How to Measure Size of Tubal Ectopic Pregnancy on Ultrasound Scan?

Short title: size of tubal pregnancy

K Rajah, V Goodhart, KP Zamora, T Amin, E Jauniaux, D Jurkovic

Early Pregnancy Unit, Institute for Women's Health, University College Hospital, London, UK(chorion

Correspondence

Mr Davor Jurkovic

Department of Obstetrics and Gynaecology

University College Hospital

250 Euston Road

London, NW1 2BU

Email: Davor.Jurkovic@nhs.net

Key words: Ectopic pregnancy, tubal, ultrasound, size, surgery

Abstract

Objective: To identify the preoperative ultrasound measurements for assessing the size of tubal ectopic pregnancy which correlate best with the findings at surgery.

Methods: We conducted a prospective study of all women with a conclusive transvaginal ultrasound diagnosis of tubal ectopic pregnancy over a 10-month period. In each case, we

measured the total size of the ectopic pregnancy by placing the calipers on the outer edges of the visible trophoblastic tissue. In ectopic pregnancies, presenting with a well-defined gestational sac we also measured the size of coelomic (chorionic) cavity using the inner borders of the trophoblastic ring as the reference points. In women with signs of intraabdominal bleeding, we measured the size of the haematosalpinx and haemoperitoneum. The surgeons were blinded to the ultrasound measurements and they were asked to estimate the size of the ectopic pregnancy and the amount of haemoperitoneum intraoperatively.

Results: A total of 105 women were diagnosed with a tubal ectopic pregnancy on ultrasound examination out of which 71/105 (67.6%) were managed surgically. We found a significant ($p<0.01$) positive correlation between all ultrasound measurements and the size of tubal ectopic pregnancy as reported during surgery. In the absence of a haematosalpinx, the mean total outer diameter of ectopic pregnancy had the highest positive correlation with the size of tubal ectopic at surgery ($r=0.65$, $P<0.001$). In cases complicated by haematosalpinx, the mean diameter of the tube was the only variable which correlated significantly ($p<0.001$) with the estimated size of ectopic pregnancy at surgery. There was a significant ($p<0.001$) positive association between the amount of haemoperitoneum on ultrasound and the estimated volume of intraperitoneal blood at surgery.

Conclusion: The mean size of haematosalpinx and the total outer mean dimeter of ectopic pregnancy on ultrasound correlate better with the surgical findings than the size of coelomic cavity. Our findings show that the standard approach to measure the size of intrauterine pregnancy on ultrasound should be adapted in women diagnosed with tubal ectopic pregnancies to include these additional measurements.

Introduction

The first successful ultrasound diagnosis of ectopic pregnancy was reported by Kobayashi et al in 1969[1]. Initially, the ultrasound diagnosis of ectopic pregnancy was based on the absence of an intrauterine pregnancy in women presenting with bleeding and pain in early pregnancy.[2] Development of high resolution transvaginal ultrasonography (TVS) has enabled to change the diagnostic approach from indirect criteria to direct visualization of ectopic pregnancy. Diagnostic accuracy has increased over time and in modern practice the majority of ectopic pregnancies are visualized on ultrasound scan prior to surgery. In particular, the increased ability to detect very small unruptured ectopic pregnancies has facilitated the development of conservative management strategies such as expectant and medical treatment[3].

Although direct visualization of ectopic pregnancy has become standard in routine clinical practice there is no consensus in the literature on the technique which should be used to measure the size of tubal ectopic pregnancy. Studies on conservative management of ectopic pregnancy often include advice on the maximum size of ectopic pregnancy which could be managed conservatively[4]. This approach and been adopted by the Royal College of Obstetricians and Gynaecologists[5] and by the National Institute of Clinical Excellence (NICE)[6] who both recommend taking into account the size of tubal ectopic pregnancy when selecting women for conservative or surgical management. Neither guideline, however, provides any advice on how to measure the size of ectopic pregnancy.

