Evaluation of Brain Microstructure Changes in Surviving Fetus of Monochorionic Twin Pregnancies With Demise of One Fetus Using Apparent Diffusion Coefficient

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Abstract

Objective

To compare the differences of brain apparent diffusion coefficient (ADC) values in surviving fetuses, twin controls and single fetus controls using diffusion weighted imaging (DWI) sequence, and to perform follow-up study to reveal the underlying cerebral microstructure changes.

Materials and methods

Thirty-two twins with demise of one fetus, 25 twins, and 20 single fetuses were included. DWI was performed and ADC map was reconstructed automatically. ADC values of certain regions were compared among three-groups, and between left- and right-hemisphere in surviving fetuses. ROC was generated to identify ADC values in surviving fetuses and twin controls.

Results

ADC values were lower in bilateral white matter of frontal lobes (left: 1.68 ± 0.19 vs. 1.91 ± 0.26, 1.88 ± 0.19, $P < 0.001$; right: 1.68 ± 0.18 vs. 1.86 ± 0.24, 1.84 ± 0.21, $P = 0.002$), parietal lobes (left: 1.80 ± 0.25 vs. 2.00 ± 0.21, 1.92 ± 0.28, $P = 0.012$; right: 1.81 ± 0.19 vs. 1.99 ± 0.24, 1.92 ± 0.26, $P = 0.012$) and occipital lobes (left: 1.72 ± 0.24 vs. 1.87 ± 0.20, 1.70 ± 0.24, $P = 0.017$; right: 1.73 ± 0.23 vs. 1.91 ± 0.22, 1.70 ± 0.27, $P = 0.005$) in surviving fetuses compared with twin controls and single fetus, respectively. In discriminating surviving fetuses and twin controls, the area-under-the-curve of ADC values in frontal, parietal and occipital lobes were range from 0.677 to 0.737. The combination of frontal and parietal lobes and gestational age had highest area-under-the-curve (0.771, 95% CI 0.648−0.894).

Conclusions

DWI is a very useful sequence for detecting underlying changes. ADC values might be effective indicators of subtle anomalies in surviving fetuses.

Trial registration:

None.

1. Background

Monochorionic twin pregnancies have some complications [1−7]. Demise of one fetus, as one of the main complications, occurs up to 20% [8], which usually has an effect on the surviving fetus, and accounts for

increasing in morbidity and mortality [9–10]. Placental sharing and vascular communications in monochorionic twins might result in clinical symptom. A clinical study including 49 monoamniotic pregnancies with single fetal demise has suggested that severe cerebral injury occurred in 26% of the survivors [11]. How to detect these abnormalities early needs to be explored.

In recent years, fetal MRI, as a valuable complementary technique, is being increasingly used to evaluate fetal brain, provides improved anatomic detail and physiologic information than ultrasound [12–16]. For surviving fetus with demise of one fetus, severe brain damage might be detected by ultrasound and prenatal MR imaging [17]. In some cases, no abnormal echo or signal of brain in the surviving fetus could be found on ultrasound or conventional MRI sequences after the death of one fetus. However, brain abnormalities were found in subsequent prenatal examination or postnatal follow-up. In the circumstances, it is necessary to identify the potential anomalies of brain in surviving fetuses by other methods. Diffusion weighted imaging (DWI) has been applied to fetal MRI to evaluate the microstructure and biophysical status of tissues and intracranial lesions [18–19], which contributes to identify abnormal ischemic tissue at an early stage. Hoffmann et al [20] reported that acute ischemic lesions can be detected on DWI within one week after the death of one fetus, which can't be detected on ultrasound or conventional MRI. Apparent diffusion coefficient (ADC) is derived from DWI sequence, which can quantitatively detect the degree of diffusion of water molecules. The decrease of ADC value may be an index of brain injuries and an early ischemic manifestation of fetal brain, which can be found before conventional MRI [21–22]. ADC value of fetus brain has been studied in many studies, about fetal maturity and fetal brain injury [23–26].

This study is to compare the differences of brain ADC values in surviving fetuses, twin controls and single fetus controls, and to perform follow-up study to find out whether abnormal ADC values exist or not in surviving fetus, in order to reveal the underlying cerebral microstructure changes.

2. Material And Methods

2.1 Subjects

This prospective study enrolled eighty-three pregnant women that were admitted to the department of obstetrics and gynecology in Peking University Third Hospital from January 2018 to March 2020. Pregnant women who were diagnosed as demise of one fetus were chosen as surviving fetus group. The inclusion criteria were as follows: 1) gestational age ≥ 20 weeks; 2) Twin pregnancy was diagnosed and one fetus died in utero which confirmed by ultrasound.3) No abnormal echo of the brain was found by ultrasound in the surviving fetus.

