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Opinion

Late-stage Cesarean section causes recurrent early preterm birth: how to tackle this problem?

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About 500 000 preterm deliveries before 37 weeks' gestation occur annually in the USA. Worldwide, this figure is estimated to be 15 million each year, with serious associated health implications and high costs to families and society. The management and prevention of preterm birth is highly variable depending on the etiology. Recent studies have shown that Cesarean section (CS) performed late in labor or at full dilatation (FDCS) is associated with recurrent early preterm birth and late miscarriage. However, the clinical problem that FDCS poses in subsequent pregnancies is still under-recognized. In addition to raising awareness, further research is needed to understand the etiology of this association and to develop prevention and management strategies, particularly in light of the escalating CS rate.

Scope of problem

The rate of CS has escalated in middle- and high-income countries in recent decades. Worldwide, CS rates have increased 3-fold, from 6.7% in 1990 to 19.1% in 2014[1]. Even in countries with already high CS rate, this continues to increase: in the USA, the CS rate in 2016 had risen from 20.7% to 31.9% over a span of 20 years[2]; similarly, a rise from 17% to 28% has been recorded in the UK in the past two decades[3,4]. Up to 20% (based on findings in a large Australian cohort of 2672 women) of emergency CS have been reported to be performed at full dilatation[5] and this proportion is increasing[6–8]. This may reflect the unwillingness of clinicians to perform assisted vaginal delivery. Retrospective review of a cohort of patients requiring intervention due to prolonged second stage of labor revealed that 28% of them underwent CS[9]. In the UK, FDCS occurs in approximately 5% of all Cesarean deliveries, which represents about 8000 deliveries per annum[6,8,10].

Maternal and neonatal complications of FDCS are well-described and include laceration of the bladder, bowel, ureter and uterine artery, and extension of the uterine incision, hemorrhage with or without blood transfusion, hysterectomy, as well as fetal lacerations and puerperal febrile episodes[6,11]. These complications may be exacerbated with increased duration of the second stage of labor.

In addition, the complication of preterm birth was recently linked to late-stage CS. Levine *et al.* exposed a 6-fold increased risk of preterm birth in a subsequent pregnancy following FDCS[12]. In their cohort, 13.5% of women who underwent FDCS had a subsequent preterm delivery compared with 2.3% of women who underwent first-stage CS (odds ratio, 5.8; 95% CI, 1.08–30.8; $P = 0.04$)[12]. In addition, there may be a longer-term impact. Watson *et al.* showed that 53% of women with a history of FDCS experienced recurrent pregnancy loss, in spite of intervention, compared with 14% of those with a history of preterm birth without FDCS (relative risk, 3.06; 95% CI, 1.22–7.71)[13]. In this study, 17/29 women in the FDCS group received intervention compared with 6/37 in the control group, while 55% (16/29) of women in the FDCS group delivered before 37 weeks compared with 19% (7/37) in the control group. Conventional treatment with vaginal cerclage did not appear to offer protection in the group of women who had a preterm birth following FDCS; of the 11/29 (38%) women with vaginal cerclage in the FDCS group, 45% (5/11) delivered preterm[13].

There appears to be a continuum of risk with regard to the degree of cervical dilatation at the time of Cesarean delivery. In a large USA study, the relative risk of spontaneous preterm delivery prior to 32 weeks' gestation was 2.48 (95% CI, 1.77–3.49) following CS at 9–10 cm dilatation, compared with 1.63 (95% CI, 1.44–1.85) when cervical dilatation was 0–4 cm[14]. A more recent large Australian cohort study reported a lower absolute risk of subsequent spontaneous preterm birth following FDCS that was still double compared with that in women with a previous first-stage CS (3.8% *vs* 1.7%)[5]. Current data do not take into account subsequent mid-trimester losses and could therefore be underestimating the actual risk of late-stage CS. Mid-trimester loss represents an important outcome that needs further evaluation in the context of a prior FDCS.

