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## Abnormalities of the Umbilical Cord

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### Abstract

Abnormalities of the umbilical cord, related to morphology, placental insertion, number of vessels and primary tumors, can influence the perinatal outcome and may be associated with other fetal anomalies and aneuploidies. The chapter investigates the most important congenital anomalies of this structure. Single umbilical artery appears to be associated with ventricular septal defects and conotruncal anomalies, hydronephrosis, dysplastic kidneys, esophageal atresia, spina bifida, holoprosencephaly, diaphragmatic hernia, and cystic hygromas. Velamentous insertion of the cord can be associated with trisomy 21, spina bifida, ventricular septal defects, and esophageal atresia. A hypoplastic umbilical artery has an artery-to-artery diameter difference of more than 50%; described anomalies include trisomy 21, polyhydramnios, congenital heart disease, and fetal growth restriction. Pseudocysts are more common than true cysts, and they are strongly associated with chromosomal defects and other congenital anomalies, especially omphalocele, hydrops, and trisomy 18. Other benign masses are teratomas, angiomyxomas, and patent urachus. Alterations in morphology and ultrastructure of the umbilical cord should extend the investigation, since there are associations with chromosomal anomalies.

**Keywords:** umbilical cord, prenatal ultrasound, congenital anomalies, fetal malformations, outcome

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## 1. Introduction

Umbilical cord makes stable interconnection between fetal well-being and placenta at the fetomaternal interface level. The prenatal ultrasonographic assessment of the umbilical cord offers the possibility to investigate the morphologic characteristics during fetal life, from early to late gestation.

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The umbilical cord structure can be demonstrated by conventional real-time ultrasound and the umbilical blood flow patterns can be analyzed by color (power) and pulsed Doppler ultrasound, which relate to its functionality [1]. Second trimester scan is able to assess four characteristics of the umbilical cord: measurement of umbilical cord area, evaluation of the number of vessels, assessment of placental umbilical cord insertion site, and determination of the coiling pattern [2].

Abnormalities of the umbilical cord related to morphology, placental insertion, number of vessels, and primary tumors can influence the perinatal outcome and may be associated with other fetal anomalies and aneuploidies. Many of these conditions are being diagnosed in utero as prenatal ultrasound becomes more sophisticated nowadays.

Using ultrasound, we can depict various congenital abnormalities of the umbilical cord, including cysts, pseudocysts, umbilical vein varix, persistent right umbilical vein, angiomyxomas, aneurysm, single umbilical artery (SUA), velamentous insertion, and teratomas.

## **2. Abnormal number of vessels**

Sometimes, during pregnancy, changes in the number of umbilical vessels may occur. Abnormal number of umbilical cord vessels includes: two-vessel cord (single umbilical artery), four-vessel cord (two veins and two arteries, one vein and three arteries), five and more vessels cord (numerous variations in conjoined twins), umbilical cord that does not keep the same number of vessels at the fetal and placental extremity [3].

### **2.1. Single umbilical artery**

It seems that the first descriptions of the single umbilical artery were made in 1543 by Vesalius in *De Humani Corporis* [4]. It may be diagnosed with the finding of two vessels on a cross-section of the cord or a vessel seen on only one side of the fetal bladder. These anomalies appear to be more common when the left umbilical artery is absent and may be associated with aneuploid fetuses and renal anomalies in euploid fetuses. Atresia, aplasia, or agenesis of one artery can lead to single umbilical artery syndrome [5].

Single umbilical artery (SUA) is the most common abnormality of the umbilical cord.

There are three theories about the absence of umbilical artery pathogenesis: (1) primary agenesis of an umbilical artery; (2) atrophy or secondary atresia of the previously normally developed umbilical artery; and (3) persistence of the original allantoic artery of the body stalk [6]. It is suggested that from the embryological point of view, the second theory would be a reasonable explanation [7].

In single umbilical artery pregnancies, chromosomal abnormalities were found in 8–11% of fetuses, more commonly trisomy 13 and 18 and less frequently trisomy 21 [8], intrauterine growth restriction (IUGR), preterm birth, placental anomalies, and perinatal mortality [9, 10].

In rare cases, both umbilical arteries are missing and the one arterial vessel is, in fact, a persistent vitelline artery, which branches off the abdominal aorta. [11]. This persistent vitelline artery appears to be associated with serious developmental defects and was classified as type II single umbilical artery (type II SUA) by Blackburn and Cooley. This anomaly accounts for 1.5% cases of single umbilical artery [12]. According to the same authors, the most common form of single umbilical artery (98%) is type I that has one artery and one vein (left), whereas type II SUA has a frequency of 1.5%. Very rare forms are type III with one artery and two veins (left and persistent right umbilical vein) and type IV with one artery and one vein (right).

There is an increased incidence of severe malformations associated with type II SUA with the implication of the caudal body wall (sirenomelia, omphalocele-exstrophy-imperforate anus-spinal defects) and urorectal like exstrophy of the bladder, anal atresia, or urogenital agenesis [13].

