

CZT-SPECT 测定的冠状动脉血流储备 对诊断冠心病的增益价值

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【摘要】 目的 探讨镉锌镉心脏专用 SPECT 仪 (CZT-SPECT) 测定冠状动脉 (简称冠脉) 血流储备 (CFR) 对心肌灌注显像 (MPI) 诊断冠脉粥样硬化性心脏病 (简称冠心病) 的增益价值。方法 回顾性分析 2017 年 11 月至 2018 年 10 月间于复旦大学附属中山医院成功完成静息/负荷 MPI 和 CFR 测定的 132 例疑似或确诊的冠心病患者 (男 89 例, 女 43 例; 年龄 40~81 岁) 影像资料, 以冠脉造影 (CAG) 结果为“金标准”, 分别计算并比较 MPI 与 MPI 联合 CFR 诊断冠心病的效能。采用 χ^2 检验或 Fisher 确切概率法分析数据。结果 132 例患者中, 冠脉狭窄 $\geq 75\%$ 者有 61 例 (46.2%), 其中单支病变 29 例 (47.5%)、双支病变 21 例 (34.4%)、三支病变 11 例 (18.0%); 396 支冠脉血管中, 狭窄程度 $\geq 75\%$ 者有 104 支 (26.3%), 狭窄程度 65%~74% 者有 25 支 (6.3%), 狭窄程度 50%~64% 者有 30 支 (7.6%)。对于冠脉狭窄程度 $\geq 75\%$ 者, MPI 在患者水平诊断冠心病的灵敏度和准确性分别为 86.89% (53/61) 和 68.94% (91/132), 联合 CFR 后分别提高至 96.72% (59/61; $\chi^2 = 3.921, P < 0.05$) 和 87.88% (116/132; $\chi^2 = 13.984, P < 0.01$); MPI 在血管水平诊断冠心病的灵敏度和准确性分别为 72.12% (75/104) 和 77.53% (307/396), 联合 CFR 后分别提高至 96.15% (100/104; $\chi^2 = 22.511, P < 0.01$) 和 85.10% (337/396; $\chi^2 = 7.479, P < 0.05$); MPI 诊断单支、双支、三支病变冠心病的灵敏度分别为 72.41% (21/29)、42.86% (9/21)、5/11, 联合 CFR 后分别提高至 93.10% (27/29; $\chi^2 = 4.350, P = 0.037$)、90.48% (19/21; $\chi^2 = 10.714, P = 0.001$)、11/11 ($P = 0.012$)。MPI 联合 CFR 检出冠脉狭窄 65%~74% 的灵敏度 [64.00% (16/25)] 高于 MPI [24.00% (6/25); $\chi^2 = 8.117, P = 0.004$]; 检出冠脉狭窄 50%~64% 的灵敏度 [76.67% (23/30)] 也高于 MPI [40.00% (12/30); $\chi^2 = 8.297, P = 0.004$]。结论 CFR 可明显提高 MPI 诊断冠心病的灵敏度和准确性, 尤其是对多支病变冠心病和冠脉轻度狭窄患者。

【关键词】 冠状动脉疾病; 血流储备分数; 心肌; 心肌灌注显像; 体层摄影术; 发射型计算机, 单光子; 镉; 锌; 镉

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Incremental value of coronary flow reserve assessed by CZT-SPECT in the diagnosis of coronary artery disease

