Trial of labor or elective cesarean delivery for low-lying placenta? A propensity score analysis.

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Précis

Trial of labor in women with low-lying placenta around term is not associated with higher risks of maternal or neonatal complications than elective cesarean delivery.

Abstract

OBJECTIVE: To compare outcomes of women with low-lying placenta by their planned mode of delivery and according to the internal os distance (IOD), while using propensity score analysis to ensure the study groups' comparability and minimize indication bias.

METHODS: Six tertiary maternity hospitals in France participated in this retrospective multicenter study of births from 2007 through 2012. Women with a low-lying placenta, defined as an IOD ≤ 20mm who gave birth after 35 weeks of gestation were included and classified in the planned trial of labor or elective cesarean groups. The main endpoint was severe postpartum hemorrhage, defined as blood loss exceeding 1,000 mL. Secondary outcomes were composite variables of severe maternal and neonatal morbidity. Using multivariable logistic regression and propensity score methods, we compared outcomes by planned mode of delivery.

RESULTS: Among 128,233 births during the study period, 171 (0.13%) women had a low-lying placenta: 70 (40.9%) in the trial-of-labor group and 101 (59.1%) with elective cesareans. The vaginal delivery rate in the trial-of-labor group was 50.0% (19/38) in the 11-20 mm subgroup and 18.5% (5/27) in the 1-10 mm subgroup. Severe postpartum hemorrhage occurred in 22.9% (16/70, 95% confidence interval [CI] 13.7–34.4) of the trial-of-labor group and 23.9% (23/101, 95%CI 15.2–32.5) of those with elective cesareans (*P*=.9); severe maternal and neonatal morbidity rates were likewise similar (respectively 2.9% versus 2.0%, *P*=.7, and 12.9% versus 9.9%, *P*=.5). Attempted labor was not significantly associated with a higher rate of severe postpartum hemorrhage after multivariable logistic regression and propensity score-weighted analysis: respectively aOR 1.42, 95%CI 0.62–3.24, *P*=0.4, and aOR 1.34, 95%CI 0.53–3.38, *P*=.5.

CONCLUSION: Our results support a policy of offering trial of labor to women with a low-lying placenta after35 weeks and an IOD of 11-20mm. An IOD of 1-10mm reduces considerably the likelihood of vaginal birth compared to 11-20mm but without increasing the incidence of severe postpartum hemorrhage or severe maternal morbidity.

Key words: low-lying placenta, placenta previa, trial of labor, cesarean delivery, maternal morbidity, propensity score, postpartum hemorrhage.

Introduction

Low-lying placenta, defined as a distance between the cervical os and the placenta (internal os distance, IOD) ≤ 20 mm is a cause of maternal and neonatal morbidity and mortality.[1-4] It increases the risk of ante-, intra-, and post-partum hemorrhage, blood transfusion, hysterectomy, sepsis, and thrombophlebitis.[5] The prevalence low-lying placenta has increased over the past two decades due to rising numbers of cesarean deliveries[6-8] and of pregnancies resulting from medically assisted reproduction.[6,9,10] Their combined prevalence of both placenta previa (defined as the placenta lying directly over the internal os) and low-lying placenta in the literature varies widely and is estimated at around 0.5% of pregnancies at term.[3,7]

All national guidelines and expert opinions on the management of placenta previa have recommended delivery by elective cesarean delivery between 36 and 38 weeks of gestation in women with uncomplicated placenta previa.[2-5,11] A broad consensus also exists to propose trial of labor at term to women with an IOD > 20 mm in the absence of other contraindications. By contrast, for women with a third-trimester asymptomatic low-lying placenta,[1] mode of delivery remains controversial. No guidelines exist in the USA[3,5] to guide this decision. Practices seem likely to be similar to those in Canada[4] where an elective cesarean is recommended for an IOD ≤ 10 mm due to the high hemorrhage risk, while individualized management is proposed when the edge is between 11 and 20 mm from the os, in the absence of antenatal complications. In the UK[2] and France,[11] the mode of delivery in women with a third-trimester asymptomatic low-lying placenta is based on her clinical background and her preferences, supplemented by transvaginal ultrasound imaging of the placental position.

Only a few studies have examined perinatal outcomes in women diagnosed with a low-lying placenta at term.[12-20] None provide data on antenatal symptoms or on the indication for either planned mode of delivery. Furthermore, most used study protocols that did not take the intended treatment into account and were thus likely to introduce a selection bias.[12-17,19,20] A randomized controlled trial might resolve this question, but difficulties in recruiting and ethical concerns undoubtedly make such a study impossible.

Our study's aim was to evaluate and compare the maternal and neonatal morbidity of women with a low-lying placenta according to their planned mode of delivery and stratified by the IOD at the last ultrasound examination before delivery, while using propensity score analysis to ensure comparability of the study groups and minimize the indication bias.

Materials and Methods

Six tertiary maternity hospitals in France participated in this retrospective multicenter study of births from 2007 through 2012. Each hospital searched their database for all consecutive case files with one of the following International Classification of Diseases, 10th edition (ICD-10) codes: ICD-10 O44 and O43.2. These codes correspond to placenta previa and low-lying placenta, with or without hemorrhage and to placenta accreta spectrum (PAS). Each paper file was first reviewed by two independent investigators (PJ and VR) to identify only low-lying placenta and avoid misclassification. Women were not eligible for the study if their medical files were incomplete, contained a classification error, or if the delivery took place outside a participating center. Then, each medical charts were reviewed to include women who met the inclusion criteria: women with singleton or multiple pregnancies who were diagnosed with a low-lying placenta (IOD less than 20 mm at the last transvaginal ultrasound before delivery) and gave birth at or after 35 weeks of gestation. Exclusion criteria included placenta previa, antenatal suspicion of PAS, and termination of pregnancy. The inclusion and diagnostic criteria were the same for all six centers.

In France, in addition to the last mandatory ultrasound performed at 32 weeks of gestation where the placental location must be mentioned, an additional ultrasound is recommended in case of placenta previa or low-lying placenta at 36 weeks of gestation to determine the IOD and therefore the planned mode of delivery.[11]

For each center, medical charts were reviewed to collect the following data: maternal baseline clinical characteristics, course of labor, mode of delivery, postpartum hemorrhage, and maternal and neonatal outcomes. We also sought to retrieve variables that might have influenced the choice of the planned mode of delivery. The

Research Ethics Committee at Angers University Hospital Center (Ref 2013/50) approved this study.

