

Peer Review File

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Reviewer A

A good narrative review. Nothing new, but this manuscript could be of interest to residents or physicians not specialised in thoracic aortic diseases. A few language editing will be needed.

Reply: Thank you for your comments. The manuscript language has been fully reviewed and edited.

Reviewer B

It is a fairly comprehensive review on the subject with many shades of gray. Here are some comments and suggestions.

1. Line 78: it would be more appropriate to say “Over the past three decades, there have been significant advancements in the management of...”

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

2. Line 87-89: it would be more appropriate to rearrange as “FET employs an aortic hybrid prosthesis (HP) which allows a single-stage total aortic arch replacement (TAR) with antegrade DTA stenting in a hybrid fashion. This approach combines the benefits of the traditional elephant trunk procedure with current advanced stenting technology.”

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

3. Line 153-155: it would be more appropriate to say “The changes in the aorta’s morphology are possible consequences of increased calcifications within the wall with thicker and less flexible membrane, which cause the aorta to become less elastic with subsequent impaired remodelling.”

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

4. Line 163-164: it would be more appropriate to say “...whereas the THP design has been found to reduce the shear stress on the intima which can explain its more favourable results in other studies.”

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

5. Line 174: it would be better to specify as “27 months”

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

6. Line 220: it would be more appropriate to say “...regardless of the location of the tear.”

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

7. Line 339: it is more appropriate to say “at 1 year follow up”.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

8. Line 381-382: it looks as if the word “outcome” is missing; therefore, it would be more appropriate to say “...with THP demonstrating a more favourable outcome compared to its market competitors.”

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

9. Line 439: avoid repeating the word “conclusion” and simply start with “FET can achieve a favourable postoperative profile in terms of survival, complications and aortic remodelling, and remains the gold-standard treatment for thoracic aortic pathologies involving the aortic arch and DTA. However, long-term follow-up is still required to maximise clinical efficacy. Several FET HPs exist; nevertheless, THP may be considered the primary choice.”

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

Reviewer C

Kayali and colleagues provide a manuscript regarding a review of FET. Although several types of FETs are widely used worldwide, FET-related complication remains an important topic and interest for surgeons. Overview of results of FET is useful and I appreciate authors’ efforts. I have several suggestions as following:

1. (Mortality and survival) Please add the causes (aortic or non-aortic) of mortality if such data is available.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 154-156 and 161-163.

2. (dSINE) dSINE is an important complication which can be life-threatening. I suggest that authors add a paper by Hiraoka et al. as a reference. Their paper reported the incidence of dSINE in 177 patients.

Ref) Hiraoka et al. Eur J Cardiothorac Surg. 2022;62:ezac325.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 195-198.

3. (dSINE) Preventive measures of dSINE are not well established. Coverage of distal edge of FET can theoretically prevent dSINE as below.

Ref) Okamura et al. Interact Cardiovasc Thorac Surg. 2022;35:ivac033.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 239-244.

4. (Endoleak) The definition of endoleak is unclear. Authors defined endoleak as a blood leak between false and true lumens in aortic dissection. However, references cited are about endoleak in true aneurysm. I recommend that authors modify the definition of endoleak.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 372-376.

5. (Reintervention) I suggest that authors add the details of reintervention in addition to reintervention rates. Yoshitake et al (reference #22) reported that TEVAR was possible in most patients in FET group although reintervention rates were similar between FET and non-FET groups.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 433, 471 and 488-489.

6. As one of future directions of FET, I recommend that authors add fenestration of FET. One or more supra-aortic vessels are perfused via fenestration of FET and excellent results are reported.

Refs)

-Roselli et al. Simplified frozen elephant trunk repair for acute DeBakey type I dissection. J Thorac Cardiovasc Surg [Internet]. 2013;145(3 SUPPL.):S197–201. (reference #47)

-Okamura et al. Eur J Cardiothorac Surg. 2021;59:765-772.

-Hashizume et al. JTCVS Tech. 2022 Nov 3;17:1-9.

Reply: Thank you for this valuable comment. Augmented, Fenestrated and custom fit FETs are in no doubt future features and configuration for aortic arch surgery. However,

scarce reports are available on the applicability and generalisation of this novice device technology. As such, we did not want to dwell on this conceptual approach in the take home message, which is more focused on the clinical outcomes of standard FET.

