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Ralf E. Harskamp, Duke Clinical Research Institute
Judson B. Williams, Duke Clinical Research Institute
Michael Halkos, Emory University
Renato D. Lopes, Duke Clinical Research Institute
Jan G. P. Tijssen, University of Amsterdam
Bruce Ferguson, Jr., East Carolina University
Robbert J. de Winter, University of Amsterdam

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Meta-analysis of minimally invasive coronary artery bypass versus drug-eluting stents for isolated left anterior descending coronary artery disease

Ralf E. Harskamp, MD\textsuperscript{a,b}, Judson B. Williams, MD, MHS\textsuperscript{a}, Michael E. Halkos, MD, MSc\textsuperscript{c}, Renato D. Lopes, MD, PhD, MHS\textsuperscript{a}, Jan G. P. Tijssen, PhD\textsuperscript{b}, Bruce Ferguson Jr, MD\textsuperscript{d}, and Robbert J. de Winter, MD, PhD\textsuperscript{b}

\textsuperscript{a}Duke Clinical Research Institute, Durham NC \textsuperscript{b}Academic Medical Center–University of Amsterdam, Amsterdam, The Netherlands \textsuperscript{c}Division of Cardiothoracic Surgery, Emory University School of Medicine, Atlanta, Ga \textsuperscript{d}Department of Cardiovascular Sciences, East Carolina University Brody School of Medicine, Greenville, NC

Abstract

**Objective**—To compare the outcomes between minimally invasive coronary artery bypass (MINI-CAB) and drug-eluting stent (DES) implantation for isolated left anterior descending artery disease.

**Methods**—Randomized and observational comparative publications were identified using MEDLINE and Google Scholar databases (January 2003 to December 2013). Studies without outcomes data, without DES use, or using conventional bypass surgery were excluded. The outcomes of interest were cardiac death, myocardial infarction, target vessel revascularization, and periprocedural stroke. Data were compared using the Mantel-Haenszel methods and are presented as odds ratios (ORs), 95% confidence intervals (CIs), and number needed to treat.

**Results**—From 230 publications, we identified 4 studies (2 randomized and 2 observational) with 941 patients (478 had undergone MINI-CAB and 463 DES implantation). The incidence of target vessel revascularization at maximum follow-up (range, 6–60 months) was significantly lower in the MINI-CAB group (OR, 0.16; 95%CI, 0.08–0.30; \(P < .0001\); number needed to treat, 13). The incidence of cardiac mortality and MI was similar between the MINI-CAB and DES groups during follow-up (OR, 1.05; 95% CI, 0.44–2.47; and OR, 0.83; 95% CI, 0.43–1.58, respectively). In addition, a similar incidence of periprocedural death (OR, 0.85; 95% CI, 0.21–3.47; \(P = .82\)), myocardial infarction (OR, 0.98; 95% CI, 0.38–2.58; \(P = .97\)), and stroke (OR, 1.36; 95% CI, 0.28–6.70; \(P = .70\)) was observed between the 2 treatment modalities.
Conclusions—Given the available evidence, MINI-CAB will result in lower target vessel revascularization rates but otherwise similar clinical outcomes compared with DESs in patients with left anterior descending artery disease.

Patients who develop coronary artery disease in the left anterior descending coronary artery (LAD) will have a large amount of viable myocardium at risk and will be prone to cardiovascular events, including myocardial infarction (MI), ischemic cardiomyopathy, and sudden cardiac death.\textsuperscript{1,2} Coronary revascularization has, therefore, been recommended to improve the symptoms and clinical outcomes of these patients. However, the optimal revascularization strategy has remained controversial.\textsuperscript{3–5} Coronary artery bypass grafting (CABG) when performed with the left internal mammary artery (LIMA) to LAD graft can provide excellent long-term outcomes but at the cost of an increased risk of complications compared with less invasive percutaneous coronary intervention (PCI). Randomized studies in the early era of PCI failed to match the outcomes obtained with CABG, primarily because of a greater need for repeat revascularization owing to restenosis.\textsuperscript{6–8} However, with the introduction of drug-eluting stents (DESs) a dramatic reduction in restenosis was seen compared with bare metal stents or balloon angioplasty alone. As such, much of the long-term advantages of CABG were thought to have been eliminated.\textsuperscript{9,10} In those settings in which the percutaneous treatment options will be equally effective, most cardiologists, as well as patients, have currently preferred PCI with DES implantation instead of CABG, primarily owing to the desire to avoid complications such as stroke and renal failure and the longer period to full recovery.\textsuperscript{11,12} However, subsequent advances in CABG have led to minimally invasive techniques that allow LIMA to LAD grafting on the beating heart using smaller sternal-sparing incisions.\textsuperscript{13–15} The major rationale for these techniques has been to avoid stroke or systemic embolization by avoiding crossclamping the aorta and avoiding the costs and morbidity associated with the cardiopulmonary bypass circuit.\textsuperscript{16} We performed a meta-analysis to compare the outcomes from minimally invasive coronary artery bypass (MINI-CAB) using LIMA to LAD grafting with PCI using DESs for the management of LAD disease.

