

Superb Microvascular Imaging of the Placenta

Natsumi Furuya¹, Junichi Hasegawa², Nao Suzuki³

ABSTRACT

Similar to ultrasound fetal morphological assessment during pregnancy, the placenta and umbilical cord should also be screened around the 20th week of gestation. Additionally, in pathologic conditions such as fetal growth restriction (FGR), preeclampsia, and various placental abnormalities, detail morphological and/or functional evaluations using Doppler methods are required. Superb microvascular imaging (SMI) is a new blood flow imaging technique that employs a unique algorithm to minimize motion artifacts by eliminating signals based on the analysis of tissue movement. While observing a placenta using SMI, dendritic blood flow from the umbilical cord indicating fetal blood flow can be seen on the background of scatter flow indicating maternal intervillous blood flow that beats in line with the mother's heartbeat. Using this modality, placental pathological findings can be obtained antenatally, especially histological findings of infarction and avascular villi. In the present review, SMI findings in the various pathologic placenta are demonstrated. These investigations may improve clinical practice in cases with placental abnormalities such as preeclampsia and FGR.

Keywords: Placental abnormalities, Pregnancy, Superb microvascular imaging.

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INTRODUCTION

In antenatal ultrasound for pregnant women, the placenta and umbilical cord should also be screened with a fetal morphological scan. So far, usually, B-mode has only been used to screen for morphological assessment of the placenta, including location in the uterus, positional relationship with the umbilical cord, and structural abnormalities. Color Doppler is occasionally applied for differential diagnosis among hematoma and hemangioma in cases with hemorrhage; however, the usefulness of color Doppler in placental assessment is limited.

Superb microvascular imaging (SMI) is one of the color Doppler imaging techniques provided by Canon medical systems that employs a unique algorithm to minimize motion artifacts by eliminating signals based on the analysis of tissue movement. Since SMI can depict flows in minute vessels clearly, peripheral blood flows in the placenta are also detectable. Therefore, we are evaluating various placental abnormalities using SMI comparing to placental pathologic findings as our pilot study.

In this review article, we demonstrate a general ultrasound assessment of the placenta and additional investigation using SMI in our experiences.

ULTRASONOGRAPHY OF THE PLACENTA

During pregnancy, the placenta should also be screened around the 20th week of gestation along with fetal screening. Positional and morphological evaluations are performed during screening. If fetal growth restriction (FGR) or oligohydramnios is observed, functional evaluation of the fetal and placental circulations is needed using various Doppler measurements (Fig. 1).

Evaluation of Placental Location in the Uterus

Placenta previa causes problems such as heavy bleeding and should be screened during the second trimester of pregnancy. During pregnancy, the uterine isthmus opens, and the uterine muscle expands until the second trimester of pregnancy. The placenta appears to move toward the uterine body; therefore, a locational diagnosis of the placenta is made after 20 weeks

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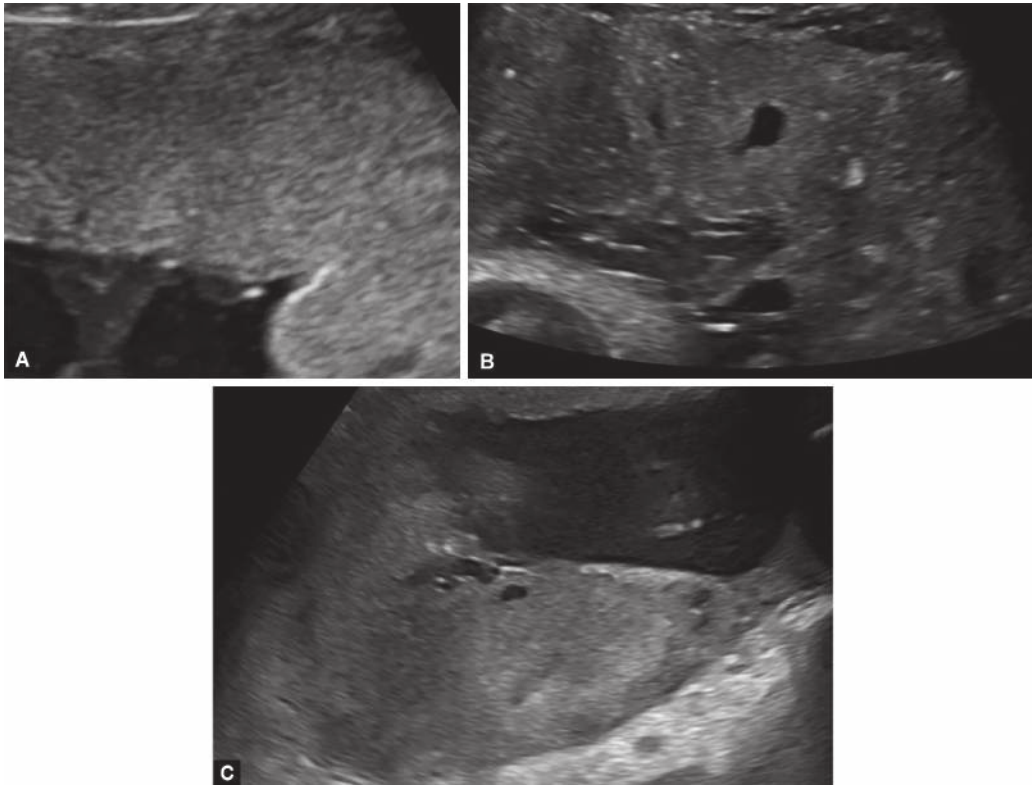
of pregnancy.¹ It is important to confirm and diagnose the positional relationship between the cervical canal, sub-uterine segment, histologically internal uterine ostium, and placental margin using transvaginal ultrasound before the sub-uterine segment is dilated.

