基于冠状动脉造影计算的微循环阻力指数在不同类型冠心病中的临床应用进展

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【摘要】冠状动脉微循环在心肌血流灌注调节中发挥关键作用,微循环阻力指数是评价微血管功能的金标准。随着计算流体力学技术的发展,基于冠状动脉造影计算的微循环阻力指数受到越来越多的关注,这种方法无需使用压力导丝和血管扩张剂,并且与基于压力导丝的微循环阻力指数有较好的诊断一致性。目前已在心肌梗死、慢性冠脉综合征和非阻塞性冠状动脉疾病中得到应用。现对基于冠状动脉造影计算的微循环阻力指数在不同类型冠心病中的临床应用价值进行综述。

【关键词】冠状动脉微循环障碍;微循环阻力指数;基于冠状动脉造影的微循环阻力指数
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Clinical Application of Coronary Angiography-Based Index of Microcirculatory Resistance in Various Types of Coronary Heart Disease

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【**Abstract**】 The coronary microcirculation plays a crucial role in the regulation of myocardial perfusion, and the index of microcirculatory resistance is the gold standard for assessing microcirculation function. With the development of computational fluid dynamics, the coronary angiography-based index of microcirculatory resistance has received increasing attention. This method does not require the use of pressure wires or hyperemic agents, and it has good diagnostic consistency with wire-based index of microcirculatory resistance. It has been applied in myocardial infarction, chronic coronary syndrome and non-obstructive coronary artery disease. This article reviews the clinical application of coronary angiography-based microcirculatory resistance index in various types of coronary heart disease.

【**Keywords**】 Coronary microvascular dysfunction; Index of microcirculatory resistance; Coronary angiography-based index of microcirculatory resistance

冠状动脉微循环由前小动脉、小动脉和毛细血管组成,在心肌血流灌注调节中发挥关键作用[1]。冠状动脉微循环障碍(coronary microcirculation dysfunction, CMD)在冠状动脉阻塞性和非阻塞性疾病中都具有重要意义,因此对微循环功能的评估至关重要[2-3]。微循环阻力指数(index of microcirculatory resistance, IMR)和冠状动脉血流储备是检测微循环功能的常见有创手段。随着计算流体力学的发展,基于冠状动脉造影计算的 IMR 的相关研究也日益广泛。现对基于冠状动脉造影计算的 IMR 在不同类型冠心病中的临床应用进展进行综述。

1　基于冠状动脉造影计算的 IMR

2003 年 Fearon 等[4]首次报道了 IMR 的检测方法,通过温度传感器测量生理盐水在冠状动脉内的通过时间(Tmn),利用压力导丝测量最大充血状态下冠状动脉远端压力(Pd),采用公式 IMR = Pd × Tmn 计算微循环阻力[5]。随着计算流体力学的发展,多个团队开发了通过两幅投射角度≥25°的冠状动脉造影图像计算血流储备分数(fractional flow reserve, FFR)的方法,包括定量血流分数(quantitative flow ratio, QFR)、冠状动脉造影血流储备分数(coronary angiography-derived fractional flow reserve, caFFR)、基于冠状动脉造影的 FFR(angiography-derived fractional flow reserve, AccuFFR)等。基于 IMR 的测量原理,de Maria 等[6]利用帧数与帧速的比值计算 Tmn,通过充血状态下的 QFR 与冠状动脉口压力(Pa)估算 Pd,提出了冠状动脉造影衍生的微循环阻力指数(angiography-derived index of microcirculatory resistance, IMR_{angio})。Scarsini 等[7]基于