METHODS

Inclusion Criteria

To be eligible for inclusion in our meta-analysis, the studies had to have (1) compared MINI-CAB with DES for LAD revascularization and (2) reported the outcomes for ≥1 clinical outcomes (ie, death, MI, stroke, target vessel revascularization [TVR]) during the periprocedural period and at ≥6 months of follow-up.

Search Strategy

A literature search was performed using MEDLINE and Google Scholar databases on all studies published of human subjects from January 1, 2003 to December 29, 2013. We used 2003 as the starting point, because DES technology was not commercially available in most catheterization laboratories before 2003. We combined 3 searches that used the following search headings: “percutaneous coronary intervention,” “PCI,” or “stent” (search 1); “minimally invasive direct,” “endoscopic atraumatic,” “totally endoscopic,” “port-access,”
or “coronary artery bypass” (search 2); and “left anterior descending,” “LAD”, or “single vessel disease” (search 3). To broaden the search, we also used the “related articles” function. All abstracts were reviewed, and no language restrictions were applied. The search resulted in 230 studies (Figure 1). After a review of the titles and abstracts, we found 20 studies that required a full text review. From these studies, we excluded those reporting on outcomes of patients with multivessel disease who had undergone multivessel revascularization (n = 1), same cohort studies with different follow-up periods (n = 1), studies using bare metal stents or balloon angioplasty (n = 12), and studies using conventional CABG with median sternotomy (n = 2). The remaining studies were included in the present meta-analysis.

Statistical Analysis

Our meta-analysis was performed in line with the recommendations from the reporting of meta-analysis guidelines for observational studies. The categorical outcomes data are reported as an odds ratio (OR) statistic, in which an OR of <1 favored the surgical group. We used a random effects model with the Mantel-Haenszel method, in which it was assumed that variation existed among the studies owing to the varying risk profiles and selection criteria among the centers. The calculated OR, therefore, had a more conservative value. Heterogeneity was assessed and reported using the Cochran C statistic. Data inconsistency was reported using I² tests, in which a score of 25%, 50%, and 75% indicated a low, moderate, or high level of data inconsistency, respectively. To translate ORs into benefits to clinical outcome, we calculated the number needed to treat, which is the inverse of the risk difference between the 2 treatment groups. For studies that contained a 0 in the cell for the number of events of interest in either 1 of the groups, we added the value of 0.5 in each cell of the 2 × 2 table for the study in question. This correction was necessary, because cells with 0 events will create problems with the computation of the ratio measures and standard errors of treatment effects. Analyses were performed using Comprehensive Meta-Analysis software, version 2 (Biostat, Englewood, NJ).

RESULTS

Study Characteristics

A total of 4 studies published from 2005 to 2013 that matched the inclusion criteria for comparing MINI-CAB versus DES implantation for isolated LAD revascularization. These studies had included 941 patients, of whom 51% had undergone MINI-CAB and 49% DES implantation. Both reviewers had 100% agreement on data extraction. The study designs involved 2 randomized controlled trials (n = 319) and 2 observational studies using propensity score methods to adjust for confounding (n = 622). The maximum follow-up ranged from 6 to 60 months. The characteristics of these studies are listed in Table 1.

