

# 冠状动脉功能学衍生技术的应用场景与发展方向\*

聂绍平<sup>1</sup> 徐洋<sup>1</sup> 王晓<sup>1</sup>

**[摘要]** 冠状动脉功能学评估是经皮冠状动脉介入治疗(PCI)临床决策的主要依据。血流储备分数(FFR)是功能学评估的金标准,但限于操作复杂、耗时长等原因,其临床应用十分有限。随着计算流体力学的发展,基于影像衍生的功能学指标(CT-FFR、QFR、caFFR、caIMR等)应运而生,其无创、高效且诊断准确率较高,在介入术前评估和术中指导中逐渐体现出优势。本文将介绍不同功能学衍生技术的应用场景,并对影像与功能学联合应用的价值进行展望。

**[关键词]** 冠状动脉疾病;血流储备分数;CT-FFR;QFR;caFFR;caIMR

**DOI:**10.13201/j.issn.1001-1439.2022.05.002

**[中图分类号]** R541.4 **[文献标志码]** C

## Application scenarios and prospects of coronary functional derived techniques

NIE Shaoping XU Yang WANG Xiao

(Beijing Anzhen Hospital, Capital Medical University, Beijing, 100029, China)

Corresponding author: NIE Shaoping, E-mail: spnie@126.com

**Summary** Coronary function assessment has become the cornerstone of clinical decision-making in percutaneous coronary intervention(PCI). Fractional flow reserve(FFR) is the gold standard for functional assessment, but its clinical application is limited due to the complicated and time-consuming procedure. With the development of computational fluid dynamics technology, imaging-derived functional indicators(CT-FFR, QFR, caFFR, caIMR, etc.) have emerged, which are non-invasive, efficient and have high diagnostic accuracy, and have advantages in pre-assessment and guidance of PCI. This article will introduce the application scenarios of different functional derived techniques, and discuss the value of the combined use of imaging and functional techniques.

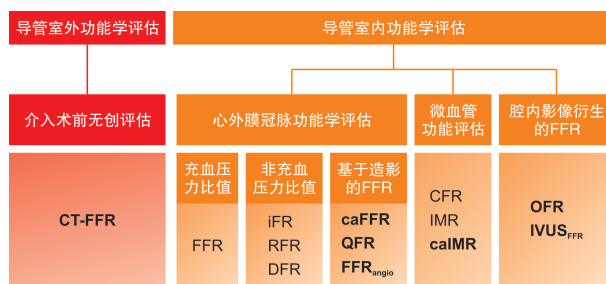
**Key words** coronary artery disease; fractional flow reserve; CT-FFR; QFR; caFFR; caIMR

冠状动脉(冠脉)功能学评估是经皮冠脉介入治疗(PCI)临床决策的基石。大量研究证实,与冠脉造影相比,基于压力导丝的血流储备分数(FFR)指导的介入治疗策略能显著改善患者预后。然而,由于操作复杂、耗时长等诸多原因,国内临床应用比例仍较低。随着计算流体力学的发展,基于无创或有创影像的各种功能学衍生技术应运而生,无论心外膜冠脉还是微血管功能评估,均体现出良好的应用前景(图1)。

### 1 传统基于冠脉导丝的功能学评估及其存在的问题

20世纪90年代,FFR的出现推动了冠脉功能学的发展<sup>[1]</sup>,实现了从单纯解剖学评估到功能学评估的新阶段。随着DEFER<sup>[2]</sup>、FAME<sup>[3]</sup>、FAME2<sup>[4]</sup>、FAMOUS<sup>[5]</sup>及COMPARE-ACUTE<sup>[6]</sup>等研究的公布,FFR的适应证从稳定型心绞痛扩展到不稳定型心绞痛、非ST段抬高型心肌梗死和ST段抬高型心肌梗死(STEMI)的非罪犯血管。目前,FFR

