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Decreased apparent diffusion coefficient in the placentas of monochorionic twins with selective intrauterine growth restriction

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A B S T R A C T

Objectives: The apparent diffusion coefficient (ADC) was associated with the onset of intrauterine growth restriction in singleton pregnancies. However, the correlation of ADC with selective intrauterine growth restriction (sIUGR) of monochorionic (MC) twin pregnancies remained unknown. In this study, we aimed to evaluate the association of ADC with sIUGR in MC twin pregnancies by exploring diffusion weighted MR imaging (DWI).

Methods: Fifty-one MC twin pregnancies, consisting 19 cases of sIUGR and 32 cases without sIUGR, were re-analyzed by DWI. ADCs were quantitated from two regions of interest, surrounding the insertion of the umbilical cord of placenta for each twin. A rADC ($ADC_{larger\ twin}/ADC_{smaller\ twin}$) in each placenta was also evaluated. Then ADCs and rADCs were compared between cases with and without sIUGR.

Results: The ADC in cases with sIUGR was significantly decreased compared with cases without sIUGR (1.846×10^3 vs $2.471 \times 10^3\ mm^2/s$, $p < 0.001$). The rADC in cases with sIUGR was significantly increased (1.346 vs 1.053, $p < 0.001$).

Conclusions: The ADC decreases and the rADC increases in the placentas of MC twins with sIUGR, suggesting that diffusion in the placenta is restricted in pregnancies with sIUGR.

1. Introduction

Twin pregnancy was subdivided in monochorionic (MC) and dichorionic defining by whether the fetuses shared one placenta. The MC twin had higher risks of complications such as selective intrauterine growth restriction (sIUGR), twin-to-twin transfusion syndrome (TTTS) et al. than dichorionic twins [1]. Selective intrauterine growth restriction (sIUGR) is one of the most common complications, with increased perinatal mortality and morbidity rates [2–4]. Previous studies have demonstrated that placentas play an important role in sIUGR [2,5–8]. Paepe et al. found a significantly higher frequency of velamentous cord insertion and uneven placental sharing in cases of sIUGR [5]. It has also been demonstrated that a decrease in placental weight and a greater number of vascular-thrombotic lesions were attributable to the discordant growth in MC twins [2,5]. However, few studies have addressed the functional properties of placentas during MC pregnancies.

Prenatal magnetic resonance imaging(MRI) not only helps delineate the morphologic alterations of the placenta during gestation [9] but also provides a new method for assessing placental function [10–12]. One of the most widely used approaches in MRI is diffusion-weighted imaging (DWI), which probes the microstructural properties of tissues by measuring the incoherent motion of water within the tissue [13,14]. Apparent diffusion coefficient (ADC) could be calculated by DWI. Bonel et al. compared the ADCs of placentas with and without intrauterine growth restriction (IUGR), and found that fetal growth restriction was associated with both restricted diffusion and a decrease in the ADC in singletons [11]. Although MC twins share one placenta, the locations of cord insertion are different between the twins, and the characteristics of the placenta may be heterogeneous in each region [5,6]. We hypothesized that DWI can be used as a helpful tool to detect placental dysfunctions within different regions, which may lead to sIUGR. In this study, we employed DWI to assess placental characteristics in MC twin pregnancies with and without sIUGR.

2. Methods

2.1. Patients

A total of 107 women with twin pregnancies who underwent fetal MRI between November 2013 and April 2015 in our hospital were involved in the study. Sixty-two out of 107 were MC twin pregnancies according to ultrasound diagnostic criteria during 11–14 weeks gestation [15]. Eleven TTTS cases were excluded. The diagnosis of TTTS was diagnosed according to Quintero et al., and staged by Quintero level I-IV [16]. A total of 51 MC cases without TTTS were eligible for this study (Fig. 1). Gestational age, estimated fetal weight (EFW), indication for

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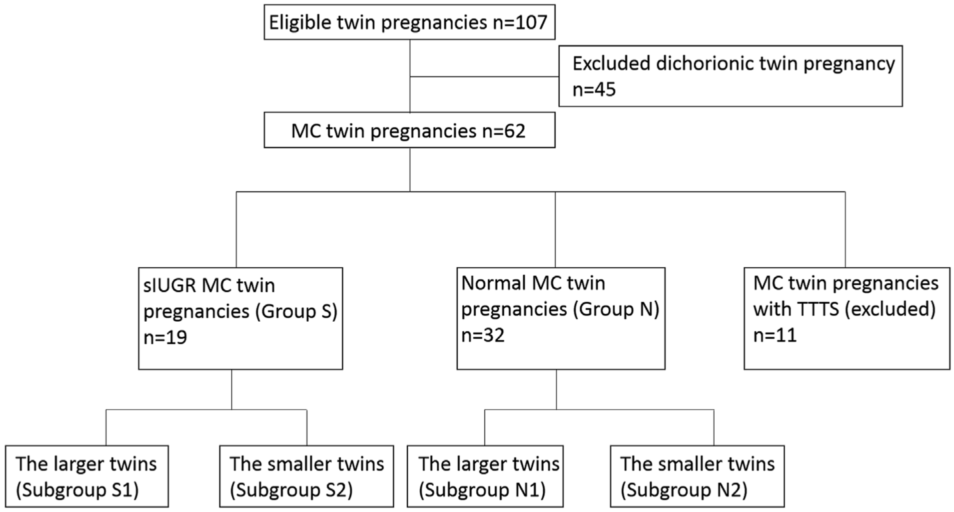

Fig. 1. Flow diagram for the patient selection process.

