Predictive Value of Computed Tomography Scans and Clinical Findings for the Need of Endoscopic Necrosectomy in Walled-off Necrosis From Pancreatitis

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Objectives: Choosing the best treatment option at the optimal point of time for patients with walled-off necrosis (WON) is crucial. We aimed to identify imaging parameters and clinical findings predicting the need of necrosectomy in patients with WON.

Methods: All patients with endoscopically diagnosed WON and pseudocyst were retrospectively identified. Post hoc analysis of pre-interventional contrast-enhanced computed tomography was performed for factors predicting the need of necrosectomy.

Results: Sixty-five patients were included in this study. Forty patients (61.5%) were diagnosed with pseudocyst and 25 patients (38.5%) with WON. Patients with WON mostly had acute pancreatitis with biliary cause compared with more chronic pancreatitis and toxic cause in pseudocyst group ($P = 0.002$ and $P = 0.004$, respectively). Logistic regression revealed diabetes as a risk factor for WON. Computed tomography scans revealed 4.62% (n = 3) patients as false positive and 24.6% (n = 16) as false negative findings for WON. Reduced perfusion and detection of solid findings were independent risk factors for WON.

Conclusions: Computed tomography scans are of low diagnostic yield when needed to predict treatment of patients with pancreatic cysts. Reduced pancreatic perfusion and solid findings seem to be a risk factor for WON, whereas patients with diabetes seem to be at higher risk of developing WON.

Key Words: endoscopic-retrograde cholangio-pancreatography, endoscopy, pancreatitis, pancreatic cysts, walled-off necrosis, pseudocysts, necrosectomy

Abbreviations: AP - acute pancreatitis, ANP - acute necrotizing pancreatitis, CI - confidence interval, ceCT - contrast-enhanced computed tomography, COPD - chronic obstructive pulmonary disease, ERCP - endoscopic retrograde cholangiopancreatography, HU - Hounsfield units, OR - odds ratio, WON - walled-off necrosis

(*Pancreas* 2017;46: 1039–1045)

Acute pancreatitis (AP) is an inflammatory process that may lead to severe complications including pancreatic necrosis (acute necrotizing pancreatitis, ANP) in approximately 5% to 10% of the patients.[1–4] Most frequently, AP is caused by gallstones or alcohol consumption in Western countries.

Acute necrotizing pancreatitis is a dynamic disease with overlapping phases, that is, early and late ANP, both coming along with their own peaks of mortality.[4–6] The course of the disease frequently includes the manifestation of peri-pancreatic fluid collections that might become infected. These are defined as 4 different types according to the revised Atlanta classification[4]: (1) acute peri-pancreatic fluid collection; (2) pancreatic pseudocyst, occurring about at least 4 weeks after the onset of AP; (3) acute necrotic collection, occurring early; and (4) the so-called *walled-off necrosis* (WON), characterized by a solid capsule and solid debris inside, again occurring rarely before 4 weeks after ANP onset. Several suggestions for the nomenclature were made during the last several years (organized pancreatic necrosis[7] or pseudocyst associated with necrosis[8]); however, Connor et al[9] suggested the term *walled-off necrosis* in 2005 and was later established during Digestive Disease Week by Peter Banks. Walled-off necrosis is a rare disease arising in 1% to 9% of all patients with AP, but if not treated early and with the right measures, lethality is high (10%–30%).[10–12]

Computed tomography (CT) is the imaging modality of choice for pancreatitis for the past decades.[13–16]

The finding of necrosis is defined by non-enhancement of pancreatic tissue in contrast-enhanced CT (ceCT), and a definable, irregular wall along with fat attenuation and solid debris distinguishes a pseudocyst from WON.[17,18] However, mostly liquefied encapsulated collections after AP are mostly referred to as pseudocysts rather than WON in radiologic imaging because radiologic criteria often are misleading. Even the Atlanta criteria suggest the use of more radiologic modalities like magnetic resonance imaging (MRI), ultrasonography, or endosonography to differentiate between pseudocysts and WON.