已被公认为冠脉功能学评估的金标准,在国内外介入治疗指南中也被列为I A类推荐<sup>[7-8]</sup>。



注:粗体示衍生技术。

图1 冠脉功能学评估及衍生技术

Figure 1 Coronary functional assessment and derived techniques

然而,2021年发表的FLOWER-MI研究<sup>[9]</sup>显示,对于STEMI合并多支病变患者,FFR指导的完全血运重建较冠脉造影指导并未显示出临床获益。2022年发表的FAME3研究<sup>[10]</sup>结果显示,对于3支病变患者,FFR指导的PCI策略较CABG

\*基金项目:北京市科技新星项目(No:Z201100006820087);北京市科技新星计划交叉学科合作项目(No:Z211100002121165)

<sup>1</sup>首都医科大学附属北京安贞医院(北京,100029)  
通信作者:聂绍平,E-mail:spnie@126.com

在1年复合终点事件(包括死亡、心肌梗死、卒中或再次血运重建)方面并未显示出非劣效性;因此,对于高危或不稳定的病变,采用FFR指导介入策略仍存在争议。另外,在临床实践中,FFR并未得到广泛应用,主要原因包括操作时间长、费用较高以及血管扩张药物的副作用,此外还与导丝操控性和压力波形需精准调控等因素有关<sup>[11]</sup>。尽管先后出现瞬时无波形比值(iFR)、静息全周期比值(RFR)、舒张期比值(DFR)等无需充血的评价方法,但仍需压力导丝和冠脉内操作,因此其使用率仍较低。

## 2 冠脉功能学评估的衍生技术与应用场景

随着计算流体力学和人工智能技术的发展,通过冠脉三维重建,可以计算出基于影像的FFR,包括无创CT血管造影(CTA)衍生的FFR(CT-FFR)和有创冠状动脉造影衍生的FFR,它们克服了基于导丝的FFR的诸多缺陷,诊断准确性与FFR一致性较高,无论在介入术前临床决策还是术中指导均体现出优势,目前已逐渐应用于临床实践。

### 2.1 介入术前无创功能学评估:CT-FFR

对于疑似冠心病患者,CTA是最常用的诊断手段,其敏感性高,但因特异性不足,常导致不必要的冠脉造影。过去10年,多种CT-FFR技术如雨后春笋般出现,通过计算流体力学或人工智能与冠脉生理学参数相结合,计算出一个心动周期内冠脉树任一点的CT-FFR值,明确CTA冠脉狭窄的功能学意义<sup>[12]</sup>。

早期大型前瞻性临床研究证实,与单纯CTA相比,CT-FFR对FFR<0.8的诊断准确性显著提高<sup>[13-14]</sup>。与传统SPECT和PET相比,CT-FFR对血管特异性缺血的诊断性能更高<sup>[15]</sup>。我们的研究显示,基于“由粗到精”血管分割技术的Ruixin CT-FFR对于缺血的诊断敏感性、特异性和准确率分别为95%、90%和92%。对于临界病变、“灰区”病变和钙化病变的诊断效能也均高于80%,显著优于冠脉CTA<sup>[16]</sup>。

对冠心病患者进行CT-FFR评估可以减少不必要的有创治疗风险,并可能降低医疗费用。一项前瞻性队列研究显示,在接受了CTA与CT-FFR评估的新发胸痛患者中,有61%的患者取消了不必要的有创冠脉造影<sup>[17]</sup>。在ADVANCE多中心注册登记的5083例患者中,与单独使用CTA相比,有2/3的受试者根据CT-FFR的结果修改了治疗策略<sup>[18]</sup>。PLATFORM研究<sup>[19]</sup>显示,采用CTA/CT-FFR减少了33%的医疗费用。然而,新近发表的FORECAST研究<sup>[20]</sup>显示,CT-FFR指导策略虽然减少了有创冠脉造影,但并未降低医疗费用。PRECISE研究<sup>[21]</sup>将进一步评估CT-FFR指导策略与传统策略对临床结局的影响。此外,针对

左主干或3支血管病变患者,基于CTA/CT-FFR的心脏团队的治疗决策与传统冠脉造影得出的决策高度一致,这表明基于CTA的功能学评估方式在临床治疗决策和规划方面具有潜在的可行性<sup>[22]</sup>。