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【Abstract】 Objective To investigate the incremental value of coronary flow reserve (CFR) assessed by cadmium zinc telluride (CZT)-SPECT as an adjunct to myocardial perfusion imaging (MPI) in the diagnosis of coronary artery disease (CAD). **Methods** Data of 132 patients (89 males, 43 females; 40–81 years) with or suspected with CAD who successfully underwent rest and stress MPI and CFR from November 2017 to October 2018 in Zhongshan Hospital Affiliated to Fudan University were retrospectively analyzed. Based on coronary angiography (CAG) as the "gold standard", the value of MPI and MPI+CFR in the diagnosis of CAD was evaluated and compared. χ^2 test or Fisher exact probability test was used for data analysis. **Results** Of 132 patients, 61 (46.2%) were CAD with stenosis of at least 75% in one vessel (47.5%, 29/61), two vessels (34.4%, 21/61), or three vessels (18.0%, 11/61). A total of 104 (26.3%) vessels with stenosis of at least 75%, 25 (6.3%) vessels with stenosis of 65%–74%, and 30 (7.6%) vessels with stenosis of 50%–64% were found in 396 vessels. For detecting coronary stenosis of at least 75%, the sensitivity and accuracy of MPI on per-patient analysis were 86.89% (53/61) and 68.94% (91/132), which in-

creased to 96.72% (59/61; $\chi^2 = 3.921$, $P < 0.05$) and 87.88% (116/132; $\chi^2 = 13.984$, $P < 0.01$) by MPI+CFR. On per-vessel analysis, the sensitivity and accuracy of MPI were 72.12% (75/104) and 77.53% (307/396) and increased to 96.15% (100/104; $\chi^2 = 22.511$, $P < 0.01$) and 85.10% (337/396; $\chi^2 = 7.479$, $P < 0.05$) by MPI+CFR. The sensitivity of MPI for predicting one, two, and three vessels disease were 72.41% (21/29), 42.86% (9/21), and 5/11 and were improved to 93.10% (27/29; $\chi^2 = 4.350$, $P = 0.037$), 90.48% (19/21; $\chi^2 = 10.714$, $P = 0.001$), and 11/11 ($P = 0.012$) by MPI+CFR. For coronary with stenosis of 65%–74%, the sensitivity of MPI was 24.00% (6/25) and was improved to 64.00% (16/25; $\chi^2 = 8.117$, $P = 0.004$) by MPI+CFR. For coronary with stenosis of 50%–64%, the sensitivity of MPI was 40.00% (12/30) and was improved to 76.67% (23/30; $\chi^2 = 8.297$, $P = 0.004$) by MPI+CFR. **Conclusion** As an adjunct to MPI, CFR can significantly improve the sensitivity and accuracy in the diagnosis of CAD, particularly for patients with mild stenosis and multivessel CAD.

【Key words】 Coronary artery disease; Fractional flow reserve, myocardial; Myocardial perfusion imaging; Tomography, emission-computed, single-photon; Tellurium; Zinc; Cadmium

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SPECT 心肌灌注显像 (myocardial perfusion imaging, MPI) 作为一种无创性检查方法, 在冠状动脉粥样硬化性心脏病 (简称冠心病) 的诊断、危险度分层和疗效评价等方面发挥了重要作用。受多支冠状动脉 (简称冠脉) 狭窄所致低估缺血程度及“平衡性缺血”等多种因素影响, MPI 诊断心肌缺血的准确性还不理想; 受 SPECT 设备本身性能的影响, 多年来 SPECT MPI 图像质量和所获得的诊断信息较难改善。得益于灵敏度和时间分辨率的提高, PET 能够进行动态采集并获得心肌血流量 (myocardial blood flow, MBF) 与冠脉血流储备 (coronary flow reserve, CFR) 相关信息, 因此提供了更多诊断与预后信息^[1-3], 被称为无创测定 MBF 与 CFR 的“金标准”^[4]。镉锌镉心脏专用 SPECT 仪 (cadmium zinc telluride-SPECT, CZT-SPECT) 较传统 SPECT 仪具有更高的灵敏度和时间分辨率, 能够像 PET 一样获得 MBF 与 CFR 信息, 提高了诊断的准确性^[5-6]。研究结果显示 CZT-SPECT 测定的 MBF 与 CFR, 与 PET 测定的结果一致性良好^[7-8], 与冠脉造影 (coronary angiography, CAG) 结果及测定的血流储备分数 (fractional flow reserve, FFR) 有较好的符合率^[9-10]。目前, 应用 CZT-SPECT 测定 CFR 临床应用的文献有限。本研究拟探讨 CZT-SPECT 测定的 CFR 对 MPI 诊断冠心病的增益价值。

