Totally laparoscopic aortobifemoral bypass surgery in the treatment of aortoiliac occlusive disease or abdominal aortic aneurysms - A systematic review and critical appraisal of literature

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Abstract

Purpose: This systematic review aims to evaluate the published literature regarding totally laparoscopic aortobifemoral bypass (LABF) surgery in the treatment of aortoiliac occlusive disease (AIOD) or abdominal aortic aneurysms (AAA), as compared with open aortobifemoral bypass (OABF) surgery.
Patients and methods: A systematic review of the medical literature between 1990 and 2016 was performed, searching the medical databases Cochrane Library, OVID Medline, Embase and PubMed. Studies concerning totally LABF with or without control group, containing more than 10 patients, were included in the analysis. Operative and aortic cross-clamping times, blood loss, rate of conversion to open surgery, mortality and morbidity within the first 30 postoperative days, hospital stay and primary and secondary patency of the graft were extracted and compared to open surgery when possible.

Results: A total number of 66 studies were deemed eligible for inclusion in this review, 16 of them matching the inclusion criteria for the quantitative synthesis. The patient material consisted of 588 patients undergoing totally laparoscopic aortobifemoral bypass, 22 due to AAA, the remaining 566 for AIOD. They were compared to 287 OABF surgeries.

The operating and aortic cross-clamping times were shorter in the open group. Conversion rates ranged from 0% to 27%. No difference in mortality between the two groups was discovered. Hospital stays ranged from 4.0 to 12.1 days in the laparoscopic group, and from 5.0 to 12.8 days in the open group.

Most of the studies provide low levels of evidence, mainly due to lack of blinding, randomization and correction of bias.

Conclusions: Totally laparoscopic aortoiliac surgery seems to be a feasible technique. The literature published this far is sparse and with inconsistent results. More randomized controlled trials are required before this method can be widely recommended.

Keywords: laparoscopy, aortobifemoral, aortoiliac occlusive disease, abdominal aortic aneurysm, open surgery

Introduction
The first laparoscopy-assisted aortobifemoral bypass was performed in 1993\(^1\). Since the performance of the first totally LABF by the same surgeon in 1996\(^2\), there has been a slow adoption of the technique and few new studies have been performed. Today, 20 years later, open surgery is still the standard approach for this procedure, lately challenged by the increasingly popular endovascular techniques. However, the endovascular approach shows patency results that seem to be inferior and reinterventions are often required\(^3\). Although several studies have shown encouraging results for laparoscopic surgery compared to open\(^4\)\(^-\)\(^6\), only one relatively small RCT has been published to date\(^5\). Oslo University Hospital is now performing a randomized controlled trial comparing totally LABF to OABF, one of the first of its kind.

Our review considers patients with severe AIOD and/or AAA in need of aortobifemoral bypass. Rouhani et al reviewed the perioperative outcomes following laparoscopic AAA repair\(^7\) in 2014, whereas the last systematic review concerning both AIOD and AAA was published in 2008 by Cau et al\(^8\). The aim of the present study was to evaluate the level of evidence concerning laparoscopic aortic surgery, compared to the open approach.

**Material and methods**

**Protocol and registration**

The review protocol was published at PROSPERO on 15 January 2015, and is publically available with the ID number CRD42015016012.

**Eligibility criteria**

This study is a systemic review and a critical appraisal of the published literature from medical databases, from 1990 until today. The inclusion and exclusion criteria are given in table 1.