For the clinic, it is of absolute importance to distinguish early on by radiology between pseudocyst and WON because the following treatment differs completely. In the past, surgery including radical approaches like complete pancreatectomy was the therapy of choice for ANP. However, the surgical approaches decreased dramatically owing to the high morbidity (50%–60%) and mortality (20%) in these patients.[19,20]

Clinical decision-making is mainly based on the gold standard of ceCT and the finding of necrosis for the choice of a conservative approach via an interventional like surgery or endoscopic treatment.

The aim of this study was 2-fold, to characterize CT findings in a cohort of patients with endoscopy secured diagnosis of pseudocysts or WONs and to find risk factors for developing WON both by a post hoc analysis of patients' data and radiologic findings. The main question we wanted to answer was whether ceCT scans according to suggested diagnosis definitions by the Atlanta criteria give us enough information for the right treatment decision.

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Received for publication October 14, 2016; accepted June 8, 2017.

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The authors declare no conflict of interest.

DOI: 10.1097/MPA.0000000000000881

MATERIALS AND METHODS

Selection of Patients

By a systematic query of the University Hospital Frankfurt clinical database, all patients with the *International Statistical Classification of Diseases*, *10th Revision*, diagnosis code K86.2 and K86.3 (pancreatic cysts or pseudocyst) and/or OPS 5-529 (surgical procedures of the pancreas) and/or text entries of "pancreatic cyst, pancreatic pseudocyst, necrosectomy, pancreas necrosis" at our hospital between January 2008 and July 2015 were identified. The study was performed in accordance with the 1975 Declaration of Helsinki. The study was approved by the ethical committee of the Frankfurt University Hospital (protocol number 274/15).

After identifying 197 patients, we had to exclude 132 patients because they were either not above 18 years of age, diagnosis of AP was too early without any developed cysts, no CT scan was done within 30 days before endoscopy, the data set was not complete, or they did not undergo endoscopic intervention. We were able to include 65 patients in this study for final evaluation.

Collected data from medical records included patient characteristics (age, sex, clinical symptoms on admission, comorbidities), imaging analysis, indication of endoscopic retrograde cholangiopancreatography and diagnosis after the procedure, sedation protocols, immediate complications and complications during follow-up, and the success and feasibility of the procedure. We used the following definitions of adverse events as used before in the literature. Perforation was defined as retroperitoneal or bowel-wall perforation identified during the procedure macroscopically or by radiological imaging after the procedure. Relevant bleeding events were defined as a decrease of hemoglobin of at least 2 g/dL after the procedure or immediate bleeding during endoscopy requiring an intervention, such as, for example, epinephrin injection. Pain was defined as the need for administration of pain relievers. Stent dislocation was defined as migration of stents more than 50% into the cyst itself or back into the lumen or nonfunctioning of the stent, respectively. Chronic comorbidities were classified as diabetes mellitus, arterial hypertension, coronary heart disease, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), and chronic renal insufficiency.

Endoscopy

All patients were diagnosed with pancreatic pseudocyst or WON and underwent endoscopic therapy. Reason for endoscopic drainage included persisting pain, intestinal compression by the cyst or WON, and/or signs of infectious disease. Treatment approach was mostly via transmural puncture of the cyst guided by endosonography. The cyst was entered with a cystostome, and after inserting guidewires, at least 2 pigtail stents (7 to 10 Fr) were placed to allow internal drainage. If pancreatic necrosis was suspected (eg, encountering solid/necrotic material), balloon dilation and placement of a metal stent or multiple plastic stents were administered. At a second treatment session, at least 2 days later, the cavity was entered by the endoscope and solid debris was removed by snare, solid baskets, and grasping forceps. Treatment sessions were repeatedly done until complete or subtotal removal of necrotic debris. The final diagnosis was in all cases made by the endoscopist, and WON was defined by the clinician by solid debris requiring removal and pseudocysts by the lack of solid material and rapid resolution after stent insertion.

