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ROLE OF FFR IN DEFINING THE NEED TO INTERVENE IN THE SIDE BRANCH IN THE TREATMENT OF TRUE BIFURCATIONS

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CONFLITO DE INTERESSE

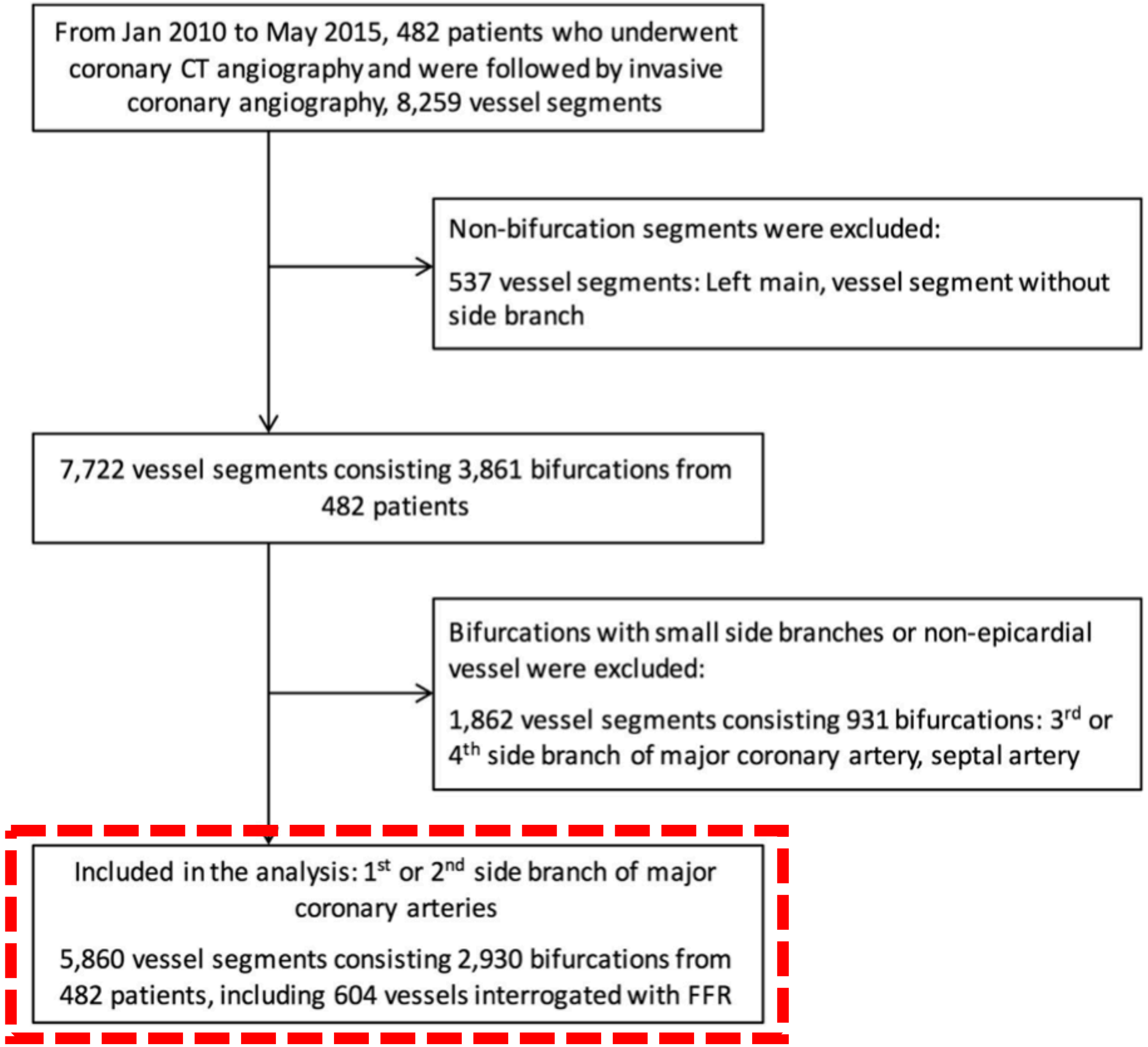
NO CONFLICTS FOR THIS ISSUE

CHALLENGES

1. Bifurcations are frequent in daily practice and account for 1 of 5 in PCI;
2. Coronary bifurcations supply 2 different territories of myocardium subtended by the main vessel and the side branch , respectively. It often necessitates simultaneous 2-balloon dilation or stent implantation in both vessels;
3. Despite advances in technology and devices, PCI of a bifurcation lesion is still limited by higher periprocedural myocardial infarction and long-term adverse events such as stent thrombosis, compared with a non-bifurcation lesion;
4. Identification of a side branch supplying a myocardial mass that benefits more from revascularization than optimal medical therapy may clarify the need of additional procedures for the SB, and may guide optimal revascularization strategy for bifurcation.

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 10, NO. 6, 2017 MARCH 27, 2017:571–81