A high prediction rate of placenta previa was obtained using transvaginal ultrasound at 20–24 weeks of gestation after the opening of the isthmus by carefully distinguishing between the cervix and isthmus.² If the placenta adheres to the anterior wall of the uterus, it was evaluated whether it has been affected by a previous cesarean section or the presence of placenta accreta spectrum (PAS).

Morphological Evaluation

As morphological abnormalities of the placenta and umbilical cord could be present, the overall size and morphology of the placenta were evaluated, and the presence or absence of lobulated and accessory placenta was confirmed. Abnormal findings, such as hematoma and infarction, were observed in the evaluation of the placental parenchyma and margins.

The umbilical cord is usually attached to the center of the placenta. A diagnosis of abnormal umbilical cord insertion, which is associated with FGR, abnormal fetal heart rate tracing, and non-reassuring fetal status, is made when the umbilical cord attaches to



Figs 1A to C: Placental growth in ultrasonography in B-mode: The placental parenchyma in the early stages of pregnancy is visualized with uniform echo-brightness, but as the number of weeks of pregnancy elapses, the lobulation becomes apparent due to the development of villous blood vessels. The grade progresses along with gestation. (A) Grade I; (B) Grade II; (C) Grade III

the placental margin (marginal insertion) or to the amnion rather than the placental parenchyma (velamentous cord insertion).³⁻⁶

Furthermore, the diagnosis of vasa previa should be made when velamentous aberrant vessels run near the internal uterine ostium. Since this causes an extremely high risk of collapse during labor or rupture of the membrane, antenatal ultrasound screening diagnosis and elective cesarean section are necessary to save infants.^{4,7,8}

Functional Evaluation

Pulsed Doppler measurement is performed to evaluate fetal and placental circulations in cases of FGR and oligohydramnios caused by the placenta. Pulsed Doppler measurement evaluates the blood flow in the umbilical artery and vein to assess the blood flow between the fetus and placenta, and the uterine artery Doppler waveform is used to evaluate the uterine-placental circulation. Both procedures evaluate the primary blood flow in the placenta and uterus.

It has been reported that when 30% of placental villous vessels are damaged, umbilical artery end-diastolic flow decreases (pulsatility index: PI/resistance index: RI increases) due to increased vascular resistance, and when 70% of placental villous vessels are damaged, umbilical artery absent end-diastolic velocity: UA-AEDV/umbilical artery reversed end-diastolic velocity: UA-REDV appears.⁹ By the time of delivery, almost all patients had elevated UA blood flow resistance ($n = 97, 93.3\%$), the majority had brain sparing ($n = 61, 58.7\%$), and approximately one-third had an elevated ductus venosus: DV Doppler index.¹⁰

NORMAL ULTRASOUND FINDINGS OF THE PLACENTA

B-mode

In early gestation, the placenta is visualized with uniform echo-brightness, but with advancing gestation, the boundary between the placenta and other chorions becomes clear, and the development of chorionic villi causes lobulation. The intervillous space of the placental parenchyma may be enlarged or calcified.¹¹

The decidual region between the placental parenchyma and the uterine myometrium can be visualized as a thin hypoechoic linear region called "clear zone".¹² At the placental margin, there is a marginal venous sinus through which blood in the villous space is discharged to the uterus, and it is visualized as a hypoechoic region with gentle blood flow inside.

The umbilical cord usually consists of two umbilical arteries and one umbilical vein. It is necessary to confirm the degree of umbilical cord twisting and insertion. The umbilical cord is usually located at the center or slightly lateral to the placenta (Fig. 2).

Conventional Color Doppler

In conventional color Doppler imaging of the placenta, the blood flow in the placenta is visualized; however, it is difficult to visualize the minute blood flow of the villous tree. Fetal blood vessels on the surface of the placenta can be evaluated using conventional color Doppler imaging. Recently developed color Doppler methods, such as Slowflow® (GE Healthcare, Chicago, Illinois, USA) and SMI® (Canon

Medical Systems, Tokyo, Japan), which can detect minute flow, improve visualization of peripheral blood flow in the villous tree.

In color Doppler imaging of the umbilical cord, two umbilical arteries and one umbilical vein are visualized in different twisting colors in a normal umbilical cord (Fig. 3).

Superb Microvascular Imaging

Superb microvascular imaging is a new blood flow imaging technique that employs a unique algorithm to minimize motion artifacts by eliminating signals based on the analysis of tissue movement. Compared with conventional blood flow imaging methods, such as color and power Doppler imaging, SMI significantly reduces motion artifacts and can visualize low-velocity blood flow in small vessels.¹³ For example, the liver, breast, thyroid, skeletal muscle, and carotid plaques have been evaluated.¹⁴

Superb microvascular imaging can depict microvessels and minute blood flow that cannot be delineated by color Doppler imaging without using an ultrasonic contrast medium. Superb microvascular imaging is also useful in assessing peripheral blood flow in the placenta because the placenta is a collection of small villous blood vessels, and the delicate maternal blood circulates in the intervillous space¹⁵⁻¹⁷ (Fig. 4).