资料与方法

1. 研究对象。回顾性分析 2017 年 11 月至 2018 年 10 月期间于复旦大学附属中山医院核医学科顺利完成静息/负荷 MPI 和 CFR 测定的疑似或已确诊的稳定型冠心病患者 132 例 (男 89 例、女 43 例, 年龄 40~81 岁) 的影像资料。纳入标准: (1) 疑似或已确诊的稳定型冠心病患者; (2) 2 周内完成 CAG 检查。排除标准: (1) 既往有冠脉介入或旁路移植手术史;

(2) 急性心肌梗死、急性心力衰竭、肥厚型或扩张型心肌病患者; (3) 已知支气管哮喘史; (4) 严重心律失常。本研究符合《赫尔辛基宣言》的原则。

2. 显像方法。检查前患者按常规准备, 显像仪器为 CZT-SPECT (型号为 D-SPECT, 以色列 Spectrum Dynamics Medical 公司), 显像剂为⁹⁹Tc^m-甲氧基异丁基异腈 (methoxyisobutylisonitrile, MIBI; 由上海欣科医药有限公司提供)。显像流程见图 1。采用迭代法对图像进行重建, 使用 Corridor 4DM 软件获得 MBF 与 CFR, 使用定量灌注 SPECT (quantitative perfusion SPECT, QPS)、定量门控 SPECT (quantitative gated SPECT, QGS) 软件获得 MPI 图像。

3. 图像分析。由 2 位有经验的核医学科医师共同协商解读 MPI 图像和 CFR 数据, 意见不一致时由第三者裁定。MPI 联合 CFR 诊断心肌缺血的标准: 先由 MPI 得出心肌灌注是否正常, 再得出 CFR 是否正常, 若两者结果一致则相互验证, 若两者结果不一致则以 CFR 为最终结果。MPI 目测分析采用 17 节段模型和 5 点评分法。CFR 诊断标准^[11]: < 2 为缺血, ≥ 2 为正常。左心室壁与冠脉的对应关系按照常规靶心图分析; CAG 发现有变异者, 以 CAG 结果为准。

4. 冠脉狭窄的定义和分级^[12]。根据 CAG 结果将患者按冠脉狭窄程度分为 $\geq 75\%$ 组 (含左主干狭窄程度 $\geq 50\%$, 并视为左前降支及左回旋支狭窄)、65%~74% 组和 50%~64% 组。多支冠脉狭窄者, 按最严重者分组, 同一支血管内有多处狭窄者取其最严重处。

5. 统计学处理。采用 IBM SPSS 25.0 软件进行统计学分析, 计数资料以频数 (百分比) 表示。分别计算并比较 MPI 与 MPI 结合 CFR 诊断冠心病的灵敏度、特异性、准确性、阳性预测值 (positive predictive value, PPV)、阴性预测值 (negative predictive value, NPV)。计数资料的比较采用 χ^2 检验或 Fisher 确切概率法, $P < 0.05$ 为差异有统计学意义。

