surgical management was 57%. High success rates were reported for both primary management with ultrasound-guided injections or in combination with systemic methotrexate (94%) and for primary management with systemic methotrexate alone (81%). Seventy-five per cent of women managed with minimally invasive surgical approaches avoided the need for more extensive surgery, but required longer follow up and additional interventions.

Conclusion Minimally invasive approaches were found to be safe and effective treatment for women desiring to conserve fertility. Ultrasound-guided intra-sac injection and laparoscopic ectopic removal procedures aimed at preserving reproductive organs should be included as minimally invasive primary management tools in addition to the well-recognised option of systemic methotrexate.

Keywords Ectopic pregnancy, methotrexate, minimally invasive, ultrasound.

Tweetable abstract Nontubal ectopics: minimally invasive procedures a safe alternative to surgery in selected cases.

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Introduction

The incidence of ectopic pregnancy is approximately 1–2% of all pregnancies, with implantation in the fallopian tubes the most common site. Nontubal ectopic pregnancies are those that implant in sites other than the fallopian tubes and account for < 10% of ectopic pregnancies.[1] There has been an increasing incidence of these rare pregnancies, especially caesarean scar ectopic pregnancies.[2] Diagnosis and management of this potentially fatal condition pose a challenge for clinicians because they are frequently diagnosed later than other ectopic pregnancies and are associated with higher morbidity and mortality rates. Serious complications may be immediate or delayed and include life-threatening haemorrhage, hysterectomy and death.[3]

The widespread use of transvaginal ultrasound with high-resolution probes, accurate and rapid serum β human chorionic gonadotrophin (β-hCG) assays and establishment

of dedicated early pregnancy units have allowed for early diagnosis.[4] This has led to the progression from predominantly radical surgical management to more conservative, fertility-sparing approaches including minimally invasive surgery, medical therapy, ultrasound-guided interventions, radiological interventions and even expectant management in selected cases.[3,5–7]

Literature in this area predominantly comprises case reports and case series with only a few studies looking into optimal management protocols. Therefore, at present there is a paucity of evidence-based guidelines for the management of these challenging cases.[8,9]

The objective of this study was to review management of nontubal ectopic pregnancies in a tertiary referral hospital setting, with a particular focus on the success of various primary treatment modalities, including ultrasound-guided intra-sac injection (USGI). We aimed to critically appraise the outcomes and guide an evidence-based approach to the management of these difficult conditions and ultimately contribute to the development of clinical practice guidelines.

Methods

This is a retrospective audit of nontubal ectopic pregnancies identified at The Royal Women's Hospital Melbourne, Australia. The hospital is a tertiary referral centre that managed 1811 ectopic pregnancies during the 11-year study period from November 2003 to November 2014. Cases were identified from an Ultrasound Picture Archiving and Communication System report, using the search term 'ectopic'. All cases were reviewed and assigned a preliminary classification according to ectopic site based on ultrasound findings.

As a retrospective, anonymised audit project, this study met the criteria for quality assurance activities outlined by the National Health and Medical Research Council.[10]

Data were collected from Ultrasound Picture Archiving and Communication System, electronic clinical reports and review of medical records. We examined demographics, previous pregnancy and gynaecological history, risk factors, clinical presentation, ectopic pregnancy sites, ultrasound and magnetic resonance imaging findings, intended primary management and the actual management for these women. Length of inpatient stay and date of discharge from outpatient care were recorded. If the actual management differed from the intended primary management, the reasons for this change were noted. Complications were noted. Both β-hCG at presentation and maximum β-hCG level were recorded. For medical regimen cases, the dates of β-hCG resolution and ultrasound resolution were recorded. Collection and management of data were performed using REDCap.[11]

Following complete investigation, including surgical and imaging findings, all nontubal ectopic cases were classified according to ectopic site; cornual-interstitial, caesarean scar, ovarian, cervical and abdominal (see Supporting information, Figure S1). Heterotopic pregnancies were classified according to the location of the nontubal pregnancy site.

