

Response to comments provided by expert reviewers.

We thank the reviewers for their insightful comments to improve the manuscript. Changes have been made in the manuscript and highlighted in yellow.

A. Comments	Response	Manuscript changes
<p>1. I strongly encourage Authors to use the abbreviation pseudoaneurysm (PA)</p> <p>2. “Sinistral portal hypertension” (Page 6) - “sinistral” portal hypertension is better.</p> <p>3. Present as worsening pain abdomen (Page 11) - abdominal pain is better. managed (Page 11) - managed is right.</p> <p>4. Multidetector CT angiography (CTA) (Page 12) - the abbreviation should be</p>	<p>We agree with the reviewers that the term pseudoaneurysm is lengthy and has a uniformly accepted abbreviation in the literature, i.e. PsA.</p> <p>Similarly, grammatical and language errors have been acknowledged and changed accordingly.</p> <p>Uniformly recognized abbreviations of other terms like CT angiography (CTA), MR Angiography (MRA), and digital subtraction angiography (DSA) have been incorporated.</p>	<p>Pseudoaneurysm abbreviated as PsA throughout the manuscript.</p> <p>(Page 6)- “Sinistral portal hypertension”- has been rephrased as “sinistral” portal hypertension.</p> <p>(Page 11)- worsening pain abdomen has been corrected to abdominal pain.</p> <p>(Page 12)- managed spellings corrected.</p> <p>(Page 12)- Multidetector CT angiography has been abbreviated as CTA throughout the text after its first description.</p>

<p>explained at the first appearance in the text.</p> <p>5. Digital subtraction angiography (Figure 4C) (Page 13) - please use the abbreviation only.</p> <p>6. A simplified approach to the approach (Page 15) - what is it?</p> <p>7. Pancreatitis related (Page 19) - pancreatitis-related is better.</p> <p>8. Chronic pancreatitis (Conclusion, twice) - please use abbreviation only.</p> <p>9. Contrast enhanced (Fig. 2 Legend) - peri gastric, contrast-enhanced is right.</p>		<p>(Page 13, Figure 4C)- Digital subtraction angiography has been abbreviated as DSA after its first description in the text.</p> <p>(Page 15)- The sentence reframed as “A simplified approach to the management of pseudoaneurysmal bleed has been illustrated in figure 5 and 6A.”</p> <p>(Page 19)- hyphen placed between pancreatitis and related (pancreatitis-related)</p> <p>(Page 20)- chronic pancreatitis abbreviated as CP.</p> <p>(Page 21, Figure 2 Legend)- hyphen placed between peri and gastric (peri-gastric); contrast and enhanced (contrast-enhanced)</p>
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<p>10. Some terms in Figure Legends can be used as abbreviations only (CP, DSA).</p>		<p>The terms in the figure legends have been used as abbreviations.</p>
<p>11. The list of References must be formatted in strict accordance with the Instructions for Authors</p>	<p>We agree with the reviewer that the references should be in accordance with the journal's guidelines for authors.</p>	<p>The references have been modified according to guidelines and both PMID and DOI of all references have been mentioned alongside.</p>
<p>B. Comments</p>	<p>Response</p>	<p>Manuscript changes</p>
<p>Please reword the following: Procedure-related bleed is not uncommon in chronic pancreatitis; is usually venous bleed and is mostly managed conservatively. Requires smother transition</p>	<p>We agree with the reviewers and have reframed the statement as mentioned.</p>	<p>Abstract- Procedure-related bleed is usually venous and mostly managed conservatively.</p>
<p>1. Please elaborate or give an example on which inflammatory mediators can activate the coagulation system</p>	<p>Vascular thrombosis in CP is due to fulfillment of 2 out of 3 of Virchow's triad criteria, namely vascular stasis due to edematous pancreas and pseudocyst and endothelial damage due to various inflammatory mediators. These</p>	<p>Page 5- Pathophysiology of venous thrombosis. Certain factors like IL-1, IL-6 and TNF-alfa released from the damaged pancreatic tissue into the blood may also trigger a</p>

	<p>inflammatory mediators have been predominantly described in acute pancreatitis and include IL-1, IL-6, and TNF-alfa mainly. Few studies have demonstrated increased levels of these cytokines in patients with venous thrombosis in CP which has been included along with references.</p>	<p>coagulation cascade, leading to thrombosis.</p>
<p>2. Which type to gastroesophageal varices is more commonly formed, based on Sarin's classification. Is IGV more common than GOV in left sided portal hypertension?</p>	<p>Most of the studies on venous thrombosis in CP and its clinical outcomes are retrospective in nature with heterogeneous patient populations. Many of these studies have described the varices as esophageal or gastric without mentioning Sarin's types. Some studies have used Sarin's classification. Usually IGV is more common, however, it is difficult to emphasize, due to the paucity of literature. All the studies with the</p>	<p>None</p>

