



Get Clarity On Generics

Cost-Effective CT & MRI Contrast Agents

**FRESENIUS
KABI**

WATCH VIDEO

AJNR

This information is current as
of August 14, 2025.

**Third Trimester Structural and Diffusion
Brain Imaging after Single Intrauterine Fetal
Death in Monochorionic Twins: MRI-Based
Cohort Study**

M. Segev, B. Djurabayev, E. Hadi, Y. Yinon, S. Rabinowicz,
C. Hoffmann and S. Shrot

AJNR Am J Neuroradiol published online 24 March 2022
<http://www.ajnr.org/content/early/2022/03/24/ajnr.A7475>

Third Trimester Structural and Diffusion Brain Imaging after Single Intrauterine Fetal Death in Monochorionic Twins: MRI-Based Cohort Study

 M. Segev,  B. Djurabayev,  E. Hadi,  Y. Yinon,  S. Rabinowicz,  C. Hoffmann, and  S. Shrot

ABSTRACT

BACKGROUND AND PURPOSE: Single intrauterine fetal death increases the risk of antenatal brain lesions in the surviving twin. We evaluated the prevalence of structural brain lesions, biometry, and diffusivity on routine third trimester MR imaging performed following single intrauterine fetal death.

MATERIALS AND METHODS: In a retrospective MR imaging–based cohort study, we compared 29 monochorionic twins complicated with single intrauterine fetal death (14 following laser ablation treatment for twin-to-twin transfusion syndrome, 8 following selective fetal reduction, and 7 spontaneous) with 2 control cohorts (49 singleton fetuses and 28 uncomplicated twin fetuses). All fetuses in the single intrauterine fetal death group underwent fetal brain MR imaging as a routine third trimester evaluation. Structural brain lesions were analyzed. Cerebral biometry and diffusivity were measured and compared.

RESULTS: Brain lesions consistent with the evolution of prior ischemic injury were found in 1 of 29 fetuses, not detected by ultrasound. No acute brain infarction, hemorrhage, or cortical abnormalities were found. Supratentorial biometric measurements in the single intrauterine fetal death group were significantly smaller than those in the singleton group, but not significantly different from those in the uncomplicated twin group. There were no significant differences in ADC values of the cerebral hemispheres, basal ganglia, and pons between the single intrauterine fetal death group and either control group.

CONCLUSIONS: Although smaller brain biometry was found, normal diffusivity in surviving twins suggests normal parenchymal microstructure. The rate of cerebral structural injury was relatively low in our cohort, arguing against the routine use of fetal brain MR imaging in twin pregnancies complicated with single intrauterine fetal death. Larger prospective studies are necessary to guide appropriate surveillance protocol and parental counseling in twin pregnancies complicated by single intrauterine fetal death.

ABBREVIATIONS: DC = dichorionic; fbMRI = fetal brain MRI; GA = gestational age; ICC = interclass correlation coefficient; MC = monochorionic; sIUFD = single intrauterine fetal death; TTTS = twin-to-twin transfusion syndrome; US = ultrasound

Monochorionic (MC) twin pregnancies are associated with increased perinatal morbidity and mortality compared with singleton or dichorionic (DC) pregnancies.¹ This increased risk is mainly related to placental architecture and vascular anastomoses in the MC placenta, which can result in fetal growth restriction or twin-to-twin transfusion syndrome. Single intrauterine fetal death (sIUFD) occurs in approximately 6% of twin

pregnancies.^{2,3} This risk is significantly higher, approximately 7- to 10-fold, in MC compared with DC twin pregnancies.¹ sIUFD considerably increases the surviving cotwin's risk of mortality and morbidity.⁴ This might be related to hypoperfusion of the surviving twin at the time of the cotwin's death due to placental vascular anastomoses. Up to 20% of surviving twins might experience adverse neurodevelopmental outcomes.^{2,3,5}

Prenatal identification of brain abnormalities in the surviving cotwin is critical for parental counseling. Expert neurosonography has a high sensitivity in detecting brain abnormalities.⁶ However, there is increasing evidence that fetal brain MR imaging (fbMRI) provides a more accurate diagnosis of brain abnormalities, specifically in detecting hemorrhage or acute ischemia.^{7,8} Relatively few studies have evaluated the utility of fbMRI for detecting brain abnormalities in cotwin survivors following sIUFD.⁴ These studies have described a range of patterns of cerebral abnormalities, mainly ischemic or hemorrhagic, in 9%–33% of surviving cotwins.^{9–12}

Received December 23, 2021; accepted after revision February 7, 2022.

From the Section of Neuroradiology (M.S., B.D., C.H., S.S.), Division of Diagnostic Imaging, Diagnostic Ultrasound Unit of the Institute of Obstetrical and Gynecological Imaging (E.H.), Department of Obstetrics and Gynecology, and Fetal Medicine Unit (Y.Y.), Department of Obstetrics and Gynecology, Sheba Medical Center, Ramat-Gan, Israel; Sackler School of Medicine (Y.Y., C.H., S.S.), Tel Aviv University, Tel-Aviv, Israel; and Pediatric Neurology Unit (S.R.), The Edmond and Lilly Safra Children's Hospital, Sheba Medical Center, Ramat Gan, Israel.

