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超声监测低体重儿的母体子宫动脉、胎儿脐动脉及大脑中动脉的作用

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摘　要

胎儿生长受限(Fetal Growth Restriction, FGR)即意味着胎儿的生长发育没有达到胎儿相应的生长潜能，在妊娠期发病率较高，在生长受限的新生儿中，围产期发病率和死亡率高出普通新生儿8倍，是新生儿发病和死亡的主要原因。胎儿生长受限又分为早发型(妊娠32周之前)和晚发型(妊娠32周及以后)，与晚发型的胎儿生长受限相比，早发型的胎儿生长受限产妇及胎儿的发病率和死亡率都比较高，值得关注的是胎儿生长受限大多集中在34周之后才能被发现，但是目前除分娩外，尚无能够逆转FGR的有效治疗方法，然而过早或过晚的分娩都会降低新生儿的存活率，而多普勒评估早已被纳入妊娠早期胎盘及胎儿疾病的预测，特别是妊娠中期的多普勒超声可以预测大多数胎儿生长受限的情况，其中子宫动脉多普勒血流参数反映了子宫胎盘血流灌注的情况，脐动脉多普勒血流参数可以有效反映胎盘与母体的血流变化，脐动脉多普勒血流参数已经被证实可以降低新生儿死亡的风险，大脑中动脉多普勒血流参数反映了胎儿脑部供血供氧的情况。

关键词

胎儿生长受限，子宫动脉，脐动脉，胎儿大脑中动脉，多普勒超声

The Role of Ultrasound in Monitoring Maternal Uterine Artery, Fetal Umbilical Artery and Middle Cerebral Artery in Low Birth Weight Infants

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Abstract

Fetal Growth Restriction (FGR) means that the growth and development of the fetus does not reach the corresponding growth potential of the fetus, and the incidence of FGR is high during pregnancy, the perinatal morbidity and mortality rate is 8 times higher than that of normal newborn, which is the main cause of neonatal morbidity and mortality. Fetal growth restriction is further divided into early-onset (before 32 weeks gestation) and late-onset (32 weeks gestation and beyond), as compared with late-onset fetal growth restriction, early-onset fetal growth restriction is associated with high maternal and fetal morbidity and mortality. It should be noted that most cases of fetal growth restriction are not detected until 34 weeks after delivery, there are no effective treatments that can reverse FGR, but early or late delivery can reduce neonatal survival, and Dopler's assessment has long been included in the prediction of placental and fetal disease in early pregnancy, in particular, Dopler ultrasound in the second trimester can predict most fetal growth restriction conditions, in which uterine artery Doppler parameters reflect uterine-placental blood flow perfusion, umbilical artery Doppler flow parameters can effectively reflect the placental and maternal blood flow changes, umbilical artery Doppler flow parameters have been proven to reduce the risk of perinatal mortality, Doppler parameters of middle cerebral artery reflect the blood and oxygen supply to the fetal brain.

Keywords

Fetal Growth Restriction, Uterine Artery, Umbilical Artery, Fetal Middle Cerebral Artery, Doppler Ultrasound

1. 简介

国际上目前对于胎儿生长受限(Fetal Growth Restriction, FGR)的诊断尚无统一标准。在没有黄金标准的情况下，FGR 几十年来一直与小于胎龄儿(Small for Gestational Age, SGA)互换使用[1]。FGR 一词用于描述胎儿超声估测体重(Estimated Fetal Weight, EFW)低于相应胎龄体重的第 10 个百分位，SGA 则是指胎儿出生体重小于胎龄相应体重 10%的新生儿[2]。我国目前对于 FGR 的定义为：FGR 是指受母体、胎儿、胎盘等病理因素影响，导致胎儿生长未达到其应有的遗传潜能，多表现为超声估测胎儿体重或者腹围低于相应胎龄的第 10 个百分位[3]。这一定义的漏洞就是过分强调了胎儿的体重，但其实有一部分胎儿的超声估测体重并没有低于第 10 个百分位，但是其实胎儿已发生了生长受限，甚至是发育受损[4]。而且胎儿的生长发育是一个动态过程，这也意味着要准确识别出胎儿是否正在发生或者将要成为生长受限胎儿，成为产科医生的第一大难题。在超声出现之前，产科医生只有靠触诊或者联合测量宫底高度及测量孕妇的腹围来评估胎儿在宫内的生长发育情况，特别是许多女性不确定自己的末次月经期(Last Menstrual Period, LMP)，或是存在月经周期紊乱的情况，那仅仅依靠产科医生的触诊及测量宫底高度和孕妇的腹围，