Ultrasound diagnosis was made on established diagnostic criteria for each of the nontubal sites.[12–18] We acknowledge that while cornual and interstitial pregnancies are different entities, they have been grouped together because the terms were often used interchangeably. In all cases the diagnosis was confirmed by an experienced ultrasonographer including review of all images at presentation and subsequent ultrasound scans. Women were counselled and managed by a team of gynaecologists and ultrasonographers: management options and treatment plans were individualised based on clinical, biochemical and imaging findings and the desire to conserve fertility.

Treatment modalities included: medical (systemic and/r local intra-sac injection), surgical, combination (combined medical and surgical) or expectant regimens. Minimally invasive approaches included USGI or surgical techniques that selectively removed the ectopic trophoblastic tissue without permanent or functional loss of organs or structures. Systemic methotrexate doses were calculated as 1 mg/kg for intramuscular injection. The protocol at our institution for USGI included transabdominal or transvaginal approaches depending on access, performed under local anaesthesia. The gestational sac was aspirated to mechanically disrupt the pregnancy before 50 mg of methotrexate was injected into the sac using an 18G chorionic villus sampling needle, followed by a saline flush; previous injection of 2 ml (30 mmol/ml) of KCl was used to achieve asystole when embryonic heart activity was present. Follow up for cases with medical or expectant management included weekly β-hCG levels. A single dose of systemic methotrexate was added for those cases where β-hCG had plateaued.

The main outcomes of interest were success of the primary management regimen and the frequency of further unplanned interventions. Primary management was considered to be successful if no further different, unplanned interventions were required.

Secondary outcomes were: success of minimally invasive approaches, time interval to discharge from all medical care, time interval to resolution (determined as achieving β-hCG levels < 20 IU/l) and time interval to resolution on imaging for medically managed cases.

Frequency of complications for the different treatment regimens are described and statistically compared (odds ratio for all categorical variables and Mann–Whitney U test for mean time to discharge from medical care).

All independent variables were considered for a binary logistic regression analysis on the likelihood of success for the primary management (1, successful; 0, unsuccessful). A model was then created including only those characteristics that yielded a significant contribution. The Hosmer and Lemeshow test has been used to test the model for significance. Nagelkerke R^2 was used to establish the amount of variance explained by the model.

Results

During the study period 114 nontubal ectopic pregnancies were diagnosed on ultrasound and managed at our hospital. Nine cases (7.9% of suspected cases) were subsequently excluded because they were found to be tubal ectopic pregnancies at surgery. One woman with a presumed caesarean scar ectopic who spontaneously miscarried was excluded because the exact pregnancy site could not be confirmed. Four cases were excluded as a result of incomplete follow up, resulting in 100 eligible cases for the study.

Demographics and clinical characteristics

Ectopic site classification following complete investigation included: 1 abdominal, 32 caesarean scar, 14 cervical, 41 cornual-interstitial and 12 ovarian (see Supporting information, Figure S2). Two heterotopic pregnancies occurred in the series, one cervical and the other an interstitial ectopic. Selected demographic and clinical characteristics are shown in Table 1.

Four women had two consecutive nontubal ectopic pregnancies and one had three during the study period. Each pregnancy was considered an individual case for the purposes of the study. The majority of these women had repeat caesarean scar ectopic pregnancies.

Twenty-four women (24%) were asymptomatic and their diagnosis was considered to be an incidental finding; many were diagnosed on routine ultrasound assessment following assisted reproductive therapy (n = 12). Three women conceived spontaneously and were asymptomatic, but presented for early assessment because they had a history of ectopic pregnancy.