Please address correspondence to Shai Shrot, MD, Section of Neuroradiology, Division of Diagnostic Imaging, Sheba Medical Center, Ramat-Gan, Israel, 2 Sheba Rd, Ramat Gan, 52621 Israel; e-mail: shai.shrot@sheba.health.gov.il

<http://dx.doi.org/10.3174/ajnr.A7475>

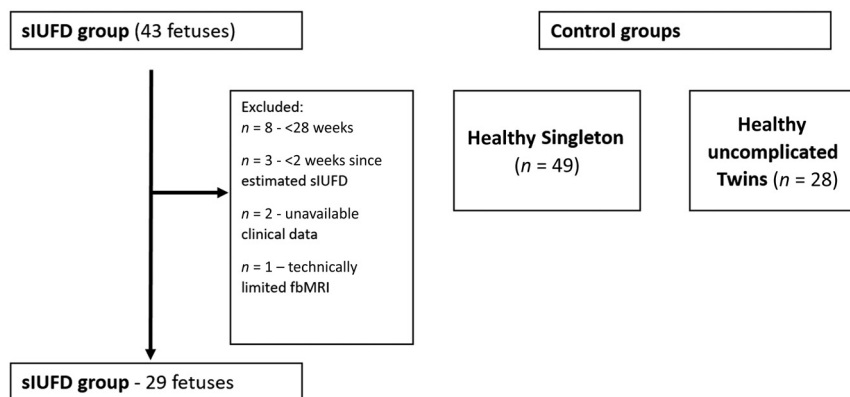


FIG 1. Study flow chart.

Relatively small cohorts, nonstandardized timing of fbMRI following the sIUFD, and lack of correlation with neurodevelopmental outcomes limit the incorporation of fbMRI into routine surveillance following sIUFD.

DWI has been shown to increase the sensitivity of structural fbMRI in diagnosing ischemic events following sIUFD, especially in the acute phase.¹³ In addition, quantitative diffusivity changes can reflect subtle structural parenchymal changes. Such changes were reported in various fetal pathologies affecting normal brain development and maturation, eg, congenital cardiac anomalies and fetal hydrocephalus.¹⁴ The effect of sIUFD on the integrity of a normal-appearing cotwin's brain, as assessed by quantitative diffusivity metrics, has not been described yet.

In Sheba Medical Center, as in other fetal medicine centers, we routinely perform a third trimester fbMRI on all MC twin fetuses following sIUFD to detect brain anomalies such as migration and proliferation disorders.¹⁵ Our objectives in the current study were to determine the utility of our practice by evaluating the prevalence of brain abnormalities as detected on surveillance third trimester fbMRI compared with a prenatal targeted ultrasound (US) and to evaluate the use of quantitative diffusivity measurements in assessing residual brain microstructural changes and brain maturation in the surviving twin following sIUFD.

MATERIALS AND METHODS

The institutional review board approved this retrospective study.

Study Design and Population

Our fetal brain imaging data base was reviewed for MC twin pregnancies following sIUFD managed in our referral center between February 2017 and June 2020. All patients in the study group underwent follow-up, which included US evaluation every 2 weeks, including targeted neurosonography. In 14 pregnancies, sIUFD occurred following laser ablation treatment for twin-to-twin transfusion syndrome (TTTS); in 8 patients, selective fetal reduction was performed; and 7 sIUFDs were spontaneous. Control groups were singleton pregnancies and uncomplicated twin pregnancies (19 were bichorionic, and 7, MC, with unavailable chorionicity data in 2 pregnancies), who had fbMRI in the same period for various indications with normal brain imaging findings. Inclusion

criteria for the sIUFD group were the following: 1) MC pregnancy, 2) documented sIUFD, 3) technically adequate third trimester fbMRI (gestational age [GA] = 28–36 weeks), and 4) fbMRI performed as a routine screening test at least 2 weeks following suspected sIUFD dating. Exclusion criteria were the following: unavailable clinical data and fbMRI performed acutely (<2 weeks) following sIUFD because of a suspected hypoxic-ischemic event in the cotwin. Inclusion criteria for control groups were singleton or uncomplicated twins with normal brain structure assessed by third trimester fbMRI with no clinical or laboratory evidence of chromosomal abnormalities or intrauterine infection.

The indications for MR imaging in the singleton control group were suspected CNS anomalies on prenatal screening US studies, not confirmed by MR imaging ($n=20$), limb abnormalities ($n=7$), abnormal outcome in previous pregnancies in siblings ($n=8$), suspected abdominal vascular abnormalities ($n=2$), polyhydramnios ($n=2$), poor quality of a US study ($n=1$), a maternal procedure during pregnancy ($n=3$), recessive genetic abnormalities of the parents ($n=1$), suspected spinal abnormality ($n=3$), familial history of CNS abnormalities ($n=1$), and exclusion of cerebral hemorrhage in fetal thrombocytopenia ($n=1$). In the twins control group, one of the fetuses was chosen randomly for imaging analysis. The indications for MR imaging were suspected CNS anomalies on prenatal screening US studies in one of the fetuses or anomalies not confirmed by MR imaging ($n=12$), mild asymmetry (<3 mm) or dilation of the lateral ventricles (<12 mm) seen on fetal US ($n=8$), limb abnormalities ($n=2$), abnormal outcome in previous pregnancies in siblings ($n=2$), twins discordance ($n=1$), and poor quality of a US study ($n=3$). A summary of study groups is presented on Fig 1.

