Cost-utility analysis comparing laparoscopic vs open aortobifemoral bypass surgery

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Objectives: Laparoscopic aortobifemoral bypass has become an established treatment option for symptomatic aortoiliac obstructive disease at dedicated centers. Minimally invasive surgical techniques like laparoscopic surgery have often been shown to reduce expenses and increase patients’ health-related quality of life. The main objective of our study was to measure quality-adjusted life years (QALYs) and costs after totally laparoscopic and open aortobifemoral bypass.

Patients and methods: This was a within trial analysis in a larger ongoing randomized controlled prospective multicenter trial, Norwegian Laparoscopic Aortic Surgery Trial. Fifty consecutive patients suffering from symptomatic aortoiliac occlusive disease suitable for aortobifemoral bypass surgery were randomized to either totally laparoscopic (n=25) or open surgical procedure (n=25). One patient dropped out of the study before surgery. We measured health-related quality of life using the EuroQol (EQ-5D-5L) questionnaire at 4 different time points, before surgery and for 6 months during follow-up. We calculated the QALYs gained by using the area under the curve for both groups. Costs were calculated based on prices for surgical equipment, vascular prosthesis and hospital stay.

Results: We found a significantly higher increase in QALYs after laparoscopic vs open aortobifemoral bypass surgery, with a difference of 0.07 QALYs, (p=0.001) in favor of laparoscopic aortobifemoral bypass. The total cost of surgery, equipment and hospital stay after laparoscopic surgery (9,953 €) was less than open surgery (17,260 €), (p=0.001).

Conclusion: Laparoscopic aortobifemoral bypass seems to be cost-effective compared with open surgery, due to an increase in QALYs and lower procedure-related costs.

Keywords: laparoscopy, aortobifemoral bypass, cost-utility, quality-adjusted life years, QALYs, EQ-5D, health-related quality of life, HRQoL, cost-effectiveness

Introduction

In patients with peripheral arterial disease (PAD), a significantly impaired health-related quality of life (HRQoL), due to reduction in walking ability and limb pain, has been reported.1-5 In patients with aortoiliac occlusive disease (AIOD), which is a manifestation of PAD, blood flow to the lower extremities can be improved with the help of either a totally laparoscopic or an open aortobifemoral bypass. The laparoscopic aortobifemoral bypass (LABF) has become an established treatment option for symptomatic AIOD at many dedicated centers.6-11 At Oslo University Hospital, we introduced the laparoscopic technique in 2005,12-14 and since February 2013, we have been conducting a randomized controlled trial,15,16 to compare the early morbidity after the two treatment methods.
Previous experiences with minimally invasive surgical techniques have been shown to improve HRQoL and reduce procedure-related expenses.\textsuperscript{17–21} The investigation concerning the relative effectiveness and safety of a new procedure compared with a standard procedure is of importance. Especially, for the health-service providers, the cost-effectiveness of any treatment is important in decision making.\textsuperscript{22} Similar to many other national health providers, the Norwegian government is increasingly focused on the cost-effectiveness of our health services, resulting in new national guidelines that describe that any new method has to be assessed for cost-effectiveness.\textsuperscript{23,24} Since we are conducting a study on a new treatment method, laparoscopic aortic surgery, it was relevant to perform a health economic evaluation.\textsuperscript{25} Rouers et al, performed a calculation of mean cost in LABF vs open aortobifemoral bypass surgery (OABF), and found decreased costs per patient in the laparoscopic group.\textsuperscript{26} However, the study was not randomized and they excluded the patients who were converted from laparoscopic to open surgery. No other known economical evaluations of LABF have been performed to this date.

The main objective of our study was to perform a cost–utility analysis by calculating QALYs and costs after totally laparoscopic vs open aortobifemoral bypass procedure.