The main endpoint was severe primary postpartum hemorrhage, defined as blood loss more than 1,000 mL within 24 hours after delivery,[21,22] measured with a collector bag in case of vaginal birth and with graduated drapes, suction canister or weighing in case of cesarean delivery.[11,23-25] This endpoint also includes intrapartum blood loss which was cumulative.[11,22] Intrapartum hemorrhage was defined by a blood loss requiring emergency cesarean delivery.[5,11,26] The main secondary endpoint was severe maternal morbidity, as previously described [24, 27-29] and defined by any one of the following: use of uterine artery embolization or emergency surgery to control postpartum hemorrhage, transfusion of more than 5 units of packed red blood cells, transfer to the intensive care unit (ICU), thromboembolic events, and death. Another secondary endpoint was severe neonatal morbidity including: 5-minute Apgar score < 7, umbilical artery pH < 7.10, need for resuscitation or intubation with transfer to the neonatal ICU (NICU), and neonatal death.[30]

Exposure was the planned mode of delivery. Each medical chart was specially reviewed by two independent investigators (PJ and VR) to ensure among other the accuracy of the planned mode of delivery. Trial of labor was defined as a planned trial of labor per medical records, regardless of ultimate mode of delivery, i.e. successful vaginal delivery or an emergency cesarean performed before or during labor for severe intrapartum bleeding, abnormal fetal heart rate, or failure to progress. An elective cesarean delivery was defined as a planned cesarean per medical records, performed before labor regardless of the indication, or during labor for women entering in labor before the planned date of cesarean delivery recorded in the medical files. Women

with a history of 2 or more cesareans CDs had elective cesareans, in accordance with French guidelines.[31]

Analyses were conducted with STATA software (version 15; StataCorp, College Station, TX). Continuous variables were described by their medians and interquartile ranges (IQR) and compared between groups by a Kruskal-Wallis test. Categorical variables were described by proportions and compared by Chi2 or Fisher's exact tests, as appropriate.

To control for confounding factors that might have influenced both the choice of the planned mode of delivery and the primary endpoint, we began the analysis with logistic regression models with multiple adjustments to estimate crude and adjusted odds ratios (aORs) and their 95% confidence intervals (CIs). Variables included in the multivariable analysis were chosen based on the literature and other hypotheses of potential confounders. Because practitioners' decisions about planned mode of delivery are probably guided by characteristics of the woman and her pregnancy rather than by chance, we performed a second analysis using a propensity score to limit potential indication bias.[32,33] An inverse probability of treatment weighting based on a propensity score was used to control for factors that might influence both management choice and primary outcome. The propensity score was defined as each woman's probability of attempting labor, based on her individual characteristics, and was estimated with a multivariable logistic regression model including the following covariates: maternal age, body mass index before pregnancy, nulliparity, previous cesarean delivery, recurrent episodes of antepartum hemorrhage, anterior placental location, and distance between the cervical os and the placenta. We assigned women planning to try labor a weight of 1/(propensity score) and those who with an elective

cesarean a weight of 1/(1−propensity score). Balance among covariates was checked by using standardized differences.

A sensitivity analysis was performed with multiple imputation of missing data. The proportion of women with missing data for any covariate included in the main multivariable model ranged from 1% to 8%. We performed multiple imputation chained equations according to Rubin's rules for those missing data (10 data sets imputed).[34] A separate analysis was performed according to IOD, i.e., 1-10 mm and 11-20 mm. A *P* value <.05 was considered significant.

Results

During the study period, the six university hospital centers recorded 128,233 births, including 1,089 coded ICD-10 O44 and O43.2. Figure 1 presents the case selection flowchart: 171 cases were available for analysis, including 70 (40.9%) in the trial-of-labor group and 101 (59.1%) in the elective cesarean group.

Table 1 summarizes maternal and pregnancy characteristics according to planned mode of delivery. Women included in the trial-of-labor group had significantly lower rates of previous cesarean delivery (*P*=.01) and higher rates of both antepartum hemorrhage (*P*<.01) and hospitalization for it (*P*<.01). Recurrent bleeding episodes were less frequent (*P*=.01) in the trial-of-labor group. The median interval (days) between delivery and the last ultrasound was shorter (4 days, IQR 0–16 versus 10.5, IQR 3–17, *P*<.01), and the median IOD was longer (13.5 mm, IQR 9–17 versus 9 mm IQR 0–13, *P*<.01) in the trial-of-labor than in the elective cesarean group.

Table 2 presents the maternal and neonatal outcomes by planned mode of delivery. The rate of severe PPH (> 1,000 mL) was similar in both groups (trial-of-labor group 22.9%, 95%CI 13.7–34.4 versus 23.0%, 95%CI 15.2–32.5, *P*=0.9). The vaginal delivery rate in those planning to attempt labor was 38.6% (27/70). Moreover, the multivariable logistic regression analysis showed that trial of labor was not significantly (aOR 1.42, 95% CI 0.62–3.24, *P*=0.4) associated with a higher rate of severe postpartum hemorrhage after adjustment for maternal age, prepregnancy BMI, nulliparity, previous cesarean delivery, and IOD (Supplemental file A). Results were similar for the multivariable analysis after multiple imputations (aOR 1.39, 95%CI 0.65–2.84, *P*=.5) and for the propensity score-weighted model (aOR 1.34, 95%CI 0.53–3.38, *P*=.5) (Figure 2). Differences in women's characteristics at baseline were well balanced between the two groups after propensity score weighting, with all standardized

differences less than 10%, except for the variable of prepregnancy BMI ≥ 30; its standardized difference was 11% after propensity score weighting (Supplemental file B).

The rate of severe maternal morbidity did not differ significantly between the trial-of-labor and elective cesarean groups (respectively, 2.9% (2/70) versus 2.0% (2/101), *P*=.7), nor did that of severe neonatal morbidity (12.9% (9/70) versus 9.9% (10/101), *P*=.5) (Table 2).

Table 3 compares the perinatal outcomes according to the IOD. In women who planned trial of labor, the rate of vaginal delivery was 50.0% (19/38) in the 11-20 mm subgroup and 18.5% (5/27) in the 1-10 mm subgroup and the rate of emergency cesarean delivery for bleeding before or during labor was 27.0% (10/37) in the 11-20 mm subgroup and 50.0% (13/26) in the 1-10 mm subgroup. Neither maternal nor perinatal outcomes differed significantly between them.

Comment

Our results indicate that almost 40% of women with a low-lying placenta at or near term who attempt labor have a successful vaginal birth with no increase in their risk of maternal or perinatal complications compared to women with elective cesareans. In particular, trial of labor did not result in a higher severe postpartum hemorrhage rate after controlling for confounding by indication with a propensity score analysis. An IOD of 11-20 mm at the last transvaginal ultrasound before delivery increased the chance of a vaginal birth compared to a measurement of 1-10 mm.

