Endoscopic Vein Harvesting for Coronary Artery Bypass Grafting is Safe and Reduces Postoperative Resource Consumption

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Abstract

**Background:** The greater saphenous vein is still frequently used as a conduit for coronary artery bypass grafting (CABG). Previously, veins were harvested through a single continuous skin incision, commonly referred to as open vein harvesting (OVH), while endoscopic vein harvesting (EVH) techniques have become increasingly popular. However, the postoperative consumption of healthcare resources remains uncertain. Therefore, the present study performed a systematic review, with meta-analysis, of outcomes relating to consumption of healthcare resources and clinical effectiveness following EVH and OVH for CABG.

**Methods:** A systematic search was performed in five databases. OVH was defined as the use of open harvesting techniques using a single continuous incision, and all studies comparing EVH to OVH for CABG were eligible.

**Results:** EVH was associated with increased duration of surgery, no difference in the length of stay in intensive care units, a reduced total length of stay in hospital, a reduced need for antibiotic treatment for leg wound infections, a reduced need for follow-up visit(s) at general practitioners/out-patient clinics, a reduced need for visit(s) by the homecare nurses, a reduced need for revision(s) of the leg wound, a reduced need for readmission(s) related to leg wounds complications and no difference in repeat cardiac catheterization(s). Furthermore, EVH reduced pain intensity approximately five days postoperatively, but not 30 days postoperatively. EVH did not increase the occurrence of mid-term myocardial infarction, recurrence of chest pain, repeat revascularization and mid-term all-cause mortality.

**Conclusions:** EVH provides safe clinical outcomes compared to OVH while reducing the short-term postoperative resource consumption. This article provides a formal synthesis of the available data on clinical effectiveness and consumption of healthcare resources following EVH and OVH for CABG, hence enabling future investigation of the long-term cost-effectiveness of methods.

Keywords: Venous grafts; Endoscopy/endoscopic procedures; Health economics; Wound infection

Introduction

Most patients suffering from multi-vessel coronary artery disease should be treated with coronary artery bypass grafting (CABG) and although the use of arterial conduits was increasing, the greater saphenous vein is still frequently used as a conduit [1]. Previously, the harvesting process involved an open vein harvesting (OVH) technique with a single continuous skin incision but today the majority is harvested using an endoscopic vein harvesting (EVH) technique, as it reduces leg wound morbidity [2-4]. Several meta-analyses have been conducted to compare OVH techniques to minimally invasive vein harvesting techniques, yet none have actually compared OVH using a single continuous skin incision to EVH using total endoscopic equipment [4-13]. Moreover, recent meta-analyses did not include several outcomes relevant to the postoperative consumption of healthcare resources that could provide essential information for the estimation of EVH’s cost-effectiveness compared to OVH which is essential to make an informed decision about vein harvesting method [14,15]. Therefore, the present study performed a systematic review with meta-analysis of outcomes relating to resource consumption and clinical effectiveness following EVH and OVH with a single continuous skin incision.

Materials and Methods

Search strategy and inclusion criteria

In May 2014, we performed a systematic search in the following databases: Cochrane, Embase, Pubmed, Scopus, and Web of Knowledge. In addition to the systematic search, a number of abstracts were identified thru secondary referencing. All studies comparing EVH to OVH for CABG were eligible, i.e. full articles, abstracts and posters were all included. OVH was defined as the use of open harvesting techniques using a single continuous incision, i.e. studies using bridging techniques were excluded. EVH was defined as: the VasoView system (Maquet, Wayne, NJ, USA), the ENDOPATH system (Ethicon Endosurgery, Cincinnati, OH, USA), the Clearglide Endoscopic Vessel Harvesting System (CardioVation, Ethicon Inc. Johnson & Johnson, Somerville, NJ, USA), the Karl Storz Endoskope (Karl Storz, Tuttingen, Germany), the Virtuoso system (Terumo Cardiovascular Corp., Ann Arbor, MI, USA), the EndoSaph Vein Harvest system (Unites States Surgical, Tyco Healthcare, Norwalk, CT, USA), a mixture of above mentioned, or if primary author’s stated EVH was used although the system was not defined. Our search was not limited by language but in case the inclusion was limited by language. Corresponding author: Jan Jesper Andreasen, Departments of Cardiothoracic Surgery and Clinical Medicine, Centre for Cardiovascular Research, Aalborg University Hospital, Høbrovej 18-22, DK-9000 Aalborg, Denmark, Tel.: +45 97664651; E-mail: jja@m.dk

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of 47 articles were included in our study (Figure 1). A list of screened for full text assessment and non-suitable articles were removed. A total and 1,420 abstracts were assessed for inclusion. 107 articles were selected of OVH versus EVH. The I² statistics were used to test for significant were retrieved from the included studies by a single author (LO).

