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Isolated Peripancreatic Necrosis in Acute Pancreatitis is infrequent and leads to severe clinical course only when extensive; a prospective study from a U.S. tertiary center

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Abstract

Goals—To explore diagnostic challenges, management, and clinical outcomes of patients with isolated peripancreatic necrosis (PPN), with emphasis to extent of involvement, and compare them to pancreatic necrosis (PN).

Background—PPN, a relatively new term, has been included as a separate entity in the Revised Atlanta Classification (RAC).

Study—Clinical data of recruited AP patients were recorded prospectively. Contrast-enhanced CT (CECT) scans were reviewed by expert radiologists blinded to clinical outcomes.

Results—Two hundred seventy one out of 400 AP patients underwent CECTs, of which 29 (11%) had PPN (14:limited; 15:extensive) and 124 (46%) PN (40:<30%; 16:30-50%; 68:>50% of parenchyma). Patients with PPN were similar to PN in age (56 years), gender (55% male), and BMI (29 kg/m^2). Nutritional support was provided in 18 (62%) patients with PPN and 97 (78%) with PN (p=0.12). Drainage/debridement was required in 2 patients (7%) with PPN and 64 (53%) with parenchymal necrosis (p<0.001). Persistent organ failure rates did not differ significantly (34% vs. 51%; p=0.17), but hospital stay was shorter in patients with PPN (15 vs. 20 days, p=0.05). Limited PPN required no intervention and had similar persistent organ failure rates and

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hospitalization length with interstitial pancreatitis (both p≥0.12). Extensive PPN mainly developed in patients with persistent organ failure (60%) and rarely required drainage (2/15).

Conclusions—PPN prevalence was lower than PN with a ratio of 1:4. PPN rarely required intervention. Utilizing the extent of involvement has the potential to classify PPN and PN with escalating clinical significance and guide management.

Keywords

Acute pancreatitis; Pancreatic necrosis; Peripancreatic necrosis

Introduction

Acute pancreatitis (AP) is currently the most common gastrointestinal disease requiring hospitalization in the U.S.[1] The incidence of AP has increased over the past two decades in the US and most European countries.[2,3] _ENREF_2 Clinical outcomes vary broadly with around 20% of the patients following a severe disease course.[4] Early prediction and management of severe AP remains challenging.[5-8]

Recently, new disease definitions and severity classifications have been proposed by international groups of experts following web-based consensus-building approaches.[4, 9] The Revised Atlanta Classification (RAC) system has been shown to be easily applicable and clinically relevant in the daily practice.[10, 11] Based on RAC, AP can be interstitial, in the majority of patients, or necrotizing. Necrotizing AP is further classified to Pancreatic Necrosis (PN), which involves the pancreatic parenchyma with/without extension to the peripancreatic tissues or Isolated Peripancreatic Necrosis (PPN)[4]

PPN has recently become an area of increasing research and clinical interest. The reported incidence of PPN has been variable with a large study suggesting that it is similar to PN.[12] Furthermore, it has been proposed that PPN follows a “milder” clinical course and requires less frequently drainage/debridement compared to PN.[12] Data correlating the extent of the PPN with disease severity is scarce.

The aim of the present study is to explore the diagnostic challenges, management, and clinical course of PPN patients as compared to those with parenchymal necrosis with special emphasis to the extent of tissue involvement.

Materials and Methods

Study design and patients

The Severity of Acute Pancreatitis/Pancreatitis-associated Risk Of Organ Failure (SAPS/PROOF) study is an ongoing observational study that started in 2004 at the University of Pittsburgh Medical Center (UPMC). It includes a prospective, well-phenotyped cohort of patients and aims to assess risks, biomarkers, management, and clinical outcomes in AP.[6, 10, 13] Ethical approval of the study was obtained by the Institutional Review Board at the University of Pittsburgh (IRB protocol ID PRO08010374). The study expanded over three chronologic periods; 2004-05, 2006-07 and 2008-14. Subjects identified within 72

hours from the onset of symptoms were consecutively enrolled during these 3 time frames after they signed a written consent form and were subsequently followed prospectively during hospitalization. For the purposes of this study, we focused on patients with PPN and PN (PPN/PN).

Data on demographics, laboratory measurements, clinical course, management, and outcomes have been recorded prospectively. All outside hospital medical records of transferred patients were retrieved and reviewed. Therefore, the present report represents a retrospective analysis of prospectively collected data.