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相同原理,提出了由静息状态的冠状动脉造影计算的非充血性 IMR_{angio}(non-hyperaemic IMR_{angio}, NH-IMR_{angio}),但其仅在 ST 段抬高型心肌梗死(ST segment elevation myocardial infarction, STEMI)患者中具有诊断价值,诊断准确性低于 IMR_{angio}。Jiang 等[8]使用相同公式通过 AccuFFR 计算得出基于冠状动脉造影的微循环阻力指数(angiography-based index of microcirculatory resistance, AccuIMR),诊断准确性高于 NH-IMR_{angio}。Fan 等[9]应用基于默里定律的 QFR 计算出冠状动脉造影微循环阻力(angiographic microvascular resistance, AMR),仅需单幅冠状动脉造影即可进行计算,较其他方法更为便捷。基于 Yong 等[10]对存在冠状动脉狭窄时 IMR 的矫正公式 $IMR = Pd \times Tmn \times (1.35 \times Pd/Pa) - 0.32$, Tebaldi 等[11]提出了存在冠状动脉狭窄时矫正侧支循环影响的基于血管的微循环阻力指数(angio-based index of microcirculatory resistance, A-IMR)公式。冠状动脉造影微循环阻力指数(coronary angiography-derived index of microcirculatory resistance, caIMR)利用 caFFR 结合充血状态下与静息状态下远段血流比值 K(K = 2.1),由静息状态下冠状动脉造影推算充血状态下的 IMR[12]。Mejia-Renteria 等[13]充血状态主动脉压与静息状态主动脉压的关系 $Pa_{充血} = Pa_{静息} - 0.1 \times Pa_{静息}$,进一步提出基于冠状动脉造影估算的 IMR(angiography-based estimation of IMR, angio-IMR)估计充血状态下的 IMR。Sheng 等[14]提出对比剂流速 QFR-固定流速 QFR(cQFR-fQFR),利用不同模型 QFR 的差值估算微循环功能。与基于导丝的 IMR 相比,基于冠状动脉造影计算的 IMR 具有较高的相关性和诊断价值,且无需应用压力导丝,除 IMR_{angio} 外,其他公式基于静息状态下的冠状动脉造影,无需使用血管扩张剂即可达到最大充血状态,这些方法的改进有利于微循环功能在临床应用中的推广。基于冠状动脉造影计算的 IMR 见表 1。

表 1 基于冠状动脉造影计算的 IMR

第一作者	使用软件	公式	相关性	敏感度	特异度	准确性	AUC(95% *CI*)
de Maria[6]	QAngio® XA 3D (Medis,荷兰)	$IMR_{angio} = Pa_{hyp} \times QFR \times \frac{Nframes_{hyp}}{fps}$	0.85	83.0%	100%	92.4%	0.96(0.92 ~ 1.00)
Scarsini[7] Kotronias[15]	QAngio® XA 3D (Medis,荷兰)	$NH\text{-}IMR_{angio} = Pa_{rest} \times QFR \times \frac{Nframes_{rest}}{fps}$	0.50	77.0%	67.0%	70.0%	0.78(0.72 ~ 0.84)
Jiang[8]	AccuIMR (脉流科技,杭州)	$AccuIMR = Pa \times AccuFFRangio \times L/V$	0.81	89.4%	92.4%	91.1%	0.92(0.88 ~ 0.96)
Fan[9]	AngioPlus Core (博动医疗,上海)	$AMR = \frac{Pa \times \mu QFR}{V_{hyp}}$	0.83	93.5%	82.7%	87.2%	0.94(0.91 ~ 0.97)
Tebaldi[11]	QAngio® XA 3D (Medis,荷兰)	$A\text{-}IMR = \frac{Pa \times (L/V) \times ([1.35 \times cQFR] - 0.32)}{100}$	0.32	70.0%	83.3%	—	0.76 (0.61 ~ 0.88)
Ai[12]	FlashAngio® (润迈德,苏州)	$caIMR = Pd_{hyp} \frac{L}{K \cdot V_{diastole}}$	0.75	86.1%	81.0%	84.2%	0.92
Mejia-Renteria[13]	QAngio® XA 3D (Medis,荷兰)	$angio\text{-}IMR = (Pa_{rest} - [0.1 \times Pa_{rest}]) \times QFR \times (L/V_{hyp})$	0.70	87.5%	85.3%	—	0.90(0.83 ~ 0.95)
Sheng[14]	AngioPlus (博动医疗,上海)	$cQFR\text{-}fQFR = cQFR - fQFR$	—	50.0%	90.7%	—	0.72(0.63 ~ 0.80)

