DOI:10.3969/j.issn.1005-202X.2023.01.011

医学影像物理

CT-FFR参数联合斑块定量技术在心肌缺血再灌注损伤预测中的应用

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【摘要】**目的：**分析基于CT的血流储备分数(CT-FFR)联合斑块定量技术在心肌缺血患者再灌注损伤预测中的应用。**方法：**回顾性分析126例行择期经皮冠状动脉介入(PCI)治疗的冠心病(CHD)患者的临床资料，所有患者在PCI术前行冠状动脉CT血管成像检查，在PCI术后8 d内行心脏磁共振或光学相干断层成像判断再灌注损伤情况，将出现心肌微循环障碍(MVO)及(或)心肌内出血(IMH)者纳入再灌注损伤组，未出现MVO及IMH者纳入非再灌注损伤组。比较两组患者性别、年龄等基线资料及PCI术前CT-FFR值及斑块定量参数差异，利用受试者工作特征(ROC)曲线分析CT-FFR值及斑块定量参数对CHD患者再灌注损伤的预测价值。**结果：**再灌注损伤组多支血管病变率显著高于非再灌注损伤组(P<0.05)，PCI后TIMI 3级率低于非再灌注损伤组(P<0.05)。两组最小管腔面积、钙化斑块体积、重构指数、偏心指数比较，差异无统计学意义(P>0.05)；再灌注损伤组CT-FFR值低于非再灌注损伤组(P<0.05)，狭窄程度、斑块长度、非钙化斑块体积及斑块总体积均高于非再灌注损伤组(P<0.05)。ROC曲线分析显示，CT-FFR值、狭窄程度、斑块长度、非钙化斑块体积、斑块总体积均对CHD患者再灌注损伤具有较高预测价值(AUC=0.758、0.943、0.865、0.928、0.891，P<0.05)，其Cut-off值分别为0.671、75.44%、38.61 mm、186.08 mm^3、305.04 mm^3，且5项联合预测价值最高(AUC=0.999，P<0.05)。**结论：**CT-FFR及斑块定量参数对预测CHD患者再灌注损伤有积极作用，可为CHD临床诊疗提供参考。

【关键词】冠状动脉；心肌缺血；再灌注损伤；血流储备分数；斑块定量技术；CT血管成像
【中图分类号】R541；R814.42 【文献标志码】A 【文章编号】1005-202X(2023)01-0066-05

Predictive value of CT-FFR combined with plaque quantification for reperfusion injury in patients with myocardial ischemia

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Abstract: Objective To analyze the value of CT-based fractional flow reserve (CT-FFR) combined with plaque quantification for predicting the reperfusion injury in patients with myocardial ischemia. **Methods** The clinical data of 126 patients with coronary heart disease (CHD) who were scheduled for percutaneous coronary intervention (PCI) were retrospectively analyzed. All patients underwent coronary CT angiography before PCI, and received cardiac magnetic resonance or optical coherence tomography within 8 d after PCI to assess the reperfusion injury. Those with myocardial microvascular obstruction (MVO) and/or intramyocardial hemorrhage (IMH) were included in reperfusion injury group, and those without MVO and IMH were enrolled as non-reperfusion injury group. The baseline data, such as gender, age, etc, and differences in CT-FFR and plaque quantitative parameters before PCI were compared between two groups. Receiver operating characteristic (ROC) curve was used to analyze the predictive value of CT-FFR and plaque quantitative parameters for reperfusion injury in CHD patients. **Results** The multivessel lesion rate in reperfusion injury group were significantly higher than that in non-reperfusion injury group (P<0.05), while the rate of TIMI grade 3 flow after PCI was lower than that in non-reperfusion injury group (P<0.05). The differences between two groups in the minimum lumen area, calcified plaque volume, remodeling index and eccentricity index were trivial (P>0.05). Compared with non-reperfusion injury group, reperfusion injury group had lower CT-FFR, but higher degree of stenosis, longer plaque length, larger non-calcified plaque volume and total plaque