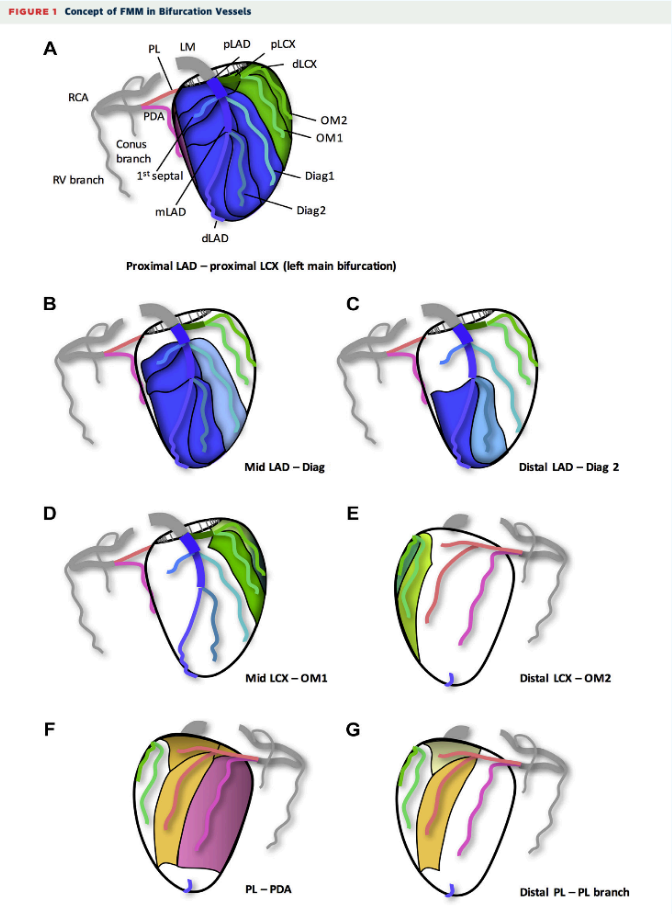
FIGURE 2 Study Enrollment

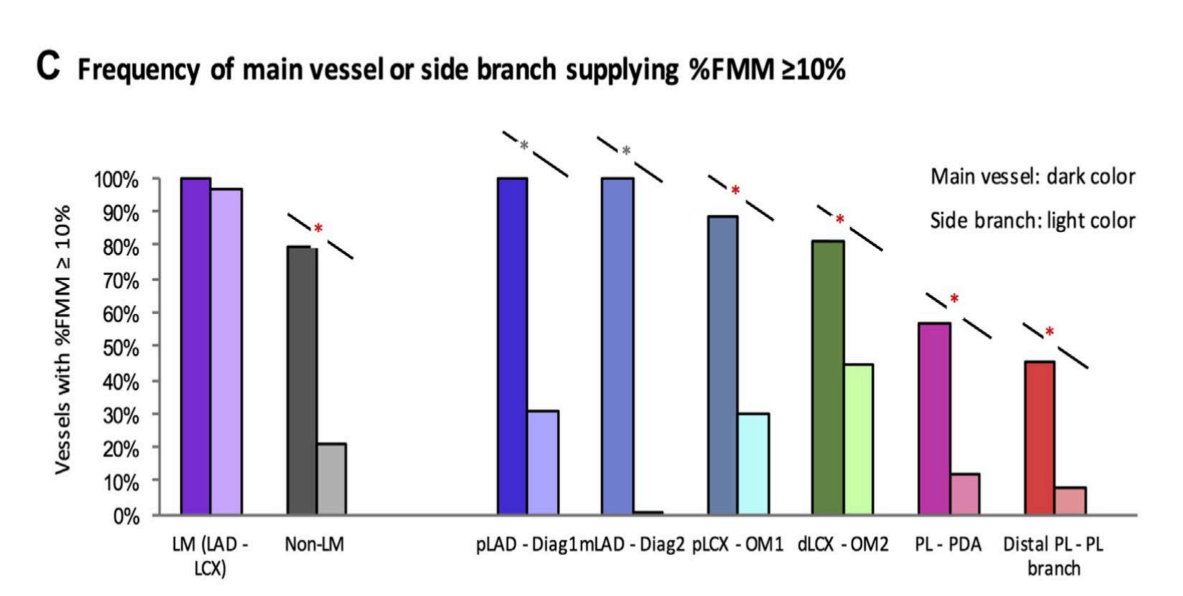


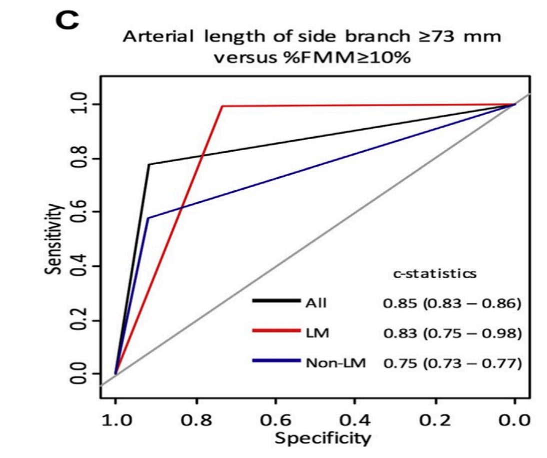
FFR = fractional flow reserve; CT = computed tomography.

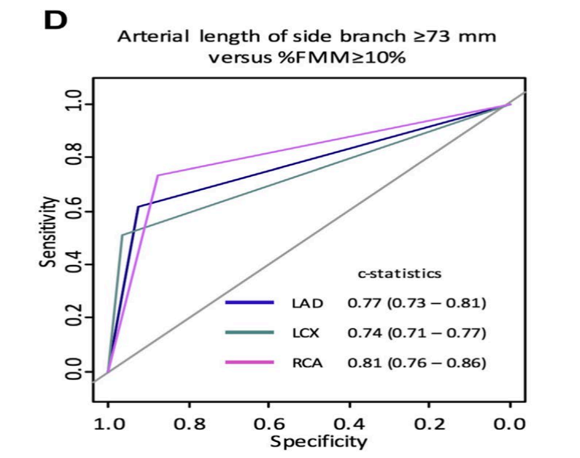
Kimetal. Myocardial Mass Subtended by Bifurcation JACC: CARDIOVASCULAR INTERVENTIONS VOL. 10, NO. 6, 2017 MARCH 27, 2017:571–81

THE BEGINING: identification of a SIDE BRANCH supplying a myocardial mass









Kimetal.
Myocardial Mass Subtended by Bifurcation
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Representative Cases of SB With %FMM >10% and SB With %FMM <10%