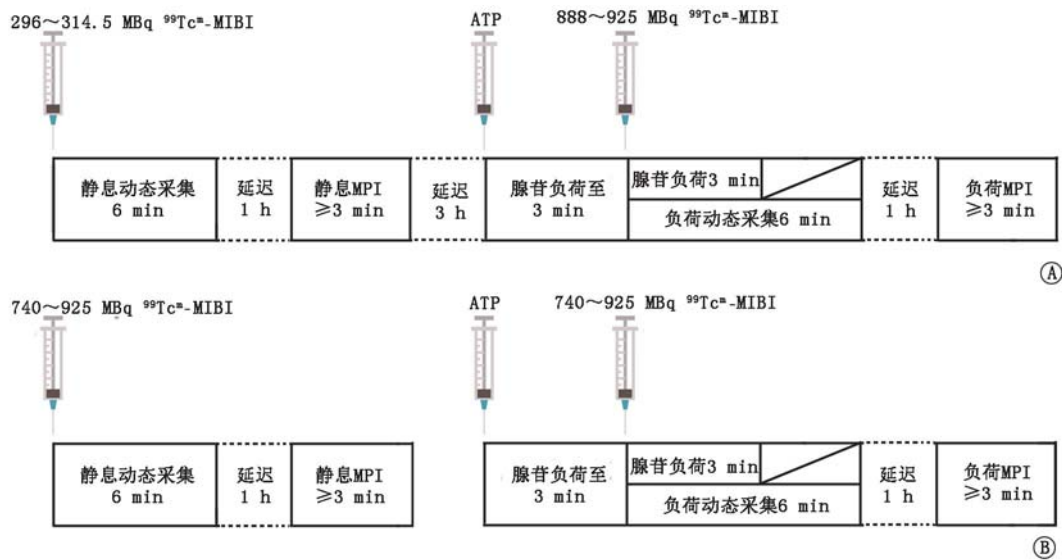


图1 锶铯镅心脏专用SPECT仪(CZT-SPECT)显像流程图[A.一日法(73例);B.两日法(59例)]。ATP采用微量注射泵注射($0.14 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$),共推注6 min,推至第3分钟时启用高压注射器注射 $^{99}\text{Tc}^{\text{m}}$ -甲氧基异丁基异脲(MIBI),并同步启动负荷动态采集。MPI为心肌灌注显像

结 果

132例患者中,吸烟者42例(31.8%),高血压者57例(43.2%),高脂血症者6例(4.5%),糖尿病患者29例(22.0%)。132例患者共计396支血管,狭窄程度 $\geq 75\%$ 者有61例(46.2%)共计104支(26.3%)血管,其中单支病变29例(47.5%)、二支病变21例(34.4%)、三支病变11例(18.0%);位于左前降支者48支(46.2%),左回旋支者27支(26.0%),右冠状动脉者29支(27.9%)。狭窄程度为50%~64%有30支(7.6%),狭窄65%~74%有25支(6.3%)。

在血管水平,MPI诊断为正常的61个节段和异常的41个节段,联合CFR后分别改判为心肌缺血和正常,诊断的准确性由77.53%(307/396)提高至85.10%(337/396; $\chi^2 = 7.479, P < 0.05$;表1;图2),诊断左回旋支的灵敏度由48.15%(13/27)提高至96.30(26/27; $\chi^2 = 15.600, P < 0.01$)。

在患者水平,MPI判断为异常者26例、正常者13例,在联合CFR后分别诊断为心肌缺血和正常,诊断的准确性由68.94%(91/132)提高至87.88%(116/132; $\chi^2 = 13.984, P < 0.01$)。联合CFR后,诊断单支、双支、三支病变冠心病的灵敏度分别由72.41%(21/29)、42.86%(9/21)、5/11提高至93.10%(27/29; $\chi^2 = 4.350, P = 0.037$)、90.48%(19/21; $\chi^2 = 10.714, P = 0.001$)、11/11($P = 0.012$;图3)。联合CFR检出冠脉狭窄50%~64%的灵敏度由40.00%(12/30)提高至76.67%(23/30; $\chi^2 = 8.297, P = 0.004$),检出冠脉狭窄65%~74%的灵敏度由

