



## Original Article

# Physiological evaluation of the provisional side-branch intervention strategy for bifurcation lesions using instantaneous wave-free ratio



Mohamed Shaheen<sup>a</sup>, Moustafa Mokarrab<sup>a</sup>, Ali Youssef<sup>b</sup>, Mansour Aref<sup>a</sup>,  
Abdelrahman Ibrahim Abushouk<sup>c,d,\*</sup>, Ahmed Elmarazy<sup>a,c</sup>, Adel Almasswary<sup>e</sup>

<sup>a</sup> Department of Cardiology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

<sup>b</sup> Department of Cardiology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

<sup>c</sup> NovaMed Medical Research Association, Cairo, Egypt

<sup>d</sup> Faculty of Medicine, Ain Shams University, Cairo, Egypt

<sup>e</sup> Department of Cardiology, Aseer Central Hospital, Abha, Saudi Arabia

## ARTICLE INFO

## Article history:

Received 2 December 2017

Accepted 16 January 2018

Available online 31 January 2018

## Keywords:

Bifurcation lesions

Coronary angioplasty

Instantaneous wave-free ratio

Physiological assessment

## ABSTRACT

**Background:** The provisional side-branch intervention strategy remains the gold standard approach for repair of coronary bifurcation lesions. We performed this study to evaluate the clinical and functional outcomes of using the instantaneous wave-free ratio (iFR) for physiological assessment in provisional side-branch repair of bifurcation lesions.

**Methods:** Fifty patients with coronary bifurcation lesions were equally divided into two groups: (I) an iFR-guided side-branch intervention group and (II) a conventional group, in which the operator selected a different interventional method. After the procedure, we performed a six-month follow-up for postoperative ejection fraction (EF) and clinical cardiac outcomes.

**Results:** Our results showed that the iFR measurement procedure was technically feasible in bifurcation lesions, with no procedural-related complications. Moreover, measuring iFR significantly predicted the side-branch percent stenosis after stenting of the main branch ( $r = -0.81$ ,  $p < 0.0001$ ). Compared to the conventional group, the iFR-guided group showed a significantly shorter procedural time (MD = -14.6 min, 95% CI [-27.7, -1.4]) and hospital stay duration (MD = -0.92 days, 95% CI [-1.6, -0.28]). However, no significant differences were recorded between the iFR-guided and conventional groups in terms of postoperative EF ( $p = 0.9$ ), six-month heart failure class ( $p = 0.89$ ), or post-interventional angina ( $p = 0.066$ ).

**Conclusion:** Using iFR for physiological assessment during the provisional side-branch intervention strategy can reduce the procedural time and length of hospital stay in patients with bifurcation lesions. Larger trials should compare the clinical outcomes of iFR to other physiological assessment methods such as the fractional flow reserve (FFR) in patients with coronary bifurcation lesions.

ClinicalTrials.gov number: NCT02785510

© 2018 Published by Elsevier B.V. on behalf of Cardiological Society of India. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Despite the remarkable advances in the field of coronary interventions, bifurcation lesions still represent a challenge in interventional cardiology.<sup>1,2</sup> The difficult anatomical position of these lesions makes their interventions technically demanding with a higher complication rate than non-bifurcation lesions.<sup>3,4</sup> Because no former study showed an additional clinical benefit for the complex systematic two-stenting procedure, the provisional

side-branch intervention strategy remains the gold standard approach for bifurcation lesions repair.<sup>5,6</sup> During this procedure, the operator needs to decide whether the jailed side-branch needs dilatation and stenting after main-branch stent implantation.

For decades, coronary angiography was the routine diagnostic method for lesion evaluation and decision-making in side-branch interventions. Given the well-documented discordance between angiographic findings and the functional severity of the lesion,<sup>7,8</sup> the advent of fractional flow reserve (FFR) allowed more accurate

Abbreviations: DEB, drug-eluting balloon; EF, ejection fraction; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; PCI, percutaneous coronary intervention.

\* Corresponding author at: Faculty of Medicine, Ain Shams University, 11591, Cairo, Egypt.

