Peer Review File

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<mark>Reviewer A</mark>

The article does not make it clear whether it is a critical review (if so, the search methodology is not clear) or whether it is personal experience.

The writing must be thoroughly revised as there are many mixed and some wrong concepts. References must be reviewed.

The purpose of the article is not clear; in fact, the title is not explained in the article.

1. The article does not contribute anything that has not already been published before (see: Aung E.YS, Khan M, Williams N, Raja U, Hamady M. Endovascular Stenting in Superior Vena Cava Syndrome: A Systematic Review and Meta-analysis. Cardiovasc.Intervent. Radiol. 45, 1236-1254 (2022) and Azizi AH, Shafi I, Zhao M, Chatterjee S, Roth SC, Singh M, Lakhter V, Baschir R. Endovascular therapy for superior vena cava syndrome: A systematic review and meta-analysis. EClinicalMedicine 37, 100970 (2021))

2. The article does not make it clear whether it is a critical review (if so, the search methodology is not clear) or whether it is personal experience

3. The writing must be thoroughly revised as there are many mixed and some wrong concepts

In my opinion it is not publishable even by doing a Major Revision

Thank you for your comments.

Comment 1: The article does not contribute anything that has not already been published before (see: Aung E.YS, Khan M, Williams N, Raja U, Hamady M. Endovascular Stenting in Superior Vena Cava Syndrome: A Systematic Review and Meta-analysis. Cardiovasc.Intervent. Radiol. 45, 1236-1254 (2022) and Azizi AH, Shafi I, Zhao M, Chatterjee S, Roth SC, Singh M, Lakhter V, Baschir R. Endovascular therapy for superior vena cava syndrome: A systematic review and meta-analysis. EClinicalMedicine 37, 100970 (2021))

We have distinguished our critical review from prior reports by commenting on how the advances of oncological treatments (e.g. new radiation techniques, immunotherapy and targeted therapies) affect how clinicians sequence treatments for superior vena cava syndrome (SVCS) based on their response rates, time to treatment response and mechanisms of action. To our knowledge, this has not been thoroughly addressed in any previously published literature reviews on SVCS. The two systematic reviews and meta-analyses of Aung et al and Azizi et al. only focused on the efficacy and risks of endovascular stenting on the treatment of SVCS. As such, this critical review serves as a guide for clinicians on when to consider endovascular stenting and how to sequence stenting with other modalities, and we hope this will be valuable and widely cited addition to the literature.

Comment 2: The article does not make it clear whether it is a critical review (if so, the search methodology is not clear) or whether it is personal experience

In our initial scoping search, we found limited literature specifically addressing the optimal sequence of treatments for malignant SVCS, especially for patients who are clinically stable. Therefore, we positioned our paper as a commentary on how clinicians should sequence treatments based on the existing clinical literature, our clinical experience, as well as new anticancer treatments for tumours that commonly cause SVCS such as lung cancer and lymphoma. We specifically stated that this paper is a "clinical practice review" instead of a "narrative review" or "systematic review" in our introduction section.

Comment 3: The writing must be thoroughly revised as there are many mixed and some wrong concepts

We have reviewed the manuscript thoroughly, including by our native English-speaking coauthors, and we have addressed necessary issues throughout. If any specific issues remain, we would be grateful if the reviewer could point out the specific sections with mixed and wrong concepts in our manuscript. We will amend them accordingly.

<mark>Reviewer B</mark>

This is a well- executed review. I have some minor suggestions

Page 3, Line 97-114

add citation: Kalra M, Sen I, Gloviczki P. Endovenous and Operative Treatment of Superior Vena Cava Syndrome. Surg Clin North Am. 2018 Apr;98(2):321-335. doi: 10.1016/j.suc.2017.11.013. PMID: 29502774

Page 3, line 114:

add citation: Haddad MM, Simmons B, McPhail IR, Kalra M, Neisen MJ, Johnson MP, Stockland AH, Andrews JC, Misra S, Bjarnason H. Comparison of Covered Versus Uncovered Stents for Benign Superior Vena Cava (SVC) Obstruction. Cardiovasc Intervent Radiol. 2018 May;41(5):712-717. doi: 10.1007/s00270-018-1906-3. Epub 2018 Feb 28. PMID: 29492630; PMCID: PMC8108479.

Page

Overall, add to discussion a few lines from following refs

Kordzadeh A, Askari A, Hanif MA, Gadhvi V. Superior Vena Cava Syndrome and Wallstent: A Systematic Review. Ann Vasc Dis. 2022 Jun 25;15(2):87-93. doi: 10.3400/avd.ra.21-00118. PMID: 35860826; PMCID: PMC9257386.

Léon D, Rao S, Huang S, Sheth R, Yevich S, Ahrar K, Huynh T, Pisimisis G, Kuban JD. Literature Review of Percutaneous Stenting for Palliative Treatment of Malignant Superior Vena Cava Syndrome (SVCS). Acad Radiol. 2022 Apr;29 Suppl 4:S110-S120. doi: 10.1016/j.acra.2021.08.016. Epub 2021 Oct 1. PMID: 34602363.

