

门控SPECT心肌灌注显像评估急性心肌梗死患者心肌挽救量的研究进展

Research progress of gated SPECT myocardial perfusion imaging in evaluating myocardial salvage in patients with acute myocardial infarction

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·综述·

门控 SPECT 心肌灌注显像评估急性心肌梗死患者 心肌挽救量的研究进展

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【摘要】 急性心肌梗死(AMI)患者经皮冠状动脉介入治疗(PCI)的目的在于尽可能地挽救濒死心肌。心肌挽救量(MS)与患者能否获益密切相关,在PCI的疗效评估及预后判断中具有重要价值。评价MS需明确初始心肌危险区面积(AAR)和心肌最终梗死面积(FIS),二者之差即为MS。通过急诊时和PCI后2次 ^{99m}Tc -甲氧基异丁基异腈门控SPECT心肌灌注显像(GSMPI)可分别定量AAR和FIS,从而获得MS,结果客观、准确,其临床价值在早期的大样本研究中已得到肯定。但在急诊时行GSMPI受到很多限制,致使AAR较难获得。近年来有学者提出的新显像方案,仅通过PCI后早期行1次GSMPI即可测定AAR,替代了2次显像法计算得到MS,其可行性及在临床中的实用价值显著提高。同时,新显像方案也扩展了核素GSMPI在AMI诊疗中的应用范围,为AMI患者的危险度分层提供了补充信息。笔者拟对GSMPI评估AMI患者MS的新显像方案的机制、应用价值、优势及发展前景作一综述。

【关键词】 心肌灌注显像; 心肌梗死; 体层摄影术, 发射型计算机, 单光子; 经皮冠状动脉介入治疗; 心肌挽救量

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Research progress of gated SPECT myocardial perfusion imaging in evaluating myocardial salvage in patients with acute myocardial infarction

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【Abstract】 The purpose of percutaneous coronary intervention (PCI) in patients with acute myocardial infarction (AMI) is to save dying myocardium as much as possible. The amount of myocardial salvage (MS) is closely related to whether the patients benefit from the PCI. MS is of great value for PCI efficacy evaluation and prognosis. To assess MS, the initial myocardial area at risk (AAR) before PCI and the final infarction size (FIS) after PCI should be determined, and the difference between the two is called MS. AAR and FIS can be quantified by double ^{99m}Tc -methoxy-isobutyl-isonitrile gated SPECT myocardial perfusion imaging (GSMPI) on emergency admission and after PCI, respectively. The results are objective and accurate, and its clinical value has been confirmed in early large sample studies. However, emergency GSMPI has many limitations that make AAR difficult to obtain. In recent years, some scholars proposed that the only one GSMPI method early after PCI could replace double imaging method for MS evaluation, which significantly improved the feasibility and expanded the application extent of GSMPI in the diagnosis and treatment of AMI, and provided supplementary information for risk stratification in patients with AMI. The principle, application value, advantages and development prospect of the new method for evaluating MS in AMI patients are reviewed by authors.

【Key words】 Myocardial perfusion imaging; Myocardial infarction; Tomography, emission-computed, single-photon; Percutaneous coronary intervention; Myocardial salvage

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近年来, 尽管经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)有效降低了急性心肌梗死(acute myocardial infarction, AMI)患者的病死率, 但AMI仍为目前冠状动脉粥样硬化性心脏病(简称冠心病)患者致死、致残的主要病因^[1]。行PCI的目的在于挽救濒死心肌, 改善AMI患者的预后。心肌挽救量(myocardial salvage, MS)对于PCI的疗效评估及预后判断具有重要价值^[2]。由MS与初始心肌危险区面积(area at risk, AAR)的比值获得的心肌挽救指数(myocardial salvage index, MSI)是AMI患者行PCI是否获益的独立预测因子^[3]。