2019年ESC慢性冠脉综合征指南推荐冠状动脉CTA作为疑似冠心病患者的一线检查手段,对于CTA功能学意义不明确者,建议功能性影像学检查明确有无心肌缺血(I类推荐)<sup>[23]</sup>,相信CT-FFR同其他经典无创影像学检查一样,有望成为侵入性冠脉造影的“守门人”。当然,CT-FFR也存在着自身局限性,比如CTA图像质量会干扰CT-FFR的分析。未来期待通过技术与算法的进一步优化,在导管室外利用无创手段为患者提供更精准的功能学评估和指导。

### 2.2 基于冠脉造影的导管室功能学评估

#### 2.2.1 心外膜冠脉功能学评估

由于不需要压力导丝和充血药物,基于冠脉造影衍生的功能学评估逐渐体现出优势,也成为近年研究热点。目前主要技术包括:定量血流分数(quantitative flow ratio, QFR)、基于计算流体力学的FFR(computational pressure-flow derived FFR, caFFR)、基于冠脉造影的血流储备分数(coronary angiography-derived FFR, FFR<sub>angio</sub>)等。其中,QFR和caFFR是研究最广泛的两种技术,不同的是caFFR结合实时主动脉压力,利用优化的流体力学公式进行计算从而模拟压力导丝回撤过程。FAVOR II China研究显示,QFR在线评估冠脉狭窄功能学意义的准确率为92.4%<sup>[24]</sup>。FLASH FFR研究显示,与金标准FFR相比,caFFR的诊断准确率高达95.7%<sup>[25]</sup>。

FAVOR III China是一项在中国26家医院进行的多中心、盲法、随机、对照试验。该研究共纳入3825例冠心病患者,结果显示,与传统造影指导治疗组相比,QFR指导组1年全因死亡、心肌梗死和缺血驱动的血运重建显著降低<sup>[26]</sup>。正在进行的FLASH II研究(NCT04575207)预计入选2134例患者,将探讨caFFR指导对比FFR指导策略对中度冠脉狭窄患者1年临床结局的影响,该研究将进一步为基于造影的功能学评估手段提供有力证据。

功能学评估在PCI术后同样发挥着不容忽视的作用。一方面,术后功能学评估能有效预测PCI后的远期临床结果。DK CRUSH VII研究<sup>[27]</sup>证实,PCI术后FFR值与靶血管失败密切相关。随后HAWKEYE研究<sup>[28]</sup>与SYNTAX II研究<sup>[29]</sup>进一步发现,PCI术后QFR越高,随访心血管不良事件的发生率越低。另一方面,术后功能学评估可能进一步优化PCI结果。Agarwal等<sup>[30]</sup>研究发现,PCI术后造影结果满意的病变有20%根据术后FFR值进行了重新分类,需要进一步干预。DEFINE PCI研究<sup>[31]</sup>对PCI成功的500例患者进行盲法iFR回

撤,结果发现,近 1/4 的患者在 PCI 术后仍存在残余缺血;值得注意的是,这些在血管造影上并不明显的狭窄仅有 38.4% 位于支架节段内,这表明 PCI 术后功能学检查在支架节段外残余病变的评估和定位中发挥更重要的作用。TARGET FFR 研究<sup>[32]</sup>显示,在采用冠脉造影指导的 PCI 患者中,高达 2/3 以上的患者冠脉功能学评估结果不理想。FFR 指导的优化策略尽管未能显著增高最终 FFR  $\geq 0.90$  的患者占比,但却明显降低了最终 FFR  $\leq 0.80$  的患者占比。关于术后功能学评估指导优化 PCI 能否改善患者临床结局仍需进一步研究,目前正在进行的 FFR REACT 研究<sup>[33]</sup>和 DEFINE-GPS 研究(NCT04451044)有望回答上述问题。

**2.2.2 微血管功能评估** 既往研究多关注心外膜冠脉,目前研究认为,微血管功能不全是非阻塞性冠心病(nonobstructive coronary artery disease, NOCAD)的主要原因。同时,对于 PCI 术后残余心绞痛的患者也应考虑微血管功能评估。目前已经开发了多种技术评估微血管功能,包括无创的超声心动图、PET-CT、CMR 等,以及有创的冠脉血流储备(CFR)、微循环阻力指数(IMR)等方法。既往研究证实,PCI 术后即刻 IMR 可预测稳定型冠心病和 STEMI 患者的心血管不良事件<sup>[34-35]</sup>。