E-mail address: [Abdelrahman.abushouk@med.asu.edu.eg](mailto:Abdelrahman.abushouk@med.asu.edu.eg) (A.I. Abushouk).

assessment of lesion severity.<sup>9–11</sup> However, FFR guidance showed similar clinical outcomes in comparison to angiography in provisional side-branch interventions.<sup>12</sup> Moreover, the need to administer adenosine to minimize the microvascular resistance for accurate FFR measurement increases the risk of adverse events such as breathlessness, chest tightness, and occasionally severe asthma.<sup>13</sup> Therefore, none of these tools (angiography or FFR) is yet validated for decision making in side-branch interventions.<sup>10</sup>

In 2012, Sen and colleagues introduced the instantaneous wave-free ratio (iFR) as an adenosine-independent index of coronary stenosis severity.<sup>14</sup> Several studies,<sup>14–18</sup> along with a recent meta-analysis,<sup>19</sup> demonstrated a high accuracy for iFR in the evaluation of coronary lesions with FFR as the standard reference. Moreover, two recent large trials (DEFINE-FLAIR and iFR-SWEDEHEART) showed that iFR was non-inferior to FFR with respect to the rate of major adverse cardiac events at 1 year post-intervention.<sup>20,21</sup>

Reviewing the literature, no former study has evaluated the clinical utility of iFR measurement in provisional repair of jailed side-branch lesions. We conducted this study to evaluate the functional aspects of iFR-guided provisional jailed side-branch interventions and compare its clinical endpoints to conventional non-iFR-guided operations.

## 2. Materials and methods

### 2.1. Patient selection

The study protocol was approved by the institutional review board of Al-Azhar University. The study was conducted in two centers: The Saudi-German Hospital (Aseer, Abha city, Saudi Arabia) and Aseer Central Hospital (Aseer, Abha, Saudi Arabia) after reviewing the approved protocol. All enrolled patients gave an informed consent after understanding the procedures and the purpose of the study. All procedures in this study were performed in accordance with the Ethical Declaration of Helsinki. All patients were subject to a complete history taking (as regard age, gender, risk factors, previous angina/myocardial infarction, previous percutaneous transluminal coronary angioplasty), full physical and cardiac examination, cardiac enzymes biomarkers (including troponin I and Creatine Kinase-MB) before and after percutaneous coronary intervention (PCI), as well as resting ECG assessment, and transthoracic echocardiography before and after PCI.

#### 2.1.1. iFR-guided side-branch intervention group

Patients with acute coronary syndrome (who were admitted to the coronary care unit) were included if they had a jailed side-branch (culprit lesion with a bifurcation anatomy) of a vessel size >2 mm, vessel length >40 mm, and an estimated lesion length <10 mm by visual estimation.

Patients were excluded from the study if they had any of the following: a significant stenosis in the left main coronary artery or the main branch proximal to the stented segment, totally occluded bifurcation lesions, primary myocardial disease, or a serum creatinine level of  $\geq 2$ .

#### 2.1.2. Conventional intervention group

The same selection criteria were applied to enroll patients in the conventional group. These patients underwent coronary intervention by operators, not involved in the iFR-guided strategy.

### 2.2. Study procedure

In both groups, culprit lesion severity was judged by multiple views, including orthogonal projections. The culprit lesion severity,

Medina bifurcation class and coronary blood flow were assessed by eyeballing, and matching with the American Heart Association classification.<sup>22,23</sup> Analysis was done by two independent experienced operators. The cut-off value for coronary intervention was a lesion stenosis of  $\geq 70\%$ .<sup>22</sup>

Coronary stenting of the main branch was performed with standard interventional techniques using drug-eluting [zotarolimus] stents. After successful stenting, a reference image was obtained. In the iFR group, pressure measurement was performed using a pressure guide wire [iFR volcano wire]. The wire was passed through the stent struts of the main branch to the side-branch and the iFR was measured at 5 mm distal to the side-branch ostium to assess the severity of stenosis. The iFR measurements were performed after stabilization of ACS by low molecular weight heparin and antiplatelet medications.

Lesions with an iFR  $\leq 0.89$  [equivalent to an FFR of 0.80] were considered to have a functionally significant stenosis and side-branch balloon dilatation (using a smaller balloon than the side-branch vessel diameter) was allowed only for these lesions. After drug-eluting balloon (DEB) inflation [PANTERALUX: Paclitaxel releasing PTCA balloon catheter], the iFR was measured again at the same site and further intervention was only recommended when iFR was  $\leq 0.89$  after DEB inflation.

In the conventional group, the decision to treat the side-branch lesion and the method of intervention were all up to the operators' discretion. Clinical follow-up, as well as angiographic follow up in the conventional group, were performed after stent implantation for six months for the following outcomes: Ejection fraction (EF), heart failure, and post-PCI angina.

