Natural History of Vasa Previa Across Gestation Using a Screening Protocol

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Objectives—The purpose of this study was to estimate the prevalence and persistence rate of vasa previa in at-risk pregnancies using a standardized screening protocol.

Methods—We conducted a descriptive study of patients with a diagnosis of vasa previa from a single ultrasound unit between June 2005 and June 2012. Vasa previa was defined as a fetal vessel within 2 cm of the internal cervical os on transvaginal sonography. Screening for vasa previa using transvaginal sonography with color flow mapping was performed routinely in the following situations: resolved placenta previa, prior pregnancy with vasa previa, velamentous insertion of the cord in the lower uterine segment, placenta succenturiata in the lower uterine segment, and twin gestations.

Results—A total of 27,573 patients were referred to our unit for fetal anatomic surveys over the study period. Thirty-one cases of vasa previa were identified, for an incidence of 1.1 per 1000 pregnancies. Twenty-nine cases had full records available for analysis. Five patients (17.2%) had migration and resolution of the vasa previa. When the diagnosis was made during the second trimester (<26 weeks), there was a 23.8% resolution rate (5 of 21); when the diagnosis was made in the third trimester, none resolved (0 of 8 cases). Of the 24 pregnancies (5 twin gestations and 19 singleton gestations) with persistent vasa previa, there was 100% perinatal survival and a median length of gestation of 35 weeks (range, 27 weeks 5 days–36 weeks 5 days). No known missed cases were identified over the study period.

Conclusions—The use of standardized screening for vasa previa based on focused criteria was found to be effective in diagnosing vasa previa, with a 100% survival rate. Vasa previa diagnosed during the second trimester resolves in approximately 25% of cases.

Key Words—obstetric ultrasound; prenatal diagnosis; vasa previa migration; vasa previa screening

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Vasa previa is defined as fetal vessels coursing within the membranes overlying or in close proximity to the cervix, the latter point which has yet to be defined in the literature. Vasa previa is a rare obstetric complication, with a reported incidence of 1 per 2500 pregnancies.[1] This condition has been associated with high fetal mortality (60%) due to rapid fetal exsanguination at the time of membrane rupture. Vasa previa has been classified into two types based on its pathologic appearance: type 1 occurring as a result of a velamentous cord insertion into the placenta and type 2 as a result of freely coursing fetal vessels connecting a main placental plate with a succenturiate lobe.[2]

Optimizing the fetal outcome depends primarily on the accurate prenatal sonographic diagnosis of this condition, with timely performance of cesarean delivery before the onset of labor and rupture of membranes. Prenatal diagnosis is based on the identification of fetal vessels passing across or near the internal cervical os and has been described using real-time grayscale, color Doppler, and 3-dimensional sonography via transvaginal or transabdominal evaluations in several case reports and series.

Several studies have noted that risk factors for vasa previa include pregnancies conceived via in vitro fertilization, multiple gestations, resolving placenta previas, velamentous cord insertions, and bilobed or succenturiate placentas.[1,3] Prior reports focusing primarily on the prenatal sonographic diagnosis of vasa previa have consisted of small case series, with the largest reporting on 18 patients.[4] In this latter series, the use of grayscale criteria of "echogenic parallel or circular lines near the cervix" with transabdominal scanning initiated further evaluation in that population.

We describe the prenatal sonographic diagnosis and management of vasa previa over 7 years from a single ultrasound unit based on a standardized protocol instituted in 2005 using focused transvaginal sonography to screen for vasa previa in at-risk pregnancies with both grayscale and color flow imaging.