Hypotheses of pathophysiology

It has been suggested that compromise of the integrity of the cervix due to cervical injury can predispose to subsequent preterm birth[12,13]. As the lower uterine segment thins out over the presenting part during labor, it is thought that the CS incision is made inadvertently too low within the cervix or even the vagina[15]. It is arguable that it is this incision within the cervical tissue, rather than an extension of the incision into the cervix, that contributes to cervical incompetence.

The difficulty of defining the border between the lower uterine segment and the cervix was well-documented by Marshall as early as 1939[16]. He described that, at full dilatation, 'the inferior limit of the lower segment can no longer be defined, by sight or touch, with absolute precision'. Marshall also described how the cervix or vaginal wall may be incised during CS late in labor[16]. In 1980, Bryan and Strickler reported that the inferior margin of the lower uterine segment, the supravaginal and vaginal cervix were seen as continuous at full dilatation, and that the difficulty in defining the marking of the cervical–corporal junction in an effaced cervix led inadvertently to primary vaginal incision[17]. It was only in 1996 that cases of incompetent cervix were described following CS carried out after prolonged pushing in the second stage[18]. This kind of trauma or laceration to the cervix was attributed to poor healing in which the cervix is 'stretched beyond tolerance'[18].

Prolonged second stage of labor (without analysis of mode of delivery or cervical dilatation) has been identified by some studies as a risk factor for preterm birth[19,20]. Second stage of labor longer than 180 min in a first pregnancy was associated with an 81% increased risk of preterm delivery in a subsequent pregnancy (adjusted hazard ratio, 1.81; 95% CI, 1.15–2.84)[21]. However, Wood *et al.* found that FDCS, but not the duration of the second stage of labor, was associated with a higher risk of delivery before 32 weeks, suggesting that it is FDCS rather than the length of the second stage that predisposes to preterm labor[14].

Levine *et al.* found that extension of the uterine incision into the cervix during FDCS increases the risk of subsequent spontaneous preterm birth[12]. However, cervical extension did not account entirely for the increased incidence of subsequent preterm birth in this cohort as the rate of preterm birth remained high even when the cases with extension were excluded from analysis (risk of spontaneous preterm birth, 9.1% following FDCS *vs* 0.9% following first-stage CS; $P = 0.02$)[12].

Injury to the cervical morphology during FDCS has been suggested as the mechanism of subsequent spontaneous preterm birth[12,13,20,22]. Recent evidence suggests that the cervix comprises a specialized sphincter at the internal os composed of 50–60% smooth-muscle cells organized circumferentially around the endocervical canal, a construction that persists down to the midcervix and then the number of smooth-muscle cells decreases gradually towards the external os, which is composed of 10–15% smooth muscle[23]. The authors proposed that the cervical smooth-muscle cells may play a role in cervical remodeling as well as initiating and/or disseminating uterine contractility. This novel sphincter morphology may be a key to investigating the mechanisms of premature and term cervical remodeling. It is thought that cervical effacement causes the internal-sphincter smooth muscle to migrate into the lower uterine segment, which can be disrupted during FDCS[20] thus resulting in incomplete recovery of cervical muscular function. Furthermore, closure of the uterine defect if it is located too low, or if extension to the cervix is required due to difficulty delivering an impacted fetal head, could equally injure the internal os[24].

These hypotheses underpinning the association between FDCS and future preterm delivery are so far unproven. The trauma alone cannot explain this relationship as over 80% of women having FDCS do not experience a subsequent preterm birth, and thus it may be that the degree of insult or the level of trauma is critical. The healing processes in Cesarean scars, the role of infection and/or ischemia, as well as the effect of the operative technique used need further consideration. This includes comparison between vertical and horizontal lower segment uterine incisions as a possible intervention, and the effect on circular sphincter competence at the internal os. Furthermore, the suture material and comparison between single- and double-layer closure warrant evaluation, as they could influence incidence of ischemia and healing. Our current prediction tools, such as cervical length and fibronectin testing, also warrant further investigation to ensure their validity in this specific population of women with history of FDCS.

