Hot Topics Left Main & MVD PCI

Insight from All Data of Left Main Revascularization (MAINCOMPARE, SYNTAX, PRECOMBAT, NOBLE, EXCEL)

Duk-Woo Park, MD

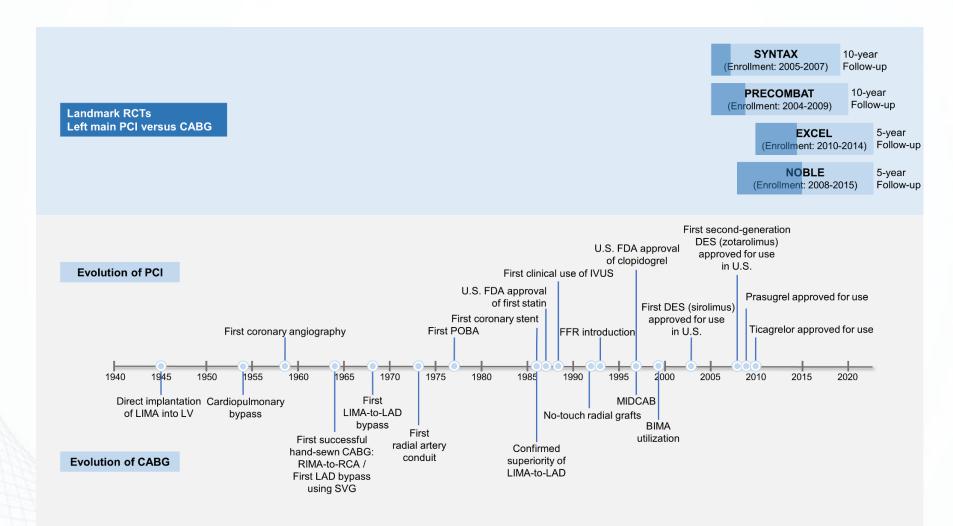
Asan Medical Center, Ulsan University College of Medicine, Seoul, Korea



Disclosure

 Institutional grant/research funding to CardioVascular Research Foundation (CVRF, Korea) and/or Asan Medical Center from Abbott, Boston Scientific, Medtronics, Daiichi-Sankyo, Edwards Lifescience, HK InnoN, Daewoong Pharm, and ChongKunDang Pharm.

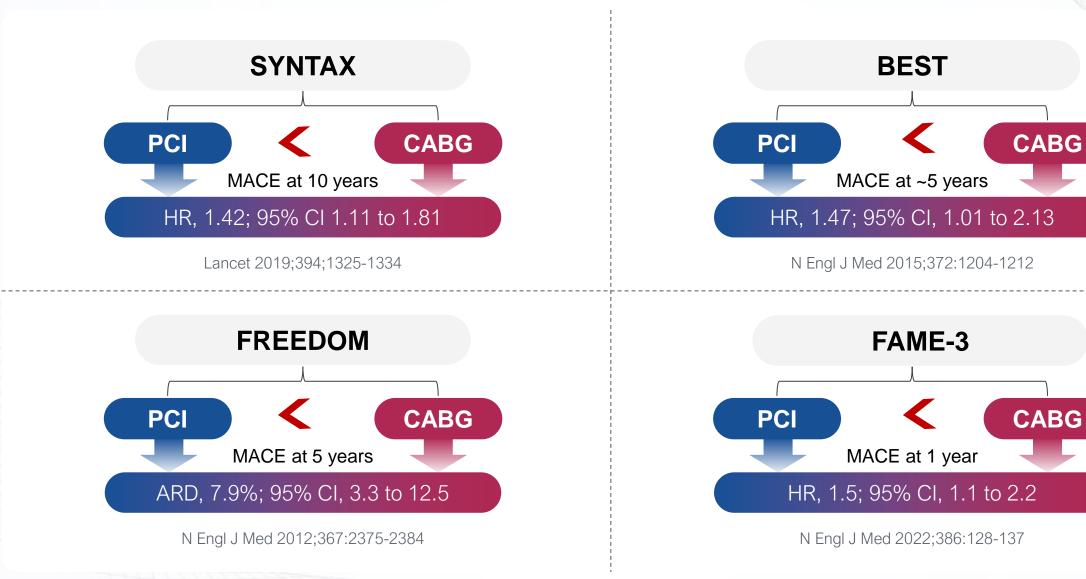
Important Milestones of PCI and CABG and Landmark trials Comparing PCI versus CABG for Left Main Disease



SW Park, DW Park et al. KCJ 2023



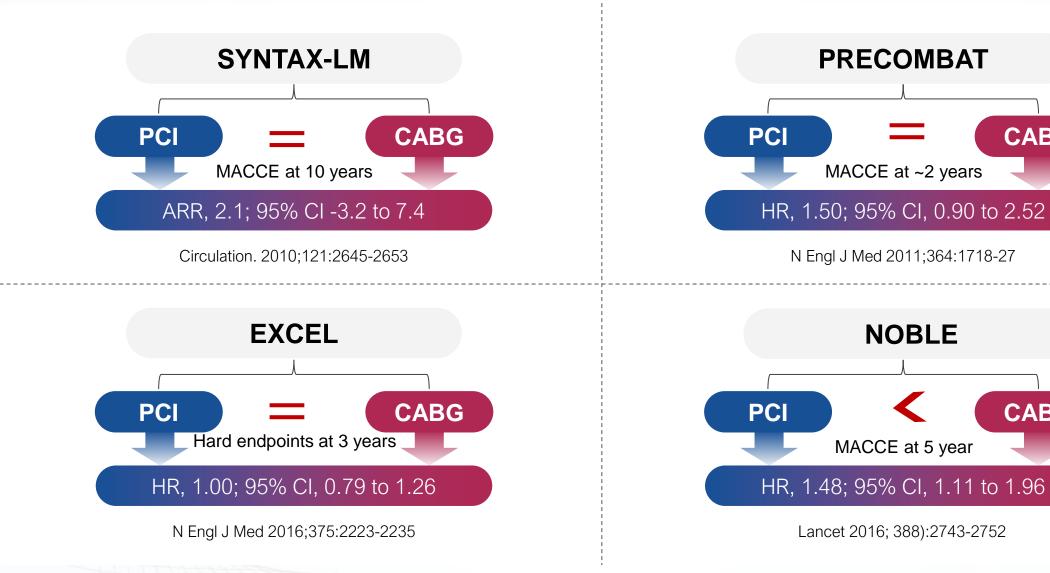
PCI or CABG for multivessel disease



28th TCTAP



PCI vs. CABG for left main disease



CABG

CABG

RCTs Comparing PCI vs. CABG for LM and MVD from Asan Medical Center

MAIN-COMPARE Registry for LM Disease

т ______

PRECOMBAT Trial for LM Disease

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

BEST Trial for Multivessel Disease

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The NEW ENGLAND JOURNAL of MEDICINE EXTABLISHED IN 1812 APRIL 24, 2008 VOL 358 NO. 17