Endoscopic retrograde cholangiopancreatography was performed by experienced endoscopists with at least 1000 endoscopies performed. All procedures were performed with standard endoscopes (GF-UCT180, GIF T 160, TJF Q180V, TJF 160V Olympus endoscopes, Olympus, Tokyo, Japan) with a working channel of 3.7 mm or 4.2 mm, respectively.

If percutaneous, image-guided, fine needle aspiration or endoscopic biopsy was positive for bacteria and/or fungi on Gram stain and culture infected cyst was diagnosed, antibiotics were administered.

CT Scan Evaluation

All patients underwent ceCT scans of the abdomen up to a maximum of 30 before endoscopy. All CT scans underwent post hoc analysis by a specialized radiologist who was blinded for the final diagnosis. As there is no consensus of solid material findings, we set the generally accepted cut-off of 30 Hounsfield units (HU). Slide thickness was 5 mm.

The finding of extraluminal gas in the pancreatic and/or peripancreatic tissues on ceCT was an indicator for infection or ongoing necrosis. Finding of any solid material plus defined wall identified WON in the CT scan according to Atlanta criteria. Contrast enhancement of the pancreas was measured and differentiated into 4 groups (<25%, 25%–50%, 50%–75%, and >75%) to measure necrotic area.

Definitions of Pancreatic Cysts

Two gastroenterologists retrospectively determined the final diagnosis based on the clinical course and endoscopic findings. Diagnosis was made according to the revised Atlanta classification criteria[4] as described below. Diagnosis of pancreatic pseudocyst was made if there was an encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas with minimal or no necrosis. Computed tomography criteria as given by Atlanta criteria include a well circumscribed, usually round or oval cyst with homogeneous fluid density and no nonliquid component. If any microbes inside the cyst were detected, diagnosis of infected pancreatic cyst was made. Diagnosis of WON was made in case of a mature, encapsulated collection of pancreatic and/or peri-pancreatic necrosis that has developed a well-defined inflammatory wall. Usually occurring more than 4 weeks after onset of necrotizing pancreatitis, ceCT criteria as given by Atlanta criteria included a heterogeneous cyst with liquid and, most importantly, nonliquid density with varying degrees of locations.

Statistical Analysis

This study was designed as a retrospective cohort study. Continuous variables are shown as median (range), and categorical variables are reported as frequencies and percentages.

Differences between different patient cohorts were determined using the Fisher's exact test or Fisher-Freeman-Halton exact test for categorical variables; for quantitative variables, we used the Mann-Whitney U test or Kruskal-Wallis test. Binary logistic regression was done for risk factor analysis. All tests were 2-sided, and P value of less than 0.05 was considered to be significant. Statistical analyses were performed with SPSS (Version 22.0, IBM, Armonk, NY).

RESULTS

Patient Characteristics

Sixty-five patients were included, 45 males (69.2%) and 20 females (30.8%). Follow-up had a median of 287 days (range, 3–2680 d). Final diagnosis of pseudocyst was made in 40 patients (61.5%), and WON was diagnosed in 25 patients (38.5%). Median age was 52 years (range, 18–81 y) in the whole cohort, and patients

in the WON group had a median age of 58 years (range, 18–78 y); however, this was not significant.

Comorbidities, namely, diabetes mellitus, arterial hypertension, coronary heart disease, cerebral vascular insufficiency, COPD, chronic renal insufficiency, or malignant neoplasia, and risk factors such as smoking, alcohol consumption, or immunosuppression showed significantly higher rates for diabetes (10% in pseudocyst group and 36% in the WON group, respectively, $P = 0.023$), arterial hypertension (37.5% vs 72%, $P = 0.01$), and smoking, which had a higher incidence in the pseudocyst group (37.5% vs 12%, $P = 0.044$). Type of pancreatitis differed as well in between both groups ($P = 0.002$), whereas AP was the main reason in the WON group in 92% (n = 23), in the pseudocyst group, only 52.5% (n = 21) were identified as AP patients. Rates of chronic pancreatitis were higher in the pseudocyst group with 35% (n = 14) versus 8% (n = 2) in the WON group. Reason for pancreatitis was significantly different as well, whereas, for 52% (n = 13) in the WON group, the cause was biliary (versus n = 7, 17.5% in the pseudocyst group), a toxic cause (n = 23, 57.5%) was higher in the pseudocyst cohort compared with WON (n = 7, 28%) ($P = 0.004$).

