



磁共振成像在胎儿侧脑室增宽中的应用进展*

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【摘要】 胎儿侧脑室增宽是产前影像学检查中常见的中枢神经系统疾病,预后从正常到严重功能障碍不等。目前仍缺少与产后个体神经发育功能相关的胎儿预测标志物,增加产前诊断和临床管理的难度。磁共振成像(magnetic resonance imaging, MRI)技术的不断进步使得其在侧脑室增宽诊断、预后评估及病因探索等方面更加准确和可靠,对预后管理和产前咨询具有重要作用。但受MRI的潜在安全隐患及经济、技术等限制,MRI不作为产前影像学诊断的首选,超声和MRI对胎儿侧脑室增宽的测量结果和分级仍存在争议。目前认为MRI测量三维体积可能为预后带来一些可靠信息,但精确分割测算脑结构是一个巨大的挑战,MRI测量侧脑室体积尚未达成共识。本文结合国内外最新研究综述MRI在产前侧脑室增宽应用中的进展,为进一步探究侧脑室体积测量在疾病诊断和管理中的作用提供理论基础,提出未来将二维宽度与三维体积结合,寻找胎儿侧脑室增宽的最佳预后预测截断值。

【关键词】 侧脑室增宽 磁共振成像 综述

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【Abstract】 Fetal ventriculomegaly is a central nervous system disorder commonly seen in prenatal imaging, and the prognosis ranges from normal health to severe dysfunction. Currently, fetal predictive markers associated with postpartum individual neurodevelopmental function are still not available, which increases the difficulty of prenatal diagnosis and clinical management. Constant advancements in magnetic resonance imaging (MRI) technology have brought better accuracy and reliability of MRI applied in the diagnosis, prognosis assessment, and etiology investigation of ventriculomegaly. MRI plays a critical role in prognostic management and prenatal consultation. Nevertheless, due to the potential safety hazards and economic and technical constraints of MRI, it is not the first choice for prenatal imaging diagnosis. Moreover, there are different opinions regarding the measurement results and grading criteria of ultrasound and MRI. At present, it is accepted that three-dimensional volume may provide reliable information for prognosis. However, accurate segmentation and measurement of brain structure remain serious challenges, and no consensus on the MRI measurement of lateral ventricle volume has been reached. In this paper, based on the latest research reports from China and around the world, we reviewed the progress in applying MRI in the prenatal diagnosis and treatment of ventriculomegaly. This review offers a theoretical foundation for further exploration of the role of lateral ventricle volume measurement in disease diagnosis and management. We suggest that researchers combine two-dimensional width with three-dimensional volume in the future to identify the optimal cutoff value for prognostic prediction of fetal ventriculomegaly.

【Key words】 Ventriculomegaly Magnetic resonance imaging Review

胎儿发育异常的产前筛查主要依靠常规超声,在影像学中检测到的部分异常可通过侵入性胎儿染色体或基因筛查进一步明确,但大部分异常往往与遗传因素无关,针对性影像学筛查及妊娠后期密切超声随访足以进行可靠的产前诊断。产前检查常见的中枢神经系统异常之一是胎儿侧脑室增宽,在妊娠15~40周内,侧脑室房部径线维持稳定,平均径线范围为5.4~7.6 mm^[1]。当影像学检查

提示侧脑室房部径线 ≥ 10 mm时认为侧脑室增宽(ventriculomegaly, VM),可由遗传、结构及感染等原因单独或组合造成,发生率为0.3%~1.5%^[2]。单纯性增宽无遗传、结构等其他异常者称为孤立性侧脑室增宽(isolated ventriculomegaly, IVM),反之为非孤立性侧脑室增宽(non-isolated ventriculomegaly, NIVM)。目前VM分度有两种方法:轻度(10~15 mm)、重度(>15 mm)或轻度(10~12 mm)、中度(13~15 mm)、重度(>15 mm)。

既往研究表明,胎儿VM不单是一种疾病,更可能是其他单个或多个中枢神经系统异常的影像学表现,其敏

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感率为88%^[3]。因此胎儿预后是医生和家庭最重视的问题。研究发现相关解剖、感染或遗传异常通常与较差的神经发育结果相关,如出生后认知、语言和行为障碍,与孤独症、癫痫、注意力缺陷等多种神经疾病有关^[4-5]。即使是孤立性轻度VM,出生后仍有6%~11%者出现神经发育异常^[2,6]。因此,临床指标与预后的差异性给产前咨询和家庭带来巨大压力,缺乏与产后个体神经发育功能相关的胎儿预测标志物是困扰临床医生的难题。在胎儿神经学领域,需要新的方法来精准监测VM胎儿的预后,更准确的工具来量化胎儿大脑发育和描述个体差异。