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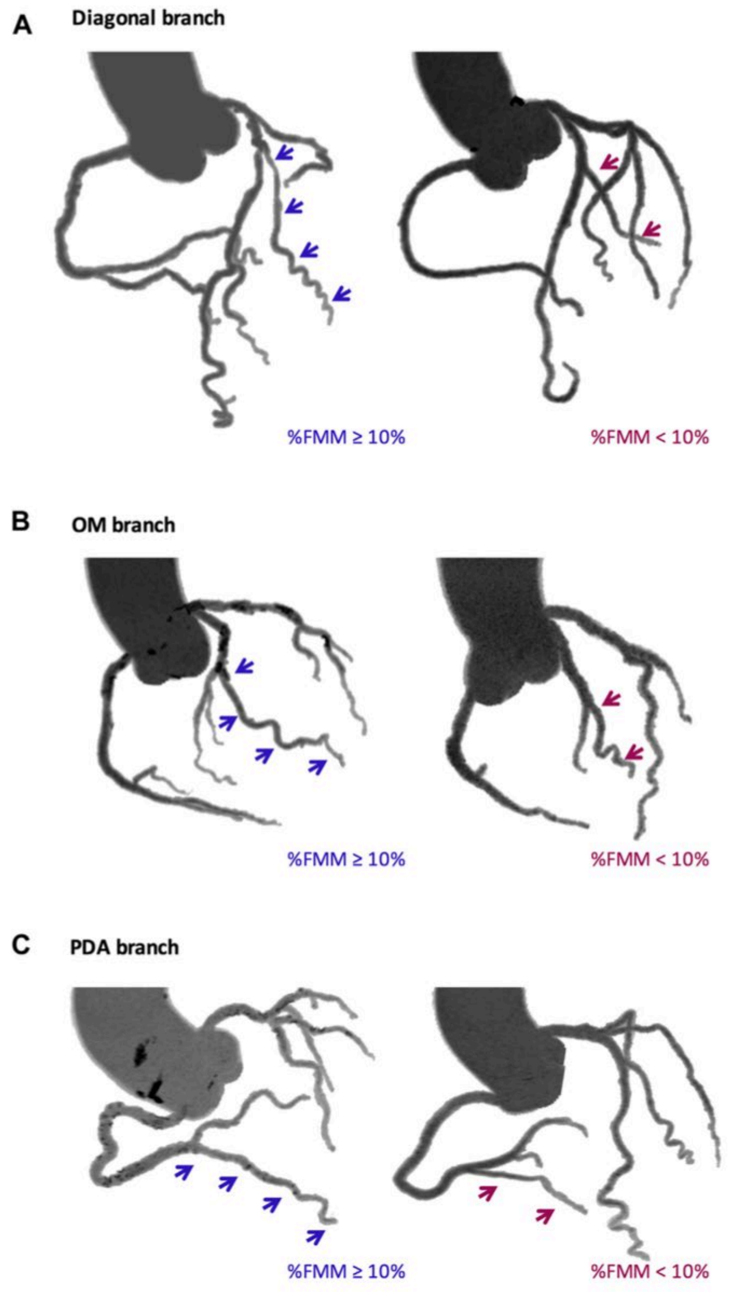
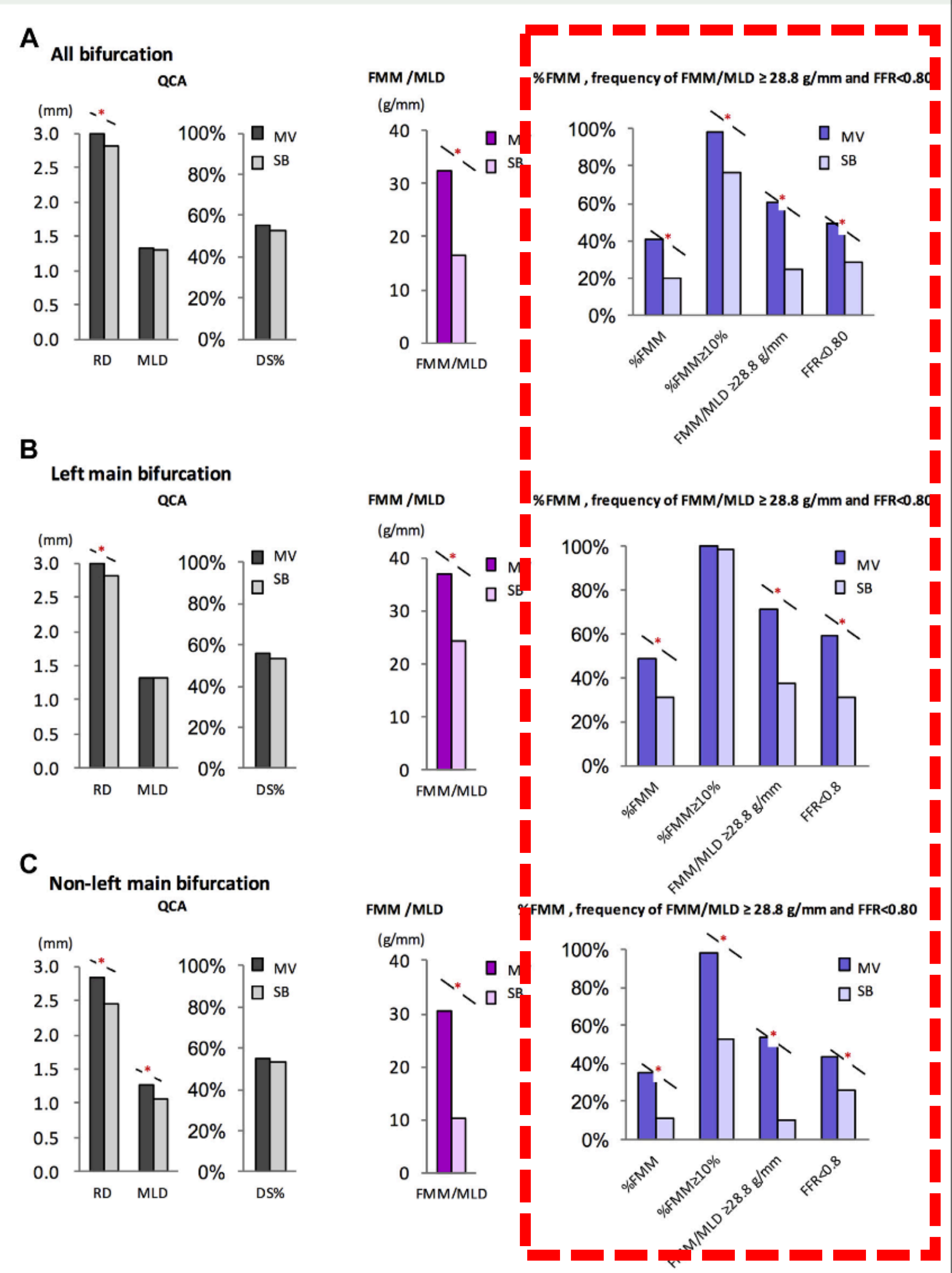
FIGURE 5 **Representative Cases of SB With %FMM ≥10% and SB With %FMM <10%**



Simulated angiography images derived from coronary computed tomography angiography (CCTA). **Colored arrows** indicate SB with %FMM ≥10% **(blue)** or <10% **(pink)**. Abbreviations as in Figures 1 and 3.

Comparison of Anatomic and Physiological Assessment Between MV and SB

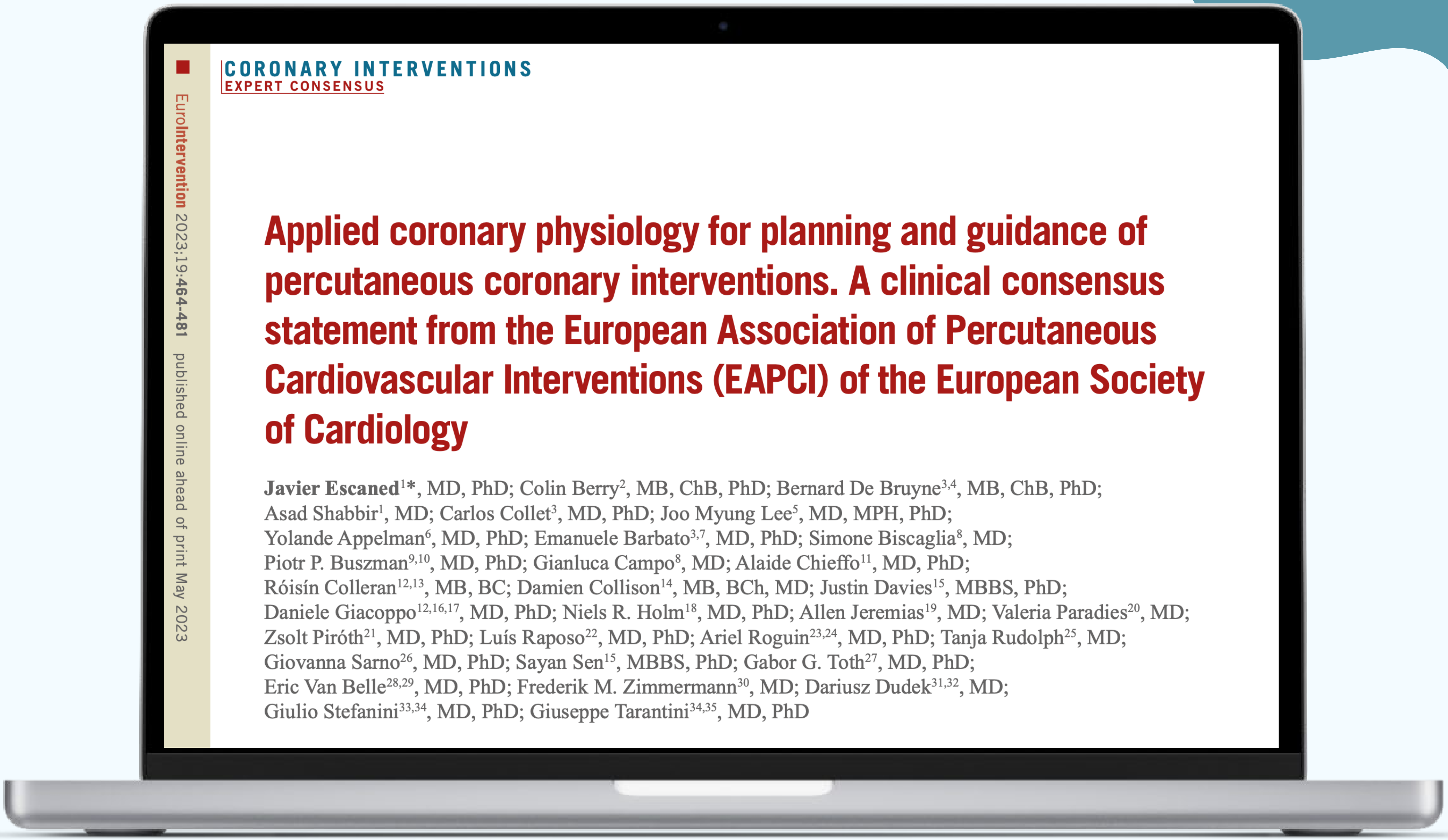
FIGURE 6 Comparison of Anatomic and Physiological Assessment Between MV and SB