The technique used to measure the size of intrauterine pregnancy was first described in 1969[7]and has been since universally adopted[8]. The calipers are placed on the inner borders of trophoblastic ring and the coelomic cavity and the mean diameter is calculated from three measurements taken in three orthogonal planes. Although this measurement does not include the

trophoblastic ring (chorion) it is routinely referred to as 'gestational sac' size. It is likely that most ultrasound examiners use the same approach to measure tubal ectopic pregnancies. However, the relative proportions of trophoblastic ring and coelomic fluid forming the gestational sac often differ in intrauterine and ectopic pregnancies and it is not known whether the measurement technique should be modified to allow for that. (Figs. 1,2) In addition, the finding of bleeding next to the gestational sac has very different implications for the planning of clinical management of ectopic compared to intrauterine pregnancies[5,9].

In this study, we carried out detailed ultrasound measurements of tubal ectopic pregnancies, haematosalpinx and haemoperitoneum and compared these measurements with the estimated size of ectopic pregnancy and amount of blood found at surgery. The aim of the study to identify measurements which correlate best with the surgical findings and to explore whether the standard approach to measure the size intrauterine pregnancy can also be used in tubal ectopic pregnancies.

Methods

This was a prospective study of women diagnosed with a tubal ectopic pregnancy and managed in the Early Pregnancy Unit (EPU) at University College London Hospital (UCLH) between November 2015 and August 2016. In our hospital all women presenting to the EPU with a positive pregnancy test and symptoms suggestive of early pregnancy complications are assessed by clinicians with expertise in early pregnancy care. Women also routinely undergo a TVS examination using a high frequency probe (Voluson E8, GE Medical Systems, Waukesha, WI, USA). The scan is performed in a standardized way. First the uterus is examined in the

transverse and longitudinal views to identify an intrauterine gestational sac. If an intrauterine pregnancy is seen, the gestational sac size is measured in the longitudinal, anterior-posterior and transverse dimensions, from the trophoblastic ring/coelomic cavity interface, as previously described by Nyberg et al.[10]. We then examine both adnexa systematically. The ovaries are examined for the presence of corpora lutea and any abnormalities. A tubal ectopic pregnancy is diagnosed when there is an adnexal swelling separate to the ovary with typical ultrasound features of ectopic pregnancy[11]. The pelvis is then assessed for any signs of haemoperitoneum.

Tubal ectopic pregnancies are categorised based on their morphological appearances into five types: solid swelling, empty gestational sac, gestational sac with yolk sac, gestational sac with an embryo without cardiac activity and a gestational sac containing a live embryo.

Women diagnosed with a tubal ectopic pregnancy and presenting with moderate to severe abdominal pain, evidence of significant haemoperitoneum and/or signs of cardiovascular instability are admitted for emergency surgery. Women who have a live tubal ectopic pregnancy or heterotopic pregnancy are also offered immediate surgical management. All other women have a blood sample taken to measure serum β-hCG. Clinically stable women with an initial serum β-hCG level <1500 IU/L are offered conservative management. Women with serum β-hCG level ≥1500 IU/L recorded either at the initial visit or during follow up are also advised to have surgery. Women undergoing conservative management are followed-up until they have a negative pregnancy test or serum hCG declines to <20IU/l.[3]

During the study period, each tubal ectopic pregnancy was measured in three perpendicular planes using the following protocol: 1) the outer to outer margins of the trophoblastic tissue were measured in all cases to include the full size of ectopic pregnancy (Figs. 3,4); 2) in ectopics presenting with a well-defined gestational sac the inner to inner margins of

the trophoblastic ring denoting the coelomic (chorionic) cavity were also measured. (Figs. 3,4) This was done in the same way as routine ultrasound measurements of coelomic cavity are carried out in cases of intrauterine pregnancies. Although this measurement does not include the trophoblastic ring, in clinical practice it is routinely referred to as the 'gestational sac' size; 3) In women with evidence of haematosalpinx the measurements were taken between the inner margins of the Fallopian tube (Figs. 3,4). We recorded the maximum and mean values of each measurement. When a gestational sac was present, we also calculated the ratio of the mean outer diameter to the mean inner diameter to assess the relative proportions of trophoblastic ring and coelomic cavity within tubal ectopic pregnancies (T/C ratio).