Studies of outcomes can be found in the supplementary file 3. Outcomes and (16) repeat cardiac catheterization. The definitions applied to each revision of leg wound, (15) readmission for leg wound complication, (10) total length of hospital stay, (11) use revascularization, (6) mid-term myocardial infarction (MI), (7) mid-term all-cause mortality, (8) total duration of surgery, (9) length of stay in intensive care unit (ICU), (11) use of antibiotics, (12) visit to physician, (13) visit by homecare nurse, (14) revision of leg wound, (15) readmission for leg wound complication, and (16) repeat cardiac catheterization. The definitions applied to each of the outcomes can be found in the supplementary file 3. Outcomes were retrieved from the included studies by a single author (LO).

Study outcomes

The included papers were reviewed for 16 outcomes which potentially affects the costs and effectiveness of treatments. These were: (1) leg wound infection (LWI), (2) pain at postoperative day five, (3) pain at postoperative day 30, (4) recurrence of chest pain, (5) repeat revascularization, (6) mid-term myocardial infarction (MI), (7) mid-term all-cause mortality, (8) total duration of surgery, (9) length of stay in intensive care unit (ICU), (10) total length of hospital stay, (11) use of antibiotics, (12) visit to physician, (13) visit by homecare nurse, (14) revision of leg wound, (15) readmission for leg wound complication, and (16) repeat cardiac catheterization. The definitions applied to each of the outcomes can be found in the supplementary file 3. Outcomes were retrieved from the included studies by a single author (LO).

Statistical analyses

Individual trials were pooled to perform a statistical comparison of OVH versus EVH. The I² statistics were used to test for significant heterogeneity between studies [19]. Significant heterogeneity was defined as I² ≥ 50%. The overall effect was calculated using fixed effects models in the absence of heterogeneity and random effects in the presence of heterogeneity.

The choice of statistical methods for comparing the pooled outcomes accounted for the fact that the outcome measures should be usable in a health economic evaluation. Categorical outcome variables were combined by calculating the log odds ratio (OR) if all studies presented the raw event counts. For some categorical outcome variables, the included studies reported either hazard ratios or raw event counts. For these outcomes the adjusted hazard ratio was extracted where possible, otherwise the rate ratios (RR) were calculated from the raw event counts. These were combined using the log RRs. A continuity correction of 0.5 was applied in studies reporting zero event count in one group. Zero-total event studies were excluded in all comparisons of categorical outcomes [20]. Continuous outcome variables were compared using weighted mean difference (WMD). Publication bias was assessed by visual inspection of funnel plots and by testing for small-studies effect using Egger’s regression statistic. P-values <0.05 were considered statistically significant. The 95% confidence intervals (CIs) were reported rather than the p-values. All statistical analyses were performed in Stata version 12.1 (StataCorp, College Station, Texas, USA).

Results

A total of 2,780 abstracts were identified. Duplicates were removed and 1,420 abstracts were assessed for inclusion, 107 articles were selected for full text assessment and non-suitable articles were removed. A total of 47 articles were included in our study (Figure 1). A list of screened and excluded studies is available upon request. The characteristics of the studies included and the pooled baseline demographics are shown in Tables 1 and 2, respectively. The quality of the studies ranged from 10 to 24 (Scale 0-28). The summary statistics are presented in Table 3 while forest plots and funnel plots related to each outcome are supplied in supplementary file 4 and 5, respectively. Unless stated otherwise, no publication bias was observed.

Outcomes mainly related to resource consumption

Fourteen studies (5 randomized controlled trials (RCTs) and 9 non-randomized controlled trials (nRCTs)) were identified for the comparison of total duration of surgery. Three studies were excluded as they did not present mean ± standard deviation. Analysis of the remaining studies showed that EVH significantly increase surgery time (WMD 15.02, 95% CI 3.07 to 26.97).

Five studies (3 RCTs and 2 nRCTs) were identified for the comparison of length of stay in ICU. A single study was excluded as it did not present mean ± standard deviation. Analysis of the remaining four showed no difference in length of stay in ICU (WMD 0.05, 95% CI -0.22 to 0.31). Sixteen studies (9 RCTs and 7 nRCTs) were identified for the analysis of total length of stay in hospital. From fifteen of these studies mean ± standard deviation could be obtained and these were analyzed. Although no difference was observed in the length of stay in ICU, the total length of stay was significantly reduced for EVH patients (WMD-0.54, 95% CI-100 to -0.09). Funnel plots showed some evidence of publication bias and this was confirmed by Egger’s
Variable | EVH (n=137,601) | OVH (n=127,647) | Availability (percentage of patients)
--- | --- | --- | ---
Age (years), mean | 64.1 | 65.3 | 93.9%
Male, % | 79.2% | 75.6% | 98.4%
Diabetes, % | 32.2% | 30.7% | 98.3%
Smoking, % | 44.1% | 44.4% | 92.7%
Body mass index (kg/m²), mean | 27.5 | 27.5 | 91.9%
Obesity *, % | 24.5% | 23.7% | 4.1%
EUROscore, mean | 4.1 | 4.5 | 1.3%

C: The Clearglide Endoscopic Vessel Harvesting System (CardioVation, Ethicon Inc. Johnson & Johnson, Somervill, NJ, USA); EVH: Endoscopic Vein Harvesting; OVH: Open Vein Harvesting; * Obesity was defined as a BMI>30 kg/m²

Table 2: Pooled baseline characteristics.