来确定胎儿生长发育的情况这一方法更是不可靠[5]，自从超声出现开始至今，超声一直被用于产前检测胎儿异常及生长发育情况，现在超声技术在评估胎儿生长发育方面已经非常成熟[5]。超声估测胎儿体重是基于Hadlock及其同事发表的Hadlock公式，此公式是目前临床上估计胎儿体重时运用得最多的公式[6] [7] [8] [9]，这使得定义中的胎儿生长受限诊断得更加准确，其次还可以结合多普勒超声监测妊娠期子宫动脉(Uterine Artery, UTA)、脐动脉(Umbilical Artery, UA)和大脑中动脉(Middle Cerebral Artery, MCA)的血流，既可以用来评估胎儿缺氧缺血的情况[10]，又可以提前对可能发生或者将要发生生长受限的胎儿进行监测及预防，这也为临床医生对于分娩时机的定制提供了的参考资料。

这篇综述旨在描述用多普勒超声监测低体重胎儿妊娠期间母体的子宫动脉(UTA)、胎儿的脐动脉(UA)和胎儿的大脑中动脉(MAC)血流参数会发挥的效用。

2. 双侧子宫动脉

众所周知，胎儿生长受限与子宫胎盘之间的血流灌注密切相关[11]，虽然当胎盘尺寸较小时，也会导致胎盘血流与脐血流的交换能力受损，但大多数的胎儿发生生长受限，并非由于胎盘尺寸较小或是胎盘的其他原因[12]。子宫动脉是胎儿进行血液循环的主要途径[13]，起源于髂内动脉。子宫动脉的升支在子宫内膜发出多个末端分支，这些分支(螺旋动脉)广泛分布于胎盘的附着处。在正常怀孕中，从妊娠3周开始，滋养细胞逐渐侵蚀和重塑子宫的螺旋小动脉，妊娠10周后，这种侵蚀浸润到达血管壁，并且会缓慢延伸到蜕膜－子宫交界处，直至28周时血管重塑达到巅峰[14] [15]。怀孕期间母体的这一生理性变化可以使子宫螺旋动脉的血管管径变粗、血管阻力降低、血流量增加，从而满足胎盘的血流供应，使胎儿获得生长发育所需的充足营养。子宫动脉血流参数可以代表子宫和胎儿之间的血流关系，而子宫动脉的舒张早期切迹又可以反映子宫动脉血管的阻力[16] [17]，若由于孕期合并症或者其他因素，导致滋养细胞的侵袭能力不能维持，从而使螺旋动脉的侵袭和重塑过程受到抑制，使这种生理性的血管重塑现象在孕28周时无法达到巅峰。那蜕膜和母体子宫内的螺旋动脉管壁中的内皮细胞和平滑肌细胞依然存在，未被滋养细胞取代，这种异常的重塑现象将导致子宫胎盘的血管阻力升高，母亲将无法向胎儿供血供氧[18] [19]，为了增加血流的供应，母体一般就会通过提高子宫动脉的阻力来代偿。但过高的阻力、和缺血、缺氧又会导致子宫动脉中的平滑肌收缩，子宫动脉的舒张期血流量不能随孕周的增加而增多，导致子宫动脉中的血流量一直不能满足孕周胎儿的所需量。让孕妇取仰卧位时先利用多普勒超声经腹部识别出宫颈－子宫交界处的子宫动脉后，就可以测量子宫动脉的搏动指数(UtA-PI)、子宫动脉阻力指数(UtA-RI)、收缩/舒张(UtA-S/D)，测量时取样线尽量平行于血流方向，控制两者夹角小于30˚ [20] [21]。这样测量出来的子宫动脉参数就可以用来综合评估子宫动脉的血流及阻力情况，在中孕期UtA-S/D、PI、RI分别为2.80、1.38、0.56，晚孕期降低为2.50、1.04、0.50 [22]，有研究将母体子宫动脉S/D、PI、RI用于预测围产儿不良预后事件的截断值定为2.35、1.11、0.47 [23]。当多种因素引起子宫胎盘内的血管损伤导致血流减少及子宫动脉阻力增加时，会使子宫动脉－胎儿血供受到影响。如果这种高阻力的情况长期存在，则会导致胎儿生长受限的发生。并且此时子宫动脉的阻力升高持续存在，胎儿生长受限将无法得到缓解，甚至可能会进一步加重[13]。如果发生了FGR甚至是在发生FGR之前胎儿的血氧供应就已经出现改变时，经多普勒超声测量就可以发现此时子宫动脉的阻力并未降低，甚至会增高。国内外研究均表明子宫动脉血流可以反映母体、子宫和胎儿之间的血流交换，可以用于预测妊娠不良结局的发生[21] [24] [25] [26] [27] [28]。双侧子宫动脉的舒张早期切迹在生长受限胎儿早期分娩方面的预测具有很高的敏感性[29]，然而最新的国际指南并未将子宫动脉血流参数作为FGR的诊断工具[30]。这就需要更多前瞻性的研究来评估利用多普勒超声测量子宫动脉血流参数是否确实可以识别出那些小于相应胎龄体重的胎儿。