Our findings are similar to those of the only study comparing maternal and neonatal outcomes according to planned mode of delivery in women with a low-lying placenta.[18] It was much smaller, including only 18 women with low-lying placentas diagnosed at 36 weeks as well as 6 with an IOD exceeding 20 mm at delivery. The authors did not control for the selection and indication biases, and the mode of delivery was determined by the women's preference.

Our results about the success of vaginal delivery according to the IOD are also consistent with those of a systematic review/meta-analysis by Jansen et al. of 10 studies, including 7 retrospective cohort studies intended to evaluate the likelihood of vaginal delivery in women with a low-lying placenta. Among the 478 such women in this meta-analysis, vaginal delivery was successful at an IOD of 0-10 mm in 43% and of 11-20 mm in 85%. The authors further stated that postpartum hemorrhage did not differ significantly by IOD in any cohorts.[35] Moreover, they underlined that only three studies[13,14,18] compared blood loss by mode of delivery, with inconsistent results[35]: one study found no difference,[14] while two others found significantly more intrapartum hemorrhages and blood transfusions in women with cesarean versus vaginal births.[13,18]

This meta-analysis nonetheless has important limitations. First, most of the studies included in this review used a methodology that did not take the intended treatment into account, and Jansen et al. provide no comparison of maternal outcomes by planned mode of delivery, i.e., cesarean or trial of labor. While they reported that 30-60% of cases chose to deliver by planned cesarean, this could have been due to unfavorable conditions for attempting labor (short IOD, for example), which might have resulted in planned cesareans for the less stable patients and thus overestimation of the success rate of vaginal delivery.[35] Simultaneously, this failure to take the intended treatment into account is likely to have introduced a selection bias by allocating to the trial-of-labor group, women who did not have a an elective cesarean because of their favorable prognosis. Moreover, their inclusion of women with an emergency cesarean during labor due to intrapartum hemorrhage after attempted labor to the cesarean group would also introduce bias by worsening the maternal prognosis in the cesarean group. This may explain why two of the three studies that assessed blood loss by actual mode of delivery found significantly higher blood loss and transfusion rates in the cesarean than in the vaginal group.[13,18] Furthermore, among the studies included in this meta-analysis reporting blood loss by the IOD or the actual rather than planned mode of delivery, only one provided information about how blood loss was assessed (with a collector bag),[18] three studies defined postpartum hemorrhage using different cutoffs for vaginal and cesarean deliveries,[16,19,21] and one did not define postpartum delivery at all.[20] All of these points limit the robustness of the results reported by Jansen et al.[35]

Our data, obtained by using a propensity score to limit indication bias, support a policy of trial of labor for women diagnosed with a low-lying placenta presenting around term with an IOD of 11 -20 mm. Attempting labor is also a possible option for

women when this distance is 1-10 mm as the incidence of blood-loss related maternal outcomes including severe postpartum hemorrhage did not differ between the trial-of-labor and elective cesarean groups. Avoiding unnecessary cesareans in women with low-lying placenta is crucial to limiting the occurrence of low-lying placenta, placenta previa, vasa previa, and placenta accreta spectrum in this population in subsequent pregnancies. Nevertheless, the shared decision-making should emphasize that the need for emergency cesarean during labor was considerably higher in women with the shortest IOD and reached about 80% in this group.

Transvaginal ultrasound has become essential in the diagnosis, follow-up, and management of women with a low-lying placenta. Most studies, including ours, have focused on the IOD. Small, observational, and retrospective studies have suggested that women with a low-lying placenta are more likely to need a cesarean delivery when the placental edge is thicker (>10 mm)[15,36] or contains a sponge-like echo[37] or marginal "sinus".[18] These additional ultrasound features are poorly defined and not routinely assessed in current practice. Their use to advise women with a low-lying placenta about mode of delivery requires further research.

The main strengths of our study were (1) the comparison of trial of labor with elective cesarean delivery, rather than women with vaginal to those with cesarean delivery, as the latter comparison is obviously biased in favor of the vaginal delivery group, and (2) use of propensity score analyses to ensure that the study groups were comparable and to minimize the impact of uncontrolled confounders and especially indication biases linked to mode of delivery.

Second, for our primary analysis, only births at or after 35 weeks' gestation were included to limit cofounding, as no perinatal center had an elective cesarean policy before this gestational age. Thus, before 35 weeks' gestation, it was likely that trial of

labor was allowed only in the most favorable conditions (preterm labor without bleeding), and elective cesarean delivery performed in the poorest conditions (severe antenatal bleeding).

The primary limitation of our cohort study lies in its retrospective design. Nonetheless, all the data of the study cases were collected according to a defined protocol. While eligible cases might have been missed, the combined prevalence of low-lying and placenta previa observed in our study (0.56%) is consistent with rates reported in the literature.[3,7]

Second, unmeasured confounders may persist despite our use of cautious statistical approaches — sensitivity, multivariable, and propensity score analyses. A randomized controlled trial would undeniably be the best study design for comparing the effects of planned mode of delivery, but its feasibility seems doubtful. Third, the infrequency of severe maternal morbidity such as second-line therapies to control postpartum hemorrhage (pelvic arterial embolization or surgical therapies), admission to intensive care, thromboembolic events, or maternal death limited our statistical power to detect potentially clinically meaningful differences between planned modes of delivery. In addition, considering the small difference in postpartum hemorrhage rates between the trial-of-labor and elective cesarean groups (respectively 22.9% versus 23.0%), we acknowledge that our study is underpowered to confirm an absence of difference in maternal adverse outcomes. Nonetheless, a post hoc analysis determined that with a sample size of 171 patients and 23% of deliveries complicated by severe postpartum hemorrhage in the unexposed group (elective cesarean group), the study would have had a power of 80% and an alpha risk of 0.05, able to detect an OR > 2.5 in the univariate logistic regression. It would also have been able to detect an OR > 2.5 in univariate logistic regression for the risk of postpartum hemorrhage

above 500 mL. Lastly, since our data are quite dated, we cannot exclude that practices of antenatal imaging and labor management may have evolved.

Conclusion

Our results support a policy of offering trial of labor to women with a low-lying placenta at or after 35 weeks of gestation and a distance of 11–20 mm between the placental edge and the internal os on ultrasound. While a distance of 1–10 mm does not increase the incidence of severe postpartum hemorrhage or severe maternal morbidity, it strongly reduces the likelihood of successful vaginal delivery, compared with 11-20 mm, from 50% to 18.5%.