Stents versus Coronary-Artery Bypass Grafting for Left Main Coronary Artery Disease

 Ki Bae Seung, M.D., Duk-Woo Park, M.D., Young-Hak Kim, M.D., Seung-Whan Lee, M.D., Cheol Whan Lee, M.D., Myeong-Ki Hong, M.D., Seong-Wook Park, M.D., Sung-Cheol Yun, Ph.D., Hyeon-Cheol Gwon, M.D.,
 Myung-Ho Jeong, M.D., Yangsoo Jang, M.D., Hyo-Soo Kim, M.D., Purn Joon Kim, M.D., In-Whan Seong, M.D.,
 Hun Sik Park, M.D., Taehoon Ahn, M.D., In-Ho Chae, M.D., Seung-Jea Tahk, M.D., Wook-Sung Chung, M.D., and Seung-Jung Park, M.D.

N Engl J Med 2008;358:1781-92

Randomized Trial of Stents versus Bypass

Surgery for Left Main Coronary Artery Disease

Seung-Jung Park, M.D., Young-Hak Kim, M.D., Duk-Woo Park, M.D., Sung-Cheol Yun, Ph.D., Jung-Min Ahn, M.D., Hae Geun Song, M.D., Jong-Young Lee, M.D., Won-Jang Kim, M.D., Soo-Jin Kang, M.D.,
Seung-Whan Lee, M.D., Cheol Whan Lee, M.D., Seong-Wook Park, M.D., Cheol-Hyun Chung, M.D., Jae-Won Lee, M.D., Do-Sun Lim, M.D.,
Seung-Woon Rha, M.D., Sang-Gon Lee, M.D., Hyeon-Cheol Gwon, M.D., Hyo-Soo Kim, M.D., In-Ho Chae, M.D., Yangsoo Jang, M.D.,
Myung-Ho Jeong, M.D., Seung-Jea Tahk, M.D., and Ki Bae Seung, M.D.

N Engl J Med 2011;364:1718-27

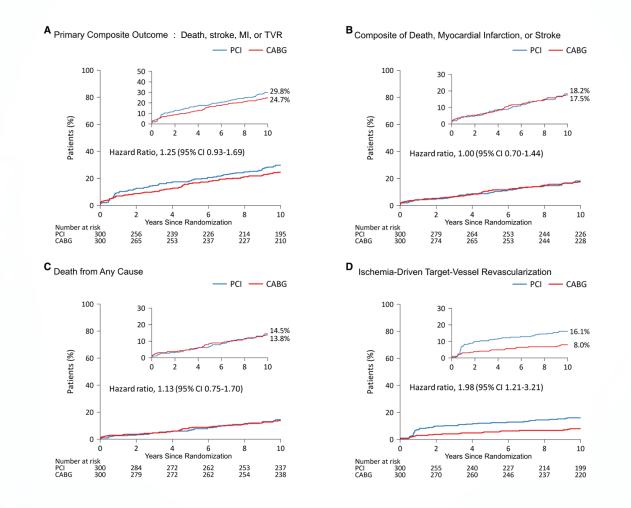
Trial of Everolimus-Eluting Stents or Bypass Surgery for Coronary Disease

Seung-Jung Park, M.D., Ph.D., Jung-Min Ahn, M.D., Young-Hak Kim, M.D., Duk-Woo Park, M.D., Sung-Cheol Yun, Ph.D., Jong-Young Lee, M.D., Soo-Jin Kang, M.D., Seung-Whan Lee, M.D., Cheol Whan Lee, M.D., Seong-Wook Park, M.D., Suk Jung Choo, M.D., Cheol Hyun Chung, M.D., Jae Won Lee, M.D., David J. Cohen, M.D., Alan C. Yeung, M.D., Seung Ho Hur, M.D., Ki Bae Seung, M.D., Tae Hoon Ahn, M.D., Hyuck Moon Kwon, M.D., Do-Sun Lim, M.D., Seung-Woon Rha, M.D., Myung-Ho Jeong, M.D., Bong-Ki Lee, M.D., Damras Tresukosol, M.D., Guo Sheng Fu, M.D., and Tiong Kiam Ong, M.D., for the BEST Trial Investigators*

N Engl J Med 2015;372:1204-12

28th TCTAF

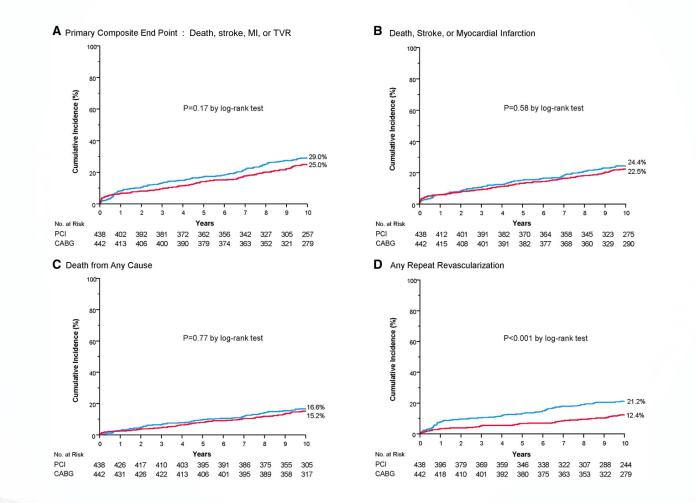
Very Long-Term (10-Year) Outcomes for LM Disease: PRECOMBAT 10-Year Report



28th TCTAF

DW Park, SJ Park et al. 2020 ACC LBCT, Circulation 2020;141:1437-1446.