### 2.3. Statistical analysis

All data were reported as means  $\pm$  standard deviations (SD) for continuous variables and as a percentages for categorical variables. All data were normally distributed; therefore, the Chi-square and Student's *t*-tests were used to compare categorical and continuous variables, respectively. Simple linear regression was employed to test the correlation between iFR value and percent stenosis of the jailed side-branch. A difference was considered significant when the *p* value was  $< 0.05$ . We used SPSS (Version 22 for Windows) to conduct the statistical analysis.

## 3. Results

Fifty patients with bifurcation coronary lesions, categorized according to Medina classification, were consecutively enrolled in this study between March 2014 and January 2017 (Fig. 1). The iFR was successfully measured in 25 patients (iFR group) and the other 25 patients (conventional group) were treated according to the operator's discretion. Age, sex, and body weight were comparable between the two groups ( $p = 0.18$ , 1, and 0.74 respectively). Baseline characteristics of enrolled patients are presented in Table 1.

### 3.1. iFR and percent stenosis values after main branch stenting

Following stenting of the main branch and before DEB inflation in the jailed side-branch, a significant reduction of stenosis in the main branch was observed in both the proximal (Mean Difference [MD] =  $-59.3\%$ ,  $p < 0.0001$ ) and distal (MD =  $-44.2\%$ ,  $p < 0.0001$ ) segments and the percent stenosis (pre-stenting =  $46.6\%$ , post-stenting =  $62\%$ ,  $p < 0.0001$ ) was markedly increased in the jailed side-branch (MD =  $15.4\%$ ,  $p < 0.0001$ ). Measuring iFR significantly predicted the side-branch percent stenosis after stenting of the main branch ( $r = -0.81$ ,  $p < 0.0001$ ).

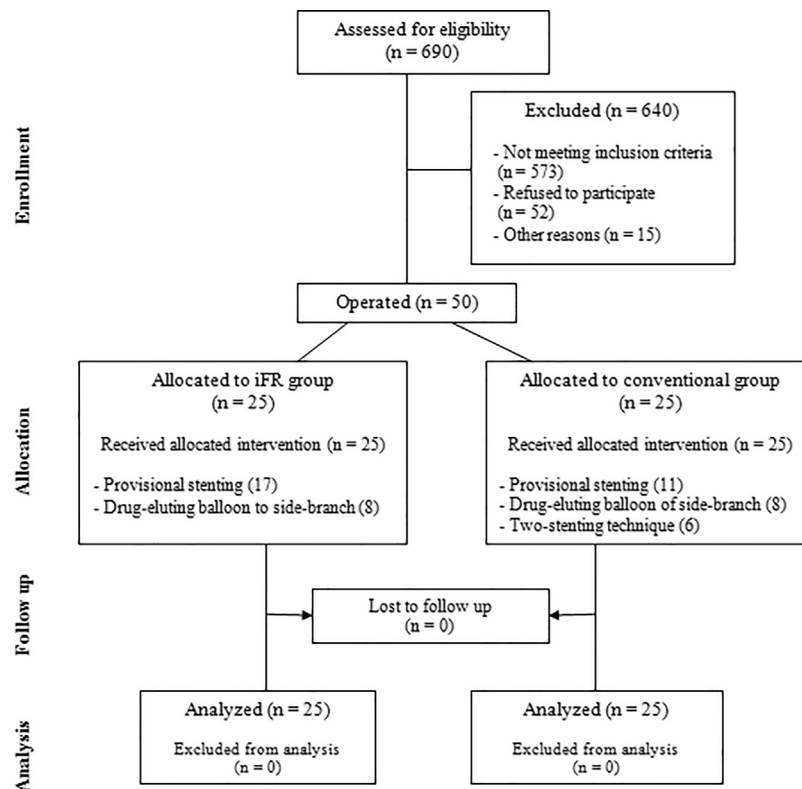


Fig. 1. Flow chart of the study.

### 3.2. iFR changes after DEB inflation of the jailed side-branch

DEB inflation was performed in 25 patients in the iFR group. The iFR measurements improved from  $0.71 \pm 0.19$  post-stenting of the main branch to  $0.90 \pm 0.16$  after side-branch balloon inflation (MD = 0.19,  $p = 0.013$ ). The proportion of patients with functionally significant stenosis after DEB inflation was 4% (1/25) in the iFR group and 12% (3/25) in the conventionally treated cohort ( $p = 0.32$ ). In the iFR group, mean iFR in the jailed side-branch on follow up was  $0.84 \pm 0.19$ . Fig. 2 shows the changes in the iFR measurements after the procedure and during follow up.

