

Letter on Genovese et al.'s "Impact of Hysterotomy Closure Technique on Subsequent Cesarean Scar Defects Formation: A Systematic Review"

Sanne I. Stegwee^{a,b} Carry Verberkt^a Judith A.F. Huirne^{a,c}

^aDepartment of Obstetrics and Gynaecology, Research Institute 'Amsterdam Reproduction and Development', Amsterdam UMC, Amsterdam, The Netherlands; ^bDepartment of Obstetrics and Gynaecology, Erasmus Medical Center, Rotterdam, The Netherlands; ^cDepartment of Obstetrics and Gynaecology, Amsterdam UMC, Amsterdam, The Netherlands

Keywords

Uterine closure · Single-layer · Double-layer · Unlocked · Meta-analysis

We have read the systematic review of Genovese et al. [1] with interest. Since the same topic has been studied by our study group, we would like to raise some issues.

This systematic review gives a good overview of the most recent evidence on this topic. We believe it is a strength that the authors compared single- and double-layer as clearly as possible by leaving out studies in which locked techniques and endometrial-saving techniques were used since they might interfere with the outcome. Furthermore, almost all included studies were performed in women undergoing a first CS, except for the study of Bamberg et al. [2] which is good to prevent confounding.

However, in our opinion, it is not right that the authors concluded that "double-layer closure ensures a better healing process of the uterine incision" when no pooling of data has taken place. As far as we are aware, no quantitative data support the statement of Genovese et al. [1] that double-layer closure after CS is superior to single-layer closure. The fact that several guidelines recommend a specific suture technique is, in our opinion, no reason to

not further elaborate on this comparison: the NICE guideline has been updated in March 2021 and now states "as there was no difference between single and double layer closure for the majority of outcomes, the committee agreed that either technique could be used" [3]. The ERASSR recommendation [4] of double-layer closure (low level of evidence, weak recommendation grade) is based on a higher prevalence of uterine rupture after single-layer closure, reported in a retrospective cohort study published in 2002 in which locked sutures were used [5], and they also state that more recent evidence does not show superiority of any of the techniques [6].

To quantitatively support the conclusions of Genovese et al. [1], we have performed a meta-analysis based on their data to compare single- with double-layer closure and included the same studies, for the outcomes "niche prevalence" (dichotomous outcome, 6 studies of which 4 RCT's included) [2, 7–11] and "residual myometrium thickness" (continuous outcome, 4 RCT's included) [2, 7, 8, 11]. There is no evidence for the superiority of double-layer closure regarding both outcomes, although no figures could be presented in this letter. Niche prevalence was not different between groups (71.8% after single-layer closure vs. 62.1% after double-layer closure, both including the endometrium, RR 1.02, 95% CI: 0.97–1.08, I^2 67%, $p = 0.42$). Residual

myometrium thickness was slightly thinner after single-layer closure including the endometrium: weighted mean difference -0.26 mm (95% CI: -0.51 to -0.01 , I^2 87%, $p = 0.05$), although the clinical relevance of this difference is of course debatable.

Although the hypothesis of our clinical trial was also that double-layer uterine closure could reduce niche prevalence and related symptoms, based on our systematic review and meta-analysis [12], we did not prove this in our large RCT the “2Close study” [11]. As stated in Table 2 in the article of Genovese et al. [1], we found a small difference in niche prevalence in favour of single-layer closure. All other short-term outcomes, including perioperative findings and ultrasound measurements after 3 months, as well as bleeding disorders and quality of life at 9 months follow-up, were not different. Our long-term results at 3 years follow-up will be published soon. We believe that this is enough evidence that single- and double-layer uterine closure can be performed equally, based on safety outcomes, ultrasound findings, and clinical symptoms.

There are, however, some recommendations to make for future studies. Not only other uterine suture factors, for example, inclusion or exclusion of the serosa and decidua but also continuous versus interrupted sutures might be topics of future studies. The level of the uterotomy, correct approximation of the wound edges of the uterotomy, and proper training of residents, and also the use of specific suture material, are additional factors that might contribute to niche development [13, 14].

Above all, more evidence is needed before solid conclusions can be drawn. For the design of new studies,

we advise to perform standardized evaluation of the sonographic scar as has been consented upon among experts [15]. To facilitate implementation, we have also developed an e-learning on how to measure the niche that is freely available [16]. Furthermore, we advise to assess, besides sonographic outcomes, also short- and in particular long-term outcomes including fertility and obstetric outcomes since these are more important for the individual patient. Properly designed studies including long-term clinical outcomes will enable us to develop future preventive strategies for the development of niche-related problems.