Regression statistic.

Seventeen studies (9 RCTs and 8 nRCTs) recorded the number of patients receiving antibiotic treatment for their LWI. One RCT was excluded as it reported zero-total events. Analysis of the remaining 16 studies showed that EVH significantly reduced the use of antibiotics (OR 0.25, 95% CI 0.19 to 0.34).

Five studies (3 RCTs and 2 nRCTs) recorded the number of patients in need of follow-up visit at their GP or at the out-patient clinic. Analysis showed that EVH significantly reduced this need (OR 0.29, 95% CI 0.17 to 0.48). Likewise, six studies (4 RCTs and 2 nRCTs) were included in the analysis of need for visits by the homecare nurse which EVH also significantly reduces (OR 0.09, 95% CI 0.04 to 0.21).

Twenty-six studies (10 RCTs and 16 nRCTs) recorded if revision of the leg wound was needed. Three of these studies (2 RCTs and 1 nRCT) were excluded as they reported zero-total events. Analysis of the remaining studies showed a significant reduction in revision for the EVH group (OR 0.09, 95% CI 0.04 to 0.21).

Twenty studies (10 RCTs and 10 nRCTs) reported the number of patients readmitted for complications related to their leg wound. Four RCTs reported zero-total events and were excluded and the analysis of the remaining studies showed that EVH significantly reduced the number of readmissions (OR 0.62, 95% CI 0.45 to 0.85).

Seven studies (3 RCTs and 4 nRCTs) reported the number of repeat cardiac catheterizations. Three out of these seven studies reported zero-total event counts and were excluded. Analysis of the remaining four studies (1 RCT and 3 nRCTs) showed no difference between treatments (OR 1.06, 95% CI 0.66 to 1.68).

Clinical outcomes

Forty-two studies (18 RCTs and 24 nRCTs) reported LWI. One RCT had zero-total events and was excluded. Analysis of the remaining 41 studies showed that EVH significantly reduced the odds of LWI (OR 0.22, 95% CI 0.15 to 0.32). The corresponding funnel plot showed evidence of publication bias and Egger’s regression statistic was significant.

Eleven studies (5 RCTs and 6 nRCTs) investigated pain intensity measured on a 10cm visual analogue scale (VAS) approximately five days postoperatively. One study was excluded as the standard deviation of the mean VAS scores was not reported. Analysis of the remaining ten studies showed that EVH was superior to OVH (WMD -1.48, 95% CI -2.45 to -0.50). Likewise, six studies (4 RCTs and 2 nRCTs) investigated pain intensity approximately 30 days postoperatively. Although EVH showed a tendency towards a reduction in the pain intensity, the difference was not statistically significant at approximately 30 days postoperatively (WMD -0.28, 95% CI -0.60 to 0.04).

Eight studies (5 RCTs and 3 nRCTs) investigated the recurrence of chest pain. Four of these studies were excluded due to zero-total events and analysis of the remaining four studies (2 RCTs and 2 nRCTs) showed no difference in the recurrence of chest pain (OR 0.98, 95% CI 0.62 to 1.55).

Eight studies (2 RCT and 6 nRCTs) reported hazard ratios or raw event counts for repeat revascularization. The seven studies (1 RCT and 6 nRCTs) which reported non-zero-total events were combined using RR as the summary measure. Analysis showed that EVH patients had a statistically significant increased rate of repeat revascularization (RR 1.20, 95% CI 1.02 to 1.42). A sensitivity analysis of repeat revascularization was conducted using studies with a Down and Black score of 20 or more. Two studies (1 RCT and 1 nRCT) were included in this sensitivity analysis and in this analysis EVH was not associated with an increased risk of repeat revascularization (RR 1.28, 95% CI 0.95 to 1.71).

Four studies (4 nRCTs) reported occurrence of MIs with a minimum follow-up of 12 months. These studies were included in the analysis of mid-term MI which showed no difference between treatments (OR 1.13, 95% CI 0.73 to 1.74).

