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Reproductive outcome after cesarean scar pregnancy: A systematic review and meta-analysis

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Conflict of Interest
None

ABSTRACT

Introduction: To evaluate subsequent reproductive among women with a prior cesarean scar pregnancy (CSP). **Material and methods:** Medline, Embase and ClinicalTrials.gov databases were searched. Inclusion criteria were women with a prior CSP, defined as the gestational sac or trophoblast within the dehiscence/niche of the previous cesarean section scar or implanted on top of it. The primary outcome was the recurrence of CSP; secondary outcomes were the chance of achieving a pregnancy after CSP, miscarriage, preterm birth, uterine rupture and the occurrence of placenta accreta spectrum disorders. Sub-group analysis according to the management of CSP (surgical vs non- surgical) was also performed. Random effect meta-analyses of proportions were used to analyze the data. **Results:** Forty-four studies (3598 women with CSP) were included. CSP recurred in 17.6% of women. Miscarriage, preterm birth and placenta accreta spectrum disorders complicated 19.1% (65/341), 10.3% (25/243) and 4.0% of pregnancies, while 67.0% were uncomplicated. When stratifying the analysis according to the type of management, CSP recurred in 21% of women undergoing surgical and in 15.2% of those undergoing non-surgical management, while placenta accreta spectrum disorders complicated 4.0% and 12.0% of cases respectively. **Conclusions:** Women with a prior CSP are at high risk of recurrence, miscarriage, preterm birth and placenta accreta spectrum. There is still insufficient evidence to elucidate whether the type of management adopted (surgical vs non-surgical) can impact reproductive outcome after CSP. Further large prospective studies sharing an objective protocol of prenatal management and long-term follow up are needed to establish the optimal management of CSP and to elucidate whether it may affect its risk of recurrence and pregnancy outcome in subsequent gestations.

KEY WORDS

Cesarean scar pregnancy, placenta accreta spectrum, reproductive outcome, surgical treatment, preterm birth, uterine rupture.

ABBREVIATIONS

CSP: cesarean scar pregnancy

PAS: placenta accreta spectrum

CS: cesarean section

KEY MESSAGE

Women with a prior cesarean scar pregnancy are at high risk of recurrence of cesarean scar pregnacy, miscarriage, preterm birth and placenta accreta spectrum.

INTRODUCTION

Cesarean scar pregnancy (CSP) is one of the most severe complications of cesarean delivery, with a reported incidence of 1.2000 pregnancies[1]. CSP refers to the implantation of the gestational sac in the area of the prior cesarean section (CS) scar, which may lead to severe haemorrhage, uterine rupture and hysterectomy. More recently, CSP has been linked with the occurrence of placenta accreta spectrum (PAS) disorders. [1-6]

Prenatal diagnosis of CSP is fundamental because it allows a pre-planned treatment in centres with high expertise in the management of such anomalies. Prenatal diagnosis of CSP is commonly accomplished on ultrasound and is based upon the visualization of the gestational sac within the area of the prior CS scar, in the presence of an empty uterine cavity and a thin myometrium.[1,4,7,8]

The natural history of CSP is unpredictable as it can lead to life-threatening conditions in early pregnancy, including uterine rupture and haemorrhage, or evolve towards PAS in the third trimester of pregnancy. Several management options for CSP, either surgical or non-surgical, have been described but there is high heterogeneity in the reported results. Furthermore, there is also a lack of consistent data on the reproductive outcome after a prior CSP. Small sample size of previously published studies, inclusion of cases with different types of management and heterogeneity of outcomes explored do not allow to extrapolate an objective evidence on the actual risk of adverse outcome in women after a prior CSP [9-11].

The primary aim of this systematic review was to evaluate subsequent reproductive among women with a prior CSP; the secondary aim was to elucidate whether the type of treatment (surgical vs non- surgical) may affect the reproductive and pregnancy outcome of women with a prior CSP.

MATERIAL AND METHODS

This review was performed according to a protocol designed a priori and recommended for systematic review. Medline, Embase and ClinicalTrials.gov databases were searched electronically on 01/12 2019 utilizing combinations of the relevant medical subject heading

(MeSH) terms, key words, and word variants for "cesarean scar pregnancy" and "outcome." Reference lists of relevant articles and reviews were hand searched for additional reports. PRISMA guidelines were followed [12,13].

Inclusion criteria were women with a prior CSP, defined as the gestational sac or trophoblast within the dehiscence/niche of the previous CS scar or implanted on top of it and diagnosed according to the following criteria[14].

