

## Peer Review File

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Comment 1-Accept: Bashir et al. rounded up a narrative clinical review on this rare condition. They also added their skills and outcomes with an amazing long-term follow-up to support the emerging evidence on the open versus endovascular approach. They debated and critically approached each entity and other applicable forms of intervention and highlighted their preferences which match the current trend dealing with Paget-Schroetter Syndrome. The optimal management of this condition remains elusive, however, in their article Bashir et al. structured their approach to support other vascular interventionalist and surgeons reading this article to follow-pursuit and use discretion based on cumulative evidence. The references used are current and the English language is well-formatted to support sufficient conclusions.

Comment 2-Accept: Paget-Schroetter syndrome is a rare condition, whose management approaches are largely guided by the accumulated expertise and clinical experience of vascular specialists. In the absence of randomized controlled trials, current practice has been guided by retrospective reviews and experience. Modern approaches and protocols appear to remain distinct between healthcare facilities but have common features including early clot lysis, surgical decompression with first rib resection, followed by adjunctive open or endovascular procedures. Further high-quality level 1 evidence and research are required to standardize treatment for this condition. The authors of this article collectively and elegantly rounded up the current evidence on this scarcity, highlighting their experience and outcomes. The structure of the article is well devised, and the article is written succinctly. The authors' take-home message is adequate and the references collated are of current and good quality. The authors have carefully considered the selective publication bias and ameliorated this with their effective outcomes to demonstrate that overall, RCT between different intervention arms is required. The shrewdness in their clinical application is in line with the current trend and I fully recommend the publication of this article which would be of interest to the CDT readership.

Comment 3: line 26- 28 - Paget-Schroetter Syndrome (PSS) is an uncommon disorder involving thrombosis of the subclavian vein, often caused by repetitive overuse of compression by surrounding anatomical structures--- please rephrase the sentence.

Reply 3: Thanks for the useful comments which we have incorporated in almost a complete rewrite of the paper. This now has a much better structure and direction with a clear message.

Change in the text: Line 26- 28 has been revised to: However, due to proximity of vital structures neurological sequelae may occur and even inadvertent removal of the second rib during surgery<sup>9</sup>.

Comment 4: As the number of cases of Paget shroetter syndrome is small and it is difficult to conduct prospective studies, the present study has a certain value. However, as it is an accumulation of a small number of cases by two vascular surgeons, there is likely to be a large bias in the selection of cases, and the results should be carefully considered. Furthermore, the results were not statistically examined in terms of outcome values, such as re-occlusions or restenosis, it would make the study a good case-series study if these aspects were improved. Or is it the aim of this study that FRR should be performed in all cases, regardless of the severity of the case or the degree of SV stenosis? We would appreciate your thoughts on these issues.

In PSS, the prognosis is generally better than in venous thrombosis of the lower limbs, and there is a lower complication rate of pulmonary embolism and cerebral infarction, so treatment options with oral anticoagulants are also considered, but this is rarely mentioned in the discussion.

Reply 4: This has been addressed in the text with the inclusion of the relevant paper.

Change in the text: Line 62.

“There is evidence anticoagulation alone may not be sufficient to reduce the incidence of post-thrombotic syndrome and open surgery is required in addition to repair the anatomical defect”.

Ref 4. Vazquez FJ, Paulin P, Poodts D & Gandara E  
Preferred management of Primary Deep Arm Vein Thrombosis  
Eur J Vasc Endovasc Surg 2017;53:744-751.

Comment 5: Because this study is a single-center study, we understand that the number of patients treated with oral anticoagulants is expected to be small. Though this was a case-series study, is it possible to examine in which cases the first rib resection was more useful and which approach was more effective. It would be better to demonstrate the superiority of surgical treatment by comparing it with medical treatment cases.

Reply 5: This was a small case series of a surgical approach for the treatment of PSS. The patients who were treated medically consisted of a different cohort and developed a dvt due to line insertion, hypercoagulable states due to carcinomatosis and were excluded as again small numbers were involved and this was a surgical paper.

Comment 6: Multiple approaches are described in this study and each study is described in Table 2. However, there is no comparison of the effectiveness or description of the advantages and disadvantages of each treatment option or indication. It would be difficult to give a general indication because of the bias in the devices and techniques available in different regions and facilities, but it would be easier to understand the content if the author could provide possible treatment algorithms and other information in such a situation.

Reply 6: This is now table 3 as a flow diagram has been inserted representing the pathway each patient with PSS follows. Hence the table illustrates the few papers dealing with the new concept of mechanical thrombectomy. Only three mention thrombectomy with only Hileman comparing thrombectomy with CDTL and this showed CDTL better as in the text.

Change in the text: Line 306.

Hileman proposed mechanical thrombectomy as an alternative to CDTL in PSS where 93% of patients showed >50% clot reduction. compared to 79% of patients treated with CDTL only<sup>20</sup>.