Very Long-Term (10-Year) Outcomes for MVD Disease: BEST 10-Year Report



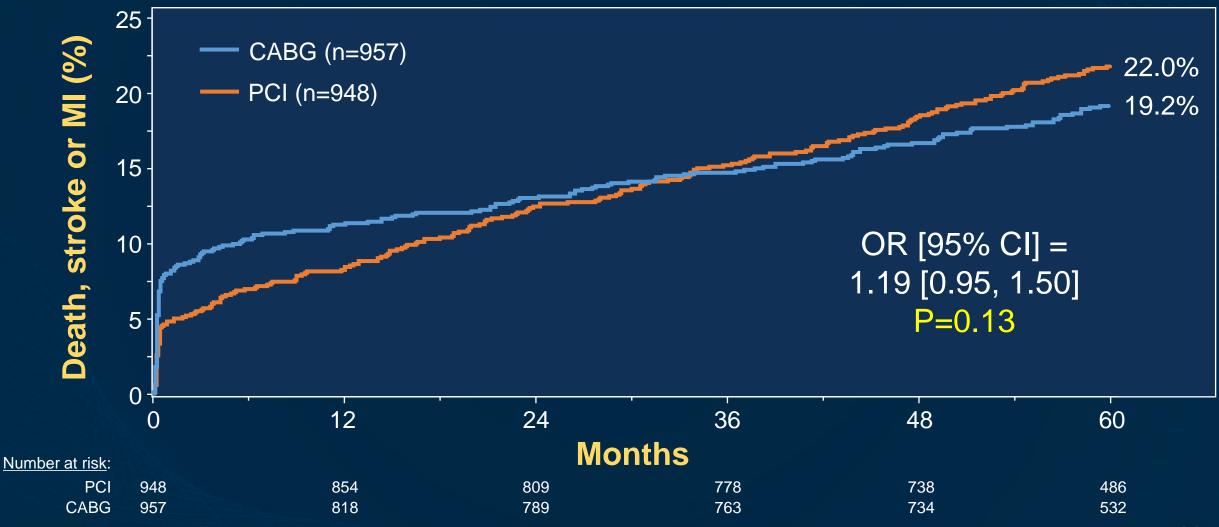
28th TCTAF

JM Ahn, DW Park, SJ Park et al. 2022 TCT LBCT, Circulation 2022;146:1581-1590.

LM PCI vs CABG Controversy = EXCEL Controversy

< Is Mortality Different?

Primary Endpoint All-cause Death, Stroke or MI at 5 Years

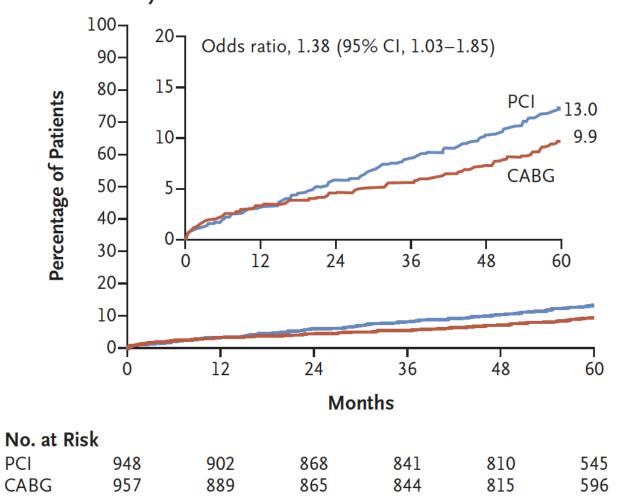


28th TCTAP

Stone GW et al. NEJM 2019;381:1820-30

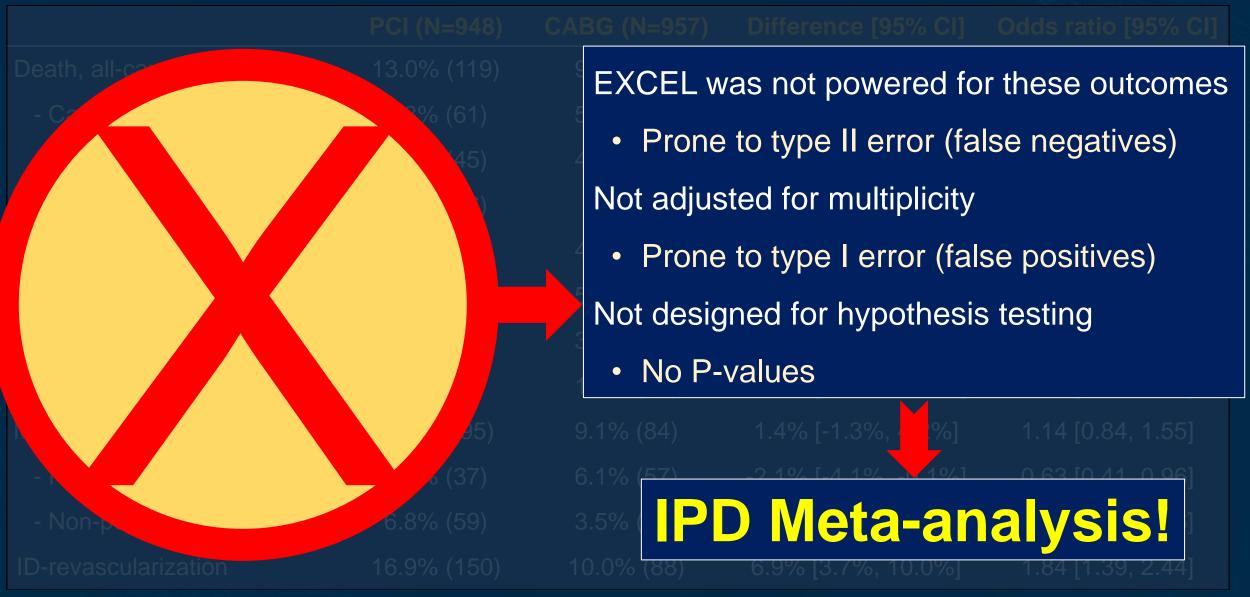
Secondary Endpoint All-cause Mortality at 5 Years