Healthy twins were chosen as twin control group, and healthy single fetuses were chosen as one fetus control group. The exclusion criteria were as follows: (1) gestational age < 20 weeks; (2)brain abnormalities diagnosed by ultrasound; and (3) any contraindications to MRI examinations.

Both the maternal age and gestational age were recorded. The current study was approved by the medical ethical committee of Peking University Third Hospital. All methods of the study were performed in accordance with the guildlines and regulations of Peking University Third Hospital ethical committee. Participants under 18 years old were not involved in this study. All the participants of the study signed written informed consents.

2.2 The followed-up clinical outcomes

The clinical outcomes were followed up after at least one year, including terminate pregnancy, died or various complication after birth. A trained researcher who was blinded to the MR images did the follow-up via telephone call after at least one year.

2.3 MR imaging protocol

The fetal MR image acquisition was performed on a 1.5-T MR scanner (Optima MR360, GE Healthcare, Milwaukee, USA). The protocol included the following sequences: (1) Single-Shot Fast Spin Echo (SSFSE) sequence: repetition time (TR)/echo time (TE) 50.4/140 ms, slice thickness 5 mm, slice interval 1 mm, scanning time 14 ~ 20 s); (2) Fast-Imaging Employing Steady-State Acquisition (FIESTA) sequence: TR/TE 4.6/2.09 ms, flip angle 60°, slice thickness 5 mm, slice interval 1 mm, scanning time 16 ~ 20 s; and (3) DWI was performed using single-shot spin-echo planar imaging (EPI) in the axial plane: TR/ TE 2831/77 ms, slice thickness 5 mm, slice interval 1 mm, FOV 320 mm^2, b = 0 and b = 600 s/mm^2, scanning time 16 ~ 20 s, 20−24 slices.

2.4 Image processing

ADC maps were obtained automatically on post-processing software (W4.7, GE Healthcare, Waukesha, Wisconsin, USA) after DWI sequence scanning. Two radiologists with more than 2 years' experience in fetal MR imaging independently drew the regions of interests (ROIs) at each axial slice. ROIs were placed bilaterally over the desired anatomical areas, including white matter of frontal lobes, parietal lobes, temporal lobes and occipital lobes, basal ganglia, thalamus and cerebellum. Each ROI was measured twice by radiologist and the average value was chosen as the final result. As large a ROI as possible was obtained, avoiding adjacent structures such as cerebrospinal fluid spaces. The areas of ROIs were 29.3 mm^2.

2.5 Statistical analysis

Statistical analyses were performed with SPSS software (version 19.0, SPSS, Inc., an IBM Company). One-way ANOVA was used to compare ADC across surviving fetuses, twin controls and single fetus controls in the same ROIs. ADC values in left hemisphere was compared with those in right hemisphere of surviving fetuses by using paired *t* test. Correlations between ADC values in surviving fetus group and time of one fetus demise, gestational age, mean maternal age were calculated by Pearson or Spearman correlation coefficients. Receiver-operating-characteristic-curve (ROC) was generated and the area-under-the-curve (AUC) of ADC values were calculated in discriminating surviving fetuses and twin controls. *P*< 0.05 (two-tailed) was considered as statistically significant.

3. Results

3.1 Demographic characteristics of the study population

A total of 83 subjects were included in this study. Six patients were excluded from analysis due to poor MR image quality with motion artifacts. There were no significant differences of gestational ages and maternal ages among three groups ($P > 0.05$) (Table 1). Of 32 demise of one twin, 27 (84.4%) had determined time of one fetus death. No significant structural and signal abnormalities in surviving fetus were found on SSFSE and FIESTA sequences (Fig. 1A-B). No significant signal abnormalities were found on DWI sequence (Fig. 1C).

Table 1
Clinical information of fetus

Information	Demise of one twin group (n = 32)	Twin controls (n = 25)	Single fetus controls (n = 20)	*F* value	*P* value
Gestational ages range (weeks)	26.0 ~ 36.0	26.0 ~ 36.0	25.0 ~ 36.0		
Mean gestational ages (weeks)	30.5 ± 3.1	30.5 ± 2.3	31.8 ± 3.2	1.637	0.202
Maternal age range (years)	24.0 ~ 38.0	25.0 ~ 38.0	24.0 ~ 37.0		
Mean maternal age (years)	30.7 ± 3.6	31.0 ± 3.4	32.0 ± 3.4	0.818	0.445