### 3.3. Comparison of clinical outcomes, procedural time and hospital stay duration between the iFR and conventional groups

The iFR group was superior to the conventional group in terms of shortening the length of hospital stay (MD =  $-0.92$  days, 95% CI [ $-1.6$  to  $-0.28$ ],  $p = 0.006$ ), procedural time (MD =  $-14.6$  min, 95% CI [ $-27.7$  to  $-1.4$ ],  $p = 0.03$ ), and fluoroscopy time (MD =  $-9.3$  min, 95% CI [ $-18$  to  $-5.2$ ],  $p = 0.038$ ). The amount of dye injection for angiography was significantly less in the iFR group ( $p = 0.03$ ), compared to the conventional group.

In terms of EF, no significant difference in the conventional group was noted before and after the intervention ( $p = 0.51$ ), while there was a significant improvement in the iFR group after the intervention, compared to baseline EF ( $p = 0.01$ ). However, EF at 6 months after the procedure was similar in the two groups ( $p = 0.9$ ). Two myocardial infarction events in the main branch occurred in the conventional group: the first took place following the PCI procedure and the patient died 10 days afterwards, while the second occurred due to late-stent thrombosis (corrected by target vessel revascularization). There was no difference between both groups with regard to the in-hospital heart failure class ( $p = 0.36$ ), six-month heart failure class ( $p = 0.89$ ), and post-PCI angina

( $p = 0.066$ ). A summary of the results of clinical outcomes is illustrated in Table 2.

## 4. Discussion

Over the past 20 years, several physiological measurements were developed to guide coronary revascularization, of which the FFR was the most promising. Measuring FFR relies primarily on the directly proportional relationship between flow and pressure under conditions of constant and minimal intracoronary resistance.<sup>24</sup> To overcome the phasic pattern in which the intracoronary resistance changes over the cardiac cycle, the FFR is measured during hyperemia (using adenosine) and time-averaged over multiple cardiac cycles (using computational methods).

Although the 2009 Focused Updates of the ACC/AHA/SCAI guidelines on PCI upgraded the level of evidence on FFR to “A” level,<sup>25</sup> its use remains restricted globally due to: 1) the lack of device reimbursement in several countries,<sup>26–28</sup> 2) multiple side effects and contraindications to adenosine administration, and 3) the apparent prolongation of the procedure time.<sup>29</sup> Five years ago (2012), Sen and colleagues calculated iFR as a ratio of trans-stenotic pressures during a diastolic wave-free period (when resistance is naturally constant and minimal); therefore, avoiding beat-to-beat pressure fluctuations and eliminating the need for adenosine administration and advanced computational methods.<sup>14,17</sup>

Our study showed that using iFR for physiological assessment of bifurcation lesions significantly reduced the procedural time (probably related to fluoroscopy time reduction and should be further confirmed), length of hospital stay, and amount of dye needed for angiography. However, we could not detect a significant change in post-operative EF, the number of patients with residual functional stenosis, or postoperative complications including

**Table 1**

Shows the baseline characteristics of enrolled patients in the study.