【收稿日期】2022-05-16
【基金项目】福建省中青年教师教育科研项目(JAT200110)；泉州市科技计划项目(2019N099S)
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volume (P<0.05). ROC curve analysis showed that CT-FFR, stenosis degree, plaque length, non-calcified plaque volume and total plaque volume had high predictive value for reperfusion injury in CHD patients (AUC=0.758, 0.943, 0.865, 0.928, 0.891; P<0.05), with the Cut-off values of 0.671, 75.44%, 38.61 mm, 186.08 mm^3, and 305.04 mm^3, respectively, and the predictive value of the combination of the 5 items was the highest (AUC=0.999, P<0.05). **Conclusion** CT-FFR and plaque quantitative parameters play a role in predicting reperfusion injury in CHD patients, and can provide a reference for the clinical diagnosis and treatment of CHD.

Keywords: coronary artery; myocardial ischemia; reperfusion injury; fractional flow reserve; plaque quantification; CT angiography

前 言

经皮冠状动脉介入(PCI)是冠心病(CHD)的主要治疗手段,可有效改善缺血心肌血流灌注,减轻心肌细胞损伤,改善患者预后[1]。虽然,再灌注治疗可缓解CHD患者心肌缺血状况,但再灌注也能引起中性粒细胞活化、补体激活、氧自由基大量堆积,导致心肌缺血损伤加剧,即再灌注损伤[2]。心脏磁共振具有无创、可定量分析等优点,可评估心肌内出血(IMH)、心肌微循环障碍(MVO)等再灌注损伤成像参数,准确性较高;光学相干断层成像分辨率高,血管三维重建效果好,也常用于再灌注损伤的评估,但两者均存在检查费用高、临床普及度不高等缺点[3-4]。血流储备分数(FFR)是一种根据压力测定冠状动脉血流的新指标,现已成为国际公认的冠状动脉狭窄功能性指标,可判断责任血管,指导PCI治疗[5]。既往FFR以冠状动脉造影为基础,造影期间利用压力导丝测试压力,这些有创性操作也使该检查受限[6]。近年来基于CT的FFR(CT-FFR)受到广泛关注,CT-FFR可在冠状动脉CT血管成像(CTA)基础上,利用Navier-Stokes方程计算流体力学特征,预测冠状动脉FFR值。有研究发现CTA能测量斑块定量参数,不仅评估患者心肌缺血状况,还能预测患者预后心血管事件发生情况[7]。基于此,本研究分析CT-FFR及CTA斑块定量参数对CHD患者再灌注损伤的预测价值,以期尽早评估患者预后,指导CHD临床诊疗。

1 资料与方法

1.1 一般资料

回顾性分析2019年6月~2021年6月间在福建医科大学附属第二医院收治的126例行择期PCI治疗的CHD患者临床资料。其中,男性76例,女性50例;年龄48~73岁,平均(58.17±5.40)岁;吸烟史75例,糖尿病37例,高血压67例,高血脂42例;左前降支病变71例,左旋支病变14例,右冠状动脉病变41例;多支血管病变54例。本研究经本院医学伦理委员会批准。

1.2 纳入与排除标准

纳入标准:(1)符合《中华人民共和国卫生标准汇编》[8]中CHD-冠脉狭窄诊断标准;(2)符合《中国经皮冠状动脉介入治疗指南(2016)》[9]中择期PCI治疗指征;(3)初次行PCI治疗;(4)影像学检查等资料完整。排除标准:(1)PCI术前行溶栓治疗;(2)既往心脏介入治疗或手术史;(3)合并原发性心肌病;(4)合并肝、肾等器官严重器质性病变;(5)凝血功能异常。

1.3 研究方法

1.3.1 冠状动脉CTA 对心率过快患者予以美托洛尔(阿斯利康制药有限公司,25 mg,H32025391)1 mg/kg舌下含服,控制心率在90次/min以下。使用128层螺旋CT机(德国西门子,型号:Definition AS),对比剂为碘海醇注射液(上海通用电气药业有限公司,含碘350 mg/mL,H20000596),经肘静脉注射50~70 mL碘海醇,注射速率4.0 mL/s,并注入30~50 mL的0.9%生理盐水;在升主动脉腔内CT值达100 HU时触发扫描;前门控扫描参数为管电压100 kV,管电流205 mAs,准直器0.6 mm,球管旋转时间0.38 s,70%RR间期重建;后门控扫描参数管电压100 kV,40%~70% RR间期管电流190 mAs,其余间期19 mAs;将原始数据传至MMWP990图像工作站,行三维重建、多平面重建、曲面重建及最大密度投影,B26f重建,重建层厚0.75 mm。