然而,由于 IMR 操作复杂、耗时并需要充血药物或 0.9% 氯化钠,其临床应用受到限制,尤其对于心肌梗死患者存在潜在风险。为了克服 IMR 的局限性,一种基于冠脉造影衍生的微循环阻力指数应运而生——caIMR。caIMR 与传统 IMR 相关性良好,诊断准确率达 85%<sup>[36-37]</sup>。对于 STEMI 患者,caIMR 与术后急性期 CMR 测量的微血管功能不全有较好的一致性<sup>[38]</sup>;同时,STEMI 术后 caIMR  $> 40$  U 的患者心源性死亡或心力衰竭再入院的风险显著升高<sup>[39]</sup>。这种无需压力导丝的非充血方法可以在术后早期识别高风险患者,从而指导临床医师制定更精准的治疗方案。

### 3 冠脉功能学评估的未来发展方向

#### 3.1 基于 OCT 衍生的 FFR

血管内光学相干断层扫描(optical coherence tomography, OCT)在评估冠脉病变形态学方面具有极高的分辨率,成为优化 PCI 治疗的重要工具,但其预测冠脉狭窄功能学意义的准确性有限,因此衍生出了基于 OCT 图像自动计算的 FFR,即 OFR。OCT 成像后,利用软件自动描绘冠脉及其侧支的管腔轮廓进行三维重建,随后计算出沿冠脉每个位置的 FFR,计算得出的 OFR 值叠加在三维重建的冠状动脉和管腔直径曲线上,同时呈现出解剖学和功能学评估结果<sup>[40]</sup>。在一项事后分析中发现,与传统有创 FFR 相比,OFR 具有良好的诊断准确性和较低的观察者变异性<sup>[41]</sup>。另外一项前瞻

性评估也显示,OFR 在真实世界中的测量结果与 FFR 保持高度一致性<sup>[42]</sup>。OFR 在提供高分辨率血管成像的同时,对狭窄病变的功能性缺血也有很好的诊断能力,可以在无诱发充血的情况下快速实现病变形态和功能学信息的整合。

#### 3.2 基于血管内超声衍生的 FFR

血管内超声(intravascular ultrasound, IVUS)利用超声波成像原理对血管的横截面进行实时成像,可以评估斑块形态、负荷并指导 PCI 治疗<sup>[43]</sup>。2018 年,Seike 等<sup>[44]</sup>开发出一种利用 IVUS 获得的解剖信息计算 FFR 的方法,用于评估心肌缺血,并且发现 IVUS-FFR 与 FFR 的线性相关性优于 IVUS 衍生的最小管腔面积。之后,通过 IVUS 影像进行血管重建也可计算 FFR(IVUS<sub>FFR</sub>),并且与有创 FFR 相比表现出良好的一致性<sup>[45]</sup>。基于类似 OFR 的计算方法,通过流体力学计算的 UFR 与 FFR 表现出很强的相关性与一致性。UFR 的计算速度快、可重复性好,有望更广泛地应用于导管室影像和功能学的综合评估<sup>[46]</sup>。

#### 3.3 冠脉影像学与功能学的联合应用

冠脉斑块形态和功能学代表冠心病的不同特征,在冠心病发生发展过程中密不可分,两者相互作用形成不同的解剖和功能学特征。尽管 FFR 阴性的患者可能有较好的预后,但同时存在高危病变的患者仍可能发生临床事件。FAME 2 研究 5 年随访发现,FFR  $> 0.8$  的延迟血运重建患者中仍有 15.7% 发生了主要终点事件<sup>[47]</sup>。一项研究对 299 例患者进行 CTA 与 FFR 分析发现,在 FFR  $> 0.80$  组中,高危特征  $\geq 3$  个的病变显示出更高的缺血事件风险<sup>[48]</sup>。COMBINE 研究显示,对于 FFR  $> 0.80$  行保守治疗的糖尿病患者,合并薄纤维帽动脉粥样硬化(TCFA)显著增加复合缺血事件风险。因此,综合考虑局部斑块负荷、高危斑块特征、局部生理学等能更好地定义易损特征,从而根据危险分层选择优化治疗策略<sup>[49]</sup>,而简单、无创的功能学评估新手段为联合应用提供了技术支撑。

