Ultrasound Obstet Gynecol 2017; **50:** 578–583
Published online 9 October 2017 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.17401

Risk of Cesarean scar defect following single- *vs* double-layer uterine closure: systematic review and meta-analysis of randomized controlled trials

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KEYWORDS: isthmocele; minimally invasive therapy; niche; scar defects; scar pregnancy; ultrasound

ABSTRACT

Objective *There is a growing body of evidence that suggests that the surgical technique for uterine closure following Cesarean delivery influences the healing of the Cesarean scar, but there is still no consensus on the optimal technique. The aim of this systematic review and meta-analysis was to compare the effect of single-* vs *double-layer uterine closure on the risk of uterine scar defect.*

Methods *MEDLINE, Scopus, ClinicalTrials.gov, PROSPERO, EMBASE and the Cochrane Central Register of Controlled Trials were searched from inception of each database until May 2016. All randomized controlled trials (RCTs) evaluating the effect of single-* vs *double-layer uterine closure following low transverse Cesarean section on the risk of uterine scar defect were included. The primary outcome was the incidence of uterine scar defects detected on ultrasound. Secondary outcomes were residual myometrial thickness evaluated by ultrasound and the incidence of uterine dehiscence and/or rupture in subsequent pregnancy. Summary measures were reported as relative risk (RR) or mean difference (MD), with 95% CIs. Quality of the evidence was assessed using the GRADE approach.*

Results *Nine RCTs (3969 participants) were included in the meta-analysis. The overall risk of bias of the included trials was low. Statistical heterogeneity within the studies was low, with no inconsistency in the primary and secondary outcomes. Women who received single-layer uterine closure had a similar incidence of uterine scar defects as did women who received double-layer closure (25%* vs *43%; RR, 0.77 (95% CI, 0.36–1.64); five trials; 350 participants; low quality of evidence). Compared with double-layer uterine closure, women who received single-layer closure had a significantly thinner residual myometrium on ultrasound (MD, −2.19 mm (95% CI, −2.80 to −1.57 mm); four trials; 374 participants; low quality of evidence). No difference was found in the incidence of uterine dehiscence (0.4%* vs *0.2%; RR, 1.34 (95% CI, 0.24–4.82); three trials; 3421 participants; low quality of evidence) or uterine rupture (0.1%* vs *0.1%; RR, 0.52 (95% CI, 0.05–5.53); one trial; 3234 participants; low quality of evidence) in a subsequent pregnancy.*

Conclusions *Single- and double-layer closure of the uterine incision following Cesarean delivery are associated with a similar incidence of Cesarean scar defects, as well as uterine dehiscence and rupture in a subsequent pregnancy. However, the quality level of summary estimates, as assessed by GRADE, was low, indicating that the true effect may be, or is even likely to be, substantially different from the estimate of the effect.* Copyright © 2017 ISUOG. *Published by John Wiley & Sons Ltd.*

INTRODUCTION

Cesarean delivery (CD) rates are rising globally[1]; in the USA, about 30% of women delivered by CD in 2015[1]. This increasing CD rate has stimulated an interest in the potential short- and long-term morbidity of Cesarean scars. In more than 50% of women with a history of CD, a uterine scar defect, also called a 'niche', defined as disruption of the myometrium in the uterine

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Accepted: 1 January 2017

scar of the Cesarean section, can be observed when examined by gel instillation sonohysterography 6–12 months after the CD[2]. Uterine scar defects detected on ultrasound several weeks or months after CD have been associated with prolonged menstrual bleeding and postmenstrual spotting[2,3], as well as an increased risk for several obstetric complications in subsequent pregnancies, including uterine dehiscence and/or rupture, scar pregnancy and placenta previa and accreta[4]. A screening method for assessing the risk of uterine scar rupture in women with a prior CD is ultrasonographic measurement of the thickness of the lower uterine segment, as pioneered by Rozenberg *et al.*[5] in 1996. A meta-analysis by Kok *et al.*[6] supports the use of measurement of residual myometrial thickness (RMT) for predicting uterine rupture during trial of labor in women with prior Cesarean section. Uterine scar defects have also been associated with lower RMT[3,5,6].

A growing body of evidence suggests that the surgical technique used for uterine closure following CD influences uterine scar healing and RMT, but there is still no consensus about the optimal method[7,8], although it is imperative to have evidence-based guidelines for each surgical step before recommending one technique over another[9,10].