1. Visualization of an empty uterine cavity.
2. Detection of the placenta and/or a gestational sac embedded in the hysterotomy scar.
3. A triangular gestational sac that fills the niche of the scar.
4. A thin (1-3 mm) or absent myometrial layer between the gestational sac and the bladder.
5. A closed cervix and empty endocervical canal.
6. The presence of embryonic/fetal pole and/or yolk sac with or without heart activity.
7. The presence of a prominent and at times rich vascular pattern at or around the choronic sac and the placenta

The primary outcome was the recurrence of CSP, defined as the occurrence of a new CSP. Secondary outcomes were:

1. The chance of achieving a new pregnancy after CSP, defined as the presence of at least a positive pregnancy test in women wishing to conceive.
2. Intra-uterine pregnancy following a prior CSP.
3. Ectopic pregnancy after a prior CSP.
4. Miscarriage, defined as intra-uterine loss of the expulsion of the product of conception before 20 weeks of gestation.
5. Preterm birth, defined as birth before 37 weeks of gestation.
6. Uterine rupture
7. Occurrence of PAS disorders
8. Uncomplicated pregnancies, defined as the number of pregnancies not experiencing major surgical complications.

Furthermore, we aimed to perform a sub-group analysis reporting all the explored outcomes according to the type (surgical vs non-surgical) treatment of the CSP. Surgical treatment included uterine curettage, hysteroscopy, laparotomic or laparoscopic resection, while non-surgical treatments included systematic administration of methotrexate, local injection of methotrexate of potassium chloride in the gestational sac, needle aspiration, high intensity focused ultrasound, Foley or Cook's catheter insertion or uterine artery embolization.
The reproductive outcome after CSP was computed only in women who wished to achieved pregnancy, while pregnancy outcome was ascertained in those with a confirmed intra-uterine pregnancy.

Only studies reporting the reproductive outcome of pregnancy with a prior CSP were considered eligible for the inclusion. Studies reporting only symptomatic women and those for which diagnosis of CSP was not clearly described were excluded (Supporting Information Table S1). Only full text articles were considered eligible for the inclusion. Conference abstracts and single case reports were excluded to avoid publication bias. Studies published before 2000 were not included, as we considered that advances in prenatal imaging techniques, improvements in the diagnosis and management of CSP make these less relevant.

Two authors (DB, FDA) reviewed all abstracts independently. Full text copies of those articles were obtained, and the same two reviewers independently extracted relevant data regarding study characteristics and pregnancy outcome. Inconsistencies were discussed and consensus was reached, or the dispute was resolved by discussion with another author. If more than one study was published for the same cohort with identical endpoints, the report containing the most comprehensive information on the population was included to avoid overlapping populations. Quality assessment of the included studies was performed using the Newcastle-Ottawa Scale *(*NOS*)* for cohort studies[15]. According to Newcastle-Ottawa Scale, each study is judged on three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment outcome of interest. Assessment of the selection of a study includes the evaluation of the representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure and the demonstration that outcome of interest was not present at start of study. Assessment of the comparability of the study includes the evaluation of the comparability of cohorts on the basis of the design or analysis. Finally, the ascertainment of the outcome of interest includes the evaluation of the type of the assessment of the outcome

of interest, length and adequacy of follow-up. According to Newcastle-Ottawa Scale, a study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp)

We used random-effect meta-analyses of proportions using random effects model were used to combine data[16]. Funnel plots displaying the outcome rate from individual studies versus their precision (1/standard error) were carried out with an exploratory aim. Tests for funnel plot asymmetry were not used when the total number of publications included for each outcome was less than ten. In this case, the power of the tests is too low to distinguish chance from real asymmetry[17,18]. Between- study heterogeneity was explored using the I^2 statistic, which represents the percentage of between- study variation that is due to heterogeneity rather than chance.[19] As previously described[62], we constructed a hypothetical model with 1000 women with a prior CSP treated medically or surgically wanting to achieve a subsequent pregnancy.

RESULTS

Study selection and characteristics

A total of 358 articles were identified, 122 were assessed with respect to their eligibility for inclusion and 44 studies included in the systematic review (Table 1, Figure 1)[9,10,20-60]. These studies included 3598 women with a prior CSP; out of these, information on subsequent pregnancy was available for 592 women.

