Relationship between the Volume Ratio of Subchorionic Hematoma to Gestation SAC in First-trimester and Pregnancy Outcome of Patients with Threatened Abortion

Xinran Wang[1], Weiping Shi[2], Jing Shi[3], Yan Ding[3], Ziyang Yu[4] and Hong Zhang[4]

[1]*Department of Ultrasound, Affiliated Hospital of Jiangnan University, Wuxi, China*
[2]*Department of Ultrasound, Affiliated Hospital of Maternal and Child Health Hospital of Nantong University, Nantong, China*
[3]*Department of Medical Ultrasound, Wuxi People's Hospital of Nanjing Medical University, Wuxi, China*
[4]*Reproductive Centre, The Second Affiliated Hospital of Soochow University, Suzhou, China*

ABSTRACT

Objective: To find the relationship between the volume ratio of subchorionic hematoma (SCH) to gestation sac measured by three--dimensional ultrasound and pregnancy outcome of patients with threatened abortion.

Study Design: Descriptive study.

Place and Duration of Study: The Second Affiliated Hospital of Soochow University, Suzhou, China, from January 2016 to December 2020.

Methodology: Medical data of patients, who were diagnosed with threatened abortion (persistent or intermittent vaginal bleeding) were collected. All included patients underwent ultrasonography for SCH at gestation age of 6-8 weeks. According to the patients' evaluation, they were classified into a case group combined with threatened abortion and SCH (n=145), and a control group with threatened abortion (n=76). The clinical data and three-dimensional ultrasound parameters of the two groups were compared to find the relationship between the volume ratio of SCH to gestation sac and pregnancy outcome.

Results: In the case group, the hospital stay was longer, the abdominal pain, its duration ≥7 days, and adverse pregnancy outcomes were higher than in the control group ($p<0.05$). Patients with moderate and severe area ratio and volume ratio of SCH to gestation sac were significantly related to higher abortion and stillbirth rates than patients with mild ratio ($p<0.05$). The area under the curve, sensitivity and specificity of the volume ratio of SCH to gestation sac in predicting abortion and stillbirth were higher than that of the area ratio of SCH to gestation sac.

Conclusion: The volume ratio of SCH to gestation sac by three-dimensional ultrasound in first-trimester plays an important role to predict pregnancy outcome.

Key Words: *Ultrasonography, Hematoma, Pregnancy outcome, Threatened abortion, ROC curve.*

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INTRODUCTION

Subchorionic hematoma (SCH) is the hematoma between the uterine wall and the decidua capsularis or the placental edge, which can lead to placental dysfunction and adverse pregnancy outcomes.[1,2] Studies have shown that small SCH hardly increases the risk of abortion, but with the increase of hematoma, the risk of abortion would gradually increase.[3]

Correspondence to: Dr. Yan Ding, Department of Medical Ultrasound, Wuxi People's Hospital of Nanjing Medical University, No. 299 Qingyang Road, Wuxi 214023, Jiangsu, China
E-mail: dingyan2001@hotmail.com
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It has been reported that 65.2% of women with large hematoma abort compared to 9.5% of those with medium hematoma and only 2.9% of those with a small hematoma.[4] Thus, the size of SCH can be a valuable factor to predict pregnancy outcomes. At present, the subjective evaluation method, the ratio of gestational sac surrounded by SCH, and the area ratio of SCH to gestation sac are used to evaluate SCH size for prediction of pregnancy outcome.[5-7] Since most of SCH are crescent and irregular, no mathematical formula can be applied to calculate its volume in the three orthogonal dimensions, the mentioned methods tend to focus on partial parameters of SCH, which are not accurate enough to evaluate the actual size of SCH.

Three-dimensional ultrasound (3-DUS) can accurately measure the volume of objects with irregular shapes, providing a novel means to visualise placental abnormalities *in utero*.[8,9] However, there is a lack of research to assess the size of SCH by three-dimensional ultrasound. On the other hand, the size of SCH based

on the fraction of gestational sac is correlated with the first-trimester miscarriage.[7] Therefore, this study was conducted to evaluate the SCH volume on 3-DUS, and obtained the SCH size by the volume ratio of SCH to gestational sac, aiming to find the relationship between the volume ratio of SCH to gestation sac and pregnancy outcome of patients with threatened abortion.