	iFR group (n = 25)	Conventional group (n = 25)	P-value (*:Significant)
Age (years)	53.44 ± 13.25	54.04 ± 10.97	0.86
Male sex (%)	23 (92%)	23 (92%)	1
Body weight (Kg)	79.52 ± 13.58	78.44 ± 8.24	0.74
Hypertension	14 (56%)	10 (40%)	0.26
Diabetes Mellitus	14 (56%)	12 (48%)	0.57
Smoking	9 (36%)	14 (56%)	0.16
Dyslipidemia	12 (48%)	12 (48%)	1
Known coronary artery disease	6 (24%)	2 (8%)	0.14
Recent myocardial infarction	6 (24%)	4 (16%)	0.48
Unstable angina	13 (52%)	14 (56%)	0.78
NYHA Class			
- 0	8 (32%)	8 (32%)	1
- 1	5 (20%)	11 (44%)	0.07
- 2	8 (32%)	3 (12%)	0.1
- 3	4 (16%)	3 (12%)	0.87
Left ventricular ejection fraction (%)	49.12 ± 9.8	50.12 ± 11.31	0.74
Culprit branch			
- Diagonal	24 (96%)	15 (60%)	0.01*
- OM	0 (0%)	8 (32%)	0.03*
- PAD	1 (4%)	2 (8%)	0.56
Medina class			
- 1,1,1	15 (60%)	9 (36%)	0.09
- 1,1,0	2 (8%)	12 (48%)	0.005*
- 1,0,1	4 (16%)	1 (4%)	0.19
- 1,0,0	4 (16%)	2 (8%)	0.4
- 0,1,1	0 (0%)	0 (0%)	
- 0,0,1	0 (0%)	1 (4%)	0.05
Main branch diameter (ml)	3.12 ± 0.28	3.03 ± 0.31	0.29
Side-branch diameter (ml)	2.54 ± 0.16	2.56 ± 0.15	0.65
Main branch proximal segment stenosis (%)	83 ± 8.17	81.2 ± 15.43	0.61
Main branch distal segment stenosis (%)	67.2 ± 23.54	76 ± 23.72	0.18
Side branch stenosis (%)	46.6 ± 8	44 ± 18.81	0.61

**Table 2**

Shows a summary of the assessed clinical outcomes.

	iFR group (n = 25)	Conventional group (n = 25)	P value (*: significant)
Length of hospital stay (day)	3 ± 0.5	3.92 ± 1.5	0.006*
Procedure time (min)	43.52 ± 10.54	58.08 ± 30.88	0.03*
Fluoroscopy time (min)	15.96 ± 5.72	25.24 ± 21.03	0.038*
In-hospital heart failure class			0.36
0	11 (44%)	10 (40%)	
1	10 (40%)	13 (52%)	
2	4 (16%)	1 (4%)	
3	0 (0%)	1 (4%)	
Six-month heart failure class			0.89
0	11 (44%)	12 (48%)	
1	11 (44%)	11 (44%)	
2	3 (12%)	2 (8%)	
3	0 (0%)	0 (0%)	
Post-PCI angina	2 (8%)	7 (28%)	0.066
Six-month ejection fraction	55.32 ± 6.05	54.96 ± 14.74	0.9
Amount of injected dye (ml)	106.4 ± 35.22	388 ± 251.36	>0.0001

angina or heart failure. The DEFINE-FLAIR study reported a significantly shorter procedural time in the iFR group ( $p = 0.001$ ), compared to the FFR group.<sup>21</sup> This is unlike the iFR-SWEDEHEART study that reported a non-significant difference ( $p = 0.09$ ) in procedural time between both groups.<sup>20</sup>

The ADVISE II and Härle et al.,<sup>15,16</sup> studies suggested adopting a hybrid of FFR-iFR guidance to enhance the diagnostic accuracy and expose fewer patients to adenosine. In the same vein, the VERIFY II study<sup>30</sup> showed that using the hybrid strategy resulted in 54% less adenosine infusion, yet a misclassification rate of 10% still disregards iFR feasibility. This approach will be further investigated in the ongoing multicenter SYNTAX II trial (NCT02015832), which applies ischemia-driven revascularization to PCI-treated patients with triple vessel disease.

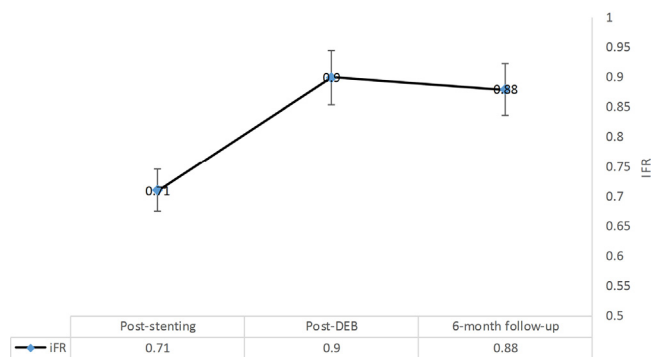
In the recently released (2017) version of the appropriate use criteria for coronary revascularization, both iFR and FFR are recommended for physiological assessment in single and multi-vessel coronary artery disease.<sup>31,32</sup> Combined with the formerly mentioned advantages over FFR, we hope that adopting iFR will increase the use of physiological assessment in interventional practice.