3.2 ADC value differences

The mean ADC values of surviving fetuses were shown in Table 2 (Fig. 1D-F). Significant differences of ADC values among surviving fetus, twin controls and single fetus controls in bilateral white matter of frontal lobes (left, F = 9.074, $P < 0.001$; right, F = 6.575, $P = 0.002$), parietal lobes (left, F = 4.710, $P = 0.012$; right, F = 4.662, $P = 0.012$) and occipital lobes (left, F = 4.327, $P = 0.017$; right, F = 5.730, $P = 0.005$) (Table 2). ADC values were lower in bilateral frontal, parietal and occipital lobes of surviving fetuses compared with that of twin controls and single fetus controls (Table 2). No significant differences of ADC values were found between the two control groups. After combined the two control groups, comparing with fetal control group, the ADC values of bilateral frontal lobes decreased in surviving fetuses (left frontal lobe: t = -4.256, $P < 0.001$; right frontal lobe: t = -3.624, $P = 0.001$). There were no significant differences of ADC values between left and right hemisphere (all $P > 0.05$) (Table 3).

Table 2
ADC values of different regions in the surviving fetus, single fetus controls and twin controls

Cerebral regions		ADC values (µm^2/ms)			F value	P value
		Surviving fetus (n = 32)	Twin controls (n = 25)	Single fetus controls (n = 20)		
Frontal lobe	Left	1.68 ± 0.19	1.91 ± 0.26	1.88 ± 0.19	9.074	0.000
	Right	1.68 ± 0.18	1.86 ± 0.24	1.84 ± 0.21	6.575	0.002
Parietal lobe	Left	1.80 ± 0.25	2.00 ± 0.21	1.92 ± 0.28	4.710	0.012
	Right	1.81 ± 0.19	1.99 ± 0.24	1.92 ± 0.26	4.662	0.012
Temporal lobe	Left	1.65 ± 0.19	1.75 ± 0.20	1.70 ± 0.14	1.891	0.158
	Right	1.70 ± 0.19	1.739 ± 0.16	1.77 ± 0.16	0.929	0.399
Occipital lobe	Left	1.72 ± 0.24	1.87 ± 0.20	1.70 ± 0.24	4.327	0.017
	Right	1.73 ± 0.23	1.91 ± 0.22	1.70 ± 0.27	5.730	0.005
Basal ganglia	Left	1.40 ± 0.14	1.43 ± 0.18	1.46 ± 0.18	0.741	0.480
	Right	1.41 ± 0.15	1.43 ± 0.17	1.45 ± 0.17	0.325	0.723
Thalamus	Left	1.30 ± 0.13	1.37 ± 0.22	1.35 ± 0.21	1.009	0.369
	Right	1.30 ± 0.16	1.35 ± 0.20	1.33 ± 0.21	0.557	0.575
Cerebellum	Left	1.41 ± 0.17	1.49 ± 0.22	1.44 ± 0.19	1.150	0.322
	Right	1.44 ± 0.18	1.54 ± 0.24	1.47 ± 0.18	1.565	0.216

Table 3
ADC values in left and right hemisphere in the surviving fetuses

Cerebral regions		ADC values (µm^2/ms, n = 32)	t value	P value
Frontal lobe	Left	1.68 ± 0.19	0.135	0.893
	Right	1.68 ± 0.18		
Parietal lobe	Left	1.80 ± 0.25	-0.176	0.862
	Right	1.81 ± 0.19		
Temporal lobe	Left	1.65 ± 0.19	-1.971	0.058
	Right	1.70 ± 0.19		
Occipital lobe	Left	1.72 ± 0.24	-0.548	0.587
	Right	1.73 ± 0.23		
Basal ganglia	Left	1.40 ± 0.14	-0.458	0.650
	Right	1.41 ± 0.15		
Thalamus	Left	1.30 ± 0.13	-0.087	0.932
	Right	1.30 ± 0.16		
Cerebellum	Left	1.41 ± 0.17	-2.030	0.051
	Right	1.44 ± 0.18		

3.3 Correlation analysis

Maternal ages were not correlated with ADC values in all selected cerebral regions (all $P > 0.05$). ADC values of bilateral frontal lobes, parietal lobes, occipital lobes, thalamus and cerebella in surviving fetuses, that of bilateral basal ganglia, thalamus, cerebella and right occipital lobe in twin controls and that of left parietal lobe, right occipital lobe, bilateral basal ganglia, thalamus and cerebella in single fetus controls, were negatively correlated with gestational age (Table 4, all $P > 0.05$).