3. 脐动脉

胎儿的脐动脉是连接胎儿跟胎盘的纽带，将血流和氧气运输给胎儿，它控制着氧气和营养的交换。脐动脉的血流变化能准确的反应出胎儿－胎盘循环的血流状态，和胎儿的生理变化。对胎儿早期缺血缺氧有明显的反映[31] [32]。脐动脉的多普勒超声测量多被用来识别因胎儿循环改变而导致的胎儿受损，可以让孕妇取仰卧位，运用彩色多普勒血流显象显示位于脐动脉游离中段的脐动脉，在此处测量脐动脉的搏动指数(UA-PI)、阻力指数(UA-RI)、收缩/舒张比(UA-S/D) [33]，脐动脉的 S/D 比值通常从孕 20 周时的约 4.0 降低至孕足月时的 2.0，在孕 30 周后小于 3.0 [34]。有研究表明在孕中期胎儿脐动脉 S/D、PI、RI 分别为 3.52、1.19、0.70，晚孕期下降为 2.47、0.83、0.52，在 28 周以后 S/D 应该<3 [22]。并将脐动脉 S/D、PI、RI 用于预测围产儿不良预后事件的截断值定为 2.59、1.12、0.67 [23]。由于脐动脉下游的血流阻力增加，舒张期脐动脉的血流缺失或逆转这两种异常也会出现[34]。在正常的妊娠期间，随着妊娠进展，脐动脉的各项指标都会随着孕周增加而逐渐降低，但是当子宫动脉形成高阻力时，不仅会导致胎儿供血供氧不足，引起胎儿生长受限，还会导致绒毛形成异常，从而导致了脐动脉的阻力升高[35]，最后出现舒张末期血流缺失和逆转的情况。而这一情况的出现代表着胎盘的组织学和功能损伤已经到达末期。特别是出现了舒张末期血流缺失和逆转已被证实与胎儿高围产期死亡率、智力发育和神经系统的长期损害有关[36]。有研究表明在早发型胎儿生长受限中，当出现舒张末期血流逆转、缺失或者两者兼有时，胎儿宫内死亡的死亡风险分别增加 7.27、3.59 和 6.8 [37]。其中出现舒张末期血流逆转的胎儿死亡的风险约为出现舒张末期血流缺失胎儿的两倍[38]，多个国内外研究表明脐动脉血流是一项常见的反应胎盘功能的指标，可以直接反应宫内环境及胎儿生长发育情况，可以用于妊娠早期预测不良的妊娠结局，特别是在胎儿生长受限方面具有更高的特异性[25] [39] [40]。

4. 大脑中动脉

大脑中动脉(MCA)是颈内动脉的主要分支，随着胎龄的增加而发育完善，直接反应了胎儿脑循环的各种动态变化，随着胎龄的增加，大脑中动脉的血流阻力也逐渐降低[31]。让孕妇取仰卧位，运用彩色多普勒血流显象显示位于基底动脉环的大脑中动脉(基底动脉环发出后 3~5 mm 处)，控制血流与声速夹角小于 30˚，尽量平行取 3 个连续、平稳波形，测量时避免探头加压，以免引起参数改变[41]，这样就可以获得大脑中动脉中段的血流参数：搏动指数(MAC-PI)、阻力指数(MAC-RI)、收缩/舒张(MAC-S/D) [21]。正常妊娠中随孕期时胎儿大脑中动脉的 RI 逐渐上升，晚孕期逐渐下降，当子宫胎盘功能不全导致子宫和脐动脉的血管阻力增加时，胎儿出现缺血缺氧。为了应对缺氧，胎儿会通过将血流重新分配至重要器官来适应。当缺氧和胎盘阻力持续存在时，胎儿的脑血管会扩张以保证脑血流量的供应。这种胎儿脑血管扩张的机制又被称为脑保护效应，此时大脑中动脉扩张，表现为搏动指数(MAC-PI)下降，当然除此之外还有大脑中动脉的阻力指数(MAC-RI)、收缩/舒张(MAC-S/D)也都会降低，当 MCA 与脐动脉的 PI 比值 ＜1 时可以作为胎儿脑保护效应的预测指标[41]，这一效应最初被认为是胎儿在应对缺血缺氧时，优先将血流供应到脑组织的一种保护性的生理代偿性反应。然而有研究表明这一效应可能无意中对胎儿有害[42]。胎儿的脑保护效应不止大脑中动脉参与，而且椎动脉(Vertebral Artery, VA)似乎更能表现整体脑血管的扩张。有研究表明椎动脉可以作为评价胎儿血流动力学的指标，可以用于预测严重的 FGR [22]，这是因为 FGR 中的脑血管的循环再分配模式是从前往后的血管扩张通路，额叶的血供最先受到优待，大脑前动脉的扩张比大脑中动脉要早或者更频繁也可以证实这一点。若血流再分配的模式真是从前往后，那为大脑前部和中部供血的血管会显示出比灌注大脑后部的血管更低的平均 PI 值，那当 VA 的 PI 值降低到第 5 个百分位时，每个胎儿至少会有一根其他的血管发生了扩张，也就是发生脑保护效应。在一项国外的研究中，参与研究的所有胎儿椎动脉血流发生改变时，这些胎儿中约有 3/8 的胎儿所有的四根脑血管都出