fbMRI

According to our protocol, all mothers had refrained from eating or drinking fluids containing sugar for 4 hours before the MR imaging examination. At our institution, a single administration of low-dose diazepam before imaging is used routinely to decrease fetal motion during the scan. Scans were obtained using a 3T MR imaging system (Ingenia 3T, Philips Healthcare, or Magnetom Prisma 3T, Siemens). Acquisition parameters for the Philips scanner were the following: a single-shot fast spin-echo T2-weighted sequence in 3 orthogonal planes, with a section thickness of 3 mm and no gap, using a flexible coil (16-channel body coil). The FOV was determined by the size of the fetal head and ranged from 230 to 290 mm. Other parameters were the following: matrix size = 224/224; TE = 90 ms; TR = approximately 2500 ms. A fast spoiled gradient-echo axial T1-weighted sequence was performed only in the axial plane (FOV = 320 mm, section thickness = 3 mm with no gap, TR = 10 ms, TE = 4.6 ms). A DWI sequence in an axial plane was then performed (FOV = 350 mm, b-value = 0 and 700 ms, section thickness = 3 mm with

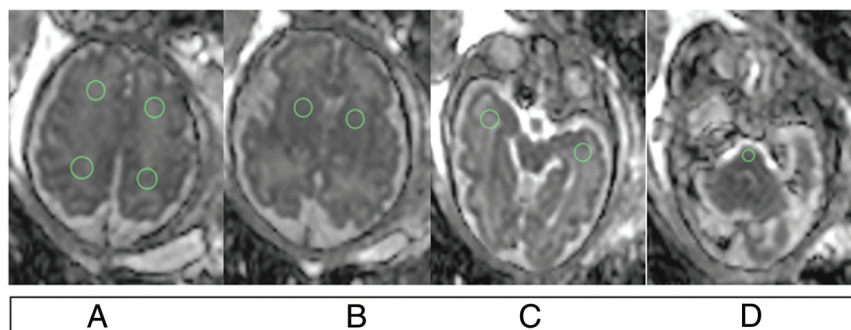


FIG 2. ROI placement on ADC map of DWI. A, Frontal and parietal lobes. B, Basal ganglia. C, Temporal lobes. D, Pons.

Table 1: Maternal and perinatal demographic and clinical features of sIUFD and control groups

	sIUFD	Singleton	Twins Control	Significance (Group 1 vs 2, Group 1 vs 3)
No.	29	49	28	
GA (mean) (wk)	30.9 (SD, 1.2)	31.5 (SD, 1.9)	31.4 (SD, 1.2)	$P = .17, P = .21$
Maternal age (mean) (yr)	31.7 (SD, 6.4)	32.3 (SD, 4.9)	33.8 (SD, 6.7)	$P = .62, P = .20$
Fetal presentation				
Head	22	38	20	$P = .53$
Breech	7	9	8	
Transverse	0	2	0	

no gap). Acquisition parameters for the Siemens scanner were the following: a HASTE T2-weighted sequence in 3 orthogonal planes (section thickness = 3 mm with no gap, using a flexible coil [16-channel body coil]). The FOV was determined by the size of the fetal head and ranged from 250 to 300 mm. Other parameters were the following: matrix size = 192/192; TE = 90 ms; TR = approximately 2500 ms. A single-shot axial T1-weighted sequence was performed only in the axial plane (FOV = 300 mm, section thickness = 3 mm with no gap, TR = 90 ms, TE = 2.35 ms). A DWI sequence in an axial plane was then performed (FOV = 256 mm, b-value = 0 and 1000 ms, section thickness = 3 mm with gaps of 0.3 mm.)

Image Analysis

Biometric measurements were read with a consensus of 2 radiologists, blinded to the clinical data (S.S., C.H.). MR imaging measurements included brain biparietal diameter (BPD), fronto-occipital diameter (FOD), length of the corpus callosum (CC), transcerebellar diameter (TCD), vermis height, vermis anteroposterior diameter, and lateral ventricle width. Fetal brain MR imaging biometry was converted to centiles using nomograms, previously published by Tilea et al.¹⁶

ADC Measurements

The acquired DWIs were transferred in DICOM format to the IntelliSpace portal, Version 10 (Philips Healthcare), and ADC maps were generated using the MR diffusion tool. To avoid inter-vendor variability in diffusivity metrics, we analyzed diffusivity data only from studies acquired on the Philips scanner (94 of 106 fbMRIs in our study). Nine circular ROIs were manually placed on

the following areas of the fetal brain (Fig 2): bilateral frontal WM, parietal WM, temporal WM, basal ganglia, and pons. ROIs ranged from 10 to 57 mm² (mean, 37.1 [SD, 12.7] mm²). ADC values were measured in the same regions of the bilateral cerebral hemisphere and basal ganglia; then, mean ADC values were calculated for each ROI. To validate the consistency of measurements and the reliability of results, 2 observers independently evaluated the first 13 consecutive fetuses (neuroradiology fellow, B.D., and a senior radiology resident, M.S.). Interobserver variability was assessed by the interclass correlation coefficient (ICC). We considered an ICC value of ≥ 0.8 as excellent agreement. ADC measurements were not available in fetuses with either degraded DWIs (ie, marked motion artifacts or field inhomogeneity) or fbMRI performed on different magnets.

