PCI for Unprotected Left Main Coronary Artery Stenosis

The impact that data from the SYNTAX and PRECOMBAT trials have had on PCI guidelines.

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Recent registries and randomized studies have shown that percutaneous coronary intervention (PCI) is safe and effective in patients with unprotected left main coronary artery (ULMCA) stenosis.[1-13] These trials have reported that drug-eluting stents (DES) yielded favorable mid- and long-term outcomes. For example, the left main substudy of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) randomized trial showed that PCI using paclitaxel-eluting stents (PES) had similar long-term safety and efficacy rates as coronary artery bypass graft (CABG) surgery in patients with ULMCA stenosis.[6]

In addition, the recent randomized PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease) trial showed that PCI with sirolimus-eluting stents (SES) was noninferior to CABG in terms of the 1-year incidence of major adverse cardiac or cerebrovascular events (MACCE).[12] These results have led to recently updated recommendations that PCI be considered as an alternative to surgery in patients who are at high surgical risk.[14,15] In this article, we review the recent data on PCI using DES and guidelines for treating ULMCA lesions.

OUTCOMES OF PCI VERSUS CABG

Before the SYNTAX left main substudy, several nonrandomized observational studies showed the safety and efficacy of DES treatment for ULMCA stenosis compared with CABG.[5] In addition to small registries, stronger evidence for feasibility of PCI as an alternative to CABG came from the recent large registry, MAIN-COMPARE (Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization).[1] This study analyzed data from 2,240 patients with ULMCA disease who were treated at 12 medical centers in Korea. Of these, 318 were treated with bare-metal stents, 784 were treated with DES, and 1,138 underwent CABG.

At 3-year follow-up, patients who were treated with stents were nearly four times as likely to need a repeat revascularization when compared to those who underwent CABG (hazard ratio [HR], 4.76; 95% confidence interval [CI], 2.8–8.11). However, the rates of death (HR, 1.18; 95% CI, 0.77–1.8) and the combined rates of death, myocardial infarction (MI), and stroke (HR, 1.10; 95% CI, 0.75–1.62) were not significantly higher with the use of stenting compared with CABG. A similar pattern was observed in patients who were treated with DES or bare-metal stents.

Another interesting finding in this study was that the majority of repeat revascularizations in PCI patients utilized repeat PCI instead of CABG.[16] Therefore, this study suggests that a routine recommendation of angiographic surveillance may not be necessary because the in-stent restenosis in the ULMCA had a benign clinical presentation.

The SYNTAX trial was a randomized controlled trial that evaluated the efficacy and safety of PCI using PES for 1,800 patients with three-vessel and/or left main disease.[17] In the left main subgroup analysis for 348 patients undergoing CABG and 357 receiving PCI, PCI demonstrated equivalent 1-year clinical outcomes of MACCE including

death, MI, stroke, and repeat revascularization compared with CABG (Table 1).

When the patients were stratified according to vascular involvement, the event rate in the PCI group was numerically higher for patients with two-vessel (19.8% vs 14.4%; *P* = .29) and three-vessel (19.3% vs 15.4%; *P* = .42) disease. However, the incidences were numerically lower in the PCI group for patients with isolated ULMCA stenosis (7.1% vs 8.5%; *P* = 1) or single-vessel disease (7.5% vs 13.2%; *P* = .27). It was of interest that the higher rate of repeat revascularization with the use of PCI (11.8% vs 6.5%; *P* = .02) was offset by a higher incidence of stroke with the use of CABG (2.7% vs 0.3%; *P* = .01).[6]

The 4-year outcomes of SYNTAX, which were presented at the 2011 Transcatheter Cardiovascular Therapeutics meeting, continued to show the same findings.[18] There were no significant differences in the rates of death (11.4% vs 11.2%; *P* = .94), MI (7.2% vs 4.8%; *P* = .2), and MACCE (33.2% vs 27.8%; *P* = .14) between PCI and CABG patients. However, the stroke rate was lower (1.5% vs 4.3%; *P* = .03), and the revascularization rate was higher (23.5% vs 14.6%; *P* = .003) after PCI. It should be noted that the analysis for ULMCA disease was not the primary objective analysis but rather the post hoc analysis, which was hypothesis generating.