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**Table 3:** Summary of results for each outcome ordered by the summary measure.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies analyzed (RCT/nRCT)</th>
<th>Sample size</th>
<th>Summary measure</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg wound infection</td>
<td>17/24</td>
<td>256,072</td>
<td>Odds ratios (95% CI) 0.22 (0.15 to 0.32)</td>
<td>83.1%</td>
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<td>Use of antibiotics</td>
<td>8/8</td>
<td>4,563</td>
<td>Odds ratios (95% CI) 0.25 (0.19 to 0.34)</td>
<td>0%</td>
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<tr>
<td>Visits to physician</td>
<td>3/2</td>
<td>1,501</td>
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<td>Visits by homecare nurse</td>
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<tr>
<td>Readmission for leg wound complication</td>
<td>6/10</td>
<td>6,609</td>
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**CI:** Confidence Interval; ICU: Intensive Care Unit; nRCT: Non-Randomized Controlled Trial; RCT: Randomized Controlled Trial; VAS: Visual Analogue Scale.

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Eleven studies (1 RCT and 10 nRCTs) supplied hazard ratios or raw event counts regarding all-cause mortality with a follow-up above 12 months. The RCT had zero-total events and was excluded. The remaining ten studies were combined using RR as the summary measure. No difference in mid-term all-cause mortality was found (RR 0.92, 95% CI 0.77 to 1.11).

**Discussion**

Compared to OVH, EVH was shown to reduce leg wound morbidity in the short-term postoperative course. The mid-term clinical outcomes did not appear different between groups. EVH was not associated with an increased risk of repeat revascularization when analyzing the studies with the highest quality scores. This proves that EVH may be used without compromising safety. Although EVH appeared to be a slightly more time consuming technique, the postoperative resource consumption was reduced. As such, EVH will reduce costs related to hospital stay, surgical revisions, follow-up visits, and antibiotics, compared to OVH. It should be noted that this is not the same as concluding that EVH is cost-saving compared to OVH.

Several other studies have conducted systematic reviews, with meta-analyses, of outcomes following minimally invasive vein harvesting techniques compared to open vein harvesting techniques [4-13]. One main difference between the present study and the previous studies should be noted: the definition of the harvesting techniques plays a crucial role in the inclusion of studies. As an example, the present study applied the same definition of EVH as Deppe et al. [5] but defined the comparator differently. Deppe et al. defined the comparator, conventional vein harvesting, as open harvesting techniques with or without a continuous skin incision (i.e., bridging technique) or the use of any other kind of non-total endoscopic instrument, including the SaphLITE System (Teleflex Medical, Research Triangle Park, NC) or the VEGA system (B. Braun-Aesculap, Tuttinglen, Germany). The meta-analysis by Sastry et al. [4] applied the same definition as the present study for OVH, while EVH was defined differently. Sastry et al. considered the SaphLITE System, which was considered a conventional harvesting technique by Deppe et al., as an endoscopic technique. These differences in the definitions of harvesting techniques, and outcomes for that matter, impede the comparison of our results to those of other meta-analyses. While point-estimates may differ slightly, the conclusions for clinical outcomes do not differ.

**Strengths and limitations**

While the present meta-analysis applied a more strict definition of OVH and EVH than previous meta-analyses it identified more relevant studies than any other met-analysis. As such, it provides a thorough comparison of OVH using a single continuous skin incision to EVH using total endoscopic equipment. However, a few limitations should be noted when interpreting the results. Firstly, none of the studies included were RCTs designed to test the long-term safety and effectiveness of EVH compared to OVH. Especially, no RCTs with a follow-up above 12 months could be included in the analysis of mid-term MI and all-cause mortality. The need for further high-quality RCTs with a longer follow-up have been acknowledged by the clinical community and two studies are expected. The ESOS trial will report events of death, MI and recurrence of angina within two year following randomization for approximately 200 patients [21]. The REGROUP trial is expected to run for approximately 6.5 years and will report events of all-cause mortality, MI and repeat revascularization for roughly 1150 patients [22]. Before the results of these studies become available, the long-term safety of EVH should be interpreted with caution. Secondly, meta-analyses of non-RCT may be prone to biased results if the individual studies contain selection bias. While this could be handled be performing secondary analysis where non-RCT are not included, it was chosen not to do so in the present study. If non-RCT were excluded in a secondary analysis, several outcomes would have no information or information from one or two studies. Hence, meta-analysis might not be that relevant. Thirdly, meta-analyses of EVH vs. OVH have been criticized for lacking information about the quality of the saphenous vein and the experience of the surgeons performing the harvest [23]. A poor-quality vein conduit is going to have poor patency, regardless of which method was used. Nevertheless, meta-analysis remains the gold standard. The key should be to interpret the meta-analyses as the, current, best available evidence.

**Conclusion**

EVH increases the intraoperative resource consumption while it reduces the postoperative resource consumption. EVH provides a reduction in short-term leg wound related morbidity compared to OVH and the major clinical outcomes are similar for both groups. Whether this translates into EVH being cost-effective compared to OVH can only be evaluated in a rigorous cost-effectiveness analysis.

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