Table 1. Inclusion and exclusion criteria applied in the evaluation of the eligibility of the articles

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<thead>
<tr>
<th>Population</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td></td>
<td>Patients with severe symptomatic AIOD and/or</td>
<td>Non-human subjects</td>
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<tr>
<td>Intervention</td>
<td>Totally LABF</td>
<td>Not total laparoscopic aortic surgery for AIOD and/or AAA treated with aortobifemoral bypass. For example:</td>
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<td>- HALS or ‘mini-laparotomy’</td>
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<td></td>
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<td>- Laparoscopic surgery for celiac artery compression syndrome</td>
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<td></td>
<td></td>
<td>- Laparoscopic management of endoleaks after endovascular treatment</td>
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<tr>
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<td>- Laparoscopic aortorenal or aortomesenteric bypass</td>
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<td>- The management of vascular injuries during a laparoscopic procedure for a “non-vascular” condition</td>
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<tr>
<td>Comparison</td>
<td>OABF or no comparison</td>
<td>Anything other than OABF and bifurcated grafts. For example:</td>
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<tr>
<td>Outcome</td>
<td>- Mortality¹</td>
<td>Not reporting any of the relevant outcomes</td>
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<td></td>
<td>- Morbidity and complications¹</td>
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<td></td>
<td>- Surgical data: operation time and clamping time.</td>
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<td>- Postoperative hospital stay</td>
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<td>- Primary and secondary</td>
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<td>- Systematic reviews</td>
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<td>- Prospective or retrospective patient series with or without control-group</td>
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<tr>
<td>- Non-systematic reviews</td>
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<table>
<thead>
<tr>
<th>Publishing year</th>
<th>Language</th>
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</thead>
<tbody>
<tr>
<td>1990-2016</td>
<td>English or Norwegian*</td>
</tr>
<tr>
<td></td>
<td>All other languages</td>
</tr>
</tbody>
</table>

Notes: *Perioperative and/or first 30 days postoperative. *Articles with an English abstract but full text in another language, was included but evaluation was purely based on the abstract. Randomized controlled trials or systematic reviews in other languages than English or Norwegian, were translated.

**Abbreviations:** AIOD, aortoiliac occlusive disease; AAA, abdominal aortic aneurysm; LABF, laparoscopic aortobifemoral bypass; OABF, open aortobifemoral bypass; HALS, hand-assisted laparoscopic surgery

**Information sources and search strategy**

Cochrane, PubMed/Medline and Embase were searched using the following keywords/MESH-terms/all-fields: Laparoscop*AND surgery AND aort* Including different MESH-terms and synonyms combined by the Boolean variable OR. The full search-strategy is included as an appendix.

The complete search was conducted together with an information specialist Hilde Iren Flaatten, Medical University library, University of Oslo, in January 2015. Before completion of the manuscript, a second literature search with the same search strategy was performed 13 May 2016 to include new publications from the recent year.

**Study selection**
All articles were evaluated for inclusion by two researchers independently (IH and AHK). In case of disagreement, the two researchers discussed the publication based on the inclusion/exclusion criteria previously described. The articles found were at first screened based on title, followed by an assessment of the abstracts of the non-excluded studies. Lastly, the full texts of the remaining publications were reviewed and articles matching all the inclusion criteria were selected for data extraction. This process was repeated for the publications added after the final literature search was performed.

**Data collection and data items**

Data was abstracted by one author (IH), and two authors reviewed the final results (IH, AHK). The authors of the different publications were not contacted for additional information regarding questions concerning methods or results.

We had further exclusion criteria concerning extraction of data from the different articles. As there are few comparative studies published to date, articles lacking a control group were included in the quantitative synthesis. Data were not obtained from studies including less than 10 patients. Publications presenting clinical research without original patient data, were not included in the quantitative analysis, hence all systematic reviews were excluded from the tables. In cases of data published several times, only the latest or largest patient series were considered. This may apply for double publications of the same results, early and mid-time results or subpopulations. All studies where this could not be verified, have been included. For further details regarding the inclusion process, see appendix 2.

We assessed differences in mortality, morbidity and complications (adverse effects and adverse events (AE), including but not restricted to pneumonia, heart attack, paralytic ileus, sepsis, renal failure, cerebrovascular events, bleeding, infection, seroma, major vascular and ischemic events) perioperatively and the first 30 days postoperative, between those undergoing totally LABF versus the group receiving OABF surgery. Technical outcomes included operating time, aortic cross-clamping time, blood loss and conversion to open or hand-assisted laparoscopic surgery (HALS). Postoperative outcomes included length of
hospital stay and patency rates. Outcome measures of eligible studies were extracted, tabulated, and then analyzed cumulatively, using a descriptive statistical approach.