Table 4
Correlations between ADC values and gestational age

Cerebral regions		Surviving fetuses, n = 32		Twin controls, n = 25		Single fetus controls, n = 20	
		r	P value	r	P value	r	P value
Frontal lobe	Left	-0.530	0.002	-0.115	0.585	0.057	0.811
	Right	-0.559	0.001	-0.222	0.287	-0.024	0.921
Parietal lobe	Left	-0.604	0.000	-0.351	0.085	-0.497	0.026
	Right	-0.539	0.001	-0.356	0.081	-0.391	0.088
Temporal lobe	Left	0.000	0.999	-0.120	0.569	0.001	0.996
	Right	-0.274	0.130	0.019	0.928	-0.084	0.725
Occipital lobe	Left	-0.454	0.009	-0.307	0.136	-0.386	0.093
	Right	-0.485	0.005	-0.430	0.032	-0.456	0.043
Basal ganglia	Left	-0.337	0.059	-0.502	0.011	-0.588	0.006
	Right	-0.276	0.126	-0.554	0.004	-0.601	0.005
Thalamus	Left	-0.394	0.026	-0.442	0.027	-0.553	0.011
	Right	-0.488	0.005	-0.473	0.017	-0.555	0.011
Cerebellum	Left	-0.479	0.006	-0.566	0.003	-0.464	0.039
	Right	-0.505	0.003	-0.471	0.018	-0.541	0.014

3.4 ROC analysis

The ROC analyses were shown in Fig. 2. In discriminating surviving fetuses and twin controls, the AUCs of ADC values in frontal lobe (left: 0.735, 95% CI 0.604−0.866; right: 0.708, 95% CI 0.568−0.847), parietal lobe (left: 0.716, 95% CI 0.584−0.849; right: 0.737, 95% CI 0.602−0.873), occipital lobe (left: 0.677, 95% CI 0.538−0.816; right: 0.719, 95% CI 0.585−0.853) were range from 0.677 to 0.737. The AUC value of frontal lobe combined with parietal lobe reached 0.751 (95% CI 0.626−0.877). After further combinations of frontal lobes, parietal lobes and gestational age, the AUC value increased to 0.771 (95% CI 0.648−0.894).

3.5 Follow-up results

Among the 32 surviving fetuses, one was terminated, and one was died after birth. Of the remaining 30 fetuses (mean gestational age, 33.4 ± 2.5 weeks; birth weight, 2739.0 ± 619.0 g), 9 (28%) were born prematurely (1 of which was complicated with congenital pneumonia and cryptorchidism). 4 (13.3%) had lower Apgar scores at birth and about 3−4 points in the first minute, 7 (23.3%) were followed up by ultrasound and MRI (3 of which had brain abnormalities, 1 of which had enhanced echoes of white

matter in the right paraventricular with effusion in the posterior fossa, and 1 had enlarged supratentorial ventricles after birth by MRI) and 1 (3.3%) had obvious growth retardation.

4. Discussion

The present study investigated the differences of ADC values of brain regions among surviving fetuses, twin controls and single fetus controls. Our study showed lower ADC values of frontal, parietal and occipital lobe in surviving fetuses compared with twin controls and single fetus controls. Furthermore, our findings showed the negative correlations between ADC values in several brain regions and gestational age.

Meta-analysis showed that the risk of neuro developmental morbidity in monochorionic twins was about 5 times higher compared with that in dichorionic twins after a single fetal death [3]. Previous study reported that cerebral hypoxic-ischemic injury might occur in the surviving fetus after demise of one fetus due to the sharing of one placenta. The surviving fetus might present with hypotension and hypoperfusion due to the loss of circulatory equilibrium and the shunting of blood flow. The reduced cerebral blood flow might be accepted as causative factors for cerebral damage in surviving fetus. In this study, compared with twin and single fetus controls, ADC values of bilateral frontal lobes, parietal lobe and occipital lobes were lower in surviving fetuses. The reduction of ADC values might be indicative of parenchymal damage and metabolic compromise while no abnormalities were detected on ultrasound and MR conventional sequences. Decrease of ADC values might reflect the intracellular/extracellular water compartmentalization [27], especially the decrease in the extracellular water content. ADC value might be more sensitive to detect the subtle anomalies, even changes of signal were not shown on DWI images. Our findings further provided evidence of the possibility of detecting potential brain damage by measuring ADC values in surviving fetuses after demise of one fetus. There were no significant differences of ADC values in all ROIs between left and right hemisphere in surviving fetuses. The characteristics of symmetry indicated that decreases of ADC values might be caused by cerebral hypoperfusion, but not a single vessel supply.

Our present study showed the negative correlations between ADC values of basal ganglia, thalamus and cerebellum and gestational age in control groups which were consistent with previous study. Decreases of ADC values in the majority of brain during fetal development were reported in previous publication [28]. Significant decreases of ADC values were detected in thalamus, basal ganglia, pons and cerebellum with gestational age, but the decrease was not detected in frontal white matter [29–30]. However, the conclusions were controversial. Hoffmann et al [20] found that a weak trend for regional ADC decline was shown in all regions which didn't reach statistical significance with brain development. In the present study, ADC values in bilateral frontal, temporal lobes were not correlated with gestational age in two control groups. The above results implied that ADC values in these regions were relatively stable and might be served as developmental indicator. However, ADC values of bilateral thalamus and cerebella, bilateral frontal lobe, parietal lobes were negatively correlated with gestational age in surviving fetuses,

which indicated the existed potential damage other than the effects of gestational age in these regions. Our findings suggested the possibility of ADC values within frontal lobes in distinguishing the potential lesions of surviving fetuses.