References

1. Reddy UM, Abuhamad AZ, Levine D, Saade GR, Fetal imaging: Executive Summary of a Joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Institute of Ultrasound in Medicine, American College of Obstetricians and Gynecologists, American College of Radiology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound Fetal Imaging Workshop. Am J Obstet Gynecol. 2014;210:387-97. doi: 10.1016/j.ajog.2014.02.028.
2. Jauniaux E, Alfirevic Z, Bhide AG, Belfort MA, Burton GJ, Collins SL et al; Royal College of Obstetricians and Gynaecologists. Placenta Praevia and Placenta Accreta: Diagnosis and Management: Green-top Guideline No. 27a. BJOG. 2019;126:e1-e48. doi: 10.1111/1471-0528.15306.
3. Silver RM. Abnormal Placentation: Placenta Previa, Vasa Previa, and Placenta Accreta. Obstet Gynecol. 2015;126:654–68. doi: 10.1097/AOG.0000000000001005.
4. Jain V, Bos H, Bujold E. Guideline No. 402: Diagnosis and Management of Placenta Previa. J Obstet Gynaecol Can. 2020;42:906-917.e1. doi: 10.1016/j.jogc.2019.07.019.
5. Gyamfi-Bannerman C. Society for Maternal-Fetal Medicine (SMFM) Consult Series #44: Management of bleeding in the late preterm period. Am J Obstet Gynecol. 2018;218:B2-8. doi: 10.1016/j.ajog.2017.10.019.
6. Jauniaux E, Silver RM. Rethinking prenatal screening for anomalies of placental and umbilical cord implantation. Obstet Gynecol. 2020;136:1211-1216. doi: 10.1097/AOG.0000000000004175.

7. Jauniaux E, Grønbeck L, Bunce C, Langhoff-Roos J, Collins SL. Epidemiology of placenta previa accreta: a systematic review and meta-analysis. BMJ Open. 2019;9(11):e031193. doi:10.1136/bmjopen-2019-031193.
8. Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: Systematic review and meta-analysis. PLoS Med. 2018;15:e1002494. doi: 10.1371/journal.pmed.1002494.
9. Jauniaux E, Moffett A, Burton GJ. Placental Implantation Disorders. Obstet Gynecol Clin North Am. 2020;47:117-32. doi: 10.1016/j.ogc.2019.10.002.
10. Petersen SH, Bergh C, Gissler M, Åsvold BO, Romundstad LB, Tiitinen A, Spangmose AL, et al. Time trends in placenta-mediated pregnancy complications after assisted reproductive technology in the Nordic countries. Am J Obstet Gynecol. 2020;223:226.e1-226.e19. doi: 10.1016/j.ajog.2020.02.030.
11. Sentilhes L, Vayssière C, Deneux-Tharaux C, Aya AG, Bayoumeu F, Bonnet M-P, et al. Postpartum hemorrhage: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). Eur J Obstet Gynecol Reprod Biol. 2016;198:12-21. doi: 10.1016/j.ejogrb.2015.12.012.
12. Matsubara S, Ohkuchi A, Kikkawa M, Izumi A, Kuwata T, Usui R, et al. Blood loss in low-lying placenta: placental edge to cervical internal os distance of less vs. more than 2 cm. J Perinat Med. 2008;36:507-12. doi: 10.1515/JPM.2008.089.
13. Bronsteen R, Valice R, Lee W, Blackwell S, Balasubramaniam M, Comstock C. Effect of a low-lying placenta on delivery outcome. Ultrasound Obstet Gynecol. 2009;33:204-8. doi: 10.1002/uog.6304.

14. Vergani P, Ornaghi S, Pozzi I, Beretta P, Russo FM, Follesa I, et al. Placenta previa: distance to internal os and mode of delivery. Am J Obstet Gynecol. 2009;201:266.e1-266.e5. doi: 10.1016/j.ajog.2009.06.009.
15. Bhide A, Prefumo F, Moore J, Hollis B, Thilaganathan B. Placental edge to internal os distance in the late third trimester and mode of delivery in placenta praevia. BJOG. 2003;110:860-4. doi: DOI:10.1016/S1470-0328(03)02991-4.
16. Al Wadi K, Schneider C, Burym C, Reid G, Hunt J, Menticoglou S. Evaluating the Safety of Labour in Women With a Placental Edge 11 to 20 mm From the Internal Cervical Os. J Obstet Gynaecol Can. 2014;36:674-7. doi: 10.1016/S1701-2163(15)30508-9.
17. Wortman AC, Twickler DM, McIntire DD, Dashe JS. Bleeding complications in pregnancies with low-lying placenta. J Matern Fetal Neonatal Med. 2016;29:1367-71. doi: 10.3109/14767058.2015.1051023.
18. Taga A, Sato Y, Sakae C, Satake Y, Emoto I, Maruyama S, et al. Planned vaginal delivery versus planned cesarean delivery in cases of low-lying placenta. J Matern Fetal Neonatal Med. 2017;30:618-22. doi: 10.1080/14767058.2016.1181168.
19. Alouini S, Megier P, Fauconnier A, Huchon C, Fievet A, Ramos A, et al. Diagnosis and management of placenta previa and low placental implantation. J Matern Fetal Neonatal Med. 2020;33:3221-6. doi: 10.1080/14767058.2019.1570118.
20. Ornaghi S, Vaglio Tessitore I, Vergani P. Pregnancy and delivery outcomes in women with persistent versus resolved low-lying placenta in the late third trimester. J Ultrasound Med. 2021. doi: 10.1002/jum.15687.

21. Bienstock JL, Eke AC, Hueppchen NA. Postpartum Hemorrhage. N Engl J Med. 2021;384(17):1635-45. doi: 10.1056/NEJMra1513247.
22. Practice Bulletin No. 183: Postpartum Hemorrhage. Obstet Gynecol. oct 2017;130(4):e168-86. doi: 10.1097/AOG.0000000000002351.
23. Deneux-Tharaux C, Sentilhes L, Maillard F, Closset E, Vardon D, Lepercq J, et al. Effect of routine controlled cord traction as part of the active management of the third stage of labour on postpartum haemorrhage: multicentre randomised controlled trial (TRACOR). BMJ. 2013;346:f1541. doi: 10.1136/bmj.f1541.
24. Sentilhes L, Winer N, Azria E, Sénat M-V, Le Ray C, Vardon D, et al. Tranexamic Acid for the Prevention of Blood Loss after Vaginal Delivery. N Engl J Med. 2018;379:731-42. doi: 10.1056/NEJMoa1800942.
25. Sentilhes L, Sénat MV, Le Lous M, Winer N, Rozenberg P, Kayem G, et al. Tranexamic Acid for the Prevention of Blood Loss after Cesarean Delivery. N Engl J Med. 2021;384(17):1623-1634. doi:10.1056/NEJMoa2028788
26. Ornaghi S, Colciago E, Vaglio Tessitore I, Abbamondi A, Antolini L, Locatelli A, et al. Mode of birth in women with low-lying placenta: protocol for a prospective multicentre 1:3 matched case-control study in Italy (the MODEL-PLACENTA study). BMJ Open. 2021;11(12):e052510. doi: 10.1136/bmjopen-2021-052510.
27. Sentilhes L, Gromez A, Razzouk K, Resch B, Verspyck E, Marpeau L. B-Lynch suture for massive persistent postpartum hemorrhage following stepwise uterine devascularization. Acta Obstet Gynecol Scand. 2008;87:1020-6. doi: 10.1080/00016340802380750.
28. Sentilhes L, Gromez A, Clavier E, Resch B, Verspyck E, Marpeau L. Predictors of Failed Pelvic Arterial Embolization for Severe Postpartum Hemorrhage. Obstet Gynecol. 2009;113:992-9. doi: 10.1097/AOG.0b013e3181a114f7.