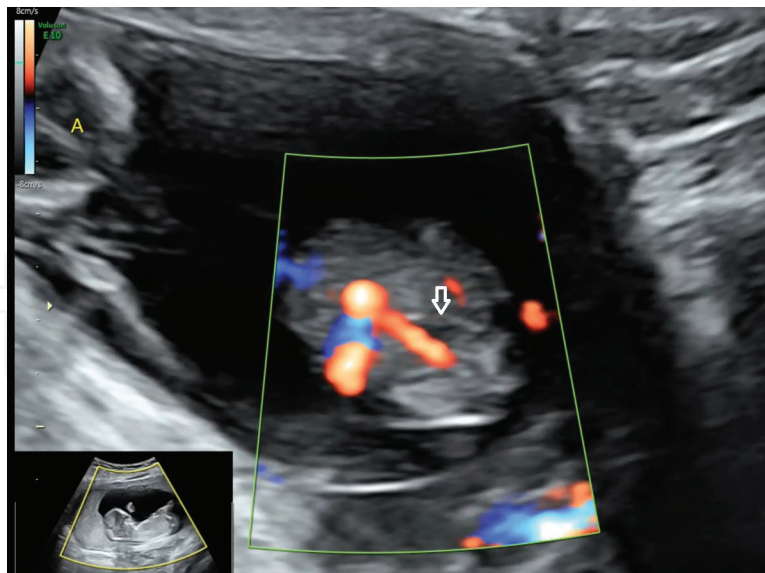
Among pregnancies with single umbilical artery associated with various malformations, two-thirds of deaths occur before birth. Regarding the other third of postnatal deaths, an increased incidence of fetal growth restriction and small placental size was found [14].

If no additional chromosomal or structural abnormalities occur, single umbilical artery is defined as an isolated SUA (iSUA) [10], and more than 90% of cases with SUA exhibit an isolated anomaly but without increasing the risk of chromosomal abnormalities [15]. Regarding adverse pregnancy outcomes and perinatal complications, studies show discordant results. A meta-analysis suggests that there is no significant association between iSUA and pregnancy outcomes [16, 17], while another meta-analysis suggests that iSUA is associated with a significant increase in adverse perinatal outcomes [18].

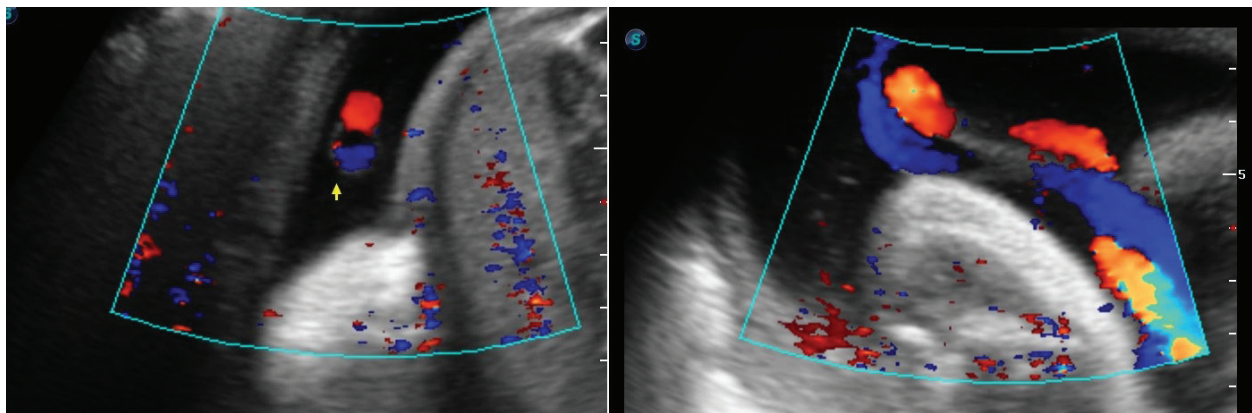
Single umbilical artery can be diagnosed in the first trimester using color Doppler and high-definition ultrasound with a low pulse repetition frequency (PRF) and a high color gain. Visualization of the umbilical arteries is preferable at the level of the fetal urinary bladder (**Figure 1**) by demonstrating the cord's perivesical course [19].

In conclusion, the easiest way to assess the number of arteries by ultrasound is by identifying the intra-abdominal portion of the umbilical artery alongside the bladder with color Doppler and/or by visualizing the cross-section of a free-floating loop of umbilical cord (**Figure 2**) [20]. In a 1991 study, Nyberg's group concluded that prenatal sonography alone was reliable in detecting any associated anomalies. They also recommended no management modification in cases with no concurrent anomalies [7]. The visualization of that anomaly should prompt a detailed sonographic assessment of the cardiovascular and genitourinary systems [3].