METHODOLOGY

This descriptive study was conducted on patients diagnosed with threatened abortion at the Second Affiliated Hospital of Soochow University from January 2016 to December 2020. Threatened abortion was defined as persistent or intermittent vaginal bleeding.[10] Inclusion criteria of patients were natural and intrauterine singleton pregnancy, threatened abortion, first ultrasound examination at 6-8 weeks of gestation, embryonic survival by sonographic evidence of cardiac tube pulsation or fetal activity, as well as being followed up until the end of the pregnancy. Patients with multiple pregnancies, adverse pregnancies by chromosome abnormality or trauma, autoimmune diseases, habitual abortion (spontaneous abortion ≥3 times) or pregnancy-related complications, including gestational hypertension, diabetes and thyroid diseases, *etc*., were excluded. After the medical data review of all patients consecutively in the electronic medical record of the hospital, a total of 211 patients meeting the mentioned inclusion and exclusion criteria were enrolled. SCH was detected by ultrasonography, which was manifested with a hypoechoic or anechoic fluid dark area between the chorionic membrane and decidua or at the edge of the placenta.[11] According to the presence of SCH by ultrasonography at gestation age of 6-8 weeks, 145 patients combined with SCH were identified as the case group, and 76 patients without SCH were the control group. This study was approved by the Ethics Committee and Review Board of the hospital (No: JD-LK-2020-118-01). All patients provided informed consent verbally, and the study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Two-dimensional ultrasonography was performed by ultrasound diagnostic instrument (GE Voluson E8, GE Healthcare, Milwaukee, USA) using a 4.0 ~ 9.0 MHz transvaginal probe and a 3.5 ~ 5.0 MHz transabdominal probe. In the dark bleeding area around the gestational sac, the circumference and area of the gestation sac and SCH on the maximum section were recorded with a trackball. According to the circumference ratio or area ratio of SCH to gestation sac, the hematoma was divided: the ratio <10% was defined as mild, the ratio between 10% and 25% was moderate, and the ratio ≥25% was severe.[7,12] Three-dimensional ultrasonography also was performed by GE Volusion E8 Expert ultrasound diagnostic instrument, and RNA5-9 abdominal volume probe with a curvature radius of 15.4 mm and frequency of 4.0 ~ 9.0 MHz was applied. After obtaining the maximum section of the gestation sac, the 3-DUS imaging system was turned on for automatic image acquisition. Then, the virtual organ computer-aided analysis measurement software (GE Healthcare, Milwaukee, USA) manually outlined the SCH shape on all obtained image layers and automatically calculated the volume of SCH. In accordance with two-dimensional ultrasonography, the hematoma also was divided into mild, moderate, and severe degrees according to the volume ratio of SCH to gestational sac.

All patients received conventional therapy for threatened abortion until the delivery, and the pregnancy outcomes, including full-term delivery, premature delivery, abortion and stillbirth, also were recorded through follow-up visits to delivery. Full-term delivery was defined as delivery ≥37 weeks of gestation, preterm delivery was defined as delivery before 37 weeks of gestation, abortion was defined as infant death or expulsion of the products of conception before 20 weeks of gestation, and stillbirth was defined as infant death at ≥20 weeks of gestation or infant weighing ≥500 g.[13]

The clinical data of patients were retrieved from the electronic medical records of the hospital, including age, gravida, parity, hospital stay, duration of vaginal bleeding, abdominal pain, duration of abdominal pain, pregnancy outcome, the circumference, area, and volume of both SCH and gestation sac. All data were reviewed and analysed anonymously by the authors using the software SPSS 20.0. The continuous variables data were expressed as mean ± standard deviation, and the comparison between the two groups was analysed by t-test. The categorical variables were expressed as percentages or rates, and compared by chi-square test. The receiver operating characteristic (ROC) curve was applied to analyse the prediction value of SCH-related indexes in pregnancy outcomes. Significant difference was considered as $p < 0.05$.

RESULTS

There were no significant differences in age, gravida, parity, and duration of vaginal bleeding between the two groups ($p > 0.05$). The proportion of patients with abdominal pain and duration of abdominal pain ≥7 days in the case group were significantly higher than those in the control group, besides, the hospital stay was significantly longer than that in the control group (all p <). As for pregnancy outcome, the proportion of patients with full-term delivery in the case group was significantly lower than that in the control group ($p < 0.001$, Table I).

According to the circumference ratio of SCH to gestational sac, 145 patients in the case group were divided into the mild (n = 47), moderate (n = 50), and severe (n = 48) groups. Based on area ratio of SCH to gestational sac, the 145 patients were divided into the mild (n = 46), moderate (n = 54) and severe (n = 45) groups. As for volume ratio of SCH to gestational sac, the 145 patients were divided into the mild (n = 47), moderate (n = 41), and severe (n = 57) groups. There was no significant difference in pregnancy outcome among the patients with mild, moderate and severe circumference ratio of SCH to gestational sac ($p > 0.05$). In the area ratio of SCH to gestational sac, the abortion and stillbirth rates of patients in the moderate, and severe groups were significantly higher than those in the mild group ($p < 0.001$).

