RISK PREDICTION OF MAJOR HAEMORRHAGE WITH SURGICAL TREATMENT OF LIVE CESAREAN SCAR PREGNANCIES

Authors Lucrezia V DE BRAUD, MD[1], Jure KNEZ PhD[2], Dimitrios MAVRELOS, MD[1], Nikolaos THANATSIS PhD[1], Eric JAUNIAUX, PhD[1], Davor JURKOVIC, PhD[1]

London, United Kingdom

[1] Institute for Women's Health, Faculty of Population Health Sciences, University College London, London.

[2]Clinic for Gynecology, University Medical Centre Maribor, Maribor, Slovenia.

Corresponding author: Professor Davor Jurkovic, Institute for Women's Health, 250 Euston Road, London, NW1 6BU, United Kingdom. Email address: d.jurkovic@ucl.ac.uk.

HIGHLIGHTS

- Surgery for cesarean scar pregnancies can be complicated by heavy bleeding
- Risk of heavy bleeding is low ≤8weeks' gestation
- Gestational age ≥9weeks' and placental lacunae are associated with major blood loss
- Advanced scar pregnancies should be treated surgically in specialized centers

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Abstract

Objective

To evaluate the association between demographic and ultrasound variables and major intra-operative blood loss during surgical transcervical evacuation of a live caesarean scar pregnancies.

Methods

This was a retrospective cohort study conducted in a tertiary referral center between 2008 and 2019. We included all women diagnosed with a live caesarean scar ectopic pregnancy who chose to have surgical management in the study center. A preoperative ultrasound was performed in each patient. All women underwent transcervical suction curettage under ultrasound guidance. Our primary outcome was the rate of postoperative blood transfusion. The secondary outcomes were estimated intra-operative blood loss (ml), rate of retained products of conception, need for repeat surgery, need for uterine artery embolization and hysterectomy rate. Descriptive statistics were used to describe the variables. Univariate and multivariable logistic regression models were constructed using the relevant covariates to identify the significant predictors for severe blood loss.

Results

During the study period, 80 women were diagnosed with a live caesarean scar pregnancy, of whom 62 (78%) opted for surgical management at our center. The median crown-rump length was 9.3mm (range 1.4-85.7). Median blood loss at the time of surgery was 100ml (range, 10-2300), and six women (10%; 95%CI 3.6-20) required blood transfusion. Crown-rump length and presence of

placental lacunae were significant predictive factors for the need for blood transfusion and blood loss >500ml at univariate analysis ($p<.01$); on multivariate analysis, only crown-rump length was a significant predictor for need for blood transfusion (OR =1.072; 95% CI 1.02 -1.11). Blood transfusion was required in 6/18 (33%) cases with the crown-rump length ≥23 mm (≥9^{+0} weeks of gestation), but in none of 44 women presenting with a crown-rump length <23mm ($p<.01$).

Conclusion

The risk of severe intraoperative bleeding and need for blood transfusion during or after surgical evacuation of live caesarean scar pregnancies increases with gestational age and is higher in the presence of placental lacunae. One third of women presenting at ≥ 9 weeks of gestation required blood transfusion and their treatment should be ideally arranged in specialized tertiary centers.

Key Words: cesarean scar pregnancy; ectopic pregnancy; suction curettage; blood transfusion; reproductive outcomes; ultrasound imaging.

1. Introduction

Caesarean scar is a relatively rare type of ectopic pregnancy which affects between 1/1800 to 2/2200 pregnancies.[1-3] It occurs when a pregnancy implants within an incompletely healed scar of a previous caesarean section. The number of diagnosed cases can be attributed to better awareness of the condition and easier access to high frequency transvaginal ultrasound which facilitates their earlier and more accurate detection. The incidence of caesarean scar pregnancies has also increased in the last two decades, due to the rising rates of caesarean section deliveries worldwide.[4] More than half of all caesarean scar pregnancies miscarry spontaneously in the first trimester, but they often require surgical management to control bleeding and facilitate recovery.[5] Live caesarean scar pregnancies can be a precursor for placenta accreta spectrum, and caesarean scar pregnancies which progress to the second and third trimester are at high risk of the complications of accreta placentation i.e. massive obstetric haemorrhage and emergency hysterectomy.[6-8] Patients with evolving caesarean scar pregnancies are informed about these risks and often opt for termination of pregnancy.[3, 5, 9-12]