Computerized Tomography scans

CT studies were performed on multi-detector helical CT scanners with 4–64 detector rows (General Electric Medical Systems, Waukesha, WI). Contiguous 5-mm–thick or 2.5-mm–thick axial sections were displayed from the diaphragm to the pubic symphysis. Patients included in the analysis of the present study received non-ionic intravenous contrast material [ioversol (Optiray 350; Mallinckrodt Imaging, Dublin, Ireland) or Isovue-370 (iopamidol injection 76%; Bracco Diagnostics Inc, Princeton, NJ)] that was administered at 3-5 mL/s at a volume of 125–150 mL. All patients were imaged in the portal venous dominant phase or underwent multiphasic scans with additional imaging in the unenhanced and pancreatic phase.

Indications of CECT scans within the first 72 hours included patients who initially presented with atypical signs and symptoms, when diagnoses other than pancreatitis were possible such as bowel perforation, and bowel ischemia or when patients developed a rapidly declining clinical course.

Imaging evaluation

All CT images were retrospectively reviewed by two subspecialty trained abdominal radiologists, who were blinded to patient outcomes. Both initial and follow-up CECT scans were reviewed. Morphologic features of AP and peri-/pancreatic fluid collections were assessed according to the definitions of the Revised Atlanta Classification (Table 1).[4] PPN was defined as non-liquefied, ill-defined, nodular areas of increased peripancreatic fat attenuation, with visual density higher than simple fluid or stranding, or as peripancreatic necrotic fluid collection *in the absence of pancreatic necrosis*. Confidence level in diagnosing PPN was recorded using a 3-point scale (1 = poorly confident or unsure; 2 = moderately confident; 3 = strongly confident). Cases initially classified as “poorly confident” were reviewed to reach a final consensus. PN was defined as devitalized pancreatic tissue, which appears as an area of parenchymal non-enhancement on CECT with or without additional peripancreatic necrosis.

PPN was quantified by recording the number of peripancreatic spaces involved; the following seven locations were considered: peripancreatic space, root of the mesentery, transverse mesocolon, gastrosplenic ligament, hepatoduodenal and/or gastrohepatic ligament, right anterior and/or posterior pararenal space, left anterior and/or posterior pararenal space. Additionally, the maximum transverse diameter of the largest peripancreatic necrotic collection was recorded. PPN was then classified as “limited” when measuring < 5

cm, and “extensive” when measuring > 5 cm or affecting >3 locations (Figure 1). The above thresholds were based on studies reporting that > 5 cm peripancreatic collections are less likely to be absorbed,[12, 14] and on our radiologists’ expert opinion.

In addition, they recorded inflammation/involvement of other abdominal organs, presence of portosplenomesenteric thrombosis, and pseudoaneurysms in the peripancreatic vessels.

Definitions

AP diagnosis, persistent organ failure, and other clinical outcomes (ICU need, hospital length of stay, mortality) were recorded as previously described.[4, 10] Walled-off necrosis was based on RAC (Table 1). Utilization of prophylactic antibiotics referred to use of carbapenem, in patients with PNN/PN and no signs of infection. Median time that CECT scans were performed was calculated from the initial admission, either this was to our institution or an outside hospital.

Interventions for PPN/PN included open surgery or minimally invasive approaches, such as laparoscopic necrosectomy, percutaneous catheter drainage (PCD) placement, and endoscopic drainage (cystenterostomy) or debridement (direct endoscopic necrosectomy). Patients were followed for ≥9 months in regards to need for intervention.

Statistical analysis

The analysis of the present study compared the management, and clinical course of patients with isolated PPN vs. those with PN (with or without concomitant PPN). A separate analysis was performed comparing 3 groups of patients: those with isolated PPN, isolated PN and those that developed both PPN and PN. No statistical significant difference in either the management or the outcomes of isolated PN versus PN+PPN was found (data not shown). Therefore, it appears that the presence of PN determines outcomes independently of concomitant PNN or not. Thus, we decided to group patients with isolated PN and those with PN+PPN together.

Continuous data were evaluated for normality by the Kolmogorov-Smirnov test and were summarized using mean and standard deviation (SD) or median and interquartile range (IQR) depending on the variable distribution. Differences between two groups with continuous data were assessed utilizing student-t test for normal and Mann-Whitney for non-normal distributions; for differences among three groups, data were tested by one-way analysis of variance (ANOVA) and Kruskal-Wallis (non-parametric ANOVA) tests. Discrete data were described using percentages and compared by the chi-square or chi-square trend test depending on the number of groups. A two-sided p-value of less than 0.05 was considered statistically significant.

