

• 临床研究 •

基于胎盘体素内不相干运动MRI和胎儿脑体积预测生长受限胎儿中的极低出生体重儿

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[摘要] 目的: 探讨胎盘体素内不相干运动(intravoxel incoherent motion, IVIM)MRI参数和胎儿脑体积对FGR中VLBWI的预测价值。方法: 回顾性纳入23例FGR孕妇, 依据胎儿出生体重分为VLBWI组(8例)和非极低出生体重儿(non-VLBWI)组(15例)。比较两组胎儿侧脑室占颅内体积百分比以及胎盘IVIM参数[真扩散系数(D)、伪扩散系数(D^{*})、血流灌注分数(f)及胎盘面积]。采用受试者工作特征(receiver operating characteristic, ROC)曲线分析各参数对VLBWI的预测效能。结果: VLBWI组胎盘D值小于non-VLBWI组[(1.38±0.04)×10⁻³ mm²/s vs. (1.44±0.07)×10⁻³ mm²/s, *t*=-2.109, *P*=0.047], 胎盘面积小于non-VLBWI组[(155.84±34.69) cm² vs. (200.41±47.95) cm², *t*=-2.315, *P*=0.031], 胎儿侧脑室占颅内体积百分比大于non-VLBWI组[(3.00±0.55)% vs. (2.53±0.33)%, *t*=2.591, *P*=0.017]。胎盘D值、胎盘面积和侧脑室占颅内体积百分比的ROC曲线下面积分别为0.767、0.783和0.792。联合胎儿侧脑室占颅内体积百分比、胎盘D值和胎盘面积可将ROC曲线下面积提高至0.892。结论: 胎盘IVIM参数和胎儿脑体积可能是帮助预测FGR中VLBWI的潜在有效影像标志物。

[关键词] 胎儿生长受限; 极低出生体重儿; 胎儿脑体积; 体素内不相干运动**[中图分类号]** R445.2**[文献标志码]** A**[文章编号]** 1007-4368(2025)03-360-07**doi:** 10.7655/NYDXBNSN241029

Prediction of very low birth weight infants in growth-restricted fetuses using intravoxel incoherent motion MRI of the placenta and fetal brain volume

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[Abstract] **Objective:** To evaluate the predictive value of placental intravoxel incoherent motion (IVIM) MRI parameters and fetal brain volume in predicting VLBWI in FGR. **Methods:** A retrospective analysis was conducted on 23 pregnant women with FGR, categorized into VLBWI group (*n*=8) and non-VLBWI group (*n*=15) based on birth weight. We compared brain structures as a percentage of intracranial volume and placental IVIM parameters [true diffusion coefficient (D), pseudo-diffusion coefficient (D^{*}), perfusion fraction (f), and placental area] between the two groups. Receiver operating characteristic (ROC) curve analysis was used to assess the predictive efficacy of each parameter for VLBWI. **Results:** The placental D value in the VLBWI group was lower than that in the non-VLBWI group [(1.38±0.04)×10⁻³ mm²/s vs. (1.44±0.07)×10⁻³ mm²/s, *t*=-2.109, *P*=0.047], and the placental area was smaller in the VLBWI group [(155.84±34.69) cm² vs. (200.41±47.95) cm², *t*=-2.315, *P*=0.031], while the percentage of lateral ventricle volume relative to intracranial volume was greater in the VLBWI group [(3.00±0.55)% vs. (2.53±0.33)%, *t*=2.591, *P*=0.017]. The areas under the ROC curve for placental D value, placental area, and lateral ventricle as a percentage of intracranial volume were 0.767, 0.783, and 0.792, respectively. Combining the fetal lateral ventricle as a percentage of intracranial volume, placental D value,

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and placental area improved the ROC curve area to 0.892. **Conclusion:** Placental IVIM parameters and fetal brain volume may serve as potentially effective imaging markers for distinguishing VLBWI in cases of FGR.