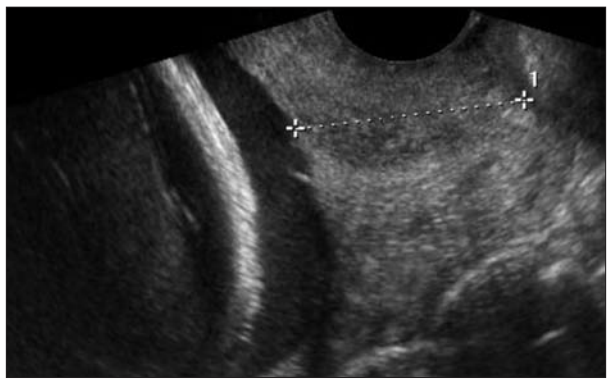
Materials and Methods

After Biomedical Research Alliance of New York Institutional Review Board approval was obtained, the charts of all patients diagnosed with vasa previa in a single ultrasound unit between June 2005 and June 2012 were reviewed. Cases were identified by *International Classification of Diseases, Ninth Revision,* code analysis of our billing system, which includes all deliveries and sonographic examinations performed by our group, as well as a separate content search analysis of the two ultrasound reporting systems used over this period (Ultra 64; Sonultra Corp, Beverly Hills, CA; and AS-Ob/Gyn; AS Software, Inc, Englewood Cliffs, NJ) using the key words "vasa previa." For the purposes of our study, vasa previa was defined as any velamentous fetal vessel (arterial or venous) noted to be within 2 cm of the internal cervical os. We excluded a funic presentation by requiring that vessels be followed from the placental edge either into another placental lobe or into the root of the umbilical cord itself.

The imaging staff consisted of multiple registered diagnostic medical sonographers and 6 maternal-fetal medicine specialists. Fetal anatomic surveys were performed between 15 and 22 weeks' gestation and in some cases on two separate occasions. Our ultrasound unit has standardized policies and protocols for the evaluation of potential vasa previa. Screening for vasa previa using transvaginal sonography with color flow mapping was performed routinely in the following clinical situations: resolved placenta previa, history of vasa previa in a prior pregnancy, velamentous insertion of the cord in the lower uterine segment, succenturiate placenta with implantation in the lower uterine segment, and twin gestations. Once a vasa previa was suspected with grayscale or color flow imaging, confirmation was performed with pulsed wave Doppler imaging to differentiate arterial and venous vessels. Grayscale sonography to delineate an aberrant vessel within 2 cm of the internal cervical os was used if linear or tubular structures were noted attached to the inner perimeter of the fetal membranes (Figure 1), and color flow imaging further identified flow within such structures (Figure 2). Delineating venous flow using pulsed wave Doppler imaging identified the type of vessel present, but the actual location of the aberrant vessel (ie, attached to the inner perimeter of the fetal membranes) was used for diagnostic accuracy. Three- and 4-dimensional technology was used in certain cases to enhance diagnosis and map out the path of the vessel(s) across the lower uterine segment (Figure 3). A variety of ultrasound equipment was used that allowed for grayscale, color Doppler, power Doppler, and 3- and 4-dimensional sonographic capabilities (Voluson 730 Expert and Voluson E8 equipment; GE Healthcare, Milwaukee, WI; and Accuvix XG equipment; Samsung Medison Co, Ltd, Cypress, CA). Serial scans were used to characterize the natural history of vasa previa.

Maternal medical records were reviewed for the following outcomes: gestational age at delivery, indication for delivery, birth weight, Apgar scores of the neonate, and

Figure 1. Two-dimensional grayscale image at 29 weeks' gestation.



placental pathologic findings. Sonograms in all cases were reviewed by a single maternal-fetal medicine specialist (A.R.) for accuracy of diagnosis. Confirmation of the sonographic findings was based on the obstetrician's surgical findings at time of delivery and the placental pathologic examination. Placental pathologic reports were reviewed in all cases to identify the incidence of velamentous cord insertions and descriptions of fetal vessels coursing freely through the fetal membranes. It was our standard practice to recommend elective admission in singleton gestations between 32 and 34 weeks based on physician discretion/patient desire and elective delivery at 35 to 36 weeks without amniocentesis for lung maturity.[1]

Results

A total of 27,573 patients were referred to our unit for fetal anatomic surveys over the study period. Thirty-two cases of vasa previa were prenatally sonographically identified by our database search strategies. The incidence of vasa previa at delivery in our population ultimately was noted to be 26 cases, or 0.94 per 1000, as 5 cases that were diagnosed with vasa previa resolved across gestation, and 1 case was misdiagnosed. Some notable baseline characteristics of the population included a median maternal age of 35 years (range, 24–58 years) with an ethnic/racial distribution of 85% white, 9% Asian, and 6% Hispanic.

