Minimally Invasive Direct Coronary Artery Bypass Graft Surgery or Percutaneous Coronary Intervention for Proximal Left Anterior Descending Artery Stenosis: A Meta-Analysis

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Background. **We conducted a metaanalysis comparing early and midterm cardiovascular adverse events associated with minimally invasive direct coronary artery bypass graft surgery (MIDCABG) and percutaneous coronary intervention (PCI), with a focus on drug-eluting stents (DES).**

Methods. **A systematic literature review (MEDLINE, EMBASE, Scopus, and so forth) yielded 12 studies (7 randomized controlled trials; 5 observational) pooling more than 2,000 patients. A random effect, inverse variance metaanalysis was conducted, and a subgroup analysis of the PCI-DES cohort was performed. Events were compared as risk ratios using a 95% confidence interval (CI). Heterogeneity of results was evaluated by Eggers I^2 test. Results are presented as early (0 to 1 year) and midterm (2 to 5 years).**

Results. **Midterm mortality in the PCI and MIDCABG groups (3.6% and 2.6%, respectively) was comparable (1.24, 95% CI: 0.66 to 2.33; $p = 0.5$; $I^2 = 0\%$). Risk of early restenosis was lower in the MIDCABG cohort compared with PCI (0.40, 95% CI: 0.16 to 0.99; $p = 0.05$; $I^2 = 57\%$). Although the early risk of recurrence of angina was comparable, over time it was 61% (43% to 74%) lower for MIDCABG patients ($p < 0.001$). Midterm results on analysis of the entire cohort demonstrated an increased risk for target vessel reinterventions (3.84, 95% CI: 2.7 to 5.5; $p < 0.001$) in the PCI cohort. Subgroup analysis revealed that the PCI-DES cohort (4 studies; 456 patients) had a higher risk of recurrent angina (risk ratio 3.4, 95% CI: 1.9 to 6.2; $p < 0.001$; $I^2 = 0\%$) and target vessel reinterventions (risk ratio 4.16, 95% CI: 2.7 to 6.6; $p < 0.001$; $I^2 = 0\%$) at midterm follow-up (2 to 5 years).**

Conclusions. **Survival rates are comparable after either MIDCABG or PCI for proximal LAD disease. However, even the use of DES was associated with significantly higher rates of angina recurrence and the need for target vessel reintervention as compared with MIDCABG.**

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Therapeutic intervention for coronary artery disease consists of percutaneous intracoronary stenting (PCI) or coronary artery bypass graft surgery (CABG). Compared with surgery, PCI is a less invasive procedure associated with lower morbidity. Minimally invasive direct coronary artery bypass (MIDCABG) is a recent introduction, where the grafting is performed through a small thoracotomy incision. It is associated with a shorter hospital stay and earlier recovery than conventional surgery.

Results comparing MIDCABG and PCI in proximal left anterior descending artery (p-LAD) disease are conflicting, especially with the recent addition of drug-eluting stents (DES). Therefore, we conducted a metaanalysis comparing clinical events associated with PCI and MIDCABG in the treatment of p-LAD disease.

Material and Methods

Inclusion Criteria

Original articles (randomized controlled trials and observational studies) comparing PCI and MIDCABG for p-LAD disease (from 2000 to May 2013) were identified. The search was limited to (1) human subjects, (2) original articles, and (3) English language. Only studies reporting clinically relevant endpoints (eg, mortality, recurrence of angina, or reinterventions during follow-up) were included. Editorials and review articles were excluded.

Technique of MIDCABG

MIDCABG consisted of harvest of the left internal thoracic artery (LITA) and its subsequent grafting to the

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Abbreviations and Acronyms

BMS = bare metal stent
CI = confidence interval
DES = drug-eluting stent
LAD = left anterior descending artery
LITA = left internal thoracic artery
MIDCABG = minimally invasive direct coronary artery bypass graft surgery
p-LAD = proximal left anterior descending artery
RCT = randomized controlled trial
RR = risk ratio
TVR = target vessel reintervention

LAD. That was most commonly accomplished through a left thoracotomy, in some cases, robotically assisted. Sequential grafting of the LITA was occasionally performed; however, only the LAD and its branches was grafted in all included studies.