We could not identify a difference in symptoms at the time of first endoscopic approach. Whereas fever seemed to occur more often in the WON group (25%, n = 6 versus 10%, n = 4; $P = 0.165$), pain seemed to have a tendency for a higher rate in the pseudocyst group (75%, n = 30 versus 52%, n = 13; $P = 0.066$).

Basic laboratory representing inflammation markers (C-reactive protein, leucocytes, procalcitonin), kidney function (serum-creatinine),

TABLE 1. Patient Characteristics and Treatment Success

Parameter	All Patients	Pseudocysts	WON	*P*
Epidemiology				
Patients, n (%)	65	40 (61.5)	25 (38.5)	
Sex, male/female, n (%)	45 (69.2)/20 (30.8)	30 (75)/10 (25)	15 (60)/10 (40)	0.271
Age, median (range), y	52.0 (18–81)	50 (18–81)	58 (18–78)	0.241
Comorbidites, n (%)				
Diabetes	13 (20.0)	4 (10.0)	9 (36.0)	**0.023**
Arterial hypertension	33 (50.8)	15 (37.5)	18 (72.0)	**0.010**
Coronary artery disease	2 (3.1)	1 (2.5)	1 (4.0)	1.0
Stroke	3 (4.6)	1 (2.5)	2 (8.0)	0.554
COPD	7 (10.8)	4 (10.0)	3 (12.0)	1.0
Malignant neoplasm	5 (7.7)	4 (10.0)	1 (4.0)	1.0
Alcohol	12 (18.5)	10 (25.0)	2 (8.0)	0.109
Smoking	18 (27.7)	15 (37.5)	3 (12.0)	**0.044**
Immunosupression	2 (3.0)	2 (5.0)	0 (0)	1.0
Chronic kidney disease	3 (4.6)	1 (2.5)	2 (8.0)	0.554
Type of pancreatitis, n (%)				**0.002**
Acute	44 (67.7)	21 (52.5)	23 (92.0)	
Chronic	16 (24.6)	14 (35.0)	2 (8.0)	
Acute on chronic	5 (7.7)	5 (12.5)	0 (0)	
Cause of pancreatitis, n (%)				**0.004**
Biliary	20 (30.8)	7 (17.5)	13 (52.0)	
Toxic	30 (46.2)	23 (57.5)	7 (28.0)	
Others (dyslipidemia, post-ERCP, unknown)	15 (23.1)	10 (25.0)	5 (20.0)	
Symptoms, n (%)				
Fever	10 (15.4)	4 (10.0)	6 (24.0)	0.165
Pain	43 (66.2)	30 (75.0)	13 (52.0)	0.066
Duodenal compression	11 (16.9)	8 (20.0)	3 (12.0)	0.509
Biliary compression	3 (4.6)	2 (5.0)	1 (4.0)	1.0
Laboratory, median (range)				
CRP, mg/dL	8.52 (0.05–34.58)	7.48 (0.05–33.33)	9.89 (0.27–34.58)	0.537
Leukocytes, count/nL	10.58 (2.53–50.22)	11.03 (3.51–31.22)	10.13 (2.53–50.22)	0.962
S-creatinine, mg/dL	0.75 (0.2–4.66)	0.67 (0.2–4.66)	0.76 (0.31–1.67)	0.143
Procalcitonin, ng/mL	0.45 (0.1–21.3)	0.5 (0.11–21.30)	0.27 (0.1–9.1)	0.368
Total bilirubin, mg/dL	0.5 (0.1–9.3)	0.5 (0.1–2.5)	0.5 (0.2–9.3)	0.915
Successful therapy, n (%)	51 (78.5)	32 (80.0)	19 (76.0)	0.762
Dead, n (%)	9 (13.8)	5 (12.5)	4 (16.0)	0.724
Days of FU, median (range), d	287 (3–2680)	492.5 (3–2680)	171 (20–1115)	0.189
Days of hospital stay, median (range), d	32 (3–262)	29 (3–161)	45 (9–262)	**0.019**

All *P* values reported are 2-sided. Statistical significance was defined as *P* value less than or equal to 0.05. Significant findings are bold.