[Key words] fetal growth restriction; very low birth weight infant; fetal brain volume; intravoxel incoherent motion

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胎儿生长受限(fetal growth restriction, FGR)是指胎儿因母体、胎儿、胎盘等病理因素影响而未达到其应有的遗传潜能,多表现为胎儿超声估测体重或腹围低于相应胎龄第10百分位^[1]。FGR胎儿出生体重通常低于正常新生儿,其中低于1 500 g者定义为极低出生体重儿(very low birth weight infants, VLBWI)^[2]。由于VLBWI常伴随早产,其死产和围产期死亡风险显著高于单纯FGR婴儿^[3-4]。因此,产前准确预测VLBWI有助于合理选择分娩时机,减少胎儿接触有害因素,从而改善母体和胎儿预后。

胎盘和胎头的发育与胎儿出生结局息息相关。胎盘-脑轴互相影响,随基因遗传学、血流动力学、结构或微结构的改变而变化,是目前研究的热点。胎儿MRI脑成像分割技术通过自动分割和测量胎儿脑体积,帮助评估FGR胎儿脑发育延迟情况及程度。既往研究显示FGR胎儿所有脑结构体积显著减小^[5],表明MRI脑分割技术用于FGR胎儿脑发育研究的可行性和灵敏度。胎盘体素内不相干运动(intravoxel incoherent motion, IVIM)可活体评估FGR胎儿胎盘的微循环灌注改变^[6]。研究表明,晚发型FGR胎儿的胎盘血流灌注分数显著降低,且与新生儿体重呈正相关^[7]。然而,大多数研究仅对胎盘IVIM参数或脑体积进行单一分析,尚未从胎儿脑结构与胎盘功能两个维度对胎儿发育进行综合评估和联合预测。

因此,本研究旨在通过联合胎儿脑体积和胎盘IVIM参数,探索其对FGR中的VLBWI的预测价值。

1 对象和方法

1.1 对象

回顾性收集2018年6月—2023年5月在南京医科大学第一附属医院接受MRI胎儿扫描的单胎孕妇。本研究经医院伦理审查委员会批准(2021-SR-407)。纳入标准:①妊娠28周及以上的单胎妊娠;②诊断为胎儿生长受限,即超声估测胎儿体重或腹围低于相应胎龄的第10百分位;③孕妇行超声检查,经多普勒血流评估存在胎盘功能不全(脐动脉间

隙大、脐动脉阻力升高、脐动脉收缩-舒张压比异常、脐动脉舒张压升高、大脑中动脉搏动指数异常以及羊水指数增厚/低);④临床资料完整;⑤孕妇接受了标准的产前MRI检查,包括胎头及胎盘MRI检查。超声检查与MRI扫描时间间隔<2周。

排除标准:①MRI图像质量差,严重图像伪影影响后续分析;②胎盘异常,如胎盘植入、胎盘早剥;③胎儿遗传性疾病和发育异常,如结构性或功能性心脏病、无脑畸形、脊柱裂;④宫内病毒、细菌或寄生虫感染;⑤MRI提示孕妇或胎儿存在实质性病变。所有FGR单胎孕妇根据出生体重分为VLBWI组(新生儿出生体重<1 500 g)和non-VLBWI组(出生体重1 500~2 500 g)。

最终,23例FGR单胎妊娠孕妇被纳入研究,其中VLBWI组8例,平均年龄(30.13±3.76)岁,non-VLBWI组15例,平均年龄(30.13±3.31)岁。

1.2 方法

1.2.1 图像采集

胎盘图像使用1.5T MRI系统(MAGNETOM Aera, Siemens公司,德国),12通道表面体线圈和2个嵌入式通道脊柱线圈对患者进行检查。患者均采用仰卧位或侧卧位成像以确保舒适度。MRI方案为:①T1加权梯度回波序列[重复时间(repetition time, TR)/回波时间(echo time, TE)=6.83 ms/2.39 ms,切片厚度=4.0 mm,视场(field of view, FOV)=380 mm×368 mm,翻转角度(flip angle, FA)=70°,面内分辨率=1.5 mm×1.5 mm];②T2加权半傅立叶获取单次涡轮自旋回波(half-fourier acquisition single-shot turbo spin-echo, HASTE)序列(TR/TE=1 300 ms/167 ms,切片厚度=4.0 mm,FOV=380 mm×309 mm,FA=70°,面内分辨率=1.5 mm×1.5 mm);③多值DWI序列(TR/TE=6 400 ms/65 ms,切片厚度=5.5 mm,FOV=320 mm×320 mm,面内分辨率=3.5 mm×3.5 mm),b值为0、50、100、150、200、500和800 s/mm²。总扫描时间<15 min。