A Death from Any Cause





Individual Outcomes at 5 Years



Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis



Marc S Sabatine^{*}, Brian A Bergmark^{*}, Sabina A Murphy, Patrick T O'Gara, Peter K Smith, Patrick W Serruys, A Pieter Kappetein, Seung-Jung Park, Duk-Woo Park, Evald H Christiansen, Niels R Holm, Per H Nielsen, Greqq W Stone, Joseph F Sabik, Eugene Braunwald

Summary

Background The optimal revascularisation strategy for patients with left main coronary artery disease is uncertain. We therefore aimed to evaluate long-term outcomes for patients treated with percutaneous coronary intervention (PCI) with drug-eluting stents versus coronary artery bypass grafting (CABG).

Methods In this individual patient data meta-analysis, we searched MEDLINE, Embase, and the Cochrane database using the search terms "left main", "percutaneous coronary intervention" or "stent", and "coronary artery bypass graft*" to identify randomised controlled trials (RCTs) published in English between database inception and Aug 31, 2021, comparing PCI with drug-eluting stents with CABG in patients with left main coronary artery disease that had at least 5 years of patient follow-up for all-cause mortality. Two authors (MSS and BAB) identified studies meeting the criteria. The primary endpoint was 5-year all-cause mortality. Secondary endpoints were cardiovascular death, spontaneous myocardial infarction, procedural myocardial infarction, stroke, and repeat revascularisation. We used a one-stage approach; event rates were calculated by use of the Kaplan-Meier method and treatment group comparisons were made by use of a Cox frailty model, with trial as a random effect. In Bayesian analyses, the probabilities of absolute risk differences in the primary endpoint between PCI and CABG being more than 0.0%, and at least 1.0%, 2.5%, or 5.0%, were calculated.

Published Online November 15, 2021 https://doi.org/10.1016/ S0140-6736(21)02334-5 See Online/Comment https://doi.org/10.1016/ S0140-6736(21)02491-0 *Contributed equally

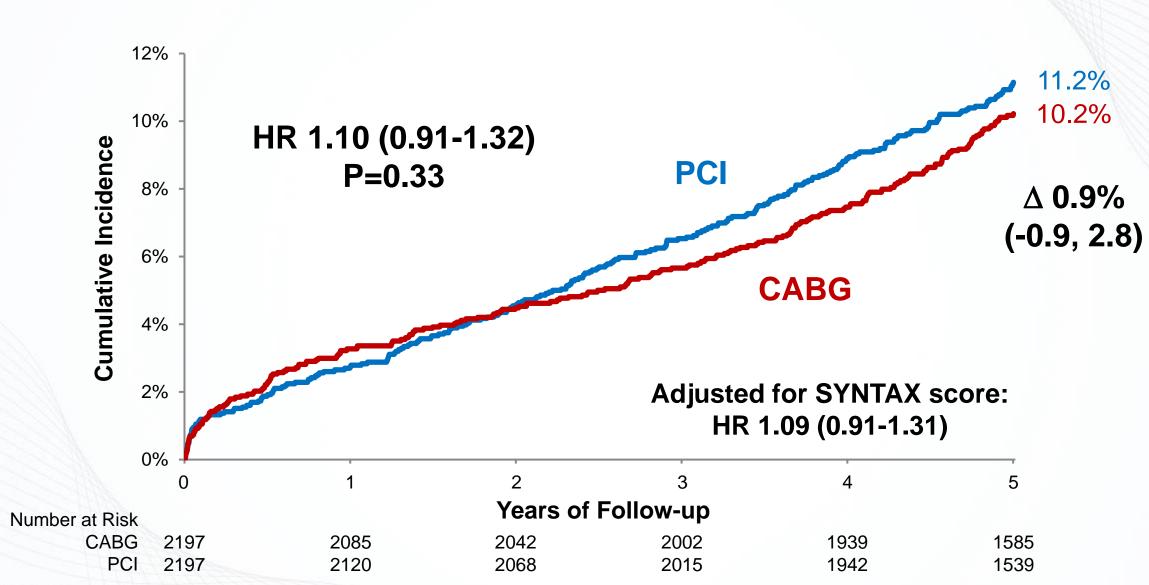
Thrombolysis in Myocardial Infarction Study Group (Prof M S Sabatine MD, B A Bergmark MD, S A Murphy MPH, Prof E Braunwald MD) and Division of Cardiovascular Medicine (Prof M S Sabatine, B A Bergmark, S A Murphy, Prof P T O'Gara MD,