Quality assessment of the included studies performed using Newcastle-Ottawa Scale[15] for cohort studies is shown in Table 2. Most of the included studies showed an overall good rate about the selection and comparability of the study groups. The main weaknesses of these studies were their retrospective design, small sample size, lack of stratification of the analysis according to type of treatment adopted (surgical vs non-surgical), gestational age at intervention and heterogeneity of outcomes observed.

CSP recurred in 17.6% (95% CI 4.6-20.8; 107/618) of cases, while 82.6% (95% CI 79.3-

85.5; 503/618) of women had an intra-uterine pregnancy (Table 3, Figure 2). Eighteen studies (300 women) reported the reproductive outcome after a prior CSP; among women who wished to conceive, pregnancy was achieved in 70.6% (95% CI 66.0-74.9) of cases.

In women experiencing an intra-uterine pregnancy after a prior CSP, the rate of uterine rupture was 1.5% (95% CI 0.5-3.4; 5/341), while miscarriage, preterm birth and PAS disorders complicated 19.1% (95% CI 15.0-23.6; 65/341), 10.3% (95% CI 6.8-14.8; 25/243) and 4.0% (95% CI 2.1-6.7; 13/327) of pregnancies. Finally, 67.0% (95% CI 61.6-72.0; 219/327) of the included cases had an uncomplicated pregnancy (Table 3).

Sub-group analysis according to the type of management adopted (surgical vs non-surgical) was affected by the small number of included cases and even smaller number of events. CSP recurred in 21.0% (95% CI 17.3-25.2; 90/428) of women undergoing surgical and in15.2% (95% CI 9.7-22.4; 21/138) of those undergoing non-surgical treatment, while the corresponding figures for the chance of achieving pregnancy were 74.4% (95% CI 69.3-79.0; 244/428) and 68.7% (95% CI 56.2-79.4; 46/67) respectively (Table 4).

Miscarriage and preterm birth complicated 16.2% (95% CI 11.8-21.6; 38/234) and 8.9% (95% CI 5.0-14.5; 14/157) of women undergoing surgical compared to 14.7% (95% CI 7.3-25.4; 14/68) and 15.2% (95% CI 7.5-26.1; 10/66) of those undergoing-non-surgical management.

Finally, 2.7% (95% CI 1.0-5.8; 6/221) of pregnancies undergoing surgical and 10.6% (95% CI 4.4- 20.6; 7/66) of those undergoing non-surgical treatment of the prior CSP experienced PAS disorders in the subsequent pregnancy.

In a hypothetical model (Figure 3) of 1000 women with a prior CSP treated medically or surgically wanting to achieve a subsequent pregnancy, 70% of those wanting to conceive, will achieve a pregnancy. Among these, 18% will experience a recurrence of CSP, while 82% will obtain a intrauterine pregnancy. In the group of women with intrauterine pregnancy, the 19% will have a miscarriage, the 10% will experience a preterm birth, and the 4% will result in PASat delivery. The 67% will have an uncomplicated pregnancy resulting in livebirth at term.

DISCUSSION

The findings from this systematic review show that, in women with a prior CSP, the risk of

recurrence is about 17%. 70% of women who wished to conceive again achieved a pregnancy. Miscarriage and preterm birth complicated about 19% and 10% of pregnancies, while PAS disorders occurred in 4% of cases. Finally, 67% of women had an uncomplicated pregnancy. In view of the small number of included studies, lack of direct comparison in the original publication and heterogeneity in outcomes observed and management options, it was not possible to fully elucidate whether the type of treatment of CSP (surgical vs non-surgical) affected the explored outcomes.

To our knowledge, this is the first systematic review assessing the reproductive and pregnancy outcome of women with a prior CSP. A recent systematic review exploring the long-term risk associated with CS, reported a higher risk of miscarriage, placenta accreta and placental abruption in women having cesarean compared to vaginal delivery[61]. In the present review, we could not compare the risk of the explored outcome in pregnancies affected compared to those not affected by a prior CSP because there was no case-control study reporting these outcomes. However, the occurrence of CSP, uterine rupture and PAS in women with a prior CSP were higher compared to what reported for women with a previous CS[1]. The small number of cases in the majority of the included studies, their retrospective non-randomized design, lack of stratification of the analysis according to the type of management adopted (surgical vs non-surgical) and heterogeneity in gestational age at treatment for most of the included studies represent the main weaknesses of the present systematic review. The assessment of the potential publication bias was also problematic, both because of the nature of outcome (rates with the left side limited to the value zero) which limits the reliability of funnel plots, and because of the scarce number of individual studies, which strongly limits the reliability of formal tests. The level of evidence for these types of studies is very low.