1.3.2 CT-FFR 使用FFR分析软件(cFFR 3.1.0,德国西门子),导入冠状动脉CTA图像后,以深度学习模式预测冠状动脉FFR值;由两名心血管诊断经验>5年的医师行双盲图像分析(CT-FFR经验>1年),软件自动识别冠状动脉中心线及管腔,识别错误时手动矫正,并生成伪彩色冠状动脉树,测量各冠状动脉血管CT-FFR值,测量时选取斑块远端2~3 cm处。

1.3.3 斑块定量参数 使用斑块分析软件(Coronary Plaque Analysis 4.2.1,德国西门子)自动提取冠状动脉树,自动识别病变斑块及血管腔径,识别错误时手动矫正,由两名心血管诊断经验>5年的医师行双盲图像分析,记录狭窄程度、最小管腔面积、斑块长度、钙化斑块体积、非钙化斑块体积、斑块总体积,并计算重构指数(冠状动脉最狭窄处管腔面积与近远端参考血管面积平均值之比)及偏心指数[(冠状动脉最狭窄处中心线与血管壁外侧最大距离-最狭窄处管腔中心线与血管壁外侧最小距离)/最狭窄处中心线

与血管壁外侧最大距离]。

1.3.4 再灌注损伤诊断　在PCI术后8 d内，使用3.0T磁共振扫描仪(荷兰飞利浦，型号：Achieva TX)判断再灌注损伤情况。4通道心电线圈，视野350 mm×350 mm，先行定常态自由进动序列扫描，检查心功能；采用T_2序列采集心尖、乳头肌水平、二尖瓣水平，以T_2现象上同病变血管分布一致的心肌内高信号区内的低信号区为IMH；接着静脉注入0.2 mL/kg造影剂钆喷酸葡胺(德国拜耳医药保健有限公司，469 mg/mL，H20080146)，10 min后采用3D翻转节段梯度回波成像观察延迟显像，以延迟显像高信号区中低信号影为MVO。将出现MVO及(或)IMH者纳入再灌注损伤组，未出现MVO及IMH者纳入非再灌注损伤组。回撤速度36 mm/s，成像速度185帧/s，回撤长度75 mm，根据采集到的图像判断再灌注损伤情况。

1.4 统计学方法

采用SPSS24.0统计软件分析；计量资料以均数±标准差表示，采用t检验；计数资料以n(%)表示，行χ^2检验或Fisher精确概率法；CT-FFR值及斑块定量参数对CHD患者再灌注损伤的预测价值采用受试者工作特征(ROC)曲线评估。$P<0.05$表示差异具有统计学意义。

2 结果

2.1 两组基线资料比较

126例患者中出现MVO及(或)IMH者54例，纳入再灌注损伤组；未出现MVO及IMH者72例，纳入非再灌注损伤组。两组性别、年龄、吸烟史、基础疾病比较，差异无统计学意义($P>0.05$)，具有可比性。再灌注损伤组多支血管病变率显著高于非再灌注损伤组($P<0.05$)，PCI后TIMI 3级率低于非再灌注损伤组($P<0.05$)。见表1。