I would like to thank the authors for sharing their work with us.

Reviewer D

I commend the authors in undertaking this challenging review of several postoperative outcomes after FET.

1. Abstract - there appears to be too many limitations and confounding factors in the referenced studies to conclude that THP should be the prime choice of prosthesis.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

2. Introduction - line 78 amend to "significant advancements have been made in the management of.."

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

3. Line 82 - suggest to remove "then in a second procedure"

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

4. Section on survival/mortality: suggest to explain some of the selection criteria or complexity of the cases involved including concomitant procedures in the relevant studies. The international series by Tan et al reported a skewed low mortality (1.5%) without commenting on case selection. Several studies in Table 1 are not so recent.

Reply: Thank you for this valuable comment. This is a narrative review that stringently followed selection methodology avoiding selection bias and publication selection taking into account control factors that could potentially skew the results and lead to incorrect conclusions. The complexities of cases in majority of studies are not sufficiently highlighted or scientifically presented. Hence, we feel that presuppositions of procedural criteria and performance will not add to the overall hypothesis of this review given the variations encountered that would impede the evidence synthesized.

5. Section on dSINE - Line 155 amend to "less elastic and subsequently impedes remodelling". Suggest to comment on the proportion of patients with dSINE that actually needed downstream intervention endovascular or otherwise and stent lengths

of the graft prostheses.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 229-231.

6. Section on aortic remodelling suggest to rename to "Aortic remodelling in aortic dissection". Suggest comment on remodelling post acute debakey I repair in FET patients versus post AMDS in those with proximal entry tears. Also the FET brands come in fixed lengths and whether THP conforms more to this optimal length.

Reply: Thank you for your input. The first comment has been incorporated into the revised manuscript. Line 256. As for the AMDS, since it is not a FET device, we believe it is outside the scope of this particular review. However, our group recently published an article comparing THP and AMDS:

Al-Tawil M, Jubouri M, Tan SZ, et al. Thoraflex Hybrid vs. AMDS: To replace the arch or to stent it in type A aortic dissection?. Asian Cardiovasc Thorac Ann. 2023;31(7):596-603. doi:10.1177/02184923221147442

7. Endoleak is often poorly reported in FET studies and is usually type Ib. Perhaps a comment may be made for the HP sizing in the referenced large international series by Tan et al.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 411-416.

8. The THP has been reported to produce thrombus within the FET and increased thromboembolic complications [<https://doi.org/10.1016/j.jtcvs.2022.08.005>]. Suggest a comment on this in the last section.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 512-519.

9. There appears to be insufficient evidence to conclude THP as a better choice for all cases due to limitations in the reviewed studies. Suggest to remove this from the conclusion and instead amend to 'further prospective evaluation of the various commercially available prosthesis devices in relation to selected indications is needed'.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

Reviewer E (Accept)

The authors of the review compiled stringent evidence that support FET implementation in aortic arch surgery with references to elective and non-elective surgery. They evolved their evidence focusing on extensive matched experiences and

evidence from the literature overall. Although FET substantially improved hybrid aortic arch operations at the benefit of FL seals and depressurization, the FL at the distal anastomosis remain variable. The authors highlighted the concept and thoughts in current evidence. There is indeed an unmet, clinical randomization from international perspective on type A dissection management with or without FET. The quality of the discussion is good and the authors referenced their evidence accordingly. The article is written in clear format and meets the reader with ease to follow. The article is well structured and methodical. This is supported by tables that collates the evidence adequately.

Reply: Thank you for your comments.

Reviewer F

I am pleased to have had the opportunity to peer review the article "Evidence-Based Frozen Elephant Trunk Practice: A Narrative Review". I have respected the tremendous efforts of the authors. Simultaneously, I approached this review process sincerely.