CSP and PAS disorders are among the most severe iatrogenic complications of cesarean delivery. There is still no adequately powered randomized controlled trial on the optimal treatment of CSP. Previously published studies differ as regard as gestational age at diagnosis and treatment, type of management (surgical vs non-surgical) and outcomes explored, thus making difficult to extrapolate an objective evidence on how to treat these anomalies [9-11]. Reproductive outcome of women with a prior CSP is another relevant issue and it has still to be fully ascertained how to counsel these women. Surgical treatment of CSP may affect the integrity of the anterior uterine wall and may sometimes end-up in unplanned hysterectomy,

especially in those cases presenting with severe life-threatening symptoms, thus affecting the future fertility of these women. Conversely, non-surgical treatment may lead to the incomplete removal of the CSP and the persistence of the cesarean scar, thus predisposing to a recurrent CSP [1-5] In the present systematic review, 17% of women with a prior CSP , this anomaly recurred, thus highlighting the need for an early ultrasound assessment during the first trimester of pregnancy in order to rule out CSP. Predicting the risk of adverse pregnancy outcome in women after CSP is also challenging. Women with CSP are at increased risk of uterine rupture and PAS, due to the anatomical weakness of the myometrium and the presence of a prior scar. This may partially explain the high incidence of uterine rupture and PAS observed in women pregnancies affected by a prior CSP and highlights the need for a thorough follow-up thorough pregnancy in order to timely detect these anomalies. [1-5]

The optimal management of CSP has still to be determined as there is no evidence form randomized controlled trials. Different treatment options for CSP, either surgical or non-surgical have been reported in the published literature, but there is still lack of data on short and long-term complications following treatment [9-11].

In the present review, CSP recurred in 21.0% (of women undergoing surgical and in15.2% of those undergoing non-surgical treatment, although a direct comparison could not be performed in view of the original design of the included studies. Uterine rupture (0.9% vs 4.4%) and PAS disorders (2.7% vs 10.6%) were relatively more common in women undergoing non-surgical compared to surgical management of PAS. A possible explanation for these discrepancies may rely on the fact that surgical treatment of CSP can partially restore the anatomy of the anterior uterine wall. Conversely, in non- surgical treatment, the persistence of the area of the prior CS scar, especially in cases presenting with a large niche, may predispose to further CSP or adverse events related to the thin myometrium over the area of the prior scar. However, this data should be interpreted with caution as none of the included studies was designed to compare different treatment modalities and it is entirely possible that other co-factors, such as gestational age at treatment, size of the prior scar and CSP may have affected the results. Furthermore, these sub-analyses were affected by the very small number of cases and even smaller number of events, thus representing a significant source of bias and highlighting the need for further studies aimed at exploring the short- and long-term consequences of the different treatment modalities for CSP.

CONCLUSION

Women with a prior CSP should be counselled on the high risk of recurrence of CSP, uterine rupture and PAS disorders in a subsequent pregnancy. In view of the original study design, it was not possible to elucidate whether the type of management adopted (surgical vs non-surgical) may affect reproductive outcome after CSP. Further large prospective studies sharing an objective protocol of prenatal management and long-term follow-up are needed in order to establish the optimal type of management of CSP and to elucidate whether it may affect pregnancy outcome in subsequent gestations.

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Supporting Information legend

Table S1: Excluded studies and reason for the exclusion.

Figure legends

Figure 1. Systematic review flowchart.

Figure 2. Pooled proportions for the occurrence of a new pregnancy, intra-uterine pregnancy and recurrence cesarean scar pregnancy after a prior cesarean scar pregnancy.

Figure 3. Hypothetical model of 1000 cesarean scar pregnancy (CSP) wanting to achieve a subsequent pregnancy.

Table 1. General characteristics of the included studies. CSP, cesarean scar pregnancy.

