

心房功能性二尖瓣反流的超声研究进展

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摘要

与心肌缺血导致左室扩大产生的二尖瓣反流不同, 心房颤动和/或射血分数保留型心力衰竭患者往往也可产生二尖瓣返流, 但其因正常的左室大小和左室收缩功能而易被忽视。这类患者的心房扩大, 随之产生的二尖瓣环扩张和小叶适应不足被认为是导致二尖瓣反流的主要原因。由于这种特殊的病理生理, 发现与鉴别尤为重要, 以便后续治疗方案的选择。超声心动图是评估二尖瓣病变的首选方法, 本文就超声心动图在心房功能性二尖瓣反流诊断与评估中的最新进展进行简要综述。

关键词

超声心动图, 心房功能性二尖瓣反流, 房颤, 射血分数保留型心力衰竭, 经食道三维超声心动图

Advances in Echocardiographic Study of Atrial Functional Mitral Regurgitation

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Abstract

In contrast to mitral regurgitation induced by left ventricular dilatation in patients with myocardial ischemia, this condition can also manifest in individuals with atrial fibrillation and/or heart failure characterized by preserved ejection fraction. However, it is frequently overlooked due to normal left ventricular size and contractility. In such cases, atrial enlargement, subsequent dilation of the mitral annulus, and inadequate adaptation of the leaflets are considered primary contributors to mitral regurgitation. Given this distinct pathophysiology, early detection and differentiation are

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crucial for informing subsequent treatment strategies. Echocardiography remains the preferred modality for evaluating mitral valve pathology. This concise review encapsulates recent advancements in diagnosing and assessing functional mitral regurgitation among patients exhibiting atrial dysfunction through echocardiographic techniques.

Keywords

Echocardiography, Atrial Functional Mitral Regurgitation, Atrial Fibrillation, Heart Failure with Preserved Ejection Fraction, Transesophageal 3D Echocardiography

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1. 引言

二尖瓣反流(mitral regurgitation, MR)是普通人群和社区中最常见的瓣膜疾病,且有随年龄增加而增高的趋势[1]。二尖瓣反流分为器质性和功能性二尖瓣反流(functional mitral regurgitation, FMR)两大类。FMR即由左心功能异常而非二尖瓣结构改变引起的二尖瓣反流,人们最初是在部分心肌梗死和心力衰竭患者中观察到,因此将这种发生在左心室扩张伴功能障碍背景下的 FMR 定义为心室功能性二尖瓣反流(ventricular functional mitral regurgitation, VFMR) [2] [3]。最近人们逐渐发现,在慢性心房颤动(atrial fibrillation, AF) [4]和射血分数保留型心力衰竭(heart failure with preserved ejection fraction, HFpEF) [5]患者中也可以出现 FMR,由于此类患者的左心房扩张明显,左心室大小和左室射血分数(left ventricular ejection fraction, LVEF)正常,因而将其定义为心房功能性二尖瓣反流(atrial functional mitral regurgitation, AFMR)。

研究显示[6], AFMR 的发生率较高,在中重度二尖瓣关闭不全患者中,约 27%为 AFMR,且 AFMR 往往发生在高龄、女性患者,常伴高血压、高血脂、糖尿病、脑血管病和外周血管疾病等,虽然该类患者 MR 程度往往低于 VFMR 患者,左室大小和射血分数正常,但却容易发生心力衰竭,死亡率较高。

超声心动图是评估二尖瓣病变的首选方法[7], AFMR 病因与发生机制与 VFMR 完全不同,且治疗方案也大相径庭,因此早期诊断与鉴别具有重要的临床意义,本文就超声心动图在 AFMR 诊断与评估中的最新进展进行简要综述。

2. 超声心动图对 AFMR 患者心脏形态评估

2.1. 二尖瓣复合体

二尖瓣复合体由瓣叶、瓣环、腱索和乳头肌组成。任何造成二尖瓣关闭力量失衡的因素都可能导致 MR 的发生[8] [9]。在心肌缺血引起的 VFMR 中,左心室扩大和 LVEF 降低会导致乳头肌与瓣叶接合点的距离增加,同时腱索对瓣叶的拉力增大(被称为心室来源的小叶拴系),从而减少二尖瓣的闭合力[10] [11]。而在非缺血性的 AFMR 中,尽管左心室的几何形状和功能相对正常,但左心房扩大会导致独立的二尖瓣环扩张,也可能增加对瓣叶的拉力(心房来源的小叶拴系),导致二尖瓣的闭合不全,从而引发 MR。这种 MR 通常是居中的、非偏心性的[12] [13]。

在 AFMR 中,小叶拴系的程度普遍较轻[14] [15]。随着左心房内压力的升高,左心房及二尖瓣环的扩张导致二尖瓣的前后叶张开,进而使二尖瓣环的鞍状形态逐步消失,瓣环的高度降低,且在左心室收缩期,小叶结构表现为平坦化[16]。在一部分经历了左心房(LA)显著重构的患者中,由于二尖瓣环的前部