胎头图像使用1.5T MRI系统(MAGNETOM Aera, Siemens公司,德国),6通道表面体线圈对患者

进行检查。母亲和胎儿都没有接受镇静剂,母亲在整个扫描过程中保持自由呼吸。MRI方案为:①轴向、冠状面和矢状面T2加权快速采集 HASTE序列,TR/TE=1 200 ms/168 ms,片厚=3.0 mm,FOV=320 mm×320 mm,矩阵大小 256×256;②轴向 T1WI vibe,TR/TE=6.83 ms/2.39 ms,片厚=3.0 mm,FOV= 380 mm×369 mm,矩阵大小 320×240;③具有 2 个不同 b 值(50 和 800 s/mm²)的 DWI 序列。收集 25 个 3 mm 厚的切片;矩阵大小 114×105;FOV= 320 mm×320 mm。T2 加权序列用于图像重建,其他序列用于排除有病变的病例。

1.2.2 胎盘扩散和灌注参数

利用 FireVoxel 软件(FireVoxel:CAL2R, Nw 纽约大学,美国)确定基于多 b 值扩散加权图像的基于 IVIM 的后处理函数参数。双指数模型的方程为: $s(b)=s_0[(1-f)\cdot e^{-b\cdot D}+f\cdot e^{-b\cdot(D+D^*)}]$ 。其中 $s(b)$ 表示信号强度, s_0 表示 $b=0$ 时的信号强度, f (灌注分数) 表示血管室的体积百分比, $1-f$ 表示剩余的体积分数、组织或细胞室。 D^* 为相关扩散系数(伪扩散系数), D 为扩散系数(真扩散系数)。

使用 MATLAB 编写的内部开发程序(The Math-Works Inc., 美国)处理胎盘面积值。使用上述相同方法在 T2WI 图像上绘制感兴趣区(ROI)。在冠状面、横切面和矢状面, ROI 覆盖整个胎盘。

1.2.3 胎头分割方法

使用 PAK-SRR(prior anatomical knowledge guided fetal brain super-resolution reconstruction)方法重建各向同性的高分辨率体积胎头 MR 图像(空间分辨率为 0.8 mm×0.8 mm×0.8 mm)。使用 Draw-EM

(developing brain region annotation with expectation-maximization)算法进一步将重建的体积图像分割成包括灰质和白质的 17 个脑区并计算体积^[8]。这种方法已被证实是可靠的晚期妊娠和新生儿脑区分割方法^[9]。

1.3 统计学方法

使用 SPSS 26.0 软件进行统计分析。采用 Kolmogorov-Smirnov 正态性检验评估参数是否符合正态分布。符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,采用独立样本 t 检验;不符合正态分布的计量资料以中位数(四分位数)[$M(P_{25}, P_{75})$]表示,采用 Mann-Whitney U 检验;分类变量以频数(百分比)表示,组间比较采用卡方检验。采用二元 Logistic 回归分析结合两组间差异有统计学意义的参数构建联合模型。采用受试者工作特征(receiver operating characteristic, ROC)曲线和曲线下面积(area under the curve, AUC)评估胎儿脑体积、胎盘 IVIM 参数及联合模型对 VLBWI 的预测价值。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 患者基本临床信息

两组患者的校正胎龄差异无统计学意义[(30.89±1.29)周 vs. (32.27±1.86)周, $P=0.078$]。临床和人口统计学数据见表 1。

2.2 两组间胎儿脑区体积百分比以及胎盘 IVIM 参数的比较

VLBWI 组胎盘 D 值小于 non-VLBWI 组[(1.38±0.04)×10⁻³ mm²/s vs. (1.44±0.07)×10⁻³ mm²/s, $t=-2.109$,