According to our hospital protocol, a longer hospital follow up is recommended in patients who receive an additional stent to the side-branch vessel. Following an accurate assessment of the side-branch lesion severity using iFR, no stents were implanted in the side-branch vessels. Therefore, these patients were discharged early from our hospital, accounting for the shorter hospital stay in the iFR group.

#### 4.1. Strength points

Although several studies have assessed the diagnostic utility of iFR in stable coronary stenosis or ACS, our study is the first to specifically investigate this point in bifurcation lesions. Unlike the majority of former studies on iFR, which were primarily focused on the functional and diagnostic accuracy outcomes, our study targeted the identification of the iFR effects on the interventional procedure characteristics and postoperative complications.

#### CHANGES IN IFR



**Fig. 2.** Changes in instantaneous wave-free ratio following main branch stenting, drug-eluting balloon inflation, and six-month follow up.

## 4.2. Limitations

Our sample size was relatively small; therefore, our results are suggestive rather than conclusive and need further confirmation in larger clinical trials. Moreover, the bifurcation-repair procedure is primarily dependent on the operator's professionalism and his skills of intervention. We did not directly compare iFR to FFR in bifurcation lesions and this head-to-head comparison is essential before the wide introduction of iFR in clinical practice.

## 5. Conclusions

Using the iFR for physiological assessment during the provisional side-branch interventional strategy is feasible and can reduce the procedural time and the length of hospital stay in patients with bifurcation lesions. However, we could not detect a significant improvement of the postoperative EF or cardiac complications. Future trials with larger sample size should directly compare the clinical outcomes of iFR and FFR assessments, especially in patients with coronary bifurcation lesions.

## 6. Conflicts of Interest

None.

## 7. Funding sources

None.

## Acknowledgement

None to declare.