Table 1. Selected demographic and clinical characteristics of women (n = 100)

Variable	Cases n (%) Mean/Median	Min.	Max.
Median maternal age	34.81	20.10	47.48
Median gravida	3.00	1	13
Median parity	3.00	0	6
History of tubal ectopic pregnancy	10		
History of nontubal ectopic pregnancy	7		
Previous caesarean section multigravid women (n = 79)	36 (46%)		
History of pelvic inflammatory disease	5		
Infertility	28		
Assisted reproductive techniques	22		
Intrauterine device 'in situ' conception	–		
Previous miscarriages (n = 99)*	33 (33.34%)		
Previous surgical termination of pregnancy (n = 99)*	29 (29.3%)		
History of other uterine surgery	13		
History of other pelvic or abdominal surgery	23		
History of endometriosis	4		
History of uterine fibroids	6		
History of congenital uterine abnormality	3		
Presentation following unsuccessful termination of pregnancy	6		
Mean gestational age at diagnosis (weeks)	7.38	4.57	11.14
Mean trophoblast mass at diagnosis (largest diameter mm) (n = 98)*	25.13	4.30	100.00
Mean fetal CRL at diagnosis (mm) (n = 47)*	9.38	2.00	55.00
Fetal cardiac activity present at diagnosis (n = 99)*	32 (32.32%)		
Median β-hCG at presentation (IU/l) (n = 98)*	7566	6	666 818
Median maximum β-hCG (IU/l) (n = 96)*	10 139	6	666 818
Mean to resolution of β-hCG (n = 78)*	52	4	150
Mean days to resolution on ultrasound (n = 18)*	144	7	398
Mean treatment length surgical regimen cases (days to discharge all care) (n = 14)	49	6	152
Mean treatment length medical regimen cases (days to discharge all care) (n = 79)*	63	4	401

CRL, crown–rump length.
*Data not available or applicable for all cases.

Most of the nontubal ectopic pregnancies (72%) were diagnosed in the latter part of the study. The Supporting information (Table S1) describes trends for ectopic sites during the study period.

Overall management

Intended primary treatment regimens for these 100 cases were: 2 expectant, 83 medical, 14 surgical and 1 combination regimen. Actual management regimens for these 100 cases were: 1 expectant, 73 medical, 11 surgical and 15 combination regimen. Ninety-one percent of primary treatment regimens used minimally invasive approaches.

Management commenced before referral to our hospital in a small proportion of cases ($n = 7$).

The primary management plan was successful in 82 (82%) of these 100 pregnancies: 64 had no complications and required no further intervention, 15 required additional interventions (systemic methotrexate doses, USGI) and three had unexpected complications arising from the planned treatment. Table 2 describes the success of management by primary treatment regimen for each ectopic site.

Approximately two-thirds (64%) of cases were managed following exactly the primary plan. The frequency of additional or unplanned interventions was 36%; of these, 16 needed a surgical procedure, with the remainder being managed with additional medical or USGI approaches.

Eighteen cases (18%) required a different, unplanned intervention and their primary management plans were considered unsuccessful. Sixteen of these unsuccessful cases (89%) required surgical procedures not included in the primary management plan.

For these 18 cases with unsuccessful management:

- Eight required surgery following failed medical treatment for rupture, haemorrhage or persistently elevated β-hCG levels.
- Two were subsequently found to have placental site/trophoblastic tumours and both required hysterectomy.
- Three cases had failed surgical management before referral to our hospital.
- Two surgical regimen cases required subsequent systemic methotrexate for persistently elevated β-hCG levels.
- One case thought to be abdominal on imaging was found at surgery to be located in a noncommunicating atrophic horn of the uterus requiring a different, unplanned procedure (resection).
- A caesarean scar case, deemed likely to resolve spontaneously (β-hCG at presentation 6 IU/l), was managed expectantly but required surgical management for persistent bleeding.
- One caesarean scar case with suspected placenta accreta chose to continue with the pregnancy against medical advice, requiring an emergency caesarean/hysterectomy at 24 weeks of gestation.