Comment 7: In the introduction, it seems somewhat redundant. If previous research is to be described, it should be focused on the main points. Part of the description should be based on the results of the case series.

Reply 7: The introduction has been rewritten and more focused.

Comment 8: L109-111. Please consider describing the neurological prognosis associated with FRR in this case series.

Reply 8: This is explained as part of the consent process. None in this series developed any neurological complications.

Comment 9: Methods, L240-245. Why was vascular surgery an Inclusion criterion for the case cluster? Please consider reflecting on PSS cases treated by other doctors and cases that were not treated. What does it mean that surgeons were included in this study? I think it could be taken as an expert opinion of two surgeons. Please describe in your discussion how this point reduces the external validity of this study.

Reply 9: This is a small case series comprising 2 surgeons in a major teaching hospital. Both provide open surgery for the management of PSS. Once referred to one of these 2 surgeons the expectations from the referring doctor is thrombolysis and then open surgery. Undoubtedly some patients may have decided upon medical management or medical opinion was that this should be the pathway.

Comment 10: L249-250. Please consider describing the extent to which patients have been referred for surgical treatment.

Reply 10: As above.

Comment 11: L253. Please consider changing the description to 7-46 % mean 15% in accordance with Reference. If possible, please also state how often this occurred in the medically treated cases in the current study.

Reply 11: This has been addressed in the text.

Change in the text: There is evidence to support surgical treatment of PSS as if treated medically (anticoagulation/ antiplatelets) there is a risk of developing a post phlebotic limb and associated morbidity in 7-46%, mean 15% of cases<sup>16</sup>.

Comment 12: L255. I don't know what 23 means.

Reply 12: Been removed.

Comment 13: L261. 28 same as above.

Reply 13: Been removed.

Comment 14: Results, L277-286. Please describe whether there are differences in outcomes by treatment route. discussion.

Reply 14: Due to small numbers and 4 different operative routes there was no difference.

Comment 15: L313-316. Based on this, it is considered necessary to consider in which cases more surgical treatment should be chosen.

Reply 15: This is a correct statement and many should or could have been referred for treatment rather than be commenced on medical therapy. Certainly, we serve a population of 1.5 million and probably should see up to 10 per yeay who may be suitable for open surgery. Also, medical practitioners in primary care particularly may not be aware there is a surgical option for these patients.

Comment 16: L325-328. Please state the reason for this, that the case selection for this study is highly biased due to the treatment at the tertiary center.

Reply 16: As above.

Comment 17: L337-338. It would be easier to make comparisons if cases where medical treatment was chosen.

Reply 17: This was deliberately done as an intervention-based study hence the medical counterpart was not studied.

Comment 18: L338-340. Please also state how often there was or was not a stroke, pulmonary infarction or local haemorrhage.

Reply 18: None of the above occurred in the 26 patients.

Comment 19: L340-353. You have described the contents of previous papers, and we ask for a discussion of what each paper means in terms of comparison with the current case series.

Reply 19: Only one paper, in this table, the Hileman paper had any sort of comparison between CDTL and mechanical thrombectomy and this was addressed.

Comment 20: L367-368. It would be better to introduce this in Table 2, in summaries, at the beginning of the paragraph from line 337, and to describe the content.

Reply 20: This is in the revised text.

Comment 21: L370-379. Were there any cases of this that were relevant in this case series? If not, we think it is unnecessary to mention it.

Reply 21: Omitted.

Comment 22: L381-382. The description of the first case of FRR in this study should be. Please consider Result.

Reply 22: This has been addressed.

Comment 23: L417-419. In the above paragraph, you mention that it is difficult because of the low incidence, why do you still state that prospective clinical studies are needed?

Reply 23: This statement has been altered in the text removing the need for prospective randomized trials.

Change in the text: Perhaps due to the low incidence of PSS, it may not be feasible for a sufficiently powered prospective randomised trial to be performed to gain a definitive answer as to the optimum surgical approach for SV decompression- particularly if the TA and PC/IC outcome differences are minimal.

Comment 24: L443-445. As for the reason for the high Secondary patency rates, please include in the Discussion the reason why the case pooling was limited to two surgeons, as case selection bias is still a major factor in this study.

Reply 24: This has been addressed in the text.

Change in the text: The surgical approach used in this current series was dependent on the surgeon with one favouring the TA and the other PC or IC approach.

Comment 25: L581, Table 1. Footnote does not explain abbreviations. If possible, please separate the table with and without occlusion for comparison.

Reply 25: Abbreviations included.

Comment 26: L585, Table 2. Please mention abbreviations in the footnote. Please change the title as it does not reflect the content.

Reply 26: This has been done.

Comment 27: The references should come before the period.

Reply 27: Been addressed.

Comment 28: If the authors add a treatment algorithm, it would be useful for readers.