While observing a normal placenta using SMI, the so-called scatter can be seen in the background of the entire placenta. It beats in line with the mother's heartbeat, and it is thought that the blood flow from the spiral artery into the villous space is depicted.¹⁵

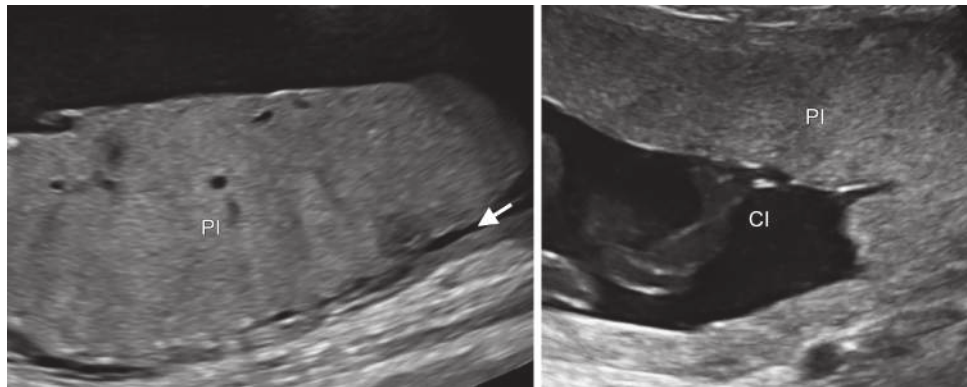
In addition, the blood flow depiction looks like a dendrite in the placenta, and upon closer examination, blood flow from the umbilical cord insertion to the placental margin can be observed. It is considered that the stem and terminal villi are observed during umbilical cord insertion.¹⁵