门控SPECT心肌灌注显像(gated SPECT myocardial perfusion imaging, GSMPI)通过计算机软件自动处理可“一站式”获得血流灌注参数及多项功能参数^[4]。在急诊PCI前注射显像剂⁹⁹Tc^m-MIBI行GSMPI检测AMI患者的初始心肌AAR的方法的临床价值已在早期的大样本研究中得到验证^[5-6], 通过与PCI后再次显像获得的心肌最终梗死面积(final infarction size, FIS)进行比较可获得MS及MSI。一项对765例AMI患者的大样本研究结果表明, 经再灌注治疗后MSI<0.5的AMI患者, 其6个月病死率明显高于MSI≥0.5者; MSI与AMI患者的6个月病死率呈独立相关, MSI能够预测AMI患者的6个月病死率^[5]。该研究结果还显示, 在用于测试AMI患者再灌注治疗疗效的临床试验中, MSI可作为病死率的替代指标, 尤其是对于新治疗方案的有效性的判断, 能够明显降低对样本量的要求, 且可行性更佳。然而, 临床实践中在急诊时行GSMPI通常很难实现, 原因包括: 核素显像剂难以及时供应、大多数单位不具备夜间急诊条件、核医学科距离急诊科或胸痛中心较远等, 以上原因导致GSMPI在AMI患者急诊时的应用受到限制^[3, 7-8]。

近年来有学者提出, 利用AMI患者行PCI后早期心肌顿抑的原理, 通过PCI后早期行1次静息状态下GSMPI即可间接获得AAR^[9-12], 从而实现MS及MSI的定量评估, 该方法的结果与2次显像法的一致性很好, 且操作简便, 同时降低了辐射剂量及检查费用, 实用价值明显提高, 对AMI患者的危险度分层、个体化治疗方案制定、疗效评价、预后判断具有重要价值。笔者拟对该新显像方案的机制、应用价值、优势及发展前景作一综述。

1 显像原理及方案

AMI发生后, 梗死相关冠状动脉闭塞导致的心肌缺血区, 即初始心肌AAR, 包括不可逆心肌损伤区(也称心肌FIS)和可逆性心肌损伤区(也称MS)。准确评估AAR及FIS是获得MS的前提。

AMI患者行PCI后早期存在心肌顿抑现象^[13], 即PCI使血流恢复正常后, 心室壁收缩功能障碍尚未恢复。早期

的一项超声研究结果显示, 这种室壁收缩异常于PCI后48 h左右开始恢复, 并将持续数日至数周才逐渐恢复正常^[14]。Main等^[15]的研究结果也表明, AMI后平均2.2 d仍可识别出这种“灌注-功能不匹配”的顿抑心肌。因此, 在PCI术后早期, 特别是2~3 d内, 在心肌顿抑仍未恢复时检测出的室壁收缩异常范围, 即可代表PCI前的初始心肌AAR。研究者正是利用这一原理, 于PCI术后早期行GSMPI, 并通过门控采集方式, 由计算机软件自动获得心室壁收缩功能参数, 识别收缩异常的心肌节段, 从而计算室壁收缩异常的范围, 间接获得AAR^[11-12]。

另外, AMI患者行PCI后FIS的评估时间也是一个关键问题。尽管有研究者于PCI术后2 d行GSMPI检测AMI患者的FIS以评价不同药物的疗效^[16], 但更多的研究者选择出院前或PCI术后至少1周, 甚至1个月或数月再行评估^[17-19]。Pellikka等^[20]在早期研究中对AMI患者分别于PCI前、治疗后18~48 h及6~14 d行GSMPI, 并比较治疗后不同时期血流灌注的改善情况, 结果显示, 术后18~48 h的低灌注区较术前改善, 但6~14 d血流灌注进一步改善, 改善的程度到后期才更明显。另外一项动物实验结果也表明, AMI后过早行GSMPI评估很可能会高估FIS, 术后1周左右评估的准确性更高^[21]。Ndrepepa等^[22]通过对1312例ST段抬高型心肌梗死(ST-segment elevation myocardial infarction, STEMI)患者于PCI术后7~14 d行GSMPI, 获得心肌FIS, 从而获得MS。

然而, 确定MS的最佳评估时间需权衡AAR及FIS 2个方面的因素, 因此有学者提出, 选择48 h至1周行GSMPI可以同时获得AAR及FIS, 是检测MS的最佳时间点^[12]。Tanaka和Nakamura^[23]观察了AMI患者再灌注后不同时段(30 min, 6 h, 1、4、20 d)心肌血流灌注的改善情况, 研究结果提示, 再灌注治疗后7 d左右行⁹⁹Tc^m-MIBI GSMPI评估MS最佳。Calabretta等^[7]对AMI患者于PCI术后3~5 d行GSMPI, 获得MS, 并证实了其可行性及临床价值。