Confounders to this new problem

Decision-making regarding the need for, as well as the execution of, second-stage delivery requires experienced operator input. The rise in FDCS is often related to increased failure of assisted vaginal delivery[8]. Moreover, there is a fear of litigation over assisted vaginal deliveries that has led to a decline in their use[25,26]. In this context, FDCS may be perceived as a safer option. In the UK, following the introduction of the European Working Time Directive, obstetric trainees work significantly fewer hours, which may limit their exposure to, and thus their confidence in, performing instrumental vaginal deliveries, therefore contributing further to this problem[6]. Maternal factors are also likely to account for the increased incidence of CS. In the UK, patient demographics are changing, with more primiparous births occurring at a higher booking body mass index and at increasing maternal age[6]. It is likely that similar trends are occurring in high-income settings worldwide.

Evidence for imaging surveillance

There have been reports of anterior cervical defects visualized on transvaginal ultrasound in women with previous FDCS. This is not looked for routinely in antenatal ultrasound scans and their relationship to preterm birth risk is unclear[16]. The screening and optimum management of cervical defects need to be further researched and resolved.

Repair of a Cesarean defect, also known as a niche or isthmocele, has been described in cases of subfertility, intermenstrual bleeding, dysmenorrhea or dyspareunia. A case series of 38 patients who underwent magnetic resonance imaging (MRI) before and after laparoscopic

repair identified significantly increased myometrial thickness following repair, a finding that was confirmed on histological analysis[27]. One hypothesis regarding niche development highlights that a low cervical incision may induce the formation of 'retention cysts' and the presence of mucus-producing glands may hamper healing[28]. Furthermore, it has been shown that a low uterine incision, which can occur, for example, when the cervix is effaced in labor, is associated with large niche development detectable by transvaginal ultrasound[29]. Incomplete uterine closure and formation of adhesions that impair healing have also been implicated in niche creation. The presence of a niche has not been commonly linked to preterm birth, partly due to subspecialty focus in research, but has been described in case studies[30].

A recent study assessing the added value of MRI in the examination of Cesarean scars compared with transvaginal monitoring found that, on MRI, it was possible to evaluate the muscle fibers remaining at the level of the scar[31]. This has not yet been correlated to preterm birth risk in the FDCS population as scars specifically within the cervix have not been investigated. Although a Cesarean scar can be identified by transvaginal ultrasound at the same time as cervical-length assessment, its value is limited in terms of analyzing the scar morphology[29,31]. Further work is needed to establish whether imaging features seen on ultrasound or MRI can predict outcome, and possibly direct intervention prior to an adverse event.

Evidence for current management

Cervical-length screening by transvaginal ultrasound is used increasingly to ascertain the risk of preterm birth. It is unknown whether this is a valid marker in women with FDCS as a risk factor. Similarly, it is unknown which interventions may reduce the risk of preterm birth in a subsequent pregnancy in these women. Decisions regarding interventions vary largely depending on clinicians' expertise, experience and preference. Limited data suggest that the failure rate of vaginal cerclage may be higher in women with prior FDCS[13]. This makes sense physiologically if the suture is confined to encircling the vaginal (distal) portion of the cervix. Transabdominal cerclage has been suggested as the most effective management option in these women[30], but larger studies are needed to support this. One can hypothesize that a transabdominal cerclage provides support above the level of the defect caused by a low incision in the cervical tissue, which logically would be the best way forward in future term pregnancy success. However, this procedure is more invasive and necessitates CS in subsequent delivery, and therefore identifying which women would benefit from this intervention needs urgent clarification.

In the first instance, greater awareness by both the public and healthcare professionals of the potential risk following likely iatrogenic injury during FDCS would increase referrals and research in this area. Since prevention is better than cure, we feel that obstetricians and personnel should be highly skilled in performing assisted vaginal deliveries. The relative merits of a higher, or perhaps vertical, uterine incision need to be evaluated. Clinical trials of screening tests (biophysical and biochemical) in women with preterm birth following FDCS are required to ascertain risk and subsequent interventions. In particular, the use of cervical scanning and MRI in evaluating the prior cervical injury and scar would be valuable. The role of higher-placed sutures, both vaginal and abdominal, should also be investigated.