In this study, we also found that average ADC values of frontal white matter in single fetus group was lower than that in previous study [28]. The possible reason was that the average gestational age in our study was larger than that in other studies. No significant differences of ADC values were found between twin controls and single fetus controls, which suggested that single fetus might serves as control group if there was no suitable twin control group in future study. The follow-up results showed that 3 fetuses subsequently developed brain abnormality by ultrasound or MRI. It indicated the underlying changes of brain might exist even through no abnormal signals on conventional and DWI sequence. The measurement of ADC values in surviving fetuses might help to detect the potential subtle anomalies earlier. Although changes of ADC values were shown in surviving fetuses, making crucial decisions (such as pregnancy termination) on the basis of DWI alone also could be very difficult. It might be more reasonable to discuss the possibility of termination of pregnancy in cases with large cerebral lesion on MR and DWI. For surviving fetuses with ADC values changes alone, the follow-up is necessary. What's more, as fast sequence, DWI has potential value of clinical application due to limitation of many sequences. It could be effective supplement to conventional fetal MRI examination and may detect the underlying changes earlier. Furthermore, the present study showed the good predictive value of ADC values in single lobe including frontal and parietal lobe in discriminating surviving fetuses and twin controls. The predictive value of combination of ADC value of frontal lobes, parietal lobes and gestational age was stronger than that of single lobe alone. The study demonstrated that ADC values might be effective indicators of subtle anomalies in surviving fetuses in future.

There were several limitations in the current study. Firstly, the sample size of the present study is small, and a larger sample group may contribute to more accurate conclusion. Secondly, there might be manual errors as ROI is selected. And thirdly, well-controlled and long-term studies are needed to reveal the relation between reduction of the ADC values and postnatal outcome.

5. Conclusion

In conclusion, decreases of ADC values were detected in surviving fetus of one fetus demise, when no visible abnormalities were detected on conventional MR. DWI, especially ADC value, is a very useful sequence for detecting underlying changes. ADC values should also be evaluated in larger clinical studies with ongoing pregnancies before adopting it as a formal work-up in cases of one fetus demise.

Abbreviations

MRI
magnetic resonance imaging; ADC:apparent diffusion coefficient; DWI:diffusion weighted imaging; SSFSE:single-shot fast spin echo; TR:repetition time; TE:echo time; FIESTA:fast-imaging employing

steady-state acquisition; EPI:echo planar imaging; ROIs:regions of interests; ROC:receiver-operating-characteristic-curve; AUC:area-under-the-curve; CI:confidence interval.

Declarations

References

1. Shek NW, Hillman SC, kilby MD. Single-twin demise: pregnancy outcome. Best Pract Res Clin Obstet Gynaecol. 2014; 28(2): 249-263.
2. WAPM Consensus Group on Twin-to-Twin Transfusion, Baschat A, Chmait RH, Deprest J, Gratacós E, Hecher K, et al. Twin-to-twin transfusion syndrome (TTTS). J Perinat Med. 2011; 39(2): 107-112.

3. Hillman SC, Morris RK, Kilby MD. Co-twin prognosis after single fetal death: a systematic review and meta-analysis. Obstet Gynecol. 2011; 118(4): 928–940.

4. Kline-Fath BM, Calvo-Garcia MA, O'Hara SM, Crombleholme TM, Racadio JM. Twin-twin transfusion syndrome: cerebral ischemia is not the only fetal MR imaging finding. Pediatr Radiol. 2007; 37(1): 47-56.

5. Merhar SL, Kline-Fath BM, Meinzen-Derr J, Schibler KR, Leach JL. Fetal and postnatal brain MRI in premature infants with twin-twin transfusion syndrome. J Perinatol. 2015; 33(2): 112-118.

6. Bekiesinska-Figatowska M, Herman-Sucharska I, Romaniuk-Doroszewska A, Jaczynska R, Furmanek M, Bragoszewska H. Diagnostic problems in case of twin pregnancies: US vs. MRI study. J Perinat Med. 2013; 41(5): 535-541.

7. Griffiths PD, Sharrack S, Chan KL, Bamfo J, Williams F, Kilby MD. Fetal brain injury in survivors of twin pregnancies complicated by demise of one twin as assessed by in utero MR imaging. Prenat Diagn. 2015; 35(6): 583-591.