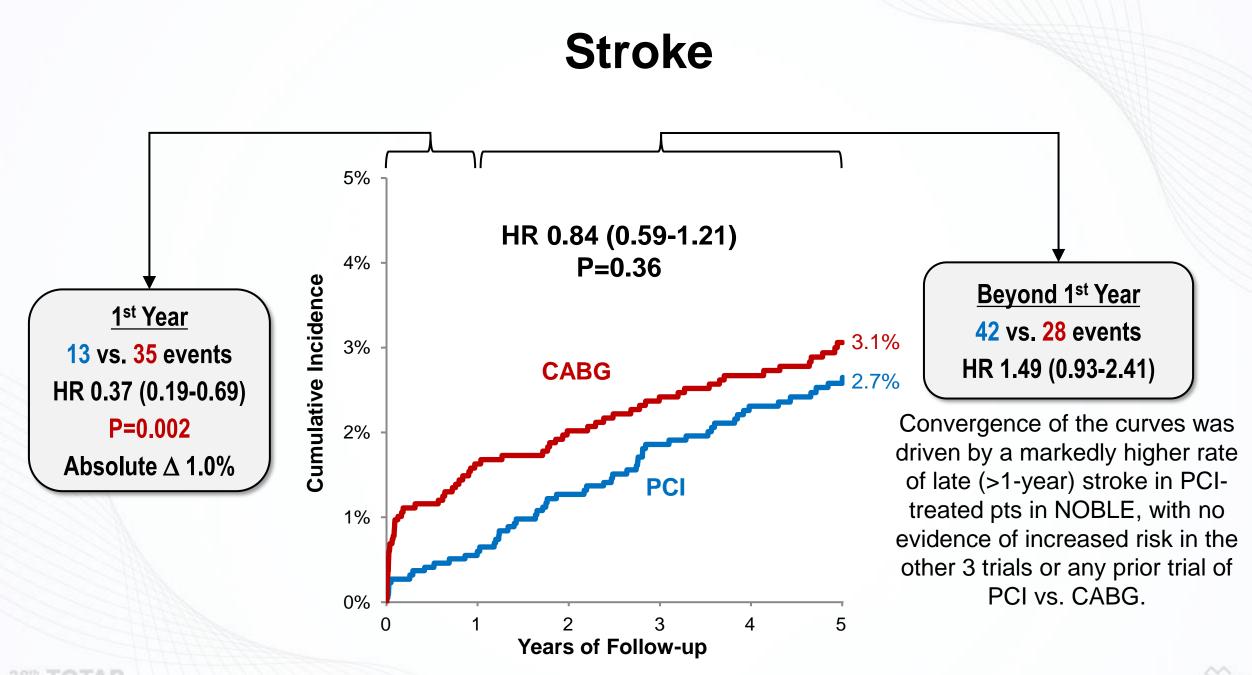
Published online November 15, 2021 https://doi.org/10.1016/S0140-6736(21)02334-5

Trial Summaries

	SYNTAX (LM)	PRECOMBAT	NOBLE	EXCEL		
N	705	600	1201	1905		
Yrs enrol.	2005-2007	2004-2009	2008-2015	2010-2014		
Regions	Europe/NA	Asia/Pacific	Europe	Europe/NA/SA/Asia/Pacific		
PEP	Death, stroke, MI, or repeat revasc	Death, stroke, MI or ID- TVR	Death, stroke, non- procedural MI, or repeat revasc	Death, stroke, or MI		
Key Inclusion	 LMCA ≥50% Stable or unstable angina or silent isch. 	 LMCA ≥50% Silent isch. stable angina, UA, or MI >1wk 	 LMCA ≥50% or FFR ≤0.80 ≤3 other complex lesions Stable angina, NSTEACS, STEMI >24h 	 LMCA ≥70% or 50-70% plus invasive¹ or non- invasive assessment Local SYNTAX ≤32 		
Key Exclusion	Prior PCI/CABGAcute MI	 Prior CABG or LM PCI Prior PCI w/in 12 mo AMI w/in 1 week Plan to treat >1 CTO LVEF <30% 	• STEMI <24 hrs	 Prior CABG or LM PCI Prior PCI w/in 12mo CK-MB >ULN 		