MRI, ultrasound reports, pregnancy outcomes and histopathologic examinations were reviewed. Gestational age calculated by combination of the last menstrual period and CRL within the first 14 weeks of gestation. The estimated fetal weight (EFW) was calculated by the Hadlock formula based on ultrasonic measurement of HC, FL, HL, AC before MRI within 2 days [17]. sIUGR was defined as an EFW in one fetus that was in the < 10th percentile for the gestational age when using a normal reference range for EFW [5,8,17,18]. Among the 51 patients, 19 suffered from sIUGR and were classified as Group S, while the other 32 without sIUGR were classified as Group N. Furthermore, we subdivided each group into two subgroups. In Group S, the larger fetus of each twin was defined as S1, the smaller one (the growth restricted twin) was defined as S2. On the other hand, the larger and smaller fetus of Group N was defined as N1 and N2 seperatively.(Fig. 1). All reports from the obstetric US and delivery ward examinations and the histopathologic reports were collected and evaluated by one prenatal doctor with more than 8 years of experience in fetal medicine (Shiyi Xiong). A histopathologic examination of the placenta was available to the parents but was not performed on a standard basis. When available, abnormal histopathologic findings suggestive of placental dysfunction (eg, infarctions, hemorrhage, and so on) were noted.

2.2. MR imaging protocol

All the patients underwent the MRI examination within 2 days after the nearest US examination. All measurements were performed with a GE OPTIMA MR360 1.5 T MRI System (GE Healthcare, Milwaukee, WI, USA). During the MRI scan, the pregnant women were placed in a supine position without maternal or fetal sedation, and an eight-channel cardiac coil was placed over the abdomen, covering the entire uterus. A fast imaging employing steady-state acquisition (FIESTA) sequence [repetition time (TR) = 4.4 m s, echo time (TE) = minimum, FOV = 380 mm*380 mm, matrix = 224*224, slice thickness/interslice gap = 6/0 mm, bandwidth = 83.13 Hz/pixel] in three orthogonal planes was obtained to provide a fetal and placental overview. Single-shot fast spin-echo (SSFSE) T2-weighted sequences (T2W) (TR = 1800–2400 m s, TE = 70–100 m s, FOV = 380 mm*380 mm, matrix = 224*224, slice thickness/interslice gap = = 5/-1 mm, bandwidth = 31.25 Hz/pixel) were performed. A T1WI fast inversion recovery motion insensitive (FIRM) sequence (TR = 7.8–8.2 m s, TE = 4.2 m s, FOV = 380 mm*380 mm, matrix = 256 *192, slice thickness/interslice gap = 6/1.0 mm, bandwidth = 15.63 Hz/pixel) was performed on the sagittal maternal plane. Diffusion-weighted image (DW image) sequences (TR = 3000–4000 m s, TE = 30–80 m s, FOV = 400 mm*400 mm, matrix = 96*128, NEX = 2, b-value = 0, 800 s/mm^2, slice thickness/interslice gap = 4/0 mm) were obtained at the end of the examination in three orthogonal directions. Apparent diffusion coefficient (ADC) maps were automatically calculated by the vendor's preset algorithm with b-values of 0 and 800 s/mm^2 using the equation $SI = SI_0 e^{-bD}$, where *SI* is the measured signal intensity, *b* is the *b*-value (800 s/mm^2), *D* is the ADC, and SI_0 is the *SI* at a *b*-value of 0. The entire protocol was valid for investigating the fetus and placenta, covering the whole uterus, and 25–40 slices were acquired in each sequence. The duration of the fetal MRI studies was 25–30 min.

2.3. Image analysis

The image quality of all sequences was evaluated by an experienced radiologist. If the MRI images did not fit the diagnostic standard, an additional scan was taken within 24 h. For evaluation purposes, the placenta was easily delineated from the myometrium on the DW images, displaying a *b*-value of 800 s/mm^2.

DW images and ADC maps were evaluated with corresponding sets of SSFSE images in the same planes as an anatomic reference. To calculate the ADC, the regions of interest (ROIs) were drawn on the ADC maps. In the SSFSE images, we selected an appropriate slice that displayed the clearest location of the umbilical cord insertion of each twin fetus. Then, according to the SSFSE images, we defined a 20-mm [2] circular ROI on the corresponding ADC maps. The ROIs were positioned near the umbilical cord insertion of each twin, and we assumed that each ROI represented the placental share of the corresponding fetus in each subgroup. Representative ADC maps are shown in Fig. 2. This procedure was performed by the consensus of two independent radiologists with more than 5 years of experience in MRI of fetuses who were blinded to the clinical outcomes. A final ROI for each twin fetus was calculated by averaging the ROIs generated by the two radiologists. Thus, in each placenta, two ROIs were calculated and marked as S1 and S2 or N1 and N2. The rADC was calculated as S1/S2 or N1/N2 in each placenta and shown as a ratio.

2.4. Statistical analysis

The independent samples *t*-test was used to examine the differences in continuous variables between groups and subgroups. Spearman's correlation coefficient was used to analyze the relationship between the EFW and ADC values. All tests were two tailed, and a p-value < 0.05 was considered statistically significant. All analyses were performed using the IBM SPSS Statistics 20 software (IBM SPSS, Inc., Chicago, IL).