考虑到成本效益,临床上常规使用超声进行筛查。相较于超声,胎儿磁共振成像(magnetic resonance imaging, MRI)具有较强的软组织对比度,可通过超快速T2加权成像最大限度地减少胎儿运动伪影,在识别胎儿中枢神经系统异常中存在巨大优势。MRI在精确测量侧脑室宽度的同时能发现如胼胝体发育异常、神经元移行障碍等额外异常,这些异常极大影响妊娠结局及神经预后。研究表明与超声相比, MRI在检测胎儿大脑异常中的诊断准确性提高了25%^[7]。但额外异常发现率受超声诊断水平及机器等影响。欧洲多中心研究发现当操作人员正确执行多平面神经超声检查时,产前MRI中检测到的额外的中枢神经系统异常的发生率仅为5.4%,主要是颅内出血和神经元迁移障碍^[8]。但毋庸置疑, MRI在探索大脑解剖和为超声诊断增加临床信息方面发挥着关键作用。同时需强调,即使产前MRI证实的IVM, 12%患者产后影像学中未发现存在额外异常^[9]。这不断提示着医务人员一个事实:侧脑室是一个立体结构,二维平面测量的增宽仅是“冰山一角”, VM仍有许多需探知的奥秘。本文拟对目前国内国外胎儿MRI在VM中的应用进展作一综述。

1 胎儿头颅MRI介绍

与儿童神经影像学类似,胎儿头颅MRI通过SSFSE及BSSFP序列扫描感兴趣区的矢、冠、轴三方位,其中横断面垂直于脑干,平行于胼胝体或颅底,并根据冠状面来调整横向对称性;冠状面、矢状面均平行于脑干,前者对称显示双侧内耳结构,正中矢状面能观察胼胝体全貌、中脑导水管以及垂体柄^[10]。虽然MRI在产前诊断中具有重要作用,但仍存在不可忽视的局限性。妊娠20周前的胎儿部分脑结构发育不完善如小脑蚓部、胼胝体,与详细的超声检查相比,该时期的MRI不能提供额外的信息。因此,胎儿头颅MRI通常在孕20周后进行。在某些情况下,可适当放宽至16~18周,但磁场对孕早期发育是否存在不良影响尚不清楚^[11-12]。其次,对于有幽闭恐惧症、金属植

人物等MRI禁忌证者无法进行该项检查。MRI常规孔径为60 cm,对于肥胖的孕妇,往往需要大孔径MRI(70 cm)才能提供较宽敞的空间及安全需要^[13]。

目前尚无文献表明MRI对胎儿发育存在有害影响^[14]。胎儿头颅MRI通常在1.5T进行,但3T MRI机型也逐渐广泛用于头颅的检查。MRI检查过程中产生的高水平噪声可能会引起母亲和胎儿的关注,导致异常运动,降低图像质量,而3T MRI具有高图像分辨率,高信号强度,增加成像的信噪比,改善解剖成像,且能量沉积不超过1.5T机型等特点。研究表明3T磁共振机更能勾勒出详细的中枢神经系统解剖结构图谱,更清晰凸显胎儿脑皮质发育异常^[15]。当然,高场强MRI存在扫描时间长、运动伪影多、组织加热增加等缺点,目前仍需大量数据证明3T机型在胎儿脑成像中的优势。

2 正常侧脑室在MRI中的描述表现

侧脑室形状不规则,分为前角、下角、后角、体部和三角区5个部分,前角、下角和后角分别位于额叶、颞叶和枕叶内。体部作为侧脑室的中心,位于额叶后部。侧脑室三角区是体部、下角和后角连接处。侧脑室表面有室管膜覆盖,脉络膜丛起源于侧脑室壁的室管膜细胞,其位置和体积在孕11周时达到最大,此时的脉络膜丛填充了75%的侧脑室。之后随着孕周增长,脉络膜丛填充脑室的体积相对较小,位置似乎更靠后^[16]。妊娠期间侧脑室的形态和形状的巨大变化与周围脑结构变化密切相关,在妊娠早期(10~13周),脑实质较薄,脑室及轴外间隙相对突出,即侧脑室占据胎儿大脑的大部分,但前角、体部及三角区的外观尚不成熟。随着灰质的成熟和大脑表面的折叠,在妊娠16~18周,侧脑室体积减小,形成4个不同的角,在成像上可以识别^[17]。