1. General comments

The Frozen Elephant Trunk (FET) procedure has recently gained popularity as a surgical approach for aortic dissection and degenerative thoracic aortic aneurysms. The primary objectives of this study were (1) to assess and evaluate the latest evidence regarding postoperative clinical outcomes of FET and (2) to provide results achieved by comparing clinical outcomes among different FET-hybrid prosthesis (HP)s available in the global market. The authors reviewed the relatively recent literature to compare FET clinical outcomes, specifically regarding mortality, distal stent graft-induced new entry (d-SINE), aortic remodeling, endoleak, re-intervention, and graft kinking. Based on this review, the authors concluded that the Thoraflex Hybrid Plexus is the prime choice among the available devices.

I conducted a peer-review based on the Scale for the Assessment of Narrative Review Articles (SANRA) and identified several points for improvement.

1) Justification of the article's importance for the readership: 1

The importance is not justified.: 0

The importance is alluded to, but not explicitly justified.: 1

The importance is explicitly justified.: 2

2) Statement of concrete aims or formulation of questions: 2

No aims or questions are formulated.: 0

Aims are formulated generally but not concretely or in terms of clear questions.: 1

One or more concrete aims or questions are formulated.: 2

3) Description of the literature search: 1

The search strategy is not presented.: 0

The literature search is described briefly.: 1

The literature search is described in detail, including search terms and inclusion criteria.: 2

4) Referencing: 1

Key statements are not supported by references.: 0

The referencing of key statements is inconsistent.: 1

Key statements are supported by references.: 2

5) Scientific reasoning: 1

(e.g., incorporation of appropriate evidence, such as RCTs in clinical medicine)

The article's point is not based on appropriate arguments.: 0

Appropriate evidence is introduced selectively.: 1

Appropriate evidence is generally present.: 2

6) Appropriate presentation of data: 1

(e.g., absolute vs relative risk; effect sizes without confidence intervals)

Data are presented inadequately.: 0

Data are often not presented in the most appropriate way.: 1

Relevant outcome data are generally presented appropriately.: 2

2. Specific comments

a) Major

1. This review predominantly addressed the clinical outcomes related to aortic dissection. However, as highlighted in the Introduction section, a review of the clinical outcomes of FET for degenerative aortic aneurysms should also be included. Readers might find it difficult to determine which conditions the clinical outcomes are being discussed. To address this, it would be beneficial to separate clinical outcomes by condition or focus primarily on aortic dissection.

Reply: Thank you for this valuable comment. Our literature search included aortic dissections and aneurysms as indications for FET. Hence, the clinical outcomes reported in this manuscript cover both pathologies. However, this comment has been incorporated into the revision by clarifying the indication/pathology in the referenced studies.

2. It is essential to incorporate stroke and spinal cord ischemia (SCI) into clinical outcomes. This inclusion is warranted because the introduction raised concerns regarding these issues. Given that stroke and SCI are significant complications that are extensively debated in the FET-related literature, they deserve a thorough review.

Reply: Thank you for this valuable comment. Whilst the authors do agree that incorporating neurological complications represented by stroke and spinal cord

ischemia (SCI) into clinical outcomes is essential, we decided to expand on this in addition to delirium in a separate study due to the amount of data on this topic in the literature as well as its importance and variability with cerebral protection techniques.

3. As mentioned by the authors, the definition of aortic remodeling may vary among studies. However, aortic remodeling occurs naturally up to the proximal descending aorta, where the stent graft is inserted. Readers are curious about the aortic remodeling rate for each region of the aorta, specifically in the downstream aorta, where no stent graft has been inserted. The authors should provide this information.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 289-295, 307-327 and 333-338.

4. While the authors suggested the use of the Thoraflex Hybrid Plexus as an answer to the differences in clinical outcomes among FET devices, the current comparison was insufficient to secure agreement from most readers. Since there are already many reviews related to FET, it is impossible to achieve originality without mentioning the clinical results between devices in detail.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

b) Minor

1. Description of the literature search

It is not necessary to describe the literature search in detail for a systematic review, but it is necessary to specify the search terms and the types of literature included.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript. Lines 109-119.

2. Referencing

Please provide references for the following statements.

Line 84-85: In 1996 the frozen elephant trunk (FET) technique was introduced, which revolutionized aortic arch repair.

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.

Line 152-153: Vessel walls in chronic aortic dissection (CAD) tend to be more fragile than those in acute aortic dissection (AAD).

Reply: Thank you for your comment. This has been incorporated into the revised manuscript.