Percutaneous Coronary Intervention Versus Coronary Artery Bypass Graft Surgery in Left Main Coronary Artery Disease

A Meta-Analysis of Randomized Clinical Data

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Objectives
The purpose of this study was to determine the safety and efficacy of percutaneous coronary intervention (PCI) compared with coronary artery bypass graft (CABG) in patients with left main coronary artery (LMCA) disease.

Background
Previous meta-analyses of PCI versus CABG in LMCA disease mainly included nonprospective, observational studies. Several new randomized trials have recently been reported.

Methods
We identified 1,611 patients from 4 randomized clinical trials for the present meta-analysis. The primary end-point was the 1-year incidence of major adverse cardiac and cerebrovascular events (MACCE), defined as death, myocardial infarction (MI), target vessel revascularization (TVR), or stroke.

Results
PCI was associated with a nonsignificantly higher 1-year rate of MACCE compared with CABG (14.5% vs. 11.8%; odds ratio [OR]: 1.28; 95% confidence interval [CI]: 0.95 to 1.72; p = 0.11), driven by increased TVR (11.4% vs. 5.4%; OR: 2.25; 95% CI: 1.54 to 3.29; p < 0.001). Conversely, stroke occurred less frequently with PCI (0.1% vs. 1.7%; OR: 0.15; 95% CI: 0.03 to 0.67; p = 0.013). There were no significant differences in death (3.0% vs. 4.1%; OR: 0.74; 95% CI: 0.43 to 1.29; p = 0.29) or MI (2.8% vs. 2.9%; OR: 0.98; 95% CI: 0.54 to 1.78; p = 0.95).

Conclusions
In patients with LMCA disease, PCI was associated with nonsignificantly different 1-year rates of MACCE, death, and MI, a lower risk of stroke, and a higher risk of TVR compared with CABG. (J Am Coll Cardiol 2011;58:1426–32) © 2011 by the American College of Cardiology Foundation

Current guidelines recommend percutaneous coronary intervention (PCI) of the left main coronary artery (LMCA) with stents as a Class IIa or IIb alternative to coronary artery bypass graft (CABG) in patients with conditions that are associated with a low risk of PCI procedural complications and/or increased risk of adverse surgical outcomes (1–3). These recommendations carry a B level of evidence, indicating the lack of data derived from multiple randomized clinical trials (RCTs) or meta-analyses (3). In fact, when the guidelines were published, only a single small randomized study (4) and a pre-specified subanalysis from a large RCT of stents versus surgery (5) were available. This lack of randomized data has prompted an overemphasis on pooled observational studies (6,7). Since the publication of the latest guidelines, 2 new RCTs have been reported that compared PCI versus CABG in patients with LMCA disease (8,9). We therefore performed an up-to-date meta-analysis of data from all RCTs.

Methods

Literature search. We searched MEDLINE and Cochrane databases from January 1980 to April 2011 using Internet-based search engines. The terms used for research included “left main,” “percutaneous coronary intervention,” “stent(s),” and “coronary artery bypass graft.” Furthermore, we searched reference lists of relevant studies, reviews, editorials, letters, and meeting abstracts. We restricted our

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Manuscript received May 7, 2011; revised manuscript received June 24, 2011, accepted July 5, 2011.
analysis to prospective RCTs or pre-specified subanalyses from RCTs that met all of the following inclusion criteria: 1) study population of LMCA disease; 2) randomization to PCI versus CABG; and 3) both safety and efficacy outcomes were reported. The quality of the identified studies was assessed to ensure minimization of bias. In detail, we evaluated information regarding control for confounders, measurement of exposure, completeness of follow-up, and blinding. No formal scoring system was used. Reviewers were not blinded to journal, authors, or institution of publication.

**Data extraction.** All data were extracted independently by 2 evaluators (D.C. and C.T.); discrepancies were resolved by consensus. The following outcomes were extracted: major adverse cardiac and cerebrovascular events (MACCE, defined as the composite of death, myocardial infarction [MI], stroke [cerebrovascular accident (CVA)], or target vessel revascularization [TVR]), all-cause death, MI, CVA, and TVR. We restricted the follow-up period to 1 year. The clinical endpoint definitions were similar among the trials.

