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Research Article

The Role of First Trimester Ultrasound in the Detection of Vasa Previa: a Systematic Review

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Abstract

Vasa previa is a rare disorder in which fetal blood vessels are left unprotected in the membranes and cross the internal os of the cervix. The risk of vessel tearing causing antepartum bleeding and fetal death due to exsanguination is highly increased. Prenatal detection drastically improves fetal outcome. The aim of this study is to scrutinize the recent evidence for the use of first trimester prenatal ultrasonography to improve the detection of vasa previa. We conducted a systematic literature review in the computerized databases Pubmed, Embase, CINAHL and Web of Science from inception to September 2022. Two first trimester sonographic markers are associated with vasa previa later in pregnancy: umbilical cord insertion in the lower one-third of the uterine cavity and a velamentous insertion. We conclude the evaluation of the umbilical cord insertion in the first trimester is feasible, not time-consuming and may identify the population at increased risk for vasa previa.

Key words: vasa previa; screening; first trimester; ultrasonography

Abbreviations

VP: vasa previa

RF: risk factor

ART: assisted reproductive technology

SR: systematic review

PPV: positive predictive value

Introduction

Vasa previa is a rare and potentially lethal obstetrical complication occurring in approximately in 0.46/1000 pregnancies (Degirmenci, Steetskamp, Macchiella, Hasenburg, & Hasenburg, 2022; Nohuz, Boulay, Gallot, Lemery, & Vendittelli, 2017; Pavalagantharajah, Villani, & D'Souza, 2020). The first type of vasa previa is associated with a velamentous cord insertion, the second type with bilobate or succenturiate placenta and the third type includes unprotected vessels along the margin of the placenta (Bohîlțea et al., 2022). If undiagnosed the fetal morbidity and mortality, caused by fetal vessel damage, is extremely high. The survival rate in undetected cases is 72.1%, versus 98.6% in prenatally detected cases, making pre-natal detection of paramount importance (Zhang et al., 2021). Prenatal detection also drastically decreases postnatal transfusion and hypoxic morbidity (Degirmenci et al., 2022; Ochiai et al., 2021; Zhang et al., 2021).

Known risk factors for vasa previa include assisted reproductive technology (ART), a low-lying placenta in second trimester, placenta previa, bilobate- or succenturiate placenta, velamentous cord insertion and multiple gestations (Degirmenci et al., 2022).

Screening for vasa previa is not universally recommended in national or international guidelines. First or second semester screening guidelines of International Society of Ultrasound in Obstetrics (ISUOG) or American College of Obstetricians (ACOG) mention visualization of placental umbilical cord insertion (Bilardo et al., 2023; Pinar et al., 2014; Salomon et al., 2022) as optional while the American Institute of Ultrasound in Medicine (AIUM) and the Australian Society for Ultrasound in Medicine (ASUM) do include the assessment of placental cord insertion as standard practice in the second trimester scan protocol ("AIUM-ACR-ACOG-SMFM-SRU Practice Parameter for the Performance of Standard Diagnostic Obstetric Ultrasound Examinations," 2018; Bethune, Alibrahim, Davies, & Yong, 2013). On the one hand, the Royal College of Obstetricians and Gynecologists (RCOG) reports in its guideline of 2018 that there is insufficient evidence to support universal screening for vasa previa at the second trimester scan (Jauniaux et al., 2019). On the other hand, the Society of Obstetricans and Gynaecologist of Canada (SOGC) and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) recommend targeted

screening in case of low-lying placenta (Gagnon, 2017; Javid, Hyett, Walker, Sullivan, & Homer, 2019).

From the 2nd trimester onwards, the accuracy of vasa previa detection by transvaginal ultrasound is high with a 100% sensitivity and a 99% specificity according to two prospective studies (Ruiter et al., 2015). In retrospective studies the overall median detection rate was 93% (Ruiter et al., 2015). In case of second trimester diagnosis, spontaneous resolution of vasa previa towards the third trimester is seen in 8.6-39% (Degirmenci et al., 2022; Erfani et al., 2019; Klahr et al., 2019; Oyelese et al., 2004). Therefore, follow-up in the third trimester is recommended.