2 临床应用

Wakabayashi等^[9]通过对AMI模型鼠再灌注后3 d行⁹⁹Tc^m-MIBI GSMPI获得AAR, 评估心肌受体在缺血再灌注后的表达情况, 结果证实了该方法的可行性及有效性。另外, Qin等^[10]通过对STEMI患者PCI术后24 h至7 d行GSMPI获得AAR, 并计算得到MS及MSI, 结果证实了MS及MSI能够用于评价心肌缺血再灌注损伤的程度。

Sotgia等^[11]的研究纳入了48例AMI患者, 于PCI术后5~10 d行1次静息⁹⁹Tc^m-MIBI GSMPI, 以室壁增厚率异常范围替代AAR, 并与血流灌注异常范围相减获得MS,

通过与 PCI 术前、术后 2 次显像灌注受损面积相减所得的 MS 进行比较, 结果证实了二者所得结果具有很好的相关性, 仅 PCI 后 1 次⁹⁹Tc^m-MIBI GSMPI 即可实现对 MS 的评估, 用室壁增厚率异常范围可替代 PCI 术前的 AAR, 以此计算 MS 的优势在于该方法的可行性明显提高。

在另一项类似的研究中, 36 例 AMI 患者于 PCI 术前注射显像剂, 于 PCI 术后 6 h 行第 1 次 GSMPI, 5 d 后再次显像, 2 次显像血流灌注异常范围相减获得 MS, 结果显示, 其与术后 5 d 1 次 GSMPI 室壁增厚率异常范围与血流灌注异常范围相减获得的 MS 相当 (Spearman 等级相关系数为 0.92, $P < 0.0001$), 且二者对患者预后进行分类的结果一致性良好 (Kappa 值=0.75)^[12]。该项研究的作者认为, 术后 1 次显像法评估 MS 将有益于对 AMI 患者不同治疗策略的效果评价。

Calabretta 等^[7]直接利用 PCI 术后 3~5 d 行 1 次 GSMPI 的方案计算 MS, 并探讨了 MS 对 STEMI 患者 PCI 术后 6 个月心功能恢复情况的预测价值。该研究中 120 例 STEMI 患者于 PCI 术后 3~5 d 行 1 次 GSMPI, 获得 MS、FIS 及术后早期左心室射血分数 (left ventricular ejection fraction, LVEF), 并于患者出院后 6 个月复查 GSMPI, 再次获得 LVEF。ROC 曲线分析结果表明, MS 能够预测 PCI 术后 LVEF 的恢复程度 ($AUC=0.79$, $P < 0.0001$); 以 23% 为临界值, MS 预测 LVEF 恢复程度的灵敏度和特异度分别为 74% 和 71%, 而 FIS 与 LVEF 恢复程度无明显的相关性 ($AUC=0.53$)。

3 与其他测定 MS 的方法的比较

3.1 双核素 GSMPI 法

近年来有研究者通过注射脂肪酸显像剂¹²³I-β-甲基-*p*-碘苯基十五烷酸 (¹²³I-β-methyl-*p*-iodophenyl pentadecanoic acid, BMIPP) 行 GSMPI 获得 AAR, 后行⁹⁹Tc^m-MIBI GSMPI 获得 FIS, 将二者相减获得 MS, 并证实了该方法用于计算 MS 的可行性^[3,8]。AMI 发生后, 缺血心肌的能量来源由脂肪酸转变为葡萄糖, 且缺血心肌的脂肪酸 β 氧化水平在心肌缺血发生后将持续降低, 因此, 应用脂肪酸显像剂¹²³I-BMIPP 于 AMI 后行 GSMPI 所显示的显像剂摄取减低区即接近于 AAR。研究显示, PCI 术后 1~2 周行¹²³I-BMIPP GSMPI, 获得的 AAR 与急诊时于 PCI 术前行⁹⁹Tc^m-MIBI GSMPI 所得的结果相当^[23]。然而, 由于¹²³I-BMIPP 的获得较为困难, 导致其在临床中的应用受到限制。

3.2 心脏磁共振 (cardiac magnetic resonance, CMR)