WHAT IS KNOWN?
In bifurcation percutaneous coronary intervention, a side branch supplying a clinically relevant amount of myocardium may deserve aggressive treatment. However, identification of such a side branch is challenging.

WHAT IS NEW?
Only one-fifth of non-left main bifurcation side branches supplied a myocardial mass 10%, which could be reasonably identified by vessel length 73 mm.

WHAT IS NEXT?
Pre-procedural recognition of myocardial mass subtended by the main vessel and side branch may guide an optimal revascularization strategy for bifurcation.


CORONARY INTERVENTIONS
EXPERT CONSENSUS

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Applied coronary physiology for planning and guidance of percutaneous coronary interventions. A clinical consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the European Society of Cardiology

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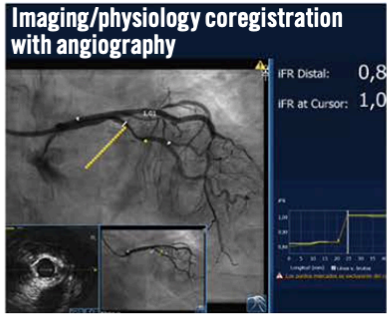
CENTRAL **ILLUSTRATION** Applications of physiology in planning and guiding PCI procedures.

Preprocedural PCI <u>**planning**</u> and <u>**simulation**</u>

– Setting of indication for PCI
– Identification of disease pattern: focal, tandem, diffuse
– Simulation of functional results with different PCI strategies

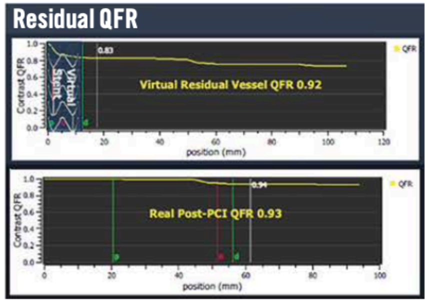
Improving the <u>**precision**</u> of PCI

– Avoidance of geographic mismatch over PCI by identifying location of target flow-limiting disease
– Intravascular imaging for accurate planning and guidance of stenting