Fetal anomalies most commonly associated with single umbilical artery include several anomalies like ventricular septal defects, hydronephrosis, cleft lip, ventral wall defects, esophageal atresia, spina bifida, hydrocephaly, holoprosencephaly, diaphragmatic hernia, cystic hygromas, and polydactyly or syndactyly. In these cases, fetal echocardiography and karyotype analysis should be considered. Usually, there are no specific fetal abnormalities to be associated with the single umbilical artery. In fact, the single umbilical artery is often found in cases with healthy neonates, with a normal size and development at term. Although, to be sure that the infant has no hidden anomalies, the pediatrician should be notified of its existence to



**Figure 1.** Visualization of the umbilical arteries at the level of the fetal urinary bladder.



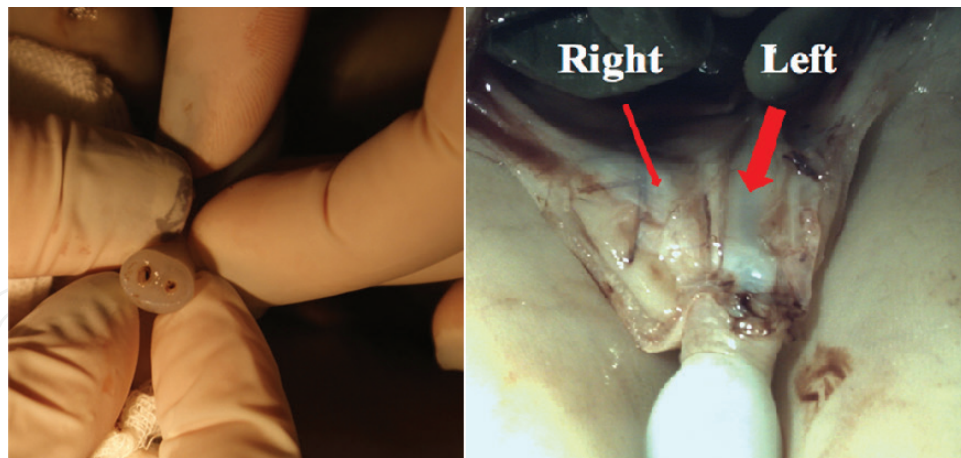
**Figure 2.** Color Doppler visualization of a free-floating loop of umbilical cord.

have a more detailed physical examination [11, 21]. Ultrasound views of the heart described in FMF's recommendations (minimum four-chamber view, outflow tract, and three-vessel view) can detect 66% of the heart malformations associated with single umbilical artery. The undiagnosed ones are minor and have a favorable outcome [22].

Nonisolated SUA requests invasive testing with chromosomal microarray because the risk of syndromes and chromosomal anomalies are substantially increased (**Figure 3**). Isolated SUA with a normal insertion of the cord does not require special precautions during labor. In these cases, the long-term outcome for children is the same as for children born with three vessels in the umbilical cord [23].

## 2.2. Persistent right umbilical vein

Unusual persistence of the right umbilical vein with left vein umbilical regression will lead to alteration in the development of embryonic vasculature, knowing that in the normal

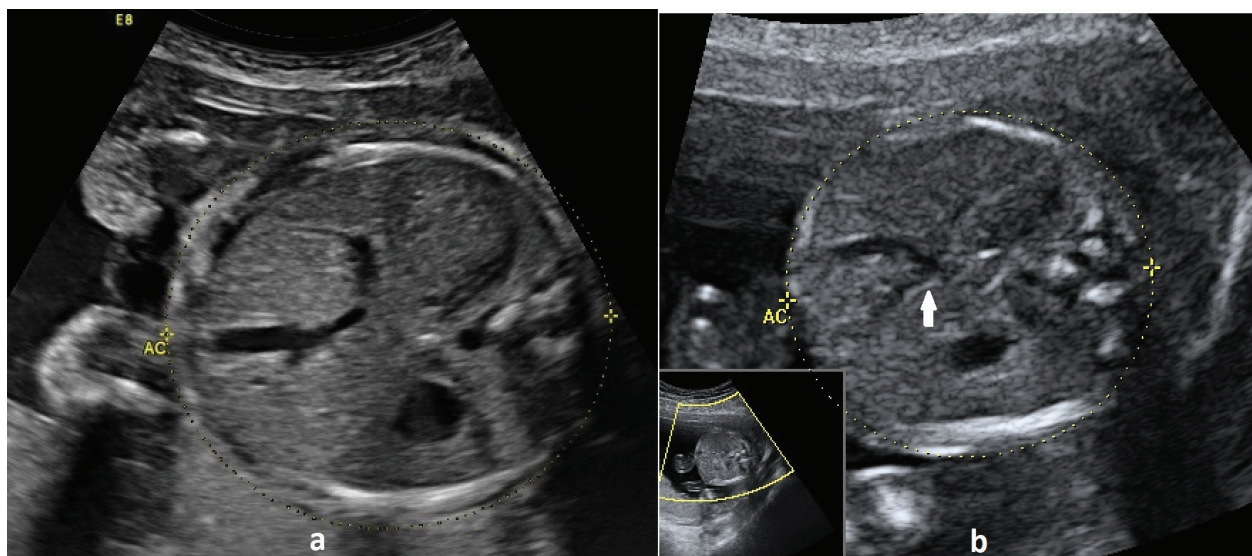


**Figure 3.** SUA at necropsy.

fetus, the right umbilical vein disappears by the seventh week of gestation. This condition does not alter the formation of ductus venosus, the distribution of blood to the fetus remaining normal [24]. First-trimester folic acid deficiency, teratogens such as retinoic acid or early obstruction of the left umbilical vein from external pressure or occlusion are considered etiologic factors [25].