ABNORMAL ULTRASOUND FINDINGS OF THE PLACENTA USING SUPERB MICROVASCULAR IMAGING

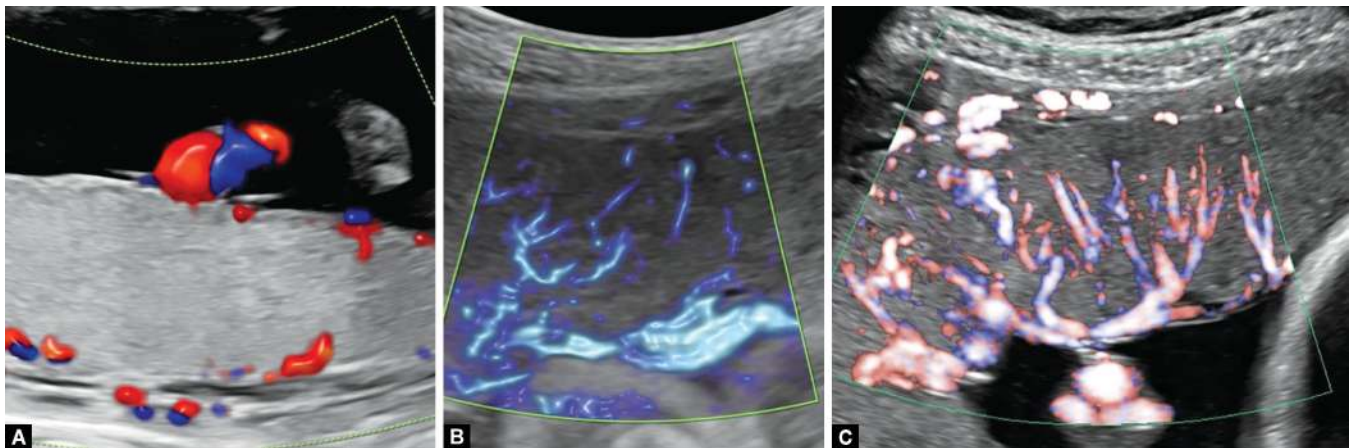
Locational Abnormalities

Cervical Pregnancy

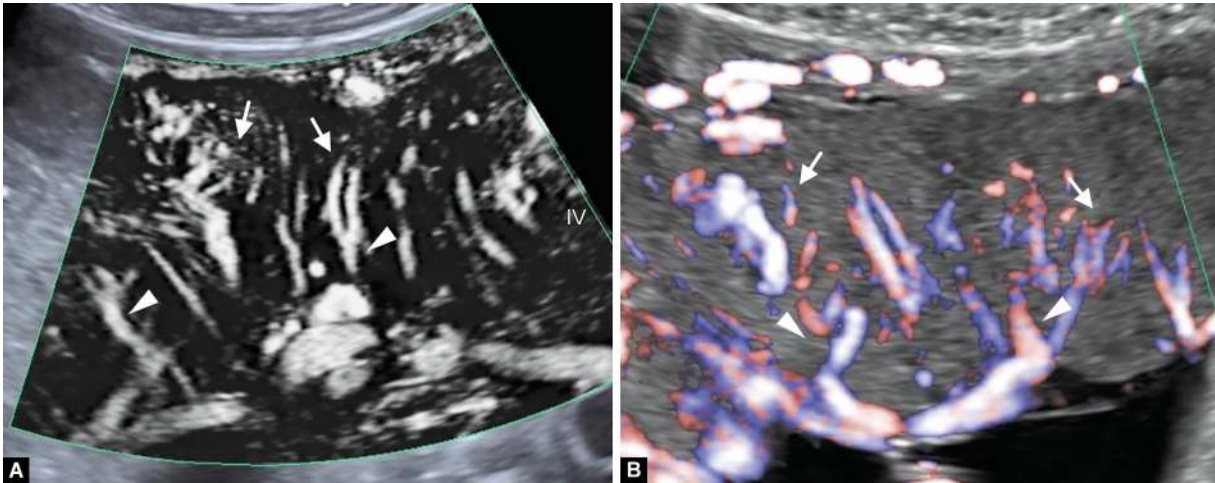
Since the blood flow is slow in early gestation, it is difficult to visualize the blood flow even with conventional color Doppler imaging. However, using SMI, it is possible to visualize the minute blood flow surrounding the villi even in the first trimester, which may be useful for diagnosing and managing cervical pregnancy and determining the therapeutic effect of treatments (Fig. 5).



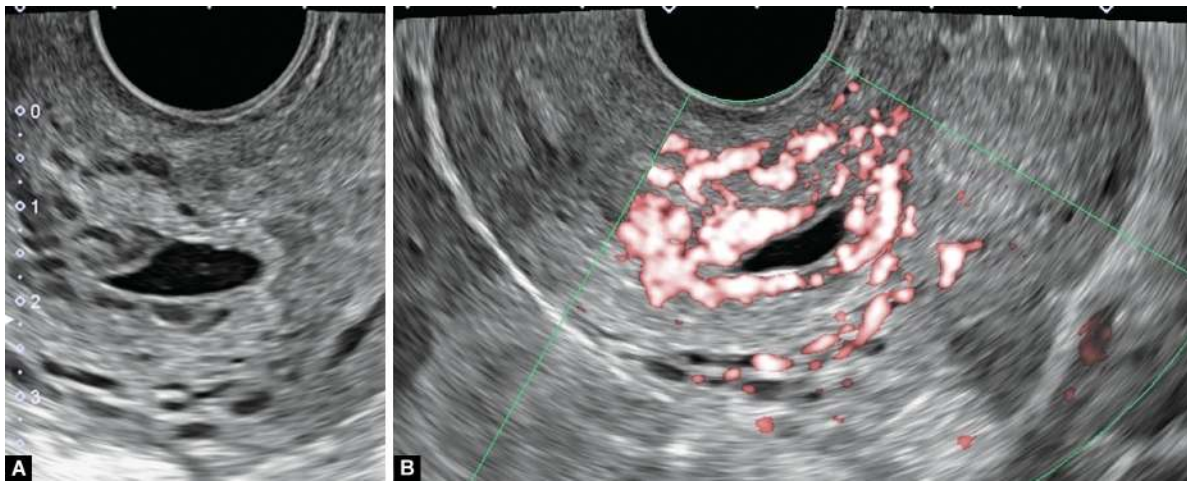
Figs 2A and B: Normal placental findings in B-mode: (A) Normally, there is a chorion between the myometrium and placenta, which is visualized as a “clear zone” using ultrasound; (B) Normally, the umbilical cord is attached to the center of the placenta. PI, placenta, CI, cord insertion, arrow: clear zone



Figs 3A to C: Normal placental findings in various color Doppler imaging: (A) Conventional color Doppler imaging; (B) recent color Doppler imaging that can depict slow flow (Slowflow®, GE Healthcare); (C) SMI® (Canon Medical Systems)



Figs 4A and B: Normal placental findings in superb microvascular imaging: When the normal placenta is observed by SMI, villous blood vessels are visualized in a dendritic manner from the umbilical cord attached to the stem and terminal villi. In addition, a squeaky “scatter” is observed in the villous space in accordance with the maternal heartbeat. (A) Monochrome SMI; (B) Color-coded SMI; IV, intervillous space, triangle: stem villi arrow: terminal villi



Figs 5A and B: Cervical pregnancy using color-coded superb microvascular imaging: SMI is also useful in diagnosing cervical pregnancy because it can visualize blood flow even when blood flow is slow in the early stages of pregnancy. (A) B-mode; (B) Color-coded SMI

Placenta Previa

Placenta previa is an abnormal placenta position that is often accompanied by a structural abnormality of the placenta, such as PAS, lobed placenta, and abnormal umbilical cord insertion.¹⁸ Because uterine vessels are often congesting around the placental attachment site in the lower uterine segment, swelling of blood vessels around the uterus can be visualized.^{19,20} Superb microvascular imaging is also useful for evaluating these blood vessels (Fig. 6).

Morphological Abnormalities

Assessing PAS during Pregnancy

Placenta accreta spectrum is a condition in which the decidua between the placenta and myometrium is missing. The conventional B-mode method is used for diagnosis by recognizing placental lacunae, the disappearance of the clear zone between the placenta and myometrium, thinning of the myometrium, and penetration of the placenta to the serosal side of the uterus.

When SMI is used under normal conditions, the placenta allows for a clear depiction of the blood flow in the myometrium, which makes it easier to distinguish between the two, SMI also helps to clearly illustrate the stasis of blood flow in the intervillous space of the placenta.