Author	Year	Country	Study design	Period considered	CSP treatment	Outcomes observed	CSP (n)	Pregnancies aft CSP (n)
Qiu[45]	2019	China	Retrospective	2013-2018	surgical	Reproductive and pregnancy outcome	62	25
Zhang[59]	2019	China	Retrospective	2015-2018	surgical	Reproductive and pregnancy outcome	154	23
Lu[39]	2019	China	Retrospective	2015-2017	surgical and/or non-surgical	Reproductive and pregnancy outcome	70	2
Elmokadem[27]	2019	Egypt	Retrospective	NS	surgical and/or non-surgical	pregnancy outcomes	7	1
Orhan[20]	2019	Turkey	Retrospective	2011-2017	surgical and/or non-surgical	pregnancy outcomes	31	9
Chen L[22]	2018	China	Retrospective	2007-2016	surgical	Reproductive and pregnancy outcome	617	103
Grechukhina[28]	2018	USA	Retrospective	2013-2018	surgical and/or non-surgical	pregnancy outcomes	30	10
Li Y[60]	2018	China	Retrospective	2006-2016	surgical	Reproductive and pregnancy outcome	301	102
Sun QL[49]	2018	China	Retrospective	2012-2015	surgical	pregnancy outcomes	395	17
Tumenjargal[50]	2018	Japan	Retrospective	2006-2017	surgical	Reproductive and pregnancy outcome	33	7

Le[35]	2018	China	Retrospective	2011-2016	surgical	pregnancy outcomes	313	19
Qi[44]	2018	China	Retrospective	NS	surgical	pregnancy outcomes	8	2
Karahasanoglu[32]	2018	Turkey	Retrospective	2009-2013	surgical	pregnancy outcomes	19	5
Li[37]	2018	China	Retrospective	2011-2015	surgical	Reproductive and pregnancy outcome	54	8
Osada[42]	2018	Japan	Retrospective	2002-2017		pregnancy outcomes	3	1
Jabeen[31]	2018	UK	Retrospective	2012-2017	Non-surgical	pregnancy outcomes	26	5
Washburn[54]	2017	USA	Retrospective	2000-2012	surgical	pregnancy outcomes	23	12
Chiang[23]	2017	Taiwan	Retrospective	1994-2015	surgical and/or non-surgical	pregnancy outcomes	90	7
Gao[9]	2016	China	Retrospective	2009-2012	surgical	Reproductive and pregnancy outcome	22	11

Donnez[25]	2016	Belgium	Retrospective	NS	surgical	Reproductive and pregnancy outcome	38	8
Uludag[51]	2016	Turkey	Retrospective	2000-2015	Non-surgical	Reproductive and pregnancy outcome	44	27
Zhang[58]	2016	China	Retrospective	2013-2014	surgical	pregnancy outcomes	8	1
Wang YQ[53]	2015	China	Retrospective	203809-2013	surgical	Reproductive and pregnancy outcome	189	32
Ko[11]	2015	Hong Kong	Retrospective	2004-2013	surgical and/or non-surgical	pregnancy outcomes	22	4
Du[26]	2015	China	Retrospective	2006-2012	surgical	Reproductive and pregnancy outcome	35	11
Timor-Tritsch[10]	2015	United States	Retrospective	2009-2018	Non-surgical	Reproductive and pregnancy outcome	96	32
Qi[43]	2015	China	Retrospective	2009-2013	surgical	pregnancy outcomes	50	4
Yang G[56]	2014	South	Retrospecti	NS	surgical	Reproductive and	3	4

		Korea	ve			pregnancy outcome		
Li[36]	2014	China	Retrospective	2009-2013	surgical and/or non-surgical	pregnancy outcomes	49	4
He[30]	2014	China	Retrospective	2005-2019	surgical	Reproductive and pregnancy outcome	58	5
Le[34]	2013	China	Retrospective	2008-2012	surgical	pregnancy outcomes	38	3
Lan[33]	2013	China	Retrospective	2004-2010	surgical	Reproductive and pregnancy outcome	79	16
Uysal[52]	2013	Turkey	Retrospective	NS	surgical and/or non-surgical	pregnancy outcomes	7	2
Zhang[57]	2012	China	Retrospective	2005-2011	surgical	pregnancy outcomes	10	4
Lian[38]	2012	China	Retrospective	2005-2009	Non-surgical	pregnancy outcomes	21	5
Shen[47]	2012	China	Retrospective	2008-2010	surgical	pregnancy outcomes	46	2
Maymon[40]	2011	Israel	Retrospecti	2000-2009	surgical and/or	Reproductive and	432	8

			ve		non-surgical	pregnancy outcome		
Yang XY[55]	2010	China	Retrospective	2003-2008	surgical	pregnancy outcomes	43	6
De Vaate[24]	2010	Holland	Retrospective	1996-2007	surgical and/or non-surgical	pregnancy outcomes	4	3
Michener[41]	2009	Australia	Retrospective	2002-2007	surgical and/or non-surgical	pregnancy outcomes	13	4
Halperin[29]	2009	Israel	Retrospective	2002-2007	surgical	pregnancy outcomes	6	1

Smorgick[48]	2008	Israel	Retrospective	2000-2006	Non-surgical	Reproductive and pregnancy outcome	5	3
Ben Nagi[21]	2007	UK	Retrospective	1999-2005	surgical and/or non-surgical	Reproductive and pregnancy outcome	29	21
Seow[46]	2004	Taiwan	Retrospective	1995-2002	surgical and/or non-surgical	pregnancy outcomes	15	8

CSP, cesarean scar pregnancy.