The ultrasound diagnosis is made in the transverse section of the fetal abdomen. Umbilical vein is abnormally connected to the right portal vein instead to the left portal vein, and fetal gallbladder is located between the umbilical vein and the stomach [26] (**Figures 4 and 5**).

It is associated with congenital anomalies: cardiac anomalies, trisomy 18, abdominal visceral situs inversus, total anomalous pulmonary venous connection, urinary tract malformation like unilateral renal agenesis, umbilical vein varix, skeletal malformations, and others [27].



**Figure 4.** Persistent right umbilical vein: (a) Normal section of abdominal circumference and (b) section of abdominal circumference with persistent right umbilical vein view.

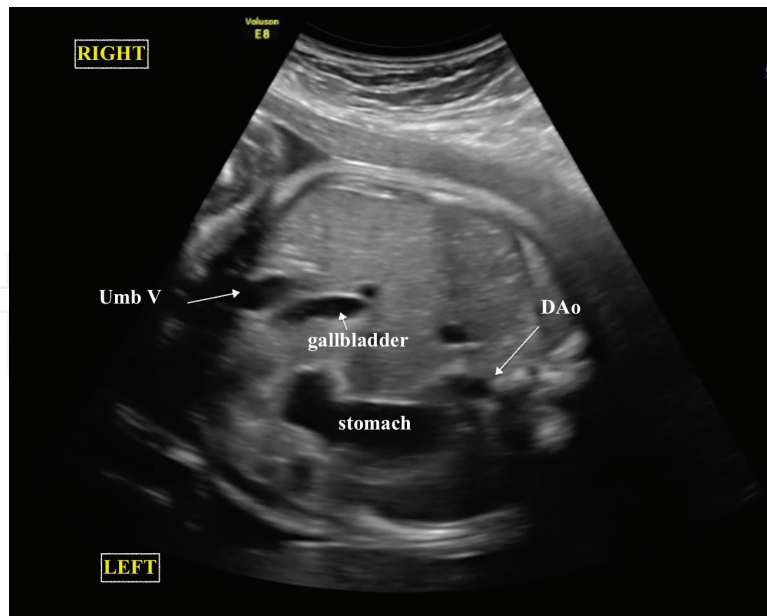


Figure 5. Persistent right umbilical vein (*DAo*, descending aorta).

### 2.3. Four-vessel umbilical cord

Five percent of umbilical cords exhibit a four-vessel structure due to the persistence of small vitelline arteries, which follow the normal twisting of the main umbilical arteries. [28].

Four umbilical vessels view is an abnormal situation that has been reported to be associated with major congenital anomalies [29]. The presence of three umbilical arteries is the most common situation of four-vessel cord, although in the specialty literature have been reported a few cases of cord with two umbilical veins and two umbilical arteries [30].

## 3. Abnormal course or connection of vessels

The insertion of umbilical cord can be located following the chorionic plate vessels using color Doppler technique. The placental insertion of the UC is better observed by ultrasound in the first trimester. Later when gestational age increases, visualization becomes difficult, especially when the placenta is posterior. The evaluation of fetal circulation is done by examining the umbilical arteries. The umbilical vascular evaluation provides information on the circulation at the fetomaternal interface level, giving the possibility of early detection of risk to the fetus [19].