24.00%(6/25)提高至64.00%(16/25; $\chi^2 = 8.117, P = 0.004$)。

讨 论

SPECT MPI临床应用虽然已有数十年,但诊断冠心病的效能还存在以下不足:(1)冠脉血管多支病变可导致低估缺血程度及“均衡性”缺血,MPI常表现为假阴性;(2)SPECT显像是高噪音影像,轻微缺血难以显示或识别;(3)以主观判断为主,诊断的准确性依赖于读片医师的经验,而客观、量化的证据有限。PET MPI的临床应用,既明显提高了图像质量,又可以提供半定量分析的CFR,使得诊断的准确性明显提高。但是受设备价格高、普及率低和显像剂供给困难等因素的影响,该检查技术难以推广。CZT-SPECT仪具有探测效率高、扫描速度快的特点,既提高了MPI的图像质量,还可以获得与PET所测结果高度吻合的CFR^[8],明显提高了诊断冠心病的准确性。

本研究中,MPI诊断冠脉狭窄程度 $\geq 75\%$ 的灵敏度和准确性分别为72.12%(75/104)和77.53%(307/396),联合CFR后分别提高到了96.15%(100/104)和85.10%(337/396),与文献报道一致^[13]。灵敏度提高主要体现在2个方面:其一是对多支病变所致心肌缺血诊断灵敏度的提高,诊断二支冠脉病变导致的心肌缺血的灵敏度由42.86%(9/21)提高至90.48%(19/21),诊断三支病变导致心肌缺血的灵敏度由5/11提高至11/11,与文献报道一致^[14];分析其原因在于MPI显像剂的分布是以心肌内显像剂分布

表 1 MPI 及 MPI 联合 CFR 在血管与患者水平对冠状动脉狭窄 $\geq 75\%$ 的诊断效能

方法	血管水平 ($n=396; \%$)				
	灵敏度	特异性	PPV	NPV	准确性
MPI	72.12 (75/104)	79.45 (232/292)	55.56 (75/135)	88.89 (232/261)	77.53 (307/396)
MPI+CFR	96.15 (100/104)	81.16 (237/292)	64.52 (100/155)	98.34 (237/241)	85.10 (337/396)
χ^2 值	22.511	0.271	2.421	18.226	7.479
P 值	<0.01	0.603	0.120	<0.01	0.006

方法	患者水平 ($n=132; \%$)				
	灵敏度	特异性	PPV	NPV	准确性
MPI	86.89 (53/61)	53.52 (38/71)	61.63 (53/86)	82.61 (38/46)	68.94 (91/132)
MPI+CFR	96.72 (59/61)	80.28 (57/71)	80.82 (59/73)	96.61 (57/59)	87.88 (116/132)
χ^2 值	3.921	11.481	6.986	4.368	13.984
P 值	0.048	0.001	<0.01	0.037	<0.01