注:hyp,充血状态;Nframes,帧数;fps,帧速;rest,静息状态;L,冠状动脉长度;V,冠状动脉血流速度;K,常数(值为 2.1);μQFR,基于莫里定律的定量血流分数。

2 基于冠状动脉造影计算的 IMR 在 STEMI 患者中的应用

STEMI 患者行经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)后,由于微循环栓塞、痉挛或再灌注损伤等原因可能会导致 CMD,进而影响患者的长期预后[16-17]。既往研究[18-19]表明 STMEI 患者直接 PCI 后 IMR > 40 U 与不良预后相关。然而,在直接 PCI 中应用 IMR 评估微循环功能可能会延长手术时间、增加手术费用,从而限制其应用[20]。目前,一些研究应用 IMR_{angio} 来评估 STEMI 患者的微循环功能。de Maria 等[6]发现 IMR_{angio} 在预测 IMR ≥ 40 U 方面表现出良好的诊断性能,ROC 曲线下面积(area under the curve, AUC)为 0.96(95% *CI* 0.92 ~ 1.00, $P < 0.001$)。此外,在非充血状态下测得的 NH-IMR_{angio} 在 STMEI 患者中同样有良好的诊断准确性(AUC = 0.82, 95% *CI* 0.74 ~ 0.90, $P < 0.001$)[7]。另一项研究[14]表明 cQFR-fQFR > 0.07 对 STEMI 患者的 CMD 也具有诊断价值(AUC = 0.716, 95% *CI* 0.628 ~ 0.803, $P < 0.001$)。

Shin 等[21]利用心脏磁共振成像评估 STEMI 患者的微循环障碍情况,发现 STEMI 术后罪犯血管 caIMR > 40 U 的患者微循环障碍发生率明显高于 caIMR≤40 U的患者(88.3% vs 32.1%, $P<0.001$)。以上研究提示多种基于冠状动脉造影计算的 IMR 对 STEMI 患者的微循环障碍均有较高的诊断价值,为 STEMI 患者的微循环障碍评估提供了更加便捷的方法。

除了诊断价值,基于冠状动脉造影计算的 IMR 对 STEMI 患者的预后也具有预测价值。Kotronias 等[15]对 262 例 STEMI 患者进行了梗死相关动脉的 NH-IMR_{angio}和 IMR 检测,中位随访时间为 4.2 年,发现 NH-IMR_{angio}预测 IMR > 40 U 的最佳截断值为 43 U, NH-IMR_{angio} > 43 U 是主要终点(全因死亡率、心搏骤停复苏和心力衰竭)的独立危险因素($HR=2.13$, 95% *CI* 1.01 ~ 4.48, $P=0.047$)。Choi 等[22]同样发现 caIMR > 40 U 是 STEMI 患者心源性死亡或心力衰竭再入院的独立危险因素($HR=2.909$, 95% *CI* 1.670 ~ 5.067, $P<0.001$)。AMR 的类似研究[23]同样证明 PCI 后 AMR≥250 mmHg × s/m 为主要不良心血管事件(major adverse cardiovascular event, MACE)的独立预测因子。此外,caIMR 还与 STEMI 患者直接 PCI 后左心室功能的恢复以及梗死面积的减少相关[24-25]。基于冠状动脉造影计算的 IMR 可用于评估 STEMI 患者 PCI 后微循环障碍的早期评价,为 STEMI 患者的微循环功能提供了一种便捷的评估方法,并且对心源性死亡或心力衰竭等心血管事件进行预后分级。