The main aim of this systematic review with a meta-analysis of randomized controlled trials (RCTs) was to compare the effect of single- *vs* double-layer uterine closure following CD on the risk of uterine scar defects detected by ultrasound. The secondary aim was to compare the effect of the two techniques on RMT and the incidence of uterine dehiscence and rupture in a subsequent delivery.

METHODS

Search strategy

The review protocol was established by two investigators (G.S., A.D.S.) prior to commencement and was registered with the PROSPERO International Prospective Register of Systematic Reviews (registration no. CRD42016046639).

Relevant RCTs were identified by two authors (A.D.S, G.S.) by searching independently the electronic databases MEDLINE, Scopus, ClinicalTrials.gov, PROSPERO, EMBASE and the Cochrane Central Register of Controlled Trials, from inception of each database until May 2016, using a combination of the following text words: 'scar pregnancy', 'scar defect', 'niche', 'minimally invasive', 'hysteroscopy', 'resection', 'bleeding', 'Cesarean', 'Caesarean', 'delivery', 'placenta', 'accreta', 'isthmocele', 'pouch', 'dehiscence', 'closure', 'layer', 'trial', 'randomized', 'randomised', 'diverticula' and 'uterus'. Agreement regarding potential relevance was reached by discussion.

Study selection

All RCTs evaluating the effect of single- *vs* double-layer uterine closure at the time of low transverse Cesarean section on the risk of uterine scar defect evaluated on ultrasound or hysterography were included. Trials not reporting outcomes of interest were excluded. Quasi-randomized trials (i.e. trials in which allocation was done on the basis of a pseudorandom sequence, such as odd/even hospital number or alternation of date of birth) were also excluded.

Data extraction and assessment of risk of bias

The risk of bias in each included study was assessed by using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions[11]. Seven domains relating to risk of bias were assessed in each included trial, since there is evidence that these issues are associated with biased estimates of treatment effect: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; and (7) other bias. Review authors' judgments were categorized as 'low risk', 'high risk' or 'unclear risk' of bias[11].

Two authors (A.D.S., G.S.) independently assessed inclusion criteria, risk of bias and data extraction. Disagreements were resolved by consensus arrived at through discussion. Data from each eligible study were extracted without modification of original data onto custom-made data collection forms. Differences were assessed and further resolved by common review of the entire process.

Primary and secondary outcomes were defined before data extraction. The primary outcome was the incidence of postpartum uterine scar defects. Secondary outcomes were postpartum RMT, evaluated by ultrasound, and incidence of uterine dehiscence and/or rupture in a subsequent pregnancy.

Uterine scar defect was defined as myometrial loss or deformity at the Cesarean scar site (or equivalent definition). RMT was defined as the distance from the delineation of the endometrium to the serosal surface at the level of the Cesarean scar, and total myometrial thickness was measured at the myometrium adjacent to the scar. Uterine dehiscence was defined as partial opening of the uterine scar with intact visceral peritoneum (or equivalent definition). Uterine rupture was defined as complete separation of the uterine scar with visceral peritoneum disruption or bladder rupture, necessitating an emergency intervention (or equivalent definition). A subgroup analysis looking at uterine dehiscence and/or rupture was performed only for women with subsequent trial of labor after Cesarean (TOLAC).

For this review, the quality of the evidence was assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach in order to assess the quality of the body of evidence relating to the primary and secondary outcomes. GRADEpro Guideline Development Tool was used to import data from Review Manager 5.3 (The Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark) in order to create 'summary-of-findings' tables. A summary of the

intervention effect and a measure of quality for each of the above outcomes was produced using the GRADE approach. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessment for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias[11].

Data analysis

The data analysis was completed independently by two authors (G.S., A.D.S.) using Review Manager 5.3[11]. The completed analyses were then compared and any difference was resolved by review of the entire dataset and independent analysis.

Meta-analysis was performed using the random effects model of DerSimonian and Laird[11] to produce summary treatment effects reported as relative risk (RR) or mean difference (MD), with 95% CIs. Heterogeneity was measured using the I^2 statistic. Potential publication bias was assessed statistically using Begg's and Egger's tests, and $P < 0.05$ was considered to be statistically significant.

The meta-analysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement[12].