**Patients and methods**

**Design**

Since February 2013, we have been conducting a multicenter randomized controlled trial, Norwegian Laparoscopic Aortic Surgery Trial (NLAST), at the Department of Vascular Surgery, Oslo University Hospital. This project is a substudy of the NLAST,\textsuperscript{15,16} where patients with AIOD classified according to the Trans-Atlantic Inter-Society Consensus II (TASC-II) as type D lesions are randomized to either LABF or OABF.\textsuperscript{27} Inclusion and exclusion were based on the following criteria.

**Inclusion criteria**

- Patient with AIOD, TASC-II type D lesions,\textsuperscript{27} and with symptoms in the form of:
  - intermittent claudication, with patient-reported, pain-free walking distance <200 m, and/or
  - chronic critical lower limb ischemia with rest pain, ischemic ulcers or gangrene, duration of symptoms >2 weeks.

**Exclusion criteria**

- Eligible for endovascular procedure
- Chronic obstructive pulmonary disease (COPD) ≥ stage IV, GOLD classification\textsuperscript{28}
- Symptomatic coronary heart disease
- Chronic heart failure, ejection fraction <40%
- Active cancer disease
- Hostile abdomen
- Abdominal aortic aneurysm ≥3.0 cm\textsuperscript{27}
- Acute critical limb ischemia, duration of symptoms ≤2 weeks

**Participants**

Three vascular surgery departments in the south-eastern region of Norway participated in the study.

**Intervention**

The patients underwent aortobifemoral bypass through a totally laparoscopic transperitoneal, retrocolic, prerenal approach described by Coggia et al\textsuperscript{29} or a traditional open technique through a midline laparotomy.

**Outcomes and perspective**

The main objectives of our study were to measure QALYs and costs after totally laparoscopic vs open aortobifemoral bypass procedure in order to assess the cost-effectiveness. Based on our cohort study, we expected a gain in HRQoL during the first 6 months and similar results in the 2 groups thereafter.\textsuperscript{13,14} The patients answered the EuroQol EQ-5D-5L questionnaire at 4 different time points; before surgery (baseline), and at 1, 3 and 6 months postoperatively.\textsuperscript{30,31} The costs included in this study are the cost of surgical equipment, prosthesis and the costs related to the hospital stay. We registered exact resource use during surgery for the first 3 open and 3 laparoscopic patients. This included all disposable and non-disposable surgical equipment. We then calculated a mean price for the resources during surgery for each group based on those 6 patients. As the 2 procedures are relatively standardized, we considered it to be sufficient to extrapolate from these 6 patients. The cost of hospital stay was calculated based on national data for price per day in a somatic ward.\textsuperscript{32} Costs included were only those that incurred during the hospital stay. We chose a health care sector perspective for the analysis.

**Randomization and blinding**

The patients were randomized to either LABF or OABF. We used block randomization and closed opaque envelopes. The sequence was random and unknown to the researchers.
Blinding of researchers, surgeons and/or participants was not considered possible.

Analysis and statistics
The EQ-5D-5L questionnaire validated in Norwegian language, was completed at all 4 time points and HRQoL was estimated based on a value set from the UK, due to the lack of any available Norwegian value set. Since these are repeated correlated measurements, we calculated QALYs using area under the curve (AUC) for both groups. Deceased patients were set to have a quality of life equal to 0 after death. One QALY was defined as 1 year of perfect health (reported by patients). Systemic morbidity was defined as all non-fatal complications related to the surgical procedure, excluding complications related to the graft and wound. No discounting of costs or health effects was performed due to the short time horizon of the analyses. Categorical variables were summarized as frequencies and continuous variables by the median and interquartile range. Comparisons between the two treatment groups were performed by using the Mann-Whitney U-test for continuous variables, and Fisher’s exact test for categorical variables. A generalized linear model with gamma family and log link function was used to analyze differences in QALYs and costs. The results were controlled for confounding factors and baseline values, including baseline EQ-5D-5L score. There were missing values for 1 patient at 3 and 6 months, we imputed the mean value for the same treatment group at each time point. To give an impression of uncertainty in the overall estimates of cost-effectiveness, we performed 1000 bootstrap samples and presented incremental cost (Δcosts) and incremental effect (ΔQALYs) between LABF and OABF. This cost-utility is a within trial analysis of a larger ongoing randomized trial, NLAST; therefore, an individual power analysis was not conducted for this sub-study. Statistical significance was set at a 5% level (p<0.05). The software used for statistical analyses were Epi Info (Epi Info™ software, Centers for Disease Control and Prevention, Atlanta, GA, USA), IBM SPSS statistics version 22.0 (IBM corporation, Armonk, NY, USA) and Microsoft Office Excel® (Microsoft, Redmond campus, Redmond, WA, USA).