Comment 1: Page 3, Line 97-114

Thank you for your comments.

add citation: Kalra M, Sen I, Gloviczki P. Endovenous and Operative Treatment of Superior Vena Cava Syndrome. Surg Clin North Am. 2018 Apr;98(2):321-335. doi: 10.1016/j.suc.2017.11.013. PMID: 29502774

Reply 1: This is added accordingly. Please see page 4, lines 13 and 16.

Comment 2: Page 3, line 114:

add citation: Haddad MM, Simmons B, McPhail IR, Kalra M, Neisen MJ, Johnson MP, Stockland AH, Andrews JC, Misra S, Bjarnason H. Comparison of Covered Versus Uncovered Stents for Benign Superior Vena Cava (SVC) Obstruction. Cardiovasc Intervent Radiol. 2018 May;41(5):712-717. doi: 10.1007/s00270-018-1906-3. Epub 2018 Feb 28. PMID: 29492630; PMCID: PMC8108479.

Reply 2: This is added accordingly. Please see page 4, line 18.

Comment 3: Page Overall, add to discussion a few lines from following refs

Kordzadeh A, Askari A, Hanif MA, Gadhvi V. Superior Vena Cava Syndrome and Wallstent: A Systematic Review. Ann Vasc Dis. 2022 Jun 25;15(2):87-93. doi: 10.3400/avd.ra.21-00118. PMID: 35860826; PMCID: PMC9257386.

Léon D, Rao S, Huang S, Sheth R, Yevich S, Ahrar K, Huynh T, Pisimisis G, Kuban JD. Literature Review of Percutaneous Stenting for Palliative Treatment of Malignant Superior Vena Cava Syndrome (SVCS). Acad Radiol. 2022 Apr;29 Suppl 4:S110-S120. doi: 10.1016/j.acra.2021.08.016. Epub 2021 Oct 1. PMID: 34602363.

Reply 3: These two literature reviews are now discussed in page 6, lines 11-21 and page 6, lines 32-33 and page 7 lines 1-9)

Reviewer C

My main question would be to what audience is the article directed? If the intended audience is to be radiation or medical oncologists, it is probably too technical for that audience. If it is intended to be IRs, it probably goes too in the weeds with medical therapies. But overall a very well written article that will add to the literature.

The authors present a well-written, well-researched review of endovascular stenting in the setting of malignant SVC obstruction. A few minor suggestions follow:

Lines 74 and 85. The references are from 1984 and 1996, respectively. More recent references are available and should be used.

Line 146. The authors state that heparin is a thrombolytic. It is an antithrombotic.

The section entitled "Technical details of endovascular stenting". This reviewer thinks that this section should be significantly shortened or removed altogether. There are many technical details presented that differ from operator to operator (e.g., line 104 stating US is often used – it is

universally used for venous access; line 109 stating that balloon dilation is performed – typically it is only performed if the stent delivery system cannot be placed). If the reader is an IR, the section is incomplete and the technique is debatable; if the reader is an oncologist, the section is unnecessary. Line 211. Refs 17 and 18 also include benign causes of SVC syndrome – this should be described. Lines 387-401. This is really a summary statement – the authors should consider moving it to the first paragraph of the conclusion section.

Thank you for your comments.

Comment 1: Lines 74 and 85. The references are from 1984 and 1996, respectively. More recent references are available and should be used.

Reply 1: Updated citations are added. Please see page 3 lines 21-22 and line 30.

Comment 2: Line 146. The authors state that heparin is a thrombolytic. It is an antithrombotic.

Reply 2: This is amended accordingly. Please see page 5, line 13.

Comment 3: The section entitled "Technical details of endovascular stenting". This reviewer thinks that this section should be significantly shortened or removed altogether. There are many technical details presented that differ from operator to operator (e.g., line 104 stating US is often used – it is universally used for venous access; line 109 stating that balloon dilation is performed – typically it is only performed if the stent delivery system cannot be placed). If the reader is an IR, the section is incomplete and the technique is debatable; if the reader is an oncologist, the section is unnecessary.

Reply 3:

We agree that the technique of stenting varies depending on the operator and with this helpful suggestion. We have shortened this section by removing some parts that are more variable, including whether ultrasound is used for vascular access, whether balloon dilatation is performed before stent deployment and the position of stent placement in relation to the site of obstruction. Please see page 4, lines 9-18.

Comment 4: Line 211. Refs 17 and 18 also include benign causes of SVC syndrome – this should be described.

Reply 4: A sentence to discuss that the systematic reviews included SVCS patients with both malignant and benign causes was added. Please see page 7 lines 6-9.

Comment 5: Lines 387-401. This is really a summary statement – the authors should consider moving it to the first paragraph of the conclusion section.

Reply 5: We would like to describe that stenting should be considered as first line treatment for patients with a poor prognosis in this paragraph. We clarified this by moving the first sentence of this paragraph to the conclusion. Please see page 13, lines 2-3.