**利益冲突** 所有作者均声明不存在利益冲突

#### 参考文献

- [1] Pijls NH, van Son JA, Kirkeeide RL, et al. Experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty[J]. *Circulation*, 1993, 87(4):1354-1367.
- [2] Pijls NH, van Schaardenburgh P, Manoharan G, et al. Percutaneous coronary intervention of functionally nonsignificant stenosis: 5-year follow-up of the DEFER Study[J]. *J Am Coll Cardiol*, 2007, 49(21): 2105-2111.
- [3] Pijls NH, Fearon WF, Tonino PA, et al. Fractional flow reserve versus angiography for guiding percuta-



- neous coronary intervention in patients with multivessel coronary artery disease; 2-year follow-up of the FAME(Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study[J]. *J Am Coll Cardiol*, 2010, 56(3):177-184.
- [4] De Bruyne B, Pijls NH, Kalesan B, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease[J]. *N Engl J Med*, 2012, 367(11):991-1001.
- [5] Layland J, Oldroyd KG, Curzen N, et al. Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction; the British Heart Foundation FAMOUS-NSTEMI randomized trial[J]. *Eur Heart J*, 2015, 36(2):100-111.
- [6] Smits PC, Abdel-Wahab M, Neumann FJ, et al. Fractional flow reserve-guided multivessel angioplasty in myocardial infarction[J]. *N Engl J Med*, 2017, 376(13):1234-1244.
- [7] 韩雅玲. 中国经皮冠状动脉介入治疗指南(2016)[J]. *中华心血管病杂志*, 2016, 44(5):382-400.
- [8] Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization[J]. *Eur Heart J*, 2019, 40(2):87-165.
- [9] Puymirat E, Cayla G, Simon T, et al. Multivessel PCI Guided by FFR or angiography for myocardial infarction[J]. *N Engl J Med*, 2021, 385(4):297-308.
- [10] Fearon WF, Zimmermann FM, De Bruyne B, et al. Fractional flow reserve-guided PCI as compared with coronary bypass surgery[J]. *N Engl J Med*, 2022, 386(2):128-137.
- [11] Kogame N, Ono M, Kawashima H, et al. The impact of coronary physiology on contemporary clinical decision making[J]. *JACC Cardiovasc Interv*, 2020, 13(14):1617-1638.
- [12] Min JK, Taylor CA, Achenbach S, et al. Noninvasive fractional flow reserve derived from coronary CT angiography; clinical data and scientific principles[J]. *JACC Cardiovasc Imaging*, 2015, 8(10):1209-1222.
- [13] Koo BK, Erglis A, Doh JH, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter DISCOVER-FLOW(Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) study[J]. *J Am Coll Cardiol*, 2011, 58(19):1989-1997.
- [14] Norgaard BL, Leipsic J, Gaur S, et al. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease; the NXT trial(Analysis of Coronary Blood Flow Using CT Angiography: Next Steps)[J]. *J Am Coll Cardiol*, 2014, 63(12):1145-1155.