Regarding all of the prenatally diagnosed vasa previa cases in which follow-up was completed, 41% of the patients had undergone some form of assisted reproductive technology, and 1 additional patient conceived using clomiphene citrate. There were 7 sets of twin pregnancies (24% of the patients): 5 dichorionic diamniotic and 2 monochorionic diamniotic pregnancies. All cases diagnosed with vasa previa had an identifiable risk factor within our protocol as follows: 25 cases had a history of a resolved placenta previa (either marginal or complete); 2 cases had velamentous cord insertions; 1 case was solely identified because of a twin gestation; and 1 case had a bilobed placenta identified. Of the 29 cases of vasa previa diagnosed at some point in gestation that were available for analysis (ie, 2 cases lost to follow-up and 1 case excluded for misdiagnosis), 5 patients (17.2%) had migration and resolution of the vasa previa across gestation, leaving 24 cases of persistent vasa previa for analysis of delivery outcomes. Of the 24 persistent vasa previa cases (5 twin gestations and 19 singleton gestations) there was 100% survival of the infants, with a median length of gestation of 35 weeks (range, 27 weeks 5 days–36 weeks 5 days). None of the dichorionic twin gestations had resolution of the vasa previa, whereas the 2 twin gestations that did have resolution of the vasa previa were notable for both being monochorionic.

Table 1 summarizes some pertinent clinical characteristics for the two groups. The median gestational age at diagnosis for the whole group was 22 weeks 6 days (range, 16 weeks 1 day–36 weeks 5 days). Eighteen patients were electively admitted to the hospital with a median gestational age at admission of 33 weeks (range, 26 weeks 1 day–36 weeks 5 days), with 100% of these cases receiving antenatal steroids before elective delivery without amniocentesis. Of the 6 cases emergently admitted, 2 were for vaginal bleeding, and 4 were for preterm labor. Two patients had müllerian anomalies (ie, didelphic uterus and a prior uterine septum after resection). In some cases in which it was not clear what type of vessel the vasa previa

Figure 2. Color flow Doppler image at 32 weeks' gestation.

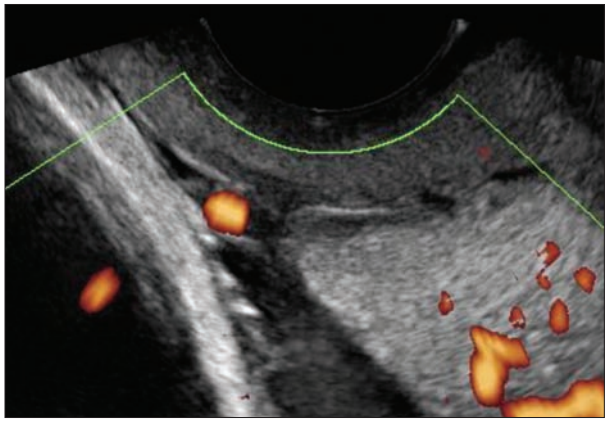
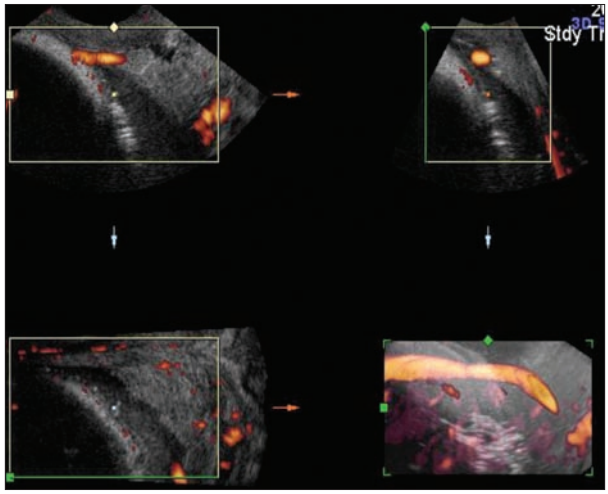


Figure 3. Three-dimensional image in the color flow angio mode at 32 weeks' gestation.



consisted of, whether arterial or venous, the uncertainty was due to lack of Doppler imaging archives or reports on the issue for the cases outlined.