Clinical Data

Demographic and clinical data included maternal age, GA at fbMRI, and fetal

presentation. Clinical data for the sIUFD pregnancies included the following: sIUFD etiology (spontaneous, following laser treatment for TTTS, and following fetal reduction), the presence of TTTS, selective intrauterine growth restriction, twin anemia polycythemia sequence, and presumed GA at sIUFD.

Statistical Analysis

Categorical variables were expressed as numbers and percentages. Continuous variables were expressed as mean (SD). The distribution of continuous variables was assessed using a histogram and quantile-quantile plot. Categorical variables were compared using the χ^2 test. Continuous variables were compared using Mann-Whitney and Kruskal Wallis tests. Linear regression was used to evaluate the effect of sIUFD on ADC values. A 2-tailed $P < .05$ was considered statistically significant. Analyses were performed with SPSS (Version 25.0, 2019; IBM).

RESULTS

Study Population

MR imaging was performed in the sIUFD group at a mean GA of 30.9 (SD, 1.2) weeks, which was not significantly different from performance in the control groups. No significant differences were found in the mean maternal age or fetal presentation (Table 1).

Clinical Characteristics of the sIUFD Group

The estimated GA at sIUFD was 19.9 (SD, 4.2) weeks. TTTS was diagnosed on the prenatal US in 14 pregnancies (Quintero stage 1–2 pregnancies, stage 2–3 pregnancies, stage 3–7 pregnancies, and one pregnancy was stage 4, TTTS stage was unavailable in one pregnancy). In 6 pregnancies, selective intrauterine growth

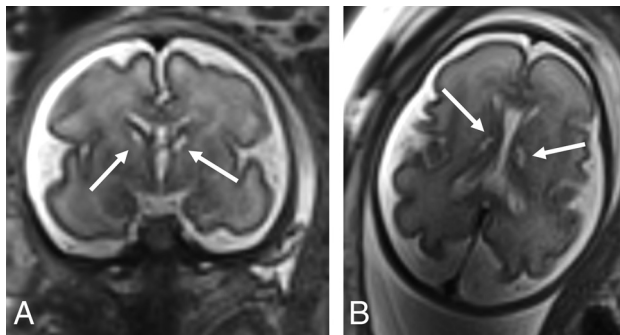


FIG 3. Coronal (A) and axial (B) T2-weighted images of a 30-week surviving twin following spontaneous sIUDF at a GA of 18 weeks, showing caudothalamic cystic changes (arrows).

restriction was found on the prenatal US, and in 2 pregnancies, a twin anemia polycythemia sequence was suspected. Post-sIUDF US did not show any major CNS abnormalities in the surviving twin (ie, infarction or hemorrhage). A minor finding of choroid plexus cyst was diagnosed in 1 fetus.

MR Imaging

fbMRI revealed a normal sulcation pattern in all surviving fetuses following sIUDF. No acute brain infarction or parenchymal hemorrhage was noted in any of the surveillance third-trimester fbMRIs performed in the sIUDF group. One fetus (~3.5% of the sIUDF group) showed bilateral caudothalamic cystic changes (Fig 3). No ventriculomegaly was observed, though 7 fetuses showed asymmetry of the lateral ventricles (compared with 5 in the singleton and 7 in the twins control groups). No cortical abnormalities, corpus callosum, septum pellucidum, or posterior fossa abnormalities were noted.

Various biometric parameters of the brain were measured in the sIUDF and control groups (Table 2). Supratentorial biometric parameters (FOD, BPD) of the sIUDF group were significantly smaller than those in the singleton group with smaller lateral ventricles. No significant differences were found in most biometric parameters between the sIUDF group and the twins control group or between the singleton and twins control groups.

ADC Analysis

DWI data were available in 22 of 29 in the sIUDF group (4 fetuses had technically degraded DWI, and fbMRI of 3 fetuses was performed on a different scanner); in 30 of 49 fetuses in the singleton cohort (12 fetuses had technically degraded DWI images, and fbMRI of 7 fetuses was performed on a different scanner); and in 15 of 28 in the twins control cohort (11 fetuses had technically degraded DWI, and fbMRI of 2 fetuses was performed on a different scanner). ADC measurements showed good-to-excellent interobserver agreement for most regions, with the ICC between 0.82 and 0.94. The ICC was considered good for the basal ganglia (ICC = 0.71).