Results

Study Cohort and Patient Demographics

A total of 400 patients with AP were prospectively enrolled into the SAPS/PROOF study until May of 2014. Of those, 271 patients (68%) underwent at least one CECT while hospitalized. Median time of 1st CECT was day 3 (IQR 1,9). Follow up CECT was

performed in 172 patients (63%) at a median of 37 days (22, 80) from admission. Based on the CECT scan findings, 118/271 patients (43%) were classified as having interstitial pancreatitis, 29/271 (11%) as PPN and 124/271 (46%) had evidence of PN (Figure 2). Ninety seven (78%) out of 124 patients with PN had also concomitant peripancreatic necrosis.

During the initial review, 35 potential cases of PPN were identified: radiologic confidence was strong in 15, moderate in 9 patients, and poor in 11 patients. Upon second review of the poorly confident cases, the diagnosis of PPN was ruled out in 6 and the remaining 5 were reassigned as moderately confident.

Patients with PPN were predominantly male (n=16; 55%) with mean age of 56 years (SD ±19). Median body mass index (BMI) was 29 kg/m^2 (IQR 24, 33). Biliary was the most common AP etiology, identified in 10 patients (35%). Twenty patients (69%) were transferred from outside facilities to our tertiary institution for advanced management. Sixteen patients (57%) had Systemic Inflammatory Response Syndrome (SIRS) on admission. The median Blood Urea Nitrogen (BUN) on admission was 10 mg/dL (5, 35). No statistically significant difference was noted in demographics and clinical characteristics of patients with PPN compared to those with PN (Table 2).

Morphologic Characteristics of Peripancreatic and Pancreatic Necrosis

PPN involved the transverse mesocolon in 21/29 patients (72%), anterior and/or posterior pararenal spaces in 21, gastrosplenic ligament in 21, root of mesentery in 19 (66%), and hepatoduodenal and/or gastrohepatic ligament in 15 patients (52%). Fifty % of the PPN patients (n=14) were stratified as having limited and 15 as extensive necrosis. In respect to PN, minimal parenchymal necrosis (<30%) was seen in 40 patients (32%), 30-50% in 16 (13%), and >50% of the gland was involved in 68 (55%).

PPN evolved to walled-off necrotic collections in 10/29 patients (34%). This rate was significantly lower when compared to PN (70/124, 56%; p=0.05). The median size of walled-off necrosis among PPN patients was 8 cm (5, 11) and did not differ significantly from PN [10 cm (6, 15); p=0.4]. All of the patients with PPN that evolved into walled-off necrosis had extensive PPN.

Occlusive thrombi involving the portosplenomesenteric system were captured in 1/29 (3%) of patients with PPN, compared to 28/124 (23%) of those with necrosis of the gland (p=0.02). Splenic was the most frequently occluded vein (n=24, 83%). Pseudoaneurysms were a rare radiologic finding in our cohort (n=3, 2%; one with IPN).

Radiologic signs attesting to inflammation of other abdominal organs were evident in 13/29 (45%) patients with PPN and 49/124 (40%) with PN (p=0.8). The organ most commonly affected in both PPN and PN groups was the stomach (69% and 55%), followed by duodenum (21% and 18%, respectively).

Management of Peripancreatic and Pancreatic Necrosis

Nutritional support was provided to 18/29 (62%) patients with PPN and 97/124 (78%) with PN (p=0.12) (Table 3). Prophylactic antibiotics were administered less frequently to patients with PPN (n=6, 21%) than those with PN (n=56, 45%; p=0.03).

In regards to need for intervention, only 2 out of 29 (7%) patients with PPN required drainage or debridement. This rate was significantly less frequent compared to PN (n=66, 53%; p<0.001). Early intervention was performed within the first 2 weeks of disease course in 11 patients (laparotomy in 9 and PCD in 2), all of which had extensive parenchymal necrosis. The indications for early intervention in these patients included abdominal compartment syndrome in 9 of them (82%) and bowel ischemia in 2 (18%). The two PPN patients and 55 (44%) with PN underwent a delayed intervention at a median of 64 (62, 66) and 53 days (28, 76) respectively (p=0.6).