CRP indicates C-reactive protein; ERCP, endoscopic retrograde cholangiopancreatography.

and liver (total bilirubin) did not show any significant differences. Patient characteristics and comorbidities are specified in Table 1.

Endoscopic Therapy

Overall number of endoscopies had a median (range) of 4 (1–38), differing significantly with 4 (1–11) in the pseudocyst group and 8 (3–38) in the WON group ($P < 0.001$). The same accounted for the number of endoscopies with cyst interventions with 2 (1–7) in the pseudocyst group and 5 (2–31) in the WON group ($P < 0.001$). Median number of necrosectomies performed in the WON group was 5 (2–31). The endoscopic approach in both groups did not differ significantly with 75.4% (n = 49) of transgastric approaches in both groups. A small number of patients, 8 (23%), underwent at least 1 percutaneous approach. Complications rate during the initial endoscopy were low and increased during the course of treatment with bleeding (12.3%, 8 patients) and stent dislocation (38.5%, 22 patients) overall with no differences in the groups. Pathogens were identified in 47.5% (n = 19) of the pseudocyst patients, whereas 76% (n = 19) were positive in the WON group ($P = 0.038$). Endoscopic findings and complications are specified in Table 2.

Imaging

Only CT scans were investigated. Time from index CT to first endoscopy was a median of 3 days (range, 0–30 d) with no differences in both groups ($P = 0.537$). Extrapancreatic location was found in 8 patients (20%) in pseudocyst group and 7 patients (28%) in the WON group ($P = 0.549$). Ascites was found in 14 (35%) of pseudocyst patients and 10 (40%) of WON patients, respectively ($P = 0.793$). Maximum Hounsfield units (HU) were 13 (range, 5–111) in pseudocysts and 15 (7–42) in WON ($P = 0.318$). Solid material was found in 3 patients (7.5%) with pseudocysts and just 9 patients (36%) with WON ($P = 0.007$). Gas as a sign of infection was found in 1 patient (2.5%) with a pseudocyst and 4 patients (16%) with WON ($P = 0.068$). Perfusion in ceCT differed significantly with less perfused areas (<50%) in 6 patients with pseudocysts (15%) and 10 patients with WON (40%) ($P = 0.039$). Wall thickness in both groups had a median of 2 mm (range, 1–6) ($P = 1.0$). Detailed findings are shown in Table 3.

Risk Factors for Diagnosis of WON

We calculated a binary logistic regression for clinical and imaging parameters separately. For clinical parameters, we included smoking, diabetes, and arterial hypertension, type of pancreatitis, reason for pancreatitis, and diagnosis of pathogens in the cyst. The only significant factor correlating with WON was diabetes in this cohort odds ratio (OR) of 8.723 (confidence interval [CI], 1.360–56.090) ($P = 0.022$). Type of pancreatitis (acute, chronic, acute on chronic) and positive pathogen showed a trend towards being significant findings ($P = 0.073$ and $P = 0.059$, respectively).

For CT parameters, we included ascites, solid material, positive gas sign, and parenchymal perfusion less than 50% in the calculation. As significant factors parenchymal perfusion less than 50% and the finding of solid debris were found (OR, 3.968; 95% CI, 1.115–14.129; $P = 0.033$ and OR, 8.194; 95% CI, 1.714–39.185; $P = 0.008$, respectively), whereas all other factors did not correlate with the diagnosis of WON (Table 4).

Treatment Success

Therapy was successful in 51 (78.5%) of all patients, 32 (80%) and 19 (76%) in the pseudocyst and WON group, respectively ($P = 0.762$). In the whole cohort, 9 patients (13.8%) died. Five (12.5%) (2 patients with sepsis, 1 metastasizing disease, 1 owing to kidney failure, and 1 owing to an unknown cause) in the pseudocyst group and 4 (16%) (3 patients with sepsis and multi-organ failure and 1 patient of uncontrollable bleeding from the pancreas necrosis) in the WON group.