Mortality



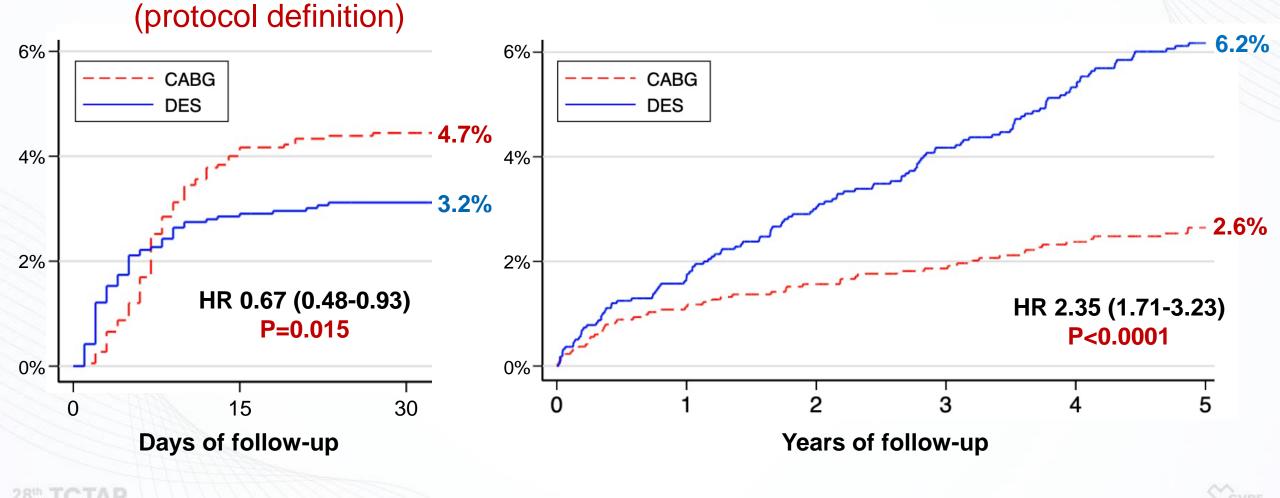


Sabatine MS et al. Lancet 2021;https://doi.org/10.1016/S0140-6736(21)02334-5

Procedural and Spontaneous MI

Procedural MI

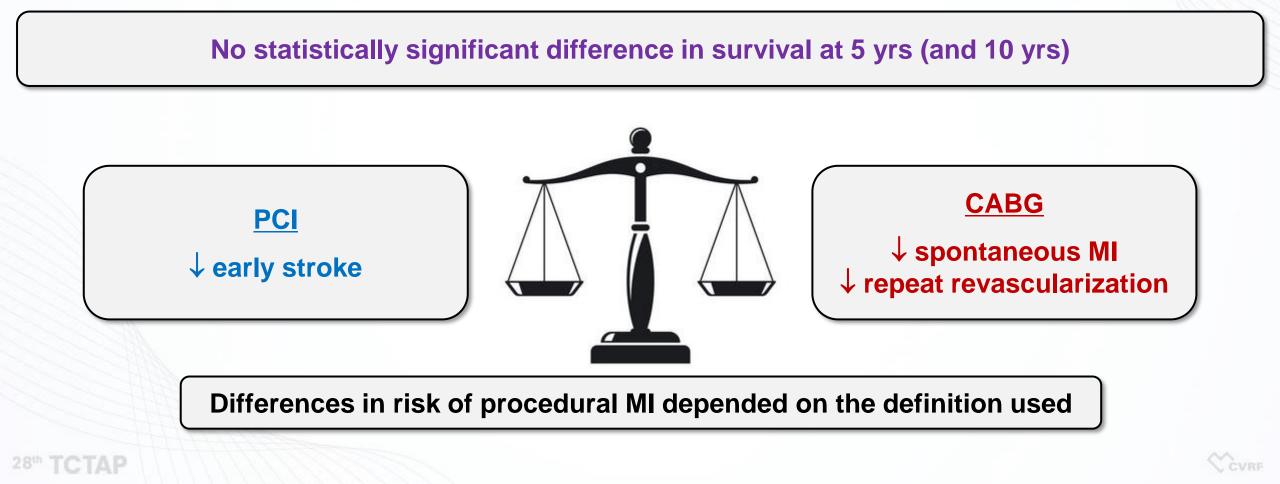
Spontaneous MI



Sabatine MS et al. Lancet 2021;https://doi.org/10.1016/S0140-6736(21)02334-5

Summary: IPD Analysis

Comparing PCI w/ DES vs. CABG in Pts w/ LM CAD, median SYNTAX score of 25, and deemed equally suitable candidates for either revascularization approach:



Contemporary Left Main Guidelines

2021 ACC/AHA/SCAI

Left main CAD

1	B-R	3. In patients with SIHD and significant left main stenosis, CABG is recommended to improve survival (9-12)					
2a	B-NR	4. In selected patients with SIHD and significant left main stenosis for whom PCI can provide equivalent revascularization to that possible with CABG, PCI is reasonable to improve survival (9).					
(Issued	after EXCE	EL)					
		2018 ESC					
Left main	CAD	2018 ESC					
		2018 ESC v SYNTAX score (0 - 22). ^{69,121,122,124,145-148}	1	Α	I	Α	
Left main	disease with low		1	AA	l Ila	A A	

(Issued before EXCEL)

Left Main and Multivessel PCI

There Are Still Unmet Needs



My understanding of available data for LM revascularization

: JACC Asia, State-of-the Art Article

JACC: ASIA

© 2022 THE AUTHORS. PUBLISHED BY ELSEVIER ON BEHALF OF THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION. THIS IS AN OPEN ACCESS ARTICLE UNDER THE CC BY-NC-ND LICENSE (http://creativecommons.org/licenses/by-nc-nd/4.0/).

STATE-OF-THE-ART REVIEW

Percutaneous Coronary Intervention for Left Main Coronary Artery Disease

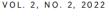
Present Status and Future Perspectives

Sangwoo Park, MD,^a Seung-Jung Park, MD, PнD,^b Duk-Woo Park, MD, PнD^b

ABSTRACT

For several decades, coronary artery bypass grafting has been regarded as the standard choice of revascularization for significant left main coronary artery (LMCA) disease. However, in conjunction with remarkable advancement of device technology and adjunctive pharmacology, percutaneous coronary intervention (PCI) offers a more expeditious approach with rapid recovery and is a safe and effective alternative in appropriately selected patients with LMCA disease. Several landmark randomized clinical trials showed that PCI with drug-eluting stents for LMCA disease is a safe option with similar long-term survival rates to coronary artery bypass grafting surgery, especially in those with low and intermediate anatomic risk. Although it is expected that the updated evidence from recent randomized clinical trials will determine the next guidelines for the foreseeable future, there are still unresolved and unmet issues of LMCA revascularization and PCI strategy. This paper provides a comprehensive review on the evolution and an update on the management of LMCA disease. (JACC: Asia 2022;2:119-138) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/ licenses/by-nc-nd/4.0/).

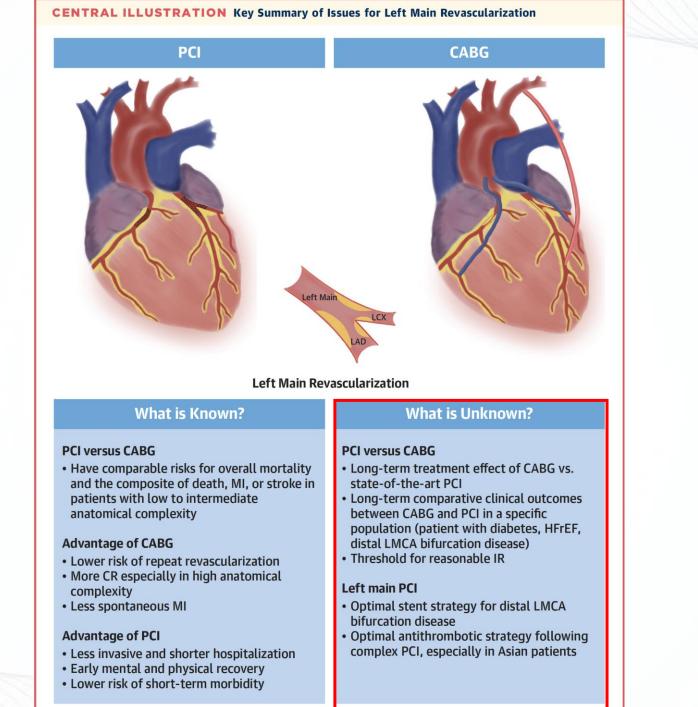
SW Park, DW Park, SJ Park et al. JACC: Asia 2022;2:119–138