Clinical Outcomes of patients with Peripancreatic and Pancreatic Necrosis

Organ failure preceded the diagnosis of PPN in 11 out of 29 patients (38%) and persisted more than 48 hours in 10 patients (34%). Five patients developed multisystem organ failure. Organ failure rates were similar between PPN and PN patients (Table 3).

Only one patient with PPN was diagnosed with pancreatic infection (n=1, 3%). The rate of infection was significantly lower when compared to PN; (n=29, 23%; p=0.01). The median length of stay for PPN patients was 15 (6, 24) days. Length of hospitalization was shorter compared to PN [20 (10, 37) days; p=0.05]. Three patients in the PPN group succumbed to their illness. Mortality rates were similar between PPN (3%) and PN groups (8%; p=0.7). All deaths occurred as a result of overwhelming multi-system organ failure.

Need for Intervention and Clinical Outcomes based on extent of Necrosis

In a post-hoc analysis, peri-/pancreatic necrosis was stratified into subcategories based on extent of involvement and management and clinical outcomes were compared (Table 4).

Nutritional support was utilized in 6/14 (43%) patients with limited and 12/15 (80%) with extensive PPN. Additionally, nutritional support was required in 58% of patients with <30% PN, 69% with 30-50%, and 93% when >50% of the gland was involved (trend p<0.001).

The need for early laparotomy or delayed/drainage debridement increased proportionally with extent of necrosis (Table 4). More specifically in the PPN group, no intervention was required for limited involvement, while 13% (n=2) of patients with extensive PPN required an intervention. In the PN group, 18% (n=7) of patients with <30%, 50% (n=8) with 30-50%, and 75% (n=51) of those with >50% of gland involvement required drainage/ debridement (trend p<0.001).

Persistent organ failure rate in the PPN group preceded in 7% of patients with limited and 60% of those with extensive necrosis (p=0.005). In the PN group, persistent organ failure was seen in 18% of patients (n=7) with <30%, 50% (n=8) with 30-50%, and 75% (n=51) of those with >50% of parenchymal involvement (trend p<0.001).

In respect to length of hospital stay, patients with limited PPN stayed for 6 days (5, 17) and those with extensive PPN for 18 days (15, 26; p=0.02). In the PN group, the length of hospitalization was 13 (7, 22), 14 (6, 19), and 32 days (19, 53) in the 3 severity groups, respectively (trend p<0.001). Of importance, patients with limited PPN had similar rates of organ failure and length of hospitalization compared to those with interstitial AP (p≥0.12).

One patient with limited PPN (7%), 2 with extensive PPN (13%), and 10 patients with >50% PN passed away during hospitalization. No deaths were captured in patients with <30% and 30-50% PN.

Discussion

To our knowledge, this is the first U.S. study to thoroughly evaluate PPN in a prospective cohort of AP patients. Demographics, management, and clinical outcomes were compared between patients with PPN and PN, as well as between subcategories based on the extent of involvement. We found that PPN is infrequent and rarely requires an intervention. Furthermore, the clinical course of limited PPN is similar to that of interstitial pancreatitis, whereas extensive PPN resembles PN.

This is the first study from our research group focusing on PPN. Previous reports derived from the same prospective cohort of patients have studied “pancreatic necrosis” as an outcome without differentiating PPN from the rest of necrotizing pancreatitis.[10, 15, 16] In the current study, presence of occlusive thrombi is reported, which complements our previous report on occlusive thrombosis and narrowing of portosplenomesenteric veins in patients with extensive “pancreatic necrosis”.[16]

PPN was first described as a separate entity of necrotizing pancreatitis in 1989 by Howard and Wagner.[17] Ten years later Sakorafas et al. described a favorable clinical course of patients with PPN versus PN.[18] The last decade, PPN has been an area of increasing research and clinical interest. Recently, the Revised Atlanta Classification of AP severity included PPN as a distinct criterion of moderately severe disease.[4] Furthermore, a large prospective study by Bakker et al. showed that patients with PPN require less interventions and have lower rates of organ failure, infected necrosis, and mortality when compared to PN.[12] Our study is in line with these findings showing a significant difference in the need for intervention, infected necrosis development, and length of hospitalization between PPN and PN.