8. Johnson CD, Zhang J. Survival of other fetuses after a fetal death in twin or triplet pregnancies. Obstet Gynecol. 2002; 99(5 Pt 1): 698-703.

9. Gomes Neto O, Marins M, Botelho RD, Nivoloni RC, Saura GE, Arias AV, et al. Feasibility and reproducibility of diffusion-weighted magnetic resonance imaging of the fetal brain in twin-twin transfusion syndrome. Prenat Diagn. 2014; 34(12): 1182-1188.

10. Weiss JL, Cleary-Goldman J, Tanji K, Budorick N, D'alton ME. Multicystic encephalomalacia after first-trimester intrauterine fetal death in monochorionic twins. Am J Obstet Gynecol. 2004; 190(2): 563-565.

11. van Klink JM, van Steenis A, Steggerda SJ, Genova L, Sueters M, Oepkes D, et al. Single fetal demise in monochorionic pregnancies: incidence and patterns of cerebral injury. Ultrasound Obstet Gynecol. 2014; 45(3): 247.

12. Glenn OA. MR imaging of the fetal brain. Pediatr Radiol. 2010; 40(1): 68-81.

13. Gonte G, Parazzini C, Falanga G, Cesaretti C, Lzzo G, Rustico M, et al. Diagnostic value of prenatal MR imaging in the detection of brain malformations in fetuses before the 26th week of gestational age. AJNR Am J Neuroradiol. 2016; 37(5): 946-951.

14. Chapman T, Matesan M, Weinberger E, Bulas DL. Digital atlas of fetal brain MRI. Pediatr Radiol. 2010; 40(2):153-162.

15. Salleen SN. Fetal MRI: An approach to practice: A review. J Adv Res. 2014; 5(5): 507-523.

16. Counsell SJ, Arichi T, Arulkumaran S, Rutherford MA. Fetal and neonatal neuroimaging. Handb Clin Neurol. 2019;162: 67-103.

17. Jelin AC, Norton ME, Bartha AI, Fick AL, Glenn OA. Intracranial magnetic resonance imaging findings in the surviving fetus after spontaneous monochorionic cotwin demise. Am J Obstet Gynecol. 2008; 199(4): 398.e1-5.

18. Arthurs OJ, Rega A, Guimiot F, Belarbi N, Rosenblatt J, Biran V, et al. Diffusion-weighted magnetic resonance imaging of the fetal brain in intrauterine growth restriction. Ultrasound Obstet Gynecol. 2017; 50(1):79-87.

19. Sartor A, Arthurs O, Alberti C, Belarbi N, Tilea B, Boizeau P, et al. Apparent diffusion coefficient measurements of the fetal brain during the third trimester of pregnancy: how reliable are they in clinical practice? Prenat Diagn. 2014; 34(4):357-66.

20. Hoffmann C, Weisz B, Yinon Y, Hogen L, Gindes L, Shrim A, et al. Diffusion MRI findings in monochorionic twin pregnancies after intrauterine fetal death. AJNR Am J Neuroradiol. 2013; 34(1): 212-216.

21. Righini A, Kustermann A, Parazzini C, Fogliani R, Ceriani F, Triulzi F. Diffusion-weighted magnetic resonance imaging of acute hypoxic-ischemic cerebral lesions in the survivor of a monochorionic twin pregnancy: case report. Ultrasound Obstet Gynecol. 2007; 29(4): 453-456.

22. Righini A, Salmona S, Bianchini E, Zirpoli S, Moschetta M, Kustermann A, et al. Prenatal magnetic resonance imaging evaluation of ischemic brain lesions in the survivors of monochorionic twin pregnancies: report of 3 cases. J Comput Assist Tomogr. 2004; 28(1): 87-92.

23. Hoffmann C, Weisz B, Lipitz S, Yaniv G, Katorza E, Bergman D, et al. Regional apparent diffusion coefficient values in 3rd trimester fetal brain. Neuroradiology. 2014; 56(7): 561-567.

24. Katorza E, Strauss G, Cohen R, Berkenstadt M, Hoffmann C, Achiron R, et al. Apparent diffusion coefficient levels and neurodevelopmental outcome in fetuses with brain MR imaging white matter hyperintense signal. AJNR Am J Neuroradiol. 2018; 39(10): 1926-1931.

25. Schneider JF, Confort-Gouny S, Le Fur Y, Viout P, Bennathan M, Chapon F, et al. Diffusion-weighted imaging in normal fetal brain maturation. Eur Radiol. 2007; 17(9): 2422-2429.

26. Kim DH, Chung S, Vigneron DB, Barkovich AJ, Glenn OA. Diffusion-weighted imaging of the fetal brain in vivo. Magn Reson Med. 2008; 59(1): 216-220.