表 1 FGR 中 VLBWI 组和 non-VLBWI 组的临床特征
Table 1 Clinical features of VLBWI and non-VLBWI group in FGR

Varibale	VLBWI(n=8)	Non-VLBWI(n=15)	t/χ^2	P
Maternal age(years, $\bar{x} \pm s$)	30.13 ± 3.76	30.13 ± 3.31	-0.005	0.996
Gestational age(years, $\bar{x} \pm s$)	30.89 ± 1.29	32.27 ± 1.86	-1.855	0.078
Hypertension[n(%)]			8.110	0.004
Yes	6(75.0)	2(14.3)		
No	2(25.0)	12(85.7)		
Diabetes[n(%)]			1.010	0.315
Yes	4(50.0)	4(28.6)		
No	4(50.0)	10(71.4)		
Neonatal gender[n(%)]			0.321	0.571
Male	3(37.5)	7(50.0)		
Female	5(62.5)	7(50.0)		
Neonatal birth weight(g, $\bar{x} \pm s$)	1 290.00 ± 87.51	2 014.00 ± 296.91	-6.670	<0.001

$P=0.047$], 胎盘面积也小于 non-VLBWI 组 $[(155.84 \pm 34.69) \text{cm}^2 \text{ vs. } (200.41 \pm 47.95) \text{cm}^2, t=-2.315, P=0.031]$, 差异有统计学意义(表2)。两组间胎盘 D*值和 f 值差异未见统计学意义 ($P > 0.05$)。VLBWI 组胎儿侧脑室占颅内体积百分比大于 non-VLBWI 组 $[(3.00 \pm 0.55)\% \text{ vs. } (2.53 \pm 0.33)\%, t=2.591, P=0.017]$, 其余脑结构所占颅内体积百分比差异均未见统计学意义 ($P > 0.05$)。

2.3 IVIM 参数、脑区体积百分比在鉴别 VLBWI 与非 VLBWI 中的价值

采用 $D=1.42 \times 10^{-3} \text{ mm}^2/\text{s}$ 作为截断值预测 VLBWI, 可获得最优的预测效能 ($\text{AUC}=0.767, 95\% \text{CI}: 0.573 \sim 0.960$, 灵敏度 66.7%, 特异度 75.0%)。以胎盘面积 = 166.90 cm^2 为截断值预测 VLBWI, 预测效能最佳 ($\text{AUC}=0.783, 95\% \text{CI}: 0.573 \sim 0.994$, 灵敏度 80.0%, 特异度 75%)。侧脑室占颅内体积百分比截断值为 2.61% 时, 预测 VLBWI 效果最佳 ($\text{AUC}=0.792, 95\% \text{CI}: 0.584 \sim 0.999$, 灵敏度 73.3%, 特异度

75.0%)。

2.4 联合预测模型的诊断价值

联合胎盘 D 值、胎盘面积和胎儿侧脑室占颅内体积百分比可将 AUC 提高至 0.892 (95%CI: 0.760~1.000, 灵敏度 80.0%, 特异度 87.5%, 图 1)。代表性 VLBWI 和 non-VLBWI 病例见图 2。

3 讨论

IVIM 技术在临床上广泛用于评估组织微观结构和微循环状况, 如肿瘤灌注和扩散特性, 为病理诊断提供参考。在胎盘中, 该技术主要用于测定胎盘灌注, 从而无创评估胎盘微循环^[10]。本研究将胎盘的 IVIM 参数和胎儿脑体积联合起来进行综合评估, 早期识别 FGR 胎儿中的高危组 (VLBWI), 辅助临床决策, 从而改善新生儿的预后。