Summary

The complications of FDCS have recently come to light and it is a sobering reminder of how our well-intentioned interventions can lead to serious harm, and of the need to remain vigilant and to audit continually our current practice. It is likely that more than 14% of women with a FDCS experience subsequent mid-trimester loss and/or preterm birth, which is recurrent and difficult to treat. By raising awareness of this important problem, we aim to focus research efforts on the optimal management, as well as avoidance, of FDCS.

REFERENCES

1. Betrán AP, Ye J, Moller AB, Zhang J, Gülmezoglu AM, Torloni MR. The increasing trend in caesarean section rates: Global, regional and national estimates: 1990-2014. *PLoS One* 2016; **11**: e0148343.
2. Downie DL. Book Review: Jessica Tuchman Mathews (Ed.), Preserving the Global Environment: The Challenge of Shared Leadership (New York: W. W. Norton & Company, 1991), pp. 362. *Pol Sci* 1994; **46**: 125–126.
3. NHS Digital. NHS Maternity Statistics, England 2017-2018. https://digital.nhs.uk/data-and-information/publications/statistical/nhs-maternity-statistics/2017-18.
4. NHS Digital. NHS Maternity Statistics - England, 2004-2005. https://digital.nhs.uk/data-and-information/publications/statistical/nhs-maternity-statistics/2004-05.
5. Cong A, de Vries B, Ludlow J. Does previous caesarean section at full dilatation increase the likelihood of subsequent spontaneous preterm birth? *Aust NZ J Obstet Gynaecol* 2018; **58**: 267–273.
6. Vousden N, Cargill Z, Briley A, Tydeman G, Shennan AH. Caesarean section at full dilatation: incidence, impact and current management. *Obstet Gynaecol* 2014; **16**: 199–205.
7. Pearson GA, MacKenzie IZ. A cross-sectional study exploring the incidence of and indications for second-stage cesarean delivery over three decades. *Int J Gynecol Obstet* 2017; **138**: 340–346.
8. Unterscheider J, McMenamin M, Cullinane F. Rising rates of caesarean deliveries at full cervical dilatation: A concerning trend. *Eur J Obstet Gynecol Reprod Biol* 2011; **157**: 141–144.
9. Tan PS, Tan JFH, Tan EL, Tan L. Comparison of Caesarean sections and instrumental deliveries at full cervical dilatation: a retrospective review. *Singapore Med J* 2019; **60**: 75–79.
10. Loudon JAZ, Groom KM, Hinkson L, Harrington D, Paterson-Brown S. Changing trends in operative delivery performed at full dilatation over a 10-year period. *J Obstet Gynaecol (Lahore)* 2010; **30**: 370–375.
11. Allen VM, O'Connell CM, Baskett TF. Maternal and perinatal morbidity of caesarean delivery at full cervical dilatation compared with caesarean delivery in the first stage of labour. *BJOG* 2005; **112**: 986–990.
12. Levine LD, Sammel MD, Hirshberg A, Elovitz MA, Srinivas SK. Does stage of labor at time of cesarean delivery affect risk of subsequent preterm birth? *Am J Obstet Gynecol* 2015; **212**: 360.e1–7.
13. Watson HA, Carter J, David AL, Seed PT, Shennan AH. Full dilation cesarean section: a risk factor for recurrent second-trimester loss and preterm birth. *Acta Obstet Gynecol Scand* 2017; **96**: 1100–1105.
14. Wood SL, Tang S, Crawford S. Cesarean delivery in the second stage of labor and the risk of subsequent premature birth. *Am J Obstet Gynecol* 2017; **217**: 63.e1–10.
15. Peleg D, Perlitz Y, Pansky S, Levit A, Ben-Ami M. Accidental delivery through a vaginal incision (laparoelytrotomy) during caesarean section in the second stage of labour. *Br J Obstet Gynaecol* 2001; **108**: 659–660.
16. Marshall C. *Caesarean Section: Lower Segment Operation*. John Wright & Sons Ltd: London, 1939.
17. Bryan B, Strickler R. Inadvertent primary vaginal incision during cesarean section. *Can J Surg* 1980; **23**: 581–583.
18. Iams JD. Preterm birth. In *Obstetrics: Normal and Problem Pregnancies*, Gabbe SG, Niebyl JR, Simpson JL (eds). Churchill Livingstone: New York, 1996; 743–810.
19. Vyas NA, Vink JS, Ghidini A, Pezzullo JC, Korker V, Landy HJ, Poggi SH. Risk factors for cervical insufficiency after term delivery. *Am J Obstet Gynecol* 2006; **195**: 787–791.