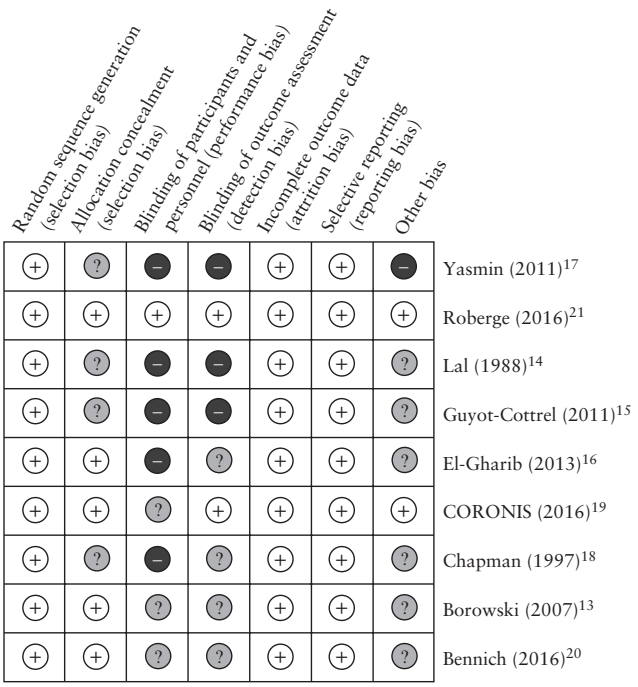

Figure 2 Risk of bias according to Cochrane Handbook[11] in randomized controlled trials included in meta-analysis. Only first author is given for each study. Risk of bias: ⊕ low; ?, unclear; ⊖, high.

RESULTS

Study selection and study characteristics

The flow of information through the different phases of the review is shown in Figure 1. Nine RCTs (3969 participants) were included in the meta-analysis[13–21].

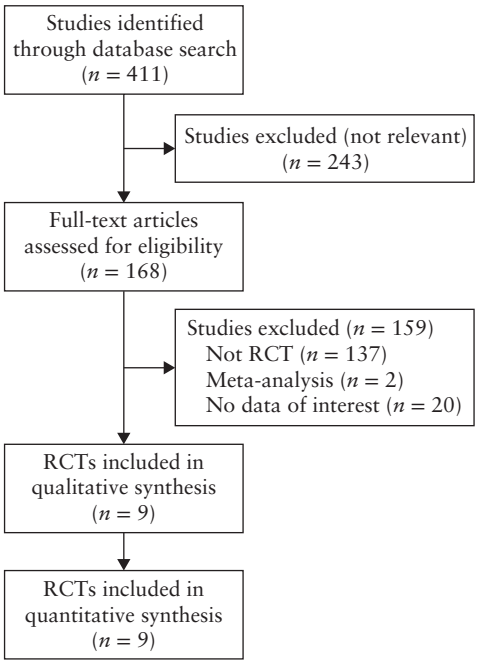

Figure 1 Flowchart summarizing inclusion of randomized controlled trials (RCTs) in systematic review.

The overall risk of bias of the included trials was low (Figure 2). All studies had a low risk of bias in random sequence generation, incomplete outcome data and selective reporting. Adequate methods for the allocation of women were used in all studies. Publication bias, assessed using Begg's and Egger's tests, was not significant ($P = 0.48$ and $P = 0.51$, respectively).

The characteristics of the included studies are shown in Table 1. All studies randomized women who underwent low transverse uterine incision during Cesarean section[13–21]. Four studies explicitly included only singleton pregnancies[13,16,17,21]. Five studies reported on the risk of uterine scar defect[13–15,20,21] and four on RMT[16,17,20,21]. Three trials reported follow-up at subsequent pregnancy and the risk of uterine dehiscence and/or uterine rupture[17–19]. Of the 3469 women included in these three trials[17–19], 756 (21.8%) underwent TOLAC and 2713 (78.2%) planned repeat CD (Table 1).

Cesarean-scar evaluation was performed by transvaginal ultrasound in four RCTs[13,15,20,21], by transabdominal ultrasound in two[16,17] and by hysterography at 3 months post CD in one[14]. Regarding single-layer uterine closure, in five trials the whole thickness of the uterine wall, including the decidual layer, was closed in a cranial/caudal position[16–18,20,21], while in the studies of Lal and Tsomo[14] and Guyot-Cottrel[15] the decidua was excluded.

