

Sponsored by Abiomed, Inc.

The Benefit of Complete Revascularization and Efficacy of Complete Revascularization in a Single Setting

Comprehensive and well-documented data demonstrate that complete revascularization has distinct clinical advantages, especially in patients with complex multivessel disease.

BY RAJAN PATEL, MD, FACC, FAHA, FSCAI

Complicated multivessel disease (MVD) remains a clinical challenge for interventional cardiologists, posing two important questions: (1) what clinical evidence shows the benefit of complete revascularization (CR) over incomplete revascularization (IR), and (2) can complex multivessel coronary artery disease be adequately treated using percutaneous coronary intervention (PCI) in a single setting?

Available data suggest that CR, potentially in a single setting as opposed to a staged procedure, has advantages, especially for patients with MVD. These advantages include:

- Reduced incidence of all-cause mortality, myocardial infarction (MI), and major cardiac and cerebrovascular events (MACCE)
- Less early recurrent ischemia and need for subsequent procedures
- Preserved, and possibly improved, left ventricular function in select patients

COMPLETE REVASCULARIZATION LEADS TO BETTER OUTCOMES

Real-world data from the New York State PCI Reporting System,¹ along with three separate trials (ARTS-1, ARTS-II, and SYNTAX) comparing revascularization of MVD patients with PCI to coronary artery bypass grafting (CABG),²⁻⁴ all showed that IR is very common, with rates approaching 70%. Yet, considerable evidence supports CR in high-risk coronary artery disease.

Improved Survival and Reduced MACCE

Using stress myocardial perfusion single-photon emission computed tomography (SPECT), Hachamovitch et al

demonstrated that coronary revascularization, compared with medical therapy alone, leads to a greater survival benefit in patients with large zones of ischemia.⁵ Figure 1 compares the cardiac death rate among patients with progressive percentages of myocardial ischemia. With increasing amounts of inducible ischemia, there was a mortality benefit among those treated with coronary revascularization compared to medical therapy alone.⁵ Revascularization in patients with > 20% ischemic myocardium was associated with a markedly lower cardiac mortality (2% vs 6.7%) than the group treated with medical therapy alone ($P < .0001$).

The SYNTAX trial⁴ randomized patients with coronary artery disease to revascularization with PCI or CABG. In the PCI group, cardiac death was lower when CR was achieved (6% with CR vs 9.1% with IR; $P = .049$), with a trend toward

Ischemic Myocardium and Mortality

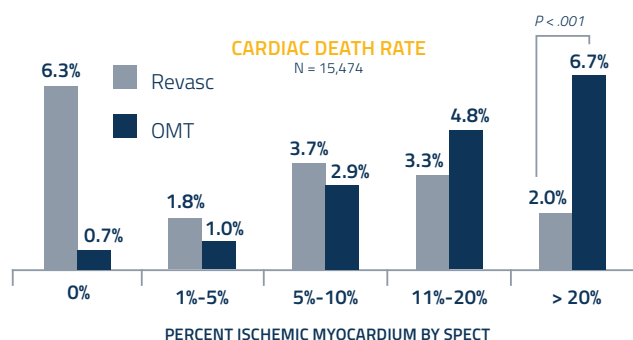


Figure 1. Mortality progressively increased in medically treated cases but not in those managed with revascularization. OMT, optimal medical therapy

all-cause mortality (11.9% vs 15.9%; $P = .052$). Cardiac death and all-cause mortality were also significantly lower among CABG group patients who received CR. In the Mayo Clinic PCI Registry, a cohort of 5,350 patients presenting with MVD who underwent PCI (either with bare-metal or drug-eluting stents), CR was associated with a survival benefit. In fact, the best survival was noted in patients without diabetes undergoing CR. The poorest survival was in diabetic patients who underwent IR.⁶

In a meta-analysis assessing three trials comparing PCI with CABG (SYNTAX, PRECOMBAT, and BEST), a reduction in MACCE was reported in the PCI cohort when CR was achieved (CR MACCE 15.3% vs IR MACCE 19.5%; $P = .025$). An even larger meta-analysis of 38 publications, including 156,240 patients with MVD undergoing PCI, showed an overall advantage with CR in terms of the death (odds ratio [OR], 0.69; 95% CI, 0.61-0.78), repeat revascularization (OR, 0.60; 95% CI, 0.45-0.80), myocardial infarction risk (OR, 0.64; 95% CI, 0.50-0.81), and postprocedural MACCE (OR, 0.63; 95% CI, 0.50-0.79).

Protected PCI With Impella® Linked to Increased Survival

The Roma-Verona Registry in Italy assessed patients with MVD and reduced left ventricular ejection fraction (LVEF) undergoing Protected PCI with Impella (Abiomed, Inc.).⁷ The registry showed patients undergoing the most CR (based on the British Cardiovascular Intervention Society

myocardial jeopardy score) had a survival advantage over those undergoing various degrees of incomplete revascularization (Figure 2).⁸

Although the primary endpoint in this study was mortality, an improvement in LVEF was also experienced by the majority of patients (Figure 3). The extent of coronary revascularization correlated with both LVEF recovery and survival.