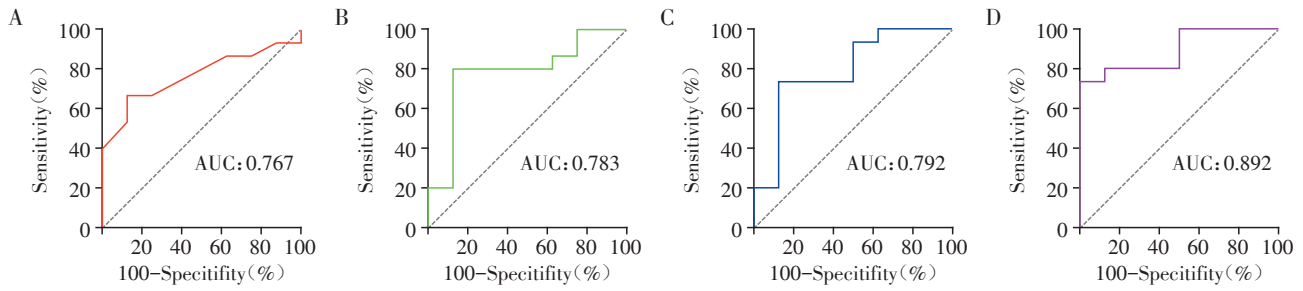
在胎盘 IVIM 参数中, VLBWI 组胎盘 D 值和胎盘面积均小于 non-VLBWI 组。先前胎盘功能与不良妊娠结局关系的研究表明, D 值与低出生体重有

表2 FGR 极低体重组和非极低体重组的脑体积和胎盘参数

Table 2 Brain volume and placental parameters of VLBWI group and non-VLBWI group in FGR

	VLBWI	Non-VLBWI	t/z	P
Percentage volume of intracranial structures in fetal MRI				
Hippocampus [% , $M(P_{25}, P_{75})$]	0.40(0.38, 0.45)	0.39(0.35, 0.42)	-0.904	0.366
Temporal lobe GM (% , $\bar{x} \pm s$)	4.30 ± 0.20	4.22 ± 0.51	0.396	0.696
Temporal lobe WM (% , $\bar{x} \pm s$)	6.57 ± 0.81	6.48 ± 0.43	0.319	0.753
Insula GM [% , $M(P_{25}, P_{75})$]	0.53(0.44, 0.56)	0.55(0.44, 0.63)	-0.839	0.428
Insula WM (% , $\bar{x} \pm s$)	1.32 ± 0.16	1.32 ± 0.17	-0.103	0.919
Frontal lobe GM (% , $\bar{x} \pm s$)	6.23 ± 0.65	6.50 ± 0.97	-0.708	0.487
Frontal lobe WM (% , $\bar{x} \pm s$)	12.43 ± 0.67	12.56 ± 0.91	-0.355	0.726
Parietal lobe GM (% , $\bar{x} \pm s$)	4.33 ± 0.34	4.22 ± 0.52	0.528	0.603
Parietal lobe WM (% , $\bar{x} \pm s$)	7.91 ± 0.60	7.87 ± 0.75	0.122	0.904
Occipital lobe GM (% , $\bar{x} \pm s$)	2.73 ± 0.19	2.93 ± 0.36	-1.409	0.173
Occipital lobe WM (% , $\bar{x} \pm s$)	3.12 ± 0.40	3.21 ± 0.36	-0.560	0.582
Cingulate gyrus (% , $\bar{x} \pm s$)	1.71 ± 0.37	1.94 ± 0.43	-1.240	0.229
Basal Ganglia (% , $\bar{x} \pm s$)	4.68 ± 0.24	4.69 ± 0.24	-0.046	0.963
Cerebellum (% , $\bar{x} \pm s$)	3.91 ± 0.23	4.30 ± 0.74	-1.705	0.105
Lateral ventricle (% , $\bar{x} \pm s$)	3.00 ± 0.55	2.53 ± 0.33	2.591	0.017
Brainstem (% , $\bar{x} \pm s$)	1.64 ± 0.07	1.59 ± 0.16	0.877	0.390
Corpus callosum (% , $\bar{x} \pm s$)	0.72 ± 0.15	0.65 ± 0.09	1.295	0.209
Cerebrospinal fluid [% , $M(P_{25}, P_{75})$]	33.99(32.28, 36.25)	34.39(31.67, 35.95)	-0.323	0.776
IVIM parameters				
D ($10^{-3} \text{ mm}^2/\text{s}$, $\bar{x} \pm s$)	1.38 ± 0.04	1.44 ± 0.07	-2.109	0.047
D* [$10^{-3} \text{ mm}^2/\text{s}$, $M(P_{25}, P_{75})$]	154.64(91.45, 190.71)	149.58(107.29, 158.90)	-0.710	0.478
f (% , $\bar{x} \pm s$)	27.87 ± 8.08	33.46 ± 5.91	-1.903	0.071
Placenta area (cm^2 , $\bar{x} \pm s$)	155.84 ± 34.69	200.41 ± 47.95	-2.315	0.031