Synthesis of results

Table 2 shows the pooled results for the primary and secondary outcomes. Statistical heterogeneity within the

Table 1 Characteristics of randomized controlled trials included in this systematic review and meta-analysis, comparing effect of single- *vs* double-layer uterine closure of Cesarean delivery (CD) incision on risk of CD scar defect

Study	Country	Sample size (n)	Inclusion criteria	Type of uterine closure: Single-layer	Type of uterine closure: Double-layer	Outcome	CD scar evaluation method	TOLAC in next pregnancy (n (%))
Lal (1988)[14]	India	100	Primary or secondary CD	Interrupted excluding decidua	Continuous unlocked	CD scar defect	Hysterography 3 months post CD	NR
Chapman (1997)[18]	USA	145	Primary or secondary CD	Continuous locked including decidua	Continuous locked	Uterine dehiscence in next pregnancy	NR	145 (100)
Borowski (2007)[13]	USA	46	Planned primary CD in singletons	NR	NR	CD scar defect	TVS 6 weeks post CD	NR
Guyot-Cottrel (2011)[15]	France	70	Primary or secondary CD	Continuous unlocked excluding decidua	Continuous unlocked	CD scar defect	TVS 6 weeks post CD	NR
Yasmin (2011)[17]	Pakistan	90	Secondary CD in singletons	Continuous locked including decidua	Continuous locked or unlocked	RMT, uterine dehiscence in next pregnancy	TAS 6 weeks post CD	0 (0)
El-Gharib (2013)[16]	Egypt	150	Primary CD in singletons	Continuous locked including decidua	Continuous locked	RMT	TAS 2 weeks post CD	NR
CORONIS (2016)[19]	Multicenter*	3234	Primary or secondary CD	Any method	Any method	Uterine dehiscence or rupture in next pregnancy	NR	611 (18.9)
Bennich (2016)[20]	Denmark	61	Planned primary CD	Continuous unlocked including decidua	Continuous unlocked	RMT, CD scar defect	TVS 5 months post CD	NR
Roberge (2016)[21]	Canada	73	Planned primary CD in singletons	Continuous locked including decidua	Continuous locked or unlocked	RMT, CD scar defect	TVS 6 months post CD	NR

Only first author is given for each study. *Argentina, Chile, Ghana, India, Kenya, Pakistan and Sudan. NR, not reported; RMT, residual myometrial thickness; TAS, transabdominal ultrasound; TOLAC, trial of labor after Cesarean; TVS, transvaginal ultrasound.

studies was low, with no inconsistency in the primary and secondary outcomes. Women who received single-layer uterine closure had a similar incidence of uterine scar defects as did women who received double-layer closure (25% *vs* 43%; RR, 0.77 (95% CI, 0.36–1.64); five trials; 350 participants; low quality of evidence). Compared with double-layer uterine closure, women who received single-layer closure had significantly thinner RMT on ultrasound (MD, −2.19 mm (95% CI, −2.80 to −1.57 mm); four trials; 374 participants; low quality of evidence) (Figure 3).

No difference was found in the incidence of uterine dehiscence (0.4% *vs* 0.2%; RR, 1.34 (95% CI, 0.24–4.82); three trials; 3421 participants; low quality of evidence) or uterine rupture (0.1% *vs* 0.1%; RR, 0.52 (95% CI, 0.05–5.53); one trial; 3234 participants; low quality of evidence) in a subsequent pregnancy. Subgroup analysis of women who underwent TOLAC was not feasible, given the lack of stratified data in the original trials.

The quality of evidence was downgraded because of serious imprecision. Outcomes were imprecise because studies included relatively few patients and few events, and thus had wide CIs around the estimate of the effect, and because the optimal information size was not reached. The quality of the evidence was also downgraded another level because of serious indirectness owing to the different interventions used.

DISCUSSION

Main findings

This meta-analysis of nine RCTs, including 3969 women, showed that single-layer closure and double-layer closure of a CD incision are associated with a similar incidence of Cesarean scar defects, as well as uterine dehiscence and/or uterine rupture in a subsequent pregnancy. Compared with single-layer closure, double-layer closure was associated with a significantly greater RMT evaluated on ultrasound, which is of unclear clinical significance. The quality level of summary estimates was low as assessed by GRADE, indicating that the true effect may be, or is even likely to be, substantially different from the estimate of the effect.