In all groups, ADC values in supratentorial WM were higher than those in the basal ganglia and pons (Fig 4). No significant differences were found in post-sIUDF ADC values of the cerebral hemispheres (frontal, parietal, temporal lobes), basal ganglia, and pons between the sIUDF group and control groups and both

singleton and twins control groups ($P = .75, .87, .38, .41$, and $.81$, respectively). After adjustment for GA, no significant differences were found between sIUDF and the singleton control groups or between the singleton and twins control groups for all evaluated brain regions. ADC measurements were similar in various sIUDF etiologies (spontaneous, following laser treatment of TTTS, or following fetal reduction, $P = .28-.9$ in different brain regions). The presence of TTTS on pre-sIUDF imaging did not result in significant ADC changes ($P = .36-.84$ in different brain regions).

DISCUSSION

In our retrospective cohort study, routine third trimester MR imaging showed structural brain lesions in approximately 3.5% of sIUDF pregnancies. These results are in agreement with Stirnemann et al,¹⁷ who also reported brain lesions in 5/239 (2.1%) surviving twins following TTTS treatment complicated by sIUDF. However, the incidence of brain lesions was relatively low compared with that in other studies. In a recent meta-analysis, Mackie et al⁴ described approximately 20% of abnormal brain findings on fbMRI of the surviving cotwin following sIUDF. There is a high variability of reported abnormal brain imaging findings in different cohorts, ranging from 9% to 33%.^{10,12,18,19} Such high variability might be attributed to the relatively small sIUDF cohorts, the indication for fetal brain examination, the timing of fbMRI following the sIUDF, and whether the sIUDF was spontaneous or following laser ablation or cord coagulation. Inconsistency in the definition of abnormal imaging findings such as mild ventriculomegaly or nonconclusive MR imaging findings such as suspected subependymal blood products are another reason for the incidence variability.²⁰ Early fbMRI, performed acutely (<2 weeks) following sIUDF or when postprocedural complications are noted, might also increase the sensitivity for diagnosing acute ischemia or hemorrhage, especially when DWI is performed.¹⁹ Early ischemic or hemorrhagic findings may spontaneously resolve and may not be detected later in pregnancy and at the time of third trimester follow-up.^{11,21}

Moreover, the risk of CNS injury in the surviving twin is obviously higher following spontaneous sIUDF versus sIUDF following laser therapy in which the twins have been dichorionized before the fetal death. On the other hand, the high proportion of sIUDF following laser therapy or cord coagulation in our cohort may explain the low rate of CNS injuries in the surviving twin found in our study. Termination of pregnancy performed in cases of major brain injury detected by post-sIUDF US or on fbMRI performed early might also contribute to the relatively low incidence of structural brain abnormalities detected on later third trimester fbMRI.

In our series, brain lesions found on MR imaging, ie, bilateral caudothalamic cystic changes, that were not detected on the prenatal US probably represent an evolution of earlier ischemic insult. Cerebral lesions in sIUDF pregnancies are usually ischemic or hemorrhagic. Ischemic injury includes focal encephalomalacic lesions or diffuse brain atrophy. Reparative cortical abnormalities such as polymicrogyria are a relatively common sequela of such focal ischemic insults. Intraventricular hemorrhage and resulting ventriculomegaly or periventricular venous infarction can also be found following sIUDF. Several possible

Table 2: Fetal MR imaging biometric parameters of sIUDF fetuses (n = 29), singleton (n = 49), and twins control (n = 28) groups^a

	sIUDF (n = 29) Mean ± SD	Singleton (n = 49) Mean ± SD	Twins Control (n = 28) Mean ± SD	Significance (P Value)		
				sIUDF vs Singleton	sIUDF vs Twins Control	Twins vs Singleton Controls
FOD (mm)	88.4 ± 4.4	91.5 ± 6.5	90.5 ± 4.9	.01 ^b	.09	.43
FOD (%)	50.7 ± 18.6	64.2 ± 22.0	59.9 ± 25.9	.01 ^b	.13	.46
BPD (mm)	68.0 ± 3.9	71.7 ± 6.2	70.4 ± 3.8	.00 ^b	.02 ^b	.25
BPD (%)	36.9 ± 17.6	56.9 ± 22.5	46.9 ± 24.4	.00 ^b	.08	.08
CC (mm)	36.8 ± 2.9	37.9 ± 2.4	37.4 ± 2.0	.08	.31	.39
CC (%)	38.9 ± 22.9	48.2 ± 17.5	43.2 ± 22.3	.07	.48	.32
TCD (mm)	37.8 ± 2.1	39.1 ± 3.7	38.4 ± 2.4	.05 ^b	.37	.29
TCD (%)	44.1 ± 21.0	51.7 ± 23.3	43.2 ± 23.5	.14	.88	.13
Vermian height (mm)	18.4 ± 1.2	18.4 ± 1.6	18.3 ± 1.1	.94	.84	.89
Vermian height (%)	61.6 ± 18.6	56.5 ± 20.1	57.0 ± 18.3	.27	.35	.92
Vermian_AP (mm)	11.8 ± 1.0	12.0 ± 1.2	11.6 ± 1.0	.59	.32	.12
Vermian_AP (%)	48.6 ± 19.5	46.5 ± 18.5	46.1 ± 16.8	.66	.60	.92
Average lateral ventricles	6.4 ± 1.3	7.3 ± 1.2	7.8 ± 1.6	.01 ^b	.00 ^b	.17

Note:—FOD indicates fronto-occipital diameter; BPD, biparietal diameter; CC, corpus callosum; TCD, transcerebellar diameter; AP, anterior-posterior.