When the initial diagnosis of vasa previa was made during the second trimester (<26 weeks), there was a 23.8% resolution rate (5 of 21); however, when the diagnosis was made in the third trimester, none resolved (0 of 8 cases). Regarding the 5 cases of resolved vasa previa, the median gestational age at diagnosis was 20 weeks 4 days (range, 16 weeks 4 days–25 weeks 2 days), and the median gestational age at resolution was 25 weeks (range, 22 weeks 5 days–30 weeks).

Regarding the delivery data for our cases: 79% of persistent vasa previa cases (19 of 24) had elective delivery at 34 to 36 weeks' gestation without lung maturity testing. Four cases were urgently delivered for preterm labor, with 1 case having preterm premature rupture of membranes, and another case was emergently delivered for vaginal bleeding at 33 weeks after the patient was hospitalized for 35 days. All cases treated as vasa previa were clinically confirmed at birth by the obstetrician performing the cesarean delivery. Regarding delivery data for the 5 resolved vasa previa cases, 4 cases delivered vaginally: 2 were electively induced, 1 was induced for development of gestational hypertension, and the fourth went into spontaneous labor. The sole patient who had a cesarean delivery did so because she had a prior cesarean delivery and declined a trial of labor.

The median time spent by the patients in the hospital was 14.5 days (range, 0–42 days). Three twin cases were admitted electively at 28 to 30 weeks' gestation at the physician's discretion. All cesarean deliveries had a low-flap transverse uterine incision.

Regarding placental pathologic reports for all 29 pregnancies with a prenatal diagnosis of vasa previa: 72% were identified with a velamentous umbilical cord insertion site, and 4% (1 case) was identified with a single umbilical artery; 82% showed fetal vessels coursing in the fetal membranes, and 17% showed either a succenturiate lobe or a bilobed placenta.

Discussion

Vasa previa has long been recognized as a cause of intrapartum mortality and fetal hypovolemic/hypoxemic neurologic morbidity. The first report of this clinical entity dates back to 1801, and it has since been regarded as an inevitable and undetectable tragedy for more than 185 years. The combination of mortality and morbidity has been estimated to be substantial with intact membranes and approximately 70% to 100% with ruptured membranes.[2] The first sonographic description of vasa previa was identified in 1987 by Gianopoulos et al.[5]

Prenatal diagnosis of vasa previa with 2-dimensional sonography has vastly improved neonatal outcomes. Antenatal management is based on expert opinions and case series because of the paucity of reported cases. In the largest series of 155 vasa previa pregnancies, Oyelese et al[1] identified a 56% risk for perinatal mortality when vasa previa was not diagnosed before delivery. Prenatal diagnosis and elective cesarean delivery before membrane rupture led to a 97% fetal survival rate. In their series, cases were obtained from a variety of sources: 4 large hospitals in the United States, 1 hospital in Israel, 1 hospital in London, and finally, a self-selected cohort of families from the Vasa Previa Foundation. In that retrospective series, there was no described

Table 1. Clinical Characteristics

Characteristic	Persistent Vasa Previa (n = 24)	Resolving Vasa Previa (n = 5)
Gestational age at diagnosis, wk	24.59 (16.14–36.71)	20.99 (16.71–25.29)
Distance of vessel from internal os at initial diagnosis, cm	0 (0–0.9)	0 (0–1.8)
Distance of vessel from internal os at last transvaginal scan, cm	0 (0–1.8)	3.2 (2.5–4.44)
Type of vessels Identified overlying internal os (pulsed wave Doppler), n		
Arterial	6	4
Venous	10	0
Arterial and venous	3	0
Not available	5	1
Gestational age at last transvaginal scan, wk	32 (26–37)	30 (26–31)
Placenta previa at some point during pregnancy (≤2 cm from internal os), n (%)	20/24 (83)	5/5 (100)
Gestational age at delivery, wk	35 (27 5/7–36 5/7)	38 (36–41)
Birth weight, g	2525 (1320–3005)	2857 (2494–3292)

Data are presented as median (range) unless otherwise specified.