Table 2. Quality assessment of the included studies according to Newcastle-Ottawa Scale (NOS) for case-control study. According to Newcastle-Ottawa Scale, a study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Author	Year	Selection	Comparability	Outcome
Qiu[58]	2019	★★★	★	★★
Zhang[59]	2019	★★	★	★★
Lu[39]	2019	★★	★	★★
Elmokadem[27]	2019	★★	★	★★
Orhan[20]	2019	★★	★	★★
Chen L[22]	2018	★★	★	★★
Grechukhina[28]	2018	★★★	★	★★
Li Y[60]	2018	★★	★	★★
Sun QL[48]	2018	★★	★	★★
Tumenjargal[50]	2018	★★	★	★★
Le[35]	2018	★★	★	★★
Qi[44]	2018	★★	★	★★
Karahasanoglu[32]	2018	★★★	★	★★
Li[37]	2018	★★	★	★★
Osada[42]	2018	★★	★	★★
Jabeen[31]	2018	★★	★	★★
Washburn[54]	2017	★★	★	★★
Chiang[23]	2017	★★	★	★★
Gao[9]	2016	★★★	★	★★

Donnez[25]	2016	★★	★	★★
Uludag[51]	2016	★★	★	★★
Zhang[57]	2016	★★	★	★★
Wang YQ[53]	2015	★★	★	★★
Ko[11]	2015	★★	★	★★
Du[26]	2015	★★	★	★★
Timor-Tritsch[10]	2015	★★★	★	★★
Qi[43]	2015	★★	★	★★
Yang G[56]	2014	★★	★	★★
Li[36]	2014	★★	★	★★
He[30]	2014	★★	★	★★
Le[34]	2013	★★	★	★★
Lan[33]	2013	★★	★	★★
Uysal[52]	2013	★★	★	★★

Zhang[56]	2012	★★★	★	★★
Lian[38]	2012	★★	★	★★
Shen[47]	2012	★★	★	★★
Maymon[40]	2011	★★	★	★★
Yang XY[55]	2010	★★	★	★★
De Vaate[27]	2010	★★	★	★★
Michener[41]	2009	★★	★	★★
Halperin[29]	2009	★★	★	★★
Smorgick[48]	2008	★★★	★	★★
Ben Nagi[23]	2007	★★	★	★★
Seow[46]	2004	★★	★	★★

Table 3. Pooled proportions for the outcomes explored in the present systematic review

Outcome	Studies (n)	Cases (n)	Raw proportions (95% CI)	I^2 (%)	Pooled proportions (95% CI)
Recurrence of CSP	44	107/618	17.31(14.4-20.5)	47.7	17.14 (14.3-20.2)
Pregnancy after CSP[a]	18	300/425	70.58 (66.0-74.9)	82.4	71.08 (66.7-75.2)
Intra-uterine pregnancy following CSP	44	503/618	812.39 (78.1-84.4)	49.8	81.62 (78.5-84.5)
Ectopic pregnancy	44	8/618	1.29 (0.6-2.5)	0	2.25 (1.2-3.5)
Uterine rupture	33	5/341	1.47 (0.5-3.4)	0	2.43 (1.1-4.3)
Miscarriage	33	65/341	19.06 (15.0-23.6)	29.9	19.37 814.2-25.1)
Preterm birth	26	25/243	10.29 (6.8-14.8)	30.2	11.67 (7.2-17.3)
PAS disorders	30	13/327	3.98 (2.1-6.7)	0	4.93 (2.9-7.5)
Uncomplicated pregnancies	30	219/327	66.97 (61.6-72.0)	53.1	66.12 (57.8-74.0)

a: only studies reporting the number of women wishing to conceive after a CSP, were included in the computation of this outcome.