紧邻主动脉根部, 其位置较为稳定, 不会出现明显的位移, 而二尖瓣的后环被牵引至左室后壁基底部的 心外膜表面, 进一步拉伸了二尖瓣的后叶, 导致二尖瓣后叶角增加, 从而使瓣环至乳头肌的距离延长(此 现象被称为“海鸥征”), 增加了心房源性栓塞的风险, 并且通过彩色多普勒超声成像表现为偏心性反流 [14] [17] [18]。据报道, 这一罕见的亚型预示着较差的预后[19] [20]。

Kagiyama 等人[21]利用经食道三维超声心动图(three-dimensional transesophageal echocardiography, 3D-TEE)技术发现, 在不伴有左室收缩功能障碍的房颤患者中, 未并发二尖瓣反流的患者相较于健康对照 组, 二尖瓣环及瓣叶面积更大, 但二尖瓣瓣叶总面积(total leaflet area, TLA)与二尖瓣瓣环面积(annular area, AA)的比值与健康人相似。而在并发 MR 的 AF 患者中, TLA 与 AA 比值较未并发 MR 的 AF 患者及健康 对照组显著降低。Kim 等人[14]也报告了相似的发现, 他们指出房颤患者的 TLA 比对照组增大 22%, AA 亦相应增大。随着 AA 增大, 二尖瓣适应性指数(包括 TLA/AA 比与 MLA 与闭合面积之比)趋于稳定, 在 合并 MR 的 AF 患者中达到最低值(对照组为 1.63, AF 且未并发 MR 组为 1.60, AF 且并发 MR 组为 1.32)。 这些研究结果揭示了 AFMR 的另一潜在机制, 即瓣膜小叶重塑不足, 这一发现也在动物实验中得到了证 实, 组织病理学检测表明, 内皮-间充质转化在这一过程中起核心作用[22]。

对二尖瓣复杂结构的定量评估可以为 MR 的严重程度提供有价值的见解, 并帮助临床医生制定全面 的治疗策略。Tomoko 等研究者利用 3D-TEE 发现, MR 的严重程度与多个参数有关, 包括 AA、二尖瓣 后叶角度、以及 AA 与前叶面积之比等[23]。此外, Cong 等研究者通过分析 168 例 AF 患者的 TEE 图像, 识别出 AA、瓣环高度与接合宽度比(annular height to commissural width ratio, AHCWR)及瓣叶下容积为 AF 患者 MR 严重程度的独立预测因子[24]。Ring 等人则定义了二尖瓣变化分数((MVA 收缩期晚期面积 - MVA 收缩期早期面积)/MVA 收缩期晚期面积 $\times 100\%$)和共适应指数((收缩早期小叶面积 - 收缩晚期小 叶面积)/收缩早期小叶面积 $\times 100\%$), 并指出这两项指标是判断 MR 程度的最强预测因素[25]。最近, Spieker 等人[26]发现接近四分之一的 AFMR 患者在进行握力实验后 MR 程度有所增加。他们提出左室长 轴切面收缩期二尖瓣前、后叶长度之和与收缩期二尖瓣环内径的比值能预测运动引起的 AFMR 严重程度 增加, 这篇研究首次分析了动态 AFMR, 揭示了运动诱发的重度 MR 的预后与静息状态下重度 MR 患者 相当, 这一发现对于识别潜在的 AFMR 患者具有重要意义。

2.2. 心脏腔室

左房的增大是 AFMR 患者中最主要的心脏腔室变化。超声心动图可以发现左房内径和左房容积指数 (left atrial volume index, LAVI)的增加, 已有研究表明, MR 的严重程度与 LAVI 密切相关[23]。在 AFMR 患者中, 无论是收缩末期还是舒张末期, 左心室大小保持正常。然而, 在有显著 MR 的情况下, 由于容 量超负荷, 可能导致左心室内径的增大和乳头肌位移。随着乳头肌的移动, 二尖瓣小叶也相应向左心室 腔内移动, 并在超声心动图中呈现出 AFMR 和 VFMR 的混合超声图像。除此之外, AFMR 的患者通常 具有较大的右心室, 右心室的面积变化率较低, 三尖瓣反流的负担也更重, 这可能归因于右心对血流动 力学改变的高度敏感性[27]。同时, 增大的右心导致三尖瓣环扩张, 三尖瓣反流更加显著, 称为功能性心 房三尖瓣反流[28] [29]。

心脏腔室大小的变化在一定程度上可以反映治疗的效果和预后。Naser 等人对 AF 和窦性心律患者中 MR 的发生率和危险因素进行了研究, 他们指出左房大小是影响 MR 的独立风险因素之一, 定期评估左 房大小有助于预测 MR 复发的风险[30]。此外, Vohra 等人的研究显示, 对于由孤立性 AF 引起的严重 MR 患者, 经过单纯二尖瓣修复术后患者的左心室舒张末期直径、左心室收缩末期直径和左房内径明显改善, 大多数患者的症状得到显著缓解, 且心房颤动得到控制[31]。