We categorized haemoperitoneum semi-quantitatively as mild when there was echogenic fluid present in the pouch of Douglas, moderate when there were visible blood clots and severe when there were blood clots and echogenic fluid present both in the pouch of Douglas and in the utero-vesical space. (Fig. 5) The indication for surgery and the findings at surgery were also recorded. The operating surgeons were blinded to the detailed measurements taken for the purpose of the study. They were asked to estimate subjectively the size haemoperitoneum immediately after the insertion of laparoscope with the patient lying supine. They were also asked to take into account the amount of blood aspirated form the pelvis during surgery to assist with their estimate. The size of ectopic was estimated subjectively during visual assessment on the affected Fallopian tube. The surgeons were not asked to attempt to measure separately the size of trophoblastic tissue and coelomic cavity.

The control group consisted of women with intrauterine pregnancies who were matched for gestational age and morphological type of gestational sac. In all cases we calculated the T/C ratio and compared the results with those from women diagnosed with tubal ectopic pregnancies.

All data were entered into an Excel spreadsheet and kept separate from the main database used for clinical treatment. We sought advice from the Joint Research Office of University College London and University College London Hospital regarding ethical approval and were advised that formal ethics approval was not needed for this study as long as patient identifiable data was not seen by anyone outside the clinical care team.

Statistical Analysis

Comparisons between ultrasound and intraoperative measurements were carried out in the subgroup of women who required surgical treatment. None of the variables were normally distributed and we thus used non–parametric statistical tests. We used Spearman's rank correlation to examine the correlation between the mean outer diameter and largest outer diameter, mean inner diameter and largest inner diameter, and mean and largest diameter of haematosalpinx. We then examined the correlation between all six ultrasonic parameters and the ectopic size reported at surgery using both correlation and regression methods.

Taking into consideration differences in the approaches to assess the size of tubal ectopic on ultrasound and during surgery, we evaluated that correlation coefficient of $r \geq 0.65$ would constitute a clinically significant result. Assuming two-sided 5% significance and 90% power, 21 women were required in each subgroup of tubal ectopics to complete the study.

We subsequently examined the joint association between the mean ultrasonic diameter values and size reported at surgery in a multivariable analysis. We only included mean ultrasonic

diameter values as the strong correlation between mean and largest ultrasonic diameter values causes problems of collinearity when the factors were included in the same regression analysis. There was no clear rationale for us choosing mean diameter over largest diameter.

We performed several multivariable analyses, considering different combinations of parameters. The size reported at surgery was found to have a positively skewed distribution and these data were analyzed following a log transformation.

We also examined the association between the severity of bleeding on ultrasound and volume of haemoperitoneum at surgery. The volume of haemoperitoneum at surgery was found to have a skewed distribution and thus we used the Mann-Whitney test to compare the two variables. As there was only one case of moderate haemoperitoneum on ultrasound, we combined moderate and severe cases for analysis.

We compared T/C ratios between the ectopic and intrauterine pregnancies. The examination of the data suggested that the values had a positively skewed distribution and a Mann-Whitney test was used for the analysis.

Results

During the study period, 120 consecutive women were diagnosed with a tubal ectopic pregnancy in the Early Pregnancy Unit. We excluded from the study nine women who did not complete the follow-up for conservative management and six women who had their surgical management in another hospital. The study group consisted of 105 women. A total of 186 women were included in the control group. Demographic characteristics of the study and control groups are presented in Table 1.

In the study group, 69/105 (65.6%, 95% CI 59.1-72.3) women presented with abdominal pain and vaginal bleeding, 21/105 (20.0%, 95% CI 4.6-35.4) with abdominal pain and 8/105 (7.6%, 95% CI -10.1-25.3) with vaginal bleeding. There were 7/105 (6.7%, 95% CI -11.2-24.7) women who were asymptomatic. Three of them had an early scan due to a previous miscarriage, other three had an early scan due to a previous ectopic pregnancy and one woman had a scan after an ectopic pregnancy was suspected on her routine first trimester scan.