	classifications and observations have been enumerated in Table 3.	
3. Why is melena more common in left sided PH, based on our experience, we have received more patients with hematemesis compared to melena in regular PH patients with varices	Authors agree with the reviewers' observation.	The common manifestation of variceal bleed is hematemesis or melena.
4. What about the performance of EUS on detecting portal vein thrombosis?	We agree with you that with the increasing availability and expertise in the use of EUS, its role in the diagnosis of portal thrombosis becomes important. Studies have shown good sensitivity and specificity of EUS in diagnosis of portal vein thrombosis with high accuracy. We have incorporated this data in the text.	Page 8- Diagnosis Endoscopic ultrasound (EUS) has been shown to have a sensitivity of 81%, specificity of 93% and accuracy of 89% for detecting thrombosis in the porto-splanchnic venous system.
5. Does it have a role in clinical settings?	The routine use of EUS solely to diagnose portal thrombosis is limited, since non-invasive cross-sectional imaging like	None

	<p>CECT have comparable accuracy in diagnosis and is non-invasive, cheap, and readily available. However, if EUS is indicated for other indications like evaluation of PsA or varices, it might simultaneously show the presence of concomitant portal thrombosis.</p>	
<p>6. Is there a role for NSBB? Especially for asymptomatic patients</p>	<p>The data on role of NSBB specifically in left-sided portal hypertension related to CP is lacking. However, their role in secondary prophylaxis has been extrapolated from studies in cirrhosis and prehepatic portal hypertension without CP. The Baveno VII consensus recommends secondary prophylaxis in EHPVO with NSBB with no definite recommendations in CP-related varices. So, a definite recommendation cannot be made; and are not being used in authors' center.</p>	<p>Page 10- Management For prophylaxis of variceal bleed, beta blockers have been recommended for secondary prophylaxis in EHPVO as extrapolated from data of cirrhotic portal hypertension with no first-hand data on their role in CP-related varices. Data on role of beta blockers for primary prophylaxis is lacking. So, a definite recommendation cannot be made on the basis of available evidence.</p>

<p>7. What is the role for anticoagulation therapy with heparin or LMWH?</p>	<p>There is a definite role for anticoagulation in certain situations as backed by data from the literature. These include acute thrombosis and thrombosis leading to bowel ischemia. The role in chronic thrombosis with collaterals is not well defined.</p>	<p>Page 9- Management Indications of anticoagulation in CP include extension of acute thrombus to portal and mesenteric vein, and development of mesenteric ischemia.</p>
<p>8. What is the role for oral anticoagulation therapy such a warfarin or newer drugs such as rivaroxaban or Pradaxa?</p>	<p>There are no controlled trials on use of newer anticoagulants in CP-related splanchnic thrombosis and hence their current indications are not well defined.</p>	<p>Page 9- Management The data on the role of anticoagulation including newer oral anticoagulants (NOACs) in venous thrombosis in the setting of CP is scarce as compared to AP, hence, no definite recommendation can be made.</p>
<p>9. How to distinguish between acute or chronic venous thrombosis? Is the a role for EUS, such as ultrasound imaging, doppler blood flow, etc?</p>	<p>The ultrasound (percutaneous or EUS) appearance of venous thrombosis includes presence of echogenic contents in the lumen along with reduced or absent flow on color doppler. The distinction between acute or chronic thrombosis is</p>	<p>None</p>

	<p>less accurate as compared to modalities like CT or MR angiography. However, some points to distinguish acute from chronic thrombosis include anechoic nature of a recently formed thrombus as compared to the echogenic nature of chronic thrombus along with other features like development of collaterals that favor chronicity.</p>	
<p>10. Please included symptoms for patients without aneurysm bleeding, such as abdominal pain, bloating, or visible abdominal mass etc</p>	<p>Patients with arterial PsA may have clinical presentation even in the absence of overt GI bleed including an acute increase in abdominal pain, abdominal distension or sudden hemodynamic worsening.</p>	<p>Page 12- Presentation Clinical manifestations of a ruptured PsA apart from overt luminal or intra-abdominal bleed include acute worsening of abdominal pain, abdominal distension, or unexplained sudden hemodynamic worsening. The reported frequency of these symptoms as per different studies has been mentioned in Table 4.</p>

<p>11. How does different management compare in terms of outcome?</p>	<p>Management of arterial PsA includes various approaches including interventional radiological, endoscopic ultrasound-guided, or surgical. The data on outcomes of these approaches comes from small retrospective studies which have been enumerated in Table 5 along with outcomes according to interventions done. However, as mentioned in the text that interventional radiological procedure is preferred choice.</p>	<p>None</p>
<p>12. Which type of management approach is more suitable for which type of aneurysm?</p>	<p>The type of approach to a particular PsA depends on various factors including size, location, neck, feeding artery and coagulation parameters of patients. Various approaches according to these factors have been explained on page 17 under management heading and illustrated in Figure 5.</p>	<p>None</p>