Minimally Invasive Extracorporeal Circulation Circuit Is Not Inferior to Off-Pump Coronary Artery Bypass Grafting: Meta-Analysis Using the Bayesian Method

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The pathophysiologic side effects of cardiopulmonary bypass have already been identified. Minimally invasive extracorporeal circulation technologies (MiECT) and off-pump coronary artery bypass graft surgery (OPCABG) aim to reduce these problems. This meta-analysis provides a comparison of MiECT and OPCABG in randomized and observational studies. A fully probabilistic, Bayesian approach of primary and secondary endpoints was conducted. MiECT does not give inferior results when compared with OPCABG. However, there is a trend to borderline significantly higher blood loss in this group in randomized controlled trials. The question whether MiECT is equivalent to OPCABG can be answered with the affirmative, but long-term follow-up data are needed to detect any advantage over time.

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REVIEW

The technique of off-pump coronary artery bypass grafting (OPCABG) was established more than 3 decades ago with the objective to reduce the unfavorable pathophysiologic side effects of conventional cardiopulmonary bypass circuits on the organ systems triggered by complement system activation through foreign surfaces, priming volume, and negative and positive pressures in the reservoir [1, 2]. To overcome these effects, the concept of minimally invasive extracorporeal circuits evolved over the last 15 years not only as an alternative to the more conventional extracorporeal circulation circuits but also as an alternative to an off-pump strategy in case of coronary artery bypass graft surgery (CABG) [3, 4]. The use of minimally invasive extracorporeal circulation technologies (MiECT) is now expanding; these systems offer several potential advantages because they reduce the systemic inflammatory response and subsequent organ dysfunction [5, 6].

The typical MiECT consists of a closed circuit, which includes the oxygenator and the pump. The circuit has no open venous reservoir. All components of the minimally invasive extracorporeal circuits are coated with heparin, and the tubing system is significantly reduced in length. These characteristics permit a reduction of the priming volume between 200 mL and 650 mL compared with the standard extracorporeal circuit [3, 7]. The OPCABG technique has shown good results as postoperative morbidity and mortality were reduced in various studies compared with CABG with conventional circuits. But the literature also presents some major drawbacks, such as a higher rate of incomplete revascularization, especially in dilated and hypokinetic hearts, due to more difficult exposure of obtuse coronary marginal branches and the lesser quality of the coronary anastomoses. For these reasons, the initial enthusiasm for OPCABG has vanished over the last years [8, 9]. Now, MiECT aims to incorporate the advantages of a traditional cardiopulmonary bypass circuit while overcoming the limitations of OPCABG [10].

With this is in mind, the main questions are these: (1) is MiECT is comparable to OPCABG in terms of operative outcomes; and (2) is the safety of a minimized heart-lung machine (with less systemic inflammatory response) even superior to OPCABG? The aim of the present meta-analysis is to overcome the low power of the limited sample sizes of the existing studies by pooling data of 3,410 patients, and to determine whether MiECT is a valid or superior alternative to OPCABG [11].

To minimize selection bias, we decided to include all studies that compare the two strategies, no matter whether the design was randomized or not. Of course,

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Abbreviations and Acronyms

AF = atrial fibrillation
CABG = coronary artery bypass graft surgery
CI = confidence interval
ICU = intensive care unit
MI = myocardial infarction
MiECT = minimally invasive extracorporeal circulation technologies
OPCABG = off-pump coronary artery bypass grafting
OR = odds ratio
RCT = randomized clinical trial
SMD = standardized mean difference

randomized trials are the gold standard in medical research because they provide the strongest evidence of treatment safety and efficacy. With respect to the comparison of MiECT versus OPCABG, randomized trials are not very common, and those trials tend to include only few patients [12]. Observational studies may provide particularly relevant information on the topic; that is the reason we decided to include observational studies. As that might considerably increase heterogeneity, we calculated all pooled estimates stratified by study design: randomized versus observational.

Material and Methods

Studies

The studies reviewed were randomized controlled trials (RCT) and observational studies that compared OPCABG and MiECT for patients undergoing CABG.

Participants

The studies reviewed involved adult patients (aged 18 years or more) who were undergoing cardiac surgery for coronary artery disease with either OPCABG or MiECT.

Search Strategy and Data Source

The search for literature was performed through PubMed, PubMed Central, Web of Science (includes MEDLINE, Conference Proceedings Citation Index, Data Citation Index CAB abstracts, Derwent Innovations Index), OvidSP (includes EMBASE, Ovid MEDLINE, HMIC, Transport Database). For the identification of RCT, the Cochrane Library was accessed. In addition, we searched Google scholar.

The searches were last updated on October 29, 2015. The search terms used for minimal extracorporeal circulation were "MECC" or "mini ECC" or "MiECT" or "minimal extracorporeal circulation" or "minimized extracorporeal circulation" or "mini-extracorporeal circulation" or "miniaturized extracorporeal circulation" or "minimal extracorporeal circulation technique" or "miniaturized extracorporeal circulation technique" or "miniaturized ECC" or "miniaturized extracorporeal circulation circuit" or "minimal extracorporeal circulation circuit."

There are no defined Medical Subject Headings (MeSH) terms for minimal extracorporeal circulation. The MeSH term for off-pump coronary artery bypass grafting was defined as "coronary artery bypass, off-pump," or search terms were used: "off-pump surgery" or "off-pump CABG" or "off-pump coronary artery bypass grafting" or "off-pump technology" or "off-pump coronary revascularization" or "off-pump coronary artery revascularization" or "off-pump coronary artery grafting" or "off-pump revascularization technology" or "off-pump coronary artery revascularization technique" or "off-pump technique" or "off-pump CABG method" or "OPCAB."

No restrictions on publication status, time, or predefined outcome were applied. Reference lists of evaluable studies, systematic reviews, meta-analyses, narrative reviews, and reports were also hand searched for additional studies eligible for inclusion. The search was conducted in compliance with the established Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) in health care interventions statement (Appendix 1) [13].

Eligibility Criteria

Two authors independently screened all titles and abstracts of the initial search, and reviewed full-text articles with respect to eligibility for inclusion. Disagreements were resolved by a third reviewer. The final decision was made on the basis of the full texts (Table 1).

Data Extraction and Analyses

Two authors (H.P.P. and B.G.) independently extracted the data into a predefined scheme; disagreement was solved by consensus, and the final decision was made by a third author (B.W.). In addition to the extraction of patient characteristics and operation details, we assessed details of the methodology, the specific study question, and inclusion criteria.

Study Design

Inhouse mortality was defined as the primary endpoint for this analysis; secondary endpoints were stroke, myocardial infarction (MI), postoperative atrial fibrillation (AF), total blood loss in milliliters, length of intensive care unit (ICU) stay in hours and length of hospital stay in days. We treated the number of anastomoses like an endpoint to use the technique of random effects analysis.

Statistical Analysis

We conducted a fully probabilistic, Bayesian analysis when events were rare, with mortality as a primary endpoint and MI and stroke as secondary endpoints. We used a Bayesian method developed for random effects meta-analysis on the odds ratio (OR) scale [14, 15]. Further details can be found in Appendix 2.

The model adequately accounts for situations with sparse event data, including zero cells in one or both treatment group and control group. Monte-Carlo Markov