There were 71/105 (67.6%, 95% CI 58.7-76.6) women with a tubal ectopic who were managed surgically whereas 34/105 (32.4%, 95% CI 23.5-41.4) women were successfully managed conservatively. Morphological and biochemical characteristics of ectopic pregnancies managed surgically and conservatively are displayed in Table 2.

In 43/105 (41.0%, 95% CI 31.6-51.4) of the cases, the ectopic pregnancies presented as solid swellings whereas in 62/105 (59.0%, 95% CI 49.6-68.4) there was a visible gestational sac. There was evidence of a haematosalpinx in 25/105 (23.8%, 95% CI 15.7-32.0) and haemoperitoneum in 32/105 (30.5%, 95% CI 21.7-39.3). 16/105 (15.2%, 95% CI 8.3-22.1) had evidence of both a haematosalpinx and haemoperitoneum. There were two cases of heterotopic pregnancy.

Surgical management was carried out in 24/25 (96.0%, 95% CI 88.3-103.4) women with evidence of a haematosalpinx and 31/32 (96.9%, 95% CI 90.6-103.0) with evidence of haemoperitoneum. The median mean outer diameter of ectopic pregnancy/trophoblastic ring was 14.0mm (IQR 10.7-19.4), the median mean diameter of coelomic cavity was 4.3mm (IQR 3.0-7.0) and the median mean haematosalpinx diameter was 21.9mm (IQR 20.0-35.5).

The serum β-hCG, serum progesterone and ultrasound measurements in women managed surgically and conservatively are shown in Table 2. A summary of the management of women presenting with different morphological types of ectopic pregnancy is provided in Table 3.

The indication for surgery was significant pain at diagnosis or during follow-up in 26.8% (95% CI 16.5-37.1), initial serum β-hCG level above 1500 IU/L in 16.9% (95% CI 8.2-26.5), sustained rise in serum β-hCG in 15.5% (95% CI 7.1-23.9), significant haemoperitoneum in 14.1% (95% CI 6.0-22.2), live embryo in 14.1% (95% CI 6.0-22.2), patient choice in 8.5% (95% CI 2.0-15.0) and heterotopic pregnancy in 4.3% (95% CI -0.4-9.0). All surgical interventions were performed laparoscopically. Tubal rupture was recorded in 3/71 (4.2%) of women. The median size of ectopic pregnancy reported at surgery was 20.0mm (IQR 20.0-30.0).

In the surgical group, the correlation coefficient between mean and largest outer diameter of ectopic pregnancy/trophoblastic ring measured on ultrasound scan was 0.98 ($p<0.001$), mean and largest coelomic cavity diameter was 0.98 ($p<0.001$) and mean and largest haematosalpinx diameter was 0.92 ($p<0.001$).

In univariate analysis all six ultrasonic parameters were significantly associated with the size reported at surgery. The results are expressed as ratios due to the log transformation of the size reported as surgery values. (Table 4)

The linear regression analysis using the size reported at surgery as a dependent variable and mean outer ectopic pregnancy/trophoblastic ring diameter, mean coelomic cavity diameter and mean haematosalpinx diameter as independent variables, found that the mean haematosalpinx diameter could be retained in the model. In women without haematosalpinx only the mean outer pregnancy/trophoblastic ring diameter was found to be significant. (Table 5)

The median blood loss at surgery was 400ml in the group with moderate/severe haemoperitoneum on ultrasound and 100ml in the group with mild haemoperitoneum on ultrasound. (Table 6)

We also assessed the relative size of the coelomic cavity to the trophoblastic ring by calculating the T/C ratio in women with intrauterine and ectopic pregnancies matched for the gestational age and morphological type. The ratio was significantly higher in all morphological types of ectopic pregnancies compared to intrauterine pregnancies. (Table 7)

