Visceral artery pseudoaneurysm in necrotizing pancreatitis: incidence and outcomes

Background: Visceral artery pseudoaneurysms (VA-PSA) occur in necrotizing pancreatitis; however, little is known about their natural history. This study sought to evaluate the incidence and outcomes of VA-PSA in a large cohort of patients with necrotizing pancreatitis.

Methods: Data for patients with necrotizing pancreatitis who were treated between 2005 and 2017 at Indiana University Health University Hospital and who developed a VA-PSA were reviewed to assess incidence, presentation, treatment and outcomes.

Results: Twenty-eight of 647 patients with necrotizing pancreatitis (4.3%) developed a VA-PSA between 2005 and 2017. The artery most commonly involved was the splenic artery (36%), followed by the gastroduodenal artery (24%). The most common presenting symptom was bloody drain output (32%), followed by incidental computed tomographic findings (21%). The median time from onset of necrotizing pancreatitis to diagnosis of a VA-PSA was 63.5 days (range 1–957 d). Twenty-five of the 28 patients who developed VA-PSA (89%) were successfully treated with percutaneous angioembolization. Three patients (11%) required surgery: 1 patient rebled following embolization and required operative management, and 2 underwent upfront operative management. The mortality rate attributable to hemorrhage from a VA-PSA in the setting of necrotizing pancreatitis was 14% (4 of 28 patients).

Conclusion: In this study, VA-PSA occurred in 4.3% of patients with necrotizing pancreatitis. Percutaneous angioembolization effectively treated most cases; however, mortality from VA-PSA was high (14%). A high degree of clinical suspicion remains critical for early diagnosis of this potentially fatal problem.

Contexte : Les faux anévrismes des artères viscérales (FAAV) surviennent en présence d’une pancréatite nécrosante; on en sait cependant peu sur leur histoire naturelle. L’objectif de l’étude était d’évaluer l’incidence et les issues des FAAV dans une grande cohorte de patients atteints de pancréatite nécrosante.

Méthodes : Nous avons examiné les données des patients atteints de pancréatite nécrosante traités entre 2005 et 2017 à l’Hôpital universitaire de l’Université de l’Indiana qui ont fait un FAAV afin d’évaluer l’incidence, les premiers signes, le traitement et les issues de cette affection.

Résultats : Vingt-huit (4,3 %) des 647 patients atteints de pancréatite nécrosante inclus (2005–2017) ont fait un FAAV. L’artère la plus souvent touchée était l’artère splénique (36%), suivie de l’artère gastroduodénale (24%). Les premiers signes les plus courants étaient la présence de sang dans les liquides évacués par drainage (32%), puis les résultats d’une tomodensitométrie effectuée pour une autre raison (21%). Le délai médian entre l’apparition de la pancréatite nécrosante et le diagnostic de FAAV était de 63,5 jours (intervalle : 1 à 957 jours). Vingt-cinq des 28 patients ayant fait un FAAV (89%) ont été traités avec succès par angiembolisation percutanée. Trois patients (11%) ont dû être opérés : 2 dès le début, et le troisième parce qu’il a recommencé à saigner après l’embolisation. Le taux de mortalité par hémorragie due à un FAAV chez les personnes atteintes d’une pancréatite nécrosante était de 14% (4 patients sur 28).

Conclusion : Dans cette étude, 4,3 % des patients atteints de pancréatite nécrosante ont connu un FAAV. L’angiembolisation percutanée s’est avérée efficace dans la plupart des cas; cependant, la mortalité associée aux FAAV était élevée (14%). Il est crucial de faire preuve d’une grande suspicion clinique afin de diagnostiquer tôt cette affection potentiellement mortelle.
A visceral artery pseudoaneurysm (VA-PSA) is a known complication following pancreatic surgery as well as in the setting of acute and chronic pancreatitis. A VA-PSA formation can lead to massive hemorrhage associated with substantial mortality, ranging from 25% to 50%. Little is known about the incidence and natural history of VA-PSA in the setting of necrotizing pancreatitis (NP), a disease that is itself associated with substantial morbidity and mortality.

An arterial pseudoaneurysm is a ruptured vessel with a surrounding hematoma in communication with the vessel lumen, and in the setting of pancreatitis it is the result of injury to the vessel from surrounding inflammation, pancreatic enzymes, infection and/or anastomotic leak; disruption of the tamponade provided by the hematoma may result in massive hemorrhage. In the setting of NP, a combination of enzymatic digestion and microcirculatory ischemia/reperfusion results in substantial local and system complications, including organ failure or large-volume pancreatic necrosis, or both. Visceral arteries are intimately associated with the mass effect and inflammation of necrosis and the development of VA-PSA is known to occur in NP. However, the available literature has not evaluated the development of VA-PSA specifically in the setting of NP. Instead, the information published to date has been limited to case reports, small case series or data from a few NP patients included in a mixed cohort of patients with chronic pancreatitis and patients who underwent pancreatic surgery.