IMPROVED OUTCOMES WITH SINGLE-STAGE REVASCULARIZATION

Reduced All-Cause Mortality

A prospective, observational, multicenter registry analysis (and the largest study of its kind) showed that single-stage CR improved long-term survival in patients with non-ST-segment elevation myocardial infarction (NSTEMI) and MVD. Outcomes from 19,980 patients, of which roughly half underwent single-stage acute CR during PCI, were compared with a propensity-matched group undergoing revascularization of only the implicated (culprit) vessel. Patients who underwent single-stage CR experienced a 5-year survival advantage for all-cause mortality ($P = .0001$) (Figure 4).⁹

Reduced MACCE and Target Lesion Revascularization Rates

Similarly, in a retrospective analysis of the SYNTAX study, staged cases were compared with patients undergoing single-setting PCI. Overall, a higher incidence

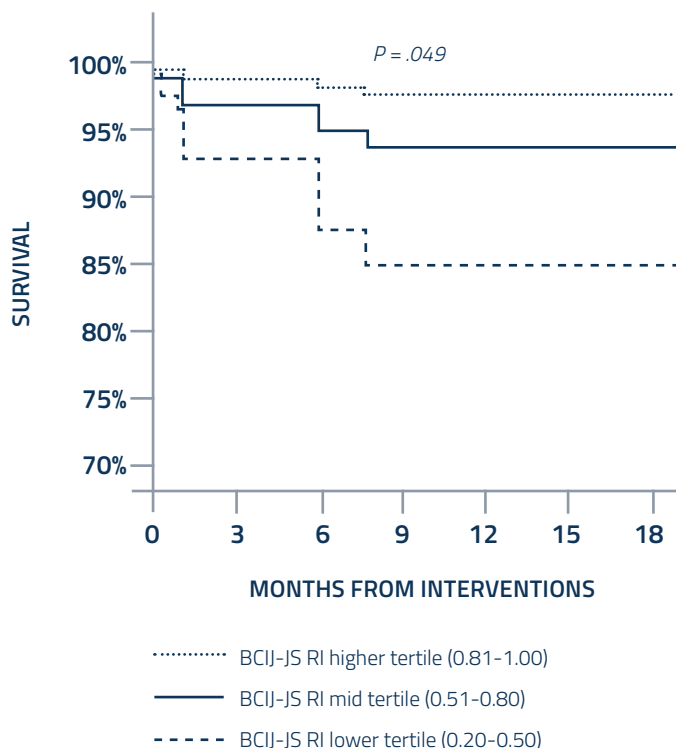


Figure 2. Survival curves according to extent of revascularization.

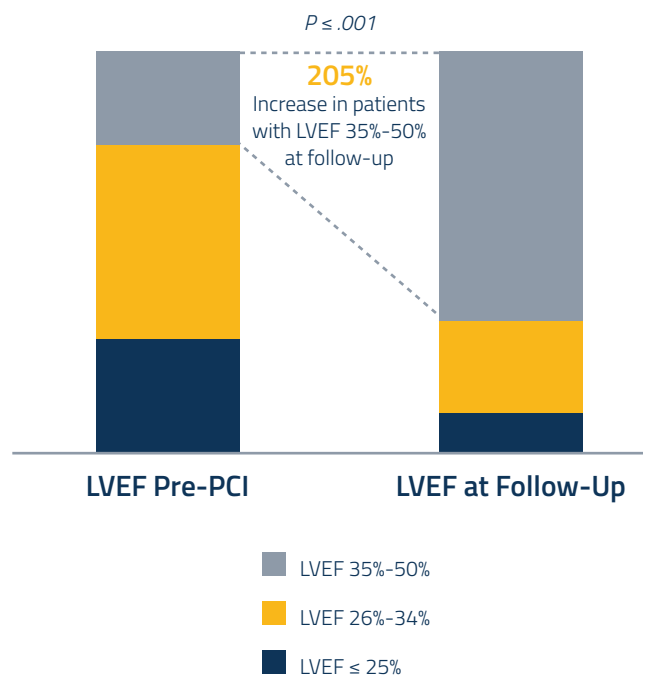


Figure 3. LVEF improvement during follow-up after Protected PCI.

Sponsored by Abiomed, Inc.