**Statistical analysis.** Data were analyzed according to intention to treat. The results of all studies were combined using a random-effects model to minimize heterogeneity between groups and confirmed by a fixed-effects model to avoid overweighting of small studies. A 2-tailed alpha of 5% was used for hypothesis testing. Statistical heterogeneity was assessed with Cochran Q via a chi-square test and quantified with the $I^2$ test. The influence of single trials was examined by excluding individual studies, and testing for systematic bias was performed using funnel plots and Begg’s test. Exploratory bivariate meta-regressions were performed to assess heterogeneous study effects. Statistical analysis was performed using Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood, New Jersey).

**Results**

**Search results.** As shown in Figure 1, 254 potentially eligible studies were identified, 4 of which met the pre-specified inclusion criteria (Tables 1 and 2). Three studies were RCTs comparing PCI and CABG in LMCA disease (4,8,9). One study was a pre-specified subanalysis of patients with LMCA disease from the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) trial (5,10). Of 1,611 randomized patients, 809 were assigned to PCI and 802 were assigned to CABG. First-generation drug-eluting stents (DES) were implanted in 96% of PCI patients, and a left anterior internal mammary artery graft to the left anterior descending artery was used in 95% of CABG patients. Distal LMCA involvement was observed in 64% of cases. The mean SYNTAX score ranged from 24 to 30, and the mean logistic EuroSCORE ranged from 2.5% to 3.9%. Complete revascularization was achieved in 71% and 76% of patients treated with PCI and CABG, respectively.

**Outcomes.** One-year outcomes are listed in Table 3. There was a nonsignificant trend toward a higher risk of MACCE with PCI versus CABG (14.5% vs. 11.8%; odds ratio [OR]: 1.28; 95% confidence interval [CI]: 0.95 to 1.72; p = 0.11) (Fig. 2), with no heterogeneity ($I^2$ = 0%; p = 0.29) or systematic bias apparent across the studies (p = 0.17). The exclusion of the study from Boudriot et al. (8), which did not include CVA among MACCE, did not significantly affect the MACCE estimate (OR: 1.25; 95% CI: 0.90 to 1.72; p = 0.18). None of the other studies was found to unduly influence the MACCE estimate.

We were not able to separate composite death/MI/CVA from MACCE from the study by Buszman et al. (4), and the study from Boudriot et al. (8) did not report CVA. Thus, death/MI/CVA estimates are drawn from SYNTAX (5) and PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery Abbreviations and Acronyms

- **CABG** = coronary artery bypass graft
- **CI** = confidence interval
- **CVA** = cerebrovascular accident
- **DES** = drug-eluting stent(s)
- **LMCA** = left main coronary artery
- **MACCE** = major adverse cardiac and cerebrovascular event(s)
- **MI** = myocardial infarction
- **OR** = odds ratio
- **PCI** = percutaneous coronary intervention
- **RCT** = randomized clinical trial
- **TVR** = target vessel revascularization
Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease (9), the 2 largest studies. The 1-year composite of death/MI/CVA occurred in 5.3% of PCI and 6.8% of CABG patients (OR: 0.77; 95% CI: 0.48 to 1.22; p = 0.26) (Fig. 2), with no heterogeneity (I² = 0%; p = 0.84).

Death at 1 year occurred in 3.0% and 4.1% of PCI and CABG patients, respectively (OR: 0.74; 95% CI: 0.43 to 1.29; p = 0.29) (Fig. 3), with no heterogeneity (I² = 0%; p = 0.58) or systematic bias (p = 0.09). The 1-year rates of MI were 2.8% and 2.9% in PCI and CABG patients, respectively (OR: 0.98; 95% CI: 0.54 to 1.78; p = 0.95) (Fig. 3), with no heterogeneity (I² = 0%; p = 0.79) or systematic bias (p = 0.17). CVA at 1 year occurred significantly less frequently with PCI compared with CABG (0.1% vs. 1.7%; OR: 0.15; 95% CI: 0.03 to 0.67; p = 0.013) (Fig. 3), with no significant heterogeneity (I² = 0%; p = 0.94) or systematic bias (p = 1.00). The CVA risk reduction with PCI versus CABG lost its statistical significance after excluding the SYNTAX LMCA subgroup (5) from the meta-analysis, although the OR was comparable (OR: 0.20; 95% CI: 0.02 to 1.71; p = 0.14). PCI was associated with a higher 1-year rate of TVR compared with that for CABG (11.4% vs. 5.4%; OR: 2.25; 95% CI: 1.54 to 3.29; p < 0.001) (Fig. 3), with no heterogeneity (I² = 0%; p = 0.72) or systematic bias (p = 0.31).