Reply 28: This has been added as table 1.

Comment 29: I think authors need to add information of surgical procedure for stenotic subclavian vein such as artificial vessel replacement and patch plasty.

Reply 29: This has been addressed in text.

Change in the text: This means access to the SV is required posterior to the manubrium and may mean a proximal venous cross clamp is placed from the IC incision when a PC approach is planned. More proximal access may mean the manubrium needs to be split to gain safe access.

Comment 30: F J Vazquez and colleagues reported big review of PSS including 1271 patients of 25 studies (Eur J Vasc Endovasc Surg. 2017; 53 :744-751(PMID 28342731)). I think this review should be included, and the authors should compare the results with this previous study.

Reply 30: This has been included as reference 4.

Change in the text: There is evidence anticoagulation alone may not be sufficient to reduce the incidence of post-thrombotic syndrome and open surgery is required in addition to repair the anatomical defect<sup>4</sup>.

Comment 31. The surgical section of the paper is incomplete. The most important advance in the surgical decompression of the extrinsic compression of the subclavian vein has been the introduction of the Robotic Transthoracic Approach. The results with this surgery have been superior to the traditional transaxillary and supraclavicular approaches. Please update the review. Please see the attached published work.

Gharagozloo F, Meyer M, Tempesta B, Gruessner S. Robotic Thoracoscopic First Rib Resection for Paget Schroetter Syndrome. European Journal of Cardiothoracic Surgery 2019; 55: 434–439.

Gharagozloo F, Meyer M, Tempesta B. Robotic First Rib Resection for Thoracic Outlet Syndrome. *J Thorac Dis* 2021;13: 6141-6154.

Gharagozloo F, Atiquzzaman N, Meyer M, Werden S. Technique of Robotic First Rib Resection. *MIS Journal*. 2021; 5:39.

Reply 31: This has been included as reference 30.

Change in the text: Recent advances in the management of PSS have included a robotic transthoracic approach which allows minimally invasive FRR and also reducing neurovascular complications<sup>30</sup>.

Comment 32: Line 132: for AngioJet, please provide manufacturer information.

Reply 32: Boston Scientific, USA.

Comment 33: Line 179-180: “The two heads.... and access between the clavicular and manubrial insertions.” I don’t understand the sentence as written. Is it saying that the access between the insertions is also identified?

Reply 33: This has been rewritten.

Change in text: The two origins of the pectoralis major muscle are from the anterior surface of the sternum (sternocostal part) and anterior surface of medial half of the clavicle (clavicular part). Between these two origins a non-muscle splitting approach enables the SV to be identified.

Comment 34: Line180-181: Is the advantage just the location of the incision? It says “advantages”.

Reply 34: This has been addressed.

Change in the text: The principal advantage of the IC approach is that an incision is made over the first rib in order to access the anteriorly located SV.

Comment 35:

Line 255: “23” appears in the body of the sentence.

Line 258-259- "FRR" was already introduced earlier in the paper.

Dealt with.

Line 261: “28” appears in the body of the sentence.

Line 267 and elsewhere: Numbers are referenced as both numerical and text. Examples: “eleven”, “15”, “three”, and “2”.

Line 274: Replace “redo” with “revision” perhaps.

Reply 35: The questions were addressed.

Comment 36: Line 293: What did the conservative treatment consist of, if known?

Reply 36: Unknown.

Comment 37: Line 350: For Trellis thrombolysis catheter, please provide manufacturer information.

Reply 37: Covidien, USA.

Comment 38:

Line 64: risk "of" PSS.

Line 79: on "the" SV.

Line 123: or urokinase "are" then infused.

Line 251: within the vein, "and" acceptance of risks.

Line 255: Abbreviation (tPA) shouldn't begin a sentence.

Line 290: occluded or re-occluded.

Line 338-339- such "as" prolonged.

Reply 38: These have all been dealt with throughout the rewritten text.

Comment 39: Paragraph starting at line 224: Schneider's paper in 2004 did not have any stent placement. The paragraph starts with citing Schneider's paper regarding PTA but then goes on to describe stents, so it is a little misleading. Perhaps separate the paragraphs or provide a separate reference for the final 2 sentences discussing stents.

Reply 39: This has been addressed.

Change in the text: Schneider et al. note that up to 60% of patients persistently exhibit recurrent thrombosis or SV stenosis following surgical decompression, and that adjunctive angioplasty in this setting was found to be highly effective.

Comment 40:

Line 255 - strike the number "23".

Line 261 - strike the number "28".

Line 269 - In some places "tPA" is written but here it is "TPA". Recommended being consistent.

Line 310 - "seem" instead of "seems".

Reply 40: Done.

Comment 41: Figures 5, 6 and 7 are not discussed in the text of the paper.

Reply 41: The number of figures has been considerably reduced in the text.