^a Variables are presented as mean (SD). MR imaging centiles in fetal CNS biometry are based on Tilea et al.¹⁶

^b Statistically significant values.

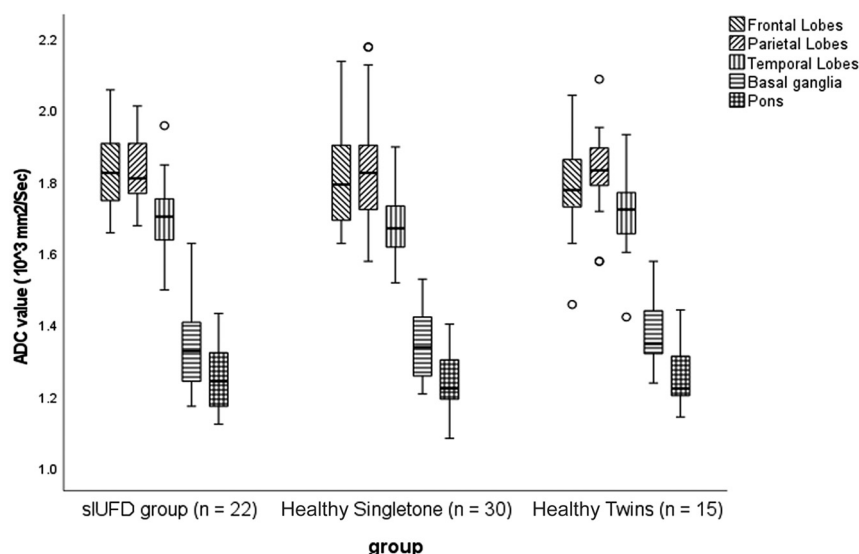


FIG 4. Boxplot of ADC values in sIUDF and control groups. No significant differences were found among various areas in different study groups.

mechanisms might lead to brain injury in survivors after sIUDF.²² Hypoxic-ischemic injury might result from the low-pressure vascular compartment of the fetus who died, leading to the survivor twin's hemodynamic fluctuations and low brain perfusion. Another theory relates to potential thrombi formed in the vascular compartment of the fetus who died and embolizing to the surviving twin through persisting placental anastomoses, resulting in ischemic injury.²³

Analyzing the biometric parameters of surviving fetuses following sIUDF revealed that most supratentorial and infratentorial brain structures were significantly smaller than in control singleton fetuses, probably related to the underlying twin pregnancy,²⁴ though there is the possibility of an underlying pathology that affects broad regions of the developing brain in surviving twins following sIUDF. Similar diffusivity values, ie, measured ADC values, found in our

study in sIUDF and control groups do not support such a hypothesis. DWI enables quantitative free-water assessment in the brain parenchyma, which reflects tissue maturation. Diffusivity changes were found in various fetal pathologies affecting normal brain development and maturation, such as congenital cardiac anomalies or fetal hydrocephalus, even with normal morphologic T2-weighted fbMRI findings.^{14,25} Transient hemodynamic fluctuations following sIUDF and resulting decreased brain perfusion might affect brain maturation. However, our results of similar diffusivity in the surviving twins on routine third trimester fbMRI support near-normal brain maturation, especially in the setting of normal morphologic-anatomic imaging findings.

Neurodevelopmental impairment in the surviving twin following sIUDF is of great concern and affects parental counseling. Hillman et al⁸ described long-term neurodevelopmental impairment in up to 26% of twins following a single fetal death. Nevertheless, formal developmental tests were not routinely performed in most cohorts, and the age at follow-up was relatively young to detect neurodevelopmental abnormalities. The association between focal or diffuse brain injury found on pre- or postnatal imaging and adverse neurodevelopmental outcomes is also controversial. Hillman et al did not find a significant correlation between abnormal brain imaging findings and neurodevelopmental impairment, possibly related to lack of imaging, underreporting, inconsistent imaging reports, and lack of consistency in imaging timing related to delivery and development of neurologic signs.⁸ Such correlation was also not found in a recently published meta-analysis by Mackie et al.⁴ Prematurity, which is very common in twin pregnancies, especially

following sIUFD,^{8,26} probably contributes significantly to long-term neurologic morbidity,^{4,8,27} which can explain the high rate of neurodevelopmental impairment, much more than reported abnormal prenatal imaging findings. The low incidence of brain abnormalities on prenatal diagnosis is not likely to reflect the low sensitivity of prenatal imaging but is probably related to the study cohort of third trimester survivors following cotwin death with normal brain maturation and development, as suggested by normal diffusivity. Many of previously reported brain abnormal findings were also strongly associated with preterm birth, obviously apparent only on postnatal imaging.