29. Sentilhes L, Trichot C, Resch B, Sergent F, Roman H, Marpeau L, et al. Fertility and pregnancy outcomes following uterine devascularization for severe postpartum haemorrhage. Hum Reprod. 2008;23:1087-92. doi: 10.1093/humrep/den049.
30. Ducarme G, Hamel J-F, Bouet P-E, Legendre G, Vandenbroucke L, Sentilhes L. Maternal and neonatal morbidity after attempted operative vaginal delivery according to fetal head station. Obstet Gynecol. 2015;126:521-9. doi: 10.1097/AOG.0000000000001000.
31. Sentilhes L, Vayssière C, Beucher G, Deneux-Tharaux C, Deruelle P, Diemunsch P, et al. Delivery for women with a previous cesarean: guidelines for clinical practice from the French College of Gynecologists and Obstetricians (CNGOF). Eur J Obstet Gynecol Reprod Biol. 2013;170:25-32. doi: 10.1016/j.ejogrb.2013.05.015.
32. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika. 70:41-55. https://doi.org/10.1093/biomet/70.1.41
33. Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. Multivar Behav Res. 2011;46:399-424. doi: 10.1080/00273171.2011.568786.
34. Rubin DB, Schenker N. Multiple imputation in health-are databases: An overview and some applications. Stat Med. avr 1991;10(4):585-98. doi: 10.1002/sim.4780100410.
35. Jansen C, Mooij Y, Blomaard C, Derks J, Leeuwen E, Limpens J, et al. Vaginal delivery in women with a low-lying placenta: a systematic review and meta-analysis. BJOG. 2019;126:1118-26. doi: 10.1111/1471-0528.15622.

36. Ghourab S. Third-trimester transvaginal ultrasonography in placenta previa: does the shape of the lower placental edge predict clinical outcome? Ultrasound Obstet Gynecol 2001;18:103–8. doi: 10.1046/j.1469-0705.2001.00420.x.
37. Saitoh M, Ishihara K, Sekiya T, Araki T. Anticipation of uterine bleeding in placenta previa based on vaginal sonographic evaluation. Gynecol Obstet Invest 2002;54:37–42. doi: 10.1159/000064695.

480 # Tables

481 **Table 1.** Maternal Characteristics of the Study Population by Planned Mode of Delivery

482 (n=171).

Maternal Characteristics	Trial of Labor group n = 70	Elective Cesarean Delivery group n = 101	*P*
Maternal age (y) median [IQR]	31 [28-35]	32 [29-35]	.7
> 30	39 (55.7)	58 (57.4)	.8
BMI before pregnancy (kg/m^2) median [IQR]	22 [19-26]	23 [20-25]	.5
<18.5	12 (18.2)	10 (10.9)	.4
[18.5-25[	37 (56.1)	60 (65.2)	
[25-30[	11 (16.7)	17 (18.5)	
≥ 30	6 (9.1)	5 (5.4)	
Tobacco use during pregnancy	11 (15.7)	23 (22.8)	.4
Drug addiction	2 (2.9)	0	.2
Preexisting hypertensive disorder	1 (1.3)	2 (2.0)	.8
Nulliparity	20 (28.6)	30 (29.7)	.9
Multiple gestation	1 (1.4)	5 (5.0)	.2
Previous uterine curettage	10 (14.3)	30 (29.7)	.05
Previous myomectomy	0	3 (3.0)	.1
Previous cesarean delivery	3 (4.3)	17 (16.8)	.01
Previous postpartum hemorrhage	5 (7.1)	5 (5.0)	.5
Previous placenta previa	2 (2.9)	2 (2.0)	.7
Previous preterm birth	3 (4.3)	7 (6.9)	.5
Medically assisted reproduction	6 (8.6)	13 (12.9)	.4
Antepartum hemorrhage *	54 (77.1)	52 (51.5)	<.01
First episode <29 weeks †	7 (13.0)	11 (21.2)	.3
Recurrent episodes ≥ 3	7 (9.4)	25 (25.0)	.01
Antepartum hospitalization	54 (77.1)	67 (66.3)	.1
for antepartum hemorrhage †	51 (82.3)	48 (60.7)	<.01
Interval between delivery and last ultrasound scan (d) median [IQR]	4 [0-16]	10.5 [3-17]	<.01
Anterior placental location	17 (24.6)	28 (28.0)	.6
Internal os distance median [IQR]	13.5 [9-17]	9 [0-13]	< .01
0-10 mm ‡	27 (41.5)	67 (68.4)	< .01

11-20 mm ‡	38 (58.5)	31 (31.6)	< .01

BMI: body mass index; IQR: interquartile range.

* Antepartum hemorrhage was defined by a blood loss during the pregnancy not requiring an immediate birth.[4,5] Gestational age of the first episode of antepartum hemorrhage < 29 weeks gestation and number of recurrent episodes of antepartum hemorrhage (≥3) are both associated with increased risk of emergency cesarean delivery.[4]

Continuous data are expressed as medians [IQR] when specified; discrete data are expressed as n (%). Kruskal-Wallis, χ2, and Fisher's exact tests were used as appropriate. A *P* value of .05 was considered significant.

† Missing data: > 10%.

‡ There were 5 and 3 missing data for the planned trial of labor and cesarean groups, respectively, because in these cases, the cervix-to-placenta distance was reported as <20 mm but not otherwise specified.

496 **Table 2**. Maternal and Neonatal Outcomes by Planned Mode of Delivery (n=171).