20. Berghella V, Gimovsky AC, Levine LD, Vink J. Cesarean in the second stage: a possible risk factor for subsequent spontaneous preterm birth. *Am J Obstet Gynecol* 2017; **217**: 1–3.
21. Quinones JN, Gomez D, Hoffman MK, Ananth CV, Smulian JC, Plante LA, Skupski DW, Fuchs KM, Scorza WE. 250: Length of the second stage of labor and risk of preterm delivery in a subsequent pregnancy. *Am J Obstet Gynecol* 2016; **214**: S147.
22. Zimmer EZ, Bardin R, Tamir A, Bronshtein M. Sonographic imaging of cervical scars after Cesarean section. *Ultrasound Obstet Gynecol* 2004; **23**: 594–598.
23. Vink JY, Qin S, Brock CO, Zork NM, Feltovich HM, Chen X, Urie P, Myers KM, Hall TJ, Wapner R, Kitajewski JK. A new paradigm for the role of smooth muscle cells in the human cervix. *Am J Obstet Gynecol* 2016; **215**: 478.e1–11.
24. Levine LD, Srinivas SK. Length of second stage of labor and preterm birth in a subsequent pregnancy. *Am J Obstet Gynecol* 2016; **214**: 535.e1–4.
25. Spencer C, Murphy D, Bewley S. Caesarean delivery in the second stage of labour. *Br Med J* 2006; **333**: 613–614.
26. Bailey PE. The disappearing art of instrumental delivery: Time to reverse the trend. *Int J Gynecol Obstet* 2005; **91**: 89–96.
27. Donnez O, Donnez J, Orellana R, Dolmans MM. Gynecological and obstetrical outcomes after laparoscopic repair of a cesarean scar defect in a series of 38 women. *Fertil Steril* 2017; **107**: 289–296.e2.
28. Vervoort AJMW, Uittenbogaard LB, Hehenkamp WJK, Brölmann HAM, Mol BWJ, Huirne JAF. Why do niches develop in Caesarean uterine scars? Hypotheses on the aetiology of niche development. *Hum Reprod* 2015; **30**: 2695–2702.
29. Vikhareva O, Rickle GS, Lavesson T, Nedopekina E, Brandell K, Salvesen KÅ. Hysterotomy level at Cesarean section and occurrence of large scar defects: a randomized single-blind trial. *Ultrasound Obstet Gynecol* 2019; **53**: 438–442.
30. Hall M, Vousden N, Carter J, Hezelgrave N, Shennan AH. Prevention of mid-trimester loss following full dilatation caesarean section: A potential role for transabdominal cervical cerclage. *J Obstet Gynaecol (Lahore)* 2015; **35**: 98–99.
31. Fiocchi F, Petrella E, Nocetti L, Currà S, Ligabue G, Costi T, Torricelli P, Facchinetti F. Transvaginal ultrasound assessment of uterine scar after previous caesarean section: comparison with 3T-magnetic resonance diffusion tensor imaging. *Radiol Medica* 2014; **120**: 228–238.