Conversely, PAS cases are often accompanied by swelling of the blood vessels around the uterus, and SMI is useful in evaluating these blood vessels (Fig. 7).

Assessment of PAS/Retained Placenta after Delivery

Retained placenta causes postpartum hemorrhage in one-fifth of cases.²¹ It is necessary to differentiate between the simply retained placenta and PAS. It is difficult to diagnose PAS during the postpartum period because the contracted uterine myometrium is thickened. Although SMI Doppler imaging clearly revealed blood flow from the myometrium to the intervillous space in the case of a simply retained placenta, the intervillous space around the invasive placenta showed low echogenicity without SMI Doppler signals, indicating an avascular or immersed intervillous space in the case



of placenta increta. Pathologically, the intervillous space is narrow or absent at the site of PAS due to adhesion between the placental tissue and uterine myometrium (Fig. 8).

Placental Abruption/subchorionic Hematoma

Acute bleeding can be visualized as an anechoic image, but over time, it changes from a heterogeneously mixed echo- to hyper-echogenicity. Placental abruption can be diagnosed if a subchorionic hematoma can be visualized ultrasonically. However, in the ultrasonographic diagnosis of placental abruption, positive predictive value: PPV was 88%, while sensitivity was 24%, making its diagnosis difficult.²² Therefore, the current diagnosis of placental abruption should be clinically made using ultrasound with physiological examination and cardiotocography.

Subchorionic hematoma is a common finding in the first and early second trimesters of pregnancy. Most of the hematomas seen in the first trimester disappear spontaneously, but some persist with

bleeding after mid-gestation occasionally resulting in placental abruption. The source of blood in the uterus after the second trimester may be due to abnormal bleeding from the placenta. When such subchorionic hematoma is observed, it is necessary to distinguish chronic subchorionic hematoma from acute placental abruption.

It is often necessary to distinguish subchorionic hematoma, such as marginal hematoma, from the marginal venous sinus or placental parenchyma. Since SMI can visualize minute blood flow, we believe that evaluation of the presence or absence of blood flow in the mass enables accurate diagnosis of placental abruption.

Furthermore, when a post placental hematoma occurs due to placental abruption, a circulatory disturbance occurs at that part from the decidual spiral artery. The oxygen exchange in the villi deteriorates at that part, and fetal hypoxia may occur acutely. However, using SMI, we demonstrated preserved intervillous blood flow even when placental abruption occurred. Superb microvascular imaging might contribute to a more accurate diagnosis of placental abruption and optimal obstetric intervention (Fig. 9).

Placental Infarction

Large placental infarction is occasionally detectable in B-mode, but blood flow around the placental infarction is difficult to evaluate in B-mode. Placental infarction can cause necrosis due to decreased blood flow in the placenta. Therefore, when SMI is used, minute blood flow can be visualized in the periphery of the normal placenta, but villous blood vessels cannot be visualized in placental infarction.¹⁶ If the decreasing blood flow over time can be detected, it can be used to evaluate the progress of infarction (Fig. 10).

Umbilical Cord Abnormalities

Even with conventional color Doppler imaging, structural abnormalities of the umbilical cord can be sufficiently diagnosed. Umbilical cord twist abnormalities, such as hyper-coiled cord and chronic compression of the umbilical cord, such as cord entanglement and true knot may reduce umbilical venous blood flow, resulting in pathological changes due to congestion of the umbilical venous flow in the placenta.^{23,24} Superb microvascular imaging can express not only vasodilatory images in the stem villi but also stagnation in the peripheral secondary villi¹⁵ (Fig. 11).

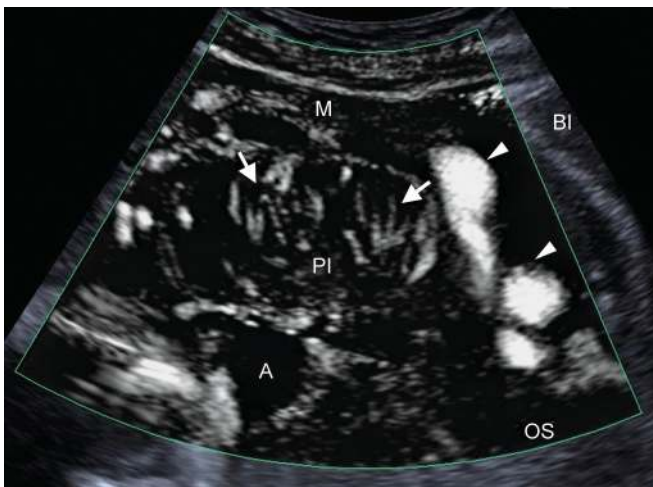
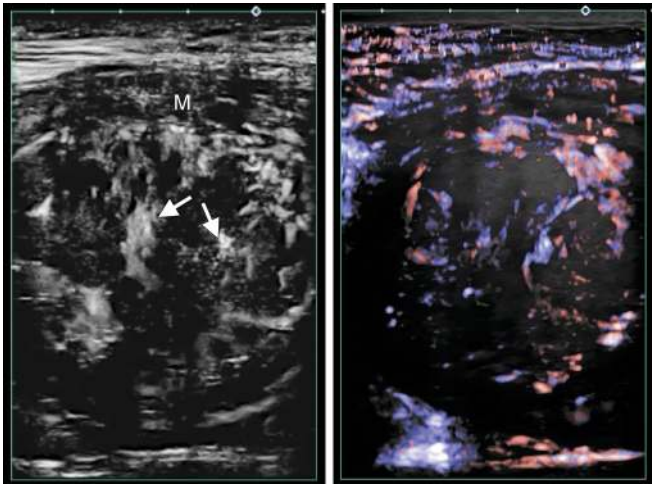