Discussion

Our results show that that in tubal ectopic pregnancies with a visible gestational sac the outer diameter of tubal ring on ultrasound was better estimate of their size compared to the diameter of the coelomic cavity using surgery as a reference standard. In tubal pregnancies complicated by haematosalpinx there was a better correlation between surgical assessment and ultrasound measurement of the size of Fallopian tube distended with blood than with the size of the outer or inner diameter of ectopic pregnancy itself. We have also found that the size of coelomic cavity is significantly smaller in relation to the total size of gestational sac in tubal compared to intrauterine pregnancies. Ectopic and intrauterine pregnancies were matched for the presence of cardiac activity and morphological type of pregnancy failure. In view of that it is likely that the observed difference in the chorion thickness was probably due to location of pregnancy. This can be explained by impaired placentation due to the absence of decidua in the Fallopian tube[12]. As a result, the ectopic trophoblastic ring appears thick, cystic and bright on ultrasound scan. In addition, the production of coelomic fluid might be reduced due to the diminished trophoblast function which could explain the finding of relatively smaller size of the coelomic cavity in

ectopic pregnancies. These functional and morphological abnormalities are the likely explanation for the higher average total trophoblastic ring to coelomic cavity ratio in ectopics compared to intrauterine pregnancies.

Our findings indicate that the approach to the measurement of ectopic pregnancy on ultrasound scan should be modified to provide estimates of its size which are more relevant to clinical practice. This is of importance regardless whether the ectopic is managed conservatively or surgically. Conservative management has a significant failure rate and there is a continuing effort to refine the selection criteria for both expectant and medical treatment[4,11]. The presence and size of the haematosalpinx is not routinely reported on ultrasound although it is likely to be associated with higher risk of adverse clinical outcomes. Our results suggest that this measurement should be routinely taken and reported. Accurate estimates of the size of ectopic pregnancy are also important in women who are selected for surgical treatment. Reporting only the size of coelomic cavity is likely to underestimate the true size of ectopic. This may result in delayed surgical treatment as very small ectopics are sometimes perceived by clinicians as being low risk. Underestimating the size of ectopic and not reporting the size of haematosalpinx may also have medico-legal implications. Women may be led to believe that the larger size of ectopic found at surgery compared to pre-operative ultrasound scan was the result of a delay in carrying out the surgical procedure rather than due to differences in the measurement techniques to determine its size.

At surgery the size of ectopic pregnancy is estimated subjectively by the operating surgeon whilst the ultrasound measurements are objective and therefore probably more reproducible and accurate. However, we decided to use the surgical findings as a reference standard which is in concordance with standard clinical practice[13]. The inconsistencies in the measurement

techniques represent a limitation of this study and it is possible that the overall correlation between ultrasound and surgical assessments of the size of tubal ectopics would have been better if pre- and intra-operative measurements had been carried out in a more uniform way. Previous studies have shown ultrasound measurements of the coelomic cavity ('gestational sac') are less reproducible than the measurements of the crown rump length[14]. Variations in measurements; however, were higher in women with larger cavities (>15mm) which we only found in 4/47 (8.5%) of women diagnosed with ectopic pregnancies in our study population.

Previous reports have shown than it is hard to provide accurate estimates of the exact amount of blood within the abdominal cavity on ultrasound scan and most authors prefer to assess severity of bleeding semi-quantitatively[14,15]. We used a similar approach in this study, but we placed particular emphasis on the presence of blood clots within the abdominal cavity. Small amount of blood tends to become diluted in the peritoneal fluid and it is seen on ultrasound as uniformly echogenic. Blood clots are an important finding because they are a sign of more severe bleeding which cannot be completely diluted in the peritoneal secretions. They also indicate that the intra-abdominal bleeding is originating form the Fallopian tubes or ovaries and it is not caused by retrograde bleeding from the uterine cavity. In the present study, the pre-operative diagnosis of haemoperitoneum was confirmed at laparoscopy in all women who underwent surgery. We also found that the presence of blood in the vesico-uterine pouch was associated with a median blood loss of 400mls. This is in agreement with the results of previous studies and we suggest that all women with this finding are offered emergency surgery without delay[15,16].

In conclusion, our study has shown that there is a need to adopt a standardized approach to the assessment of ectopic pregnancy size including detailed measurement of the entire gestational sac, the surrounding haematosalpinx and assessment of the severity of the

haemoperitoneum. This should help to refine selection criteria for different management option and result in better clinical outcomes. A standardized approach to the measurement of ectopic pregnancy would also facilitate further research into the management of ectopic pregnancy and ensure consistency in reporting the outcomes in clinical audit and research.