**Risk of bias**

All articles included in the data abstraction were evaluated using the 'Risk of bias tool' and the 'Quality Assessment tool for Quantitative Studies', recommended by the Cochrane institute. For all major outcomes, the GRADE assessment tool was used to grade the level of evidence and describe our confidence in the result.

**Statistics**

Results from studies with prospective or retrospective patient series are presented as comparative tables to assess the safety of the procedure. We used Microsoft Office Excel 2010© (Microsoft Redmond campus, Redmond, Washington, United States) in the creation of the tables. As the data did not allow for meta-analysis to be performed, the results are narratively reported in the text, illustrated with tables.

**Results**

**Study selection**

The initial search yielded 983 articles from the different databases. 110 full-text articles were assessed for eligibility after removal of the studies excluded based on title and abstract, together with duplicates. This resulted in 62 publications matching our inclusion/exclusion criteria, 11 of them concerning robotic surgery.

Our final search, performed on 13 May 2016, resulted in 101 additional articles published over the last year. Four of them met the inclusion criteria and were added to the review, resulting in a total of 66 articles included at last. See figure 1.
Figure 1. Flow chart of systematic search for literature and inclusion regarding laparoscopic aortobifemoral bypass surgery compared with open aortobifemoral bypass.

Notes: A total of 66 articles met the inclusion criteria. 16 of them were also eligible for inclusion in the quantitative synthesis.
An unsystematic search performed after the final search made us aware of two more studies. One is regarding the long-term results of totally laparoscopic aortobifemoral bypass\textsuperscript{6}, whereas the other study by Krog et al\textsuperscript{9} concerns the acute phase response after laparoscopic versus open aortobifemoral bypass surgery. They were not systematically reviewed and hence left out from the analysis.

\textbf{Study characteristics}

This systematic review comprises 66 articles; six systematic reviews, one randomized controlled trial, seven comparative studies and 52 cohort studies. Of the 52 cohort studies, 24 studies had a patient group smaller than 10 patients, and were not included in the tables. 18 articles did not report a uniform patient group or procedure, either mixing the results from patients suffering from AIOD and AAA, or not separating patient groups receiving tube grafts and aortounifemoral bypass from the patients receiving aortobifemoral bypass. Two comparative studies were excluded from the tables for similar reasons. Finally, 16 studies were deemed eligible for inclusion in the quantitative synthesis, only two of them concerning robotic surgery and one of them regarding AAA surgery.

The publication years ranged from 1997 to 2016, the one lastly added being a prospective comparative cohort study using propensity score matching in order to diminish bias\textsuperscript{10}. The sample size ranged from 11\textsuperscript{11} to 139 patients\textsuperscript{12} in the intervention group, the equivalent numbers for the open control group are 11\textsuperscript{13} to 156\textsuperscript{4} patients. Most patients were classified as C or D according to the Trans-Atlantic Inter-Society classification\textsuperscript{14}, with two publications also including TASC B lesions\textsuperscript{15,16}. Seven articles did not report the TASC classification. Two of the studies made use of robotic technology to create the aortic anastomosis\textsuperscript{16,17}.

\textbf{Peri- and postoperative outcomes}

A total of 588 patients underwent totally LABF surgery, 566 for AIOD and 22 due to AAA. In total, 287 patients underwent open surgery, and serve as the control group. The different outcomes after LABF surgery for AIOD are reported in table 2-4.
Due to inconsistency in the use of mean and median between the publications, the results from the studies are reported individually in the tables. No summary or combining of the results was possible, making the planned meta-analysis inappropriate.

