



# Totally endoscopic coronary artery bypass surgery: A meta-analysis of the current evidence

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## ARTICLE INFO

### Article history:

Received 24 October 2017

Received in revised form 18 December 2017

Accepted 20 December 2017

### Keywords:

Totally endoscopic coronary artery bypass grafts  
TECAB

Endoscopy/endoscopic procedures

Minimally invasive heart surgery

Robotic heart surgery

## ABSTRACT

**Background:** Totally endoscopic coronary artery bypass (TECAB) has emerged as an alternative to other minimally invasive techniques. However, limited TECAB results are available to date. The purpose of this systematic review is to examine the existing literature to give an objective estimate of the outcomes of TECAB using a meta-analytical approach.

**Methods:** A comprehensive online review was performed in Ovid MEDLINE®, Ovid EMBASE and The Cochrane Library from 2000 to July 2017. Eligible studies included single arm TECAB studies as well as comparative studies (TECAB vs minimally invasive direct coronary artery bypass (MIDCAB)). Pooled event rates and odds ratios (ORs) for operative mortality, perioperative myocardial infarction (MI), perioperative stroke, graft patency and repeat revascularization were estimated. Single arm and pairwise comparisons were performed.

**Results:** Seventeen single arm TECAB articles (3721 patients, weighted mean follow-up 3.3 years) were included. The pooled event rate was 0.80% (95%CI: 0.60–1.2%) for operative mortality, 2.28% (95%CI: 1.7–3%) for perioperative MI, 1.50% (95%CI: 1.1–2.0%) for perioperative stroke, 2.99% (95%CI: 1.6–5.4%) for repeat revascularization and 94.8% (95%CI: 89.3–97.5%) for early graft patency (weighted mean follow-up 10.1 months). On pairwise meta-analysis 376 patients (263 TECAB and 113 MIDCAB) were included. No difference in operative mortality (OR = 0.25, 95%CI: 0.02–2.83), perioperative MI (OR = 3.09, 95%CI: 0.37–26.12) or perioperative stroke (OR = 1.33, 95%CI: 0.17–10.26) was found between the two techniques.

**Conclusions:** TECAB has an acceptably low operative risk and a good early patency rate. The incidence of perioperative MI requires further investigation. The dearth of data comparing TECAB to open approaches compels the need for future comparative trials.

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## 1. Introduction

Since the Food and Drug Administration approval of the da Vinci robotic surgical system for cardiac surgery in 2002, there has been an increase in cardiac procedures performed either robotically or with robotic assistance [1]. While robotic mitral valve surgery has been well established, the limits of the robot for other cardiac procedures continue to be expanded [2]. One developing use of the robot is for coronary artery bypass graft surgery (CABG). In most centers, robotic

assistance is used for the harvesting of the left internal mammary artery (LIMA), while the distal anastomosis is performed under direct visualization through a small thoracotomy [3].

In totally endoscopic coronary artery bypass (TECAB) however, the entire procedure is performed through trocar accesses, without any surgical incision. While the majority of TECAB is performed robotically, there are some centers which use endoscopic instruments [3]. To date, data on TECAB are limited to single center experiences, with obvious limitations in terms of sample size and generalizability. For this reason, it is difficult for a surgeon to give an objective assessment and estimate of the risks and benefits of TECAB when counseling a patient.

The purpose of this manuscript is to use a meta-analytic approach to provide physicians and patients an objective estimate of the outcomes of TECAB in the current era.

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## 2. Methods

This study was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [4].

### 2.1. Search strategy

A medical librarian performed comprehensive searches to identify studies that evaluated the impact of totally endoscopic coronary artery bypass surgery. Search terms included: TECAB, endoscopic coronary artery bypass, minimally invasive coronary artery bypass surgery, MIDCABG and left anterior small thoracotomy bypass.

Searches were run on June 19, 2017 in the following databases from 2000 to present: Ovid MEDLINE® (In-Process & Other Non-Indexed Citations and Ovid MEDLINE® 1946 to Present); Ovid EMBASE (1974 to present); and The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register). The full search strategy for Ovid MEDLINE is available in supplement (Supplementary Table 4).

### 2.2. Inclusion criteria

The literature was reviewed for any article published starting in the year 2000. There were no language restrictions or article type restrictions on the search strategy. The articles had to include >40 patients in each study. Additionally, the authors had to provide data on in-hospital stay along with follow-up data, if available. The description of the procedure had to specify that there was no open surgical incision involved.

### 2.3. Study selection

The searches across the chosen databases were conducted. After results were de-duplicated, 2 independent reviewers (J.L., M.R.) screened the citations. Discrepancies were resolved by consensus and a third reviewer's (M.G.) opinion. Titles and abstracts were reviewed against predefined inclusion/exclusion criteria. Articles considered for inclusion involved randomized clinical trials (RCTs), controlled trials, or cohort studies in which human, adult patients with coronary artery disease underwent minimally invasive coronary artery bypass surgery.

Full text was then pulled for the selected studies for a second round of eligibility screening. Reference lists for articles selected for inclusion in the study were also searched (i.e. backward snowballing); from these, additional, relevant articles were screened. In case of multiple publications with the same patients' cohort, studies with the most recent, complete, data were included in the final analysis. Studies that did not have adequate information on a particular outcome were not included in that event analysis.