现了异常[43]，脑血管从前往后的循环再分配模式也导致了 VA 成为最后分配的血管，使其受到损害，而 VA 供应的区域为小脑半球、蚓部和脑干，这些区域受损导致 VA 异常的胎儿将面临着更为严重的损害和更差的围产期结局[43] [44]。大脑中动脉已被证实是比脐动脉更为敏感的预测胎盘功能不全的指标[45] [46]，国内外研究表明胎儿大脑中动脉可反应出胎儿缺血缺氧的状态[21] [46]。胎儿脑血流的重新分布也成为了妊娠晚期胎儿发生了宫内受损的一个指标[47]。多个研究表明对大脑中动脉进行多普勒监测可以用于辅助 FGR 的诊断，并可以用于不良妊娠结局的预测[48] [49] [50]。

5. 概括

胎儿生长受限(FGR)是一种与不良妊娠结局有很大相关性的产科并发症，而多普勒超声可以通过监测高危妊娠中母体的子宫动脉、胎儿的脐动脉和大脑中动脉的血流参数，来综合评估胎儿在宫内生长发育的情况，帮助确定分娩时机从而改善妊娠结局[51]。针对于胎儿生长受限，2020 年母胎医学协会(Society for Maternal-Fetal Medicine, SMFM)指南建议：生长受限的胎儿可以通过每 1~2 周进行 1 次超声检查，特别是监测胎儿的脐动脉血流来评估胎儿情况[2] [52]。另外 FGR 不仅是导致围产儿患病和死亡的重要原因[53]。而且它的远期不良结局危害巨大，包括青春期肥胖、糖尿病、胰岛素抵抗等的风险增加，并且心脑血管及智力发育的影响将伴随终生[54]。国际妇产科联合会(Federation of International of Gynecologists and Obstetricians, FIG)根据美国妇产科学院(American College of Obstetricians and Gynecologists, ACOG)的唯一一项孕足月研究中不成比例的宫内生长干预试验(DIGITAT)研究和专家意见做出了建议：EFW 低于第 3 个百分位数的胎儿应该在孕 36 周至 38 周之间就终止妊娠，而对于 FGR 和在妊娠早期就有轻微的多普勒血流参数异常的胎儿应该在妊娠 34 周至 37 周之间就终止妊娠，并且也有研究表明在妊娠 30 周之前对 FGR 进行干预会有显著的效果，但是在妊娠 36 周后再进行干预的效果甚微[55] [56]。尽管 FGR 围产期的发病率及死亡率较高，也并不建议对诊断为 FGR 的所有孕妇都进行剖宫产。FGR 并不是阴道分娩的绝对禁忌，但是在进行阴道分娩时，必须在分娩期间连续地监测胎儿的心率，并且要在进行阴道分娩前就做好一切应对不良结局的预防措施[57]。这也再一次强调了在妊娠中期甚至是早期就需要确诊 FGR 或者预测 FGR 发生的重要性，虽然 FGR 是多种因素共同参与的结果，但是超声检查与适时监测的作用无可替代[58]。而且利用多普勒超声对高危妊娠的监测及母婴围产期的不良结局的预测有一定的价值，又不会对胎儿及母体产生任何损伤，能够尽早预测胎儿发生 FGR 的风险，从而进行预防及改善不良妊娠结局。

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