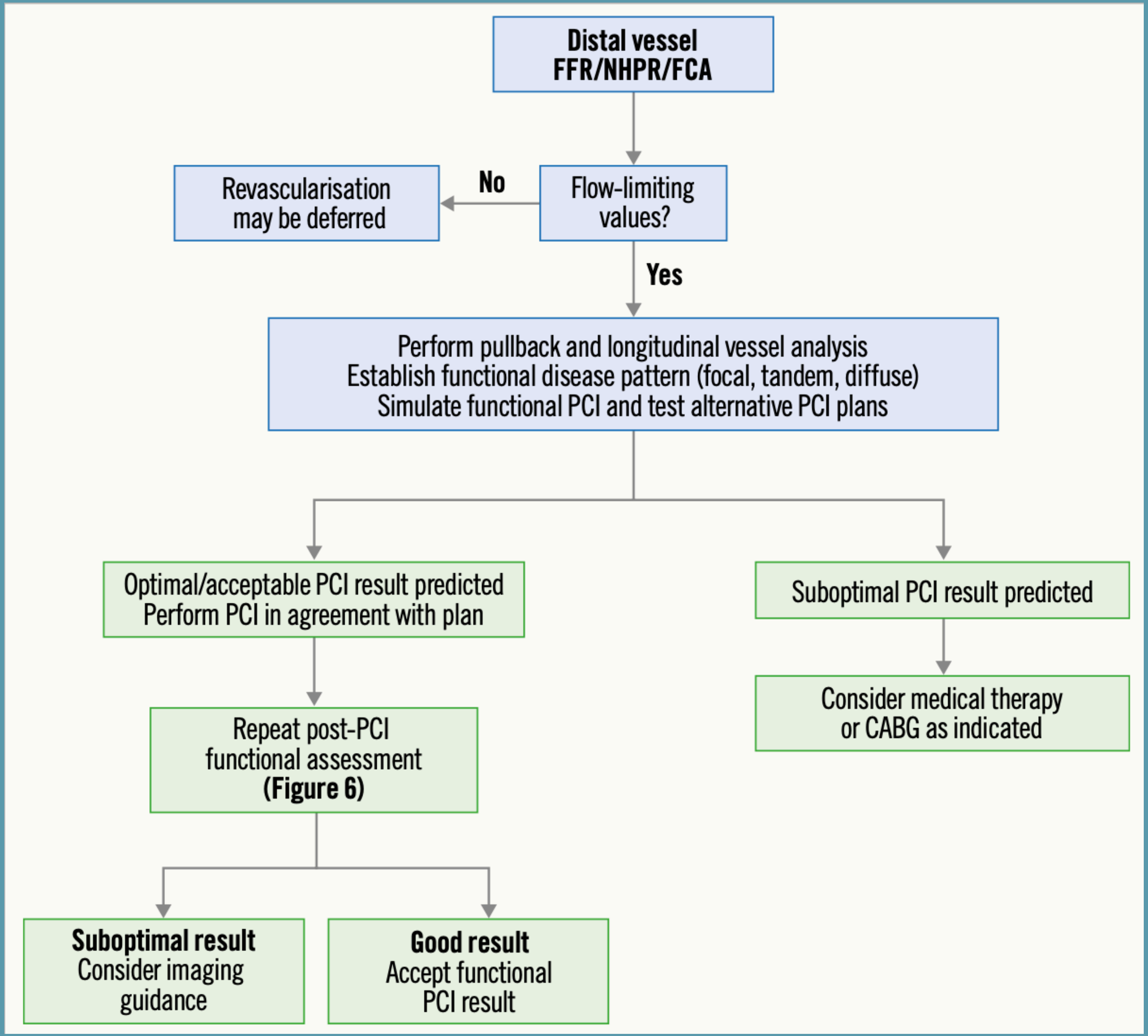


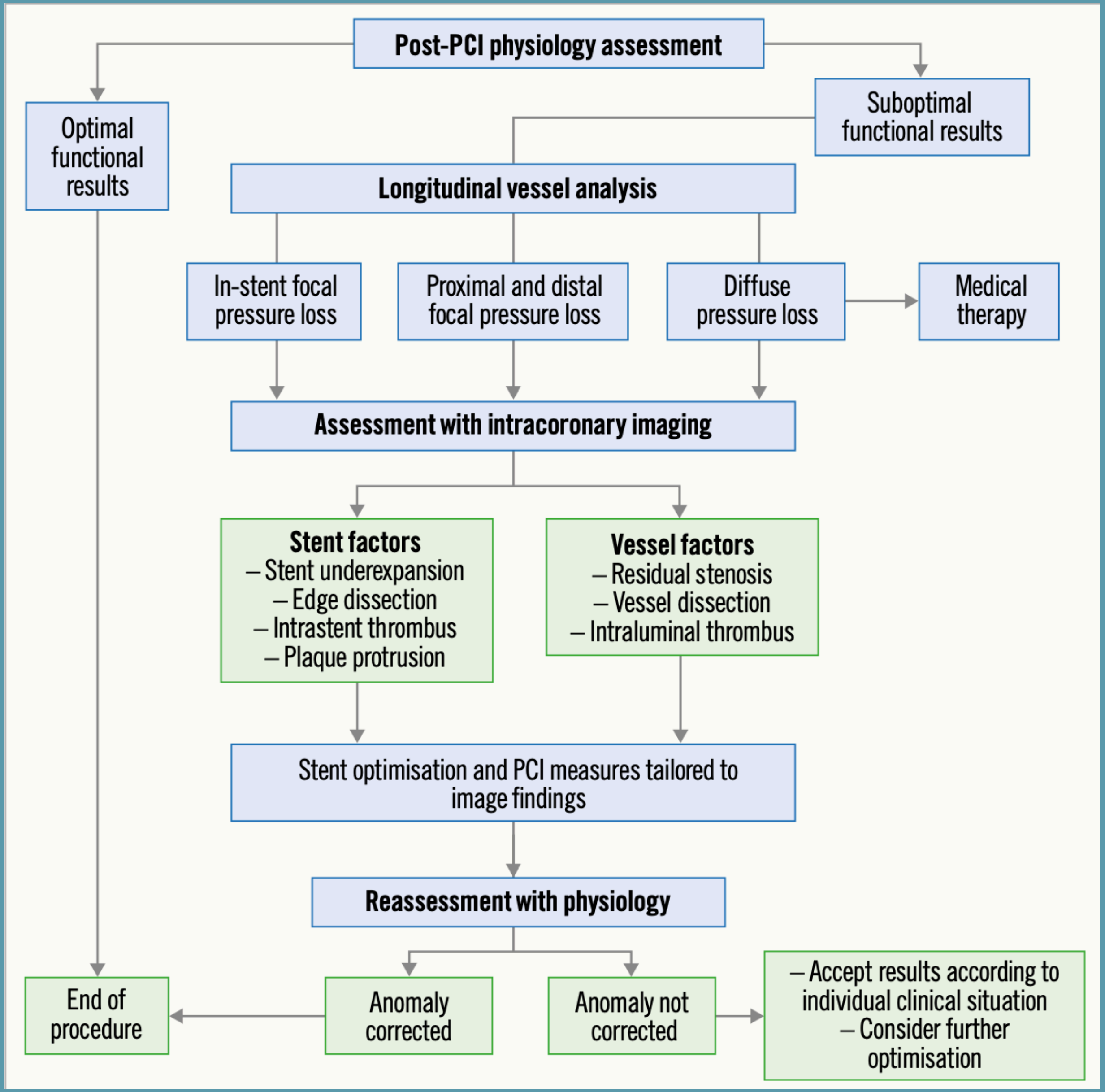
Postprocedural assessment and <u>**optimisation**</u>

– Longitudinal physiology analysis to rule out flow-limiting disease
– Focal patterns may be amenable to post-PCI optimisation



iFR: instantaneous wave-free ratio; PCI: percutaneous coronary intervention; PPG: pullback pressure gradient; QFR: quantitative flow ratio


Distal vessel
FFR/NHPR/FCA
Revascularisation may be deferred
No
Flow-limiting values?
Yes
Perform pullback and longitudinal vessel analysis
Establish functional disease pattern (focal, tandem, diffuse)
Simulate functional PCI and test alternative PCI plans
Optimal/acceptable PCI result predicted
Perform PCI in agreement with plan
Suboptimal PCI result predicted
Consider medical therapy or CABG as indicated
Repeat post-PCI functional assessment
(Figure 6)
Suboptimal result
Consider imaging guidance
Good result
Accept functional PCI result



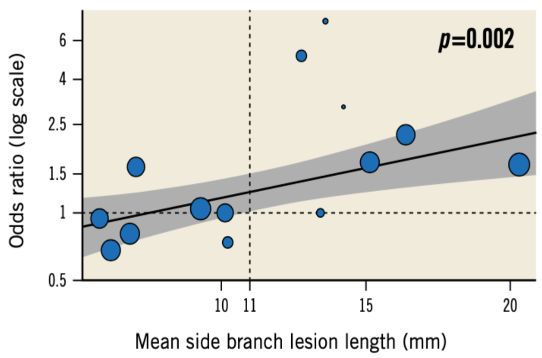
Post-PCI physiology assessment
Optimal functional results
Suboptimal functional results
Longitudinal vessel analysis
In-stent focal pressure loss
Proximal and distal focal pressure loss
Diffuse pressure loss
Medical therapy
Assessment with intracoronary imaging
Stent factors
– Stent underexpansion
– Edge dissection
– Intrastent thrombus
– Plaque protrusion
Vessel factors
– Residual stenosis
– Vessel dissection
– Intraluminal thrombus
Stent optimisation and PCI measures tailored to image findings
Reassessment with physiology
End of procedure
Anomaly corrected
Anomaly not corrected
– Accept results according to individual clinical situation
– Consider further optimisation

Table 1. Objectives of physiological planning and guidance of PCI.