3 胎儿MRI脑室及脑室周围其他结构的二维测量

准确的侧脑室定性和定量评估研究关系到VM的诊断和临床管理。超声一般使用横切面测量侧脑室宽度,该切面上清晰显示透明隔腔及侧脑室后角,且脉络膜丛未填充整个侧脑室。胎儿MRI可以从冠状面和横切面进行测量,冠状面经侧脑室三角区脉络膜丛血管球水平,垂直侧脑室长轴测量侧脑室两侧壁内缘最短连线^[18]。目前多项研究多注重超声和MRI两种测量方式在疾病管理和诊断中一致性和差异性的比较。BEHRENDT等^[19]认为产前MRI测量的胎儿侧脑室宽度比超声测量的宽度仅大约1 mm,对脑室扩张的分级没有影响。JEZBEROVA等^[20]认

为超声和MRI在VM疾病诊断中一致性最好(kappa值为0.817),但在胼胝体和皮质发育异常疾病中诊出率较差。DHAIFALAH等^[21]通过MRI对妊娠中期超声检测异常进行复核发现MRI与超声诊断的一致率为80%,其中MRI在VM和神经管缺陷中的诊断率较高,分别为86%和83%。而在另一个系统评价中发现超声和MRI的VM检出率分别为85%和95%,假阳性率分别为23%和20%^[22]。BARZILAY等^[23]发现在完善针对性超声后,孕晚期产前MRI发现额外异常概率仅为5.9%,其中轻、中、重度增宽额外异常率分别为0%、6%、25%,增宽的程度与额外异常发现率相关。因此,超声和MRI诊断一致性较高。虽然目前对于轻度VM病例中使用MRI的重要性尚未确定,但上述发现表明对于这类患者,即使不进行MRI检查,在神经超声检查中漏检的概率也很低。

4 胎儿MRI在侧脑室体积测量中的应用

目前国内外研究者聚焦于胎儿MRI多维度评估脑部发育如局部结构体积增长、脑沟脑回发育、皮质发育等。多项研究通过3D切片,尽可能清晰勾勒出大脑即脑室结构,通过测量脑室容积判断其与预后的相关性,但不同研究采用不同增宽标准、3D重建模式及运动矫正方法,结果具有较大异质性,因此目前尚缺乏正常胎儿脑结构体积规范数据库。

KYRIAKOPOULOU等^[24]发现,正常胎儿幕上脑组织以每周11.65%的相对增长率增加,皮质体积以13.15%的相对增长率增长,侧脑室体积以3.43%的相对增长率缓慢增加。孙姗姗等^[25]通过研究不同程度IVM对脑实质体积的影响发现,不同程度增宽的侧脑室体积、宽度及大脑半球体积均存在差异,实质厚度及体积无明显差异。与正常组相比,增宽组扩张侧脑室实质厚度减小,脑实质体积未见明显差异。结果与SCOTT等^[26]研究相似,他们认为轻中度VM胎儿除侧脑室体积增加外,其余幕上脑结构无明显异常。Di MASCIO等^[27]发现脑室前后角直径和侧脑室体积是活产预测指标,而脑实质体积与妊娠结局无对应关系。ZHU等^[28]认为VM胎儿脑实质存在“追赶生长”模式,即随着孕周增加,两侧不对称的脑实质发育最终趋于一致。当然,有学者认为实质厚度减小但体积未见差异的原因可能是脑组织水分子扩散受限,即使实质受到VM的影响而向外移位,但脑组织水肿使得脑实质体积近似正常,他们研究了脑实质的表观扩散系数(apparent diffusion coefficient, ADC)值,发现相较于ADC值未发生明显改变的轻度VM组,重度VM组多部位ADC值均下降,进而表明微观结构的改变可能是神经发育异常的潜

在危险因素^[29]。CHEN等^[30]基于侧脑室形态学、混合皮质或/和皮质下放射组学特征建立回归模型发现,侧脑室枕角扩张周围的皮质下脑实质放射组学可能与VM引起的病理生理变化显著对应,即皮层下实质的微结构改变可以作为VM胎儿出生后神经发育的预测指标。