Ethics
The project was voluntary and participants gave an informed, written consent. The trial was approved by the Regional Committee for Medical and Health Research Ethics (REC, region south-east of Norway, registration number 2012/1367). The trial was registered at www.clinicaltrials.gov, with the registration number NCT01793662.

Results
Participant flow and recruitment
Fifty consecutive patients from the participating hospitals were included from February 2013 to February 2016. They were randomized to either LABF (n=25) or OABF (n=25). The participant flow is described in Figure 1. The baseline characteristics of the patients in the two groups are given in Table 1. One laparoscopic procedure was converted from laparoscopic to open surgery due to bleeding. The patient was analyzed in the laparoscopic group, in accordance with the “intention-to-treat” principle. No patients were excluded after randomization. One patient dropped out after randomization and another did not wish to complete the follow-up program. One patient in the open group died of an acute myocardial infarction on the second postoperative day. This within trial analysis was completed after the inclusion of 50 patients.

Outcomes and estimation
Operative data and postoperative results are described in Table 2. Operation time was significantly longer in the

- Patients with symptomatic AIOD eligible for aortobifemoral bypass surgery. February 2013–February 2016 (n=50)
- Randomization
- Drop outa (n=1)
- LABF (n=25)
- OABF (n=24)
- Mortality (n=1)

Figure 1 Flow chart of patient population with AIOD TASC-II type D lesion treated with either totally LABF or OABF.

Notes: aPatient dropped out after randomization; he was randomized to open surgery.
Abbreviations: AIOD, aortoiliac occlusive disease; LABF, laparoscopic aortobifemoral bypass; OABF, open aortobifemoral bypass; TASC, Trans-Atlantic Inter-Society Consensus.
LABF group, but they had shorter postoperative hospital stay than the open group, 4.0 vs 7.0 days, \( p < 0.001 \). There was no statistically significant difference between the two groups in terms of morbidity and mortality; however, there seem to be a tendency toward less total morbidity after LABF, \( p = 0.058 \).

HRQoL-scores based on EQ-5D-5L for the two groups, at baseline and during follow-up are presented in Figure 2. HRQoL is higher during follow-up in the laparoscopic group at all survey time points. Although, there is a small difference in HRQoL at baseline, this difference was not statistically significant. At the single time point measurements; only the difference at 1 month is statistically significant. AUC was calculated for these repeated correlated measurements of HRQoL in both groups. Total QALYs gained were calculated by AUC as HRQoL multiplied by follow-up time. The LABF group had a significantly higher gain in QALYs, with a difference of 0.07 QALYs, \( p = 0.001 \). The costs of resources (hospital stay, surgical equipment and vascular prosthesis) are presented in Table 3.32 The operative equipment was more expensive in the LABF group. However, the total cost per patient is much less in the LABF group compared with the OABF group, 9,953 € vs 17,260 €, \( p = 0.001 \) (Table 4). The higher gain in QALYs and lower costs are also demonstrated in a scatter plot showing costs and QALYs for each patient (Figure 3A). The open group has more extreme values, both with regard to costs and HRQoL. The uncertainty surrounding the mean estimates of incremental costs and QALYs, based on bootstrapping, are demonstrated in Figure 3B. The Figure 3B shows a high probability that LABF is both more effective and less costly than OABF.

We used a generalized linear model to control for possible confounding effects. The difference in QALY’s was still significantly in favor of laparoscopy after controlling for possible confounding effects.