standardized protocol used to diagnose vasa previa; therefore, the outcome rather than the feasibility of prenatal diagnosis appeared to be the focus of the study. In their retrospective analysis, more than 60% of vasa previa cases had a history of resolved second-trimester placenta previa or low-lying placentas; 32.9% of cases had succenturiate and bilobed placentas; 10% of cases had undergone in vitro fertilization; and 4.5% of cases were twin gestations. As a result, the authors recommended that women with pregnancies complicated by vasa previa be offered elective cesarean delivery at 35 weeks or earlier in a singleton gestation if fetal lung maturity was documented. Identification and selection biases inherent in their analysis limit the clinical utility of that article. Nomiyama et al[6] identified 2 cases of vasa previa while screening for velamentous cord insertions in 587 patients at 18 to 20 weeks. In that report, only 1 of the 2 cases identified was confirmed at delivery, whereas the other seemed to resolve and migrate across gestation. Interestingly, that article appears to be the first report in the literature describing probable migration and resolution of a prenatally diagnosed vasa previa across gestation.

In one of the largest retrospective series to evaluate the prenatal diagnosis of vasa previa,[4] grayscale criteria of "echogenic parallel or circular lines near the cervix" identified during transabdominal scanning was the basis used to initiate further transvaginal evaluations in more than 93,000 screened pregnancies over an 8-year period. A total of 18 cases were identified by this contingency technique, in which 3 cases appeared to be described as resolved on follow-up evaluation, thus leaving 15 true vasa previa cases. The authors stated that the "relative movement was probably caused by differential growth between the lower uterine segment and the placenta." Furthermore, they stated that despite second-trimester diagnosis, confirmation in the third trimester is essential because of "evolutionary changes." That article appears to be the second and last report of vasa previa migration across gestation with prenatal diagnosis of vasa previa.

Catanzarite et al[7] prospectively collected 10 cases over an 8-year period from 1991 to 1998. However, the authors noted that scanning techniques used for screening for vasa previa had evolved over that period. Transabdominal scanning was used with grayscale imaging to initially "screen for fetal vessels over the cervix" with a filled bladder. Color flow Doppler sonography was used only when fetal vessels were suspected until 1995, at which point it was also used in patients with low-lying placentas with accessory lobes. Only in the last year of data collection (ie, 1998) was "routine color Doppler or color power angio 'sweep' across the lower uterine segment" specifically used. In that study, transvaginal imaging was only used "when necessary." Limitations of the study to extrapolate to other populations included the lack of a standardized approach to diagnosis secondary to a temporal bias as well as the inability to determine the detection rates of the varied approaches.

It is interesting to note that transabdominal scanning is associated with a false-positive rate of 25% for the diagnosis of placenta previa, whereas transvaginal imaging is quoted to have 87.5% sensitivity, 98.8% specificity, and, more importantly, a 97.6% positive predictive value.[2] These data highlight the limitations of prior US studies, which had used transabdominal diagnostic techniques to delineate at-risk pregnancies for vasa previa. Finally, a recent series published by Hasegawa et al[8] prospectively examined the usefulness of predicting vasa previa by detecting cord insertion sites in 1270 Japanese patients using both transvaginal and transabdominal scanning with color flow Doppler imaging at 9 to 13 weeks. In that study, 139 cases were identified with subjectively delineated low uterine segment cord insertion sites, in which follow-up second- and third-trimester scans ultimately identified 3 cases of vasa previa, whereas there were no cases identified in the control group. In a recent comprehensive review of the literature on vasa previa, the authors identified a total of 28 cases of prenatally diagnosed vasa previa among 17 publications over 16 years.[9] They suggested adoption of a protocol to specifically seek vasa previa by careful examination of the placental location and umbilical cord insertion site transabdominally, which they hypothesized should substantially decrease the number of unsuspected cases at delivery. Their proposed protocol for focused evaluation of vasa previa using established risk factors had similar criteria as we have chosen, except they did not advise routine transvaginal imaging.[9] However, this protocol is in contrast to an obstetrician's views that it is not feasible to have a policy of screening for vasa previa in England and Wales. The authors of that article agreed that increased awareness of risk factors is important but thought that a screening strategy based on these factors is "too complex for daily clinical practice."[10] Recently, a cost-utility analysis of the addition of targeted and universal screening strategies for vasa previa in singleton and twin pregnancies was performed in Canada. The authors concluded that, compared to current practice, screening all twin pregnancies for vasa previa was cost-effective. In singleton gestations, the use of color Doppler imaging at all transabdominal sonographic examinations and the targeted use of transvaginal sonography for in vitro fertilization pregnancies or when placen-

tas have been found to be associated with 1 or more risk factors (ie, accessory lobes and velamentous cord insertions) are also cost-effective. The authors concluded that a policy in which women with multiple gestations, low-lying placentas, in vitro fertilization conceptions, accessory placental lobes, velamentous cord insertions, or marginal cord insertions are referred for transvaginal sonography to screen for vasa praevia should be considered for adoption.[11]