TABLE 2. Endoscopic Treatment and Complications

Parameter	All Patients	Pseudocyst	WON	*P*
Number of endoscopies, median (range)	4 (1–38)	4 (1–11)	8 (3–38)	**<0.001**
Number of endoscopies with cyst intervention, median (range)	2 (0–31)	2 (1–7)	5 (2–31)	**<0.001**
Number of necrosectomies, median (range)	0 (0–30)	0 (0)	2 (1–30)	**<0.001**
Type of drainage, n (%)				0.837
Transgastric	49 (75.4)	29 (72.5)	20 (80.0)	
Transduodenal	6 (9.2)	4 (10.0)	2 (8.0)	
Percuteanous	8 (12.3)	6 (15.0)	2 (8.0)	
Transpapillary	1 (1.5)	1 (2.5)	0 (0)	
Initial complications, n (%)				
Bleeding	4 (6.2)	2 (5.0)	2 (8.0)	0.635
Perforation	1 (1.5)	1 (2.5)	0 (0)	1.0
Air embolus	0 (0)	0 (0)	0 (0)	
Sedation related	2 (3.1)	1 (2.5)	1 (4.0)	1.0
Late complications, n (%)				
Bleeding	8 (12.3)	3 (7.5)	5 (20.0)	0.243
Perforation	3 (4.6)	2 (5.0)	1 (4.0)	1.0
Air embolus	1 (1.5)	0 (0)	1 (4.0)	0.385
Fistulation	8 (12.3)	4 (10.0)	4 (16.0)	0.700
Stent dislocation	22 (33.8)	12 (30.0)	10 (40.0)	0.432
Positive pathogens in the cyst, n (%)	38 (38.5)	19 (47.5)	19 (76.0)	**0.038**

All *P* values reported are 2-sided. Statistical significance was defined as *P* value less than 0.05. Significant findings are bold.

TABLE 3. Radiological Findings in ceCT Scans

Parameter	All Patients	Pseudocyst	WON	*P*
Days from CT to endoscopy, median (range), d	3 (0–30)	3.5 (0–30)	3 (0–25)	0.537
CT findings				
Extrapancreatic localization of fluid collection, n (%)	15 (23.1)	8 (20.0)	7 (28.0)	0.549
Ascites, n (%)	24 (36.9)	14 (35.0)	10 (40.0)	0.793
Maximal Hounsfield units, median (range), HU	15 (5–111)	13 (5–111)	15 (7–54)	0.139
Solid material, n (%)	5 (10.8)	3 (7.5)	9 (36.0)	**0.007**
Gas inclusion within the fluid collection, n (%)	5 (7.7)	1 (2.5)	4 (16.0)	0.068
Thickness of wall, median (range), mm	2 (1–6)	2 (1–6)	2 (1–4)	
Perfusion of pancreatic tissue, n (%)				0.156
<25	11 (16.9)	4 (10.0)	7 (28.0)	
25–50	5 (7.7)	2 (5.0)	3 (12.0)	
50–75	12 (18.5)	9 (22.5)	4 (16.0)	
>75	36 (55.4)	25 (62.5)	11 (44.0)	
Perfusion <50%, n (%)	16 (24.6)	6 (15.0)	10 (40.0)	**0.039**

All *P* values reported are 2-sided. Statistical significance was defined as *P* value less than 0.05. Significant findings are bold.

Length of hospital stay differed significantly with 29 days (range, 3–161) in the pseudocyst group and 45 (range, 9–262) in the WON group ($P = 0.019$) (Table 1).

DISCUSSION

Treatment decision for AP fluid collections is a clinical challenge. In the present study, we evaluated prediction of ceCT and clinical parameters in 65 patients, who underwent endoscopic treatment, thereby establishing the interventional golden standard of the diagnosis of pseudocyst versus WON.