注:CFR 为冠状动脉血流储备, MPI 为心肌灌注显像, NPV 为阴性预测值, PPV 为阳性预测值; 括号内为用例数比

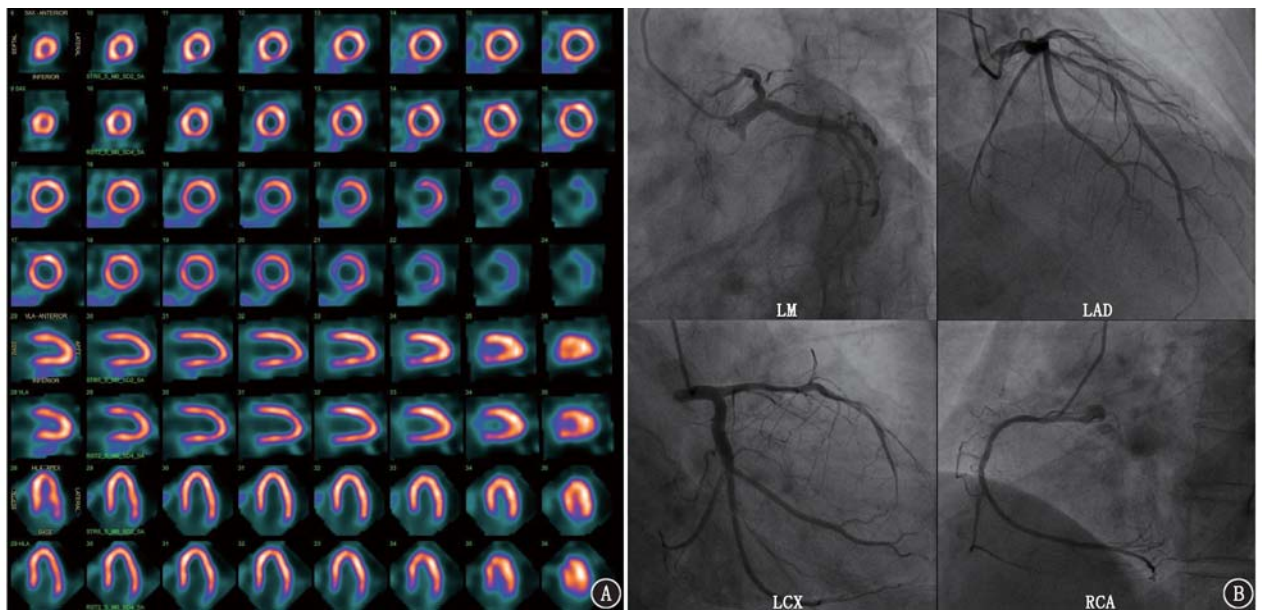


图 2 冠状动脉粥样硬化性心脏病患者(男, 57 岁)碲铊钼心脏专用 SPECT 仪心肌灌注显像(MPI)图及冠状动脉造影(CAG)图。A. MPI 表现为左心室下壁心尖部可逆性心肌缺血(第 1、3、5、7 排为负荷显像, 第 2、4、6、8 排为静息显像), 左前降支(LAD)、左回旋支(LCX)、右冠状动脉(RCA)血流储备分别为 2.24、2.85、2.25; B. CAG 示各支冠状动脉均未见狭窄(LM 为左主干)

最多部位为 100% 的正常参考区域, 其他部位以此为参考标准按比例递减, 因此在多支病变冠心病中, 指定的正常参考区域实际上也可能是异常的, 三支病变可能因为“平衡性缺血”被判断为正常, 降低了诊断的灵敏度, 而 CFR 通过客观评估, 不仅可以发现最显著的病变冠脉, 还可以发现被误认为是正常参考区域的病变血管, 从而揭示各支冠脉狭窄的真实程度, 弥补了 MPI 的不足。其二是对左回旋支供血的侧壁病变诊断的灵敏度由 48.15% (13/27) 提高至 96.30% (26/27), 分析其原因可能为侧壁最厚导致散射效应更加明显, 以及部分容积效应使轻微心肌缺血难以显示, 导致诊断灵敏度下降^[15], 而 CFR 则弥补了该不足。

目前临床将冠脉狭窄 $\geq 50\%$ 作为诊断冠心病的标准, 一般将狭窄 $\geq 75\%$ 作为进行介入治疗的指征, 而对于狭窄 50%~74% 的临界病变冠脉是否进行介入治疗的决策依据之一是病变冠脉是否引起心肌缺血^[16-17]。有文献表明, 临界病变冠脉 MPI 在很大程度上并无心肌缺血征象^[18], 与本研究中 MPI 诊断狭窄 65%~74% 与 50%~64% 冠脉的灵敏度分别为 24.00% (6/25) 和 40.00% (12/30) 的结果相似。相比于 MPI, CFR 能够客观反映病变冠脉的狭窄程度^[19]。本研究中, MPI 联合 CFR 诊断狭窄 65%~74% 与 50%~64% 冠脉的灵敏度分别提高至 64.0% (16/25) 和 76.67% (23/30), 表明 CFR 对 MPI 诊断轻度狭窄冠状动脉具有较好的增益价值, 能够为患