Patient and Procedural Characteristics

An overview of the patient and procedural characteristics is listed in Table 2. The patients were, on average, in their mid-60s (range, 61–66 years) and were predominantly male (range, 64%–80%). The occurrence of diabetes ranged from 21% to 60%, and most patients had preserved left ventricular ejection fraction without a history of MI. Coronary
angiography showed that the treated lesions were predominantly complex lesions, either type B2 or C. In the 2 observational studies, the total occluded LAD lesions were numerically more common than in the MINI-CAB group.\textsuperscript{18,19} Sirolimus-eluting stents were used exclusively in 2 studies.\textsuperscript{12,18} Overall, sirolimus-eluting stents were used in 70% of patients (n = 324) and paclitaxel-eluting stents in 30% of patients (n = 139). Surgical access was performed using a left anterolateral thoracotomy (5–8 cm) between the fourth or fifth intercostal space. In 3 studies, the ribs were retracted to allow LIMA harvesting and anastomosis to the LAD under direct vision.\textsuperscript{12,18,20} In 1 study, the LIMA was harvested using a thoracoscopic approach, and the anastomosis was performed using endoscopic stabilization devices without rib retraction.\textsuperscript{19} All procedures were performed without the use of cardiopulmonary bypass.

**Postprocedural Outcomes**

As shown in Figure 2, the postprocedural outcomes for death, MI, stroke, and TVR were infrequent and also not significantly different statistically between MINI-CAB and DES implantation. Two studies reported the postprocedural hospital days, and both showed a longer length of stay after MINI-CAB than after DES implantation (mean, $4.4 \pm 2.0$ days vs $3.6 \pm 1.5$ days; $P = .017$; and median, 8 days; range, 7–9; vs median, 1; range, 1–1; $P < .0001$).\textsuperscript{12,20}

**Cardiac Death at Maximum Follow-up**

All 4 studies reported on cardiac mortality at the maximum follow-up point. A meta-analysis of the studies did not show any significant differences in cardiac death at the maximum follow-up point between the 2 groups (OR, 1.05; 95% confidence interval [CI], 0.44–2.47; Figure 3). Information on all-cause mortality was also available in all studies and rendered similar results (OR, 1.16; 95% CI, 0.69–1.95; $P = .58$).

**MI at Maximum Follow-up**

Similar to cardiac death, a meta-analysis of the 4 studies did not show any significant difference in the incidence of MI at the maximum follow-up point between the 2 groups (OR, 0.83; 95% CI, 0.43–1.58; Figure 3).

**TVR at Maximum Follow-up**

A meta-analysis of the included studies showed a significantly lower incidence of TVR after MINI-CAB (2.5%) than after DES implantation (12.3%) at the maximum follow-up point, with an OR of 0.16 (95% CI, 0.08–0.30; $P < .0001$). The risk difference between MINI-CAB and DES was 7.7% (range, 1%–14%; number needed to treat, 13; Figure 3).

**DISCUSSION**

Revascularization of patients with isolated LAD disease has evolved significantly by advances in interventional and surgical techniques. The current guidelines support the use of a revascularization strategy in patients with significant proximal LAD disease (using angiographic and fractional flow reserve criteria) to alleviate symptoms and improve the prognosis.\textsuperscript{5} PCI with DESs has become the first-line intervention for most patients with
isolated proximal LAD lesions. However, the findings from our meta-analysis suggest that for isolated LAD revascularization, the use of MINI-CAB will result in more definitive revascularization compared with DESs, although at the expense of a longer initial postprocedural recovery. A number of reasons could explain the difference in outcomes between MINI-CAB and PCI. First, a significant proportion of the treated LAD lesions in our meta-analysis were lesions with high complexity. Previous studies have shown that lesion complexity is an important predictor for procedural success and repeat revascularization procedures after DES implantation. Surgical techniques will be much less affected by lesion complexity and as such will have lower TVR rates. Second, unlike the LIMA graft, coronary stents that include DESs only treat the affected segment but will not be effective in providing revascularization in progressive coronary artery disease in the LAD.

**MINI-CAB and Newer Generation DESs**

Recent studies have shown that newer generation DESs, such as the everolimus-eluting and zotarolimus-eluting stents, will further reduce the risk of MI, reintervention, and stent thrombosis compared with sirolimus-eluting and paclitaxel-eluting stents. Currently, a number of randomized studies are ongoing to assess the comparative effectiveness of these newest generation DESs against conventional CABG in patients with multivessel disease and/or unprotected left main disease (ClinicalTrials.gov Identifiers, NCT01205776 and NCT01311323). Given the rapid advances in surgical techniques to further reduce postprocedural morbidity, future studies are also needed to assess the efficacy and safety of these techniques in the setting of proximal LAD disease compared with conventional stenting.