It is of the highest importance to diagnose a pancreatic cyst as WON because the endoscopist might directly, after puncture of the cyst, insert stents for following necrosectomy, which yields the best results with lowest mortality to date.[21] The aim of treating WON is the complete removal of necrotic material and later solution of the cyst[22]; however, the treatment options have massively changed during the last several years. Back in 1985, Kozarek et al[23] introduced a transluminal endoscopic access to pancreatic pseudocysts as a treatment option in high-risk patients. One option of treating ANP and its complications is CT-guided puncture and drainage; however, this does not allow necrosectomy, and morbidity rates are around 40% with a success rate of 50% to 80%.[24] Therefore, the transgastric approach to the retroperitoneal cavity with the possibility of necrosectomy was established as the treatment of choice.[25,26] This approach secures the diagnosis, allows the endoscopist to start treatment immediately, and has high success rates up to 80% as in our cohort with quite low complication rates.

In blindly evaluating all CT scans that had been performed before patients underwent endoscopic treatment, we were able to identify a reduced perfusion of less than 50% of the pancreatic tissue and the finding of solid material as a predictor of necrosectomy required in the clinical course of the patient. In this cohort, 16 patients (24.6%) provided no sign of any solid necrotic material in the CT scan; nonetheless, the patient had to undergo transmural necrosectomy later on. In comparison, 3 patients (4.6%) were detected with solid material inside the cyst but did not need necrosectomy. Thirty-seven (56.9%) of the patients had no solid necrotic material detected and did not need necrosectomy, whereas 9 patients (13.8%) had solid findings and needed necrosectomy. In this cohort, this equals 4.6% (3 patients) which thereby were false positive and 24.6% (n = 16) false negative when just taking the finding of solid debris inside the cyst into account for the diagnosis of WON, which is by Atlanta criteria the main difference to pseudocysts.

In another study as well aiming at defining CT characteristics for WONs, solid debris was diagnosed in 43% of all WON patients and 25% of all pseudocyst patients, whereas gas inclusions were found in 12% of the WON patients and 5% of the pseudocyst patients, which is absolutely comparable with our findings[27]; however, there are huge variances in detection of solid debris in ceCT, for example, in another study in just 17.3% of patients.[28] Magnetic resonance imaging scans seem to be of much higher sensitivity compared with CT for detection of solid debris inside cysts as it was shown in an early small study in 1997[29] and some small following studies[30,31]; however, larger evaluations are still missing and MRI is still way less used for this indication. In Figure 1, we show examples of misleading findings in ceCT and the use of an MRI. Furthermore, an accompanying

TABLE 4. Logistic Regression Analysis for Clinical and Radiological Risk Factors Associated With Necrosectomy

Parameter	OR	95% CI	*P*
Clinical parameters			
Smoking	3.421	0.406–28.854	0.258
Diabetes	8.734	1.360–56.090	**0.022**
Arterial hypertension	1.911	0.501–7.292	0.343
Chronic pancreatitis	0.206	0.037–1.158	0.073
Biliary pancreatitis	2.615	0.487–14.024	0.262
Positive microbiology culture from cyst	3.931	0.949–16.278	0.059
CT parameters			
Ascites	1.596	0.489–5.205	0.439
Solid material	8.194	1.714–39.185	**0.008**
Gas positive	7.225	0.652–80.111	0.107
Extrapancreatic localization	1.120	0.301–4.170	0.866
Parenchymal perfusion <50%	3.968	1.115–14.129	**0.033**

All *P* values reported are 2-sided. Statistical significance was defined as *P* value less than 0.05. Significant findings are bold.