**Laparoscopic surgery due to AIOD without control group**

See table 2. Overall, the operating time ranged from 240\(^{18}\) to 376 minutes\(^{19}\) in the nine cohorts concerning AIOD, with aortic cross-clamping time ranging from 60 to 121 minutes in the same studies. The perioperative blood loss ranged from 497\(^{15}\) to 1150\(^{16}\) ml. Between 5%\(^{15}\) and 27%\(^{11}\) of the procedures resulted in conversion to open surgery or HALS. The overall mortality in this group was low, a total of three patients died (1.5%). This is excluding the study of Barbera et al\(^{11}\), which did not report 30-day mortality. The morbidity range was quite consistent between the studies, ranging from 16-18%. Two studies reported slightly higher rates of 33%\(^{19}\) and 23.8%\(^{18}\), respectively. Length of hospital stay was reported by seven studies and ranged from 5\(^{15}\) to 10.1\(^{11}\) days. In terms of patency, the different studies demonstrated large variation in follow-up times. Consequently, this outcome is left out from the tables.

**Comparative studies concerning AIOD**

For further information, see table 3. Six of the studies were comparative in nature, including one RCT. In the laparoscopic group, the operating time ranged from a mean of 231 minutes\(^{20}\) to a median of 273 minutes\(^{5}\), and the aortic cross-clamping time stretched from median 48 minutes\(^{5}\) to median 89.5 minutes\(^{21}\). Both mean/median operating and clamping times were shorter for all the open procedures. Four publications found the difference in operating and cross-clamping time between the laparoscopic and open group to be statistically significant. Two studies did not report p-values\(^{5,21}\).

A median blood loss of 400mL\(^{22}\) was reported as the lowest for the laparoscopic group, with a median of 725 mL\(^{5}\) being the most substantial amount of hemorrhage occurring. In the open group, the blood loss ranged from 642 mL\(^{13}\) to 1010mL\(^{4}\). One study did not report this
outcome at all. Two studies found the difference between the two groups to be statistically significant, two did not report p-values, and in two papers the difference did not reach statistical significance.

Numbers regarding conversion rate, mortality, morbidity and length of hospital stay are reported in table 4. The conversion rate in the laparoscopic group ranged from 2% in one study, to 22% in the one reporting the highest rate of conversion. In one project, all the surgeries could be performed successfully without need for conversion. However, this publication presented the smallest patient group, with only 14 patients in the laparoscopic group.

Regarding mortality, three studies in the laparoscopic group and three studies in the open group, reported no mortality. None of the findings were significant. In contrast, significant differences in mortality between the two groups were obtained by Kazmi et al, reporting a p-value of 0.005 in favor of less mortality in the laparoscopic group. In this regard, it is worth pointing out that the latter study reported the total mortality at the end of the study, not after 30 days.

The morbidity rate displayed a wide range in both groups. One study found this difference to be statistically significant, with higher morbidity in the open group.

The shortest length of hospital stay was a median of four days in the laparoscopic group and five days following open surgery, both outcomes originating from the same study. The longest duration of hospital stay after the laparoscopic approach was a mean of 12.1 days, and a mean of 12.8 days in the open group. This difference was found to be statistically significant in all studies but one. The latter reported a p-value of 0.304.

Not all publications described patency rates, and the studies displayed great diversity in follow-up-time and the patency definition. Hence, this is left out from the table.

**Abdominal aortic aneurysm repair**
Only one study concerning AAA surgery was included in the quantitative synthesis\textsuperscript{23}, and included 22 patients. Originating from one study, these outcomes are not reported in the tables. An operating time of 391 minutes and a clamping time of 146 minutes were reported. Blood loss was not an outcome. Two of the 22 procedures (9\%) were converted to open surgery, both of them due to difficulty in exposure of the aorta. Two patients died, from myocardial infarction and multiorgan failure, respectively. Both were high-risk patients enrolled early in the trial before the introduction of a global risk assessment scoring system. Nine patients developed perioperative complications, most of them suffering from transient postoperative ileus. The average length of hospital stay was 6.2 days.