References

1. Kobayashi M, Hellman LM, Fillisti LP. Ultrasound: an aid in the diagnosis of ectopic pregnancy. Am J Obstet Gynecol 1969;103:1131-40
2. Crochet JR, Bastian LA, Chireau MW. Does this woman have an ectopic pregnancy? The rational clinical examination systematic review. JAMA 2013;309:1722-9.
3. Hajenius PJ, Mol F, Mol BWJ, Bossuyt PMM, Ankum WM, Van der Veen F. Interventions for tubal ectopic pregnancy. Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.: CD000324. DOI: 10.1002/14651858.CD000324.pub2.
4. Mol F, Mol BW, Ankum WM, van der Veen F, Hajenius PJ. Current evidence on surgery, systemic methotrexate and expectant management in the treatment of tubal ectopic pregnancy: a systematic review and meta-analysis. Hum Reprod Update. 2008; 14:309-19.
5. Elson CJ, Salim R, Potdar N, Chetty M, Ross JA, Kirk EJ on behalf of the Royal College of Obstetricians and Gynaecologists. Diagnosis and management of ectopic pregnancy. BJOG 2016;123:e15–e55.
6. National Institute for Health and Care Excellence. Ectopic pregnancy and miscarriage: diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage. London: National Institute for Health and Care Excellence; 2012.
7. Hellman LM, Kobayashi M, Fillisti L, Lavenhar M, Cromb E. Growth and development of the human fetus prior to the twentieth week of gestation. Am J Obstet Gynecol. 1967;99:662-70.

8. Grisolia G1, Milano K, Pilu G, Banzi C, David C, Gabrielli S, Rizzo N, Morandi R, Bovicelli L. Biometry of early pregnancy with transvaginal sonography. Ultrasound Obstet Gynecol 1993;3:403-11.

9. Bennett GL, Bromley B, Lieberman E, Benacerraf BR. Subchorionic hemorrhage in first-trimester pregnancies: prediction of pregnancy outcome with sonography. Radiology. 1996;200:803-6.

10. Nyberg DA, Mack LA, Laing FC, Patten RM. Distinguishing normal from abnormal gestational sac growth in early pregnancy. J Ultrasound Med 1987;6:23-7.

11. Mavrelos D, Nicks H, Jamil A, Hoo W, Jauniaux E, Jurkovic D. Efficacy and safety of a clinical protocol for expectant management of selected women diagnosed with a tubal ectopic pregnancy. Ultrasound Obstet Gynecol 2013;42102-7.

12. Stock RS. Gross pathology and microscopic histopathology. In Sovall TG, Ling FW.(eds.) Extrauterine Pregnancy. New York: Mc Grow Hill; 1993. p.65-96.

13. Cacciatore B, Stenman UH, Ylostalo P. Comparison of abdominal and vaginal sonography in suspected ectopic pregnancy. Obstetrics and Gynecology 1989; 73:770-4.

14. Pexsters A, Luts J, Van Schoubroeck D, Bottomley C, Van Calster B, Van Huffel S, Abdallah Y, D'Hooghe T, Lees C, Timmerman D, Bourne T. Clinical implications of intra- and interobserver reproducibility of transvaginal sonographic measurement of gestational sac and crown-rump length at 6-9 weeks' gestation. Ultrasound Obstet Gynecol 2011;38:510-5.

15. Fauconnier A, Mabrouk A, Salomon LJ, Bernard JP, Ville Y. Ultrasound assessment of haemoperitoneum in ectopic pregnancy: derivation of a prediction model. World J Emerg Surg 2007;2:23.

16. Bignardi T, Condous G. Does tubal ectopic pregnancy with hemoperitoneum always require surgery? Ultrasound Obstet Gynecol. 2009;33:711-5.

Figure Legends

Figure 1: An image of tubal ectopic pregnancy. Coelomic cavity (calipers) appears relatively small in comparison to the surrounding hyperechoic trophoblastic ring.

