Characterisation of Placental Diffusion in Twin Pregnancies using Diffusion-Weighted Magnetic Resonance Imaging

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INTRODUCTION

Functional MRI, particularly diffusion-weighted imaging (DWI), has gained a lot of attention due to its superior capability of detecting pathologies earlier than morphological MRI. The placenta is of particular interest in this field of study, as DWI has been shown to surpass sonography in sensitivity and accuracy for the detection of placenta-related pathologies such as placenta increta[1], abruptio placentae[2], placental insufficiency[3], and intrauterine growth restriction[4]. Although still at its infancy, this field of study shows potential in further expanding the fetal applications of MRI. In fact, multiple studies have aimed at better characterising placental diffusion using DWI by investigating potential correlation with factors such as gestational age[5-6] and pre-eclampsia[7]. Most DWI studies, however, investigate singleton fetuses. The few ones investigating twin pregnancies are directed at specific rare pathological entities, such as twin reversed arterial diffusion[8] or Twin-Twin Transfusion Syndrome[9]. In this retrospective study, we hypothesis that placental diffusion as measured by DWI in twin pregnancies would not be significantly different compared to normal singletons.

METHODS

Pregnant patients referred for fetal MR evaluation subsequent to a level 2 ultrasound from January 2009 to December 2014 were retrospectively reviewed to select all twin pregnancies as well as normal singleton controls. Those studies with DWI where the placenta was fully or partially contained within the field of view were included in this study. Imaging was performed using a 1.5T MR imaging system with the following DWI parameters: TR 8000 msec, TE 80 msec, 5-mm thickness, and two b-factor values of 0 and 800-1000. The DW image with b=0 that captured the largest portion of each placenta was used for analysis and reconstruction of apparent diffusion coefficient (ADC) maps using the FuncTool post-processing software. Two ADC quantification methods were conducted and compared using the paired t-test: the first employs manually outlining the visualised portion of the placenta in its entirety, wherein the other, 3 regions of interest (ROI) each with a 5-mm diameter were placed on each border as well as at the centre of the visualised placenta. For those pregnancies with separate (non-fused) placental discs, ADC values were compared between each twin disc pair using the paired t-test. The study was divided into two arms: twin (experimental) and normal singleton (control) and each arm was further divided into two groups according to gestational age (GA): GA $\leq$ 24 weeks and GA > 24 weeks. ADC values within each group were compared between the two arms using the t-test. A p-value less than 0.05 was considered to indicate statistical significance.

RESULTS

The study yielded 10 twin pregnancies equally distributed between the two GA groups (mean GA 25+1 weeks [19+5 – 31+1]), and 6 normal singleton pregnancies, 4 with a GA $\leq$ 24 (mean GA 23+5 weeks [18+2 – 34+3]). Comparison of the two quantification methods revealed no significant difference in the singleton arm, as opposed to the twin arm, wherein ADC values were significantly higher using the manual outlining method compared to the multiple ROI one (p=0.014). Four of the 10 twins had separate placental discs, and no significant difference in ADC was found between those placental pairs using either quantification method. Due to quantification discrepancy, further analysis was based on the manual outlining method. When comparing the two study arms, the one near-term singleton with a GA of 34+3 weeks and ADC value of $(2.97\pm0.83)\times10^{-3}$ was excluded. In the GA $\leq$ 24 weeks group, no significant ADC difference existed between twins [mean $(1.93\pm0.33)\times10^{-3}$; range $1.39\times10^{-3} - 2.39\times10^{-3}$] and singletons [mean $(2.03\pm0.15)\times10^{-3}$; range $1.90\times10^{-3} - 2.18\times10^{-3}$]. In the GA > 24 weeks group, the twin arm [mean $(1.81\pm0.33)\times10^{-3}$; range $1.27\times10^{-3} - 2.27\times10^{-3}$] could not be statistically compared to the singleton arm as it contained only a single subject with a GA of 26+0 and ADC value of $(2.15\pm0.46)\times10^{-3}$.

DISCUSSION

Prior to assessing diffusion –expressed in ADC values– within the placenta, two approaches to ADC quantification were examined. The statistically significant discrepancy between the two examined methods, suggesting a non-uniform diffusion pattern within the placenta, demonstrates the crucial impact of quantification method on image interpretation. As such, manual outlining of the visualised placenta was chosen as the preferred ADC quantification method in this study in order to eliminate sampling bias. One limitation to this method is the subjectivity of 'manual' determination of placental tissue, which may erroneously incorporate adjacent myometrium and amniotic fluid. Similar lack of accuracy and reproducibility in ADC quantification has been documented in the literature, yet not thoroughly investigated[10-11]. Further assessment using varying numbers, sizes, and locations of ROI in a larger sample size is required for ADC quantification standardisation.

Comparing diffusion within separate twin placenta disc pairs showed no significant differences irrespective of GA or fetal status (i.e. normal, abnormal or demised).

When comparing the placental pool with GA $\leq$ 24 weeks, twins and normal singletons were found to have statistically similar placental diffusions. While such finding supports our hypothesis, it is important to note that of the 5 twins in this group, 2 had a demised fetus and 2 had an abnormal fetus, which might have resulted in the 'physiological' twins behaving as 'functional' singletons. While it would be ideal to assess placental diffusion in healthy twins and singletons, most fetal MRIs conducted at our institution are of abnormal fetuses, with the primary indication being sonographic anomaly. Comparing diffusion between twins and singletons with GA >24 weeks could not be carried out due to paucity of data at this stage of pregnancy in our cohort.

Lastly, while acknowledging the small sample size limitation of this study, no obvious trend was noted between diffusion and GA, a finding that had been documented by Sivrioğlu et al[5]. However, the one near-term singleton (GA > 34) had an ADC value that was far higher than all others, which might suggest a relationship between ADC and GA, as suggested by Manganaro et al[6]. The advanced GA and associated high ADC value of this fetus in comparison to the rest of the sample pool, setting it as an outlier, was the basis for our decision to exclude it from analysis. Another limitation of this retrospective study was the variability in b-value due to the recently implemented change in fetal DWI protocol at our institution from 1000 to 800.

CONCLUSIONS

Our study suggests that no placental diffusion difference exists within double-disc placentas or between twins and normal singletons with GA $\leq$ 24 weeks. A dedicated prospective study is required for further assessment of placental diffusion and validation of these findings.

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