**Methodological quality**

Of the 16 studies included in the quantitative synthesis, only one of them was randomized\textsuperscript{5}. One publication attempted to correct for bias, making use of a propensity score matching system\textsuperscript{24}. As this article reported the results together for aortobifemoral bypass and other procedures applying tube graft, it was not eligible for inclusion in the quantitative analysis.

After evaluating the quality of the individual articles using Risk of bias tool recommended by the Cochrane Institute, only the RCT was rated as ‘strong’\textsuperscript{5}, two as ‘moderate’\textsuperscript{18,19} and the rest as ‘weak’. The systematic reviews were evaluated similarly and also displayed variable quality. Three studies were assessed to be of low methodological quality\textsuperscript{8,25,26}, two of moderate quality\textsuperscript{7,27} and one of high quality containing a satisfactory methodological chapter\textsuperscript{28}.

**Discussion**

In this review, we have seen that totally LABF seems to achieve satisfactory results compared to OABF, with shorter hospital stay, longer operating and clamping times and perhaps less peri- and postoperative complications in the laparsoscopic group. The research conducted this far provides a low level of evidence.
An international consensus for the management of peripheral disease was last updated in 2007, recommending aortobifemoral bypass as the procedure of choice for most patients with severe (TASC C or D) AIOD. Despite several studies demonstrating the feasibility of totally laparoscopic aortic surgery, the widespread use of this technique has remained relatively low. A rapid development of endovascular methods has led to few centers adopting the procedure.

This review demonstrates that the quality of the research and evidence is low, with great diversity between the studies and their way of reporting results. Heterogeneity of the studies and selection of the patients made comparison difficult. Nevertheless, it seems quite evident that laparoscopic surgery is related to longer operating and clamping times, with four of the comparative studies showing p-values <0.05 for this result. Similarly, four studies reported p-values <0.05 in favor of shorter hospital stay for the laparoscopic group, leading us to believe that laparoscopic surgery might result in a shorter postoperative course. This may have an impact on decision making and health economy.

The results regarding intraoperative blood loss and postoperative morbidity were less conclusive, but there is a tendency towards less postoperative complications. Morbidity was defined differently in the studies and makes comparison unfortunate. However, significantly shorter hospital stay in the laparoscopic group can be a result of fewer intra- and postoperative complications, and possibly less intraoperative blood loss in the laparoscopic group, as these outcomes both are indirect measures of intraoperative problems encountered. The two studies that in fact did report p-values for differences in morbidity, had the largest patient selection of all the studies. Kazmi et al. reported results over a period of six years, and included a thorough analysis of the complications faced. From these results, it seems possible that less morbidity come at the expense of longer operating and clamping times.

Overall, most studies provide evidence that laparoscopic surgery is comparable to open surgery regarding survival and safety of the procedure. This is in great contrast to the only
study so far reporting negative results. The latest study by Ricco et al\textsuperscript{24} suggests that the laparoscopic approach significantly increases the risk of adverse events (AE) compared to open surgery. However, the study combines the results of aortobifemoral bypass surgery for AAA and AIOD. AAA surgery entails a higher risk of complications and it seems as the benefit of laparoscopic surgery might be less in this group. This cohort attempts to reduce the recruitment bias by using propensity score matching, a method originally introduced by Rosenbaum and Rubin in 1983\textsuperscript{37}. Propensity score is meant to limit selection bias by predicting the likelihood that a patient with given characteristics will receive a specific treatment. In this particular study, 50 patients from the laparoscopy group were matched with 50 patients from the laparotomy group showing similar scores. Both the propensity score matched group and the overall series, found significantly higher risk of AE after undergoing LABF compared to OABF. As the results from AAA and AIOD were grouped together in this publication, it could not be included in our final analysis, but it still brings a few new and noteworthy points into the discussion.