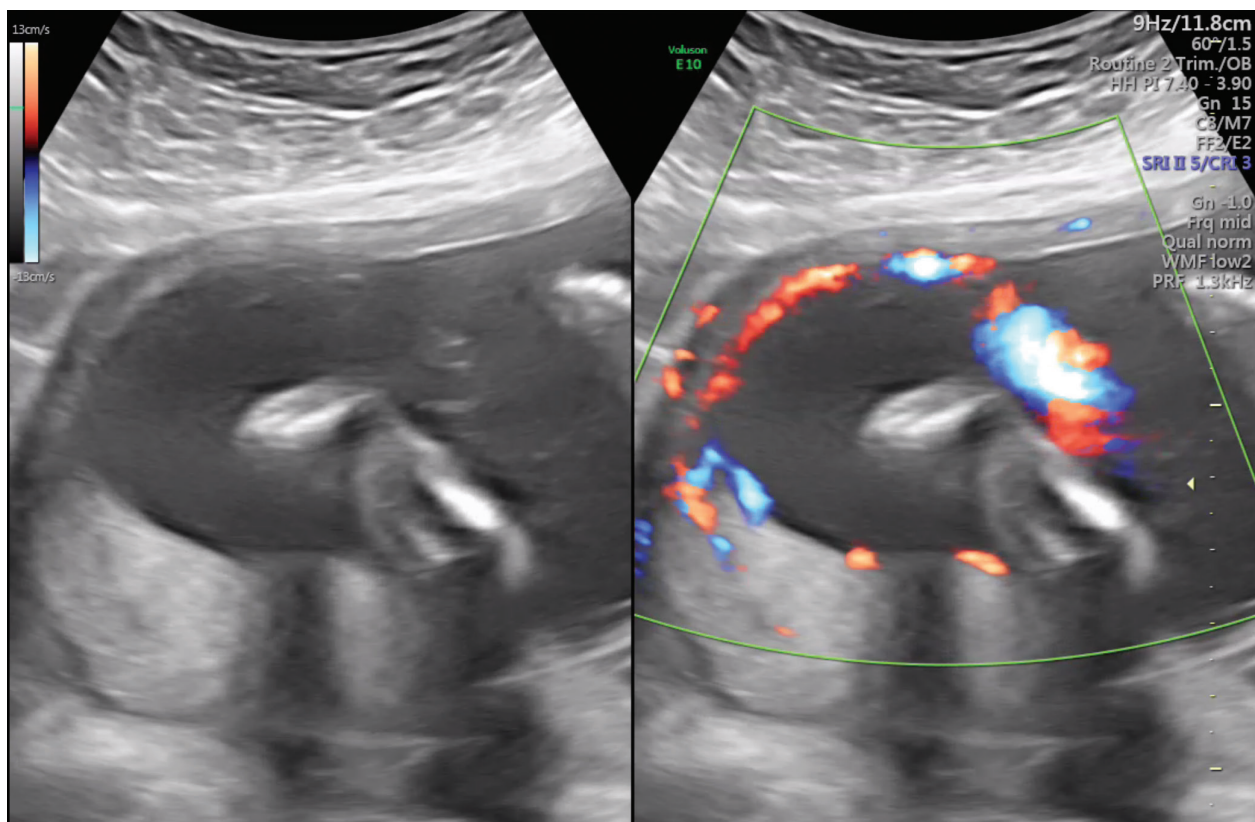
### 3.1. Velamentous insertion of the cord

The umbilical cord insertion is located on the placental mass in about 99% of cases, into the central portion of the placenta. The velamentous insertion is the condition in which the umbilical vessels are configured between amnion and chorion before reaching the placenta on the chorioamniotic membranes [31]. That abnormal insertion occurs when the cord implants in the trophoblast anterior to the decidua capsularis or when placental tissue grows laterally,

leaving an area which becomes atrophic. The umbilical cord inserts into the chorion leave at a point away from the placental mass and appears as membranous umbilical vessels at the placental insertion site (velamentous vessels are not protected by Wharton's jelly), the rest of the cord is usually normal. This type of pathological insertion of the cord occurs in 1–2% of singleton pregnancies. In multiple pregnancies, the incidence of velamentous cord insertion is 10-fold higher than in singleton pregnancies [32] (**Figure 6**).

Heinonen et al. [33] in this aberrant attachment, such as at the margins or to the membranes, found an association with higher maternal serum human chorionic gonadotropin (hCG) and lower maternal serum alpha-fetoprotein (AFP). However, until further data is available, no specific recommendations can be made.

Prenatal identification of these pregnancies is an important issue. There is a higher risk for an adverse perinatal outcome like intrauterine growth retardation, preterm birth, placental abruption, vasa previa, low Apgar scores at 1 and 5 min, neonatal death, congenital anomalies, and fetal bleeding [34]. Associated anomalies include trisomy 21, spina bifida, ventricular septal defects, esophageal atresia, obstructive uropathies, congenital hip dislocation, and asymmetrical head shape. It has been noted that a higher rate of deformations occur instead of malformations or disruptions [34]. Velamentous insertion associated with vasa previa appears to have an increased rate of congenital malformations. Also, 13% cases of single umbilical artery are associated with velamentous insertion [14].



**Figure 6.** Velamentous cord insertion.



## Vasa previa

It is important to be aware that velamentous cord insertion is associated with an increased rate of vasa previa. Vasa previa is a form of velamentous cord insertion in which velamentous vessels pass through the fetal membranes of the lower uterine segment and incidence is estimated to be 0.04% [35]. These fetal vessels may break when membrane rupture occurs and the result is fetal exsanguination. Intrapartum diagnosis is very difficult in this case [36].