497

Outcomes	Trial of Labor group n = 70	Elective Cesarean Delivery group n = 101	*P*
Maternal outcomes			
Primary outcome			
Severe PPH ≥ 1,000 mL	16 (22.9)	23 (23.0)	.9
Mode of delivery			
Cesarean delivery	43 (61.4)	101 (100.0)	<.01
Emergency cesarean before labor for hemorrhage*,†	15/68 (22.1)	21/31 (67.7)	<.01
Emergency cesarean during labor for hemorrhage*,†	10/68 (14.7)	1/31 (3.2)	<.01
General endotracheal anesthesia	13/43 (30.2)	26/101 (25.7)	.6
Vaginal delivery	27 (38.6)	0	< .01
Operative vaginal delivery	2 (2.9)	0	0.2
Estimated blood loss (mL) ‡ median [IQR]	500 [300-950]	675 [350-1000]	.8
Postpartum hemorrhage ≥ 500 mL	32 (45.7)	53 (53.0)	.4
Use of additional uterotonic agent	5 (7.1)	7 (6.9)	.9
Blood transfusion			
Red blood cells	6 (8.6)	7 (6.9)	.7
> 5 units of packed red blood cells transfused	0	1 (1.0)	.4
Fresh frozen plasma	2 (2.9)	2 (2.0)	.7
Fibrinogen	1 (1.4)	0	.2
Pelvic arterial embolization	1 (1.4)	0	.2
Second-line surgical therapies §	1 (1.4)	1 (1.0)	.7
Admission to intensive care	0	1 (1.0)	.4
Length of hospital stay (days) median [IQR]	5 [4-6.5]	6 [5-6]	.2
Postpartum anemia (< 10 g/dL) during hospital stay	48 (69.6)	68 (67.3)	.7
Thromboembolic events	0	0	
Postpartum fever ‖	0	1 (1.0)	
Sepsis ‖	0	1 (1.0)	
Maternal death	0	0	
Severe maternal morbidity ¶	2 (2.9)	2 (2.0)	.7
Neonatal outcomes			
Gestational age at delivery median [IQR]	38 [36-40]	37 [37-38]	.05

between 35^0 and 36^6 weeks	20 (28.6)	20 (19.8)	.2
between 37^0 and 39^6 weeks	33 (47.1)	79 (78.2)	<.01
≥ 40^0 weeks	17 (24.3)	2 (2.0)	<.01
Birthweight (g) median [IQR]	3050 [2665-3460]	2985 [2780-3275]	.5
Umbilical cord arterial pH < 7.10	1 (1.7)	1 (1.0)	.8
Apgar score < 7 at 5 minutes	5 (7.3)	3 (3.0)	.2
Respiratory distress syndrome	9 (12.9)	5 (5.0)	.06
Need for resuscitation or intubation	5 (7.1)	8 (7.9)	.8
Transfer to neonatal intensive care unit	14 (20.0)	11 (10.9)	.1
Neonatal death	1 (1.4)	0	.2
Severe neonatal morbidity #	9 (12.9)	10 (9.9)	.5

IQR: interquartile range

Continuous data are expressed as medians [IQR] when specified; discrete data are expressed as n (%). Kruskal-Wallis, $\chi 2$, and Fisher's exact tests were used as appropriate. A *P* value of .05 was considered significant.

* Missing data: > 10%.

† Other indications for cesarean deliveries were abnormal fetal heart rate without hemorrhage during labor and protracted labor.

‡ There were 15 and 21 missing data for the planned trial of labor group and 21 for elective cesarean groups.

§ Second-line surgical therapies: uterine compression sutures, vessel ligation, and peripartum hysterectomy for management of massive primary postpartum hemorrhage after uterine massage and uterotonic agents failed to stop bleeding.

‖ Postpartum fever was defined by an isolated postpartum fever higher than 38.5°C, and sepsis by a positive blood culture.

¶ Severe maternal morbidity, defined by any one of the following: uterine artery embolization or emergency surgery to control PPH (i.e., vessel ligation and/or uterine compression sutures and/or peripartum hysterectomy), transfusion of more than 5 units of packed red blood cells, transfer to intensive care unit, thromboembolic events, or death.

Severe neonatal morbidity, defined by any one of the following: 5-minute Apgar score less than 7, umbilical artery pH less than 7.10 (umbilical artery blood gas values were routinely measured), need for resuscitation or intubation, and neonatal death.

520 **Table 3.** Maternal and Neonatal Outcomes by Planned Mode of Delivery for Women

521 with Cervix-to-Placenta distances of 1-10 mm and 11-20 mm (n=163)*.

Outcomes	**Internal Os Distance: 1-10 mm**			**Internal Os Distance: 11-20 mm**		
	Trial of Labor n = 27	Elective Cesarean Delivery n = 67	*P*	Trial of Labor n = 38	Elective Cesarean Delivery n = 31	*P*
Maternal outcomes						
Severe postpartum hemorrhage ≥1,000 mL	5 (18.5)	19 (28.8)	.3	10 (26.3)	4 (12.9)	.2
Mode of delivery						
Cesarean delivery	22 (81.5)	67 (100)	<.01	19 (50.0)	31 (100)	<.01
Emergency cesarean delivery before labor for hemorrhage †,‡	6/26 (23.1)	15/21 (71.4)	<.01	9/37 (24.3)	5/9 (55.6)	.1
Emergency cesarean delivery during labor for hemorrhage †,‡	7/26 (26.9)	1/21 (4.8)	.02	1/37 (2.7)	0	.5
General endotracheal anesthesia	4/22 (18.2)	21/67 (31.3)	.2	7/19 (36.8)	6/31 (19.4)	.1
Vaginal delivery	5 (18.5)	0	<.01	19 (50.0)	0	<.01
Instrumental delivery	1 (3.7)	0	.1	0	0	-
Estimated blood loss (mL) median [IQR]	500 [300-650]	800 [400-1100]	.4	650 [300-1000]	500 [300-800]	.9
Postpartum hemorrhage ≥ 500 mL	13 (48.2)	38 (57.6)	.4	18 (47.4)	14 (45.2)	.8
Use of additional uterotonic agent	2 (7.4)	7 (10.5)	.7	3 (7.9)	0	.1
Blood transfusion						
Red blood cells	2 (7.4)	7 (10.5)	.7	4 (10.5)	0	.06
Fresh frozen plasma	0	2 (3.0)	.4	2 (5.4)	0	.2
Fibrinogen	0	0	-	0	0	-
Pelvic arterial embolization	1 (3.7)	0	.1	0	0	-
Second-line surgical therapies §	0	1 (1.5)	.5	1 (2.6)	0	.4
Admission to intensive care unit	0	1 (1.5)	.5	0	0	-
Length of hospital stay (days) median [IQR]	6 [4-7]	6 [5-7]	.2	5 [4-6.5]	5 [5-6]	.2
Postpartum anemia (< 10 g/dL) during hospital stay	19 (70.4)	44 (65.7)	.7	27 (73.0)	21 (67.7)	.6
Thromboembolic events	0	0	-	0	0	-
Postpartum fever ‖	0	1 (1.5)	.5	0	0	-
Sepsis ‖	0	1 (1.5)	.5	0	0	-
Maternal death	0	0	-	0	0	-
Severe maternal morbidity ¶	1 (3.7)	2 (3.0)	.9	1 (2.6)	0	.4
Neonatal outcomes						