This publication is interesting for more than one reason. On one hand, higher probability for AE in the laparoscopic group has not previously been reported. However, the study is operating with a composite endpoint grouping together different AE such as death, post-operative hemorrhage, myocardial infarction, stroke, post-operative respiratory failure and problems related to the prosthesis and anastomosis. A similar method is applied by Kazmi et al\textsuperscript{22}. Employing composite endpoints in the analysis is a way of generating significant results in smaller patient series, but may pose interpretation difficulties as an increased risk for the individual events are not necessarily related to each other. Contrasting to Ricco’s publication, Kazmi et al found significantly less morbidity in the laparoscopic group even by means of a composite endpoint, a similar outcome to other publications. It should be noted that this study differs from the others included in our review in that it reports the results using ‘patient years’.

On the other hand, propensity score matching has been criticized and errors are often made when applying this method in statistical analysis\textsuperscript{38}. Without knowing the full implication this might have, it is worth mentioning that medical complications were balanced out between
LABF and OABF. This might imply that the risk of AE following LABF is closely linked to surgical technique, particularly completion of the anastomosis. The complexity of the procedure is indicated by a considerable learning curve\textsuperscript{18}, which is overcome at approximately 25-30 procedures\textsuperscript{12}. Lately, robots have been attempted to shorten the operating time by assisting in the creation of the anastomosis. So far, it seems to be a viable technique\textsuperscript{39}, that may enhance the surgical procedure\textsuperscript{16,25}. There is a distinct need for further research on this field of laparoscopic surgery.

This systematic review has several limitations, mostly due to poor quality of the individual studies and great diversity in terms of procedure type and reporting manners. A metanalysis could not be performed and the results could not be summarized, as there was no uniformity in the way they were described. Few publications reported standard deviations as part of their analysis, and even less studies made use of P-values if comparing to other groups. Consequently, range became the most objective measurement of reporting the results. Unfortunately, this is substantially less reliable than performing a meta-analysis.

Some of the publications seem to report repeated patient material. Nevertheless, all the mentioned studies were included, as this assumption could not be verified. What impact this has on the results, can hardly be quantified.

In addition to the problems encountered above, numerous studies reported diverse patient and procedure groups, and the larger part of the studies were excluded from the quantitative synthesis for this reason. These studies carry a significant risk of bias, assuming operating and clamping times are considerably longer for AAA than for AIOD\textsuperscript{8,40}, and vary between the procedure types. Most of Stadler’s publications\textsuperscript{41-45} were affected by this decision and could not be included, despite large patient material in most of the studies.

Most studies were observational, and the description of the characteristics of the consecutive patients in the cohorts was inadequate for the larger part of them. We must assume a considerable selection bias, as none of the studies describe attempts to correct confounders
existing in the different groups of participants. The only randomized study was closed prematurely at 28 patients, as an ethical committee eventually found it unethical to randomize patients originally referred for laparoscopic surgery. An overall ‘weak’ rating as the end-point when assessing the quality of the individual studies using the ‘Risk of bias tool’ recommended by the Cochrane Institute, requires the poorest score in two of the six individual components evaluated in the tool. This was easily achieved for the larger part of the publications, as a result of the limitations described earlier.

**Conclusion**

To conclude, laparoscopic aortoiliac surgery is still sparsely utilized despite promising results. It seems reasonable to claim that laparoscopic aortobifemoral bypass can be performed safely, with shorter hospital stay, less intraoperative hemorrhage and possibly less peri- and post-operative complications and morbidity compared to open surgery. Open surgery delivers shorter operating and aortic cross-clamping times. The mortality rate appears unaffected by surgical approach. However, few centers and surgeons are performing this procedure. The published literature to date is of sparse quality and the level of evidence is low. There is a need for further research.

**Acknowledgements**

We thank medical librarian Hilde Iren Flaatten at the University of Oslo for her help during the literature search. We also thank Truls Erik Bjerklund Johansen at the Department of Urology, Oslo University hospital, for helpful advice and critical revision.

**Author contribution**

Conception and design: AHK, IH, JJJ
Data collection: IH, AHK
Analysis and interpretation: IH, AHK
Statistical analysis: IH
Writing the article: IH, AHK
Disclosure

There are no conflicts of interest or external funding. All expenses were covered fully by the University of Oslo.

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