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STATE-OF-THE-ART PAPER

Unprotected Left Main Coronary Disease and ST-Segment Elevation Myocardial Infarction

A Contemporary Review and Argument for Percutaneous Coronary Intervention

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Acute occlusion involving the unprotected left main coronary artery (ULMCA) is a clinically catastrophic event, often leading to abrupt and severe circulatory failure, lethal arrhythmias, and sudden cardiac death. Although coronary artery bypass grafting (CABG) is the standard of care for ULMCA disease in patients with stable ischemic heart disease, uncertainty surrounds the optimal revascularization strategy for patients with ST-elevation myocardial infarction (MI) and ULMCA occlusion who survive to hospitalization, and treatment guidelines in this setting are vague. Percutaneous coronary intervention (PCI) is technically feasible in most patients, has the advantage of providing more rapid reperfusion compared with CABG with acceptable short- and long-term outcomes, and is associated with a lower risk of stroke. PCI of the ULMCA should be considered as a viable alternative to CABG for selected patients with MI, including those with ULMCA occlusion and less than Thrombolysis In Myocardial Infarction flow grade 3, cardiogenic shock, persistent ventricular arrhythmias, and significant comorbidities. The higher risk of target vessel revascularization associated with ULMCA PCI compared with CABG is an acceptable tradeoff given the primary need for rapid reperfusion to enhance survival. (J Am Coll Cardiol Intv 2010;3:791–5) © 2010 by the American College of Cardiology Foundation

Although the previous version of the guidelines stated that the standard of care for patients with significant unprotected left main coronary artery (ULMCA) disease is coronary artery bypass grafting (CABG), the 2009 American College of Cardiology (ACC)/American Heart Association (AHA) focused guidelines for percutaneous coro-

nary intervention (PCI) state that ULMCA stenting may be considered in patients with anatomic conditions that are associated with a low risk of procedural complications and clinical conditions that predict an increased risk of adverse surgical outcomes (class IIb) (1,2). Acute occlusion involving the ULMCA, which accounts for 0.8% of patients who undergo primary PCI (3), is a clinically catastrophic event, often leading to abrupt and severe circulatory failure, lethal arrhythmias, and sudden cardiac death. Patients with ULMCA disease with ST-segment elevation myocardial infarction (STEMI) who survive to hospitalization are typically critically ill, may suffer from cardiogenic shock, and have high mortality rates, and both the acuity of the event and critical condition of the patient may preclude the opportunity for emergency CABG (4).

Uncertainty surrounds the optimal revascularization strategy for STEMI patients and ULMCA

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disease, and treatment guidelines in this setting are vague. The 2004 revised ACC/AHA STEMI guidelines indicate that PCI is class Ia indication in cardiogenic shock and a class Ia indication for CABG if there is suitable coronary anatomy, but again do not provide specific treatment recommendations for ULMCA disease (5). Considering the clinical dilemma that ULMCA disease presents in the setting of STEMI, there is a need to better understand the evidence base regarding ULMCA revascularization strategies and to establish treatment recommendations. The present report critically evaluates the current evidence to elucidate the role of primary PCI for ULMCA occlusion, supporting PCI as superior to medical therapy alone and as a suitable alternative to surgical revascularization in selected cases.

Procedural, In-Hospital, and Long-Term Outcomes With PCI for STEMI Due to ULMCA Occlusion

Abbreviations and Acronyms

ACC = American College of Cardiology

AHA = American Heart Association

CABG = coronary artery bypass grafting

DES = drug-eluting stent(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

ULMCA = unprotected left main coronary artery

As with less complex lesions and clinical settings, procedural success has improved considerably when percutaneous revascularization with stenting (compared with angioplasty alone) is performed for ULMCA disease in STEMI. Although data on long-term follow-up are limited in this indication, patients who survive to discharge following ULMCA PCI have a favorable prognosis. In a retrospective multicenter international registry, angiographic success was achieved in all 23 patients, with no deaths after the first month in patients with STEMI who underwent UL-

MCA PCI with drug-eluting stents (DES) (6). Although the in-hospital mortality rate was 44% in 18 patients (cardiogenic shock present in 78%) who underwent primary PCI, Lee et al. (7) reported no subsequent death or MI during a follow-up period of 39 ± 22 months. In another study of 16 patients (cardiogenic shock present in 69%) who underwent ULMCA PCI with DES for STEMI, despite an in-hospital mortality rate of 44%, there were no subsequent deaths at a mean follow-up of 215 days (8). Prasad et al. (9) reported an in-hospital mortality rate of 35% among 28 patients who underwent primary PCI for ULMCA occlusion, yet there was only 1 death at a follow-up of 26 ± 12 months.

