Peer Review File
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Reviewer A
Comment 1: Methods section, was the thoracic duct ligated?
Reply 1: This is clarified in the methods section by added the following text on page 9, line 143.
Changes in the text:
Methods section page 9, line 143
The thoracic duct was not ligated unless iatrogenic injury occurred.

Comment 2: Discussion section, lines 269-271, can you clarify this statement?
Reply 2: We have clarified the statement, see page 15, lines 270-273.
Changes in the text:
Discussion section, page 15, lines 279-280.
If patients are offered open Ivor Lewis esophagectomy or HMIE, it is usually due to frozen section examination on specific ~~perioperative~~ lymph nodes ~~harvest~~ before proceeding the operation e.g. lymph node near the adrenal gland or lower paratracheal lymph nodes.

Reviewer B
Comment 1: There are some grammatical issues that would need to be addressed.
Reply 1: We agree, and we have thoroughly corrected all the grammatical errors.
Changes in the text: Please see the manuscript – all changes are marked with red and strikethrough.

Reviewer C
Comment 1: It is mentioned the surgeons were trained and skilled already. How many previous experiences with esophagectomy did the surgeons have? Can this be quantified?
Reply 1: This is quantified in the discussion section, page 14, line 266-268.
Changes in the text:
Discussion section, page 15, line 270-272.
Approximately 500 esophagectomies was performed by the surgical team of two general surgeons and two thoracic surgeons in the ten years prior to implementation of TMIE in 2016.

Comment 2: Was there any difference between groups in baseline parameters?
Reply 2: As described on page 12, lines 205-210, The aim was not to compare the results of the 120 TMIE patients to any other groups of patients undergoing esophagectomy in the study period, since these patients was a different type of patients with bigger tumors and more comorbidity, especially pronounced in the beginning of the implementation phase. Therefore, there is no comparison of baseline parameters between groups in the paper.
Changes in the text: None

Comment 3: Please add an ethical statement to the methods section. Was informed consent obtained?
Reply 3: The study was conducted after approval from the hospital administration and Central Denmark Region. This approval allowed data extraction without informed consent according to The Danish Health Care Act Section 42d Subsection 2.) This statement is added to method section as advised, and the ethical section in the footnote section is modified.

Changes in the text:
Change a, methods section, page 10, line 165-167: The study was approved by the hospital administration and Central Denmark Region. This approval allowed data extraction without informed consent according to The Danish Health Care Act Section 42d Subsection 2.

Change b, footnote section, page 16, line 308-311. The study was approved by the hospital administration and Central Denmark Region and was conducted according to the Declaration of Helsinki. This approval allowed data extraction without informed consent according to The Danish Health Care Act Section 42d Subsection 2. ~~has been proved by the Central Denmark Region and was conducted according to the Declaration of Helsinki.~~

Comment 4: As the authors say, these are the results in a single high-volume tertiary institution by dedicated esophageal cancer specialists with advanced laparoscopic and thoracoscopic skills this limits the generalizability of the study. Do the authors think centralization would help to overcome compilations in general?
Reply 4: We believe centralization is crucial for advanced oncological surgery, including esophagectomy, especially implementation of complex minimal invasive procedures like TMIE. See added text on centralization esophagectomy in general and centralization in Denmark in discussion section, page, line
Changes in the text:
Discussion section, page 12, line 221-225
Since the presented implementation strategy took place in a single high-volume tertiary institution by dedicated esophageal cancer specialists with advanced laparoscopic and thoracoscopic skills, it might not be the same results in another institution with another setup. In addition to that, the importance of centralization of advanced upper gastrointestinal cancer surgery has been shown in several studies (10-12), and in Denmark, the centralization occurred in 2003 to 2006 where the numbers of centres treating esophageal cancer was reduced from 26 centres to just four centres. This improved the quality of care with lower anastomotic leakage and lower 30- and 90-day mortality (13).

Reviewer D
Comment 1: Thank you for asking me to review this manuscript. I congratulate the authors on their clinical outcomes, which are clearly impressive.
Unfortunately, I feel the paper simply reports on the clinical outcomes of a series of esophageal resections rather than what is proposed in the title.

The retrospective nature of the study and the data collection is an inherent problem, but, more significantly, the paper does not show a "roadmap" for conversion from open to minimally invasive esophagectomy, which is essentially its premise.

The reported step-wise progression is common practice for most centres embarking on MIE. The paper would have added a new dimension had it compared 2 groups (ie one surgeon going from open straight to totally minimally invasive, another taking the reported 2-step approach), but this is not the case.
There is no assessment of the learning curves (for either hybrid or totally minimally invasive approaches) making it difficult to contextualise the results. In the context of the title, I feel this is a pre-requisite.

I don't feel that this manuscript describes an implementation method for the adoption of totally minimally invasive esophagectomy and, as such, unfortunately does not add a great deal to what's known or done currently.

Reply 1: Thank you for your comment. We agree with some of your remarks. A comparison of the results from two surgeons taking two different strategies to TMIE in matched patients from the same center would be interesting. There is no comparison to the HMIE group either, but this was never the aim of the study. The retrospective investigation was performed after inspiration from the Dutch studies who investigated and found learning curve associated increased risk of anastomotic leakage during the implementation period. This was found not to be the case in our patients, probably due to a stepwise implementation strategy by advanced minimal invasive surgeons in carefully selective patients. Therefore, the comparison should not be done to other groups of our patients, but as a comparison and comment to the Dutch finding and serve as inspiration for other surgeons aiming to implement TMIE without risking increased morbidity.

There is no assessment of the learning curve in relation to anastomotic leakage as seen in the Dutch studies, however, the anastomotic leakages in the present study did no differ and did not reach more than 10% during the implementation, suggesting that the learning curve was already flattened, or at least not resulting in increased morbidity.

We agree that the title implies a comparison, therefore, we have changed the title.

Changes in the text: The title is changed to Safe and efficient 2-step implementation of totally minimally invasive esophagectomy