Gestational age at delivery, median [IQR]	37 [36-40]	37 [37-38]	.05	38 [37-39]	38 [37-39]	.06
between 35^0 and 36^6 weeks	11 (40.7)	15 (22.4)	.07	8 (21.1)	4 (12.9)	.4
between 37^0 and 39^6 weeks	10 (34.0)	51 (76.1)	<.01	22 (57.9)	26 (83.9)	.02
≥ 40^0 weeks	6 (22.2)	1 (1.5)	<.01	8 (21.1)	1 (3.2)	.03
Birthweight (g) median [IQR]	2810 [2620-3430]	2950 [2690-3330]	.5	3150 [2670-3520]	3030 [2870-3230]	.4
Umbilical cord arterial pH < 7.10	0	0	-	1 (3.1)	1 (3.5)	.9
Apgar score < 7 at 5 minutes	3 (11.5)	2 (3.0)	.1	2 (5.3)	1 (3.2)	.7
Respiratory distress syndrome	4 (14.8)	3 (4.5)	.08	5 (13.2)	2 (6.5)	.4
Transfer to neonatal intensive care unit	3 (11.1)	7 (10.5)	.9	2 (5.3)	1 (3.2)	.7
Neonatal death	1 (3.7)	0	.1	0	0	-
Severe neonatal morbidity #	5 (18.5)	7 (10.5)	.3	4 (10.5)	3 (9.7)	.9

IQR: interquartile range.

Continuous data are expressed as medians [IQR] when specified; discrete data are expressed as n (%). Kruskal-Wallis, $\chi 2$, and Fisher's exact tests were used as appropriate. A *P* value of .05 was considered significant.

* There were 5 and 3 missing data for the planned trial of labor and elective cesarean groups, respectively, because in these cases, the internal os distance was reported as <20 mm but not otherwise specified.

† Missing data: > 10%.

‡ Other indications for cesarean deliveries were abnormal fetal heart rate without hemorrhage during labor and protracted labor.

§ Second-line surgical therapies: uterine compression sutures, vessels ligation, and peripartum hysterectomy for management of massive primary postpartum hemorrhage after uterine massage and uterotonic agents failed to stop bleeding.

‖ Postpartum fever was defined by an isolated postpartum fever higher than 38.5°C, and sepsis by a positive blood culture.

¶ Severe maternal morbidity, defined by any one of the following: uterine artery embolization or emergency surgery to control PPH (i.e., vessel ligation and/or uterine compression sutures and/or peripartum hysterectomy), transfusion of more than 5 units of packed red blood cells, transfer to intensive care unit, thromboembolic events, and death.

Severe neonatal morbidity, defined by any one of the following: 5-minute Apgar score< 7, umbilical artery pH < 7.10 (umbilical artery blood gas values were routinely measured), need for resuscitation or intubation, and neonatal death.

Figures

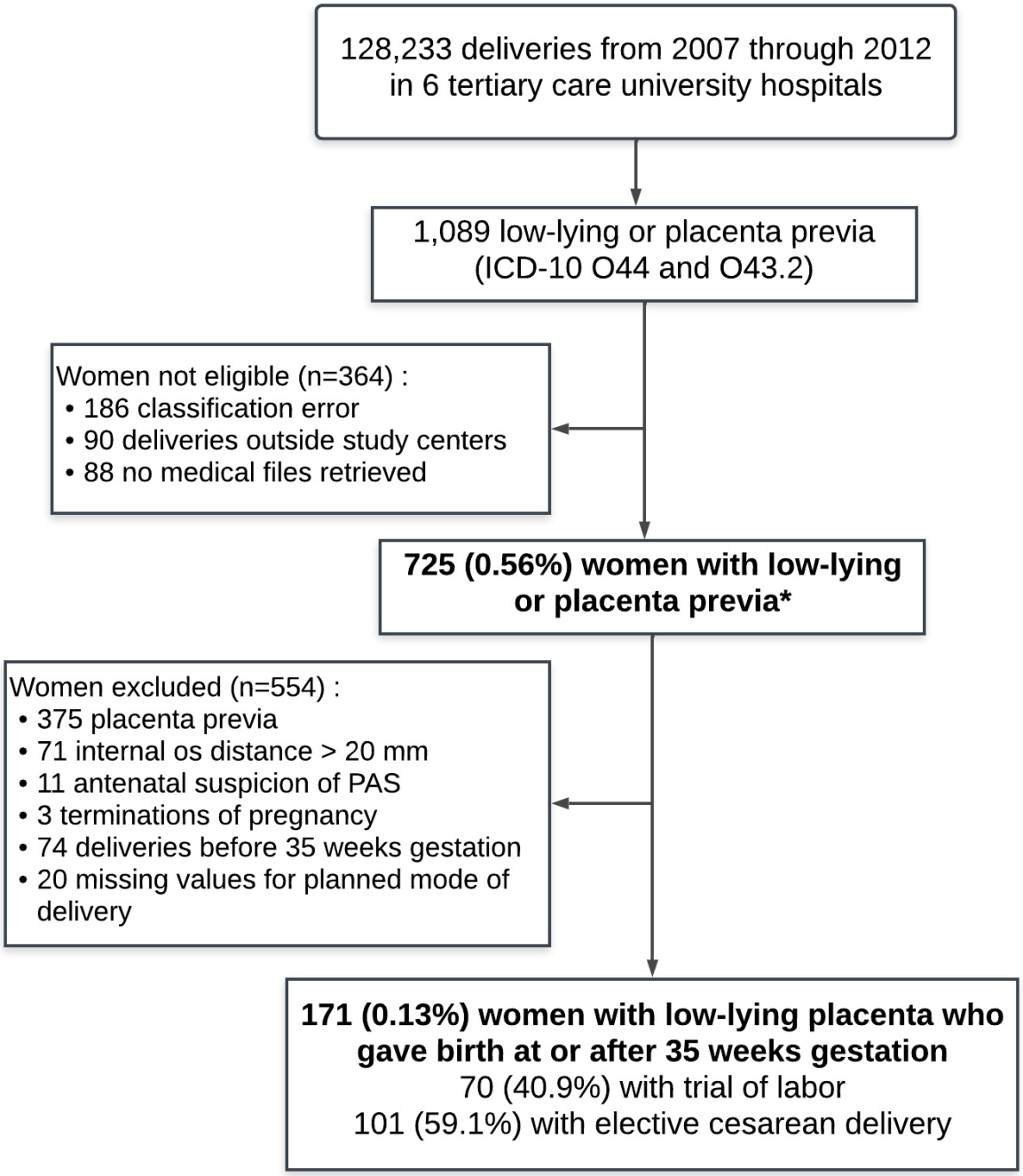


Figure 1. Study flow chart.