Conflict of Interest Statement

Judith Huirne received a grant from ZonMw for the execution of the 2Close trial; she received a grant from PlantTec for the execution of a pilot study (4DryField) to study the effect of adhesion barrier on niche formation and gynaecological complaints. Both funders had no role in the preparation of the currently presented data or the creation of the current manuscript. She received a grant from Samsung and a fee from Olympus, all outside the submitted work. The remaining authors report no conflict of interest.

Author Contributions

Sanne I. Stegwee performed the analyses and drafted the first version of the manuscript. Carry Verberkt and Judith A.F. Huirne interpreted the data and critically revised the manuscript. All authors approved the current version to be published.

References

- 1 Genovese F, Schiattarella A, D’Urso G, Vitale SG, Carugno J, Verzi G, et al. Impact of hysterotomy closure technique on subsequent cesarean scar defects formation: a systematic review. *Gynecol Obstet Invest*. 2023;88(2):81–90.
- 2 Bamberg C, Hinkson L, Dudenhausen JW, Bujak V, Kalache KD, Henrich W. Longitudinal transvaginal ultrasound evaluation of cesarean scar niche incidence and depth in the first two years after single- or double-layer uterotomy closure: a randomized controlled trial. *Acta Obstet Gynecol Scand*. 2017;96(12):1484–9.
- 3 Excellence NifHaC. *Caesarean birth*. NICE guideline; 2023.
- 4 Caughey AB, Wood SL, Macones GA, Wrench IJ, Huang J, Norman M, et al. Guidelines for intraoperative care in cesarean delivery: enhanced recovery after surgery society recommendations (Part 2). *Am J Obstet Gynecol*. 2018;219(6):533–44.
- 5 Bujold E, Bujold C, Hamilton EF, Harel F, Gauthier RJ. The impact of a single-layer or double-layer closure on uterine rupture. *Am J Obstet Gynecol*. 2002;186(6):1326–30.
- 6 Dodd JM, Anderson ER, Gates S, Grivell RM. Surgical techniques for uterine incision and uterine closure at the time of caesarean section. *Cochrane Database Syst Rev*. 2014;(7):Cd004732.
- 7 Bennich G, Rudnicki M, Wilken-Jensen C, Lousen T, Lassen PD, 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(4):417–22.
- 8 Hanacek J, Vojtech J, Urbankova I, Krcmar M, Křepelka P, Feyereisl J, et al. Ultrasound cesarean scar assessment one year postpartum in relation to one- or two-layer uterine suture closure. *Acta Obstet Gynecol Scand*. 2020;99(1):69–78.
- 9 Hayakawa H, Itakura A, Mitsui T, Okada M, Suzuki M, Tamakoshi K, et al. Methods for myometrium closure and other factors impacting effects on cesarean section scars of the uterine segment detected by the ultrasonography. *Acta Obstet Gynecol Scand*. 2006;85(4):429–34.
- 10 Kataoka S, Tanuma F, Iwaki Y, Iwaki K, Fujii T, Fujimoto T. Comparison of the primary cesarean hysterotomy scars after single- and double-layer interrupted closure. *Acta Obstet Gynecol Scand*. 2016; 95(12):1352–8.
- 11 Stegwee SI, Voet L, Ben A, Leeuw R, Ven P, Duijnhoven RG, et al. Effect of single- versus double-layer uterine closure during caesarean section on postmenstrual spotting (2Close): multicentre, double-blind, randomised controlled superiority trial. *BJOG*. 2020;128(5): 866–78.

- 12 Stegwee SI, Jordans IPM, van der Voet LF, van de Ven PM, Ket JCF, Lambalk CB, et al. Uterine caesarean closure techniques affect ultrasound findings and maternal outcomes: a systematic review and meta-analysis. *BJOG*. 2018;125(9):1097–108.
- 13 Stegwee SI, van der Voet LFL, Heymans MW, Kapiteijn K, van Laar J, van Baal WMM, et al. Prognostic model on niche development after a first caesarean section: development and internal validation. *Eur J Obstet Gynecol Reprod Biol*. 2023;283: 59–67.
- 14 Sholapurkar SL. Etiology of cesarean uterine scar defect (Niche): detailed critical analysis of hypotheses and prevention strategies and peritoneal closure debate. *J Clin Med Res*. 2018;10(3):166–73.
- 15 Jordans IPM, de Leeuw RA, Stegwee SI, Amso NN, Barri-Soldevila PN, van den Bosch T, et al. Sonographic examination of uterine niche in non-pregnant women: a modified Delphi procedure. *Ultrasound Obstet Gynecol*. 2019;53(1):107–15.
- 16 Verberkt C, Jordans IPM, Van den Bosch T, Timmerman D, Bourne T, de Leeuw RA, et al. How to perform standardized sonographic examination of uterine niche in non-pregnant women. *Ultrasound Obstet Gynecol*. 2022;60(3):420–4.