表1 两组基线资料比较

Table 1 Comparison of baseline data between two groups

基线资料	再灌注损伤组(n=54)	非再灌注损伤组(n=72)	t/χ^2值	P值
性别(例，男/女)	33/21	43/29	0.025	0.875
年龄(岁，$\bar{x}\pm s$)	57.83±5.60	58.42±5.27	0.605	0.546
吸烟史[例(%)]	34(62.96)	41(56.94)	0.200	0.655
基础疾病[例(%)]				
糖尿病	17(31.48)	20(27.78)	0.204	0.651
高血压	31(57.41)	36(50.00)	0.680	0.410
高血脂	19(35.19)	23(31.94)	0.146	0.703
病变血管[例(%)]			1.844	0.398
左前降支	31(57.41)	40(55.56)		
左旋支	8(14.81)	6(8.33)		
右冠状动脉	15(27.78)	26(36.11)		
多支血管[例(%)]	29(53.70)	25(34.72)	4.540	0.033
PCI后TIMI 3级[例(%)]	48(88.89)	72(100.00)	-	0.005*

*：Fisher精确概率法

2.2 两组CT-FFR值及斑块定量参数比较

两组最小管腔面积、钙化斑块体积、重构指数、偏心指数比较，差异无统计学意义($P>0.05$)；再灌注损伤组CT-FFR值低于非再灌注损伤组($P<0.05$)，狭窄程度、斑块长度、非钙化斑块体积及斑块总体积均高于非再灌注损伤组($P<0.05$)。见表2。

2.3 CT-FFR值及斑块定量参数对CHD患者再灌注损伤的预测价值分析

ROC曲线分析显示，CT-FFR值、狭窄程度、斑块长度、非钙化斑块体积、斑块总体积均对CHD患者再灌注损伤具有较高预测价值(AUC=0.758、0.943、0.865、0.928、0.891，$P<0.05$)，其Cut-off值分别为0.671、75.44%、38.61 mm、186.08 mm^3、305.04 mm^3，且5项联合预测价值最高(AUC=0.999，$P<0.05$)。见表3和图1。

3 讨论

MVO及IMH是PCI术后的主要再灌注损伤，也与心源性死亡、心肌梗死再发等不良心血管事件密切相关[10]。再灌注治疗后，内皮细胞肿胀、斑块碎片等形成

表2　两组CT−FFR值及斑块定量参数比较($\bar{x} \pm s$)

Table 2 Comparison of CT−FFR and plaque quantitative parameters between two groups (*Mean*±*SD*)

项目	再灌注损伤组(*n*=54)	非再灌注损伤组(*n*=72)	*t*值	*P*值
CT-FFR值	0.62±0.10	0.73±0.12	5.595	<0.001
狭窄程度/%	79.14±3.74	70.02±4.11	12.796	<0.001
最小管腔面积/mm^2	4.64±0.13	4.97±1.04	1.819	0.071
斑块长度/mm	43.51±5.50	35.10±5.51	8.483	<0.001
钙化斑块体积/mm^3	121.48±18.95	116.10±20.02	1.526	0.130
非钙化斑块体积/mm^3	207.51±19.67	166.83±19.11	11.681	<0.001
斑块总体积/mm^3	328.99±27.64	282.93±25.74	9.631	<0.001
重构指数	1.20±0.24	1.13±0.21	1.741	0.084
偏心指数	0.51±0.12	0.44±0.11	1.943	0.054

表3　CT−FFR值及斑块定量参数对CHD患者再灌注损伤的预测价值分析

Table 3 Predictive value of CT−FFR and plaque quantitative parameters for reperfusion injury in CHD patients

指标	Cut-off值	灵敏度/%	特异度/%	约登指数	AUC	95% CI
CT-FFR值	0.671	77.78	68.06	0.459	0.758	0.675~0.841
狭窄程度	75.44%	85.19	93.06	0.783	0.943	0.904~0.982
斑块长度	38.61 mm	87.04	76.39	0.634	0.865	0.803~0.927
非钙化斑块体积	186.08 mm^3	87.04	86.11	0.731	0.928	0.882~0.973
斑块总体积	305.04 mm^3	81.48	84.72	0.662	0.891	0.833~0.950
5项联合	-	98.15	95.83	0.967	0.999	0.997~1.000

