

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007;356. DOI: 10.1056/NEJMoa070829.

Electronic Supplementary Appendix

Inclusion Criteria (all 4 criteria must be met)

Patients with a $\geq 70\%$ lesion in ≥ 1 vessel subtending a large area of myocardium with one of the following:

- Prior PCI or CABG with evidence of ischemia
- Chronic stable angina, CCS class I-III
- Post-MI patients without class IV angina, severe LV dysfunction, or arrhythmia
- Asymptomatic ischemia detected by exercise or perfusion scintigraphy or 24-hour ambulatory ECG recording

Patients who meet criteria adapted from one of the existing AHA/ACC Joint Task force Class I or II indications for PCI:

- Patients with single-vessel CAD who are asymptomatic to severely symptomatic and who have a large area of ischemic myocardium subtending a significant ($>50\%$ diameter reduction) coronary stenosis (AHA/ACC Class I indication) or a moderate area of ischemia (AHA/ACC Class II indication).
- Patients with multivessel CAD who are asymptomatic to severely symptomatic. Asymptomatic or minimally symptomatic patients must have a large ischemic area or moderate ischemic area (AHA/ACC Class II indication) to qualify.

Has at least 1 vessel for angioplasty meeting one of the following criteria:

- Right coronary artery: proximal to the posterior descending artery in a right dominant vessel
- Left circumflex coronary artery: proximal to 1 or 2 OM branches or proximal to the posterior descending artery and posterolateral branches in a left dominant vessel
- LAD: proximal or mid vessel
- SVG or LIMA: graft must supply the same regions as outlined previously or, in the opinion of the interventionalist, the coronary stenosis subtends a major mass of myocardium

Has objective evidence of myocardial ischemia or severe symptoms with marked coronary stenosis including one of the following:

- Spontaneous new ST-T changes on resting ECG defined as either ≥ 1.0 mm ST-segment deviation from the baseline (80 mm from J point) or >2.0 mm T-wave inversion (or pseudonormalization, if T waves were previously inverted) in a minimum of 2 contiguous leads within 1 of 3 ECG lead groups (anterior V1-V4; inferior II, III, aVF; lateral I, aVL, V5-V6)
- Objective evidence of stress-induced myocardial ischemia as detected by standard 12-lead exercise stress test, exercise or pharmacologic stress (adenosine or dipyridamole) coupled with perfusion scintigraphy, exercise or pharmacologic stress (dobutamine) coupled with 2-dimensional echocardiography, or exercise radionuclide ventriculography, based on one of the following:
 - >1.0 mm ST-segment deviation from baseline on standard treadmill exercise using 12-lead ECG
 - ≥ 1 Scintigraphic perfusion defects during exercise technetium 99m sestamibi or thallium-based isotope imaging
 - ≥ 1 Perfusion defects (reversible or partial reversible) with pharmacologic stress (dipyridamole, adenosine) during technetium 99m sestamibi or thallium imaging
 - ≥ 1 Wall motion abnormalities during exercise radionuclide ventriculography
 - 2-Dimensional echocardiography (exercise or dobutamine)
 - Severe angina (CCS class III) and coronary stenosis $\geq 80\%$

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; MI, myocardial infarction; ECG, electrocardiogram; AHA, American Heart Association; ACC, American College of Cardiology; CAD, coronary artery disease; OM, obtuse marginal branch; LAD, left anterior descending coronary artery; SVG, saphenous vein graft; LIMA, left internal mammary artery.

Exclusion Criteria

- Unstable angina and symptoms refractory to maximal oral and intravenous medical therapy (persistent CCS class IV)
- Post-MI course complicated by persistent rest angina, shock, and persistent CHF for which the need or likelihood of urgent myocardial revascularization is high
- Coronary angiographic exclusions:

- Patients with no prior CABG and left main coronary disease $\geq 50\%$
- Coronary arteries technically unsuitable or hazardous for PCI
- Patients with nonsignificant CAD in whom PCI would not be considered appropriate or indicated
- Patients with restenosis of a lesion previously treated with PCI and no other target lesion
- EF $< 30\%$ ($< 35\%$ if patient has 3-vessel disease including $> 70\%$ LAD proximal stenosis)
- Cardiogenic shock
- Pulmonary edema or heart failure unresponsive to standard medical therapy
- CABG or PCI within the last 6 months
- Concomitant valvular heart disease likely to require surgery or affect prognosis during follow-up
- Congenital or primary cardiac muscle disease likely to affect prognosis during follow-up
- Resuscitated out-of-hospital sudden death or symptomatic sustained or nonsustained ventricular tachycardia
- Significant systemic hypertension (BP $> 200/100$ mm Hg) unresponsive to medical therapy
- Markedly positive stress test (significant ST segment depressions or hypotensive response during stage I of the Bruce protocol)
- Severe noncardiovascular comorbidity limiting survival

CCS, Canadian Cardiovascular Society; MI, myocardial infarction; CHF, congestive heart failure; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; EF, ejection fraction; LAD, left anterior descending coronary artery; BP, blood pressure.

Sample Size Calculation Assumptions

We projected a 3-year composite event rate of 21% in the medical therapy only arm and 16.4% in the PCI plus medical therapy arm (relative difference of 22%, absolute difference of 4.6%). Sample size estimates are predicated on the following assumptions:

- a trial duration of 7 years;
- patient accrual for 54 months, 2/3 rate for first year, full rate thereafter;
- minimum follow-up duration of 30 months (average follow-up duration of 55 months);
- cross-over rate from PCI to medical therapy of 1% during the first 6 months, none thereafter;
- cross-over rate from medical therapy to PCI of 3% for the first 2 years, 2% for the next 2 years, and 1% thereafter;
- two-sided tests of significance at an $\alpha = 0.05$;
- annual loss to follow up rate of 1%;

The program published by Joanna Shih in CCT (1995) 16:395-407 was used for the calculations. Accordingly, a sample size of 1,984 patients would have 80% power and 2,270 patients would have 85% power. The latter corresponds to 602 endpoints or 614 after an adjustment of 2% for sequential monitoring. Using the above assumptions the sample size achieved by the study group has 85% power to detect a 22% relative difference and 80% power to detect a 20.9% relative difference.

Supplementary Appendix

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