GM=Gray matter; WM=White matter; D=true diffusion coefficient; D*=pseudo-diffusion coefficient; f=perfusion fraction.



A: ROC of D. B: ROC of placental area. C: ROC of lateral ventricle. D: ROC of combined model.

图1 单一MR模型以及联合模型诊断效能的ROC曲线

Figure 1 ROC curves for diagnostic performance of the single MR model and the combined model

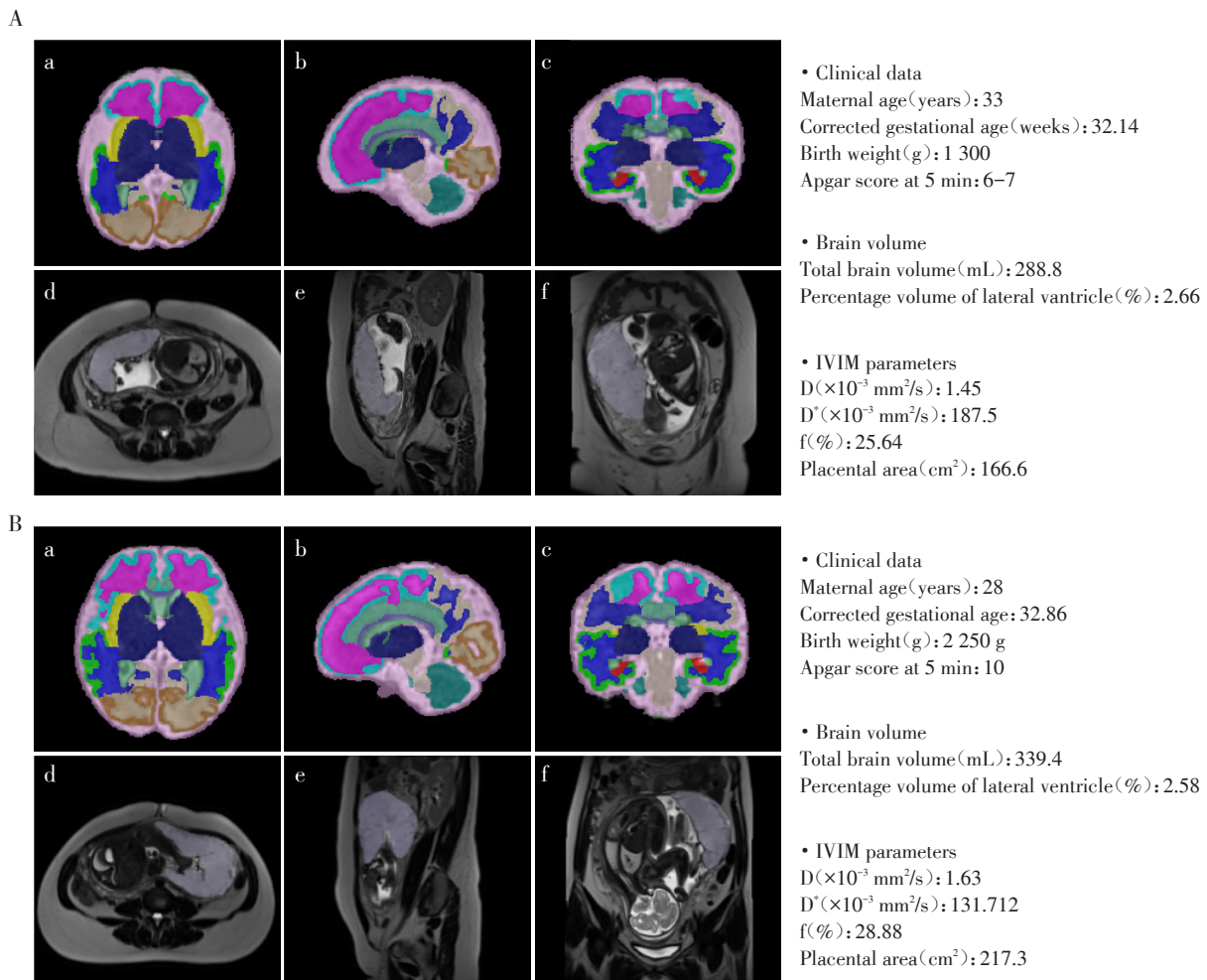


图2 VLBWI组胎儿(A)和non-VLBWI组胎儿(B)的胎头体积(a~c)及胎盘面积图像(d~f)

Figure 2 Images of fetal brain volume (a-c) and placental area (d-f) of the VLBWI fetuses (A) and non-VLBWI fetuses (B)

显著关联^[11],这与本研究结果一致。D值反映的是单纯水分子扩散,VLBWI组D值降低与胎盘的细胞密度增加,细胞间隙更窄,结构更加紧密有关^[12],限制了水分子的扩散,这可能反映了灌注异常所导致的胎盘间质梗死、纤维化和钙化^[13],影响氧气和营养物质的转运,从而导致新生儿的体重减低。一项病例对照结果指出,胎盘面积减少与出生体重下降

密切相关,且增加了FGR的风险^[14]。本研究也证明了FGR胎儿中胎盘面积与出生体重之间的相关性。较小的胎盘面积可能会减少子宫胎盘动脉的数量^[15],降低氧气和营养运输的效率^[16],导致出生体重下降。

Kuula等^[17]研究极低出生体重早产儿与正常出生体重足月儿20岁时脑体积差异,结果表明极低出