Topics	Controversial Points (Why This Issue Is Nonuniform Or Undefined? How Can We Resolve This Issue?)
MI definition	Because there is still no uniform definition of MI that does not penalize one of the revascularization approaches, different protocol definitions of MI were used in trials comparing PCI and CABG for LMCA disease. The interstudy heterogeneity for MI definitions ca result in wide variability across trials and imprecision in estimating the overall treatment effect. Additional studies and efforts b trialists are warranted to improve standardization of the MI definition for future clinical trials comparing PCI and CABG.
Complete (CR) or incomplete revascularization (IR)	Reducing the burden of ischemia would improve clinical outcomes, and current evidence supports complete revascularization. Previous studies investigating the clinical impact of CR and IR have lacked standardized definitions of IR. Also, because of inherent selection bia on the results of previous studies, IR was more frequently associated with sicker patients and more anatomically complex CAD. There is discrepancy in the long-term clinical outcomes of IR between PCI and CABG. In brief, clinical outcomes following IR seem more favorabl after CABG than after PCI. Efforts are needed to standardize the definitions of CR and IR in future studies. Further study is required t validate the optimal degree of revascularization and a reasonable level of IR for acceptable long-term outcomes according to the revascularization strategy. Also, it is needed to identify some subsets of patients with LMCA disease who would benefit more from CF
Role of IVUS or FFR	 With regard to the clinical impact of IVUS guidance for left main PCI, there has been no large, multicenter, randomized clinical trial Based on previous observation, IVUS was more frequently used in a substantially younger and less comorbid population, which might have influenced clinical outcomes. These studies rarely included a prespecified protocol for IVUS guidance and stent optimization. Although the potential role of IVUS in reducing LMCA restenosis and stent thrombosis-related complications may b clinically meaningful, a true clinical effect of IVUS guidance for LMCA PCI can be confirmed only through RCTs. Because it is highl unlikely that the efficacy of IVUS guidance in LMCA PCI is tested in RCTs, trials comparing IVUS-guided LMCA PCI with a prespecifie optimization protocol vs CABG might provide further insight. CR based on the functional definition is the preferred strategy for PCI. However, the role of functional guidance for CABG is less clear The clinical use of resting distal coronary pressure-to-aortic pressure ratio and iFR in guiding revascularization of LMCA disease is yet to be fully validated in RCTs. Further RCTs are needed to conclude these issues.
All-cause mortality or cardiac mortality	Controversy exists regarding whether all-cause mortality or cardiac mortality is preferred as a study endpoint in RCTs comparing PCI t CABG. There has been a debate over conflicting all-cause and cardiac mortality findings shown in the 5-y results of the EXCEL tria The use of cardiac-specific mortality may exclude deaths related to the procedure, either through noncardiac mechanisms or because of misclassification. On the other hand, all-cause mortality is the most unbiased endpoint; however, it may lead to oversimplification by including death that is less attributable to the procedure. Efforts should also be made to find a better consensus and definition of cardiac mortality while discussing which mortality endpoint should be preferred.
Long-term follow-up data beyond 5 or 10 y	Until recently, long-term follow-up studies comparing contemporary PCI and CABG beyond 5 y were still limited. Limited follow-up could have penalized the CABG group because the long-term benefits of CABG over PCI have not typically been fully evident until to 10 y after the procedure. Also, a substantial interaction between treatment effect and time for the risk of major adverse event was noted in EXCEL and NOBLE. Study participants in EXCEL and NOBLE will be followed up beyond 5 y, which will provide additional valuable information.
Optimal antithrombotic strategy and DAPT duration	The optimal strategy for DAPT following complex PCI, such as LMCA bifurcation PCI using the 2-stent technique, still remains unclear Furthermore, it was suggested that the East Asian population tends to have a higher risk of bleeding events but a relatively lower risk of thrombotic events, namely, the East Asian paradox. A guideline and unique regimen specifically for Asian patients or the unique ischemic/bleeding risk score of Asian patients might be useful in tailoring DAPT for this population.
Role of SYNTAX score	The current guideline recommendation for LMCA revascularization is mainly based on the anatomic SYNTAX score. The SYNTAX score failed to clearly differentiate the comparative outcomes between CABG and PCI in EXCEL and NOBLE. The current role of the SYNTAX score as the key factor in decision making for optimal LMCA revascularization needs to be further debated in contemporar clinical practice settings. Also, the SYNTAX score should be interpreted with caution in the context of heart team discussion.

TABLE 6 Unmet Issues on Left Main Revascularization

28th TCTAP



What Are Big Deal? Left Main or Complex PCI in the Contemporary PCI



Can Average Interventional Cardiologists Perform Average-Quality Left Main or Complex Multivessel PCI?