Prenatal diagnosis is key to prevent neonatal morbidity and mortality caused by vasa previa, yet there is no consensus on routine prenatal screening. Given that vasa previa is rare, an early phase, non-invasive and easy screening could help to identify a high-risk population. This systematic review (SR) is to make a broad search to find all reports about vasa previa and first trimester screening using ultrasound and hereby evaluate the possibility of an early risk stratification.

Material and methods

1. Search strategy

A systematic review of the literature was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

By the support of a medical librarian, a comprehensive search string of Pubmed, Embase, CINAHL and Web of Science the core collection was designed by KDV and TVDB. The search included reports from inception until September 2022. There were no language restrictions. The search strategy consisted of subject headings (MeSH, SH) and words in title and abstract for vasa previa or related conditions (‘vasa previa, ‘velamentous cord insertion’, ‘marginal placental cord insertion’) AND ultrasound or risk factor synonyms. (Supplementary Data 1).

This search was adapted to fit the search system of the three other databases. Duplicates were removed. The reference lists of the reviews and systematic reviews were screened for additional reports.

2. Study selection

For the screening process, Rayyan was used. Two researchers (KDV and KDW) independently screened titles, abstracts and full texts. After the full-text screening, conducted by the same two independent researchers, unresolved discrepancies were decided with the senior researcher (TVDB).

Inclusion criteria are full text journal publications on first trimester ultrasonography and risk of vasa previa. Exclusion criteria are absent relation with the first trimester (i.e., up until 14 weeks gestational age), absent relation with vasa previa, review without a new case nor study material, systematic review, conference abstracts, letters to the editors or a commentary.

3. Data extraction

The number of vasa previa cases, the total number of the population and the prevalence of the identified risk factor or sonographic feature were retrieved by one reviewer (KDV).

4. Quality Assessment: assessment of risk of bias

The QUIPS checklist for the systematic assessment of the methodological quality is used to score the included cohort studies. Two reviewers scored the studies independently.

Results

1. Study selection

The search resulted in 2337 records of which 1368 duplicates were removed. The title and abstract of 969 reports were screened, of which 286 were included for full-text screening.

The full text was not available online for 44 records, mainly manuscripts from before 1995.

The full texts of 242 reports were screened. Based on the inclusion and exclusion criteria, 9 papers were selected including five cohort studies and four case studies. One retrospective cohort and four prospective cohort studies were identified in this search. No additional reports were extracted from the reference list of the reviews and systematic reviews.