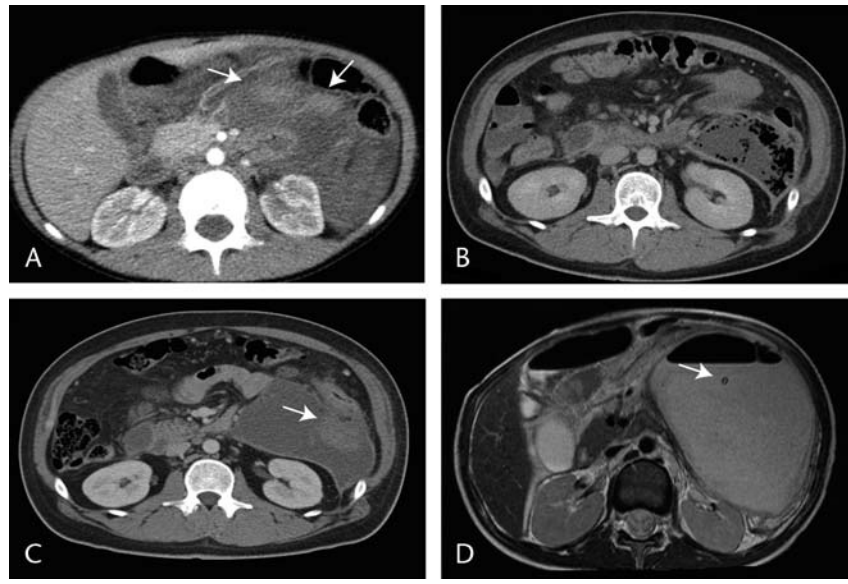

FIGURE 1. A and B show ceCT scans in a patient with AP 5 weeks before (A) with irregular cyst and probable solid debris (arrows) and (B) after the first necrosectomy and diagnosed WON, the solid material being huge necrosis. C and D show a ceCT scan (C) in a young patient after traumatic AP some weeks before again with irregular cyst and solid material (arrow); however, the same patient after T2-weighted MRI scan was done (D) after placement of a drainage shows no solid material. The patient was misdiagnosed as having WON. Treatment was successful after stent placement.

magnetic resonance cholangiopancreatography could be valuable for the detection of disconnected duct syndrome, because of a strong association of this finding and WON.[32,33] Nonetheless, MRI has lower availability, higher costs, and additional drawbacks in comparison with other image modalities that may limit its use as the imaging modality of choice.

The diagnosis of pancreatic pseudocyst as suggested by the Atlanta criteria is made by a definable wall without any solid material. The emergence of a solid wall is believed to derive from a disruption of the main pancreatic duct or branches without any recognizable pancreatic necrosis, thereby probably explaining the significant differences in contrast enhancement in CT scans comparing WON and pseudocyst reflecting the different extents of necrosis. In our cohort, significantly more patients in the WON group had a history of AP caused by biliary stones, whereas pseudocysts developed more in patients with chronic/acute on chronic pancreatitis caused by toxic agents (mainly alcohol). The development of a pseudocyst is a rare event during AP, probably explaining the significant finding of more patients with AP in the WON group. However, a "disconnected duct syndrome" during AP can form pseudocysts as well.[34]

Interestingly, when looking at clinical parameters, we found significantly more patients with diabetes and arterial hypertension in the WON group and less patients with smoking as a risk factor. In a logistic regression model, diabetes remains a significant risk factor for the onset of WON. A connection of diabetes and developing pancreatitis is well established in large cohorts; however, the reasons for that still remain speculative, for example, the accompaniment with other comorbidities (obesity, gallstones) or diabetes medication increasing the pancreatitis risk.[35,36] However, a connection between diabetes and the development of WON has not been described so far to our knowledge. Concerning clinical symptoms (fever, pain, duodenal compression with nausea/vomiting) or laboratory results, we could not identify any significant differences, which fits previous data, showing that WON can be asymptomatic in about 50%.[37,38]

In sum, ceCT scans can be of low diagnostic yield helping to decide whether or not necrosectomy will be necessary. Magnetic resonance imaging scans are not routinely recommended; however, for diagnosis of solid material inside the cysts, T2-weighted scans should be considered as suggested by Atlanta criteria and others,[4,38,39] especially if endoscopic treatment is planned (Fig. 1). Further prospective trials evaluating ceCT, MRI, and ultrasound for the prediction of the need of necrosectomy seem to be warranted. Furthermore, special attention should be paid to patients with history of AP owing to biliary cause and diabetes as comorbidity because these patients seem to be at higher risk for developing WON.

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