**Meta-regression and subgroup analyses.** Meta-regression analysis did not disclose statistically significant interactions for any of the previously mentioned outcomes between PCI versus CABG and the log-OR of the number of enrolled patients, diabetes, distal LMCA involvement, mean SYNTAX score, mean logistic EuroSCORE, or complete revascularization (all p = nonsignificant).

The SYNTAX (5) and PRECOMBAT (9) trials reported MACCE stratified by number of vessels involved. In pooled analyses of these 2 studies, the 1-year MACCE rates were nonsignificantly different with PCI compared with those for CABG for isolated LMCA disease (OR: 0.66; 95% CI: 0.18 to 2.40; p = 0.53), LMCA plus 1-vessel disease (OR: 0.58; 95% CI: 0.22 to 1.51; p = 0.26), and LMCA plus 2-vessel disease (OR: 1.28; 95% CI: 0.74 to 2.23; p = 0.38), but higher with PCI in patients with LMCA plus 3-vessel disease (OR: 1.80; 95% CI: 1.06 to 3.07; p = 0.03) (Figs. 4 and 5).

**Discussion**

In this meta-analysis of RCTs involving patients with LMCA disease, PCI was found to be nonsignificantly different than CABG with respect to composite MACCE at 1-year follow-up. In addition, the 2 groups had similar rates of the combined endpoint of death/MI/CVA and of the individual components of death and MI. However, CVA occurred less frequently and TVR occurred more frequently in patients treated with PCI compared with CABG.

In a previous meta-analysis from Naik et al. (11) of 10 studies (8 of which were registries), PCI was associated with a nonsignificant 16% reduction in 1-year MACCE compared with CABG, with an approximately 4-fold

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**Table 1**  
**Studies Included in the Meta-Analysis**

<table>
<thead>
<tr>
<th>Study/First Author (Ref. #)</th>
<th>Year</th>
<th>Design</th>
<th>N</th>
<th>PCI, n</th>
<th>DES, %</th>
<th>CABG, n</th>
<th>LIAD, %</th>
<th>Primary Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEMANS (4)</td>
<td>2008</td>
<td>RCT</td>
<td>105</td>
<td>52</td>
<td>35</td>
<td>53</td>
<td>81</td>
<td>Cardiac death, MI, CVA, repeat revascularization, and/or acute/subacute in-stent thrombosis</td>
</tr>
<tr>
<td>SYNTAX Left Main (5)</td>
<td>2009</td>
<td>Pre-specified subanalysis from RCT</td>
<td>705</td>
<td>357</td>
<td>100</td>
<td>348</td>
<td>97</td>
<td>All-cause death, CVA, MI, and repeat revascularization</td>
</tr>
<tr>
<td>Boudriot et al. (8)</td>
<td>2010</td>
<td>RCT</td>
<td>201</td>
<td>100</td>
<td>100</td>
<td>101</td>
<td>99</td>
<td>All-cause death, MI, and repeat revascularization</td>
</tr>
<tr>
<td>PRECOMBAT (9)</td>
<td>2011</td>
<td>RCT</td>
<td>600</td>
<td>300</td>
<td>100</td>
<td>300</td>
<td>94</td>
<td>All-cause death, CVA, MI, and repeat revascularization</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass graft; CVA = cerebrovascular accident; DES = drug-eluting stent(s); LAD = left anterior descending; LEMANS = Left Main Coronary Artery Stenting; LIMA = left internal mammary artery; MI = myocardial infarction; PCI = percutaneous coronary intervention; PRECOMBAT = Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease; RCT = randomized clinical trial; SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

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**Table 2**  
**Patients and Procedural Characteristics of Included Studies**

<table>
<thead>
<tr>
<th>Study/First Author (Ref. #)</th>
<th>Age, yrs</th>
<th>Male, %</th>
<th>Diabetes, %</th>
<th>Distal LMCA Disease, %</th>
<th>No. of Diseased Vessels, 0/1/2/3, %</th>
<th>SYNTAX Score, Mean</th>
<th>Logistic EuroSCORE, Mean %</th>
<th>Complete Revascularization, Overall/PCI/CABG, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEMANS (4)</td>
<td>61</td>
<td>67</td>
<td>18</td>
<td>58</td>
<td>0/9/23/68</td>
<td>25</td>
<td>3.4</td>
<td>84/79/89</td>
</tr>
<tr>
<td>SYNTAX Left Main (5)</td>
<td>65</td>
<td>74</td>
<td>25</td>
<td>61</td>
<td>13/20/31/36</td>
<td>30</td>
<td>3.9</td>
<td>68/65/73</td>
</tr>
<tr>
<td>Boudriot et al. (8)</td>
<td>68</td>
<td>75</td>
<td>36</td>
<td>71</td>
<td>29/31/27/14</td>
<td>24</td>
<td>2.5</td>
<td>98/98/97</td>
</tr>
<tr>
<td>PRECOMBAT (9)</td>
<td>62</td>
<td>77</td>
<td>32</td>
<td>65</td>
<td>10/17/32/41</td>
<td>25</td>
<td>2.7</td>
<td>69/68/70</td>
</tr>
</tbody>
</table>