Figure 2: A case of an intrauterine miscarriage at 7 weeks' gestation. Most the gestational sac is occupied by coelomic cavity whilst the trophoblastic ring appears thin in comparison.

Figure 3: A schematic illustration of ultrasound measurements of tubal ectopic pregnancy carried out in this study.

Figure 4: An example of ultrasound measurement of coelomic cavity ('gestational sac')

( ), trophoblastic ring ( ) and haematosalpinx ( ) in a woman diagnosed with tubal ectopic pregnancy.

Figure 5: A case of severe haemoperitoneum in a woman diagnosed with a tubal ectopic pregnancy. Note the presence of free fluid and hyperechoic blood clots both in the pouch of Douglas and in the vesico-uterine pouch.

Table 1: Demographic characteristics of women and the study and control groups

	Study Group (N=105)	Control Group (N=186)
Age [median (IQR)]	32 (28-35)	32 (28-37)
Parous *	36; 34.3% (21.6-46.8)	81; 43.5% (35.4-51.6)
Previous tubal ectopic pregnancy*	9; 8.6% (-9.0-26.2)	16; 8.6% (-4.6-21.8)
Previous miscarriage*	28; 26.7% (12.6-40.8)	67; 36.0% (26.8-45.2)
Previous termination of pregnancy*	20; 19.0% (3.5-34.5)	35; 18.8% (7.1-30.5)
Conception:		
Spontaneous*	94; 89.5% (87.5-91.5)	172; 92.5% (91.4-94.0)
Ovulation induction*	2; 1.9% (-16.9-20.7)	2; 1.1% (-13.3-15.5)
Superovulation & IUI*	2; 1.9% (-16.9-20.7)	-
IVF/ICSI*	7, 6.7% (-11.3-24.7)	12; 6.5% (-7.0-20.0)

*n; % (95% CI)

Table 2 Comparison of the size and serum biochemistry in women managed surgically or medically (N=105)

Variable	Surgical		Expectant		P-value
	N	Median (IQR)	N	Median (IQR)	
Serum hCG (IU/L)	60	1239 (676, 3382)	34	168 (82, 480)	**<0.001**
Serum progesterone (IU/L)	57	19.9 (11.4, 36.7)	34	12.6 (4.4, 44.1)	0.19
Outer mean diameter (OMD)	71	15.9 (10.9, 20.4)	34	12.5 (10.2, 14.7)	**0.02**
Outer largest diameter (LD)	71	17.5 (13.7, 23.9)	34	14.3 (10.8, 17.2)	**0.01**
Inner mean diameter (ID)	47	4.8 (3.5, 8.1)	15	3.7 (2.4, 4.8)	**0.02**
Inner largest diameter (ILD)	47	5.4 (4.0, 10.8)	15	3.7 (2.9, 6.2)	**0.01**
HS mean diameter (HMD)	24	24.2 (20.0, 35.8)	1	20.0 (-)	-
HS largest diameter (HLD)	24	34.9 (24.4, 45.8)	1	31.0 (-)	-

Table 3: Morphological types of ectopics in the surgical and conservative groups (N=105)

Morphological type of tubal ectopic	Surgical [N=71]	Conservative [N=34]
Solid swelling n (%) (95% CI)	24 (33.8) (22.8-44.8)	19 (55.9) (39.2-72.6)
Empty gestational sac n (%) (95% CI)	27 (38) (26.7-49.3)	15 (44.1) (27.4-60.8)
Gestational sac with yolk sac n (%) (95%CI)	8 (11.3) (3.9-18.6)	0
Embryo without cardiac activity n (%) (95%CI)	3 (4.2) (0.1-8.9)	0
Embryo with cardiac activity) n (%) (95%CI)	9 (12.7) (4.9-20.4)	0

Table 4. Comparison of different ultrasound measurements of the size of tubal ectopic with subjective assessment of ectopic size at surgery (N=71)