3　基于冠状动脉造影计算的 IMR 在慢性冠脉综合征患者中的应用

由于 CMD 导致微血管性心绞痛是慢性冠脉综合征(chronic coronary syndrome, CCS)的一个重要原因,《2019 ESC 慢性冠脉综合征诊断和管理指南》[26]建议将 IMR≥25 U 或冠状动脉血流储备 < 2.0 作为 CCS 患者微循环功能异常的标准。Fan 等[27]研究发现 AccuIMR 与 IMR 呈显著相关($r=0.75$, $P<0.001$),并且显示出较高的诊断价值(AUC = 0.918, 95% *CI* 0.841 ~ 0.966, $P<0.001$)。Dai 等[28]纳入 138 例冠心病行 PCI 的患者,中位随访时间 28 个月,发现 caIMR≥25.1 U 是心源性死亡或心力衰竭再入院的独立危险因素($HR=9.66$, 95% *CI* 2.04 ~ 45.65, $P=0.004$),可用于评估预后风险。糖尿病患者更容易合并 CMD, Zhang 等[29]共纳入 290 例 CCS 患者,以 caIMR≥25 U 作为 CMD 的诊断界值,发现糖尿病患者较非糖尿病患者的 CMD 患病率更高(57.8% vs 38.3%, $P=0.001$),而且 caIMR≥25 U 是 CCS 合并糖尿病患者包括心血管死亡、非致命性心肌梗死、心力衰竭和由缺血导致的血运重建等 MACE 的独立危险因素($HR=2.760$, 95% *CI* 1.066 ~ 7.146, $P=0.036$)。提示对于合并糖尿病的 CCS 患者,应用基于冠状动脉造影计算的 IMR 评估微循环功能对于预后判断具有重要意义。

4　基于冠状动脉造影计算的 IMR 在非阻塞性冠状动脉疾病中的应用

缺血伴非阻塞性冠状动脉疾病(ischaemia with non-obstructive coronary arteries, INOCA)是具有缺血性胸痛症状或心肌缺血的客观证据,但在冠状动脉造影或 CT 血管成像检查中未发现阻塞性冠状动脉狭窄的疾病[3,30]。因缺血而导致心肌损伤且无明显冠状动脉阻塞的心肌梗死被称为冠状动脉非阻塞性心肌梗死(myocardial infarction in the absence of obstructive coronary artery disease, MINOCA)[31]。微循环障碍是非阻塞性冠状动脉疾病的重要原因之一。Mejía-Rentería 等[32]发现在 INOCA 患者中, Angio-IMR 与 IMR 有良好的相关性($r=0.76$, $P<0.001$)及诊断价值(AUC = 0.865, $P<0.001$)。FLASH IMR 研究[33]前瞻性纳入 113 例 INOCA 患者,发现以基于导丝的 IMR 为参照,caIMR 的诊断准确性为 93.8%, AUC 为 0.963 (95% *CI* 0.928 ~ 0.999)。这些结果提示基于冠状动脉造影计算的 IMR 在 INOCA 患者中具有较好的诊断性能。Abdu 等[34]发现在 MINOCA 患者中,以 caIMR > 43 U 作为界值分组,高 caIMR 患者的 MACE(包括心血管死亡、非致死性心肌梗死、心力衰竭、卒中和因心绞痛再住院)发生率显著高于低 caIMR 患者(36.4% vs 13.0%, $P=0.005$), caIMR > 43 U 是 MACE 的重要危险因素($HR=3.40$, 95% *CI* 1.26 ~ 9.18, $P=0.016$)。目前尚无基于冠状动脉造影计算的 IMR 与 INOCA 患者预后的相关研究,未来需更多的大样本前瞻性研究以验证基于冠状动脉造影计算的 IMR 对其预后的危险分层及指导意义。

5　结语

CMD 在多种疾病中都发挥重要作用,并且对疾病的预后产生影响。因此,便捷而有效的评估方法对于理解微循环功能至关重要。基于冠状动脉造影计算的 IMR 为微循环功能的评估提供了新方法,不需要压力导丝以及应用血管扩张剂,使得微循环功能的评估变得更加方便和易于实施。目前的研究已证实,基于冠状动脉造影计算的 IMR 与基于压力导丝的 IMR 具有较好的相关性和诊断一致性,为评估疾病的机制和预后提供了可靠的方法。未来仍需进行大规模的前瞻性研究,以进一步探究不同模型在真实世界中对预后的预测价值,以及在不同类型冠心病患者中的适用性,为疾病的诊断和治疗提供更为精准和便捷的指导。

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