Comparison with existing literature

Our data support earlier findings of a prior systematic review of RCTs[7]. Roberge *et al.*[7] found no statistically significant difference in CD scar defect and uterine dehiscence, and also found that single-layer uterine closure was associated with significantly lower RMT. However, the authors did not include in their systematic review all currently available studies, such as the CORONIS trial[19] and the trials by Bennich *et al.*[20] and Roberge *et al.*[21], and the quality of evidence was not assessed[7]. In a large cohort study including more than 7600 women with prior CD, Hesselman *et al.*[22] observed a similar rate of uterine rupture after single-layer closure of the CD incision

Table 2 Primary and secondary outcomes in randomized controlled trials comparing effect of single- *vs* double-layer uterine closure of Cesarean delivery (CD) incision on risk of CD scar defect, residual myometrial thickness (RMT) and uterine dehiscence or rupture in subsequent pregnancy

Outcome	*Trials (n[refs])*	*Participants (n)*	*Single-layer closure**	*Double-layer closure**	*RR or MD (95% CI)*	I^2 *(%)*	*Quality of evidence*
Scar defect found at US	5[13–15,20,21]	350	41/164 (25.0)	80/186 (43.0)	0.77 (0.36 to 1.64)	10	Low
RMT at US (mm)	4[16,17,20,21]	374	13.5	15.4	−2.19 (−2.80 to −1.57)†	19	Low
Uterine dehiscence in next pregnancy	3[17–19]	3421	7/1693 (0.4)	3/1728 (0.2)	1.34 (0.24 to 4.82)	30	Low
Uterine rupture in next pregnancy	1[19]	3234	1/1610 (0.1)	2/1624 (0.1)	0.52 (0.05 to 5.53)	—	Low
Uterine dehiscence or rupture in next pregnancy	3[17–19]	3421	8/1693 (0.5)	5/1728 (0.3)	1.43 (0.54 to 3.79)	30	Low

*Values given as *n*/*N* (%) or mean. †Statistically significant. MD, mean difference; RR, relative risk; US, ultrasound scan.

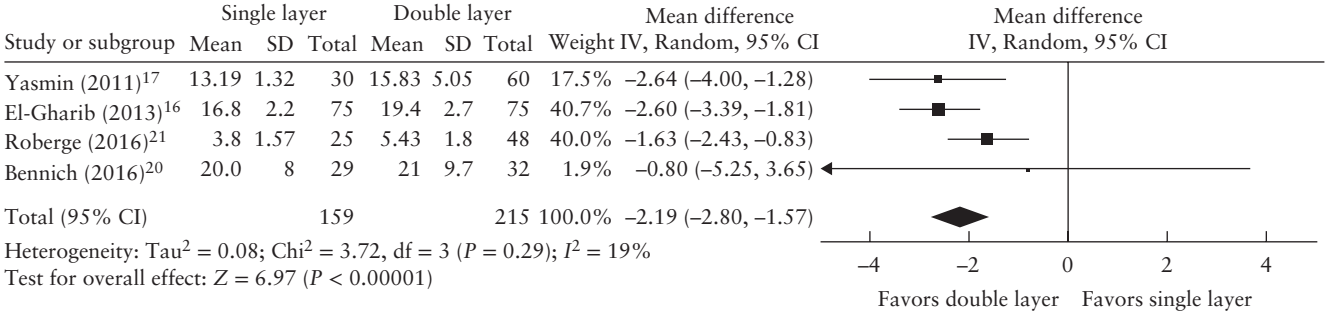

Figure 3 Forest plot of mean difference in residual myometrial thickness (in mm) after single- *vs* double-layer uterine closure of Cesarean delivery incision. Only first author is given for each study.

compared with double-layer closure (adjusted RR, 1.13 (95% CI, 0.75–1.70)). This finding is in agreement with our pooled data.

Strengths and limitations of the study

One of the strengths of our study is the inclusion of only RCTs. Our meta-analysis included all studies published to date on the topic. The studies were of high quality, with a low risk of bias according to the Cochrane risk-of-bias tools, and of low statistical heterogeneity. In addition, publication bias was not apparent by statistical analysis. Intention-to-treat analysis was used and both random- and mixed-effects models were used when appropriate. These are key elements in evaluating the reliability of a meta-analysis[11].