Table I: Comparison of the demographic data between the two groups.

	Control Group (n=69)	Case Group (n=145)	p
Age, n (%)			0.618[a]
<35 years	37(53.62%)	83(57.24%)	
≥35 years	32(46.38%)	62(42.76%)	
Gravida, n	2.32±1.25	2.41±1.42	0.646[b]
Parity, n	0.33±0.14	0.31±0.10	0.233[b]
Hospital stay, days	4.33±3.35	7.12±5.26	<0.001[b]
Duration of vaginal bleeding, n (%)			0.893[a]
<14 days	46(66.67%)	98(67.59%)	
≥14 days	23(33.33%)	47(32.41%)	
Abdominal pain, n (%)			<0.001[a]
No	48(69.57%)	48(33.10%)	
Yes	21(30.43%)	97(66.90%)	
Duration of abdominal pain, n (%)			0.001[a]
<7 days	34(49.28%)	37(25.52%)	
≥7 days	35(50.72%)	108(74.48%)	
Pregnancy outcome, n (%)			<0.001[a]
Full-term delivery	47(68.12%)	32(22.07%)	
Premature delivery	12(17.39%)	38(26.21%)	
Abortion	8(11.59%)	35(24.14%)	
Stillbirth	2(2.90%)	40(27.59%)	

a: chi-square test; b: t-test.

Table II: Correlation between SCH-related indexes and pregnancy outcome.

Group	Full-term delivery (n=32)	Premature delivery (n=38)	Abortion (n=35)	Stillbirth (n=40)	p
SCH/gestation sac circumference					0.183[a]
<10%	13(8.97%)	15(10.34%)	8(5.52%)	11(7.59%)	
10%~25%	10(6.90%)	16(11.03%)	13(8.97%)	11(7.59%)	
≥25%	9(6.21%)	7(4.83%)	14(9.66%)	18(12.41%)	
SCH/gestation sac area					<0.001[a]
<10%	15(10.34%)	20(13.79%)	5(3.45%)	6(4.14%)	
10%~25%	13(8.97%)	11(7.59%)	17(11.72%)	13(8.97%)	
≥25%	4(2.76%)	7(4.83%)	13(8.97%)	21(14.48%)	
SCH/gestation sac volume					<0.001[a]
<10%	18(12.41%)	22(15.17%)	4(2.76%)	3(2.07%)	
10%~25%	9(6.21%)	10(6.90%)	14(9.66%)	8(5.52%)	
≥25%	5(3.45%)	6(4.14%)	17(11.72%)	29(20%)	

a: chi-square test.

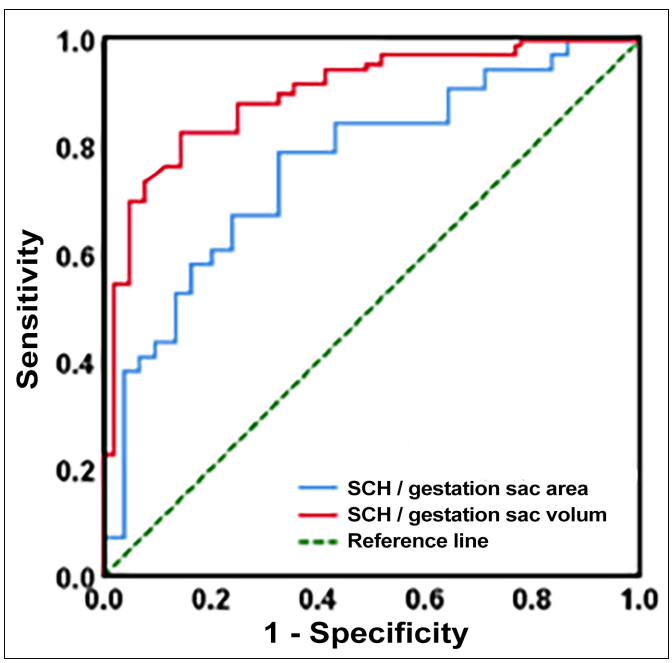

Figure 1: Predictive value of area and volume ratio of SCH to gestation sac on pregnancy outcome by ROC curve.

In the volume ratio of SCH to gestational sac, the abortion and stillbirth rates in the moderate and severe groups also were significantly higher than those in the mild group (p <0.001). On the contrary, the full-term delivery and premature delivery rates of patients with mild area and volume ratio of SCH to gestational sac were significantly higher than those with moderate and severe ratios (p <0.001, Table II).