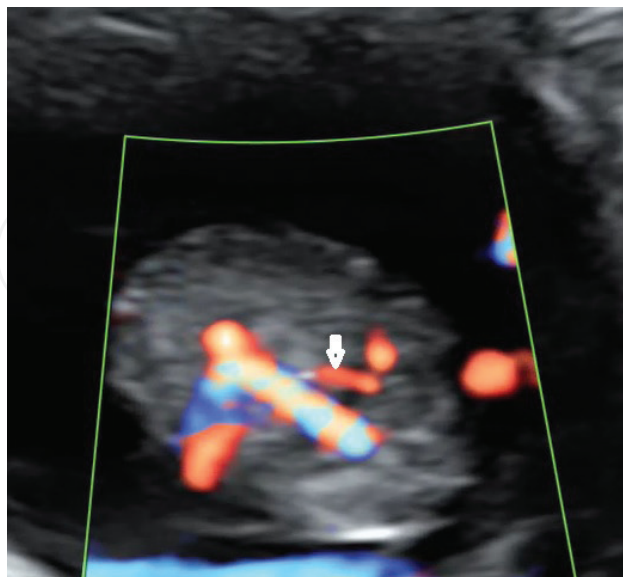
## 4. Abnormal structure or configuration of vessels

### 4.1. Hypoplastic umbilical artery

A hypoplastic umbilical artery has a smaller diameter than the contralateral artery, showing by ultrasonography an artery-to-artery diameter difference of more than 50% [37] (**Figure 7**).

It seems that the hypoplastic umbilical artery represents a mild form of the single umbilical artery. Described anomalies include trisomy 21, polyhydramnios, congenital heart disease, stillbirth, trisomies, and fetal growth restriction. The presence of discordant umbilical arteries is a sign of different umbilical artery blood flow indices and of placental disease [38]. This condition increases the risk of IUGR, placental infarction, umbilical cord hematoma, and abnormal umbilical cord insertion. It is also known that the fetal prognosis is better for hypoplastic umbilical arteries compared with SUA syndrome [37].

Karyotyping is not indicated in isolated hypoplastic umbilical artery because there is no evidence of increased risk of chromosomal defects.



**Figure 7.** Hypoplastic umbilical artery.

#### 4.2. Umbilical vein varix

Umbilical vein varix is a rare condition which occurs in the intrahepatic portion of the umbilical vein presents an incidence of 2.8:1000 [39]. Ultrasound scan usually discovers a circular vessel dilation  $\geq 9$  mm, 59 or more than 50% over the diameter of the intrahepatic UV [40]. The condition is associated with chromosomal anomalies in up to 12% of cases, especially trisomy 21 and poor fetal outcome with emergent cesarean delivery [41].

Complete follow-up includes karyotyping, regular fetal testing, and third trimester interval growth studies [42]. Because the incidence is very low, the clinical significance remains controversial.

#### 4.3. Umbilical artery aneurysm

Umbilical artery aneurysm is an extremely rare vascular anomaly usually associated with high risk of fetal aneuploidy, IUGR, and fetal demise. Fetal demise is a result of compression of the dilated artery on the umbilical vein, thrombus formation, or due to associated fetal anomaly like trisomy 18 [43]. This condition is a vascular anomaly which appears as an anechoic cyst close to cord insertion with a hyperechogenic rim in which color flow and spectral Doppler examinations show nonpulsatile and turbulent blood flow within the artery [44].

It is important to consider karyotype analysis given the high incidence of aneuploidy associated with umbilical artery aneurysm.

Tumors of the Umbilical Cord

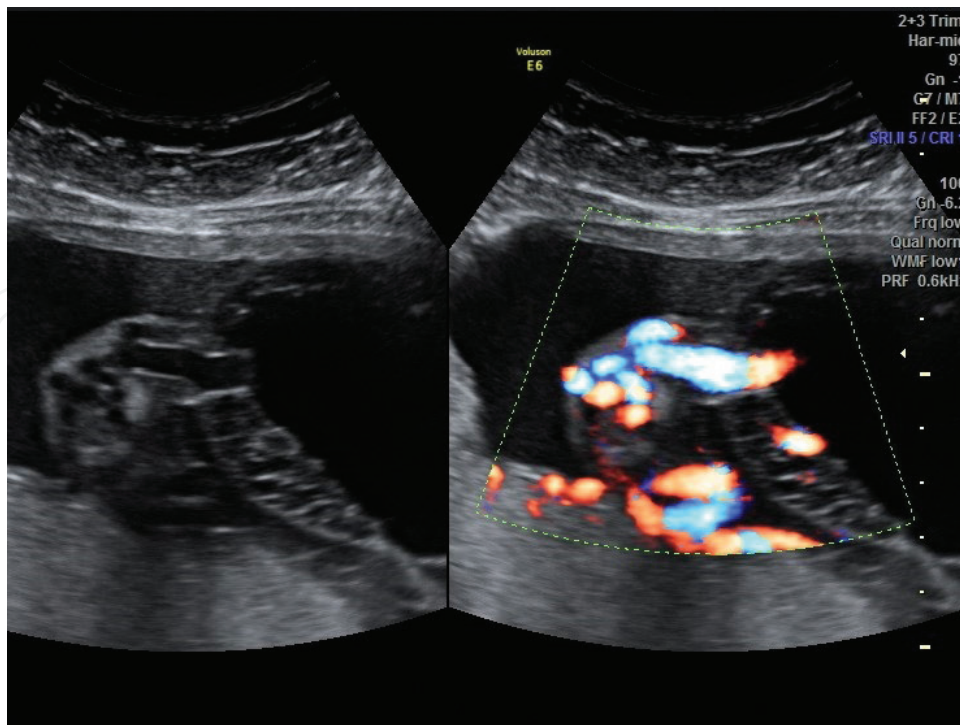
#### 4.4. Cord cysts

Cord cysts have no clinical relevance and develop from the remnants of the allantois or the omphalomesenteric duct. The finding of an isolated umbilical cord cystic mass should lead to further detailed sonographic evaluation and karyotype testing should be done when IUGR or other anomalies are found [45]. The majority of first-trimester cysts are transient ultrasound findings that have no influence on pregnancy outcome [46]. The prognosis of persistent cysts appears to be similar to that of second-trimester cysts [47].