Pre-PCI physiology assessment		
Objective	**Technique**	**Benefit**
Determining the indication for PCI	Pressure wire or FCA to identify the presence of flow-limiting disease	– Management of significant stenoses may confer prognostic or symptom benefit – Deferral of non-flow-limiting disease avoids unnecessary PCI
Identifying patterns of flow-limiting disease	Longitudinal physiological vessel analysis to identify focal, tandem, and diffuse patterns of flow-limiting disease	– Assists in gauging effectiveness of PCI – Aids with planning the length of stent and/or number of stents – Reconsider PCI when a suboptimal result is anticipated
Simulate impact of stenting in specific locations	NHPR and imaging-based functional assessments to simulate relief of stenosis virtually	– Plan effectiveness of PCI before stent deployment – Allows for several simulations prior to PCI
Facilitating precision stent deployment	Correlating physiology and angiography using either coregistration technologies or visual assessment, use of concomitant intracoronary imaging	– Avoidance of geographical miss during stenting, missing flow-limiting lesions – Accurate sizing of balloons and stents
Post-PCI physiology assessment		
Objective	**Technique**	**Benefit**
Ensuring an optimal functional result of PCI	Physiological measurements in PCI target vessel after satisfactory angiographic result, jailed side-branch interrogation	– Early identification of residual flow-limiting disease in the PCI target vessel after the intervention
Identifying potential targets of functional optimisation of PCI	Post-PCI longitudinal vessel analysis	– Establishing the cause of suboptimal functional PCI results – Establishing the feasibility and mode of PCI optimisation
Assessing the impact of PCI optimisation	Repeat physiological measurements after physiology-based optimisation	– Residual disease not amenable to PCI may identify need for directed medical therapy or surgical revascularisation

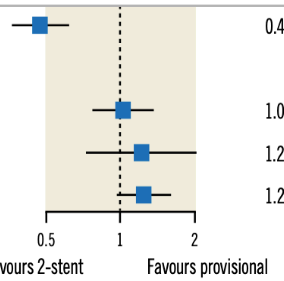
FCA: functional coronary angiography; NHPR: non-hyperaemic pressure ratio; PCI: percutaneous coronary intervention

C Meta-regression by mean side branch lesion length



D Network meta-analysis of 22 RCTs (6,726 patients)

Technique	OR	95% CI	p-value	p-score
DK-crush	0.47	[0.36-0.62]	<0.01	1.00
Provisional	Reference		NA	0.57
Culotte	1.03	[0.77-1.36]	0.86	0.51
T-stenting	1.22	[0.73-2.03]	0.45	0.26
Crush	1.24	[0.97-1.60]	0.09	0.16



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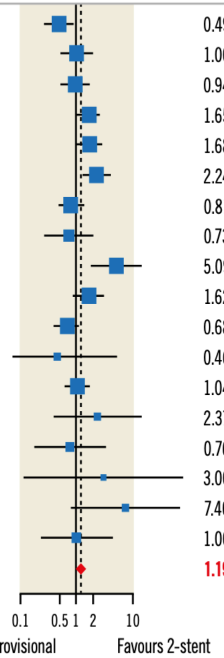
CENTRAL ILLUSTRATION Primary endpoints: major adverse cardiac events at the longest follow-up.

A Pairwise meta-analysis of 18 RCTs (5,022 patients)

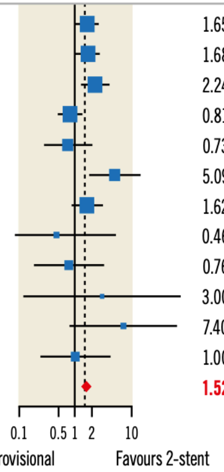
Study	OR	95% CI	Weight
BBC ONE, 2010	0.49	[0.27-0.86]	7.7%
BBK I, 2015	1.00	[0.52-1.93]	7.0%
CACTUS, 2009	0.94	[0.53-1.68]	7.6%
DEFINITION II, 2022	1.65	[1.04-2.62]	8.7%
DKCRUSH-II, 2017	1.68	[1.00-2.83]	8.1%
DKCRUSH-V, 2019	2.24	[1.27-3.96]	7.8%
EBC MAIN, 2021	0.81	[0.49-1.32]	8.4%
EBC TWO, 2016	0.73	[0.28-1.94]	4.8%
Lin et al, 2010	5.09	[1.85-13.97]	4.6%
NBBS IV, 2020	1.62	[0.88-3.00]	7.4%
NBS, 2013	0.68	[0.41-1.12]	8.3%
Pan et al, 2004	0.46	[0.04-5.22]	1.2%
PERFECT, 2015	1.04	[0.63-1.71]	8.4%
Ruiz-Salmerón et al, 2013	2.37	[0.40-13.96]	2.1%
SMART-STRATEGY II, 2021	0.76	[0.18-3.28]	2.8%
Ye et al, 2010	3.00	[0.12-77.17]	0.7%
Ye et al, 2012	7.40	[0.81-67.20]	1.4%
Zhang et al, 2016	1.00	[0.24-4.23]	2.9%
Random effects model	1.19	[0.90-1.58]	



Heterogeneity: I^2=58% [29%; 75%], τ^2=0.1874, χ^2_{17}=40.41 (p<0.01)

B Sensitivity analysis of true bifurcations (3,082 patients)

Study	OR	95% CI	Weight
DEFINITION II, 2022	1.65	[1.04-2.62]	15.5%
DKCRUSH-II, 2017	1.68	[1.00-2.83]	14.4%
DKCRUSH-V, 2019	2.24	[1.27-3 96]	13.5%
EBC MAIN, 2021	0.81	[0.49-1.32]	14.9%
EBC TWO, 2016	0.73	[0.28-1.94]	7.8%
Lin et al, 2010	5.09	[1.85-13.97]	7.4%
NBBS IV, 2020	1.62	[0.88-3.00]	12.7%
Pan et al, 2004	0.46	[0.04-5.22]	1.8%
SMART-STRATEGY II, 2021	0.76	[0.18-3.28]	4.3%
Ye et al, 2010	3.00	[0.12-77.17]	1.0%
Ye et al, 2012	7.40	[0.81-67.20]	2.1%
Zhang et al, 2016	1.00	[0.24-4.23]	4.4%
Random effects model	1.52	[1.08-2.13]	



Heterogeneity: I^2=46% [0%; 72%], τ^2=0.1370, χ^2_{17}=20.37 (p<0.04)
Test for overall effect: z=2.40 (p=0.02)

Clinical outcomes following different stenting techniques for coronary bifurcation lesions: a systematic review and network meta-analysis of randomised controlled trials