CMR 具有较高的空间分辨率, 通过对 AMI 患者 PCI 后 1 周左右行 T2 加权成像可实现对 AAR 的检测, 联合延迟增强扫描可获得 FIS, 从而可计算得到 MS^[24]。其中, 准

定量 AAR 是获得 MS 的重要前提, 也是研究的难点。

CMR 检测 AAR 的标准化技术为 T2 加权成像, 其中 T2 加权短时间反转恢复序列 (T2-STIR) 的组织对比度更佳^[25]。研究者将 T2 加权短时间反转恢复序列 (T2-STIR) 及对比度增强的稳态自由进动成像 (CE-SSFP) 获得的 AAR 与 GSMPI 所得结果进行比较, 发现二者与 GSMPI 所得结果均具有良好的 consistency ($r=0.81$, $P < 0.001$; $r=0.86$, $P < 0.001$)^[26]。另有研究结果显示, GSMPI 与 MRI 对于透壁性心肌梗死的评价一致性良好, 但对于未完全坏死仍存活的心肌, GSMPI 较 MRI 明显高估了 MS^[27]。

然而也有研究者发现, T2 加权成像易低估 AAR, 且 T2 加权短时间反转恢复序列 (T2-STIR) 无法完全抑制心内膜下“慢血流”效应, 易出现高信号伪影, 导致过度诊断^[28]。因此, T2 加权成像技术测量 AAR 的准确性及可重复性有待进一步研究证实。近年来, 随着纵向弛豫时间定量成像 (T1 mapping)、横向弛豫时间定量成像 (T2 mapping) 技术的发展, CMR 可更加客观、准确地评估 AAR^[29], 其中 T1 mapping 具有更高的灵敏度, T2 mapping 在降低伪影干扰上具有明显的优势, 且能够直观地显示心肌水肿的变化, 但结果受 MR 扫描仪场强、MR 序列及心肌节段等因素的影响较大, 其测量一致性仍需进一步提高, 以上原因均导致目前其在临床中的实际应用受到限制^[30]。此外, 某些特殊人群, 如幽闭恐惧症及体内有金属植入物无法行 MRI 的患者, 行 CMR 存在困难; 且并非所有医院都能实现这种理想的成像模式, 加之 CMR 对操作者本身的要求较高等, 均限制了其在临床中的普遍开展。

3.3 ⁸²Rb PET 心肌灌注显像

研究结果显示, 应用⁸²Rb PET 心肌灌注显像评估 AMI 患者行 PCI 后的 MS 是可行的, 通过 1 次显像即可获得 AAR、FIS、MS 以及心功能等多项定量参数^[31]。Ghotbi 等^[32]将⁸²Rb PET 显像与 GSMPI、CMR 测定的 MS 结果进行对比, 结果显示 PET 获得的 AAR、FIS 均低于 GSMPI 及 CMR, 而 3 种方法获得的 MSI 的差异无统计学意义。

但是, PET 显像的成本较高, 核素的获得相对较困难。研究结果表明, 当 PCI 术后早期 PET 显像显示的灌注缺损与 AAR 的一致性不能确定时, 需要进行第 2 次 PET 显像^[24]。以上原因均限制了⁸²Rb PET 显像在 MS 测定中的临床应用。

4 小结与展望

综上, 无创性量化 AMI 患者的 MS 具有重要的临床价值, GSMPI 是冠心病诊疗中的常用检查方法, 其优势在于可通过简单的方法“一站式”获得血流灌注、心功能等多项信息, 而 GSMPI 用于 AMI 患者 MS 及 MSI 的评估, 能够

为患者出院前的危险度分层提供补充信息,同时为后续个体化随访计划的制定及用药指导提供更多的参考依据。未来仍需更大样本量的研究以评价 GSMPI 在 AMI 患者疗效评估及预后判断中的临床价值。

随着核医学显像设备的不断更新,碲铋镅心脏专用 SPECT 仪已投入临床使用,其能将图像的空间分辨率大大提高,同时降低显像剂的注射剂量,缩短采集时间,最终获得更加优质的图像^[33]。因此,未来 GSMPI 在 AMI 的诊疗中将发挥更广泛的评估作用,其应用前景值得期待。

利益冲突 所有作者声明无利益冲突

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