The critical value of the area ratio of SCH to gestation sac to predict abortion and stillbirth was 33.43%, the AUC was 0.766 with 95%CI of 0.703~0.830, the sensitivity was 89.89% and the specificity was 94.40%. However, the critical value of the volume ratio of SCH to gestation sac to predict abortion and stillbirth was 29.76%. Moreover, the AUC of volume ratio of SCH to gestation sac to predict abortion and stillbirth was 0.900 (95% CI: 0.858~0.941), with the sensitivity of 89.89% and specificity of 94.40%, which was higher than those of area ratio of SCH to gestation sac (Figure 1).

DISCUSSION

In this study, the higher SCH/ gestational sac volume ratio by 3-DUS measurement, the higher the stillbirth rate and

abortion rate, and the lower the full-term delivery rate, which was consistent with previous studies.[14] It is believed that SCH in large volumes would increase the risk of spontaneous abortion or premature delivery, while SCH in a smaller volume has a better prognosis. This is probably due to a constant threat of SCH to pregnancy through the pressure-volume effect directly, causing the adverse pregnancy outcome. However, there are still many studies suggesting that the intrauterine SCH volume in patients with threatened abortion has no correlation with adverse pregnancy outcomes and is meaningless in predicting abortion and premature delivery.[15,16] The controversy may be owing to the differences in the calculation method of SCH. The largest diameter, area, volume, and relative size (the product of vertical diameter, transverse diameter and anteroposterior diameter) can be used to evaluate the size of SCH, but these parameters cannot accurately calculate the actual size of irregular SCH, resulting in deviations of research results.[14-16] It is reported that the relative value of SCH to gestational sac (expressed as a percentage) showed a good correlation between SCH and adverse pregnancy outcomes.[7,17,18] For example, when the volume ratio of SCH to the gestational sac is less than 40%, the prognosis is good. In this study, the relevant parameters of SCH and gestation sac were measured by 3-DUS, and the AUC of volume ratio of SCH to gestation sac in predicting spontaneous abortion and stillbirth was 0.900, the sensitivity and specificity were 89.89% and 94.40%, respectively, which were higher than that of the area ratio of SCH to gestation sac. It suggests that the volume ratio of SCH to gestation sac could more accurately assess the disease severity of patients than the circumference ratio and area ratio, and the 3-DUS can effectively evaluate the SCH size for prediction of pregnancy outcome.

Abdominal pain and vaginal bleeding are the common symptoms of threatened abortion. In this study, the proportion of patients with abdominal pain and the duration of abdominal pain ≥7 days in the case group were significantly higher than those in the control group ($p<0.05$). The result indicates that abdominal pain and its duration are the risk factors for adverse pregnancy, and increase the possibility of abortion and stillbirth. Previous studies have suggested that the severity and duration of abdominal pain had a close relationship to pregnancy outcome, which is consistent with this study.[19] The relationship between abdominal pain and pregnancy outcome might be related to placenta damage and adverse uterine contraction induced by SCH. Studies have shown that SCH accompanied by clinical bleeding, especially with bleeding time for longer than 14 days, can significantly increase the risk of premature delivery and fetal death.[20] There was no significant relationship between the duration of vaginal bleeding and pregnancy outcome, which might be related to sample selection and sample size in this study.

However, there are also some limitations and shortcomings, including small sample size, and lack of analysis on progesterone, human chorionic gonadotropin levels, as well as uterine artery blood flow parameters, which can be further included in the subsequent study to explore their impact on pregnancy outcome. Due to lack of research about SCH classification, the literature supporting the distribution of patients with mild, moderate, and severe SCH is a little weak and not authoritative enough, and this results also need to be further verified by prospective studies. Although this study has suggested that the higher volume ratio of SCH to gestation sac is related to adverse pregnancy outcomes, it is still necessary to combine it with other clinical factors to make a comprehensive evaluation of patients. Moreover, the development of a risk stratification system to assess and predict pregnancy outcomes will be of great importance to the subsequent treatment of patients.

CONCLUSION

SCH size in first-trimester and explore the relationship between SCH-related indexes and pregnancy outcome. This indicates that the volume ratio of SCH to gestation sac is more accurate and effective to evaluate the SCH size for the prediction of pregnancy outcome than the circumference ratio and area ratio of SCH to gestation sac.

ETHICAL APPROVAL:

This study was approved by the Ethics Committee and Review Board of the Second Affiliated Hospital of Soochow University (No. JD-LK-2020-118-01), and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

PATIENTS' CONSENT:

All patients enrolled in this study provided informed consent verbally.

COMPETING INTEREST:

The authors declared no competing interest.

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AUTHORS' CONTRIBUTION:

All of the authors declare that they have all participated in the study design and execution, data collection and analysis, manuscript writing and revision, and they have approved the final version.

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