TARUI等^[31]研究了20例孤立性轻度侧脑室增宽(10~15 mm为轻度)胎儿MRI图像,通过软件在冠状面上分割脑结构并进行体积重建和测量,发现与同孕周正常胎儿脑部体积相比,增宽组全脑、皮质板、皮质下实质和大脑的体积明显增加,以孕20~25周为甚。该团队开发了一种基于相似性指数的沟发育模式分析,发现增宽组两侧大脑半球的脑沟位置发育以及脑沟位置、深度、面积的综合特征均发生改变,强调脑沟位置变化与侧脑室体积变化无关,是一种独特的变异,作者表示脑沟发育模式个体差异性可考虑作为胎儿MRI生物标记物来关联个体未来的神经发育功能。

动物实验证明距状沟内折叠程度可作为评价脑成熟程度的解剖学标志^[32]。LI等^[33]通过高场强MRI成像(3T和7T)对84例14~35孕周的死胎进行了三维重建侧脑室和距状沟,并进行定量测量。发现侧脑室容积在妊娠14~23周时逐渐减小,在妊娠24~35周时迅速增大。随着孕周增加,距状沟发育,侧脑室后角收缩,距状沟深度与后角长度具有较好的线性相关性。因此,距状沟的深度可能为侧脑室异常提供重要线索。

5 人工智能在胎儿脑MRI上的应用

在MRI成像的过程中,通过改变影响MR信号产生的因素,产生多种序列,因为脑部结构部位在不同的序列下的表现不同,只根据一种序列不能准确判断结构的位置、大小等信息,因此MRI具有较多序列,目前超声和MRI诊断VM主要是放射科医师进行阅片手动测量,大量的2D序列识别需要花费较长时间,且受放射科医生水平影响,若没有正确识别最大二维脑室宽度的切片或者切面质量较差,诊断易受到干扰。因此,国内外学者逐渐着手于建立基于人工智能深度学习模型自动化识别侧脑室区域^[34]。但是不可否认的是,受胎儿运动干扰及MRI序列强度的不均质性,自动分割具有较大难度。多年来,包括U-net在内的深度学习算法在医学图像分析领域的应用频率显著增长,深度学习算法通过实现一系列任务,包括分类、检测和定位,彻底改变了图像处理^[35]。研究表明,人工智能模型可应用于脑MRI预测胎龄^[36]和脑病理分类^[37]以及功能性胎儿脑MRI^[38]。在一项对50例胎儿VM的病例对照研究中,PISAPIA等^[39]从胎儿MRI中提取多种成像特

征,并通过机器学习进行整合,建立了一个产后进行脑脊液分流术预测模型,准确率为82%。在一项独立的重复队列研究中,该模型达到了91%的准确率,突出了基于图像预测模型的高准确性以及预后预测的可靠性。SHE等^[40]提出了一种基于图像分割的人工智能辅助测量方法,通过分割和测量两步实现胎儿脑MRI生物特征参数的快速准确自动测量,提供了24~37周胎儿生长、生长曲线的参考值和95%的预测区间,该研究证实了VM的宽度与孕周无统计学意义,左侧侧脑室宽度平均为(6.44±1.83) mm,右侧平均为(5.88±1.65) mm。自动分割和精确脑室测量的结合显示了人工智能在临床实践中提高诊断能力和简化胎儿大脑异常评估方面的潜力。

6 小结和展望

胎儿VM的程度及进展与预后密切相关,多数可能是正常变异,神经发育正常,但也可能发生严重神经发育障碍如孤独症、癫痫等,预后不确定性是产前诊断和咨询的难点和重点。侧脑室的立体结构和胎儿运动伪影的干扰使得二维测量宽度已不能满足临床需求。如何精准测量侧脑室各部径线是待解决的问题。胎儿MRI已成为临床实践中广泛使用的工具,不仅提高了二维及三维先天性脑发育异常产前诊断的准确性,更提供了准确的产前咨询,优化围产期管理。且随着图像重建、运动校正、分割工具等方法的不断精进,侧脑室模型及体积测算已然是不可或缺的影像学预测因子。未来在不断扩大胎儿VM研究队列和人工智能的运用下,建立胎儿大脑发育的规范化数据库是提高产前诊断准确性和疾病预测特异性的重点。

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