Strengths of our study included its large number of patients screened, the standardized approach to evaluation using transvaginal imaging in at-risk populations, and the largest vasa previa population prenatally identified. Additionally, it provides for the analysis of the natural history of prenatally diagnosed vasa previa across gestation in the largest series collected by a single center with a standardized approach. Despite this standardized approach, on review of all the images of our study, we reclassified a single case, as it was not correctly identified as a vasa previa. This image actually represented a marginal sinus at the edge of the placenta and was not actually representative of a fetal vessel. The vessel delineated was on the outer perimeter of the fetal membranes, thus indicating a placental sinus rather than a vasa previa. Our observation of migration of vasa previa, particularly related to gestational age at the time of diagnosis, seems to warrant further research and we believe it is an interesting and novel observation. This finding further suggests that vasa previas should be serially assessed across gestation for the possibility of resolution based on gestational age at diagnosis. Finally, our data further support a recent decision analysis suggesting that elective preterm delivery at 34 to 35 weeks without verification of fetal lung maturity allows for 100% survival.[12]

Our study had several limitations, which are difficult to overcome in a retrospective analysis. We have the inability to assess the detection rate of sonography in the diagnosis of vasa previa because of the need for outcome data on all pregnancies scanned. We do not have the data systems in place to obtain outcome information on normal sonograms, but it is our experience that our referring physicians, practically all of whom deliver in 1 of 5 Manhattan hospitals, provide us with feedback if adverse fetal outcomes occur. We do not know of any missed cases of vasa previa over the time included for analysis in this study. As other authors have observed, vasa previa shared an *International Classification of Diseases, Ninth Revision*, code with velamentous cord insertion until only recently; therefore, medical discharge code analysis at our collaborating hospitals would not be reliable in identifying cases.

We also address an interesting management dilemma. In some of our cases, the vasa previa migrated from the internal os. Nonetheless, remaining aberrant vessels were in proximity to the internal os (<2 cm away). This finding is similar to a low-lying placenta or marginal previa that is between 0.1 mm and 3.0 cm from the cervical os. The tendency to bleed and the need for cesarean delivery are increased when the placental edge is within 3.0 cm of the internal os.[13] More recently, some authors have suggested that the term "low-lying placenta" should only be used if the placental edge is located farther than 2 cm but within 3.5 cm from the internal cervical os, as these patients can safely undergo labor and vaginal delivery, and the risk of bleeding is low.[14] Therefore, we suggest that patients with aberrant velamentous fetal vessels within 2.0 cm of the internal os should be treated like patients with placentas overlying or near the internal os because of a risk of severe fetal hemorrhage and fetal mortality with cervical dilatation or membrane rupture.

In summary, our standardized screening protocol for vasa previa was effective in diagnosing vasa previa during the second and third trimesters. Vasa previa diagnosed during the second trimester resolves in approximately 24% of cases; however, no case of vasa previa diagnosed during the third trimester resolved by the time of delivery in our population. We recommend that patients at risk of vasa previa (ie, those with multiple gestations, a history of a low-lying placenta or placenta previa in the second trimester, a velamentous cord insertion in the lower uterine segment, or a succenturiate lobe in the lower uterine segment) should be evaluated with transvaginal sonography of the cervix and lower uterine segment for signs of vasa previa using grayscale and color flow imaging modalities. We agree with the previous reviews suggesting that elective delivery at 35 weeks is optimal for the best planned outcome. Scheduled cesarean delivery at 35 to 36 weeks after corticosteroid use for fetal lung maturity seems reasonable, as the likelihood of spontaneous labor rises after that gestational age.

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