For surgically managed caesarean scar pregnancies, there is general consensus that the risk of complications and emergency hysterectomy increases with advancing gestation. However, the threshold of gestational age beyond which the risk of major blood loss and hysterectomy becomes significant is unknown. The objective of this study was to evaluate the association between demographic and ultrasound variables and the risk of major blood loss during surgical evacuation of live caesarean scar pregnancies and help clinicians when counselling women about surgical and other treatment options.

2. Materials and Methods

We conducted a retrospective cohort study of consecutive pregnant women diagnosed with a live caesarean scar pregnancy undergoing surgical management at University College Hospital of London (UCLH) between January 2008 and October 2019. Patient's demographic data, previous obstetric, gynaecological and medical history, clinical and ultrasound data and images were recorded and stored in a specialized database (Viewpoint Version 5, Bildverargeritung GmbH, Munich, Germany).

All women attending the early pregnancy unit at UCLH with suspected early pregnancy complications have an ultrasound examination to ascertain the viability and location of pregnancy. The scans are carried out transvaginally and/or transabdominally using high resolution ultrasound equipment (Voluson E8, GE Medical Systems, Milwaukee, WI, USA).

Viability of the pregnancy was confirmed by the visualization of the embryonic or fetal pole with evidence of cardiac activity. Gestational age was calculated by measuring the crown-rump length (CRL).[16] Implantation of pregnancy within the previous caesarean section scar was diagnosed according to the previously published criteria[17].

Colour Doppler imaging (CDI) with a default pulse repetition frequency of 0.9 kHz, gain of 0.8 and low wall motion filter (40 Hz) was used to assess the vascularity around and within the gestational sac. A semi-quantitative colour score method with a scale from 1 to 4 was used to describe pregnancy blood supply as previously reported.[18] In brief, a score of 1 was given when there was no detectable blood flow, 2 for minimal blood flow, 3 for moderate blood flow and 4 for high vascularity. The presence of placental lacunae, defined as multiple irregular vascular spaces within the placental parenchyma was also recorded.[19]

All women received extensive counselling regarding the prognosis and potential risks of continuing with the pregnancy. The advice was based on the evolving medical evidence available at the time.[1, 5, 6] Asymptomatic women and those with mild symptoms were offered a choice between conservative and surgical management. Women presenting with moderate or severe bleeding were offered immediate surgical treatment. Medical treatment with methotrexate as a first line choice or adjuvant treatment prior to surgery was not used during the study period. Only women with live caesarean scar pregnancy who underwent surgical treatment in our unit were included into the final study group.

All surgical procedures were performed transcervically, using suction curettage under transabdominal or transrectal ultrasound guidance. A Shirodkar cervical suture was inserted selectively to secure haemostasis following evacuation of pregnancy as previously described.[20] All women who had Shirodkar cervical suture inserted during the surgical procedure were reviewed in the outpatient clinic 2-3 days after their operation for ultrasound examination and suture removal under local anaesthesia.

All material aspirated from the uterus was collected in a graduated volume suction bottle and total blood loss was measured adding the volume in the bottle to weighing surgical swabs. In addition, the surgeon assessed the amount of blood collected on surgical drapes. At the surgical procedure, the principal surgeon and theatre staff compared their blood volume loss estimates and the higher estimate was recorded as the intraoperative blood loss.

All patients were managed according to our centre's protocol. Ethical committee approval (NHS Health Research Authority 18/WM/0328) was obtained prior to the start of this study.