Comparisons of Outcomes With PCI Versus CABG for STEMI Due to ULMCA Occlusion

Nonrandomized and randomized data examining ULMCA PCI in nonemergency cases compared with CABG have not

demonstrated significant differences in the outcomes of death or MI (10–12). This has led to increasing interest surrounding the role of PCI in more acute situations involving ULMCA disease, in which patients are often too critically ill and hemodynamically unstable to undergo CABG.

Studies evaluating surgical revascularization of ULMCA occlusion in patients with acute MI are limited but indicate high clinical risk for such patients. In a study of 13 patients with acute MI due to ULMCA occlusion, the in-hospital mortality rate after emergency CABG was 46% (13).

Limitations to the Current Evidence Comparing Revascularization Strategies in ULMCA Disease and MI

Among existing studies reporting outcomes in MI related to ULMCA disease, 3 themes have emerged regarding treatment strategies: 1) clinical outcome is improved with any revascularization compared with medical therapy alone (14–16); 2) among revascularization patients, a treatment bias favoring performance of PCI rather than CABG in higher clinical risk patients prohibits direct comparison between the 2 revascularization modalities; and 3) despite differences in patient groups and decisions for treatment, ULMCA PCI in STEMI is associated with similar survival rates compared with CABG (16).

Aside from the small sample size of individual trials, which limits any definite conclusion, the observational, nonrandomized design of these trials enables significant confounding and imbalance in factors like patient variability (e.g., age, illness severity, cardiogenic shock, and coronary anatomy), different primary end points, and various periods of follow-up between treatment groups that are only partially accounted for through multivariable and propensity score adjustments. Subjective assessment of each patient by a physician and a nonobjective means of deciding the appropriate intervention are oftentimes very difficult. Patients undergoing emergency PCI are often more unstable than ones undergoing CABG because their higher risk precludes surgical revascularization. Further, lack of application of the intention-to-treat principle challenges comparisons between PCI and CABG; specifically, patients considered for CABG who do not survive to surgery or are later deemed ineligible are not represented in CABG-related outcomes. Conversely, if the very same patients underwent PCI and subsequently died, they nonetheless would be considered PCI-related deaths despite the fact that death would have occurred no matter what revascularization strategy was chosen.

Advancing ULMCA PCI as a Standard in STEMI

Multicenter randomized trials are necessary to evaluate the role of PCI while taking into account the limitations mentioned earlier. However, it is unlikely that a randomized controlled trial with sufficient size for this indication will ever be conducted given the logistic complexities of such a study and the treatment biases that favor one therapy over another. Nevertheless, there is an opportunity through studies to further refine our understanding of ULMCA PCI in STEMI. Fundamental issues specific to PCI in this setting that still require clarification include: 1) possible advantages of PCI with respect to more rapid reperfusion compared with CABG; 2) the safety and efficacy of DES along with technical considerations regarding the treatment of the distal ULMCA; 3) duration of dual antiplatelet therapy; 4) possible advantages of PCI with respect to lower risk of stroke compared with CABG; 5) role of catheter-based hemodynamic support; and 6) strategy of complete revascularization with treatment of infarct-related and noninfarct-related arteries in patients with cardiogenic shock.

PCI may be performed more expeditiously than CABG and promptly reperfuse the infarcted artery, potentially reversing arrhythmic and hemodynamic instability. Delays to reperfusion with CABG, which may take an hour or longer during off-peak hours to establish cardiopulmonary bypass, can be catastrophic in this situation. Hence, we advocate the consideration of emergency PCI as a preferred alternative to CABG in the following situations and when PCI can be performed in a timely fashion by experienced operators (5): 1) ULMCA occlusion with less than Thrombolysis In Myocardial Infarction (TIMI) flow grade 3; 2) cardiogenic shock and/or life-threatening arrhythmias; or 3) coexisting illnesses or conditions that pose excessive risk of CABG-related complications (e.g., chronic obstructive pulmonary disease, cerebrovascular disease). If there is TIMI flow grade 3 and the patient is not in cardiogenic shock, then time is less critical, and the decision regarding PCI versus CABG can be made based on whether the anatomy is favorable for PCI (ostial or midshaft as opposed to distal bifurcation disease), whether there is multivessel disease, and whether there are other comorbidities that would make surgery a less attractive alternative.

The antirestenotic benefit of DES is less of an immediate issue in ULMCA PCI than is survival itself. Surgeons commonly use the saphenous vein graft rather than the left internal mammary artery to anastomose the left anterior descending coronary artery in these critically ill patients. Furthermore, PCI of the ostial or midshaft ULMCA is less technically challenging and are associated with lower restenosis rates compared with the distal bifurcation, especially when 2 stents are required (17,18). Although lesion localization and complexity in guiding decisions regarding the

appropriate revascularization modality are important to consider, PCI is still a reasonable initial strategy even in patients with distal bifurcation disease, as restenosis can be managed in most cases with a repeat percutaneous approach (84%) or with subsequent CABG (19).