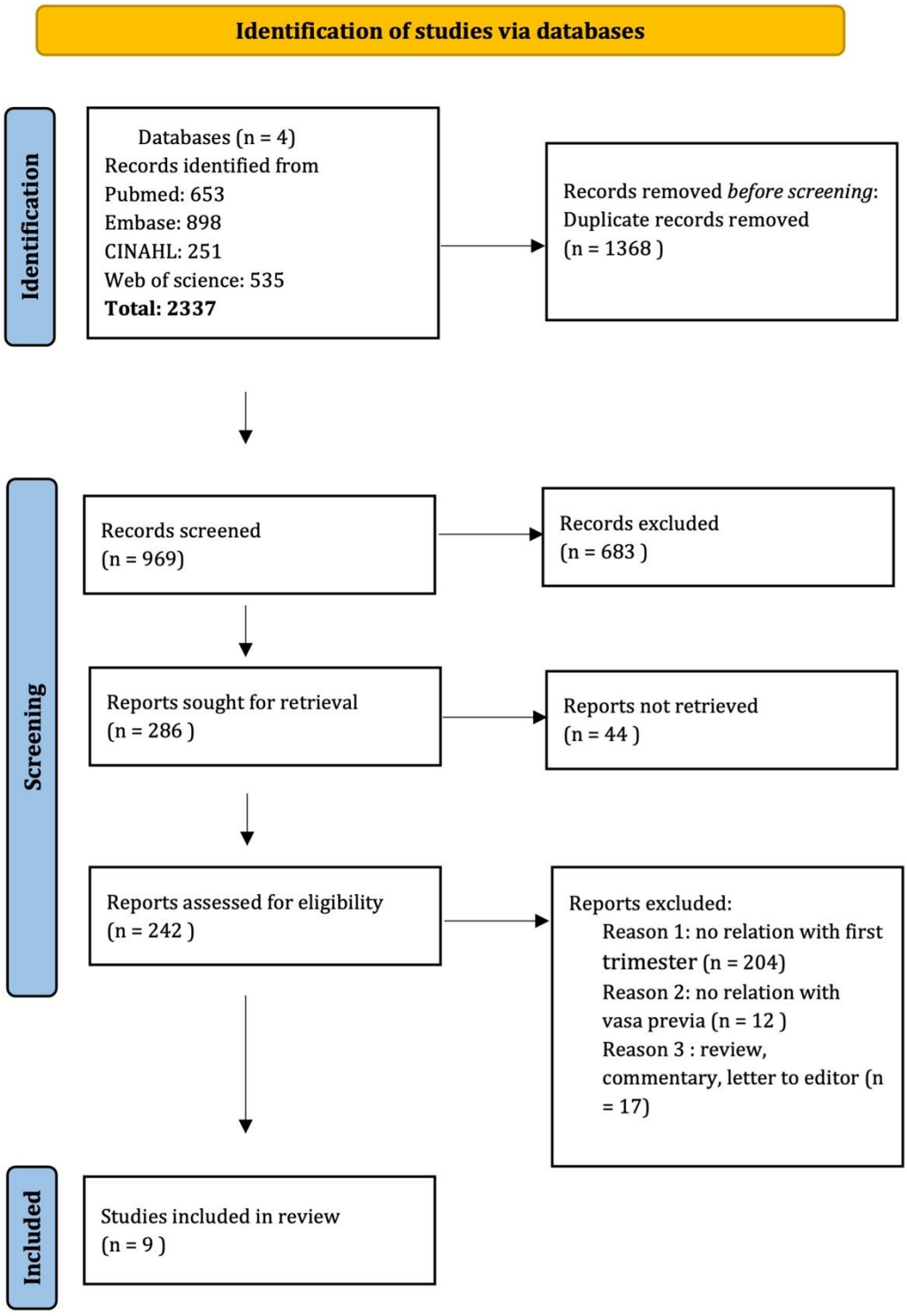

Figure 1: Study selection

2. Quality assessment

The consensus of the quality assessment of the included cohort studies was framed in table 1. Our risk of bias due to missing reports or studies is low because of the initial broad search strategy.

The included cohort studies scored low or moderate for risk of bias except the short report of Hasegawa et al. (2012) due to missing information and including a cohort overlapping with the two other included studies of Hasegawa et al. (2006, 2011).

Study	Year	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Study Confounding	Statistical Analysis and Reporting
Hasegawa	2006	low	low	low	low	low	low
Hasegawa	2011	low	low	low	low	low	low
Hasegawa	2012	moderate	high	high	moderate	high	high
Derisbourg	2021	low	low	low	moderate	low	low
Zhang	2020	low	moderate	low	low	low	low

Table 1: Risk of bias assessed by QUIPS quality assessment tool

3. Data extraction and interpretation

3.1 Case reports

The search identified 4 case reports on vasa previa at delivery, reporting on first trimester sonographic findings as well.

At 8 weeks gestational age, the first case had a placenta lying over the internal ostium with a marginal insertion of the umbilical cord (Ochiai et al., 2021). The author of the second case described a low-lying placenta at 13 weeks without information about the cord insertion (Sauerbrei & Davies, 1998).

Both the third and fourth case report mentioned a cord insertion in the lower uterine segment at 11 and 12 weeks of gestation (Degirmenci et al., 2022; Hasegawa et al., 2007).

3.2 Cohort data synthesis (table 2)

Five cohort studies were included, published between 2006 and 2020. The cohort size varies between 318 and 26 830 patients. Three out of five cohort studies also included multiple gestations (Hasegawa et al., 2006; Hasegawa et al., 2012; Hasegawa et al., 2011), which have a higher incidence of vasa previa. The cohort of Hasegawa et al. published in 2012 interferes with two previous cohorts by Hasegawa et al. published in 2006 and 2011. Therefore, the 2012 study was not deemed of additional value.