### Table 1 Baseline characteristics of patients treated with either totally laparoscopic or open aortobifemoral bypass for AIOD

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Laparoscopy, (N=25)</th>
<th>Open surgery, (N=24)</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, median (IQR)</td>
<td>62.0 (58.0–66.0)</td>
<td>66.0 (58.5–70.0)</td>
<td>0.170*</td>
</tr>
<tr>
<td>Female gender N (%)</td>
<td>15 (60.0)</td>
<td>14 (58.3)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Current smoker N (%)</td>
<td>12 (48.0)</td>
<td>15 (62.5)</td>
<td>0.393*</td>
</tr>
<tr>
<td>Hypertension (HT) N (%)</td>
<td>19 (76.0)</td>
<td>17 (70.8)</td>
<td>0.466*</td>
</tr>
<tr>
<td>COPD N (%)</td>
<td>4 (16.0)</td>
<td>6 (25.0)</td>
<td>0.335*</td>
</tr>
<tr>
<td>Diabetes mellitus (DM) N (%)</td>
<td>1 (4.0)</td>
<td>0 (0)</td>
<td>0.510*</td>
</tr>
<tr>
<td>Coronary heart disease (CHD) N (%)</td>
<td>2 (8.0)</td>
<td>7 (29.2)</td>
<td>0.060*</td>
</tr>
<tr>
<td>ASA classification, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA class 2.</td>
<td>0 (0)</td>
<td>1 (4.2)</td>
<td>c</td>
</tr>
<tr>
<td>ASA class 3.</td>
<td>25 (100.0)</td>
<td>22 (91.7)</td>
<td></td>
</tr>
<tr>
<td>ASA class 4.</td>
<td>0 (0)</td>
<td>1 (4.2)</td>
<td>c</td>
</tr>
<tr>
<td>Fontaine classification, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fontaine class 2b.</td>
<td>19 (76.0)</td>
<td>19 (79.2)</td>
<td>c</td>
</tr>
<tr>
<td>Fontaine class 3.</td>
<td>5 (20.0)</td>
<td>5 (20.8)</td>
<td></td>
</tr>
<tr>
<td>Fontaine class 4.</td>
<td>1 (4.0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>EQ-5D-5L score, median (IQR)</td>
<td>0.58 (0.46–0.73)</td>
<td>0.48 (0.39–0.61)</td>
<td>0.157 a</td>
</tr>
</tbody>
</table>


**Abbreviations:** IQR, interquartile range; AIOD, aortoiliac occlusive disease; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists classification.

### Table 2 Operative and postoperative characteristics of patients treated with either totally laparoscopic or open aortobifemoral bypass for AIOD

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Laparoscopy, N=25</th>
<th>Open surgery, N=24</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation time (minutes), median (IQR)</td>
<td>221 (203–248)</td>
<td>196 (160–230)</td>
<td>0.024*</td>
</tr>
<tr>
<td>Postoperative stay in hospital(days), median (IQR)</td>
<td>4.0 (3.0–5.0)</td>
<td>7.0 (6.0–9.0)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Thirty-day hospital readmission, N (%)</td>
<td>2 (8.0)</td>
<td>4 (16.7)</td>
<td>0.314*</td>
</tr>
<tr>
<td>Thirty-day mortality, N (%)</td>
<td>0 (0)</td>
<td>1 (4.2)</td>
<td>0.490*</td>
</tr>
<tr>
<td>Thirty-day systemic morbidity, N (%)</td>
<td>2 (8.0)</td>
<td>6 (25.0)</td>
<td>0.111 b</td>
</tr>
<tr>
<td>Thirty-day total morbidity (systemic and local*), N (%)</td>
<td>7 (28.0)</td>
<td>13 (54.2)</td>
<td>0.058 b</td>
</tr>
</tbody>
</table>

**Notes:** *Mann-Whitney U-test, *Fisher’s exact test, *systemic morbidity was defined as all non-fatal complications related to the surgical procedure, excluding complications related to the graft and wound, *local morbidity was defined as complications related to the graft and wound.