- [15] Driessen RS, Danad I, Stuijzand WJ, et al. Comparison of coronary computed tomography angiography, fractional flow reserve, and perfusion imaging for ischemia diagnosis[J]. *J Am Coll Cardiol*, 2019, 73(2):161-173.
- [16] Wang X, Zeng Y, Tang Z, et al. Diagnostic accuracy of computed tomography-based fractional flow reserve with a new coarse-to-fine subpixel algorithm in detecting hemodynamically significant stenosis[P]. Paper presented at: ACC, March 8, 2022, Washington DC.
- [17] Douglas PS, Pontone G, Hlatky MA, et al. Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs. usual care in patients with suspected coronary artery disease; the prospective longitudinal trial of FFR(CT): outcome and resource impacts study[J]. *Eur Heart J*, 2015, 36(47):3359-3367.
- [18] Fairbairn TA, Nieman K, Akasaka T, et al. Real-world clinical utility and impact on clinical decision-making of coronary computed tomography angiography-derived fractional flow reserve; lessons from the ADVANCE Registry[J]. *Eur Heart J*, 2018, 39(41):3701-3711.
- [19] Hlatky MA, De Bruyne B, Pontone G, et al. Quality-of-life and economic outcomes of assessing fractional flow reserve with computed tomography angiography: PLATFORM[J]. *J Am Coll Cardiol*, 2015, 66(21):2315-2323.
- [20] Curzen N, Nicholas Z, Stuart B, et al. Fractional flow reserve derived from computed tomography coronary angiography in the assessment and management of stable chest pain; the FORECAST randomized trial[J]. *Eur Heart J*, 2021, 42(37):3844-3852.
- [21] Nanna MG, Vemulapalli S, Fordyce CB, et al. The prospective randomized trial of the optimal evaluation of cardiac symptoms and revascularization: Rationale and design of the PRECISE trial[J]. *Am Heart J*, 2022, 245:136-148.
- [22] Collet C, Onuma Y, Andreini D, et al. Coronary computed tomography angiography for heart team decision-making in multivessel coronary artery disease[J]. *Eur Heart J*, 2018, 39(41):3689-3698.
- [23] Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes[J]. *Eur Heart J*, 2020, 41(3):407-477.
- [24] Xu B, Tu S, Qiao S, et al. Diagnostic accuracy of angiography-based quantitative flow ratio measurements for online assessment of coronary stenosis[J]. *J Am Coll Cardiol*, 2017, 70(25):3077-3087.
- [25] Li J, Gong Y, Wang W, et al. Accuracy of computational pressure-fluid dynamics applied to coronary angiography to derive fractional flow reserve: FLASH FFR[J]. *Cardiovasc Res*, 2020, 116(7):1349-1356.
- [26] Xu B, Tu S, Song L, et al. Angiographic quantitative flow ratio-guided coronary intervention(FAVOR III China): a multicentre, randomised, sham-controlled trial[J]. *Lancet*, 2021, 398(10317):2149-2159.