Several studies concluded that morphologic features of cord cyst (single, multiple) correlate with fetal abnormalities like abdominal wall defects and patent urachus [48].

Umbilical cord cysts are classified as true cysts or pseudocysts. True cysts have an incidence of 3.4% in first trimester of pregnancy and have no clinical significance, and are sometimes associated with fetal structural anomalies and aneuploidy [45]. True cysts are derived from the embryological remnants of either the allantois or the omphalomesenteric duct, are located typically toward the fetal insertion of the cord and range from 4 to 60 mm in size [49].

The exact cause of umbilical cyst is not known, but it is thought to be due to raised hydrostatic pressure in the umbilical vessels (**Figure 8**).



**Figure 8.** Large umbilical cyst in the second trimester.

Pseudocysts are more common than true cysts and can be located anywhere along the cord; they have no epithelial lining and represent localized edema and liquefaction of Wharton's jelly (known as Wharton jelly cysts). It is rarely possible to differentiate between true cysts and pseudocysts on ultrasound imaging [50]. But differentiation between the two entities is not very important because both are associated with anomalies. Pseudocysts are more common than true cysts and they are strongly associated with chromosomal defects and other congenital anomalies, especially omphalocele, hydrups, and trisomy 18 [51]. Usually, ultrasonography monitoring is sufficient, invasive tests not being typically needed. A higher risk of fetal anomalies is associated with the following: detection of cysts in the second or third trimester, persistence after the first trimester, large size, and location near fetal or placental end. Also, trisomy 18, 13, and 21 are known to be associated, in such cases, chromosomal analysis may be warranted [52].

They might be associated with omphalocele, Meckel's diverticulum, patent urachus, and hydronephrosis. False cysts are most commonly found at the fetal end of the cord, do not have an epithelial lining and might be associated with omphalocele, patent urachus, and chromosomal anomalies [53]. Twenty percent of cord cysts, no matter what type they are, are associated with structural or chromosomal anomalies [54].

When the umbilical cyst is detected antenatally, especially in second or third trimesters, it is recommended a detailed ultrasonographic examination of the fetus, and it should be carefully looked for any associated defects. In case of any suspicion should be done the karyotyping analysis.

#### 4.5. Umbilical cord teratomas

They are rare benign lesions, only 12 cases reported in the literature, which may lead to adverse fetal outcomes. These tumors are the only true neoplasms of the umbilical cord which

have a very polymorphic presentation and should be evaluated when the lesion contains calcifications [55].

It can also be associated with severe fetal anomalies such as anencephaly, intestinal anomalies, and abdominal wall defects. The outcome in extragonadal teratomas can be affected by the presence of associated anomalies and surgical complications after correction of the congenital malformations [56].

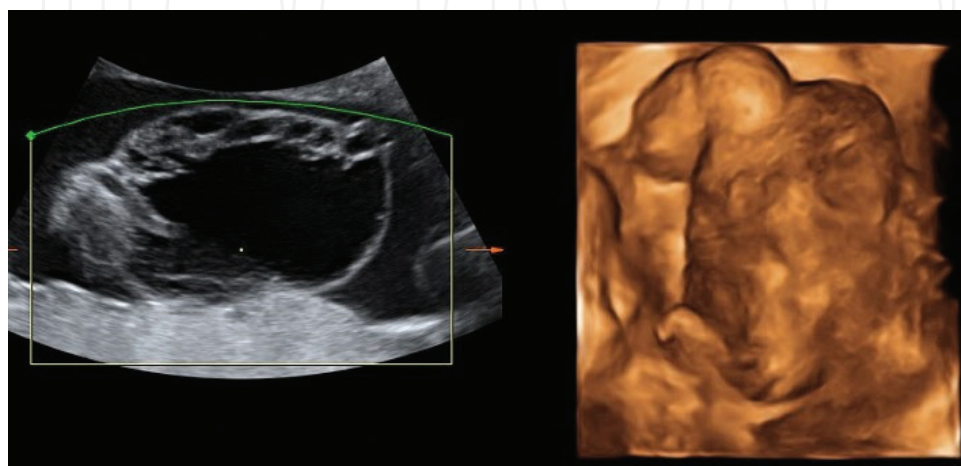
Angiomyxomas are benign solid masses which may be associated with fetal demise. Associated complications are premature delivery, cardiovascular anomalies, nonimmune hydrops fetalis, hydatidiform mole, polyhydramnios, and stillbirth [57]. The management of pregnancy with angiomyxoma in the third trimester is not well defined.