The two studied risk factors in the first trimester include a low cord insertion in the uterine cavity and a velamentous cord insertion.

Low cord insertion is defined by Hasegawa et al. (Derisbourg et al., 2021; Hasegawa et al., 2006; Hasegawa et al., 2012; Hasegawa et al., 2011) as the insertion of the umbilical cord in the lower one-third of the uterine cavity. The incidence of low cord insertion was similar in all three prospective cohort studies: 11%, 10.6% and 11.9% respectively (Derisbourg et al., 2021; Hasegawa et al., 2006; Hasegawa et al., 2011). Lower third cord insertion is not only associated with vasa previa, but also with low-lying placenta in second and third trimester and with velamentous and marginal cord insertion at birth (Hasegawa et al., 2006; Hasegawa et al., 2011). The relative risk for vasa previa in case of a first trimester low cord insertion is 9.3 (Hasegawa et al., 2006; Hasegawa et al., 2011).

Velamentous cord insertion at the inferior part of the placenta between 11-13 weeks gestation was described as risk factor for vasa previa by Zhang et al. (2020) and detected in 0.3% of the study population (Zhang et al., 2020).

From 9 weeks onwards a low cord insertion is detectable, whereas a velamentous cord insertion is detectable from 11-13 weeks gestational age onwards (Derisbourg et al., 2021; Hasegawa et al., 2006; Hasegawa et al., 2011; Zhang et al., 2020). Before 11 weeks, the trophoblast covers most of the uterine cavity and umbilical cord insertion into the placenta may be difficult to determine. Therefore, Hasegawa et al. (2006) proposed to determine the position of the insertion of the cord in the uterine cavity instead of insertion in the placenta. After 11 weeks of gestational age Sepulveda et al. (2006) demonstrated the feasibility to determine a velamentous cord insertion (Sepulveda, 2006).

Except for Hasegawa et al. (2011) and Derisbourg et al. (2021) who reported on vasa previa in mid-trimester, the other cohorts documented the outcome at the time of delivery. Hasegawa et al. (2012) described no changes in diagnosis between 20 weeks and just prior to delivery (Hasegawa et al., 2012).

Zhang et al. (2020) followed vasa previa cases detected in the mid-trimester and only 1 in 22 cases resolved at 24 weeks (Zhang et al., 2020).

Hasegawa et al. (2011) tried to identify maternal risk factors for lower cord insertion in the first trimester. Multiparity, previous dilatation and curettage, multiple gestations, maternal age > 40y, smoking, alcohol drinking and in vitro fertilization were the examined possible risk factors but no associations were found (Hasegawa et al., 2011).

3.3 Incidence and detection rate (table 3)

The incidence of vasa previa in the included studies varies between 0.08 and 0.31%.

The incidence of vasa previa in the studies of Hasegawa (2006, 2011, 2012) and Derisbourg et al. (2021) was almost three times higher than in the series by Zhang et al. (2020).

A high sensitivity for vasa previa is noted with the sonographic assessment of the umbilical cord in the first trimester. Two out of three studies report 100% sensitivity for a low cord insertion in the first trimester as screening test for vasa previa, whereas one study reports a remarkably lower sensitivity of 25%.

A 76.2% sensitivity and even higher specificity for detecting vasa previa has been associated with velamentous cord insertion in the first trimester (Zhang et al., 2020). The positive predictive value for vasa previa is almost ten times higher for velamentous insertion than for a low cord insertion in the uterine cavity (Zhang et al., 2020).

Author (year of publication)	Study design	Population (n)	Inclusions	Risk factor (RF)	Gestational age at risk assessment	Cases RF + n (%)	Outcome (VP)	VP cases (n)
Hasegawa (2006)	Prospective cohort	318	All pregnancies	Low cord insertion	9-11 weeks	35 (11%)	36 weeks or delivery*	1
Hasegawa (2011)	Prospective cohort	1311	All pregnancies	Low cord insertion	9-13 weeks	139 (10.6%)	20 weeks	3
Hasegawa (2012)	Prospective cohort	3647	Unclear	Low cord insertion	First trimester	/	20 weeks and delivery**	10
Derisbourg (2021)	Prospective cohort	1620	Singleton pregnancies	Low cord insertion	11-14 weeks	192 (11.9%)	20 weeks	4
Zhang (2020)	Retrospective cohort	26830	Singleton pregnancies	Velamentous insertion	11-13 weeks	79 (0.3%)	Delivery*	21

Table 2: Summary of data extraction (VP: vasa previa, RF: risk factor)

Discussion

Although vasa previa is a rare obstetrical condition, the associated high fetal morbidity and mortality, may justify an appropriated screening. We performed a meticulous and broad search to evaluate the current evidence for the use of first trimester sonography in vasa previa screening.