The primary outcome was the rate of blood transfusion following surgical evacuation of caesarean scar pregnancy. The secondary outcomes were the total blood loos during surgery, length of hospitalization, rate of retained products of conception, need for re-intervention, need for uterine artery embolization and hysterectomy rate.

2.1 Statistical analysis

SPSS version 26.0 (SPSS Inc., Chicago, IL, USA) data analysis and statistical software package was used to analyse the data. A standard Kurtosis analysis indicated that some values were not normally distributed and the data are therefore presented as median and range. Proportions were indicated as percentages. Spearman's non-parametric coefficient was calculated to assess the correlation between continuous variables. Univariate logistic regression was performed using need for blood transfusion and severe blood loss as the dependent variables. Age, parity, gestational age, gestational sac diameter, crown-rump length, vascularity score and the presence of placental lacunae were considered as independent variables. A multivariable logistic regression model using the relevant covariates was constructed. A P value <0.05 was considered significant.

3. Results

A total of 238 caesarean scar pregnancies were diagnosed in the 12-year period, 80 (34%) of whom contained a live embryo. The study group included 55/80 (69%) women referred to our unit from other hospitals and 25/80 (31%) first diagnosed in our centre.

After receiving counselling about management options, 11 (14%) out of 80 women opted to continue with the pregnancy, two women (3%) opted for surgical treatment

in their local hospitals and three women (4%) were lost to follow up. The remaining 63 (79%) patients underwent surgical termination of pregnancy at our centre. One patient was excluded because of incomplete records, leaving 62 cases for the final analysis (Fig. 1).

Patients baseline characteristics are summarized in Table 1. Out of 62 women included in the study, 2 (3%) had a recurrent caesarean scar pregnancy. The median CRL was 9.3 mm (range 1.4-85.7) and the median gestational sac diameter was 23.2 mm (range 6.3-82.7). The median gestational age based on CRL was 48 days (range 37-102) or 6^{+6} weeks (range 5^{+4} weeks and 14^{+4} weeks). A simple suction curettage without additional haemostatic measures was performed in 32 (52%) cases and the remaining 30 (48%) cases required a Shirodkar cervical suture to control the bleeding. The suture was successful in achieving haemostasis in 29 out of 30 (97%, 95% CI 82.8 – 99.9) cases. One patient with an advanced caesarean scar pregnancy required an emergency uterine artery embolization to achieve haemostasis. There were no cases of uterine perforation and no emergency hysterectomy was required. In 52 cases, the procedure was performed as day surgery, while 10/62 (16%) women were admitted overnight for monitoring. For these patients, median admission time was 3 days (range 1-4).

The median blood loss at the time of surgical procedure was 100 ml (range 10-2300), and nine (15%, 95%CI 6.9-25.8) patients had a blood loss >500ml (Fig. 2). The median amount of intra-operative blood loss increased with higher vascularity of the pregnancy (Table 2). Placental lacunae (Fig. 3 and Fig. 4) were recorded in 13 cases. In 12 (92%) of these cases, the presence of placental lacunae was associated with increased blood flow and vascularity score of 3 or 4 (Fig. 5).

Six out of 62 patients (10%; 95%CI 4-20) of the final study group required blood transfusion (Fig. 6). The univariate analysis indicated that CRL was a significant predictor for the need for blood transfusion (OR =1.07; 95% CI 1.02 -1.11). None of the 44 women with CRL <23 mm required a blood transfusion. In women presenting with CRL ≥23mm (9^{+0} weeks of gestation) the transfusion rate was 6/18 (33%). In the subgroup of women with CRL ≥40mm (11^{+0} weeks) transfusion rate was 4/9 (44%). The presence of placental lacunae and CDI score ≥3 were also significant predictive factors for the need for blood transfusion and blood loss >500mls in a univariate analysis (Table 3 and Table 4).