US is the main imaging technique used on routine follow-up of twin pregnancies. It enables evaluation of fetal growth and the diagnosis of hemodynamics and MC twin complications. However, it has limited sensitivity in diagnosing ischemia, hemorrhage, or cortical malformations.^{7,11,28} Currently, fbMRI is gaining widespread acceptance as an important adjunct to US, especially in high-risk twin pregnancies. There is currently little evidence to guide the optimal timing of fbMRI (relative to the occurrence of the twin complication, including sIUFD) to improve the detection of brain insult and prognostication. In our cohort, fbMRI performed routinely in the mid-late third trimester for all surviving twins had a relatively low incidence of cerebral injury (~3.5%), which argues against routine use of fbMRI in an MC twin pregnancy complicated with sIUFD. fbMRI, performed earlier, especially following US evidence of fetal compromise (ie, intrauterine growth restriction, flow abnormalities, or abnormal brain findings), will probably have increased diagnostic ability and, similar to previous studies, will show a higher incidence of cerebral injury.^{13,29} A follow-up third trimester fbMRI is highly recommended to evaluate the sequelae of acute injury and reparative malformations in these cases of early brain injury.

The retrospective nature and the relatively small population are major limitations of our study. Study recruitment was noncontrolled, so our data describe the observed rates of brain abnormalities in third trimester routine fbMRI rather than reflecting the true prevalence of brain abnormalities. Selection bias, either related to referral to our tertiary center or for exclusion of acute complications in the sIUFD group that might result in termination/reduction due to concern for injury to the surviving fetus is an important limitation of our study. Our control cohorts of singleton and uncomplicated twins were also relatively heterogeneous and underwent fbMRI due to various indications, though in all cases, fbMRI findings were normal. Our study is also limited by the lack of correlation of fetal MR findings with neurodevelopmental outcomes. However, the high prematurity rate in this subgroup of twin pregnancies is an important confounding factor in assessing long-term outcomes. Future studies should include prospective fetal monitoring protocols, including US and fbMRI, following twin pregnancies complicated by sIUFD. Evidence-based parental counseling requires a correlation between specific brain abnormalities demonstrated on fbMRI and postnatal imaging and neurodevelopmental outcomes. Currently, such correlation is lacking in large-scale cohorts.

CONCLUSIONS

In surviving twins following sIUFD, routine third trimester fbMRI showed persistent small biometry, though normal diffusivity

suggests normal parenchymal maturation and microstructure. The rate of cerebral structural injury, not detected by US, was relatively low in our relatively small cohort (1/29, ~3.5%), which argues against routine use of fbMRI in an MC twin pregnancy complicated by sIUFD. fbMRI should be performed following sonographic evidence of a fetal compromise or brain injury. Larger prospective studies with expert fetal neurosonography and standardized timing of pre- and postnatal MR imaging, including formal neurodevelopmental assessment, are necessary to evaluate the appropriate surveillance protocol better and guide parental counseling in twin pregnancies complicated with sIUFD.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

REFERENCES

1. D'Antonio F, Thilaganathan B, Dias T, et al; Southwest Thames Obstetric Research Collaborative (STORK). **Influence of chorionicity and gestational age at single fetal loss on risk of preterm birth in twin pregnancy: analysis of STORK multiple pregnancy cohort.** *Ultrasound Obstet Gynecol* 2017;50:723–27 [CrossRef Medline](#)
2. Pharoah PO, Adi Y. **Consequences of in-utero death in a twin pregnancy.** *Lancet* 2000;355:1597–1602 [CrossRef Medline](#)
3. Saito K, Ohtsu Y, Amano K, et al. **Perinatal outcome and management of single fetal death in twin pregnancy: a case series and review.** *J Perinat Med* 1999;27:473–77 [CrossRef Medline](#)
4. Mackie FL, Rigby A, Morris RK, et al. **Prognosis of the co-twin following spontaneous single intrauterine fetal death in twin pregnancies: a systematic review and meta-analysis.** *BJOG* 2019;126:569–78 [CrossRef Medline](#)
5. Ong SS, Zamora J, Khan KS, et al. **Prognosis for the co-twin following single-twin death: a systematic review.** *BJOG* 2006;113:992–98 [CrossRef Medline](#)
6. van der Knoop BJ, Zonnenberg IA, Verbeke JIML, et al. **Additional value of advanced neurosonography and magnetic resonance imaging in fetuses at risk for brain damage.** *Ultrasound Obstet Gynecol* 2020;56:348–58 [CrossRef Medline](#)
7. Aertsen M, Van Tieghem De Ten Berghe C, Deneckere S, et al. **The prevalence of brain lesions after in utero surgery for twin-to-twin transfusion syndrome on third-trimester MRI: a retrospective cohort study.** *Eur Radiol* 2021;31:4097–4103 [CrossRef Medline](#)
8. Hillman SC, Morris RK, Kilby MD. **Co-twin prognosis after single fetal death: a systematic review and meta-analysis.** *Obstet Gynecol* 2011;118:928–40 [CrossRef Medline](#)
9. Griffiths PD, Sharrack S, Chan KL, et al. **Fetal brain injury in survivors of twin pregnancies complicated by demise of one twin as assessed by in utero MR imaging.** *Prenat Diagn* 2015;35:583–91 [CrossRef Medline](#)
10. Jelin AC, Norton ME, Bartha AI, et al. **Intracranial magnetic resonance imaging findings in the surviving fetus after spontaneous monochorionic cotwin demise.** *Am J Obstet Gynecol* 2008;199:398 e391–95 [CrossRef Medline](#)
11. Robinson A, Teoh M, Edwards A, et al. **Fetal brain injury in complicated monochorionic pregnancies: diagnostic yield of prenatal MRI following surveillance ultrasound and influence on prognostic counselling.** *Prenat Diagn* 2017;37:611–27 [CrossRef Medline](#)
12. van Klink JM, van Steenis A, Steggerda SJ, et al. **Single fetal demise in monochorionic pregnancies: incidence and patterns of cerebral injury.** *Ultrasound Obstet Gynecol* 2015;45:294–300 [CrossRef Medline](#)
13. Hoffmann C, Weisz B, Yinon Y, et al. **Diffusion MRI findings in monochorionic twin pregnancies after intrauterine fetal death.** *AJNR Am J Neuroradiol* 2013;34:212–16 [CrossRef Medline](#)
14. Schonberg N, Weisstanner C, Wiest R, et al. **The influence of various cerebral and extracerebral pathologies on apparent diffusion**