Percutaneous Intervention

Percutaneous coronary intervention was performed in the routine manner. Studies used a relatively uniform strategy of stent deployment with at least 90% patients having undergone either bare-metal stent (BMS) or DES insertion. A separate subgroup analysis of articles reporting outcome with DES was also conducted.

Studied Endpoints

Clinical endpoints compared were duration of hospital stay, mortality, recurrence of angina, myocardial infarction, and need for reintervention. All results were assimilated into two periods: early (0 to 1 year) and midterm (2 to 5 years).

Search Strategy

We conducted a systematic search of articles on EMBASE, Scopus, Web of Science, and MEDLINE using the terms "single vessel disease," "left anterior descending artery," "percutaneous intervention," "drug-eluting stent," "coronary artery bypass," "minimally invasive coronary artery bypass," and "MIDCABG" in various combinations.

Two of the authors (V.S., S.V.D) independently screened abstracts and retrieved the full text articles. All full text articles were then evaluated independently to conform to the inclusion criteria. Discrepancies were resolved by consensus. Data were obtained from the studies using a prespecified data abstraction form.

Statistical Analysis

Statistical analysis for binary data was performed using the "meta" package for R 3.0.1 [1, 2]. The risk ratio (RR) was implemented as the effect estimate. In the inverse weighted model, each study contributes a percentage of the final pooled estimate [3]. That is presented in each forest plot under the column of weight (W). As per Bate's correction, 0.5 was added to each cell of the two-by-two table in case the study or control arm had zero events [4]. The cutoff for the p value is 0.05; data are presented with 95% confidence intervals (CI). To compare the hospital stay, studies were pooled using the standardized mean difference as the effect estimate.

Results are presented as a forest plot, depicting each individual risk ratio (RR) as well as the overall composite effect estimate. A risk ratio with its 95% CI less than 1 would favor MIDCABG. A random effects model has been implemented as both randomized controlled trial (RCT) and retrospective studies have been pooled [3]. Heterogeneity is defined as the variation among studies that would contribute to the overall results. It was evaluated using the Eggers I^2 test and further stratified into low (25% to 49%), moderate (50% to 74%), and high (>75%) heterogeneity [3]. A subgroup analysis was performed after excluding the observational studies and compared to the overall effect. A separate subgroup analysis was conducted of studies implementing DES as their technique of percutaneous intervention.

Publication bias was excluded by a visual inspection of the contour-enhanced funnel plot symmetry and determined using the Begg-Mazumdar rank correlation test. The results are presented as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for metaanalysis of observational studies [5, 6].

Results

The initial search criteria yielded 312 articles. Exclusion of duplicates and further refinement of Medical Subject Headings yielded 193 abstracts, which were evaluated for inclusion. The detailed PRISMA flow diagram is presented in Figure 1. Two articles were excluded to avoid patient duplication. A total of 14 articles [7–19] discussing the results of 12 studies (seven RCTs and five observational studies) fulfilled the selection criteria. Two articles presented results of the same randomized controlled trial at a follow-up period of 6 months and 5 years [9, 10]. Etienne and colleagues [7, 8] have presented two articles discussing a retrospective analysis of data from two institutions. Drenth and associates [16, 20] have also presented their data initially in 2002 and then results of a longer follow-up in 2004. Blazek and colleagues [21] presented data regarding results of BMS at the end of 10 years of follow-up. As other articles failed to present data with such a long follow-up period, it was excluded from the metaanalysis. Herz and coworkers [22] was excluded because the study included patients with triple vessel disease. Care was taken to ensure nonduplication of data during analysis.

The detailed patient demographics are presented in Tables 1 and 2. As the majority of patients were part of RCTs, patient population between cohorts is relatively well matched. In four articles [10, 11, 15, 16], angiographic evaluation was performed at the end of the follow-up period. Drug-eluting stents were implemented as the interventional strategy in five studies (463 patients). Sirolimus- or paclitaxel-eluting stents were used for