Therefore, the aim of this study was to define the incidence, presentation, treatment and outcomes of VA-PSA in NP.

**Methods**

This retrospective analysis was approved by the Indiana University (IU) institutional review board and was compliant with the Health Insurance Portability and Accountability Act. Data for all patients with NP who were treated at IU Health University Hospital between 2005 and 2017 were prospectively collected into the institution’s NP database. This cohort includes patients who required intervention as well as those who recovered without the need for mechanical débridement of necrotic tissue. This database was queried for patients with an admission or discharge diagnosis of pseudoaneurysm of the visceral arterial tree. Additionally, all computed tomography and angiography reports were reviewed for those studies diagnosing pseudoaneurysm. At our institution, we generally obtain imaging for patients on a weekly basis until resolution of pancreatic necrosis.

Acute pancreatitis and severe acute pancreatitis were defined according to the revised Atlanta classification. Necrosis was defined as a lack of pancreatic parenchymal enhancement and/or findings of peripancreatic necrosis such as acute necrotic collection (ANC) or walled-off necrosis (WON) on contrast-enhanced cross-sectional imaging. Organ failure was defined according to the modified Marshall scoring system for organ dysfunction. Infected necrosis was suspected by the presence of gas within an ANC or WON on contrast-enhanced cross-sectional imaging and confirmed with steriley obtained cultures during intervention on pancreatic necrosis. A computed tomography severity index (CTSI) score was calculated for all patients according to the definitions outlined in the 2004 modification of the CTSI.

Clinical characteristics of patients who had NP with and without VA-PSA were reviewed. Descriptive statistics were applied to define the incidence, presentation, treatment and outcomes of patients with VA-PSA. The clinical characteristics of patients with VA-PSA were compared with those of patients without VA-PSA to identify potential risk factors for pseudoaneurysm development. Categorical data are expressed as frequencies with percentages and were compared using the $\chi^2$ test. Nonparametric continuous data are reported as median values with ranges and were compared using the Wilcoxon rank-sum test. Parametric continuous data are reported as mean values with the standard error of the mean (SEM) and were compared using the Student t test. Odds ratios (ORs) were calculated for significant risk factors and are reported with 95% confidence intervals (CIs). A $p$ value less than 0.05 was considered significant.

**Results**

**Incidence and presentation**

A total of 647 patients with NP were treated at IU Health University Hospital between 2005 and 2017. The mean duration of follow-up was 44.4 months (SEM 1.7 mo). Follow-up to disease resolution or death was achieved in 633 patients (97.8%); 14 patients were lost to long-term follow-up. Twenty-eight (4.3%) of the patients developed VA-PSA, 5 of whom developed VA-PSA at multiple sites. The median time from onset of pancreatitis to diagnosis of PSA was 63.5 days (range 1–957 d). The presenting symptoms of VA-PSA in the study cohort are shown in Table 1. The most common presentation was bloody

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. (%) of patients</th>
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<tbody>
<tr>
<td>Blood in drain (surgical or percutaneous)</td>
<td>9 (32)</td>
</tr>
<tr>
<td>Incidental computed tomography finding</td>
<td>6 (21)</td>
</tr>
<tr>
<td>New or changed abdominal pain</td>
<td>5 (18)</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Hemorrhagic shock</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Decreased hemoglobin/hematocrit</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Incidental finding at operation</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>
drain output (9 patients, 32%), followed by incidental computed tomography (CT) findings (6 patients, 21%). Diagnosis of VA-PSA was established by CT (14 patients, 50%), by traditional angiography (12 patients, 43%) or at the time of operation (2 patients, 7%). The locations of the VA-PSAs in the study cohort are shown in Figure 1; the most common artery involved was the splenic artery (12 VA-PSAs, 36%) followed by the gastroduodenal artery (8 VA-PSAs, 24%). Pseudoaneurysm developed in several additional visceral arteries, including the gastroepiploic, pancreaticoduodenal, gastric, dorsal pancreatic, hepatic and superior mesenteric arteries.