Logistic regression analysis

A binary logistic regression model was performed for treatment success. All independent variables were considered for inclusion in the model. Maternal age, maternal body mass index, parity, smoking status, trophoblastic mass size and presence of a heartbeat did not yield a significant fit and were therefore not included in the final model. The level of β-hCG at presentation was included in the model but did not make a significant contribution in the prediction of

Table 2. Success of primary management by ectopic site

Site of ectopic pregnancy	Total no of. cases by site	Median gestational age (weeks)	Primary management expectant		Primary management medical (systemic/local)		Primary management surgical	
			n	Successful *n* (%)	*n*	Successful *n* (%)	*n*	Successful *n* (%)
Abdominal	1	5.430	–	–	–	–	1	0 (0%)
Caesarean scar	32	6.710	2	0 (0%)	29	25 (86%)	1	1 (100%)
Cervical	14	6.785	–	–	14*	12 (86%)	–	–
Cornual or interstitial	41	7.000	–	–	35**	31 (89%)	6***	4 (67%)
Ovarian	12	7.215	–	–	6	6 (100%)	6	3 (50%)
Total cases all sites	100		2	0 (0%)	84	74 (88%)****	14	8 (57%)****

*Includes the primary combination regimen case with heterotopic intrauterine and cervical ectopic pregnancy that was principally managed with intra-sac injection in combination with a uterine artery coil embolisation procedure to prevent complications.
**Includes one heterotopic intrauterine and cornual ectopic pregnancy.
***Includes management of one ectopic pregnancy located in a noncommunicating uterine horn; considered unsuccessful as an unplanned extension of the surgical procedure was required.
****Statistically significant difference ($P = 0.01$ OR = 0.18) between the success rates of the planned management medical regimen group ($n = 84$), and surgical regimen group ($n = 14$) using two-sided Fisher's exact test.

treatment success. According to the Hosmer and Lemeshow test, the final binary logistic regression model was statistically significant: $\chi^2(8) = 19.015$, $P = 0.015$. The model explained 24% of the variance in success of the primary management for ectopic pregnancy and correctly classified 88% of cases. The maximum β-hCG level was significant to the model but did not affect the odds of the outcome for the primary management. Gestational age in days was significant to the model: an increase in the gestational age in days was associated with a reduction of the likelihood of success of the primary management (see Supporting information, Table S3).

Systemic methotrexate

Systemic methotrexate was included in the primary management for 75 cases, but was included in the actual management for 83. The mean intramuscular dose for single-dose systemic methotrexate was 80 mg (range 50–100 mg; $n = 25$). The mean total dose for multi-dose systemic methotrexate was 288 mg (range 120–602 mg; $n = 57$) and the median number of doses was four (range two to nine doses).

Ultrasound-guided intra-sac injection

Forty-two (42%) of the 100 cases had USGI included in their management; 18 had intra-sac methotrexate, 22 had both KCl and intra-sac methotrexate, and two had only intra-sac KCl. The use of this approach peaked in 2012–14, when it was used in 61% of cases (see Supporting information, Table S2).

Ectopic site classification for these 42 cases included: 19 caesarean scar, 6 cervical and 17 cornual-interstitial ectopic pregnancies, including two heterotopic pregnancies. Most doses of USGI were administered transvaginally ($n = 25$ or 60%). Seventeen (40%) had transabdominal administration. The mean dose of methotrexate used for USGI was 38 mg (range 7–70 mg).

Of the 42 cases, USGI was included in the primary management for 36 cases. The six remaining cases had USGI following systemic methotrexate for rising β-hCG levels, increasing fetal size or persistent heartbeat. Table 3 compares the success of management for cases with USGI and those managed with systemic methotrexate.

All eight cases with planned USGI as the primary management were considered to be successful; three of these cases with caesarean scar ectopic pregnancies required a single dose of systemic methotrexate for plateauing β-hCG levels as per protocol.

Of the 28 cases of USGI commenced in conjunction with systemic methotrexate; 22 were considered successful and did not require any further intervention, two were considered successful but required further doses of systemic methotrexate for persistent β-hCG levels, two were considered successful but experienced unexpected complications (pneumonia, blood loss requiring transfusion), two cases were considered unsuccessful and further unplanned management was required. One of these unsuccessful cases was in a woman with a caesarean scar ectopic pregnancy and rising β-hCG levels: ectopic rupture occurred and emergency uterine wedge resection was performed. The other unsuccessful case was a caesarean scar ectopic pregnancy requiring total abdominal hysterectomy and salpingectomy for a placental site tumour.