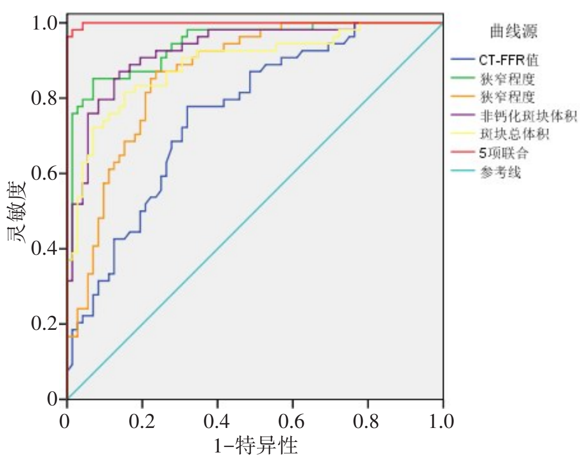

图1　CT−FFR值及斑块定量参数预测CHD患者再灌注损伤的ROC曲线

Figure 1 ROC curves of CT−FFR and plaque quantitative parameters for predicting reperfusion injury in CHD patients

微栓塞,及介入操作引起的炎症反应,均能诱发MVO[11]。长时间微循环障碍可造成组织严重缺血缺氧,毛细血管壁被破坏,再灌注治疗后,红细胞大量外渗,诱发IMH[12]。研究发现MVO及IMH在PCI术后常见,即使是成功的PCI,术后再灌注损伤发生率仍高达40%[13]。本研究中再灌注损伤组PCI后TIMI 3级率低于非再灌注损伤组,但其TIMI 3级率为88.89%,处于较高水平,与上述研究结果一致。故对于PCI术成功者,也不可掉以轻心,应密切监测其心肌微循环恢复情况,及时发现再灌注损伤。是否能预测并尽早发现MVO和IMH,也是近年研究的热点。

目前认为狭窄程度、心肌缺血范围等均与CHD再灌注损伤相关,心肌缺血越严重,越容易发生再灌注损伤[14-15]。本研究结果显示,再灌注损伤组多支血管病变率显著高于非再灌注损伤组,提示病变越多时越易发生再灌注损伤,与目前研究结果一致。CT-FFR是基于CTA图像的一种新型无创测量法,与有创性血管造影FFR测量值具有较高一致性,在冠状动脉缺血疾病诊断中准确性良好[16-17]。CT-FFR可评估狭窄病变对远端心肌血流的影响,CT-FFR值越低提示病变远端心肌血流灌注压越低,病变部位心肌缺血越严重[18]。本研究中再灌注损伤组CT-FFR值低于非再灌注损伤组,且CT-FFR值对CHD患者再灌注损伤具有较高预测价值,其Cut-off值为0.671。目前,临床常用CT-FFR值≤0.80作为缺血性病变的阳性标准[19],本研究结果也提示CT-FFR值越低者PCI术后越易发生再灌注损伤,且低于0.671

时发生MVO、IMH风险极高,需临床予以重视。

另据文献报道斑块性质也是影响CHD患者再灌注损伤及预后的重要因素,脂质斑块包含丰富的氧化应激及局部炎症,可引起局部内皮功能障碍,故脂质斑块越多、占比越大者,易引起MVO等再灌注损伤[20-21]。本研究中再灌注损伤组非钙化斑块体积及斑块总体积均高于非再灌注损伤组,且非钙化斑块体积、斑块总体积均对CHD患者再灌注损伤具有较高预测价值,提示不稳定斑块也是引起再灌注损伤发生的关键因素[22]。本研究还发现狭窄程度、斑块长度也对CHD患者再灌注损伤具有较高预测价值,考虑与病变部位狭窄越严重、斑块越长时,局部内皮细胞及毛细血管壁损伤越严重,导致再灌注时易出现MVO与IMH有关[23-24]。不仅如此,CT-FFR值与上述CTA斑块定量参数联合检测对CHD患者再灌注损伤预测价值最高,提示在CTA基础上,测量FFR值及斑块参数可更全面评估心肌缺血情况,对预测PCI术后再灌注损伤更有利[25]。

综上所述,CT-FFR值联合CTA斑块定量参数可综合评估CHD患者心肌缺血状况,预测PCI术后再灌输损伤发生风险,指导临床治疗。

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(编辑:黄开颜)