**Risk factors**

The clinical characteristics of the patients who developed VA-PSA and those who did not were compared. The cause of pancreatitis was not associated with VA-PSA development (Table 2). Preexisting medical conditions, including alcohol misuse, cardiac disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes, hyperlipidemia, hypertension, obesity and tobacco misuse were evaluated; none of these correlated with an increased risk for developing VA-PSA (p value range 0.12–0.86). Clinical factors associated with a statistically significant increased risk of VA-PSA development include age older than 50 years (OR 2.51, 95% CI 1.1–6.0, p = 0.038) and the development of any organ failure (OR 2.1, 95% CI 1.0–4.6, p = 0.048) (Fig. 2). The presence of infected necrosis or disconnected pancreatic duct syndrome did not increase the risk of VA-PSA formation (p = 0.11 and 0.40, respectively). No difference was seen in the CTSI score when we compared patients who developed VA-PSA (mean CTSI score 7.1, SEM 0.3) and those who did not (mean CTSI score 6.7, SEM 0.1) (p = 0.3). Additionally, the degree of necrosis was not found to be associated with VA-PSA development (Table 3). No difference in the incidence of VA-PSA was observed between patients who required intervention for pancreatic necrosis (20 of 525 patients, 4%) and patients who did not require intervention (8 of 122 patients, 7%) (p = 0.18). A drainage catheter (either operatively or percutaneously placed) was present in 359 patients (58%) who did not develop a VA-PSA and in 13 patients (46%) who did develop VA-PSA. The presence of a drainage catheter did not increase the risk of developing VA-PSA (p = 0.2).

**Management and outcomes**

All patients were treated within 24 hours of VA-PSA diagnosis. Twenty-six of the patients with VA-PSA (93%) underwent percutaneous angioembolization. Two patients had primary operative repair (7%); 1 patient underwent emergent operation for hemorrhagic shock, and 1 VA-PSA was discovered and treated at the time of elective operation for disconnected pancreatic duct syndrome. These 2 cases account for both of the instances of VA-PSA identified at the time of operation. Percutaneous angioembolization was technically successful in all patients. The procedure was clinically successful in 25 of the 26 patients who underwent it (96%); 1 patient rebled and required operative management. The median transfusion requirement was 1.5 (range 0–32) units of packed red blood cells. In 4 patients, hemorrhage from a VA-PSA resulted in uncorrectable multiple organ system failure that led to death, despite the rapid control of hemorrhage. Therefore, the mortality rate directly

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**Table 2. Comparison of the causes of pancreatitis in patients who developed visceral artery pseudoaneurysm and those who did not***

<table>
<thead>
<tr>
<th>Cause of pancreatitis</th>
<th>No. (%) of patients</th>
<th>p value</th>
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<tbody>
<tr>
<td></td>
<td>No VA-PSA</td>
<td>VA-PSA</td>
</tr>
<tr>
<td>Biliary</td>
<td>307 (50)</td>
<td>14 (50)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>121 (20)</td>
<td>10 (36)</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>38 (6)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>PEP</td>
<td>37 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other</td>
<td>116 (19)</td>
<td>3 (11)</td>
</tr>
</tbody>
</table>

*PEP = postendoscopic retrograde cholangiopancreatography pancreatitis; VA-PSA = visceral artery pseudoaneurysm.  
*Categorical variables were compared using the χ² test.
attributable to hemorrhage from a VA-PSA was 14% (4 of 28 patients). The mortality rate before NP disease resolution among all patients who developed VA-PSA was 25% (7 of 28 patients) and the mortality rate among patients who did not develop VA-PSA was 7.6% (47 of 619 patients). The development of VA-PSA was associated with a 4.1-fold (95% CI 1.6–10.0, \( p = 0.002 \)) increased risk of death before resolution of NP.

**DISCUSSION**

This large contemporary series provides important insight into VA-PSA in the setting of NP. It is a well-known complication of chronic pancreatitis and a recognized complication following pancreatic surgery;\(^{12,13} \) however, our understanding of the incidence and natural history of VA-PSA in the setting of NP is limited. Available publications include case reports or data for small numbers of NP patients included in reports of patients with chronic pancreatitis.\(^ {13–18,27} \) Given the prevalence of NP, this analysis provides important information on VA-PSA complicating NP, including its incidence, presentation, risk factors and treatment.

The true incidence of VA-PSA in NP is unknown; a wide range of 1.3%–10% has been reported in patients with “pancreatitis.”\(^ {14–18,27} \) However, most patients included in these studies had chronic pancreatitis and/or the studies included fewer than 10 patients with NP. Our group previously conducted a study of 37 patients who developed VA-PSA between 1995 and 2005. This report included 11 patients who underwent pancreatectomy and 22 patients
with chronic pancreatitis; only 4 patients developed VA-PSA in the setting of NP.\textsuperscript{12} On the basis of the existing data, VA-PSA has been thought to be a rare complication of NP. The current series demonstrates VA-PSA to be a much more common complication of NP than generally accepted, with an incidence of 4.3%. Importantly, the current series of NP patients includes both patients managed medically and patients who required intervention. This series provides a much more accurate estimate of the incidence of VA-PSA in the NP population. The retrospective nature of this study is a minor limitation, as we achieved follow-up to disease resolution (or death) in nearly all patients. Further, in these patients we are capturing ongoing follow-up data to expand the understanding of long-term problems and outcomes in this challenging group.