Table 3. Comparison of success for intra-sac and systemic medical management by ectopic site

Site of ectopic	Total medical management cases by site	Primary management USGI with/without systemic methotrexate		Primary management systemic methotrexate only		Primary management systemic methotrexate with subsequent USGI	
	n	*n*	Successful *n* (%)	*n*	Successful *n* (%)	*n*	Successful *n* (%)
Abdominal	_	_	_	_	_	_	_
Caesarean scar	29	16	14 (88%)	10	8 (80%)	3	3 (100%)
Cervical	14	6*	6 (100%)	8	6 (75%)		
Cornual or interstitial	35	14**	14 (100%)	18	14 (77%)	3	3 (100%)
Ovarian	6	_	_	6	6 (100%)	_	_
Total all sites	84	36	34 (94%)***	42	34 (81%)***	6	6 (100%)***

*Heterotopic live intrauterine and live cervical ectopic pregnancy; local injection of methotrexate and KCl to both cervical and intrauterine pregnancies with systemic single dose methotrexate and performed with surgical procedure of uterine artery coils/embolisation.
**Includes one heterotopic failed intrauterine and live cornual ectopic pregnancy; local injection of methotrexate and KCl to cornual ectopic and systemic multidose methotrexate.
***No statistically significant difference ($P = 0.177$, OR = 3.4) between the success rates of the primary management USGI with/without systemic methotrexate ($n = 36$), and combined primary management systemic methotrexate only and primary management systemic methotrexate with subsequent USGI ($n = 48$) regimens using two-sided Fisher's exact test.

Surgical management

Primary surgical management was planned for 14 women, but was eventually undertaken for 25. Four (29%) of these 14 women were clinically unstable and required urgent surgical procedures. One multigravida aged 47 with an unplanned pregnancy did not wish to preserve fertility and had primary surgical management. Three (22%) had failed surgical procedures performed externally before referral to the study site. Six (43%) were clinically stable but were considered complex and directed towards primary surgical management.

Subsequent unplanned surgical management was required for 13 women: two women with primary surgical management, 11 women with primary medical or expectant management.

To preserve fertility a minimally invasive surgical approach of selective enucleation or resection of the ectopic trophoblastic tissue was the primary procedure for five women. Four of these five women required further management:

- Two required systemic methotrexate for plateauing β-hCG levels.
- One ovarian ectopic pregnancy initially managed externally required salpingo-oophorectomy.
- A primigravida with a ruptured cornual-interstitial pregnancy required multidose systemic methotrexate for rising β-hCG levels and a laparoscopic wedge resection for residual trophoblastic tissue 4 months after treatment commenced.

Three further cases were successfully treated with minimally invasive surgical procedures as an additional, unplanned treatment: two cornual-interstitial ectopic pregnancies following multidose systemic methotrexate and one caesarean scar ectopic pregnancy managed expectantly.

Combined management

Combined management was planned for only one woman with a cervical heterotopic pregnancy, but was eventually undertaken for 15 cases (n = 15%). Ten arose from the primary medical regimen group; the additional four stemmed from the primary surgical regimen group.

Treatment length

Time to discharge from all medical care, including outpatient follow up, was known for 94 cases (Table 1). The mean time to discharge for the primary medical regimen group (n = 79) was not significantly different to those (n = 14) with a primary surgical approach (U = 377.5, P = 0.059).

Complications

Complications according to the different treatment regimens are described in Table 4. Hysterectomy was required for seven women and the clinical details of these particular cases are described in the Supporting information (Table S4).

Subsequent pregnancies and fetal anomalies

In our cohort of 100 cases, 42 women were known to have 52 subsequent pregnancies: 46 intrauterine and six repeat nontubal ectopics; no tubal ectopics occurred. Three intrauterine pregnancies were affected by a fetal anomaly: one trisomy 15, one absent ductus venosus and one skeletal anomaly.