Variables	N	Correlation analysis		Regression analysis	
		Correlation	P-value	Ratio (95% CI)(*)	P-value
Mean outer/trophoblastic ring diameter	71	0.65	**<0.001**	1.26 (1.18, 1.34)	**<0.001**
Largest outer /trophoblastic ring diameter	71	0.65	**<0.001**	1.18 (1.12, 1.24)	**<0.001**
Mean coelomic cavity diameter	47	0.37	**0.01**	1.19 (1.07, 1.33)	**0.002**
Largest coelomic cavity diameter	47	0.32	**0.03**	1.13 (1.05, 1.23)	**0.002**
Mean haematosalpinx diameter	24	0.86	**<0.001**	1.18 (1.13, 1.23)	**<0.001**
Largest haematosalpinx diameter	24	0.90	**<0.001**	1.15 (1.11, 1.18)	**<0.001**

(*) Ratios given for a 5-unit increase in each parameter

Table 5: Association between ultrasound measurements and reported size of ectopic pregnancy at surgery in women with different morphological types of tubal ectopic pregnancy

Morphological type of tubal ectopic	N	Variable	Ratio (95% CI) (*)	P-value
Gestational sac with haematosalpinx	14	Mean trophoblastic ring diameter	0.99 (0.85, 1.15)	0.89
		Mean coelomic cavity diameter	0.92 (0.76, 1.12)	0.38
		Mean haematosalpinx diameter	1.22 (1.10, 1.35)	**0.001**
Solid swelling with haematosalpinx	24	Mean outer diameter	0.98 (0.89, 1.07)	0.62
		Mean haematosalpinx diameter	1.19 (1.12, 1.27)	**<0.001**
Gestational sac without haematosalpinx	47	Mean trophoblastic ring diameter	1.37 (1.21, 1.56)	**<0.001**
		Mean coelomic cavity diameter	0.87 (0.75, 1.02)	0.08

(*) Ratios given for a 5-unit increase in each parameter

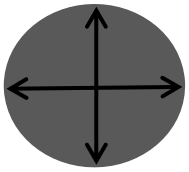
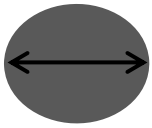
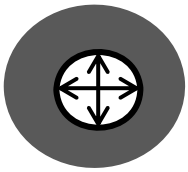
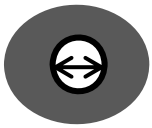
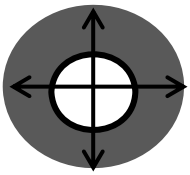
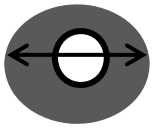
Table 6: Association between degree of haemoperitoneum on ultrasound and volume of haemoperitoneum at surgery

Degree of haemoperitoneum on ultrasound	N	Volume of haemoperitoneum at surgery (ml) Median (IQR)	P-value
Mild	23	100 (50, 200)	**<0.001**
Moderate / Severe	8	400 (300, 900)	

Table 7: Comparison of the trophoblast/coelomic cavity ratios (T/C) in different morphological types of tubal and intrauterine pregnancies

Type	Ectopic		IUP		P-value
	N	Median (IQR)	N	Median (IQR)	
GS, YS-, EM-	42	3.1 (2.3, 4.7)	126	1.5 (1.2, 1.7)	**<0.001**
GS, YS+, EM-	8	3.2 (2.4, 4.6)	24	1.3 (1.2, 1.4)	**<0.001**
GS, EM+, HR-	3	2.7 (2.5, 3.2)	9	1.2 (1.1, 1.2)	**0.01**
GS, EM+, HR+	9	1.8 (1.7, 2.3)	27	1.2 (1.1, 1.2)	**<0.001**
All combined	62	2.8 (2.3, 4.2)	186	1.3 (1.2, 1.6)	**<0.001**

GS – gestational sac, YS – yolk sac, EM – embryo, HR – heart rate

Morhological type of tubal ectopic	Transverse plane (mm)	Longitudinal plane (mm)
<u>Solid swelling</u> Outer diameter (outside to outside)		
<u>With gestational sac</u> Coelomic cavity (inside to inside)		
Trophoblastic ring (outside to outside)		
<u>Haematosalpinx</u> Haematosalpinx diameter (inside to inside)