**Adoption of MINI-CAB in Current Clinical Practice and Future Prospects**

MINI-CAB could present an attractive alternative to conventional CABG, because it omits the risks of deep sternal wound infections and the problems with sternal healing and results in a shorter length of hospital stay and interval to full recovery, with equal safety and efficacy in experienced surgical centers. Despite these advantages, the adoption of MINI-CAB has been slow, and the use of coronary stents for isolated LAD disease has been the default revascularization strategy. The low use of MINI-CAB can, in part, be explained by the greater technical demands of this procedure compared with conventional CABG, its restriction to revascularization of isolated LAD and diagonal disease, and finally, its invasiveness compared with DES. However, the use of MINI-CAB could regain popularity, because recent studies of “hybrid coronary revascularization” (in which MINI-CAB is combined with DESs for non-LAD lesions) have shown promising results compared with conventional surgery.

The findings of our meta-analysis have reinforced the need for a multidisciplinary heart team approach to discuss all treatment options for patients with isolated LAD disease, including the role of MINI-CAB, and to select the most appropriate treatment strategy for individual patients. Although the current guidelines have provided recommendations for the use of MINI-CAB, a recently published statement document on optimizing outcomes and
the future prospects of CABG proposed including MINI-CAB in the decision tree for revascularization in patients with isolated LAD disease.29

Study Limitations

Our study had several limitations. First, the inclusion criteria, study design, treatment protocols, and outcome assessment varied across the studies. Second, our study included observational data, which is prone to selection bias and confounding, despite applying proper adjustment methods. Third, among the randomized studies, both the treatment allocation and the assessment of clinical outcomes were unblinded. Fourth, owing to the variation in definitions of events and data collection and the use of scheduled angiographic follow-up, we noted increased heterogeneity among some of the outcomes among the included studies. Finally, a publication bias could not be ruled out, because meta-analyses can only report on the outcomes of published studies.

CONCLUSIONS

In patients who underwent isolated LAD revascularization, the use of MINI-CAB resulted in lower TVR rates and similar rates of cardiac death and MI at midterm follow-up compared with PCI with DESs.

Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>coronary artery bypass grafting</td>
</tr>
<tr>
<td>DES</td>
<td>drug-eluting stent</td>
</tr>
<tr>
<td>LAD</td>
<td>left anterior descending artery</td>
</tr>
<tr>
<td>LIMA</td>
<td>left internal mammary artery</td>
</tr>
<tr>
<td>MI</td>
<td>myocardial infarction</td>
</tr>
<tr>
<td>MINI-CAB</td>
<td>minimally invasive coronary artery bypass</td>
</tr>
<tr>
<td>PCI</td>
<td>percutaneous coronary intervention</td>
</tr>
</tbody>
</table>

References


FIGURE 1.
Consort diagram. LAD, Left anterior descending artery.
FIGURE 2.
Summary of average differences in periprocedural outcomes. MINI-CAB, Minimally invasive coronary artery bypass; DES, drug-eluting stent; OR, odds ratio; CI, confidence interval.
FIGURE 3.
Forest plot showing results from meta-analysis of studies reporting cardiac death, myocardial infarction, and repeat revascularization after minimally invasive coronary artery bypass compared with drug-eluting stents. MINI-CAB, Minimally invasive coronary artery bypass; DES, drug-eluting stent; OR, odds ratio; CI, confidence interval; MI, myocardial infarction; TVR, target vessel revascularization.
### TABLE 1

Characteristics of studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hong and colleagues(^{20})</th>
<th>Ben-Gal and colleagues(^{18})</th>
<th>Thiele and colleagues(^{12})</th>
<th>Etienne and colleagues(^{19})</th>
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<td>Study design</td>
<td>RCT</td>
<td>Cohort</td>
<td>RCT</td>
<td>Cohort</td>
</tr>
<tr>
<td>Year published</td>
<td>2005</td>
<td>2006</td>
<td>2009</td>
<td>2013</td>
</tr>
<tr>
<td>Country</td>
<td>South Korea</td>
<td>Israel</td>
<td>Germany</td>
<td>Belgium</td>
</tr>
<tr>
<td>Patients (n)</td>
<td>189</td>
<td>166</td>
<td>130</td>
<td>456</td>
</tr>
<tr>
<td>MINI-CAB</td>
<td>Direct vision</td>
<td>Direct vision</td>
<td>Direct vision</td>
<td>Thoracoscopic</td>
</tr>
<tr>
<td>Stent type</td>
<td>PES/SES</td>
<td>SES</td>
<td>SES</td>
<td>PES/SES</td>
</tr>
<tr>
<td>Follow-up (mo)</td>
<td>6</td>
<td>23</td>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>Contact</td>
<td>Office visit</td>
<td>Telephone, records</td>
<td>Office visit</td>
<td>Office, records</td>
</tr>
<tr>
<td>Catheterization at follow-up</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
| Definition proc MI      | Q-wave, CK-MB                  | —                               | Q-wave, CK-MB                   | Q-wave, troponin                 