LMCA = left main coronary artery; other abbreviations as in Table 1.
increased risk of TVR and no differences in mortality. The lack of randomization in the majority of studies resulted in only moderate internal validity, with moderate/high chance for selection and attrition bias in 30% of studies included and moderate performance and detection bias in all of them. Reliance on registries can lead to incorrect conclusions because of the influence of unassessed confounding variables (e.g., comorbidities, terminal illness, low socioeconomic status); only randomization can provide an unbiased estimation of the effects of a treatment (12). Importantly, our meta-analysis included only randomized data from 4 trials, making the risk of residual confounding unlikely. The present study might also be more reflective of current treatment practice than the earlier meta-analysis (11) because 96% of PCI patients received DES and 95% of CABG patients were revascularized with a left anterior internal mammary artery graft.

The SYNTAX (5) and PRECOMBAT (9) trials were designed as noninferiority trials and were individually un-

### Table 3 1-Year Outcomes in Left Main Patients Revascularized by PCI or CABG

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>PCI (n = 809)</th>
<th>CABG (n = 802)</th>
<th>Absolute Difference (95% CI)</th>
<th>Number Needed to Treat</th>
<th>Number Needed to Harm</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACCE</td>
<td>14.5 (117/807)</td>
<td>11.8 (93/790)</td>
<td>2.7 (0.6 to 6.0)</td>
<td>—</td>
<td>37</td>
<td>0.11</td>
</tr>
<tr>
<td>Death/MI/CVA</td>
<td>5.3 (35/655)</td>
<td>6.8 (43/636)</td>
<td>−1.5 (−4.1 to 1.2)</td>
<td>67</td>
<td>—</td>
<td>0.26</td>
</tr>
<tr>
<td>Death</td>
<td>3.0 (24/807)</td>
<td>4.1 (32/790)</td>
<td>−1.1 (−3.0 to 0.8)</td>
<td>91</td>
<td>—</td>
<td>0.29</td>
</tr>
<tr>
<td>MI</td>
<td>2.8 (23/807)</td>
<td>2.9 (23/790)</td>
<td>−0.1 (−1.8 to 1.6)</td>
<td>1.000</td>
<td>—</td>
<td>0.95</td>
</tr>
<tr>
<td>CVA</td>
<td>0.1 (1/707)</td>
<td>1.7 (12/689)</td>
<td>−1.6 (−2.9 to −0.6)</td>
<td>63</td>
<td>—</td>
<td>0.013</td>
</tr>
<tr>
<td>TVR</td>
<td>11.4 (92/807)</td>
<td>5.4 (43/790)</td>
<td>6.0 (3.3 to 8.7)</td>
<td>—</td>
<td>17</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are % (n/N) unless otherwise indicated.

CI = confidence interval; CVA = cerebrovascular accident; MACCE = major adverse cardiac and cerebrovascular event(s); TVR = target vessel revascularization; other abbreviations as in Table 1.

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### Major Adverse Cardiac and Cerebrovascular Events

<table>
<thead>
<tr>
<th>Model</th>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Events / Total</th>
<th>Odds ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
</tr>
<tr>
<td>Fixed</td>
<td>LEMANS</td>
<td>1.368 (0.579–3.229)</td>
<td>16/52</td>
<td>13/53</td>
</tr>
<tr>
<td>Fixed</td>
<td>SYNTAX left main</td>
<td>1.181 (0.774–1.801)</td>
<td>56/355</td>
<td>46/336</td>
</tr>
<tr>
<td>Fixed</td>
<td>Boudriot et al.</td>
<td>1.450 (0.686–3.086)</td>
<td>19/100</td>
<td>14/101</td>
</tr>
<tr>
<td>Fixed</td>
<td>PRECOMBAT</td>
<td>1.328 (0.725–2.436)</td>
<td>26/300</td>
<td>20/300</td>
</tr>
<tr>
<td>Random</td>
<td>Pooled estimate</td>
<td>1.276 (0.950–1.715)</td>
<td>106</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pooled estimate</td>
<td></td>
<td></td>
<td>PCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
</tbody>
</table>