27. Griffiths PD, Russell SA, Mason G, Morris J, Fanou E, Reeves MJ. The use of in utero MR imaging to delineate developmental brain abnormalities in multifetal pregnancies. AJNR Am J Neuroradiol. 2012; 33(2):359-365.

28. Righini A, Bianchini E, Parazzini C, Gementi P, Ramenghi L, Baldoli C, et al. Apparent diffusion coefficient determination in normal fetal brain: a prenatal MR imaging study. AJNR Am J Neuroradiol. 2003; 24(5): 799-804.

29. Schneider MM, Berman JI, Baumer FM, Glass HC, Jeremy RJ, Esch M, et al. Normative apparent diffusion coefficient values in the developing fetal brain. AJNR Am J Neuroradiol. 2009; 30(9): 1799-1803.

30. Boyer AC, Gonçalves LF, Lee W, Shetty A, Holman A, Yeo L, et al. Magnetic resonance diffusion-weighted imaging: reproducibility of regional apparent diffusion coefficients for the normal fetal brain. Ultrasound Obstet Gynecol. 2013; 41(2):190-197.
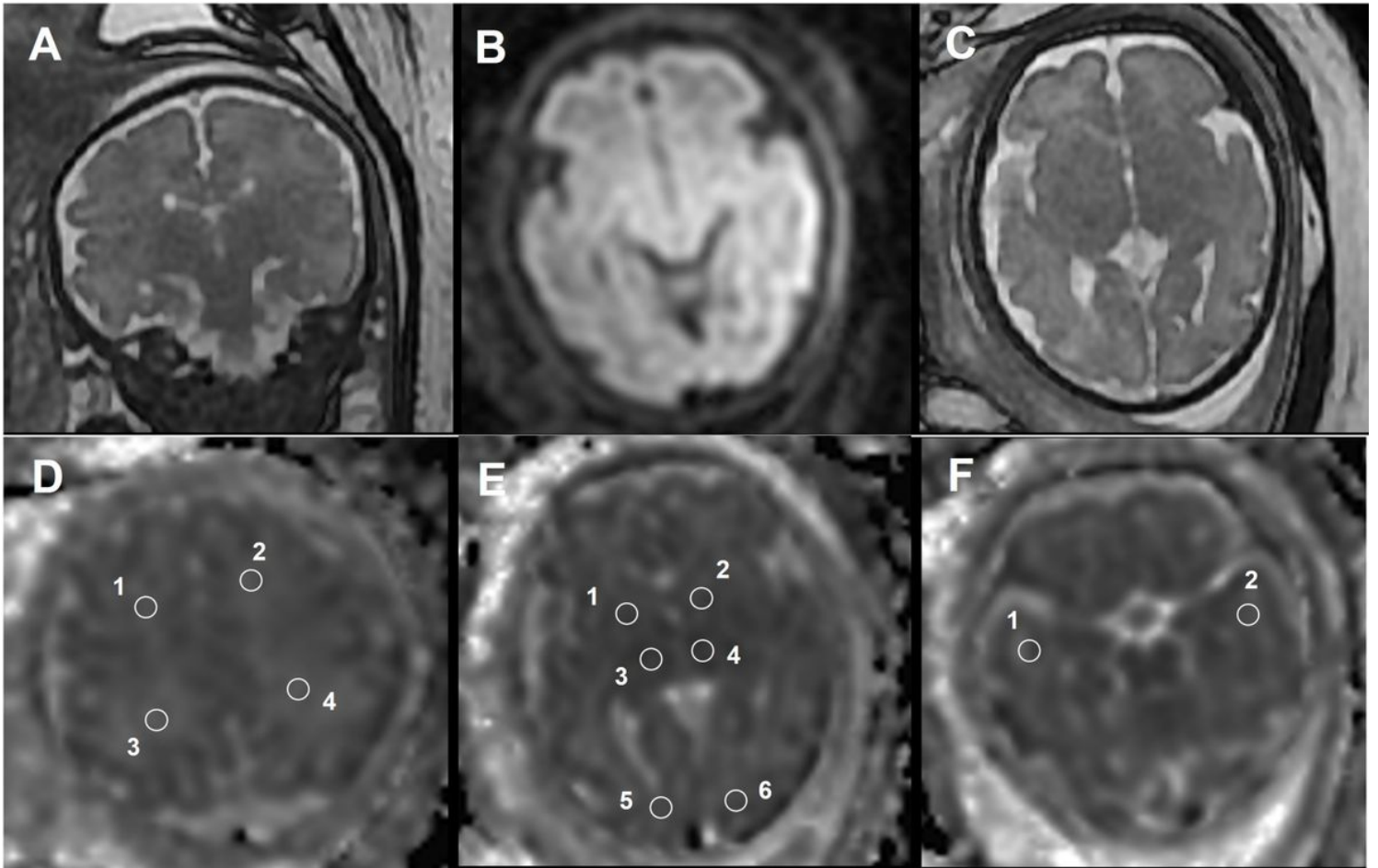
Figures