The ultimate proof of the relative values of PCI versus CABG for ULMCA stenosis clearly depends on the results of randomized clinical trials comparing the two treatment strategies. The PRECOMBAT trial randomized 600 patients with ULMCA to either CABG or PCI with SES in a noninferiority study in Korea.[12]

As shown in Table 1, PCI was noninferior to CABG for the 1-year MACCE rate, which was the primary endpoint, (absolute difference, 2%; upper margin of 95% CI, 5.6%; HR, 1.56; *P* for noninferiority = .011). At 2 years, the MACCE rate (12.2% vs 8.1%; HR, 1.5; 95% CI, 0.9–2.52; *P* = .12) and the composite rate of death, MI, or stroke (4.4% vs 4.7%; HR, 0.92; 95% CI, 0.43–1.96; *P* = .83) remained comparable between the PCI and CABG groups. However, the 2-year rate of ischemia-driven target vessel revascularization was significantly higher in the PCI group than in the CABG group (9% vs 4.2%; HR, 2.18; 95% CI, 1.1–4.32; *P* = .022).

The results of a small randomized study were also in line with these studies.[11] The incidence of the composite end-

TABLE 1. OUTCOMES OF CABG AND PCI USING DES FOR ULMCA STENOSIS

Variables	**SYNTAX[6]**		**PRECOMBAT[12]**	
Study Design	Substudy of a Randomized Study		Randomized Study	
Treatment type	PCI using PES	CABG	PCI using SES	CABG
No. of patients	357	348	300	300
Age (mean)	65	66	62	63
Male sex (%)	72	76	76	77
Diabetes mellitus (%)	24	26	34	30
EuroSCORE (mean)	3.9	3.9	2.6	2.8
SYNTAX score (mean)	30	30	24	26
Bifurcation left main stenosis (%)	74	69	67	62
Three-vessel disease (%)	38	35	41	41
1-Year Events (%)				
Death from any cause	4.2	4.4	2	2.7
Myocardial infarction	4.3	4.1	1.3	1
Stroke	0.3[a]	2.7	0	0.3
Repeat revascularization	12[b]	6.7	6.1[c]	3.4
MACCE[d]	15.8	13.6	8.7	6.7

[a]P = .009 between PCI and CABG.

[b]P = .02 between PCI and CABG.

[c]Ischemia-driven target vessel revascularization in the PRECOMBAT study.

[d]MACCE includes all-cause death, myocardial infarction, stroke, or repeat revascularization.

TABLE 2. UPDATED GUIDELINES OF PCI FOR STABLE PATIENTS WITH ULMCA STENOSIS

Organization	Class of Recommendations		Level of Evidence
ACCF/AHA/SCAI (2011)[20]	IIa	Low risk for PCI (eg, low SYNTAX score ≤ 22, ostial or trunk LM stenosis)	B
		High risk for CABG (eg, STS-predicted operative mortality ≥ 5%)	
	IIb	Intermediate risk for PCI (eg, low-to-intermediate SYNTAX score < 33, bifurcation LM stenosis)	B
		Increased risk for CABG (eg, moderate-to-severe COPD, disabled stroke, previous cardiac surgery, or STS-predicted operative mortality > 2%)	
	III	Unfavorable anatomy for PCI and good candidates for CABG	B
ESC/EACTS (2010)[15]	IIa	Ostial or shaft LM disease with zero- or single-vessel disease	B
	IIb	Bifurcation LM disease with zero- or single-vessel disease	B
		LM disease with two- or three-vessel disease and SYNTAX score ≤ 32	
	III	LM disease with two- or three-vessel disease and SYNTAX score ≥ 33	B

Abbreviations: ACCF, American College of Cardiology Foundation; AHA, American Heart Association; COPD, chronic obstructive pulmonary disease; EACTS, European Association for Cardio-Thoracic Surgery; ESC, European Society of Cardiology; LM, left main; SCAI, Society for Cardiovascular Angiography and Interventions; STS, Society of Thoracic Surgeons.

point of cardiac death, MI, and repeat revascularization at 1 year was 13.9% after CABG and 19% after PCI, which met the noninferiority hypothesis (*P* for noninferiority = .019).