We constructed a multivariable logistic regression model for predicting blood loss >500 mL which retained CRL (aOR 1.07; 95% CI 1.01 – 1.13) and placental lacunae (aOR 35.0; 95% CI 2.71 – 451.7) as significant variables. In predicting the need for blood transfusion, only CRL was an independent significant predictor with an aOR of 1.06; 95% CI 1.01-1.11) whilst the presence of placental lacunae was not significant (aOR 9.39; 95% CI 0.78 – 113.2).

Forty-two (68%) patients attended for post-operative follow-up scans, which showed retained products of conception (RPOC) in nine (15%, 95%CI 7-26) cases. Second procedure to remove RPOC was carried out in six out of 62 (10%, 95%CI 4-20) cases. In two of these cases the blood loss was 1000 mL and one of these patients required a repeated blood transfusion. One patient developed a broad ligament hematoma after the second evacuation, which was managed expectantly. All 30 patients who were given Shirodkar cervical sutures had their sutures successfully removed in the clinic without the need for re-admission and general anaesthesia.

Discussion

Our data add to prior studies suggesting an association between advanced gestational age and complication rate in women presenting with caesarean scar pregnancy.[21] We found a strong positive association between the gestational age as expressed by fetal CRL and the risk of severe intraoperative bleeding requiring blood transfusion. In addition, the vascularity of gestational sac as expressed by the CDI score and the presence of placental lacunae were also associated with the increased risk of blood transfusion on the univariate analysis.

Using our previously described suction curettage under ultrasound guidance technique for patients opting for pregnancy termination,[20] we found that additional haemostatic measures were required in less than half of all cases of live caesarean scar pregnancies and no patient required emergency hysterectomy to control the bleeding.

Our data also show that none of 40 patients with live caesarean scar pregnancy managed before completed eight weeks of gestation (CRL ≤15mm) had recorded blood loss >500 ml. These findings suggest that early live caesarean scar pregnancy could be treated by general obstetricians gynaecologists without particular expertise in managing complex early pregnancy complications. As live caesarean scar pregnancy develops, trophoblastic cells reach the deep uterine blood supply of the radial and arcuate arteries [22,23] resulting in a higher blood loss when the placental bed is disrupted during the surgical procedure.

Surgical management of caesarean scar pregnancy appears to be associated with a high success rate, low complication rate and short post-treatment follow up.[5] Two main surgical management options have been proposed with or without adjunctive therapies i.e. transcervical suction aspiration and surgical excision via multiple routes.[24]

We have previously shown that simple suction curettage under ultrasound guidance is efficient and safe in over 50% of women presenting with a live or non-viable caesarean scar pregnancy at ≤14 weeks of gestation.[20] In the present study, which included only live caesarean scar pregnancies, we found a similar efficacy of Shirodkar suture to secure haemostasis by tamponade in cases at high risk of intraoperative bleeding. Transcervical suction curettage with selective insertion of Shirodkar suture is a relatively simple treatment, easier to learn and considerably less expensive than hysteroscopic resection or laparoscopic excision of caesarean scar pregnancy.[24] Another minimally invasive treatment option is the placement of a cervical ripening double-balloon catheter which can be used both to terminate the pregnancy and achieve hemostasis.[25] However, this method can only be used in very early pregnancies up to eight weeks of gestation.

The rate of retained products of conception in the present study was higher than the rates reported following surgical treatment of miscarriage,[26] but this is not unexpected as caesarean scar pregnancy often implants deep into the uterine wall and sometimes invading into the broad ligament. In addition, in some cases complicated by major blood losses, the procedure had to be stopped to secure haemostasis before the pregnancy could be completely evacuated. Furthermore, all women who had Shirodkar suture inserted had routine detailed post-operative follow-up scans which could have contributed to the higher rate of diagnosed RPOC.

The main strength of our study compared to other contemporary published studies is to have included only patients with live caesarean scar pregnancy. Previous studies have included both live and caesarean scar pregnancy with no embryonic/fetal heart activity. As the majority of the patients in the latter subgroup are likely to miscarry without any further intervention,[8] their inclusion in a management cohort does not

allow the accurate evaluation of outcomes of a particular strategy. Our study provides also data on a gestational cut-off after which the risk of intraoperative complications increases significantly. As most caesarean scar pregnancies are diagnosed around 7 weeks of gestation,[8, 20] this gives the patients a few days to consider different management options.