Fig. 6: Placenta previa using monochrome superb microvascular imaging: In placenta previa, the blood flow in the placental parenchyma is also clearly visualized. M, myometrium; BI, bladder; PI, placenta; Os, internal uterine ostium; arrow, placental cotyledon; triangle, congested intramural veins; A, amniotic space



Figs 7A and B: Placenta accreta spectrum using superb microvascular imaging: Since the uterine myometrium is thinning at the placental attachment site, villous vessels can be detected near the myometrium. PAS is often accompanied by swelling of blood vessels around the uterus. (A) B-mode; (B) Monochrome SMI; S, stem villi; L, placental lacunae; Large arrow, maternal blood flow in the uterine myometrium; triangle, lack of myometrial blood flow indicating site of placental invasion; small arrow, villous vessel



Figs 8A and B: Retained placenta using superb microvascular imaging: SMI Doppler imaging clearly revealed blood flow from the myometrium to the intervillous space in case of simply retained placenta: (A) Monochrome SMI; (B) color-coded SMI, M, uterine myometrium; arrow, intervillous blood flow

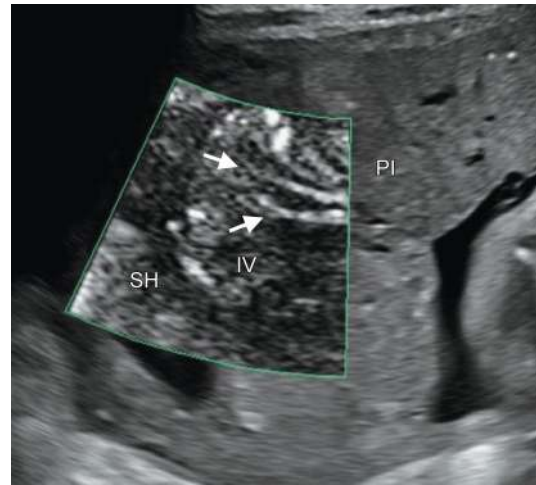
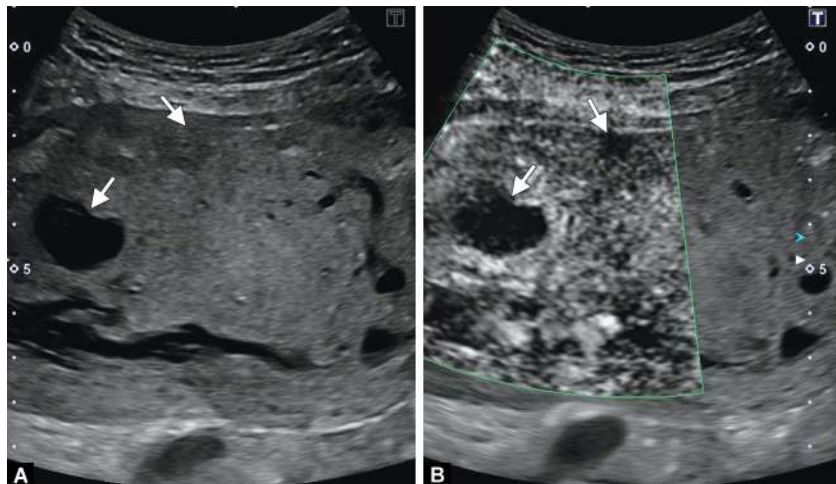


Fig. 9: Subchorionic hematoma in case of placental abruption using monochrome superb microvascular imaging: Lack of blood flow may help diagnose placental abruption, as SMI is capable of delineating fine blood flow. PI, placenta, arrow: terminal villi; SH, subchorionic hematoma; IV, intervillous blood flow



Figs 10A and B: Placental infarction using superb microvascular imaging: Fine blood flow can be visualized in the periphery in a normal placenta, but villous blood vessels cannot be visualized in placental infarction: (A) B-mode; (B) Monochrome SMI; arrow, infarction

Functional Abnormalities

Preeclampsia

Preeclampsia is associated with placental dysplasia during early pregnancy.²⁵ Among the pathological abnormalities of the placenta due to insufficient oxygen supply of maternal blood from the uterus, called maternal vascular malperfusion,²⁶ pathological findings of infarction and avascular villi have been reported. We antenatally demonstrated the placental pathological findings associated with preeclampsia using SMI.¹⁵

Placental infarction is a pathological condition in which the villus space and villi are agglomerated due to ischemia, and the infarct findings on SMI are “anechoic” because blood flow in the villus space and villi is not locally observed.