\(^{RCT\text{, Randomized clinical trial; MINI-CAB, minimally invasive coronary artery bypass; PES, paclitaxel-eluting stent; SES, sirolimus-eluting stent; proc MI, procedural myocardial infarction; CK-MB, creatine kinase MB-fraction.}}\)

\(^{*}\text{Enrollment varied between the 2 groups: in the surgical group, the patients were included from 1997 to 2011 and, in the matched coronary stent group, from 2002 to 2005.}\)
### TABLE 2

Patient and procedural characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>MINI-CAB</th>
<th>DES</th>
<th>MINI-CAB</th>
<th>DES</th>
<th>MINI-CAB</th>
<th>DES</th>
<th>MINI-CAB</th>
<th>DES</th>
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<tbody>
<tr>
<td><strong>Patient characteristics</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients (n)</td>
<td>70</td>
<td>119</td>
<td>83</td>
<td>83</td>
<td>65</td>
<td>65</td>
<td>260</td>
<td>196</td>
</tr>
<tr>
<td>Age (y)</td>
<td>61 ± 10</td>
<td>61 ± 10</td>
<td>&gt;70 (39)</td>
<td>&gt;70 (39)</td>
<td>66 (59–71)</td>
<td>66 (59–72)</td>
<td>63 ± 12</td>
<td>62 ± 12</td>
</tr>
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<td>Male gender (%)</td>
<td>64</td>
<td>64</td>
<td>80</td>
<td>80</td>
<td>71</td>
<td>69</td>
<td>75</td>
<td>74</td>
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<td>Diabetes (%)</td>
<td>49</td>
<td>37</td>
<td>29</td>
<td>30</td>
<td>25</td>
<td>28</td>
<td>21</td>
<td>60</td>
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<tr>
<td>Previous MI (%)</td>
<td>23</td>
<td>22</td>
<td>34</td>
<td>29</td>
<td>23</td>
<td>23</td>
<td>12</td>
<td>21</td>
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<tr>
<td>CVD (%)</td>
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<td>3</td>
<td>—</td>
<td>—</td>
<td>9</td>
<td>3</td>
<td>—</td>
<td>—</td>
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<tr>
<td>UA (%)</td>
<td>43</td>
<td>50</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>41</td>
<td>40</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>52 ± 9</td>
<td>53 ± 9</td>
<td>&lt;30 (7)</td>
<td>&lt;30 (1)</td>
<td>65 (60–70)</td>
<td>65 (60–66)</td>
<td>&lt;30 (8)</td>
<td>&lt;30 (1)</td>
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<td><strong>Procedural characteristics</strong></td>
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<tr>
<td>Total occlusion (%)</td>
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<td>0</td>
<td>24</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>13</td>
<td>3</td>
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<tr>
<td>Bifurcation lesion (%)</td>
<td>—</td>
<td>—</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>—</td>
<td>—</td>
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<tr>
<td>B2C lesion (%)</td>
<td>76</td>
<td>76</td>
<td>—</td>
<td>—</td>
<td>54</td>
<td>62</td>
<td>—</td>
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<tr>
<td>Lesion length (mm)</td>
<td>19 ± 4</td>
<td>20 ± 5</td>
<td>—</td>
<td>—</td>
<td>12 (10–18)</td>
<td>12 (10–17)</td>
<td>—</td>
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<tr>
<td>Stent length (mm)</td>
<td>23 ± 5</td>
<td>—</td>
<td>—</td>
<td>13 (13–18)</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Stent diameter (mm)</td>
<td>2.9 ± 0.3</td>
<td>—</td>
<td>—</td>
<td>3 (3–3.5)</td>
<td>—</td>
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</table>

Data presented as mean ± standard deviation or median (range), except as noted. MINI-CAB, Minimally invasive coronary artery bypass; DES, drug-eluting stent; MI, myocardial infarction; CVD, cerebrovascular disease; UA, unstable angina; LVEF, left ventricular ejection fraction.

*Data in parentheses are number of patients.