The primary limitations of our cohort study lie in its retrospective nature and that the number of advanced pregnancies (≥12 weeks' gestation) was relatively small, therefore our findings in this subgroup of women should be interpreted with caution. This could explain why data on the vascularity of the gestational sac and the presence of placental lacunae which both increase with advancing gestational age showed a significant association with surgical outcomes in the univariate analysis ($p<.01$) but not in the multivariate analysis. All the procedures in our study were performed by surgeons experienced in carrying out second trimester surgical terminations of pregnancy and in diagnosing and managing caesarean scar pregnancies. This could influence the low rate of major complications in our cohort and our findings may not be replicated in those with less experience in performing ultrasound-guided intrauterine procedures.

Conclusions

The risk of major bleeding during evacuation of live caesarean scar pregnancies increases with advancing gestation and higher vascularity around the gestational sac is associated with the amount of blood loss during surgical management. Ultrasound-guided suction curettage is a successful treatment option for women with live caesarean scar pregnancy <15 weeks' gestation who wish to preserve their fertility. Early diagnosis of caesarean scar pregnancy is important as the surgical treatment

before completed nine weeks' gestation is simple and safe. These patients could probably be safely treated locally by teams without particular expertise in managing complex early pregnancy complications. By contrast, women with more advanced pregnancies, particularly those presenting at ≥11 weeks of gestation, are at significant risk of suffering major bleeding and they should be referred for treatment to regional expert centres.

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None declared.

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Details of ethics approval:

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Table 1. Patients' baseline characteristics and presenting symptoms (n=62)

Patients' characteristics	**N=62**
Age (median, range)	35 (26-42)
Gravidity (median, range)	4 (2-14)
Parity (median, range)	2 (1-6)
Number of previous Caesarean deliveries (median, range)	2 (1-5)
Presenting symptoms	
Vaginal bleeding (n, %)	14 (23%)
Abdominal pain (n, %)	8 (12%)
Vaginal bleeding and pain (n, %)	24 (39%)
Asymptomatic (n, %)	16 (26%)

Table 2. Colour Doppler score and intraoperative blood loss during surgical evacuation of caesarean scar pregnancy (n=62)

Colour Doppler Score	**n (%)**	***Estimated blood loss (mL)***
1	0 (0)	-
2	36 (58,0)	100 (10 - 600)
3	19 (31,6)	300 (10 -1500)
4	7 (11,6)	1300 (50 – 2300)

Data are expressed as median (range).

Table 3. Results of univariate analysis showing association between several demographic and ultrasound variables and the need for blood transfusion (n=62)

Variable	**OR**	***p***
Maternal age	0.99 (0.81 – 1.21)	*0.905*
Parity	0.83 (0.40 – 1.72)	*0.624*
CRL*	1.07 (1.03 – 1.12)	*0.001*
Gestational sac diameter	1.15 (1.04 – 1.27)	*0.005*
Colour Doppler score	5.27 (1.49 – 18.66)	*0.01*
Placental Lacunae	26.1 (2.72-250.8)	*0.005*

*CRL: Crown-rump length.

Table 4. Results of univariate analysis showing association between various demographic and ultrasound variables and intraoperative blood loss >500ml (n=62)

Variable	**OR**	***p***
Maternal age	0.98 (0.82 – 1.16)	*0.779*
Parity	0.63 (0.32 – 1.25)	*0.188*
CRL*	1.08 (1.03 – 1.13)	*0.001*
Gestational sac diameter	1.17 (1.06 – 1.29)	*0.001*
Colour Doppler score	4.76 (1.63 – 13.87)	*0.004*
Placental Lacunae	62.7 (6.63 – 592.1)	*0.001*

*CRL: Crown-rump length.