Figure 1

The images of fetal brain of a woman with 31 weeks of gestation. (A) Coronal view in FIESTA sequence; (B) Axial view in FIESTA sequence; (C) Axial view in DWI sequence. (D) frontal lobe and parietal lobe; (E) Occipital lobe, basal ganglia and thalamus; (F) Temporal lobe.
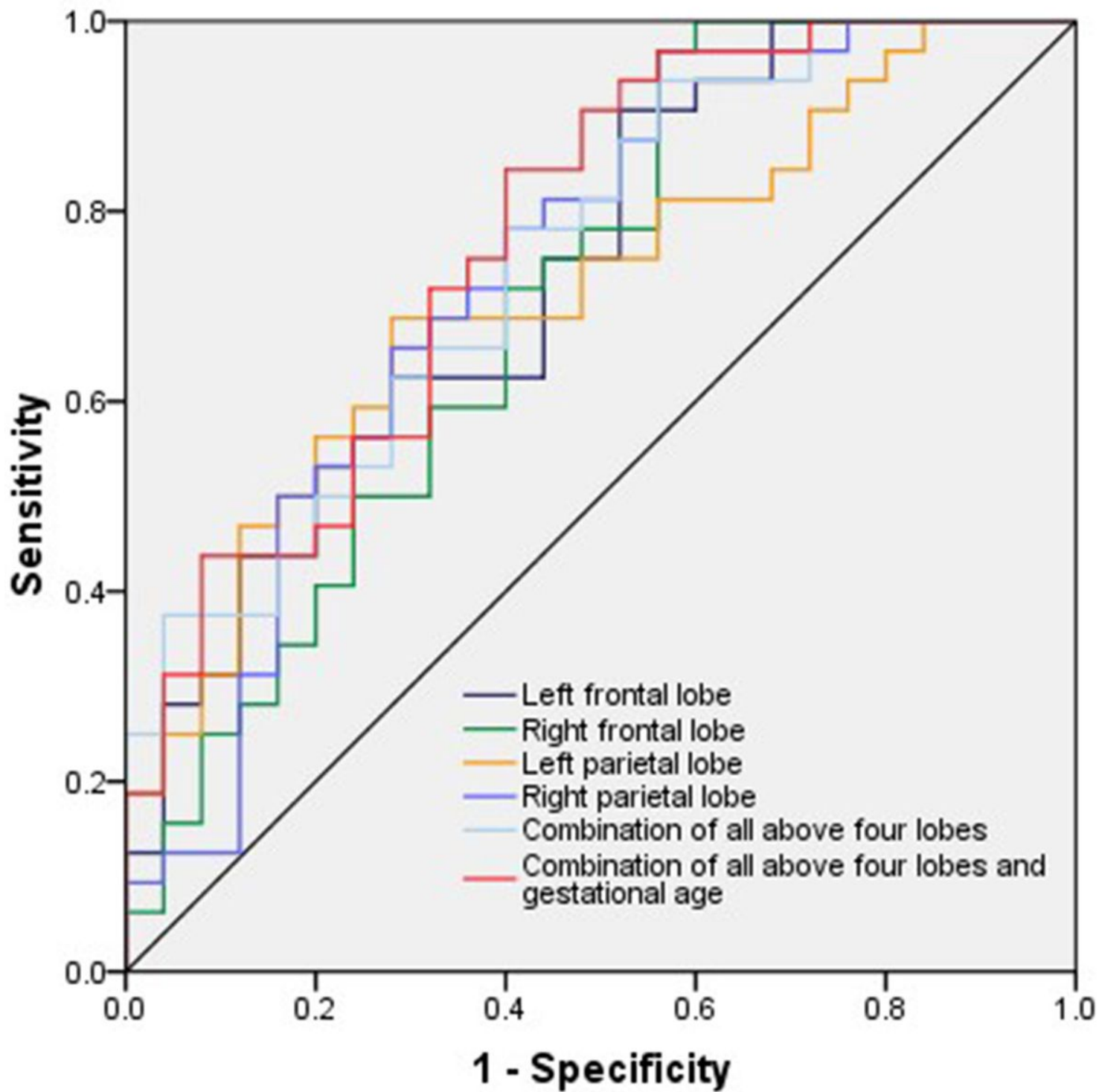
Figure 2

ROC curves for ADC values of different lobes in surviving fetuses and twin controls.