- coefficient values in the fetal brain. *J Neuroimaging* 2020;30:477–85 [CrossRef Medline](#)
15. Khalil A, Rodgers M, Baschat A, et al. **ISUOG Practice Guidelines: role of ultrasound in twin pregnancy.** *Ultrasound Obstet Gynecol* 2016;47:247–63 [CrossRef Medline](#)
 16. Tilea B, Alberti C, Adamsbaum C, et al. **Cerebral biometry in fetal magnetic resonance imaging: new reference data.** *Ultrasound Obstet Gynecol* 2009;33:173–81 [CrossRef Medline](#)
 17. Stirnemann J, Chalouhi G, Essaoui M, et al. **Fetal brain imaging following laser surgery in twin-to-twin surgery.** *BJOG* 2018;125:1186–91 [CrossRef Medline](#)
 18. Conte G, Righini A, Griffiths PD, et al. **Brain-injured survivors of monochorionic twin pregnancies complicated by single intrauterine death: MR findings in a multicenter study.** *Radiology* 2018;288:582–90 [CrossRef Medline](#)
 19. Weisz B, Hoffmann C, Ben-Baruch S, et al. **Early detection by diffusion-weighted sequence magnetic resonance imaging of severe brain lesions after fetoscopic laser coagulation for twin-twin transfusion syndrome.** *Ultrasound Obstet Gynecol* 2014;44:44–49 [CrossRef Medline](#)
 20. Hochberg A, Silber R, Avnet H, et al. **Fetal and neonatal brain lesions following laser ablation for twin-to-twin-transfusion-syndrome as detected by pre- and post-natal brain imaging.** *Prenat Diagn* 2021;41:1531–40 [CrossRef Medline](#)
 21. Shrot S, Hoffmann C, Katorza E. **Reversible parenchymal ischemic injury on fetal brain MRI following fetoscopic laser coagulation- Implication on parental counseling.** *Radiol Case Rep* 2020;15:1369–72 [CrossRef Medline](#)
 22. Shek NW, Hillman SC, Kilby MD. **Single-twin demise: pregnancy outcome.** *Best Pract Res Clin Obstet Gynaecol* 2014;28:249–63 [CrossRef Medline](#)
 23. Patten RM, Mack LA, Nyberg DA, et al. **Twin embolization syndrome: prenatal sonographic detection and significance.** *Radiology* 1989;173:685–89 [CrossRef Medline](#)
 24. Ghi T, Prefumo F, Fichera A, et al; Societa Italiana di Ecografia Ostetrica e Ginecologica Working Group on Fetal Biometric Charts. **Development of customized fetal growth charts in twins.** *Am J Obstet Gynecol* 2017;216:514 e1–17 [CrossRef Medline](#)
 25. Yaniv G, Katorza E, Bercovitz R, et al. **Region-specific changes in brain diffusivity in fetal isolated mild ventriculomegaly.** *Eur Radiol* 2016;26:840–48 [CrossRef Medline](#)
 26. Cimpoca B, Syngelaki A, Chi Mu A, et al. **Twin pregnancy with two live fetuses at 11-13 weeks: effect of one fetal death on pregnancy outcome.** *Ultrasound Obstet Gynecol* 2020;55:482–88 [CrossRef Medline](#)
 27. Lopriore E, Ortibus E, Acosta-Rojas R, et al. **Risk factors for neurodevelopment impairment in twin-twin transfusion syndrome treated with fetoscopic laser surgery.** *Obstet Gynecol* 2009;113:361–66 [CrossRef Medline](#)
 28. Griffiths PD, Bradburn M, Campbell MJ, et al. **Use of MRI in the diagnosis of fetal brain abnormalities in utero (MERIDIAN): a multicentre, prospective cohort study.** *Lancet* 2017;389:538–46 [CrossRef Medline](#)
 29. Lanna MM, Consonni D, Faiola S, et al. **Incidence of cerebral injury in monochorionic twin survivors after spontaneous single demise: long-term outcome of a large cohort.** *Fetal Diagn Ther* 2020;47:66–73 [CrossRef Medline](#)