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FIGURE 1 Study Flowchart

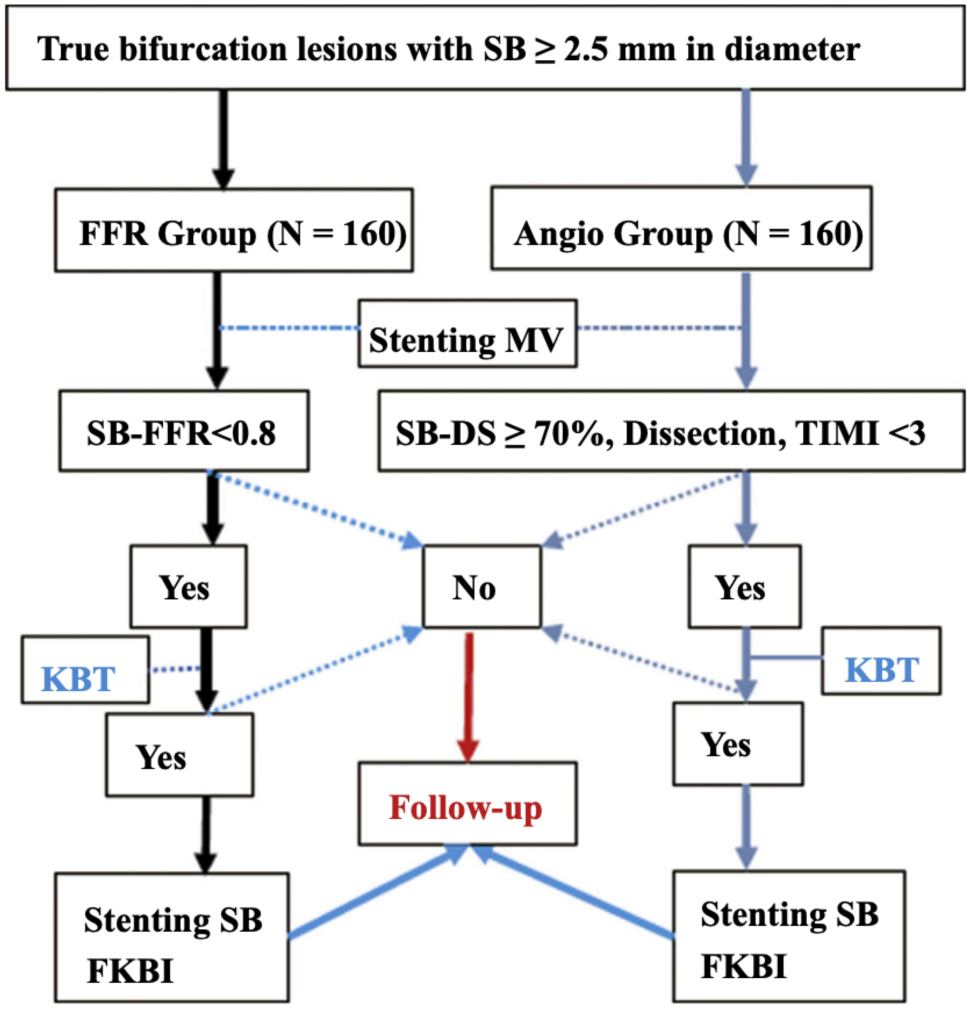
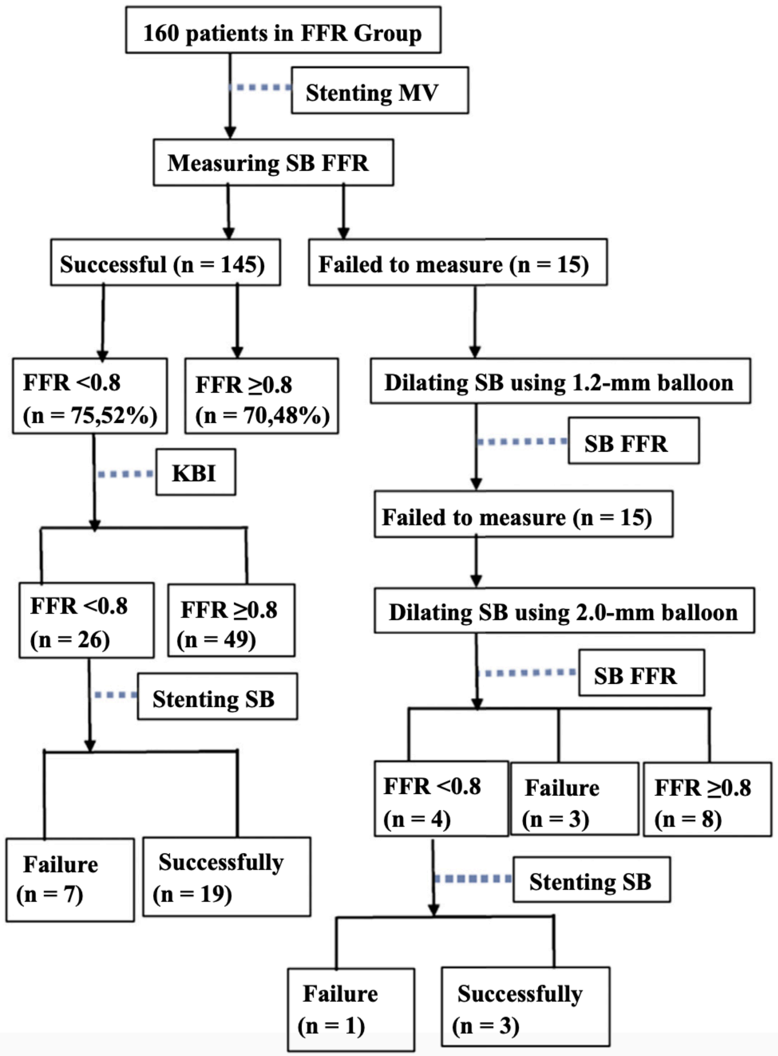


FIGURE 2 Description of the Study Flow in the FFR-Guided Group



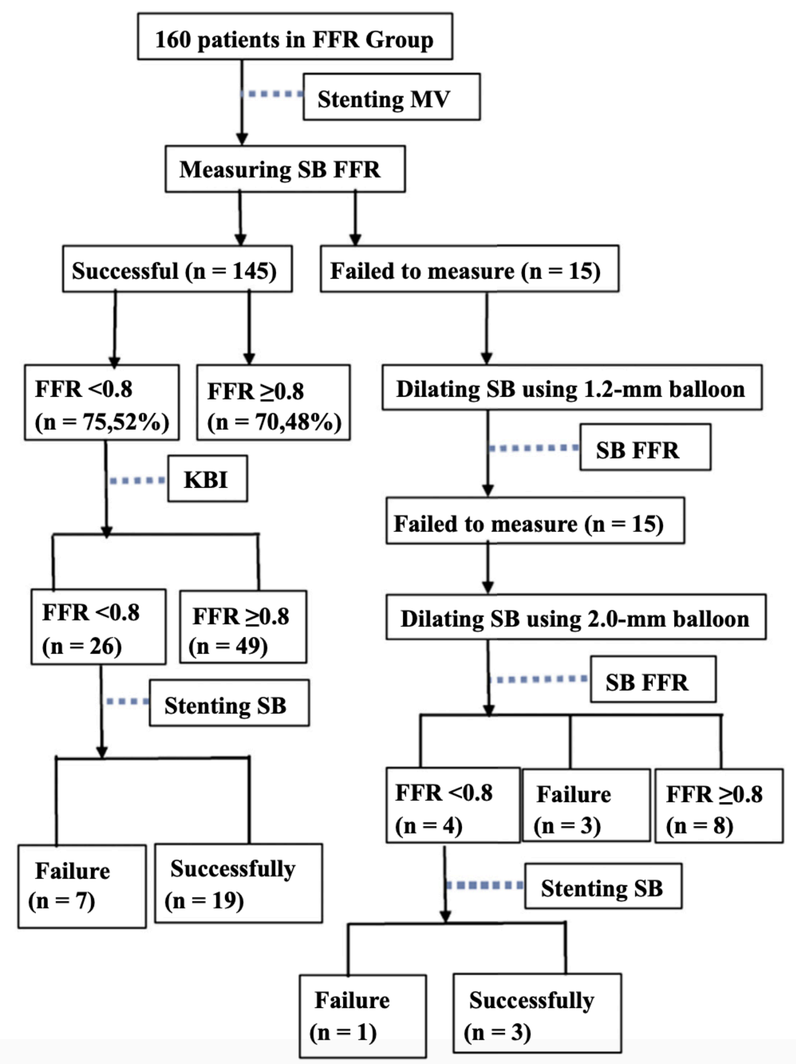
JACC: CARDIOVASCULAR INTERVENTIONS VOL. 8, NO. 4, 2015 APRIL 20, 2015:536–46