In contrast, the present study reports a significant lower rate of PPN compared to PN (ratio 1:4). Bakker et al. showed a higher ratio between PPN and PN of 1:1,[19] and a group from Spain reported a ratio of almost 2:1.[11] The different PPN/PN ratios between these studies likely reflect variations in defining PPN by radiologists rather than “true” institutional variations of PPN prevalence. The RAC refers to PPN as “heterogeneous collections with areas of fat surrounded by fluid density and areas with a slightly greater attenuation than seen in collections without necrosis”. In the present study, a stricter definition of PPN was used as described in Table 1. Furthermore, the level of confidence in diagnosing PPN was recorded and “poorly confident” cases were reviewed a second time by our radiologists for

final consensus. In addition, multiple CECT scans per patient were reviewed, which clarified the diagnosis for cases with inconclusive findings in the initial imaging. Additional studies comparing different radiologic definitions of PPN are required to clarify which approach should be adopted in clinical practice.

The findings of the present study can be implemented in clinical practice as follows: Evidence of PPN in AP patients who survive organ failure during the early phase of disease, suggest that the likelihood of delayed drainage/debridement is small. Such patients will require prolonged nutritional support, but PPN tends to improve with conservative management. In contrast, more than half of patients with parenchymal necrosis on CECT scan will remain symptomatic despite nutritional support and eventually undergo pancreatic intervention.

Studies trying to quantify the extent of PPN are scarce. In the present study, we classified PPN based on its size and extrapancreatic sites involved utilizing conventional CECT reading. This approach is readily applicable to daily practice. A recent work by Meyrignac et al. aimed to measure the volume of PPN using software for imaging segmentation. The authors reported that a volume of PPN ≥100ml is associated with organ failure, infection, prolonged hospitalization, mortality, and need for intervention.[20] Such promising approaches may become accessible in the near future with the fast evolution of technology.

In the present study, half of patients with PPN were stratified as having limited and the other half as extensive involvement. In the limited PPN group, none of the patients required drainage/debridement and the rate of persistent organ failure and length of stay were similar to interstitial pancreatitis. These findings suggest that limited PPN has no or minimal impact on AP morbidity and mortality. On the other hand, extensive PPN was commonly associated with persistent organ failure, prolonged hospitalization, but rarely required pancreatic intervention.

Persistent organ failure usually develops within the first days of AP onset following SIRS. It consists the main determinant of severe disease during the early phase. Based on our findings, persistent organ failure is associated with the development of extensive PPN/PN, which suggests that extensive necrosis is part of a systemic inflammatory syndrome. On the other hand, limited PPN/PN is likely a local process reflecting the magnitude of pancreatic injury.

The present study has several strengths. The prospective and continuous nature of patient enrollment eliminates selection bias. All patients were thoroughly phenotyped following the RAC severity definitions. Two expert abdominal radiologists blinded to the patients' clinical outcomes reviewed available CECT scans. A diagnostic confidence level for PPN was recorded using a 3-point scale and cases initially classified as "poorly confident" were reevaluated to reach a final consensus. Finally, additional analysis was performed between patients with PPN after classifying them into two subcategories based on PPN extent.

This study has potential limitations. Firstly, our institution is a referral center that treats "sicker" patients with higher rates of organ failure than reported in the literature. Therefore, the results of this study may not be representative of a community healthcare setting.

Second, the definitions of AP severity and local complications were recently refined in RAC. Therefore, in the earlier phase of the study, clinicians could have been unaware of the entity of PPN while managing many of the enrolled patients. Third, the definition of limited and extensive PPN used was arbitrary, mainly based on the opinion of our expert radiologists. Additionally, the median time that a CT scan was performed in our study was the day 3 from admission; thus, PPN could have been missed in those patients with early imaging who did not undergo follow-up scan. Another potential limitation is that CT scan may under-diagnose PPN and in some cases ultrasonography or MRI might have been more sensitive in detecting necrotic components in peripancreatic collections. Finally, CECT scans were performed at the discretion of treating physicians. Thus, a small number of local complications could have been overlooked in patients who did not undergo CECT scans.

In conclusion, PPN was less common and rarely required drainage/debridement compared to PN in the present study. Limited PPN had a benign clinical course similar to interstitial pancreatitis. Extensive PPN, on the other hand, was frequently associated with organ failure and a prolonged clinical course. Growing experience with RAC terminology by radiologists will improve interdisciplinary communication among physicians and standardize documentation of local complications among institutions. Adding the extent of involvement has the potential to sub classify PPN/PN into grades of escalating clinical significance and guide management decisions.