3. 超声心动图对 AFMR 患者心脏功能评估

3.1. 左心房功能

无论是 AF 还是 HFpEF, 随着间质纤维化逐步取代了可收缩的心房肌组织, 左房的硬度增加, 从而改变了房室顺应性[32][33]。斑点追踪超声心动图是一项新兴的超声心动图技术, 能够对心肌形变进行客观量化[34]。最近研究表明, 尤其是左心房峰值应变的分析, 可以有效检测左心房壁的纤维化[35]。此外, 左心房应变与左心房的顺应性以及 MR 患者组织样本中通过 Masson 三色染色检测到的左心房壁纤维化量有关[36][37]。因此, 无论是 AF、HFpEF 还是 MR, 都可能损害左心房功能, 导致患者更加不利的临床预后。

已证实 AFMR 患者左心房应变降低与平均左心房和肺动脉收缩压升高有关, 左心房 V 波的幅度相对于二尖瓣反流量不成比例地增加, 这可能是由于左心房顺应性受损所致[38], 这一现象值得进一步探究。Cramariuc 等人[39]通过评估 LA 存储应变(left atrial reservoir strain, LASr)和存储功(left atrial reservoir work, LAWr)来分析左心房功能。在对 515 例中重度 AFMR 患者的研究中, 他们发现 AF 组的左心房容积最大, 而合并 HFpEF 和 AF 的患者组中, 左心房功能参数受损最严重, 并且这与较差的预后密切相关。研究进一步指出, 左心房的存储功能是预测中重度 AFMR 预后的一个可靠因素。另一方面, Tamargo 等人[27]的研究表明, 与非 MR-HFpEF 患者相比, MR-HFpEF 患者的 LASr 和辅泵应变表现较差, 左心房顺应性也更低。左心房功能障碍的发生率(定义为 LASr 小于 24.5%)在 MR-HFpEF 患者中是非 MR-HFpEF 患者的两倍(56%对 23%, $P < 0.0001$)。

3.2. 左心室功能

AFMR 对左心室功能的影响目前尚存在广泛争议。此前一段时间人们认为 AFMR 是局限于左心室的疾病, 并不会对左心室的功能产生影响, 无论是收缩功能还是舒张功能。Tomoko 等人的研究[23]对健康对照组与不同程度 MR 的房颤患者进行了 TTE 相关参数的比较。他们发现, 患有中重度 MR 的 AF 患者的二尖瓣 E 峰值显著高于轻度 MR 患者及对照组。同样, 这些中重度 MR 的患者在 e' 和 E/e' 值上也明显超过对照组。Tomoko 认为, 这可能反映了血流动力学的改变伴随着一定程度的左心室舒张功能不全, 这表明 AFMR 可能不仅仅是由心房的单一变化引起, 左心室功能的变化也是其疾病进展的一部分。此外, Naser 等人的研究也得出了类似的结论, 他们指出左心室舒张功能减退是 AF 患者发生 MR 的一个重要危险因素[30]。

随着超声心动图斑点追踪技术的引入, 人们开始从心肌应变的角度评估左心室功能。Meucci 等人的研究[40]显示, 在患有严重 AFMR 的患者中, 左室全长应变(global longitudinal strain, GLS)的损害与不良预后独立相关, 而左房应变则与预后无显著关联。这项研究还发现, 引入 LV GLS 可以显著提高预测患者预后的模型精度, 左室 $GLS \leq 16.3\%$ 的患者尽管 LVEF 正常, 但生存率较低。值得注意的是, 多种因素可能解释 AFMR 患者左室 GLS 的损害, 除了慢性容量过载的不利影响外, 其他因素包括全身炎症、微血管灌注不足、心室钙处理的干扰和氧化应激等。此外, Tamargo 等人[27]通过斑点追踪技术分析了 280 名 HF-HFpEF 患者的超声心动图, 发现即使只有 42% 的患者表现为轻至中度 MR (无重度 MR 病例), MR-HFpEF 组患者的左室 GLS 和二尖瓣 s' 速度也普遍低于非 MR-HFpEF 组。从病理生理学角度看, AFMR 与左室 GLS 受损之间的关系可能是双向的, 左室的损伤可能既是 MR 的原因也是结果, 这需要在未来的研究中进一步明确。

4. 小结

AFMR 是最近描述的一种疾病亚型, 鉴于 AF 和 HFpEF 的患病率在全球范围内均呈上升趋势——过

去 50 年增加了三倍, 据预测, 它可能在未来成为最常见的 MR 类型[41]。AFMR 的定义在外科研究中存在较大差异, 回顾性研究中关于纳入与排除 AFMR 患者的标准也不一致。同时, 关于 AFMR 的最有效治疗方法仍是一个有争议的话题, 还需要更多的研究来探讨。随着超声技术的迅速发展, 我们现在能够更深入地研究 AFMR 的机制、评估药物及手术治疗的效果和预后, 从而帮助患者在出现严重症状、不可逆的心肌损伤和晚期心力衰竭之前, 进行早期的最佳药物和介入治疗。

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