Table 4. Frequency of complications according to treatment regimen and comparison between medical and surgical groups

	Total cases (n = 100)	Primary management medical (n = 84)	Primary management surgical (n = 14)		Primary management expectant (n = 2)
	n	n (OR = 1)	n	OR (95% CI)	n***
Hysterectomy	7	5	1	0.82 (0.09–7.62)	1
Rupture during course of treatment	4	3	1**	0.48 (0.05–4.99)	–
Blood transfusion or excessive bleeding requiring treatment	13	10	2	0.81 (0.16–4.16)	1
Admission to ICU or Complex Care	3	1	1	0.16 (0.01–2.66)	1
Unplanned hospital admission	30	25*	5	0.76 (0.23–2.50)	–
Residual trophoblastic lesion or tumour	4	3	1	0.47 (0.05–4.87)	–
Specific surgical complications	2	–	2	–	–
Side effects from systemic methotrexate	25	25	–	–	–

*Includes combined management heterotopic case managed with USGI and uterine artery embolisation.
**Ruptured before planned surgery was able to be performed.
***Expectant case numbers too small for a meaningful statistical comparison.

Discussion

Main findings

This study reviews the management of women diagnosed with nontubal pregnancies in different anatomical sites, analysing the efficacy of different treatment regimens.

A high rate of success (82%) is demonstrated for all management regimens, with minimal morbidity and no deaths occurring following the diagnosis of these complex pregnancies. The primary management in stable women was predominantly conservative, with minimally invasive approaches comprising 90% of cases; 83 women were managed medically, two were managed expectantly, one received combined USGI and minimally invasive surgical management and four others underwent minimally invasive surgical procedures. For women who were clinically unstable or who did not wish to preserve fertility, surgical procedures were chosen as primary management (10%).

This study supports the emerging evidence[9,19] that minimally invasive approaches are safe and effective treatment options for nontubal ectopic pregnancies in women desiring to conserve fertility. Higher success rates were shown when primary management was systemic or intra-sac injection (88%) when compared with primary surgical management (57%); this result was found to be statistically significant.

This study offers additional insights into the role of USGI and minimally invasive surgical procedures, aimed at preserving reproductive organ structures and function. This series highlights the possibility of including them as tools in addition to the well-recognised option of systemic methotrexate. This is supported by the similarly high success rates reported for primary management with USGI alone or in combination with systemic methotrexate (94%) and for primary management with systemic methotrexate alone (81%). In addition, 75% of the eight women managed with minimally invasive surgical approaches avoided more extensive surgery; some however, required lengthy follow up and additional management with systemic methotrexate.

To our knowledge this is the largest case series (n = 42) of consecutive nontubal ectopic pregnancies which USGI has been used as part of the management plan. USGI was shown to play an important role in the management of women with caesarean scar, cervical and cornual-interstitial pregnancies. We compared the success rates according to anatomical site for all medically managed cases and reported a higher success rate (94%) for cases managed primarily with USGI alone or when used in conjunction with systemic methotrexate compared with 81% for cases managed with systemic methotrexate alone. The benefit of subsequent USGI for the six failed cases (with persistently elevated β-hCG levels or a growing live fetus) is illustrated by the 100% rate of success. This is in keeping with observations from other large series (Doubilet et al.[20], Verma et al.[5]), which reported similar rates of successful outcomes.

Forty-two women achieved a subsequent pregnancy following this potentially catastrophic diagnosis and three were affected by a fetal anomaly. The pregnancy diagnosed with skeletal anomaly was conceived 3 weeks following treatment for an ovarian ectopic with systemic methotrexate. Currently there is no consensus on how long to wait to conceive after the use of methotrexate. At our institution the suggested interval between methotrexate administration and a new pregnancy is 4 months. In view of the increased possibility of fetal anomalies if conception happens soon after the administration of methotrexate, we recommend that these women should undergo detailed early fetal anomaly scans.

Strengths and limitations

To our knowledge this is one of the largest series of consecutive nontubal ectopic pregnancies treated predominantly by minimally invasive approaches, including a significant proportion of cases managed with USGI.