The studies included in our SR report a slightly higher incidence of vasa previa than other papers, reporting 0.02% and 0.22% incidence figures (3, 24). The latter lower incidence figures may be due to underreporting in retrospective series, in which some vasa previa cases may have been missed at cesarean section (Hasegawa et al., 2012). The study design of the included studies in our SR had a low risk for selection bias. The incidence reported in our SR may therefore be considered more reliable for the overall pregnant population.

Adequate and clinically relevant risk screening for vasa previa should be non-invasive, easy and performant with a high sensitivity and a reasonable specificity, meaning the test should not miss any vasa previa, while the number of the group stratified as high risk should be acceptable. First trimester screening provides the opportunity to identify a high-risk population for this rare entity. Most of the studies in this SR report a significant association between first trimester sonographic assessment of the umbilical cord insertion and vasa previa later in pregnancy, yet results are conflicting.

The first trimester sonographic assessment of the cord implantation in the uterine cavity may meet the condition of a suited risk stratification tool. According to our SR, one in ten pregnancies would be stratified as higher risk and referred for mid-trimester transvaginal ultrasound scan. In case of a lower cord insertion, vasa previa will eventually be diagnosed in 0.5-2.9% (table 3). The latter positive predictive value (PPV) of 0.5-2.9% for low cord insertion is remarkable lower than the PPV of 16% reported in the meta-analysis of Ruiter et al. (2016) (Ruiter et al., 2016). The explanation for this difference is found in the inclusion of the study of Hasegawa et al. (2010), which was not included in our SR. This study reports on low cord insertion in the mid-trimester instead of the first trimester, which results in a much higher PPV in the meta-analysis of Ruiter et al. (2016) (Hasegawa et al., 2010).

Furthermore, the undeniable difference in sensitivity between the studies of Hasegawa et al. (2006, 2011) and Derisbourg et al. (2021) must be clarified in the future.

The second sonographic risk factor in the first trimester is velamentous insertion, but only investigated as screening tool in one study. The two-step screening model from Zhang et al. (2020) is the first screening model which includes first trimester velamentous insertion and shows a higher detection rate than other second trimester risk factors. The latter author reporting sensitivity of 57% and 38% respectively for low-lying placenta and bilobed placenta in the second trimester as screening method for vasa previa, in contrast with a sensitivity of 76.2% with first trimester assessment (Zhang et al., 2020).

This method combined with appropriate monitoring and delivery would decrease overall stillbirths by 10%. They made this assumption by calculating the potential stillbirths in cases of non-detecting the vasa previa at all (Zhang et al., 2020).

Evaluation of the umbilical cord insertion in the first trimester is easy. Detection of the insertion of the umbilical cord becomes more difficult with progressing gestational age, viz 72% detection in the third trimester, versus 95% in the early second trimester (Padula et al.). Furthermore, Bohiltea et al. (2022) argues evaluation in the first trimester hardly requires extra time, viz less than 30 seconds, while it may be lifesaving (Bohîlțea et al., 2022; Hasegawa et al., 2006; Sepulveda, 2006).

The limitations of this SR are the low number of studies fulfilling inclusion criteria and the conflicting results. Although the search syntax was developed to be as broad as possible; the limited studies hinder us to draw precise conclusions. Derisbourg et al. (2021) reports a remarkably low sensitivity in contrast with the two studies of Hasegawa et al. (table 3). The sonographic assessment in the cohort by Derisbourg et al. (2021) was performed by 38 different sonographers. Part of them had been informed at a meeting at the start of the study while the other had the protocol mailed to them. This may illustrate the importance of a proper teaching program for the sonographers on how to perform a first trimester ultrasound scan including the assessment of the umbilical cord insertion.