CHOOSING A REVASCULARIZATION STRATEGY BASED ON RISK STRATIFICATION

The SYNTAX study group created the SYNTAX score to classify angiographic complexity and predict outcomes of patients who are treated with revascularization.[19] The score takes into account anatomic complexities including calcification, bifurcation lesions, total occlusion, thrombus, and long lesions. In spite of some limitations, such as absence of clinical profiles and wide interobserver variation, the score is considered to be a useful predictor for the extent of coronary disease and provides important information for deciding the revascularization strategy. In the SYNTAX study, the low (0–22; 26% vs 28.4%; *P* = .6) and intermediate SYNTAX (23–32; 29.5% vs 29.7%; *P* = .9) score groups had comparable 4-year incidences of MACCE between PCI and CABG groups.[18] However, in the high score group (≥ 33), PCI showed a higher incidence of MACCE than CABG (42.6% vs 26.3%; *P* < .003).

Although the SYNTAX score can be used to identify high-risk patients, the score has several limitations. For instance, the relationship between SYNTAX score and event rates after CABG is flat,[21] as the outcomes were primarily determined by patients' clinical morbidity. In addition, the calibration and discrimination power might be better with use of the EuroSCORE rather than the SYNTAX score with either PCI or CABG for ULMCA stenosis.[21]

This finding indicates that additive risk stratification should be performed using important clinical variables such as age, presence of diabetes mellitus, chronic renal failure, unstable presentation, pulmonary function, and neurologic abnormality.[6,22] Therefore, other clinical risk scores, such as EuroSCORE ACEF (age, creatinine, and ejection fraction) score, Mayo Clinical risk score, or Society of Thoracic Surgeons score also need to be considered to predict outcomes and determine an optimal revascularization strategy.[23] In fact, the combined risk stratification with SYNTAX score and EuroSCORE provided better performance to predict long-term outcomes of ULMCA revascularization.[20,24]

In addition to the extent of associated coronary disease and patient comorbidity, the presence of ULMCA bifurcation stenosis is an important consideration when the appropriate revascularization strategy is chosen. In contrast with ostial or shaft stenosis, PCI in the ULMCA bifurcation has been more challenging, although the prevalence was > 60% across prior studies. A previous study assessing the outcomes of PCI with DES for ULMCA stenosis showed

that the risk of target vessel revascularization was six-fold (95% CI, 1.2–29) in bifurcation stenosis compared with nonbifurcation stenosis (13% vs 3%).[25]

However, fortunately, a substudy of the recent PRECOMBAT study showed that the treatment effect between PCI and CABG was not affected by the presence of bifurcation stenosis.[12] If stenting was performed by experienced operators, either single- or two-stent techniques for bifurcation yielded a comparably feasible long-term outcome compared to CABG, even for bifurcation ULMCA stenosis.[26]

GUIDELINES AND CONCLUSIONS

Because of the recent randomized and nonrandomized studies favoring the safety and efficacy of PCI using DES for ULMCA stenosis, the practice guidelines updated the recommended indication of PCI, as shown in Table 2. The American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Interventions[20] and European Society of Cardiology/European Association for Cardio-Thoracic Surgery[15] stated that PCI for ULMCA stenosis is a class IIa or IIb indication for those patients with ULMCA lesions who have nonextensive coronary disease and are at a low stenting risk or a high surgical risk.

In summary, current data and guidelines support PCI as a reasonable alternative to CABG for patients with ULMCA stenosis. The decision regarding which revascularization strategy is appropriate should be made based on the angiographic and clinical complexities of patients. Additional randomized trials comparing PCI using new-generation DES with CABG, such as the NOBLE (Nordic-Baltic-British Left Main Revascularization) study or the EXCEL (Evaluation of Xience Prime Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial are ongoing to further clarify the differential treatment effect of PCI versus CABG for ULMCA stenosis. ■

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