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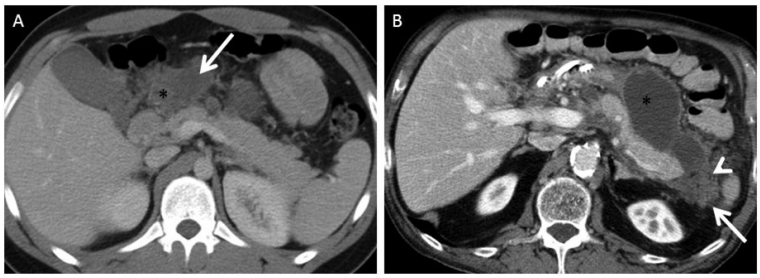

Figure 1.

A. Limited isolated peripancreatic necrosis (heterogeneous collection with high attenuation [*] and low attenuation [arrow] areas) anterior to pancreatic neck and body measuring 4 cm. Pancreatic parenchyma enhances normally. B. Extensive isolated peripancreatic necrosis around the normally enhancing pancreatic body and tail extending into the left anterior pararenal space (arrow). The heterogenous 11 cm collection has low (*) and high (arrow head) attenuating areas. Pancreatic parenchyma enhances normally.

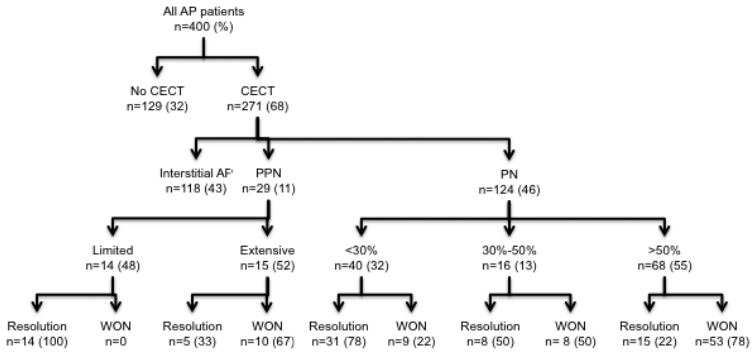

Figure 2. Contrast enhanced CT scan findings in our cohort of 400 AP patients

AP: acute pancreatitis; CECT: contrast-enhanced computerized tomography; PPN: isolated peripancreatic necrosis; PN: pancreatic necrosis; WON: walled-off necrosis

Table 1

Definitions of imaging findings derived by the Revised Atlanta Classification

Edematous pancreatitis	Localized or diffuse enlargement of the pancreas, with normal homogeneous enhancement or slightly heterogeneous enhancement of the pancreatic parenchyma related to edema
Peripancreatic stranding	Inflammatory changes within the peripancreatic tissue, which appears as “mistiness”, visualized as subtle and ill-defined increase in attenuation (stranding, hardening) of the peripancreatic fat
Pancreatic necrosis	Devitalized pancreatic tissue, which appears as an area of parenchymal non-enhancement with or without additional peripancreatic necrosis. The extent of pancreatic necrosis is recorded as percentage of pancreatic parenchyma affected: 1 <30%; 2 30-50%; 3 >50%
Isolated peripancreatic necrosis *	Heterogeneous areas of non-enhancement that contain *non-liquefied* components, visualized as ill-defined, nodular areas of increased peripancreatic fat attenuation with visual density higher than simple fluid and much higher than simple stranding or peripancreatic necrotic fluid collection, in the absence of pancreatic necrosis. Confidence level in diagnosing peripancreatic necrosis was recorded using a 3-point scale: 1 poorly confident or unsure; 2 moderately confident; 3 strongly confident
Pancreatic / Peripancreatic fluid or fluid collections (PFC)	Fluid or fluid collections located within the pancreas or around the pancreas. The definition of the fluid collection is according to Revised Atlanta Classification: acute pancreatic fluid collection; acute necrotic collection; Pseudocyst; walled-off necrosis
Thrombus	Venous filling defect partially or completely occluding the vein
Pseudoaneurysm	Focal aneurysmal arterial dilatation
Inflammation of adjacent organs	Present when the inflammation extends to the adjacent organ causing wall thickness (stomach, duodenum, jejunum, colon); kidney involvement is considered present when the inflammation extends into the perinephric space

* For isolated peripancreatic necrosis, a detailed definition was followed complementing the RAC terminology based on radiologist expertise.