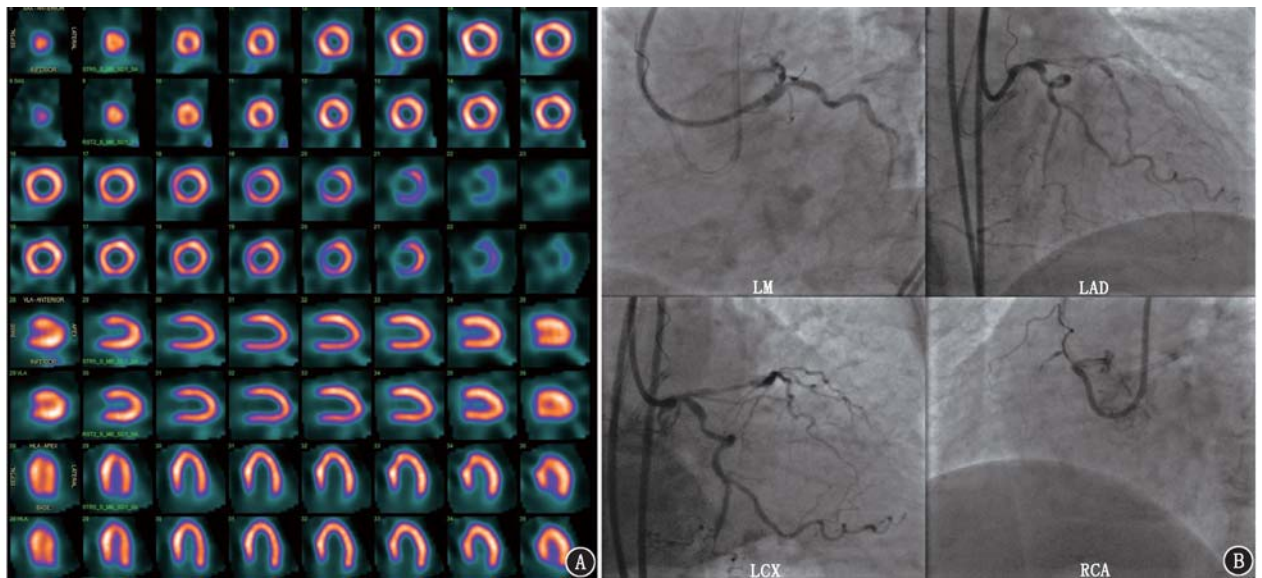


图3 冠状动脉粥样硬化性心脏病患者(女,79岁)碲铊心肌灌注显像(MPI)图及冠状动脉造影(CAG)图。A. MPI未见明显缺血征象(第1,3,5,7排为负荷显像,第2,4,6,8排为静息显像),左前降支(LAD)、左回旋支(LCX)、右冠状动脉(RCA)血流储备分别为1.84、1.45及1.51;B. CAG示左主干(LM)近段狭窄80%;LAD全程弥漫性病变,开口狭窄90%,近中段狭窄70%,中远段弥漫性狭窄40%~60%;LCX中段狭窄50%;RCA近段起完全闭塞

者的治疗决策提供更准确的参考依据。

冠心病心肌缺血的主要机制分别为冠脉狭窄、痉挛及微血管病变^[20],CAG仅能识别出冠脉狭窄与痉挛,而MPI和CFR还可以反映冠脉微血管循环的信息^[21-22],因此能够诊断出CAG无法识别的微血管病^[23],并提供更多的预后信息^[24]。因此,当以CAG为参考标准时,MPI或MPI联合CFR出现的假阳性不一定是真实的假阳性。影响心肌血流的因素还有狭窄部位及侧支循环情况等,冠脉也存在解剖变异的可能。CFR是一项新的检查技术,影响CFR检查结果的因素很多,因此本研究在患者入组时,对可能导致CFR结果偏倚的因素进行了排除。

综上,CFR是客观评价冠脉血流异常的定量指标。MPI联合CFR能够明显提高对冠心病的诊断效能,尤其是对冠脉轻度狭窄与多支病变冠心病。

利益冲突 所有作者均声明不存在利益冲突

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