## 5. Patent urachus

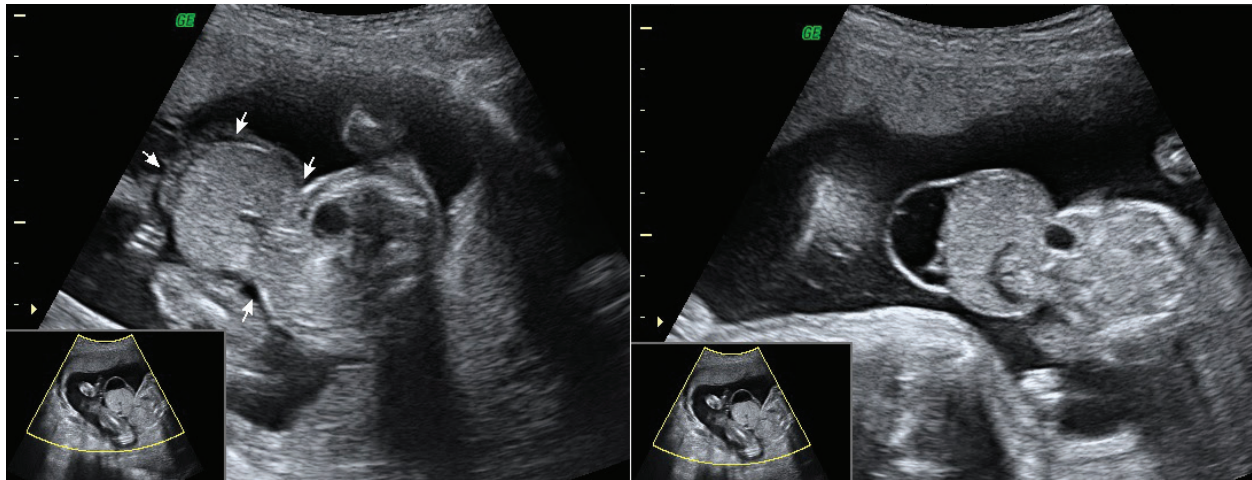
Urachus represents a vestigial structure formed by the bladder dome and the obliterated umbilical arteries. Patent urachus represents 10–15% of all urachal anomalies in the literature [58] and may lead to urination through umbilicus and infections. It is a rare condition because urachal lumen typically closes at week 17 post-conception [59]. Alterations in the morphology of the umbilical cord should extend the investigation, since there are associations with chromosomal anomalies. It has been associated with bladder exstrophy and anterior abdominal wall defects.

## 6. Congenital hernia of the umbilical cord

Congenital hernia of the umbilical cord (CHUC) is a rare congenital entity recognized as a distinct entity since the 1920s but is often misdiagnosed as a small omphalocele. During the first 5th–6th week of gestation, the bowel herniates into the developing umbilical cord and withdraws into the abdominal cavity until the 10th–12th week of gestation [60]. Return of



**Figure 9.** Large umbilical cyst 3D view.



**Figure 10.** Congenital hernia of the umbilical cord.

physiologically herniated bowel or failed closure of umbilical ring (**Figures 8 and 9**). A review of the literature described associated malformations like pulmonary stenosis, cleft lip and palate, ear tag, small and large bowel atresia and stenosis, short bowel syndrome, tetralogy of Fallot, Meckel's diverticulum, persistent cloaca, and congenital glaucoma [61] (**Figure 10**).

## 7. Congenital umbilical arteriovenous malformation

The literature reported extremely rare cases of congenital umbilical arteriovenous malformation, less than 10 cases communicated in literature because congenital arteriovenous malformations are found most commonly in the brain, liver, and extremities. Congenital umbilical arteriovenous malformation is congenital lesions presented as a multitude of arteries and veins connected by a fistula. This condition can be asymptomatic but can also lead to congestive heart failure and massive hemorrhagic shock [62].

## 8. Conclusion

Invasive (diagnostic and therapeutic) procedures implying the puncture of the umbilical circulation are widely guided by ultrasound. Therefore, perinatal management may be enhanced by a prenatal ultrasonographic depiction of the morphology of the umbilical cord. In early pregnancy should be undertaken targeted examination because many details of cord development become difficult to identify on ultrasound with increasing gestational age. It is known also the association with structural (especially cardiovascular) and chromosomal anomalies, and for that further extended investigation should be needed in case of detection of abnormalities in the number, structure, or course of cord vessels. Most cases with isolated congenital anomalies of UC have a favorable outcome. Particular attention should be paid to umbilical cord insertions, both fetal and placental one. In apparently isolated single umbilical

artery, further ultrasound scans during the late pregnancy and continuous fetal-heart-rate monitoring during labor should be offered. The single umbilical artery assumes an additional risk and the parents should be advised of the need for extra surveillance; they have to be also aware regarding the possibility of detection of some possible associated abnormality only after delivery.

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