Randomized Comparison of FFR-Guided and Angiography-Guided Provisional Stenting of True Coronary Bifurcation Lesions

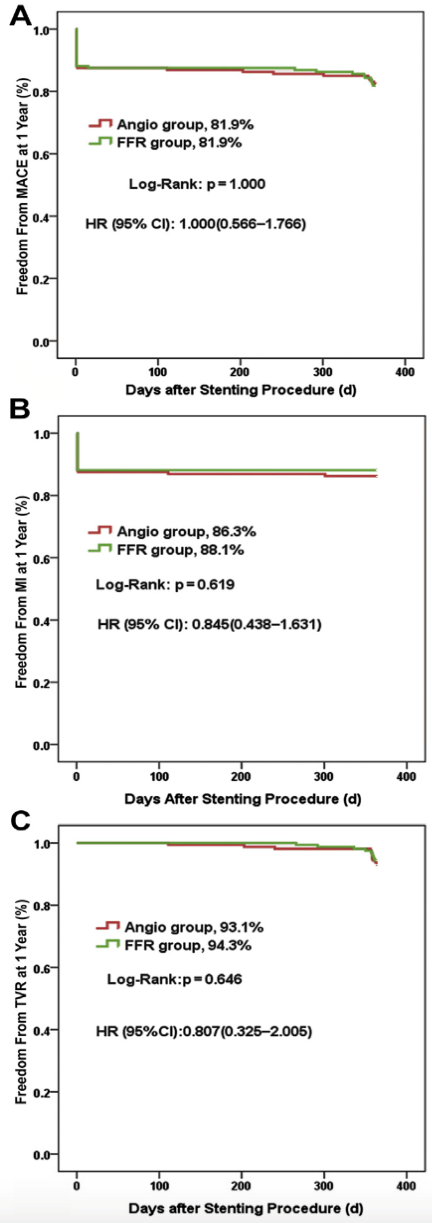
The DKCRUSH-VI Trial (Double Kissing Crush Versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions VI)

Shao-Liang Chen, MD,[*,†] Fei Ye, MD,[*] Jun-Jie Zhang, PhD,[*] Tian Xu, MBBS,[‡] Nai-Liang Tian, MD,[‡] Zhi-Zhong Liu, PhD,[‡] Song Lin, MD,[§] Shou-Jie Shan, MD,[*] Zhen Ge, MD,[*] Wei You, MD,[‡] Yue-Qiang Liu, MD,[§] Xue-Song Qian, MD,[||] Feng Li, MD,[¶] Song Yang, MD,[#] Tak W. Kwan, MD,[**] Bo Xu, MBBS,[††] Gregg W. Stone, MD[‡‡]

FIGURE 2 Description of the Study Flow in the FFR-Guided Group



Event-Free Survival During Follow-Up



JACC: CARDIOVASCULAR INTERVENTIONS VOL. 8, NO. 4, 2015 APRIL 20, 2015:536–46

CONCLUSIONS OF METANALYSIS

1. **There was no significant difference between PS and 2-stent techniques.**

2. **RCTs with true bifurcation lesions were included, there was a lower risk of MACE in patients treated with 2-stent techniques.**

3. **The benefits of the 2-stent strategy were more apparent in patients with longer side branch lesions; this was especially observed in RCTs with a mean lesion length greater than 11 mm.**

4. **When considering all bifurcation strategies individually, DK-crush was associated with the lowest event rates compared to the observed rates of other techniques within each of the included trials.**

Euro**Intervention** 2023;19:**664-675**
Clinical outcomes following different stenting techniques for coronary bifurcation lesions: a systematic review and network meta-analysis of randomised controlled trials

Intracoronary physiological assessment is acknowledged as a valuable strategy to identify the presence of flow-limiting epicardial stenoses in patients with chronic coronary syndromes.

When prior evidence of myocardial ischaemia is not available, FFR or instanta- neous wave-free ratio (iFR) are recommended by the guidelines to assess the haemodynamic relevance of intermediate-grade coronary stenoses. FFR can also be considered in patients with multivessel disease undergoing PCI.

Improving preprocedural planning and simulation, 2) improving intraprocedural precision of PCI in addressing flow- limiting disease, and 3) guiding procedural optimisation of subopstimal PCI results.

A post-PCI FFR ≥0.90 has been associated with a significantly lower risk of repeat PCI and MACE in a systematic review of 7,470 patients.

The most robust recent data, obtained in a patient-level meta-analysis of 5,869 vessels treated with modern drug-eluting stents, reported optimal post-PCI FFR cut-off values of 0.86 for target vessel failure and 0.80 for the composite of cardiac death or target vessel myocardial infarction.

For NHPR, a post-PCI iFR ≥0.95 was associated with improved patient outcomes in the DEFINE PCI study. An optimal cut-off for post-PCI distal coronary pressure/aortic pressure (Pd/Pa) ratio of >0.96 has also been proposed.

Bifurcation lesions and jailed side branches

1. There is a paucity of studies evaluating bifurcation lesions with invasive physiology.

2. Angiographic guidance, the standard approach to guide PCI of bifurcation lesions, frequently overestimates side branch (SB)-lesion severity.

3. Physiologic assessment of bifurcation anatomy may further assist PCI strategy and indicate the necessity of adopting a non-provisional strategy in some instances. In the Nordic-Baltic Bifurcation Study III, systematic kissing-balloon (KB) led to higher SB FFR values (0.92 versus 0.85 with no-KB; P=0.011), but the difference was not clinically relevant, and attenuated over time (0.91 versus 0.87; P=0.19).

4. Compared with an angiography-guided approach, an FFR-guided PCI strategy in bifurcation PCI provided similar rates of functionally adequate revascularisation and hard cardiac events with less stent implantation and was associated with numerically lower rates of TVF and stent thrombosis.

5. In the DKCRUSH-VI study, patients were randomly assigned to FFR or angiography guided SB-PCI, which led to fewer stents being placed (25.9% in the FFR arm versus 38.1% in the angiography arm, P=0.01), less main branch (MB) restenosis in the physiology guided group (1.2% versus 9.2%, P=0.01), and no difference in MACE.

6. Thus, provided that coronary flow is normal, and signs of acute ischemia are absent after main- branch stenting, current evidence suggests that a pressure-wire based provisional approach is feasible, yielding reliable clinical outcomes.

7. Recent work has also supported the use of jailed pressure guidewires for continuous SB monitoring, which seems safe and feasible, even with high-pressure MB inflations using non-compliant balloons, however large prospective studies are lacking.

THANK YOU

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