- [27] Li SJ, Ge Z, Kan J, et al. Cutoff value and long-term prediction of clinical events by FFR measured immediately after implantation of a drug-eluting stent in patients with coronary artery disease: 1-to 3-year results from the DKCRUSH VII Registry Study[J]. *JACC Cardiovasc Interv*, 2017, 10(10):986-995.
- [28] Biscaglia S, Tebaldi M, Brugaletta S, et al. Prognostic value of QFR measured immediately after successful stent implantation; the international multicenter prospective HAWKEYE Study[J]. *JACC Cardiovasc Interv*, 2019, 12(20):2079-2088.
- [29] Kogame N, Takahashi K, Tomaniak M, et al. Clinical implication of quantitative flow ratio after percutaneous coronary intervention for 3-vessel disease [J]. *JACC Cardiovasc Interv*, 2019, 12(20):2064-2075.
- [30] Agarwal SK, Kasula S, Hacıoglu Y, et al. Utilizing post-intervention fractional flow reserve to optimize acute results and the relationship to long-term outcomes [J]. *JACC Cardiovasc Interv*, 2016, 9(10):1022-1031.
- [31] Jeremias A, Davies JE, Maehara A, et al. Blinded physiological assessment of residual ischemia after successful angiographic percutaneous coronary intervention; The DEFINE PCI Study[J]. *JACC Cardiovasc Interv*, 2019, 12(20):1991-2001.
- [32] Collison D, Didagelos M, Aetesam-Ur-Rahman M, et al. Post-stenting fractional flow reserve vs coronary angiography for optimization of percutaneous coronary intervention(TARGET-FFR)[J]. *Eur Heart J*, 2021, 42(45):4656-4668.
- [33] van Zandvoort LJC, Masdjedi K, Tovar Forero MN, et al. Fractional flow reserve guided percutaneous coronary intervention optimization directed by high-definition intravascular ultrasound versus standard of care: Rationale and study design of the prospective randomized FFR-REACT trial[J]. *Am Heart J*, 2019, 213:66-72.
- [34] Fearon WF, Low AF, Yong AS, et al. Prognostic value of the Index of Microcirculatory Resistance measured after primary percutaneous coronary intervention[J]. *Circulation*, 2013, 127(24):2436-2441.
- [35] Nishi T, Murai T, Ciccarella G, et al. Prognostic value of coronary microvascular function FFR measured immediately after percutaneous coronary intervention in stable coronary artery disease: an international multicenter study[J]. *Circ Cardiovasc Interv*, 2019, 12(9):e007889.
- [36] Ai H, Feng Y, Gong Y, et al. Coronary angiography-derived index of microvascular resistance [J]. *Front Physiol*, 2020, 11:605356.
- [37] Mejia-Renteria H, Lee JM, Choi KH, et al. Coronary microcirculation assessment using functional angiography: Development of a wire-free method applicable to conventional coronary angiograms [J]. *Catheter Cardiovasc Interv*, 2021, 98(6):1027-1037.
- [38] Shin D, Kim J, Choi KH, et al. Functional angiography-derived index of microcirculatory resistance validated with microvascular obstruction in cardiac magnetic resonance after STEMI[J]. *Rev Esp Cardiol(Engl Ed)*, 2022.
- [39] Choi KH, Dai N, Li Y, et al. Functional coronary angiography-derived index of microcirculatory resistance in patients with ST-segment elevation myocardial infarction[J]. *JACC Cardiovasc Interv*, 2021, 14(15):1670-1684.
- [40] Tian F, Yu W, Huang J, et al. First presentation of integration of intravascular optical coherence tomography and computational fractional flow reserve[J]. *Int J Cardiovasc Imaging*, 2019, 35(4):601-602.
- [41] Yu W, Huang J, Jia D, et al. Diagnostic accuracy of intracoronary optical coherence tomography-derived fractional flow reserve for assessment of coronary stenosis severity[J]. *EuroIntervention*, 2019, 15(2):189-197.
- [42] Gutierrez-Chico JL, Chen Y, Yu W, et al. Diagnostic accuracy and reproducibility of optical flow ratio for functional evaluation of coronary stenosis in a prospective series[J]. *Cardiol J*, 2020, 27(4):350-361.
- [43] van Zandvoort LJC, Ali Z, Kern M, et al. Improving PCI outcomes using postprocedural physiology and intravascular imaging [J]. *JACC Cardiovasc Interv*, 2021, 14(22):2415-2430.
- [44] Seike F, Uetani T, Nishimura K, et al. Intravascular ultrasound-derived virtual fractional flow reserve for the assessment of myocardial ischemia [J]. *Circ J*, 2018, 82(3):815-823.
- [45] Bezerra CG, Hideo-Kajita A, Bulant CA, et al. Coronary fractional flow reserve derived from intravascular ultrasound imaging: Validation of a new computational method of fusion between anatomy and physiology [J]. *Catheter Cardiovasc Interv*, 2019, 93(2):266-274.
- [46] Yu W, Tanigaki T, Ding D, et al. Accuracy of intravascular ultrasound-based fractional flow reserve in identifying hemodynamic significance of coronary stenosis [J]. *Circ Cardiovasc Interv*, 2021, 14(2):e009840.
- [47] Xaplanteris P, Fournier S, Pijls NHJ, et al. Five-year outcomes with PCI guided by fractional flow reserve [J]. *N Engl J Med*, 2018, 379(3):250-259.
- [48] Lee JM, Choi KH, Koo BK, et al. Prognostic implications of plaque characteristics and stenosis severity in patients with coronary artery disease[J]. *J Am Coll Cardiol*, 2019, 73(19):2413-2424.
- [49] Yang S, Koo BK, Narula J. Interactions between morphological plaque characteristics and coronary physiology: from pathophysiological basis to clinical implications [J]. *JACC Cardiovasc Imaging*, 2021, S1936-878X(21):00775-0.