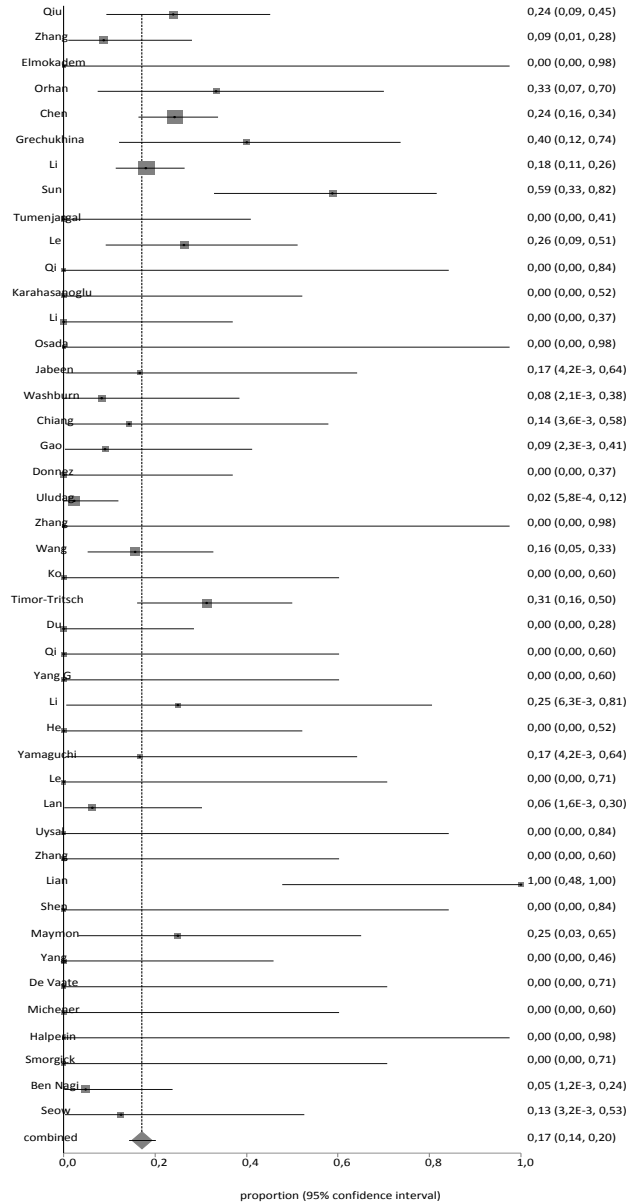
CSP, cesarean scar pregnancy. PAS, placenta accreta spectrum.

Table 4. Pooled proportions for the outcomes explored in the present systematic review in women with a prior cesarean scar pregnancy (CSP) undergoing surgical or non-surgical treatment.

Outcome	Studies (n)	Cases (n)	Raw proportions (95% CI)	I^2 (%)	Pooled proportions (95% CI)
	Surgical treatment				
Recurrence of CSP	27	90/428	21.02 (17.3-25.2)	63	21.01 (13.9-29.2)
Pregnancy after CSP	11	244/328	74.39 (69.3-79.0)	72	72.23 (60.6-82.5)
Intra-uterine pregnancy following CSP	27	331/428	77.34 (73.1-81.2)	63	77.70 (69.4-85.0)
Ectopic pregnancy	27	7/428	1.64 (0.6-3.3)	0	2.38 (1.2-4.0)
Uterine rupture	20	2/233	0.86 (0.1-3.1)	0	1.84 (0.5-3.9)
Miscarriage	21	38/234	16.24 (11.8-21.6)	30.8	16.43 (10.5-23.4)
Preterm birth	16	14/157	8.92 (5.0-14.5)	0	9.71 (5.7-14.79
PAS disorders	19	6/221	2.71 (1.0-5.8)	0	4.00 (1.9-6.9)
Uncomplicated pregnancy	19	143/221	64.71 (58.0-71.0)	76.9	61.61 (46.2-75.9)
	Non-surgical treatment				
Recurrence of CSP	17	21/138	15.22 (9.7-22.4)	63	15.65 (6.3-28.2)
Pregnancy after CSP	5	46/67	68.66 (56.2-79.4)	16.4	79.90 (57.0-83.0)
Intra-uterine pregnancy following CSP	17	116/138	84.06 (76.9-89.7)	63.1	82.96 (70.1-92.8)
Ectopic pregnancy	17	1/138	0.72 (0.01-4.0)	0	2.50 (0.6-5.6)
Uterine rupture	13	3/68	4.41 (0.9-12.4)	23	6.00 (1.8-12.5)
Miscarriage	13	14/68	14.71 (7.3-25.4)	0	21.41 (12.9-31.4)
Preterm birth	11	10/66	15.15 (7.5-26.1)	56.4	16.59 (5.5-32.1)
PAS disorders	11	7/66	10.61 (4.4-20.6)	0	12.04 (5.6-20.5)
Uncomplicated pregnancy	11	42/66	63.64 (50.9-75.1)	0	62.44 (51.0-73.2)

PAS, placenta accreta spectrum.