Limitations of this study include its retrospective nature and a relatively heterogeneous approach to similar clinical presentations, especially in earlier years where management plans were less well structured. We acknowledge a potential for selection bias as more unstable or urgent cases may have been directed towards surgical treatment, therefore resulting in relatively poorer outcomes for this treatment regimen group. It is also valid to observe that the study spans over 11 years, a period during which technological advances have favourably impacted diagnostic and treatment modalities such as ultrasound and laparoscopy. During this 11-year period we documented an increment in the total number of nontubal ectopic cases and in particular of caesarean scar ectopics. This rise in frequency was accompanied by a corresponding increase in the choice of USGI as the primary treatment regimen in all ectopic sites.

Unfamiliarity with these infrequent ectopic pregnancies can lead to misdiagnosis and suboptimal management.[5] Twenty-four cases were referred to our hospital after failed treatment, following inability to locate the pregnancy or following failed termination of pregnancy. This contributed to a delay in diagnosis and advancing gestational age increases risks and complexity of care.

Interpretation

Our success rates for the conservative management of nontubal ectopic pregnancies are in keeping with similar studies.[5,9]

The cornual-interstitial group (41%) and the caesarean scar ectopic group (32%) were the largest groups in this series. The high incidence reflects the rising caesarean section rates, increasing rates of assisted reproduction techniques, advances in ultrasound technology and increasing availability of early ultrasound to diagnose these cases.[5,21] Both of these groups were predominantly managed medically with success rates of 86% and 88%, respectively; these results are similar to other series in the literature.[19,22]

Seven of the 100 women in this series required hysterectomy (7%); within these cases, caesarean scars were the most common ectopic site (n = 5; 71%). Similar rates of hysterectomy are reported in other series including Birch Petersen et al.[23] (6%).

The major criticisms of medical management include lengthy follow up, prolonged bleeding or haemorrhage, risk of persistent trophoblastic disease and risk of rupture even after β-hCG levels decrease.[19,22] These criticisms are supported in our study: two women required hysterectomy following unexpected rupture; lengthy follow up in women managed medically (mean time to β-hCG resolution 52 days; mean time to ultrasound resolution 144 days). Four women had residual lesions months after resolution of β-hCG, prompting surgical intervention in two, who were subsequently found to have placental site or trophoblastic tumours and required hysterectomy.

Conclusion

Nontubal ectopic pregnancies may be safely treated by minimally invasive procedures in selected cases. USGI and surgical procedures aimed at preserving reproductive organ structures and function should be included as primary management tools in addition to the well-recognised option of systemic methotrexate. These options are relevant for women desiring to conserve fertility. The disadvantages may be the longer resolution times, the risk of residual trophoblastic disease and the need for unplanned surgery.

Acknowledgements

Study data were collected and managed using REDCap electronic data capture tools hosted at The University of Melbourne.[11] REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources.

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Disclosure of interests

None declared. Completed disclosure of interests form available to view online as supporting Information.

Contribution to authorship

RPD, JR, WCA, GRK and KLR all contributed to the study design, data collection, analysis and interpretation. JR, KLR and RPD wrote the manuscript. RPD, WCA and GRK critically reviewed the manuscript for accuracy and intellectual content.

Details of ethics approval

Human Research and Ethics Committee approval for a retrospective anonymised audit project that met the criteria for quality assurance activities outlined in the National Health and Medical Research Council guideline 'Ethical Considerations in Quality Assurance and Evaluation Activities'[10] was obtained. Correspondence confirming this was received from The Royal Women's Hospital HREC on 21 October 2014.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. (A) Transvaginal ultrasound image of gestational sac within the cervical canal with decidual reaction and blood in the endometrial cavity.

Figure S2. Nontubal ectopic cases by site (n = 100).

Table S1. Trends over time: nontubal ectopic pregnancies by site.

Table S2. Trends in USGI for management by ectopic site.

Table S3. Binary logistic regression—variables in the equation.

Table S4. Clinical characteristics for cases requiring hysterectomy. ■

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