Critical appraisal of eligible studies was assessed via the Newcastle-Ottawa Quality Assessment Scale (NOS) for Cohort Studies (Supplementary Table 2) [5]. Studies with scores of six or more were included in our meta-analysis.

The full PRISMA flow diagram outlining the study selection process is available in Supplementary Fig. 1.

### 2.4. Outcomes of interest

For the single arm analysis, the primary outcome was the pooled event rate of operative mortality, while secondary outcomes were the pooled event rate of perioperative myocardial infarction (MI), perioperative stroke, graft patency and repeat revascularization.

For the pairwise comparison with minimally invasive direct coronary artery bypass (MIDCAB), the primary outcome was operative mortality and secondary outcomes were perioperative MI, perioperative stroke, and repeat revascularization.

### 2.5. Data extraction and statistical analysis

Data extraction of all included studies was performed independently by 2 investigators (J.L., M.R.) and in case of disagreement a third investigator (M.G.) was included and an agreement was negotiated. Microsoft Office Excel 2010 (Microsoft, Redmond, Washington) was used for data extraction.

Extracted variables included the following: study name, publication year, study design, number of patients, interventions, age, sex, diabetes mellitus (%), peripheral vascular disease (PVD), extent of coronary artery disease (CAD), ejection fraction % (EF%), EuroSCORE, surgical procedure, operative mortality, perioperative MI, stroke, graft patency, repeat revascularization, graft patency follow-up time, and follow-up survival time.

The data could be synthesized only when the number of studies equals or exceeds two. Measurement data reported as mean  $\pm$  SD were adopted. Pooled event rates and odds ratio (OR) with 95% Confidence Interval were calculated.

Postoperative morbidities and mortality risks were pooled on a logarithmic scale using a random effects model I (inverse variance method) [6]. The Cochran Q statistic and the  $I^2$  test were used to assess studies' heterogeneity. If heterogeneity was significant ( $I^2 > 75\%$ ), a leave one out sensitivity analysis was performed [7].

Funnel plots and Egger's regression test were used to assess for potential publication bias in our meta-analysis. If publication bias was suspected, visual assessment of cumulative forest plot as well as Classic and Orwin's fail-safe N tests were used for further

assessment. If significant publication bias was found, Duval and Tweedie's trim and fill method was used to adjust for the possible bias.

Comprehensive Meta-Analysis V 3.0 (Biostat, Inc., Englewood, NJ) was used for statistical analysis.

## 3. Results

### 3.1. Eligible studies and characteristics of studies

Among 3536 retrieved searched articles, 17 single arm TECAB articles were finally eligible with a total of 3721 included patients. From the seventeen articles, 2 comparative studies were identified which included a total of 376 patients: TECAB 263 (69.9%) and MIDCAB 113 (30.0%).

Among included patients the mean age was 60.6 years, 70.2% were males, mean EF was 56.8%, 25.9% had diabetes, and 8.1% had pulmonary disease. Only 30.9% of the population underwent procedures on 2 or more coronary vessels while 69.1% had only 1 vessel treated.

The majority of cases were performed using cardiopulmonary bypass and antegrade cardioplegia (62.1%). The weighted mean cross-clamp and cardiopulmonary bypass times were 67.9 min and 100.4 min, respectively.

The weighted mean clinical follow-up time was 3.3 years. In those studies which aimed to assess graft patency, 90.9% of eligible patients had assessment of the graft by either coronary angiography or computed tomographic angiography for study purposes. The weighted mean angiographic follow up time was 10.1 months.

### 3.2. Study quality

The results of our Newcastle-Ottawa scale assessment yielded 11 studies with 6 stars, 4 studies with 7 stars and 2 studies with 8 stars (Supplementary Table 2).

### 3.3. Meta-analysis of postoperative outcomes

#### 3.3.1. Operative mortality

The pooled event rate for operative mortality was 0.80% with 95%CI of 0.60–1.2%. 3676 patients were assessed for this outcome and recruited from 16 included articles (Fig. 1A).

On pairwise meta-analysis, no difference in operative mortality was identified (OR = 0.25 (95%CI: 0.02–2.83; Fig. 2)).

#### 3.3.2. Perioperative myocardial infarction

The pooled event rate for perioperative MI was 2.28% with 95%CI of 1.7–3%. 2556 patients were assessed for this outcome and recruited from 14 included articles (Fig. 1B).

On pairwise meta-analysis, no difference in perioperative MI was identified (OR = 3.09 (95%CI: 0.37–26.12; Fig. 2)).

#### 3.3.3. Perioperative stroke

The pooled event rate for perioperative stroke was 1.50% with 95%CI of 1.1–2.0%. 3353 patients were assessed for this outcome and recruited from 15 articles (Fig. 1C).

On pairwise meta-analysis, no difference in perioperative stroke was identified (OR = 1.33 (95%CI: 0.17–10.26; Fig. 2)).

#### 3.3.4. Repeated revascularization

The pooled event rate for follow-up repeated revascularization was 2.99% with 95%CI of 1.6–5.4%.

1,217 patients were assessed for this outcome and recruited from 9 articles (Fig. 1D).

Pairwise meta-analysis was not performed due to insufficient number of studies.

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