Recurrence of CSP



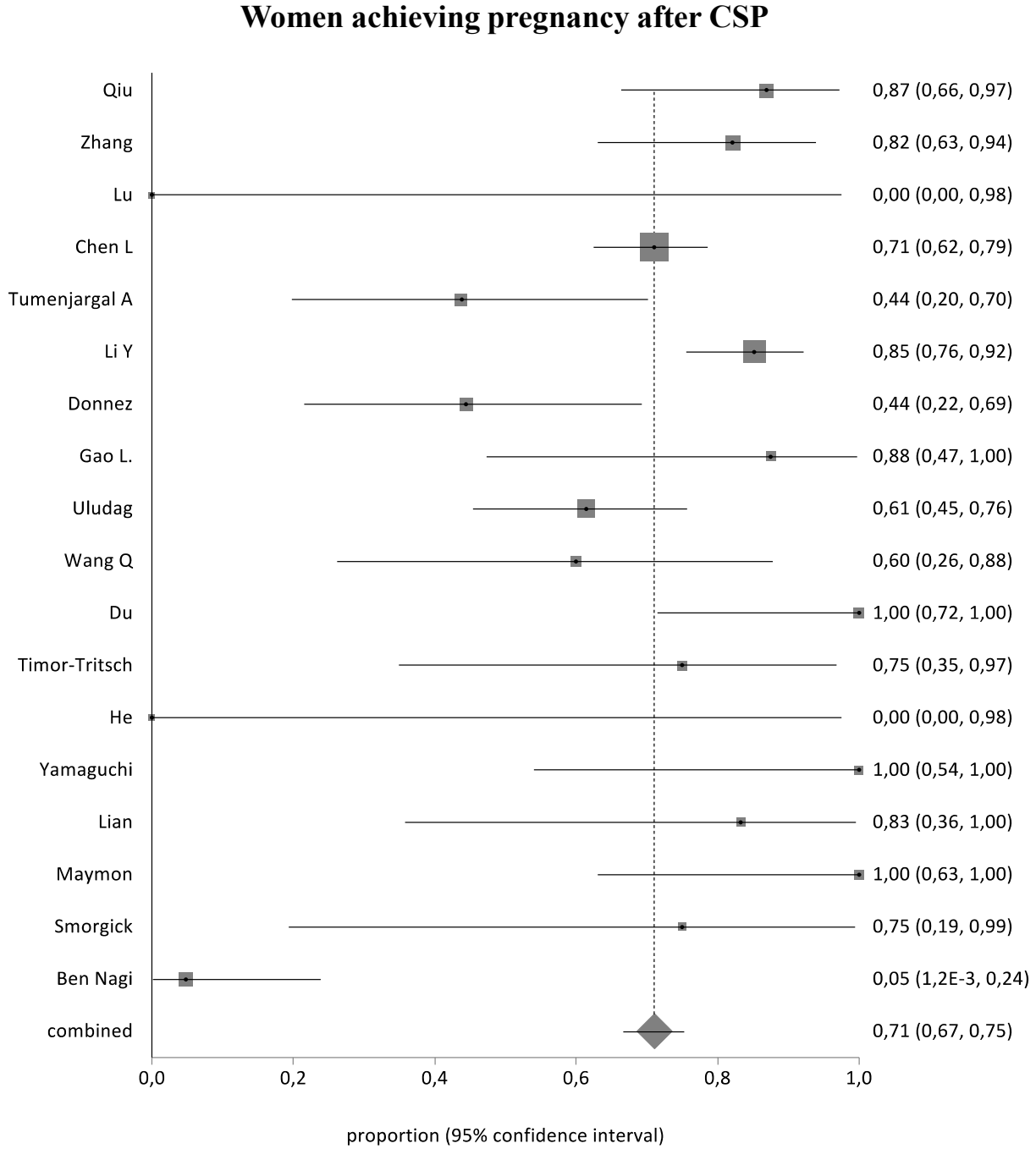


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Figure 3 - Hypothetical model of 1000 CSP wanting to achieve a subsequent pregnancy.