Stent thrombosis is a dreaded and catastrophic complication of ULMCA PCI, typically resulting in either large MI or death. The risk of stent thrombosis is generally higher in patients who undergo primary PCI in MI than elective PCI (20,21), raising uncertainty about the use of DES in ULMCA PCI in acute MI. Although the optimal adjunctive pharmacotherapy and duration of antiplatelet therapy is still uncertain, primary PCI with DES is still challenged by difficulty ascertaining the patient's likelihood for compliance with dual-antiplatelet therapy. In the PREMIER (Prospective Registry Evaluating Myocardial Infarction: Events and Recovery), 13.6% of MI patients who underwent primary PCI with DES discontinued clopidogrel within 30 days of discharge (22). Compared with patients who were compliant with long-term dual-antiplatelet therapy, early discontinuation was associated with significantly higher death and rehospitalization at 1 year. The consequences of premature antiplatelet therapy discontinuation are likely to be even greater after ULMCA stenting. Therefore, if possible, the cardiologist should discuss with the patient the importance of dual-antiplatelet therapy for at least 12 months prior to the implantation of DES and inquire about any impending surgery in the next 12 months that would require premature discontinuation of dual-antiplatelet therapy. If likely compliance remains a concern, bare-metal stents should be used rather than DES.

A consideration in evaluating the safety profiles of CABG and PCI is the risk of stroke, especially in the elderly. In the subset of patients with ULMCA disease in the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) trial, CABG was associated with a higher rate of stroke compared with PCI (2.7% vs. 0.3%, $p = 0.009$) (12). The reason for this may be that CABG patients are exposed to surgical risks such as perioperative thromboemboli or surgical manipulation or cannulation of the aorta.

Intra-aortic balloon counterpulsation is recommended by the ACC/AHA for STEMI patients with cardiogenic shock who undergo primary PCI (5). Although there are no data regarding the use of intra-aortic balloon counterpulsation in emergent ULMCA PCI in MI, its elective use in non-emergent PCI may decrease the risk of intraprocedural events in higher-risk patients (23). Percutaneous left ventricular assist devices have not been studied specifically in STEMI patients who underwent ULMCA PCI. Although percutaneous left ventricular assist devices provide superior hemodynamic support in patients with cardiogenic shock compared with intra-aortic balloon counterpulsation, the use of these devices did not improve early survival (24).

More data are required before percutaneous left ventricular assist devices can be routinely recommended as first-line therapy in the mechanical management of cardiogenic shock.

It is imperative to achieve TIMI flow grade 3, as it is associated with the lowest mortality in patients with MI complicated by cardiogenic shock (25,26). Incomplete revascularization is an independent predictor of in-hospital mortality in patients who undergo emergency ULMCA PCI for acute MI (27). PCI of the noninfarct-related artery to provide complete revascularization in patients with concomitant multivessel disease should be considered in patients that remain hemodynamically unstable after ULMCA PCI, especially if there is regional wall motion in the distribution of the noninfarct-related artery (5). On the contrary, CABG may be preferred if complete revascularization cannot be achieved with PCI, or when a mechanical complication such as severe mitral regurgitation or a ventricular septal defect is present.

Conclusions

Primary PCI of the ULMCA is technically feasible in most patients and has the advantage of providing more rapid reperfusion compared with CABG, with acceptable short-term and long-term outcomes with a lower risk of stroke. Although there remains controversy regarding the role of ULMCA PCI in elective settings, primary PCI in ST-segment elevation MI should be considered a suitable alternative to CABG in patients with ULMCA occlusion and TIMI flow grade <3, critically ill patients with cardiogenic shock, persistent ventricular arrhythmia, and significant comorbidities. The higher risk of target vessel revascularization associated with ULMCA PCI is acceptable given the severity and time urgency of effective reperfusion in this setting. Although a multicenter trial would be preferred to definitively establish the optimal treatment strategy for acute MI involving the ULMCA, it is unlikely that a randomized trial of sufficient size will be conducted for this indication given the logistical complexities of such an undertaking. Absent a randomized trial, it is our belief that physicians and guidelines committees should recognize primary PCI as the preferred reperfusion modality for selected patients with ULMCA occlusion and TIMI flow grade <3. For non-ST-segment elevation acute coronary syndrome and ULMCA disease, a randomized trial comparing CABG and PCI is warranted.

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