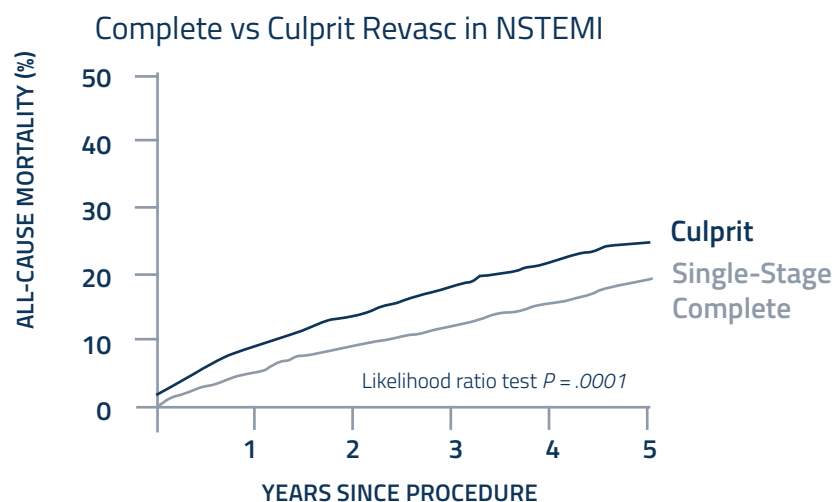


Figure 4. Kaplan-Meier curves show improved all-cause mortality after PCI with complete, single-stage CR in patients with MVD and NSTEMI.

of all-cause mortality was demonstrated in staged cases versus PCI in a single setting at 5 years ($n = 778$; 21.9% vs 12.6%; $P = .006$). Additionally, staging was associated with an increased incidence of urgent revascularization (32.8% vs 24.8%; $P = .035$), stroke (5.4% vs 1.9%; $P = .031$), and MACCE (48.1% vs 35.5%; $P = .004$) (Figure 5).¹⁰ The SMILE randomized controlled trial was designed to examine the effects of staging coronary revascularization among NSTEMI patients with MVD. The primary endpoints (rates of MACCE, reinfarction, rehospitalization for unstable angina, and repeat coronary revascularization)

were compared between a single-stage and multistage CR procedures. In SMILE, 584 patients were randomized during their index hospitalization either to one-stage PCI ($n = 264$) or to multistage PCI ($n = 263$). Results showed a significant reduction in both MACCE rates (hazard ratio [HR], 0.549; 95% CI, 0.363-0.828; $P = .004$) and target vessel revascularization rates (HR, 0.522; 95% CI, 0.310-0.878; $P = .013$) in the subgroup that received CR in a single setting.¹¹

Protected PCI With Impella Reduces Acute Kidney Injury During Single-Stage, Multivessel PCI

Because CR in a single setting often requires longer procedure times and larger amounts of contrast, acute kidney

injury (AKI) is a concern. Studies have shown that patients with AKI after PCI have higher in-hospital mortality rates.¹² A retrospective single-center study of PCI with Impella support during high-risk PCI found that mechanical circulatory support reduced the overall AKI risk, even in those cases in which there was preexisting chronic kidney disease.⁶

Furthermore, treatment of MVD in a single setting may induce hemodynamic instability that can be mitigated with the Impella heart pump. Impella has demonstrated positive patient outcomes in several clinical studies and postmarket registries.¹³⁻¹⁵

SYNTAX: 5-Year Outcome of Staged PCI (72 hours–14 days)

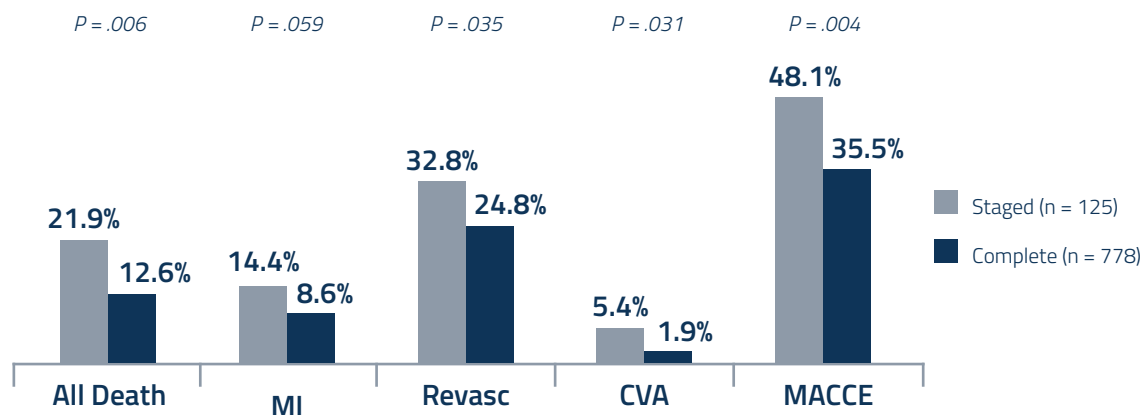


Figure 5. SYNTAX data shows improved 5-year outcomes with CR compared to staged procedures. CVA, cerebrovascular accident.