Limitations of our study are inherent to the limitations of the included RCTs. The majority of women included in the analysis came from one large trial[19], which therefore drives the summary statistics. Several trials, including the largest one, included women with more than one CD, which could have influenced the results, while some trials had a number of participants lost to follow-up. The quality of evidence was judged as moderate to low, as a low number of studies and women were included for each outcome. Our data were underpowered to detect modest differences in rare but serious events (i.e. incidence of uterine dehiscence and uterine rupture), which may be considered more clinically meaningful than the primary outcome (i.e. incidence of uterine scar defects). Assessment of the primary outcome was performed using different methods and at different times after CD among the included trials (Table 1). The planned subgroup analysis to evaluate only women who underwent TOLAC was not feasible.

No significant difference was seen when comparing the effect of the two techniques on the primary outcome, i.e. uterine scar defects detected on ultrasound. The secondary outcome of RMT did reveal differences, as the single-layer technique resulted in lower myometrial measurements. However, from a clinical standpoint, the question is whether single-layer uterine closure increases the risk of subsequent uterine rupture in women undergoing TOLAC, but this analysis was underpowered to detect such a difference. For the outcome of uterine rupture at subsequent delivery, selection bias may have been present, as those with a thin segment might not be allowed to attempt vaginal birth after CD. This could potentially underestimate the risk of uterine rupture after single-layer closure. Lal and Tsomo[14] used hysterography at 3 months post CD to detect uterine scar defects, whereas the other RCTs used ultrasound. The study by Guyot-Cottrel[15] was published only as an abstract.

Implications of the study

The only significant finding of our meta-analysis was that single-layer uterine closure at CD is associated with

a thinner RMT, as evaluated by ultrasound, compared with double-layer closure. Interestingly, uterine scar defects were more common in the double- than in the single-layer uterine closure group, but the difference was non-significant (Table 2). The biological basis to explain these findings is not completely clear. In previous studies[5,6], a thinner RMT has been associated with a higher risk of uterine dehiscence and/or rupture, but the presence of a uterine scar seen on ultrasound after CD has also been associated with a higher incidence of uterine dehiscence and/or uterine rupture[4]. It is possible that the presence of a uterine scar defect and/or thinner RMT is related to technical aspects of the CD. For example, uterine closure was usually done 'full-thickness' in most of the included trials, i.e. performed with inclusion of the inner part of the uterine wall (decidua/endometrium) in the scar tissue. Full-thickness uterine closure has been associated with impaired CD scar healing and uterine scar defects[23], but with a lower incidence of incomplete healing of the CD incision in the only randomized trial comparing these two techniques of uterine closure[24]. A possible explanation for these seemingly contradictory findings may be that the RMT is an inappropriate surrogate marker of CD-scar healing.

Conclusions

The results of this meta-analysis provide low- to moderate-quality evidence that single- and double-layer closure of the uterine incision following CD are associated with similar incidences of uterine scar defects detected by ultrasound after CD, and uterine dehiscence and rupture in subsequent pregnancy. Given the rarity of uterine dehiscence and uterine rupture, and based on the current RCTs, we cannot yet recommend a specific technique for uterine closure, and larger trials are needed.