**Abbreviation:** IQR, interquartile range; AIOD, aortoiliac occlusive disease.
for the confounding effects of coronary heart disease, COPD, hypertension, diabetes, EQ-5D-5L score before surgery, smoking and chronic critical ischemia (p=0.008).

The multivariate regression analysis also showed that the difference in total cost per patient were significantly in favor of laparoscopy, after controlling for the confounding effects of coronary heart disease, COPD, hypertension, EQ-5D-5L before surgery and chronic critical ischemia (p<0.001).

**Discussion**

**Summary**

We found significantly higher gain in QALYs and lower costs after laparoscopic vs open aortobifemoral bypass surgery. This gain maintained its statistical significance even after controlling the results for baseline differences in HRQoL and other confounding variables.

**Discussion**

EQ-5D is the most commonly used quality of life questionnaire in health economic evaluations, and it is easy and highly tolerated by patients.36,37 Another tool might detect smaller differences, but as long as the results are unambiguous in favor of laparoscopy, this would likely not influence our conclusions.36 We chose a generic quality of life questionnaire to capture the differences between the two groups. A disease specific tool could have been better to assess symptoms and deterioration in HRQoL due to PAD, but would not necessarily capture the differences comparing laparoscopy with laparotomy, which was our main objective.38 Additionally, neither of the disease-specific questionnaires are validated for the economic analysis25 nor made available in the Norwegian language. Although we used a UK tariff for valuing EQ-5D, we do not think the results would have been altered if a Norwegian value set had been available.

HRQoL is the primary indication of treatment and main benefit in revascularization surgery in patients with PAD.2,3 Some have argued the lack of “hard data”, like morbidity and mortality, in these cost-utility evaluations and have also uttered concerns about the use of QALYs and its role in decision making.22,39,40 However, there are no known differences in

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**Table 3** Resources and estimation of cost per patient comparing totally LABF with OABF

<table>
<thead>
<tr>
<th>Resources</th>
<th>Laparoscopy, unit cost (€)</th>
<th>Open surgery, unit cost (€)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 day of postoperative hospital stay</td>
<td>1,726</td>
<td>1,726</td>
<td>SAMDATA 2014, Norwegian Health Directorate (Huseby et al32)</td>
</tr>
<tr>
<td>Surgical equipment</td>
<td>1,457</td>
<td>516</td>
<td>Estimated mean price of all surgical equipment (disposable and non-disposable) from 3 LABF and 3 OABF. (price based on 2014)</td>
</tr>
<tr>
<td>Vascular prosthesis</td>
<td>419</td>
<td>419</td>
<td>Manufacturer (price based on 2014)</td>
</tr>
</tbody>
</table>

*Abbreviations: LABF, laparoscopic aortobifemoral bypass; OABF, open aortobifemoral bypass.*

**Table 4** Comparing mean total costs in Euro (€) and quality-adjusted life years (QALYs) after LABF vs OABF

<table>
<thead>
<tr>
<th></th>
<th>LABF</th>
<th>OABF</th>
<th>Direct estimate</th>
<th>Regression estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean total cost per patient (€)</td>
<td>9,953</td>
<td>17,260</td>
<td>-7,307</td>
</tr>
<tr>
<td></td>
<td>Differences</td>
<td></td>
<td>P-value</td>
<td>Differences</td>
</tr>
<tr>
<td>QALYs</td>
<td>0.45</td>
<td>0.38</td>
<td>0.067</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

*Notes: *Mann–Whitney U-test.*

*Abbreviations: LABF, laparoscopic aortobifemoral bypass; OABF, open aortobifemoral bypass; QALY, quality-adjusted life years.*
morbidity or mortality between LABF and OABF for AIOD to this day.9,11 Hence, a cost-utility is an appropriate tool for comparing two procedures, combining the patient-reported quality of life with an economic perspective.

