CLINICAL RESEARCH STUDY

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The Impact of Revascularization on Mortality in Patients with Nonacute Coronary Artery Disease

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ABSTRACT

BACKGROUND: Although early revascularization improves outcomes for patients with acute coronary syndromes, the role of revascularization for patients with nonacute coronary artery disease is controversial. The objective of this meta-analysis was to compare surgical or percutaneous revascularization with medical therapy alone to determine the impact of revascularization on death and nonfatal myocardial infarction in patients with coronary artery disease.

METHODS: The Medline and Cochrane Central Register of Controlled Trials databases were searched to identify randomized trials of coronary revascularization (either surgical or percutaneous) versus medical therapy alone in patients with nonacute coronary disease reporting the individual outcomes of death or nonfatal myocardial infarction reported at a minimum follow-up of 1 year. A random effects model was used to calculate odds ratios (OR) for the 2 prespecified outcomes.

RESULTS: Twenty-eight studies published from 1977 to 2007 were identified for inclusion in the analysis; the revascularization modality was percutaneous coronary intervention in 17 studies, coronary bypass grafting in 6 studies, and either strategy in 5 studies. Follow-up ranged from 1 to 10 years with a median of 3 years. The 28 trials enrolled 13,121 patients, of whom 6476 were randomized to revascularization and 6645 were randomized to medical therapy alone. The OR for revascularization versus medical therapy for mortality was 0.74 (95% confidence interval [CI], 0.63-0.88). A stratified analysis according to revascularization mode revealed both bypass grafting (OR 0.62; 95% CI, 0.50-0.77) and percutaneous intervention (OR 0.82; 95% CI, 0.68-0.99) to be superior to medical therapy with respect to mortality. Revascularization was not associated with a significant reduction in nonfatal myocardial infarction compared with medical therapy (OR 0.91; 95% CI, 0.72-1.15).

CONCLUSION: Revascularization by coronary bypass surgery or percutaneous intervention in conjunction with medical therapy in patients with nonacute coronary artery disease is associated with significantly improved survival compared with medical therapy alone.

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Whereas timely coronary artery revascularization significantly reduces the incidence of death and nonfatal myocardial infarction in the setting of acute coronary syndromes,[1] data regarding the impact of revascularization on patients with nonacute coronary artery disease are scarce.[2-4] Early randomized trials comparing surgical revascularization (coronary artery bypass grafting) with medical therapy found that mortality was reduced by bypass surgery only in specific high-risk subsets of patients, such as those with severe left main coronary artery stenosis or 3-vessel coronary artery disease with reduced left ventricular systolic function.[5] However, these trials consistently demonstrated that coronary bypass

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grafting was more effective than medical therapy at relieving angina.[6,7] Similarly, randomized clinical trials comparing percutaneous coronary intervention with medical therapy demonstrated a reduction in anginal symptoms and anti-anginal medication without a major impact on mortality after coronary intervention.[8-10]

However, prior studies of revascularization versus medical therapy alone were powered inadequately to detect significant mortality differences. Even the relatively large Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation trial[10] was vastly underpowered to demonstrate a mortality difference between the 2 arms.

Prior meta-analyses have compared a single form of revascularization (surgical or percutaneous) with medical therapy and have not included recently completed trials.[4,11] Repeatedly, both forms of revascularization have been found to be equivalent in preventing death or myocardial infarction in patients with coronary artery disease.[12-18] Consequently, we conducted a systematic review and meta-analysis of all randomized clinical trials that compared the effect of coronary revascularization by either percutaneous intervention or bypass grafting with medical therapy alone on outcomes of patients with nonacute coronary artery disease.

CLINICAL SIGNIFICANCE

- In patients with nonacute coronary artery disease, the odds ratio for revascularization versus medical therapy for mortality was 0.74 (95% CI, 0.63-0.88, $P<.001$), indicating a significant mortality reduction with coronary revascularization.
- A stratified analysis according to revascularization mode revealed both coronary artery bypass grafting and percutaneous coronary intervention to be superior to medical therapy with respect to mortality.
- Revascularization was not associated with a significant reduction in nonfatal myocardial infraction compared with medical therapy.

MATERIALS AND METHODS

Search Strategy and Inclusion Criteria

This meta-analysis considered randomized clinical trials comparing coronary revascularization by percutaneous coronary intervention or bypass grafting in combination with medical therapy with medical therapy alone for the treatment of patients with nonacute coronary artery disease. Comprehensive searches of the Medline and Cochrane Central Register of Controlled Trials databases were performed using Web-based engines (PubMed and OVID) for studies published between 1977 and January 2008. Search terms included *coronary revascularization, balloon angioplasty, stent, coronary artery bypass grafting, medical therapy, angina, stable, coronary artery disease,* and combinations. In addition, bibliographies of retrieved articles were searched for other relevant studies.

For inclusion, studies were required to be prospective, randomized trials of coronary revascularization versus medical therapy alone in patients with stable coronary disease with the individual outcomes of death or nonfatal myocardial infraction reported at a minimum follow-up of 1 year. Multiple study designs were accepted, including trials with 2 arms in which patients were randomized to percutaneous intervention versus medical therapy or bypass grafting versus medical therapy; trials with 2 arms in which patients were randomized to any revascularization strategy versus medical therapy alone; and trials with 3 arms in which patients were randomized to percutaneous intervention or bypass grafting or medical therapy alone. Although studies randomizing patients with acute coronary syndromes were excluded from the analysis, studies of stable patients after a completed myocardial infraction were included. Studies were included irrespective of the presence of documented ischemia or any functional assessment of the hemodynamic significance of a coronary stenosis. Study eligibility was assessed by 2 authors; disagreements were resolved by consensus with a third author.

End Points

End point definitions were those used in the individual trials. All-cause mortality was death from any cause (cardiac or noncardiac) and preferentially used unless only cardiac deaths were reported. Myocardial infarction was generally defined as an elevation of serum markers of myocardial necrosis more than 3 times the upper limit of normal or electrocardiographic changes. End points were extracted from each trial at the primary prespecified follow-up. The follow-up periods for each trial are provided in Table 1. Event rates at the end of the follow-up period for each study were those used for the analysis.

Statistical Analysis

Because individual patient-level data from each trial were not available, a meta-analysis of summary statistics from individual trials was performed using Comprehensive Meta Analysis software (Biostat, Englewood, NJ). Data were analyzed according to the intention-to-treat principle. Methods based on odds ratios (OR) (Peto's method) were used to calculate the OR for the 2 primary outcomes of interest: death and nonfatal myocardial infarction. Although the Q statistic failed to indicate statistical heterogeneity ($P = .15$), given the heterogeneous nature of the included studies, a random-effects model was used to calculate a summary OR from the ORs and 95% confidence interval (CI) for each end point in each study. Cumulative meta-analysis was performed by sequentially adding studies one at a time according to date of publication (from earliest to latest). As each trial is added, a new summary OR incorporating the new