Avascular villi are pathologically a condition in which blood flow in the intervillous space is normal, but the capillaries in the villi have disappeared. The only finding of avascular villi in SMI is

the background “scatter”, and the dendritic villus blood flow is not visualized.¹⁵

Unlike the abovementioned infarct findings associated with placental abruption and subchorionic hematoma, preeclampsia presents placental pathology due to problems with villous growth from early gestation; therefore, these findings are diffused throughout the placenta (Fig. 12).

Fetal Growth Restriction

Fetal growth restriction is often caused by dysfunction of the uteroplacental circulation from early gestation, similar to preeclampsia. In our experience, using SMI, poorer visualization of villous blood vessels and avascular villi could be observed in FGR with preeclampsia than in placental abnormalities.

Pathologically, when the placenta becomes ischemic, the number of capillaries in the villi may increase to compensate for the decrease in blood flow. This finding was observed in SMI

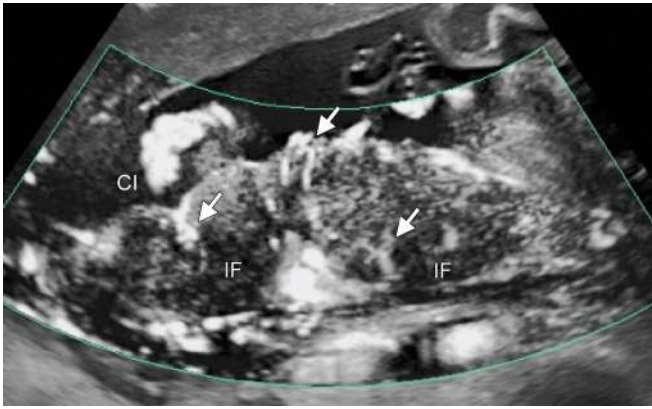


Fig. 11: Placental findings in a hyper-coiled cord using monochrome superb microvascular imaging: A hyper-coiled cord may reduce umbilical venous blood flow, resulting in pathological changes due to congestion of the umbilical venous flow in the placenta. CI: cord insertion arrow: congested stem villi, IF: infarction



Fig. 12: Placental findings at the avascular villi using monochrome superb microvascular imaging: When the blood flow in the placenta decreases, infarctions occur frequently in the placenta. Further, when the blood flow is further reduced, the capillaries in the villi disappear and lead to the formation of avascular villi. Arrow, terminal villi, A, avascular villi

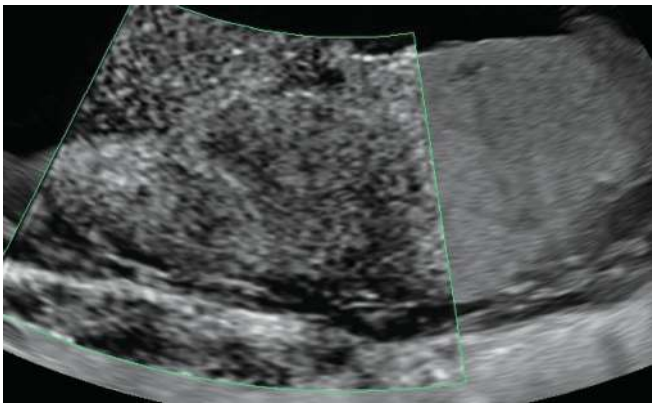


Fig. 13: Whole placental findings in fetal growth restriction using monochrome superb microvascular imaging: FGR is also attributed to impaired circulation in the placenta, with small infarctions and avascular villi scattered throughout the placenta

as fluffy villous vessels. Furthermore, if the blood flow in the placenta deteriorates because it cannot be compensated, the aforementioned SMI findings of infarctions or avascular villi may increase.¹⁵

In a case of severe preeclampsia complicated with FGR who underwent SMI 4 hours before intrauterine fetal death: IUFD, villous blood vessels were not visualized in the placenta, and only the background “scatter” was observed. We believe that this was because peripheral villous blood flow insufficiency preceded the process of FGR deterioration and fetal placental circulation disruption (Fig. 13).

CONCLUSION

Not only fetal morphologic scans but also systematic scans for the placenta and umbilical cord should be performed antenatally. In pathologic cases such as FGR and preeclampsia, at present, the main arterial flow including the umbilical artery or uterine artery is only evaluated. However, since SMI can depict peripheral blood flow, SMI findings indicate the possibility of predicting pathological findings, and then these findings might show us new insights into

fetal and placental compromise in these diseases. We believe such investigations may improve clinical practice in cases related to placental pathology.