Table 2

Demographics and clinical characteristics of patients with peri-/pancreatic

	PPN n=29	PN n=124	p-value
Age, mean in years (SD)	56 (19)	50 (16)	0.2
Gender, male (%)	16 (55)	82 (66)	0.4
BMI, median in kg/m^2 (IQR)	29 (24, 33)	29 (26, 34)	0.7
Transfers (%)	20 (69)	93 (75)	0.7
Sentinel AP (%)	21 (72)	82 (66)	0.7
Etiology:			
• Biliary (%)	10 (35)	45 (36)	0.97
• Alcoholic (%)	1 (3)	29 (24)	0.02
• Other (%)	18 (62)	50 (30)	0.06
Positive SIRS admission (%)	16/28 (57)	61/112 (54)	0.97
Positive SIRS 48 hrs (%)	14/26 (54)	66/106 (62)	0.6
BUN admission, median in mg/dL (IQR)	13 (9, 24)	16 (11, 21)	0.3
BUN 48 hrs, median in mg/dL (IQR)	10 (5, 35)	15 (8, 39)	0.07

p-values represent comparisons between PPN and PN groups.

AP: acute pancreatitis; PPN: isolated peripancreatic necrosis; PN: pancreatic necrosis; SD: standard deviation; IQR: interquartile range; BMI: body mass index; SIRS: systemic inflammatory response syndrome; BUN: blood urea nitrogen

Table 3

Management and clinical outcomes of patients with peri-/pancreatic necrosis

	PPN n=29	PN n=124	p-value
Nutritional support (%)	18 (62)	97 (78)	0.12
Prophylactic Carbapenems (%)	6 (21)	56 (45)	0.03
Intervention (%)	2 (7)	66 (53)	<0.001
Early (wthin 2 weeks;%)	0	11 (9)	
Delayed drainage/debridement (%)	2 (7)	55 (44)	<0.001
Time of delayed drainage/debridement, median days (IQR)	64 (62, 66)	53 (28, 76)	0.6
Organ failure (%)	11 (38)	66 (53)	0.2
Persistent organ failure (%)	10 (34)	63 (51)	0.17
Multi-system organ failure (%)	5 (17)	39 (31)	0.17
Infected necrosis (%)	1 (3)	29 (23)	0.01
ICU need (%)	11 (38)	71 (57)	0.09
Hospital LOS, median (IQR)	15 (6, 24)	20 (10, 37)	0.05
Mortality (%)	3 (10)	10 (8)	0.7

p-values represent comparisons between PPN and PN groups.

AP: acute pancreatitis; PPN: isolated peripancreatic necrosis; PN: pancreatic necrosis; IQR: interquartile range; ICU: intensive care unit; LOS: length of stay

Table 4

Clinical outcomes of patients with peri-/pancreatic necrosis stratified based on the extend

	Limited PPN n=14	**Extensive PPN n=15**	**PN <30% n=40**	**PN 30-50% n=16**	**PN >50% n=68**	**p-values: w/x/y/z**	**Trend p-value**
Nutritional Support (%)	6 (43)	12 (80)	23 (58)	11 (69)	63 (93)	0.06/0.2/ 0.55/0.02	<0.001
Need for intervention (%)	0	2 (13)	7 (18)	8 (50)	51 (75)	NA/1/ 0.02/0.07	<0.001
Persistent organ failure (%)	1 (7)	9 (60)	7 (18)	8 (50)	51 (75)	0.005/ 0.006/0.02 /0.07	<0.001
Hospital LOS, median days (IQR)	6 (5, 17)	18 (15, 26)	13 (7, 22)	14 (6, 19)	32 (19, 53)	0.02/0.047 /0.74/ <0.001	<0.001
Mortality (%)	1 (7)	2 (13)	0	0	10 (15)	1/NA/NA/ NA	0.8

w: p-value that resulted from comparison of limited PPN to extensive PPN

x: p-value that resulted from comparison of extensive PPN to PN<30%

y: p-value that resulted from comparison of PN<30% to PN 30-50%

z: p-value that resulted from comparison of PN 30-50% to PN>50%

Trend p-values represent trend test comparisons between the 5 necrotizing AP groups.

AP: acute pancreatitis; PPN: isolated peripancreatic necrosis; PN: pancreatic necrosis; IQR: interquartile range; LOS: length of stay