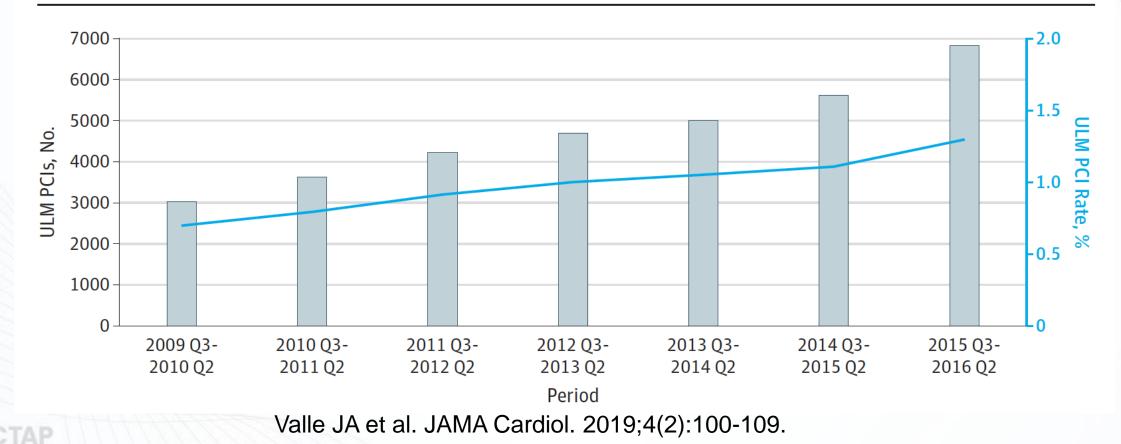


Contemporary Use and Trend of Left Main PCI: US NCDR Database

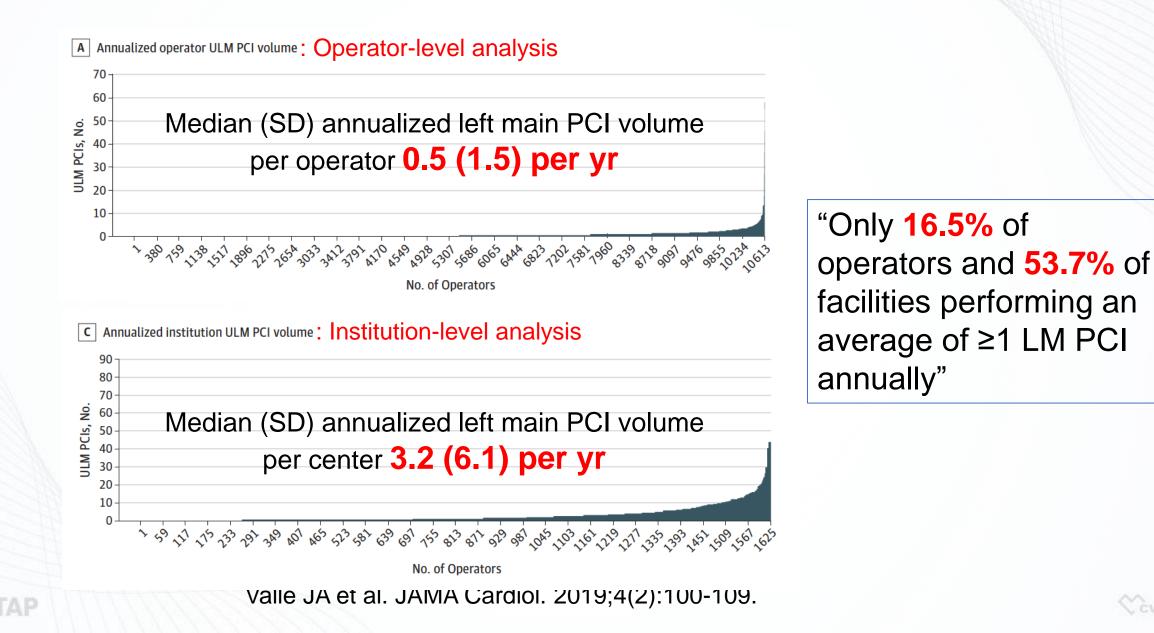
Unprotected left main PCI represented **1.0%** of all procedures,

modestly increasing from 0.7% to 1.3% over time

Figure 1. Temporal Trends in Unprotected Left Main (ULM) Percutaneous Coronary Intervention (PCI)



Contemporary Use and Trend of Left Main PCI



"State-of-the-Art (Cutting Edge)" PCI for LM Disease



Key Component of State-of-the Art Left Main PCI "Imaging and Physiologic Concept"

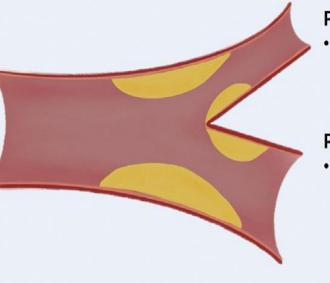
Role of IVUS

Pre-PCI

- Can provide additional information on the ischemic burden of LMCA lesion
- Provide more reliable information on lesion characteristics than angiography
- Helpful in planning PCI strategy (especially for distal LMCA bifurcation lesion)

Post-PCI

- Ensure stent optimization with subsequent postdilatation
- Identify procedural complications



Role of FFR

Pre-PCI

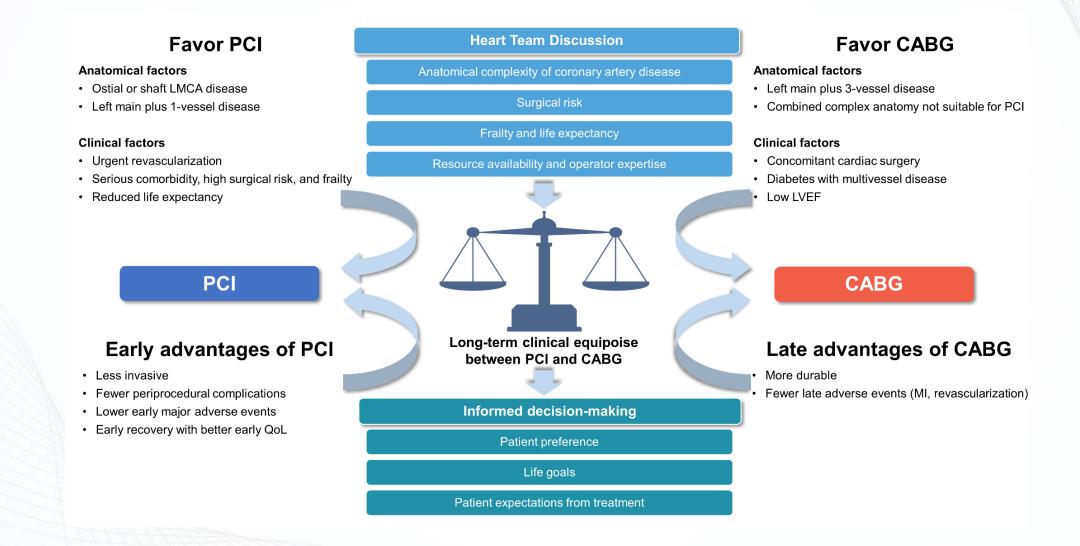
Provide accurate information on the functional status of angiographic intermediate or ambiguous LMCA lesion

Post-PCI

· Assessment for jailed branches after left main PCI



Optimal Heart Team Approach for LM Revascularization



SW Park, DW Park et al. KCJ 2023,

Key Summary: Data Understanding and My Practice 2023 for Left Main Revascularization

- With remarkable advancements in PCI, clinical outcomes of left main PCI have substantially improved.
- Contemporary evidences demonstrated that PCI was comparable to CABG in mortality and hard clinical endpoints for left main PCI.
- Imaging- and physiology-guided contemporary "state-of-the-art" left main PCI will provide better clinical outcomes.
- Owing to the gap between clinical practice and the available clinical evidence, no unified algorithm can be applied to various clinical scenarios; therefore, decision-making should be on a case-by-case basis and the Heart-Team approach should be emphasized.