Early diagnosis and swift treatment are critical as VA-PSA presents the potential for massive hemorrhage. Early diagnosis requires awareness of presenting symptoms. In the setting of chronic pancreatitis, the most common presenting symptom is abdominal pain and gastrointestinal bleed.\textsuperscript{19,20,28,29} Patients with NP presented differently: abdominal pain was the presenting symptom in a minority of patients (18%). The most common presenting symptom in the NP population was bloody output from a surgical or percutaneous drain (32%) followed by incidental CT findings (21%). These differences are probably explained by the increasing use of percutaneous drainage and CT-surveillance imaging in the modern era.\textsuperscript{10–31} It is noteworthy that 18% of patients presented with new or changed pain, 11% presented with gastrointestinal bleed and 2 patients (7%) presented acutely with catastrophic hemorrhage and shock. These findings highlight the diverse presentation of VA-PSA and illustrate the need for awareness of this pathology.

The splenic artery (36%) and the gastroduodenal artery (24%) were the arteries in which VA-PSA most commonly developed in the setting of NP. However, our data also highlight the fact that nearly any visceral artery may be involved in VA-PSA. This finding may be explained by the propensity for necrosis to track down either paracolic gutter, down the root of the small bowel mesentery and even into the pelvis. This knowledge is important when initial imaging fails to disclose VA-PSA; evaluation of the entire visceral arterial tree, including the celiac axis and branches of the superior mesenteric artery, is critical.

Wide use of percutaneous angioembolization in the treatment of VA-PSA over the last several decades has improved the morbidity and mortality associated with this condition. Traditionally, surgical management was the only option to treat VA-PSA. Operative treatment of VA-PSA was associated with mortality ranging from 10% to 50%.\textsuperscript{14,21,14,35} Percutaneous angioembolization efficacy ranges from 79% to 100%, with contemporary mortality rates of approximately 10%–20%.\textsuperscript{12,17,22,23,36,37} In the current series, the success rate of angioembolization was 96% (1 patient developed rebleeding that was managed operatively). Despite swift and successful treatment, mortality remained high at 18%. The overall severity of illness in patients with NP, including the association of organ failure with VA-PSA development, probably contributed to the high mortality rate we observed.

Two specific risk factors for VA-PSA development in the population of patients with NP include age older than 50 years and the presence of any organ failure. No other study to date has identified specific risk factors for VA-PSA in this population. A substantial limitation of this study is the lack of clinical severity analysis using the Acute Physiology and Chronic Health Evaluation (APACHE) II, the Bedside Index of Severity in Acute Pancreatitis (BISAP) or Ranson’s criteria. The vast majority of NP patients treated at our institution are transferred after days or weeks of treatment at an outside facility and our ability to retrospectively evaluate these severity metrics is very limited. However, CTSI has been shown to correlate reliably with clinical severity metrics,\textsuperscript{38} and in the current series NP severity as assessed by CTSI was not associated with an increased risk of VA-PSA development. Perhaps the prolonged systemic inflammation that results in persistent organ failure\textsuperscript{39} may be a contributing factor in the development of VA-PSA. Given that organ failure is present in the most severe cases of NP, VA-PSA may be considered a marker of disease severity. Interestingly, the presence of infected necrosis was not a risk factor. Perhaps this is related to more rapid evacuation of necrosis as infection is diagnosed. These risk factors (age and organ failure) should be taken into consideration by treating clinicians, and when they are present in combination with new hemodynamic instability and/or signs and symptoms of hemorrhage, prompt evaluation for VA-PSA with contrast-enhanced imaging should be performed.

This study raises important questions about the management of NP-associated VA-PSA. For example, following treatment of an identified VA-PSA, should the necrosis be evacuated more aggressively to prevent the development of further VA-PSA? If intervention is necessary, what is the appropriate timing of intervention following VA-PSA treatment? In patients with VA-PSA, which necrosectomy approach is safest? Clinical questions involving low-incidence events in NP provide motivation for developing a national or international multicentre consortium to study this relatively uncommon disease.

**CONCLUSION**

A VA-PSA is a potentially lethal complication in patients with NP. In this study its incidence was 4.3%, which is substantially higher than previously appreciated, and substantial heterogeneity exists in terms of presentation and location. A high degree of clinical suspicion should be held, and early diagnosis sought, because despite advances in diagnosis and treatment, the mortality rate among patients with NP who develop VA-PSA remains high.
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Competing interests: None declared.

Contributors: T. Maatman, M. Heimberger, A. Roch, M. House, E. Ceppa, M. Schmidt and N. Zyromski designed the study. T. Maatman, M. Heimberger, K. Lewellen, A. Roch and N. Zyromski acquired the data, which all authors analyzed. T. Maatman, M. Heimberger, A. Roch, M. House and N. Zyromski wrote the article, which all authors critically reviewed. All authors gave final approval of the article for publication.

References