REFERENCES

1. Hamilton BE, Martin JA, Osterman MJ. Births: Preliminary data for 2015. *Natl Vital Stat Rep* 2016; **65**: 1–15.
2. Bij de Vaate AJ, Brölmann HA, van der Voet LF, van der Slikke JW, Veersema S, Huirne JA. Ultrasound evaluation of the Cesarean scar: relation between a niche and postmenstrual spotting. *Ultrasound Obstet Gynecol* 2011; **37**: 93–99.
3. van der Voet LF, Bij de Vaate AM, Veersema S, Brölmann HA, Huirne JA. Long-term complications of caesarean section. The niche in the scar: a prospective cohort study on niche prevalence and its relation to abnormal uterine bleeding. *BJOG* 2014; **121**: 236–244.
4. Vervoort AJ, Uittenbogaard LB, Hehenkamp WJ, Brölmann HA, Mol BW, Huirne JA. Why do niches develop in Caesarean uterine scars? Hypotheses on the aetiology of niche development. *Hum Reprod* 2015; **30**: 2695–2702.
5. Rozenberg P, Goffinet F, Phillippe HJ, Nisand I. Ultrasonographic measurement of lower uterine segment to assess risk of defects of scarred uterus. *Lancet* 1996; **347**: 281–284.
6. Kok N, Wiersma IC, Opmeer BC, de Graaf IM, Mol BW, Pajkrt E. Sonographic measurement of lower uterine segment thickness to predict uterine rupture during a trial of labor in women with previous Cesarean section: a meta-analysis. *Ultrasound Obstet Gynecol* 2013; **42**: 132–139.
7. Roberge S, Demers S, Berghella V, Chaillet N, Moore L, Bujold E. Impact of single- vs double-layer closure on adverse outcomes and uterine scar defect: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014; **211**: 453–460.
8. Roberge S, Chaillet N, Boutin A, Moore L, Jastrow N, Brassard N, Gauthier RJ, Hudic I, Shipp TD, Weimar CH, Fatusic Z, Demers S, Bujold E. Single- versus double-layer closure of the hysterectomy incision during caesarean delivery and risk of uterine rupture. *Int J Gynaecol Obstet* 2011; **115**: 5–10.
9. Berghella V, Baxter JK, Chauhan SP. Evidence-based surgery for cesarean delivery. *Am J Obstet Gynecol* 2005; **193**: 1607–1617.
10. Xodo S, Saccone G, Cromi A, Ozcan P, Spagnolo E, Berghella V. Cephalad-caudad versus transverse blunt expansion of the low transverse uterine incision during cesarean delivery. *Eur J Obstet Gynecol Reprod Biol* 2016; **202**: 75–80.
11. Higgins JPT, Green S (eds). Cochrane handbook for systematic reviews of interventions, version 5.1.0 (update March 2011). The Cochrane Collaboration, 2011. Available at: www.cochrane-handbook.org. (accessed May 16 2016).
12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009; **62**: 1006–1012.
13. Borowski K, Andrews J, Hocking M, Hansen W, Fleener D, Syrop C. Ultrasonographic detection of cesarean scar defects in a trial of single versus double layer closure. *Am J Obstet Gynecol* 2007; **197**: S62.
14. Lal K, Tsomo P. Comparative study of single layer and conventional closure of uterine incision in cesarean section. *Int J Gynaecol Obstet* 1988; **27**: 349–352.
15. Guyot-Cottrel A. *Essai* CHORUS: Comparaison de l'aspect échographique de la cicatrice de césarienne selon une fermeture utérine en un plan ou en deux plans. Abstract. Faculté de Médecine, Université Paris Descarte: Paris, 2011.
16. El-Gharib MN, Awara AM. Ultrasound evaluation of the uterine scar thickness after single versus double layer closure of transverse lower segment cesarean section. *J Basic Clin Reprod Sci* 2013; **2**: 42–45.
17. Yasmin S, Sadaf J, Fatima N. Impact of methods for uterine incision closure on repeat cesarean section scar of lower uterine segment. *J Coll Physicians Surg Pak* 2011; **21**: 522–526.
18. Chapman SJ, Owen J, Hauth JC. One- versus two-layer closure of a low transverse cesarean: the next pregnancy. *Obstet Gynecol* 1997; **89**: 16–18.
19. CORONIS collaborative group, Abalos E, Addo V, Brocklehurst P, El Sheikh M, Farrell B, Gray S, Hardy P, Juszczak E, Mathews JE, Naz Masood S, Oyarzun E, Oyieke J, Sharma JB, Spark P. Caesarean section surgical techniques: 3 year follow-up of the CORONIS fractional, factorial, unmasked, randomised controlled trial. *Lancet* 2016; **388**: 62–72.
20. Bennich G, Rudnicki M, Wilken-Jensen C, Lousen T, Lassed PN, Wojdemann K. Impact of adding a second layer to a single unlocked closure of a Cesarean uterine incision: randomized controlled trial. *Ultrasound Obstet Gynecol* 2016; **47**: 417–422.
21. Roberge S, Demers S, Girard M, Vikhareva O, Markey S, Chaillet N, Moore L, Paris G, Bujold E. Impact of uterine closure on residual myometrial thickness after cesarean: a randomized controlled trial. *Am J Obstet Gynecol* 2016; **214**: 507.e1–6.
22. Hesselman S, Högberg U, Ekholm-Selling K, Råssjö EB, Jonsson M. The risk of uterine rupture is not increased with single- compared with double-layer closure: a Swedish cohort study. *BJOG* 2015; **122**: 1535–1541.
23. Roberge S, Bujold E. Closure of uterus and the risk of uterine rupture. *BJOG* 2015; **122**: 1542.
24. Yazicioglu F, Gökdogan A, Kelekci S, Aygün M, Savan K. Incomplete healing of the uterine incision after caesarean section: Is it preventable? *Eur J Obstet Gynecol Reprod Biol* 2006; **124**: 32–36.