## References

- Pan M, de Lezo J, Medina A, Romero M, Segura J, Rapamycin-eluting stents for the treatment of bifurcated coronary lesions: a randomized comparison of a simple versus complex strategy. *Am Heart J*. 2004;148:857–864.
- Colombo A, Moses J, Morice M, Ludwig J. Randomized study to evaluate sirolimus-eluting stents implanted at coronary bifurcation lesions. *Circulation*. 2004;109:1244–1249.
- Mathias DW, Moony JF, Lange HW, et al. Frequency of success and complications of coronary angioplasty of a stenosis at the ostium of a branch vessel. *Am J Cardiol*. 1991;67:491–495.
- Mishra S. Dedicated bifurcation stents—Mechanistic, hardware, and technical aspects. *Indian Heart J*. 2016;68:841–850.
- Al Suwaidi J, Berger PB, Rihal CS, et al. Immediate and long-term outcome of intracoronary stent implantation for true bifurcation lesions. *J Am Coll Cardiol*. 2000;35:929–936.
- Yamashita T, Nishida T, Adamian MG, et al. Bifurcation lesions: two stents versus one stent—immediate and follow-up results. *J Am Coll Cardiol*. 2000;35:1145–1151.
- Chen S-L, Xu B, Chen JB, et al. Diagnostic accuracy of quantitative angiographic and intravascular ultrasound parameters predicting the functional significance of single de novo lesions. *Int J Cardiol*. 2013;168:1364–1369.
- Tonino PAL, De Bruyne B, Pijls NHJ, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *New Engl J Med*. 2009;360:213–224.
- Koo B-K, Kang H-J, Youn T-J, et al. Physiologic assessment of jailed side branch lesions using fractional flow reserve. *J Am Coll Cardiol*. 2005;46:633–637.
- Koo B-K, Park K-W, Kang H-J, et al. Physiological evaluation of the provisional side-branch intervention strategy for bifurcation lesions using fractional flow reserve. *Eur Heart J*. 2008;29:726–732.
- Ye F, Zhang J-J, Tian N-L, et al. The acute changes of fractional flow reserve in DK (double kissing), crush, and 1-stent technique for true bifurcation lesions. *J Intervent Cardiol*. 2010;23:341–345.
- Chen S-L, Ye F, Zhang J-J, et al. Randomized comparison of FFR-guided and angiography-guided provisional stenting of true coronary bifurcation lesions: the DKCRUSH-VI trial (double kissing crush versus provisional stenting technique for treatment of coronary bifurcation lesions VI). *JACC: Cardiovasc Interv*. 2015;8:536–546.
- McGeoch RJ, Oldroyd KG. Pharmacological options for inducing maximal hyperaemia during studies of coronary physiology. *Catheter Cardiovasc Interv*. 2008;71:198–204.
- Sen S, Escaned J, Malik IS, et al. Development and validation of a new adenosine-independent index of stenosis severity from coronary wave-intensity analysis: results of the ADVISE (ADenosine Vasodilator Independent Stenosis Evaluation) study. *J Am Coll Cardiol*. 2012;59:1392–1402.
- Escaned J, Echavarría-Pinto M, García-García HM, et al. Prospective assessment of the diagnostic accuracy of instantaneous wave-free ratio to assess coronary stenosis relevance: results of ADVISE II international, multicenter study (adenosine vasodilator independent stenosis evaluation II). *JACC Cardiovasc Interv*. 2015;8:824–833.
- Härle T, Bojara W, Meyer S, Elsässer A. Comparison of instantaneous wave-free ratio (iFR) and fractional flow reserve (FFR)—first real world experience. *Int J Cardiol*. 2015;199:1–7.
- Indolfi C, Mongiardo A, Spaccarotella C. The instantaneous wave-free ratio (iFR) for evaluation of non-culprit lesions in patients with acute coronary syndrome and multivessel disease. *Int J Cardiol*. 2015;178:46–58.
- Petraco R, Al-Lamee R, Gotberg M, Sharp A. Real-time use of instantaneous wave-free ratio: results of the ADVISE in-practice: an international, multicenter evaluation of instantaneous wave-free ratio in clinical practice. *Am Heart J*. 2014;168:739–748.
- Man W, Hu J, Zhao Z, et al. Diagnostic performance of instantaneous wave-free ratio for the evaluation of coronary stenosis severity confirmed by fractional flow reserve: a PRISMA-compliant meta-analysis of randomized studies. *Medicine*. 2016;95:e4774.
- Götberg M, Gudmundsdottir IJ, Sandhall L, et al. Instantaneous wave-free ratio versus fractional flow reserve to guide PCI. *New Engl J Med*. 2017;376:1813–1823.
- Davies JE, Dehbi H-M, Al-Lamee R, et al. Use of the instantaneous wave-free ratio or fractional flow reserve in PCI. *New Engl J Med*. 2017;376:1824–1834.
- Ryan TJ, Faxon DP, Gunnar RM, et al. F. D. P. guidelines for percutaneous trans-luminal angioplasty: a report of the American College of Cardiology/American Heart Association task force on assessment of diagnostic and therapeutic cardiovascular procedures (subcommittee on percutaneous trans luminal angioplasty). *Circulation*. 1998;78:502–786.
- Medina A, de Lezo JS, Pan M. A new classification of coronary bifurcation lesions. *Rev Esp Cardiol*. 2006;59:183.
- Spaan JA, Piek JJ, Hoffman JJ, Siebes M. Physiological basis of clinically used coronary hemodynamic indices. *Circulation*. 2006;113:446–455.
- Kushner FG, Hand M, Smith SC, et al. Focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update). *Catheter Cardiovasc Interv*. 2009;74: 2009.
- Dattilo PB, Prasad A, Honeycutt E, Wang TY, Messenger JC. Contemporary patterns of fractional flow reserve and intravascular ultrasound use among patients undergoing percutaneous coronary intervention in the United States: insights from the National Cardiovascular Data Registry. *J Am Coll Cardiol*. 2012;60:2337–2339.
- Puymirat É, Muller O, Sharif F, et al. Fractional flow reserve: concepts, applications and use in France in 2010. *Arch Cardiovasc Dis*. 2010;103:615–622.
- Lakhter V, Zack CJ, Bove AA, Bashir R. National utilization rates of fractional flow reserve in guiding coronary revascularization. *Circulation*. 2012;126: A18105–A18105.
- Samady H, Gogas BD. Does flow during rest and relaxation suffice? *J Am Coll Cardiol*. 2013;61:1436.
- Hennigan B, Oldroyd KG, Berry C, et al. Discordance between resting and hyperemic indices of coronary stenosis severity. *Circ Cardiovasc Interv*. 2016;9: e004016.
- Patel MR, Calhoon JH, Dehmer GJ, et al. C. J. H. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2017;69:2141–2212.
- Patel MR, Calhoon JH, Dehmer GJ, et al. C. J. H. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2016 appropriate use criteria for coronary revascularization in patients with acute coronary syndrome: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2017;69:570–591.