CONCLUSION

CR leads to improved outcomes in terms of mortality, MI, repeat revascularization, and MACCE rates. Perhaps more controversial is the view that single-stage CR in patients with MVD is associated with better outcomes in MACCE and revascularization rates when compared with multistage PCI. Interventional cardiologists should consider achieving CR in a single setting based on a growing data set that CR has clinical advantages for patients with MVD. ■

1. Hannan EL, Racz M, Holmes DR, et al. Impact of completeness of percutaneous coronary intervention revascularization on long-term outcomes in the stent era. *Circulation*. 2006;113:2406-2412. doi: 10.1161/CIRCULATIONAHA.106.612267
2. Serruys PW, Unger F, van Hout BA, et al. The ARTS study (Arterial Revascularization Therapies Study). *Semin Interv Cardiol*. 1999;4:209-219. doi: 10.1006/siic.1999.0107
3. Samo G, Garg S, Onuma Y, et al. Impact of completeness of revascularization on the five-year outcome in percutaneous coronary intervention and coronary artery bypass graft patients (from the ARTS-II study). *Am J Cardiol*. 2010;106:1369-1375. doi: 10.1016/j.amjcard.2010.06.069
4. Farooq V, Serruys PW, García-García HM, et al. The negative impact of incomplete angiographic revascularization on clinical outcomes and its association with total occlusions: the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) trial. *J Am Coll Cardiol*. 2013;61:282-294. doi: 10.1016/j.jacc.2012.10.017
5. Hachamovitch R, Hayes SW, Friedman JD, et al. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. *Circulation*. 2003;107:2900-2906. doi: 10.1161/01.CIR.0000072790.23090.41
6. Jiménez-Navarro MF, López-Jiménez F, Barsness G, et al. Long-term prognosis of complete percutaneous coronary revascularization in patients with diabetes with multivessel disease. *Heart*. 2015;101:1233-1239. doi: 10.1136/heartjnl-2014-307143
7. Burzotta F, Russo G, Ribichini F, et al. Long-term outcomes of extent of revascularization in complex high risk and indicated patients undergoing Impella-protected percutaneous coronary intervention: report from the Roma-Verona registry. *J Interv Cardiol*. 2019;5243913. doi: 10.1155/2019/5243913

8. De Silva K, Morton G, Sicard P, et al. Prognostic utility of BCIS myocardial jeopardy score for classification of coronary disease burden and completeness of revascularization. *Am J Cardiol*. 2013;111:172-177. doi: 10.1016/j.amjcard.2012.09.012
9. Rathod KS, Koganti S, Jain AK, et al. Complete versus culprit-only lesion intervention in patients with acute coronary syndromes. *J Am Coll Cardiol*. 2018;72:1989-1999. doi: 10.1016/j.jacc.2018.07.089
10. Watkins S, Oldroyd KG, Preda I, et al. Five-year outcomes of staged percutaneous coronary intervention in the SYNTAX study. *EuroIntervention*. 2015;10:1402-1408. doi: 10.4244/EIJV10I12A244
11. Sardella G, Lucisano L, Garbo R, et al. Single-staged compared with multi-staged PCI in multivessel NSTEMI patients: the SMILE trial. *J Am Coll Cardiol*. 2016;67:264-272. doi: 10.1016/j.jacc.2015.10.082
12. Tsai TT, Patel UD, Chang TI, et al. Contemporary incidence, predictors, and outcomes of acute kidney injury in patients undergoing percutaneous coronary interventions: insights from the NCDR Cath-PCI registry. *JACC Cardiovasc Interv*. 2014;7:1-9. doi: 10.1016/j.jcin.2013.06.016
13. Dixon SR, Henriques JP, Mauri L, et al. A prospective feasibility trial investigating the use of the Impella 2.5 system in patients undergoing high-risk percutaneous coronary intervention (the PROTECT I trial): initial U.S. experience. *JACC Cardiovasc Interv*. 2009;2:91-96. doi: 10.1016/j.jcin.2008.11.005
14. O'Neill WW, Kleiman NS, Moses J, et al. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. *Circulation*. 2012;126:1717-1727. doi: 10.1161/CIRCULATIONAHA.112.098194
15. Popma JJ. PROTECT III 2-year interim report with ongoing enrollment. Presented at the Transcatheter Cardiovascular Therapeutics 2019 annual meeting; September 24-28, 2019; San Francisco, California.

Rajan Patel, MD, FACC, FAHA, FSCAI
 Director, Interventional Cardiology Fellowship
 Program

John Ochsner Heart & Vascular Center
 Ochsner Medical Center
 New Orleans, Louisiana
 rapatel@ochsner.org

*Disclosures: Consulting fees/honoraria for Abiomed;
 speaker's bureau for Boston Scientific Corporation.*