The implementation of laparoscopic aortic surgery, has been slow.11 However, gradually there has been published evidence that the LABF combines the benefits of a minimally invasive technique with the excellent long-term patency rates of OABF for the treatment of AIOD.7,13 In the present study, we have demonstrated higher postoperative HRQoL combined with lower costs after LABF compared with OABF. This is an important finding and should be of interest to health providers, as well as for the patients suffering from AIOD in need of an aortobifemoral bypass.

The incremental cost-effectiveness ratio (ICER) can be defined as a price per effect (health) gained. The level of willingness to pay for a treatment can be used as a threshold. The ICER should be below this threshold, and thereby can be used as a tool in decision making. Norway is a country where hospital expenses are fully covered by the government. There are no strict requirements, for the time being, for the reporting of HRQoL in health technology assessment processes in Norway, but the focus is increasing. Although a threshold on the price of a QALY has not been set, a recent attempt of estimating the threshold empirically for Norway, resulted in a range of €43,000 to 94,000 per QALY gained.41 Interventions resulting in increased health and decreased resource use, as is the case of LABF in our study, are in health economics regarded as “dominant”.42 In easier terms; “one saves money and provide a better result”. By definition, these dominant interventions are below the suggested or estimated thresholds, and should be considered as replacement for the comparative treatment.42 Based on these assumptions and the result of our study, one may suggest that the patients with symptomatic AIOD TASC II type D lesions should be offered a LABF instead of an OABF procedure.

We have followed the patients in this study for only 6 months. In other patient groups, it has been shown that the benefits of laparoscopic surgery are mostly gained during the first year.38,43,44 In our pilot study, the main effect on HRQoL was during the first 6 months.14 Even if the difference between the 2 groups would later during follow-up decrease, there is no indication that the benefits in terms of HRQoL and spared economic costs will be in favor of other than LABF. There also seem to be no negative long-term effects of LABF for AIOD.7 Given the assumption of laparoscopy being a dominant intervention at 6 months, which was also confirmed by our analyses, we found no reason to include longer term considerations in the analysis.

We have, in our study, found the main cause of costs is the hospital stay, which is significantly shorter after laparoscopic surgery, mean 4.0 vs 7.0 days. All doctors with the vascular departments were involved in the postoperative evaluation and care of the patients, and all patients were discharged when they met the following discharge-criteria; able to walk, oral intake of food, normal urination/defecation and no untreated ongoing local or systemic complication. We have no indication of any protocol-driven resources.

We used national data for cost per day in hospital.32 This number is calculated as a mean for all types of admissions in somatic specialist health care in Norway, and may not apply for our patients and wards. We know that laparoscopic
equipment is expensive, there is more use of disposable equipment and also the operation time is longer. However, the total length of stay in hospital is significantly lower in the LABF group. This might outweigh any increased equipment costs and operation time costs. An opportunity cost evaluation and a micro cost analysis would be useful to assess the costs of the procedure and hospital stay even more specifically.

Generalizability and external validity are of importance when combining an economic evaluation with a clinical trial. We aimed to include all patients eligible for surgery and our inclusion/exclusion criteria reflect the clinical world. Multiple testing and repeated measurements on a small population can weaken the statistical analysis. This influences the strength of the conclusion. However, our results are strong and highly significant. We are the first to investigate these outcomes in a randomized setting, and this might affect decision makers. Further research is necessary to investigate the validity of the results and possible clinical implications.

Conclusion

LABF leads to an increase in QALYs gained and lower treatment costs, and seems to be cost-effective compared with open surgery.

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Author contributions

Conception and design: AHK, SSHK, TW, JOS. Data collection: AHK, MS, EMP, SSHK. Analysis and interpretation: AHK, TW. Statistical analysis: TW, AHK. Writing the article: AHK, SSHK, TW. Critical revision of the article: AHK, SSHK, TW, EMP, MS, JOS. Final approval of the article: AHK, SSHK, TW, EMP, MS, JOS. Overall responsibility: AHK, SSHK. All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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