REFERENCES

- Goto M, Hasegawa J, Arakaki T, et al. Placenta previa with early opening of the uterine isthmus is associated with high risk of bleeding during pregnancy, and massive haemorrhage during caesarean delivery. *Eur J Obstet Gynecol Reproduct Biol* 2016;201:7–11. DOI: 10.1016/j.ejogrb.2016.03.012.
- Hasegawa J, Kawabata I, Takeda Y, et al. Improving the accuracy of diagnosing placenta previa on transvaginal ultrasound by distinguishing between the uterine isthmus and cervix: a prospective multicenter observational study. *Fetal Diagn Ther* 2017;41(2):145–151. DOI: 10.1159/000446212.
- Hasegawa J, Arakaki T, Ichizuka K, et al. Management of vasa previa during pregnancy. *J Perinat Med* 2015;43(6):783–784. DOI: 10.1515/jpm-2014-0047.
- Hasegawa J. Ultrasound assessment of the umbilical cord. *Donald School J Ultrasound Obstet Gynecol* 2014;8(4):382–390. DOI: 10.5005/jp-journals-10009-1378.
- Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol* 2006;107(4):927–941. DOI: 10.1097/01.AOG.0000207559.15715.98.
- Hasegawa J, Matsuoka R, Ichizuka K, et al. Velamentous cord insertion into the lower third of the uterus is associated with intrapartum fetal heart rate abnormalities. *Ultrasound Obstet Gynecol* 2006;27(4):425–429. DOI: 10.1002/uog.2645.
- Furuya N, Sasaki T, Homma C, et al. Ultrasound screening and management of vasa previa in Japan. *J Obstet Gynaecol Res* 2020;46(7):1084–1089. DOI: 10.1111/jog.14254.
- Hasegawa J. Ultrasound screening of umbilical cord abnormalities and delivery management. *Placenta* 2018;62:66–78. DOI: 10.1016/j.placenta.2017.12.003.
- Morrow RJ, Adamson SL, Bull SB, et al. Acute hypoxemia does not affect the umbilical artery flow velocity waveform in fetal sheep. *Obstet Gynecol* 1990;75(4):590–593.
- Turan OM, Turan S, Gungor S, et al. Progression of Doppler abnormalities in intrauterine growth restriction. *Ultrasound Obstet Gynecol* 2008;32(2):160–167. DOI: 10.1002/uog.5386.

11. Grannum PA, Berkowitz RL, Hobbins JC. The ultrasonic changes in the maturing placenta and their relation to fetal pulmonic maturity. *Am J Obstet Gynecol* 1979;133(8):915–922. DOI: 10.1016/0002-9378(79)90312-0.
12. Jauniaux E, Bhide A. Prenatal ultrasound diagnosis and outcome of placenta previa accreta after cesarean delivery: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2017;217(1):27–36. DOI: 10.1016/j.ajog.2017.02.050.
13. Hasegawa J, Yamada H, Kawasaki E, et al. Application of superb micro-vascular imaging (SMI) in obstetrics. *J Matern Fetal Neonatal Med* 2018;31(2):261–263. DOI: 10.1080/14767058.2016.1278206.
14. Jiang ZZ, Huang YH, Shen HL, et al. Clinical applications of superb microvascular imaging in the liver, breast, thyroid, skeletal muscle, and carotid plaques. *J Ultrasound Med* 2019;38(11):2811–2820. DOI: 10.1002/jum.15008.
15. Furuya N, Hasegawa J, Homma C, et al. Novel ultrasound assessment of placental pathological function using superb microvascular imaging. *J Matern Fetal Neonatal Med* 2020. 1–4. DOI: 10.1080/14767058.2020.1795120.
16. Hasegawa J, Suzuki N. SMI for imaging of placental infarction. *Placenta* 2016;47:96–98. DOI: 10.1016/j.placenta.2016.08.092.
17. Hasegawa J, Kurasaki A, Hata T, et al. Diagnosis of placenta accreta spectrum using ultra-high-frequency probe and Superb microvascular Imaging. *Ultrasound Obstet Gynecol* 2019;54(5):705–707. DOI: 10.1002/uog.20207.
18. Hasegawa J. Sonoembryological evaluations of the development of placenta previa and velamentous cord insertion. *J Obstet Gynaecol Res* 2015;41(1):1–5. DOI: 10.1111/jog.12531.
19. Hasegawa J, Matsuoka R, Ichizuka K, et al. Predisposing factors for massive hemorrhage during cesarean section in patients with placenta previa. *Ultrasound Obstet Gynecol* 2009;34(1):80–84. DOI: 10.1002/uog.6426.
20. Saitoh M, Ishihara K, Sekiya T, et al. Anticipation of uterine bleeding in placenta previa based on vaginal sonographic evaluation. *Gynecol Obstet Investigat* 2002;54(1):37–42. DOI: 10.1159/000064695.
21. Al-Zirqi I, Vangen S, Forsen L, et al. Prevalence and risk factors of severe obstetric haemorrhage. *BJOG* 2008;115(10):1265–1272. DOI: 10.1111/j.1471-0528.2008.01859.x.
22. Glantz C, Purnell L. Clinical utility of sonography in the diagnosis and treatment of placental abruption. *J Ultrasound Med* 2002;21(8):837–840. DOI: 10.7863/jum.2002.21.8.837.
23. Redline RW. Clinical and pathological umbilical cord abnormalities in fetal thrombotic vasculopathy. *Human Pathol* 2004;35(12):1494–1498. DOI: 10.1016/j.humpath.2004.08.003.
24. Hasegawa J, Furuya N, Doi M, et al. Sono-embryological assessments of a true knot that developed into a hypercoiled cord and circumvallate placenta. *J Matern Fetal Neonatal Med* 2019. 1–5. DOI: 10.1080/14767058.2019.1704247.
25. Roberts JM, Hubel CA. The two stage model of preeclampsia: variations on the theme. *Placenta* 2009;30 Suppl A(Suppl A):S32–S37. DOI: 10.1016/j.placenta.2008.11.009.
26. Ernst LM. Maternal vascular malperfusion of the placental bed. *APMIS* 2018;126(7):551–560. DOI: 10.1111/apm.12833.