Author (year of publication)	Incidence VP	Test	PPV	NPV	TP (n)	FN (n)	Sensitivity	Specificity
Hasegawa (2006)	0.31%	Low cord insertion	2.9%	100%	1	0	100%	89.3%
Hasegawa (2011)	0.23%	Low cord insertion	2.2%	100%	3	0	100%	89.6%
Hasegawa (2012)	0.27%	Low cord insertion	-	100%	10	0	-	-

Derisbourg (2021)	0.25%	Low cord insertion	0.5%	99.8%	1	3	25%	88.2%
Zhang (2020)	0.08%	Velamentous insertion	20.3%	99.9%	16	5	76.2%	99.8%

Table 3: Positive predictive value (PPV), negative predictive value (NPV), FN (false negative), TP (true positives), sensitivity and specificity of first trimester screening for vasa previa.

A general limitation in studies about vasa previa is the lack of postnatal confirmation of the diagnosis. Examination of the membranes and placenta in relation with the cervical os is not always feasible. The reported numbers of vasa previa are based on sonographic assessment in second or third trimester and therefore reliant on the experience and skills of the sonographer.

In the future, we need large multicentric prospective studies using a strict protocol on the added value of low cord insertion and velamentous cord insertion in the first trimester as predictive marker for vasa previa. Providing a high sensitivity is confirmed, this marker creates opportunities for risk stratification of the unselected population of pregnancies.

Furthermore, the benefit of early risk stratification in the first trimester above screening at the mid-trimester scan is yet unknown. Screening at mid-trimester by determining placental cord insertion followed by transvaginal ultrasound if marginal or velamentous cord insertion was detected (7.7%) seemed to be feasible and efficient. Although the confirmation of the screen-positive group and follow-up of the screen-negative group was limited. From the 21 cases of prenatal detected vasa previa; 16/21 cases could be confirmed postnatally and only 11/18 cases were confirmed in the third trimester. (Gross, Markota Ajd, Specht, & Scheier, 2021)

Conclusion

First trimester sonographic assessment of the umbilical cord insertion is feasible and may allow for stepwise risk stratification for vasa previa highlighting a high-risk population. If classified as high risk, focused follow-up with diagnostic transvaginal ultrasound with doppler evaluation in the second trimester would be indicated. Although the incidence is low, vasa previa is a life-threatening condition for the fetus. Therefore, we suggest validation of the evaluation of the placental umbilical cord insertion in the first trimester as risk stratification tool for vasa previa.

Statements

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Statement of Ethics

An ethics statement is not applicable because this study is based exclusively on published literature.

Study approval statement: This study protocol did not need approval by the ethical committee by the University Hospital Leuven after submitting a questionnaire.

Consent to participate statement: Informed consent was not needed because of the use of published literature.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Karlijn De Vocht: identification studies, writing original draft

Kobe Dewilde: conceptualization, identification studies, writing review and editing

Thierry Van den Bosch: conceptualization, writing review and editing

Anne Pexsters: writing review

Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.

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Supplementary data 1:

Pubmed:

("Vasa Previa"[Mesh] OR "Vasa Praevia*"[tiab] OR "vasa previa*"[tiab] OR ("Pregnancy Complications "[Mesh:NoExp] AND "umbilical cord"[Mesh:NoExp]) OR "velamentous cord insertion"[tiab] OR "velamentous insertion"[tiab] OR "marginal placental cord insertion"[tiab] OR "marginal cord insertion"[tiab] OR "umbilical cord insertion"[tiab]) AND ("Ultrasonography, Prenatal"[Mesh:NoExp] OR "Ultrasonography"[Mesh:NoExp] OR "Ultrasonograph*"[tiab] OR "ultrasound"[tiab] OR "Ultrasonic"[tiab] OR "sonograph*"[tiab] OR "echograph*"[tiab] OR "diagnos*"[tiab] OR "Prenatal Diagnosis"[Mesh:NoExp] OR "imag*"[tiab] OR "screen*"[tiab] OR "risk"[tiab] OR "risks"[tiab] OR "predict*"[tiab] OR "prenatal"[tiab]).

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