生体重组的绝对脑体积较小,脑室体积较大。本研究将研究节点提前至胎儿期,结果与其相似。脑室扩张可能是多种因素的共同作用。长期慢性缺氧和低血供会导致神经元减少和白质发育受损,脑实质体积减小,脑室体积相对增大。缺氧会增加脑水肿的风险^[18],使脑室压力增加,脑室扩张。此外,FGR中的VLBWI往往经历缺氧和氧化应激,影响中枢神经系统发育,包括脑脊液的生成、流动和吸收^[19],导致脑室扩大。研究表明,侧脑室增宽程度与中枢神经系统异常的发生率呈正相关^[20]。脑室扩张可能间接反映了脑实质的发育不良,更易导致VLBWI的发生。

本研究也有一定局限性。首先,本研究为回顾性研究,样本量较小。随着对FGR危害的重视,临床上对FGR胎儿的定期评估、母体的营养支持和健康管理显著降低了VLBWI的发生率。此外,本研究样本需满足超声多普勒、胎头MRI及胎盘MRI等检查要求,并符合图像重建与分割的质量标准,严格的入组条件进一步缩小了样本量。未来需在更大样本的基础上,利用放射组学或人工智能方法更深入研究FGR中VLBWI与non-VLBWI的鉴别方法。此外,本研究纳入了28~35周胎儿,鉴于胎儿脑发育的复杂性与长期性,未来研究应进行更全面、动态的分析。

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所有作者声明无利益冲突。

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Author's Contributions:

KONG Lingnan was responsible for drafting the manuscript and revising the manuscript; HUANG Shijie was responsible for the data processing; ZHANG Xuan, JI Liangyu, and ZHOU Xin were responsible for analyzing and interpreting the data; WU Feiyun and ZHAO Meng proposed the research plan, supervised the research implementation, revised the paper, and provided funding.

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