Favors PCI   Favors CABG

### Death, Myocardial Infarction or Stroke

<table>
<thead>
<tr>
<th>Model</th>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Events / Total</th>
<th>Odds ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
</tr>
<tr>
<td>Fixed</td>
<td>SYNTAX left main</td>
<td>0.745 (0.430–1.291)</td>
<td>25 / 355</td>
<td>31 / 336</td>
</tr>
<tr>
<td>Fixed</td>
<td>PRECOMBAT</td>
<td>0.828 (0.352–1.946)</td>
<td>10 / 300</td>
<td>12 / 300</td>
</tr>
<tr>
<td>Random</td>
<td>Pooled estimate</td>
<td>0.769 (0.484–1.220)</td>
<td>264</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pooled estimate</td>
<td></td>
<td></td>
<td>PCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
</tbody>
</table>

Favors PCI   Favors CABG

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**Figure 2** Effect of PCI on MACCE and the Composite of Death, MI, or Stroke

CI = confidence interval; LEMANS = Left Main Coronary Artery Stenting; MACCE = major adverse cardiac and cerebrovascular event(s); MI = myocardial infarction; PRECOMBAT = Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease; SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery; other abbreviations as in Figure 1.
Figure 3  Effect of PCI on Death, MI, Stroke, and Repeat Revascularization

Pooled odds ratios are from fixed and random models. Abbreviations as in Figures 1 and 2.
derpowered for the composite rate of death/MI/CVA. Even for MACCE, wide noninferiority margins (6.6% to 7.0%) were necessary. In the present 1,611-patient meta-analysis, a nonsignificant 2.7% treatment effect in favor of CABG was evident. However, CVA was more frequent with CABG, whereas TVR was more frequent with PCI. Many clinicians believe that TVR is of less clinical importance than death, MI, or stroke, arguably being more comparable to numerous other adverse outcomes such as bleeding, renal failure, or atrial fibrillation. The present study may thus be informative to guide future trials comparing PCI and CABG for LMCA disease with a more relevant endpoint, such as the composite of death/MI/CVA. In the EXCEL (Evaluation of Xience Prime or Xience V Versus CABG for Effectiveness of Left Main Revascularization) trial, approximately 2,600 patients with left main disease and SYNTAX score ≤32 will be randomized to stent implantation with the second-generation DES Xience stent (Abbott Vascular, Santa Clara, California) or CABG. Of note, EXCEL is including only patients with mild to moderate anatomic complexity (SYNTAX score ≤32), for which the advantages of CABG over PCI may be less evident (13). The SYNTAX score roughly correlates with the extent of coronary atherosclerosis (14), and our meta-analysis supports revascularization by CABG in patients with 3-vessel disease.

### Figure 4
**Effect of PCI on MACCE Stratified by Burden of Coronary Artery Disease**

Pooled odds ratios are from fixed and random models. LMCA = left main coronary artery; other abbreviations as in Figures 1 and 2.

### Figure 5
**Differences in 1-Year MACCE Between PCI and CABG in the Pooled Analysis of the SYNTAX Left Main and PRECOMBAT Studies After Stratification by Burden of Coronary Artery Disease**

Abbreviations as in Figures 1, 2, and 4.
Study limitations. Variation in study design, endpoint definitions, and possible publication bias are limitations of all meta-analyses. Similarly, meta-regressions are prone to misleading results (15). Even with 1,611 patients in the present study, our analysis cannot exclude small differences among the procedures. The present study reflects the outcomes that may be expected when comparing CABG with first-generation DES. Of note, both PCI and CABG procedures continue to improve over time. Finally, because the long-term advantage of CABG over PCI may accrue over time, a fair assessment of the 2 revascularization techniques is likely to require longer follow-up than in the present study.

Conclusions

From the available RCT data, no significant differences were present between PCI and CABG in patients with LMCA disease for the occurrence of 1-year MACCE and the component endpoints of death or MI. However, PCI was associated with higher rates of TVR but with fewer CVAs compared with CABG. Based on the present study, revision of the guidelines regarding left main PCI (1,2) is warranted, raising the level of evidence of current recommendations from B to A.

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REFERENCES


Key Words: coronary artery bypass graft • left main • percutaneous coronary intervention.