* low-lying placenta was defined as a distance between the placental edge and the cervical os of less than 20 mm at the last transvaginal ultrasound scan before delivery; placenta previa was defined as the placenta lying directly over the cervical os.[1]

PAS, placenta accreta spectrum.

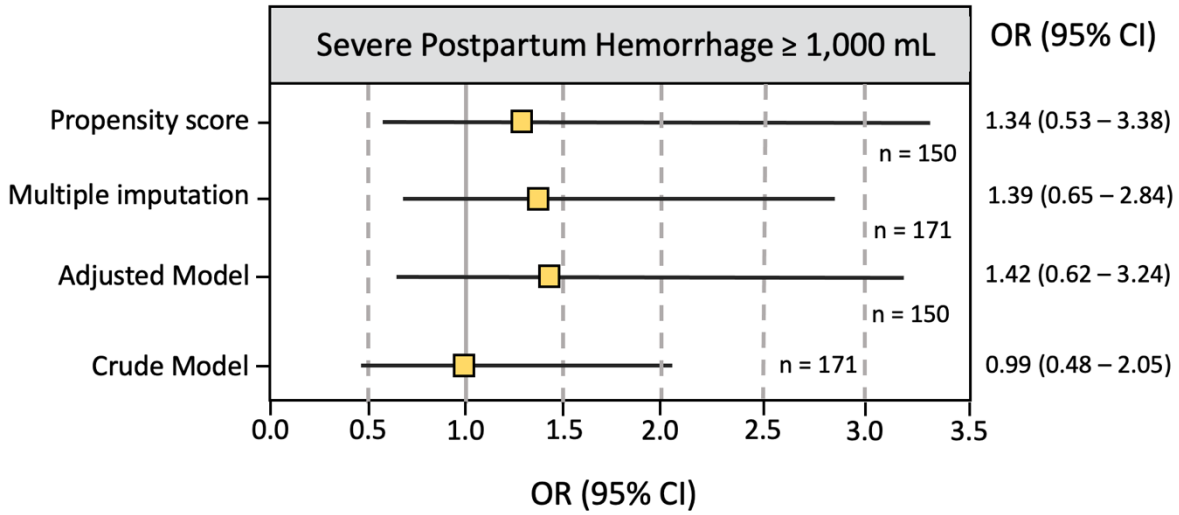


Figure 2. Risk of severe postpartum hemorrhage in the trial-of-labor group (reference: elective cesarean delivery) for the main analysis, including all deliveries at and after 35 weeks gestation (n=171).

CI, confidence interval; OR, odds ratio.

Supplemental files

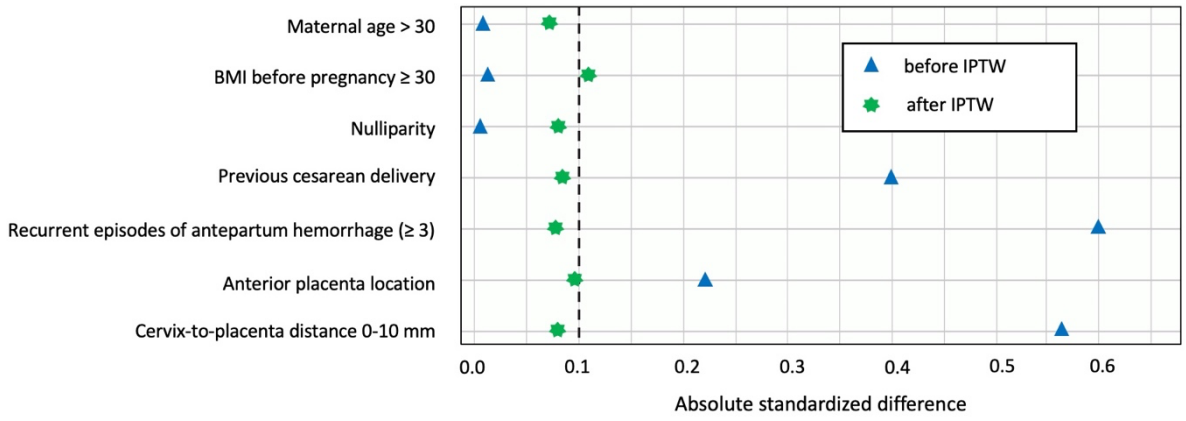
Appendix A. Univariate and multivariate analysis of severe postpartum hemorrhage according to the planned mode of delivery.

	Severe Postpartum Hemorrhage ≥ 1000 mL		
	Crude OR (95% CI)	Adj. OR (95% CI)	*P* *
Planned mode of delivery			
Elective cesarean delivery	Ref	Ref	
Trial of labor	0.99 (0.48-2.05)	1.42 (0.62-3.24)	.5
Maternal age >30 (years)	1.46 (0.70-3.06)	1.68 (0.71-3.94)	.2
BMI before pregnancy ≥ 30 (kg/m²)	2.04 (0.56-7.39)	2.04 (0.53-7.23)	.3
Nulliparity	0.55 (0.23-1.29)	0.70 (0.27-1.88)	.5
Previous cesarean delivery	3.27 (1.24-8.61)	2.28 (0.69-4.87)	.2
Tobacco use during pregnancy	1.52 (0.66-3.49)	-	-
First episode of antepartum hemorrhage <29 weeks	0.43 (0.09-2.00)	-	-
Recurrent episodes of antepartum hemorrhage (≥ 3)	1.14 (0.56-2.32)	-	-
Anterior placental location	0.56 (0.26-1.22)	-	-
Internal os distance, 0-10 mm	1.37 (0.65-2.89)	1.51 (0.66-3.47)	.3

OR, odds ratio; CI, confidence interval; BMI, body mass index.

* Adjusted logistic regression analyses. Adjustment for maternal age, BMI, nulliparity, previous cesarean delivery, and cervix-to-placenta distance. The number of adjustment variables included is limited due to the low number of events (n=39).

Appendix B. Absolute standardized differences



Absolute standardized differences between women with planned trial of labor or elective cesarean delivery, for the variables included in the propensity score, before (total population) and after propensity score weighting (propensity score-weighted population).

Absolute standardized difference is a measure of effect size between two groups that is independent of sample size. It is the absolute value of the mean difference divided by the pooled standard deviation.

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