

Value of clinical criteria to indicate a CT-FNA in the diagnosis of infected acute pancreatitis

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SUMMARY Objective: To assess the value of clinical criteria in detecting pancreatic infection (PI) on or after the seventh day of acute pancreatitis attack (AP). **Methods:** We determined as clinical criteria of suspicion of PI (SPI): the presence, persistence or recurrence of fever $\geq 38^\circ\text{C}$, leukocytosis $\geq 12,000/\text{mm}^3$ and organ failure (OF) in the absence of extrapancreatic infection. Patients with SPI criteria underwent computed tomography - fine needle aspiration (CT-FNA), if CT-FNA was negative and SPI criteria for 72 hours CT-FNA was repeated. **Results:** We prospectively studied 369 patients with AP and found 48 patients who met SPI criteria (mean age 37 yr, 17-70 yr), 30 male and 18 female. Etiology was biliary (56.2%), alcohol (35.4%) and others (8.4%). We performed 53 CT-FNA in 48 patients and 28 were diagnosed with PI. At the time of CT-FNA 50% of patients had OF. Mean time for CT-FNA in patients with PI was 12.5 ± 7 days. Mean clinical follow-up after hospital discharge was one month. No patients with SPI criteria and negative CT-FNA or patients without SPI criteria developed clinical signs of PI. The SPI criteria had a sensitivity of 100%, specificity of 94% (CI 95% 92-97), PPV of 58% (IC 95% 44-72) and NPV of 100%. **Conclusions:** The application of SPI criteria on or after the seventh day of onset of AP can be a useful tool in making the decision and defining the time to perform a CT-FNA in order to clarify the clinical scenario between SIRS and sepsis related PI. Our approach can lead to better strategic treatments in the management of these difficult cases.

RESUMEN Objetivo: utilidad de criterios clínicos para indicar una punción guiada por tomografía axial computarizada (PG-TAC) para el diagnóstico de infección pancreática a partir del séptimo día de iniciado el evento de pancreatitis aguda. **Material y métodos:** los criterios clínicos de sospecha de infección pancreática (CSIP) fueron los siguientes: presencia, persistencia o recurrencia de fiebre ($\geq 38^\circ\text{C}$), leucocitosis $\geq 12,000$ y/o falla de órganos en ausencia de datos de infección extra-pancreática. Los pacientes con sospecha de infección pancreática fueron enviados a una PG-TAC y cuando era negativa y los CSIP persistían (> 72 horas) una nueva PG-TAC era indicada. **Resultados:** en forma prospectiva se estudiaron 369 pacientes con pancreatitis aguda y 48 pacientes presentaron CSIP (edad promedio 37 años, 17 a 70 años), 30 hombres y 18 mujeres. Etiología biliar (56%), alcohol (35.4%) y otras (8.4%). Se realizaron 53 PG-TAC en 48 pacientes y en 28 pacientes se diagnosticó infección pancreática. Al momento de la PG-TAC el 50% de los pacientes presentaban falla orgánica. El tiempo promedio del diagnóstico de infección pancreática fue de 12.5 ± 7 días. Ningún paciente con CSIP y PG-TAC negativa o pacientes sin CSIP desarrolló datos clínicos de infección pancreática durante el tiempo promedio de seguimiento después desde su egreso (un mes). Los CSIP tuvieron una sensibilidad de 100%, especificidad de 94% (IC 95% 92-97%), valor predictivo positivo de 58% (IC 95% 44-72) y valor predictivo negativo del 100%. **Conclusiones:** la aplicación de CSIP a partir del séptimo día de iniciado el cuadro clínico de la pancreatitis aguda puede ser una herramienta útil en la toma de decisiones y en definir el tiempo para indicar una PG-TAC tratando de diferenciar entre respuesta inflamatoria sistémica y sepsis relacionada a la infección pancreática.

Key words: *Pancreatic infection, clinical criteria, CT-FNA, acute pancreatitis.*

ca. Nuestro abordaje puede llevar a mejorar las estrategias de manejo en estos difíciles casos.

Palabras clave: *infección pancreática, criterios clínicos, punción guiada por tomografía axial computarizada, pancreatitis aguda.*

INTRODUCTION

Acute pancreatitis (AP) is self-limiting in most cases. About 25% of patients with AP may develop severe or life threatening complications. Infection of pancreatic necrosis is one of the most severe complications in AP. This is the major risk factor for sepsis - related multiple organ failure (OF) and mortality. The bacterial contamination of the necrotic pancreatic tissue has been detected in experimental models as early as several hours and one clinical study reported pancreatic bacterial contamination of 23.8% in the first seven days of the AP attack. Prevalence of PI ranges from 12% to 23% of cases and mortality rate increases to almost 40% when sterile pancreatic necrosis becomes infected.¹⁻⁴ Once PI is diagnosed, surgery becomes the gold standard treatment.^{5,6} Yet recently, the use of endoscopic and radiologic treatment for infected pancreatic necrosis has been reported.⁷⁻⁹

Different methods to make the diagnosis of infected pancreatic necrosis such as serum C reactive protein and procalcitonin have been used.^{3,10,11} Computerized tomography (CT) does not differentiate between pancreatic necrosis and PI and recently, the use of Gallium-67 single-photon emission computed tomography (SPECT) has shown some usefulness in detecting PI.¹² The non-surgical gold standard method to diagnose PI is by fine needle aspiration (FNA) guided by abdominal ultrasound or CT for bacterial testing of the pancreatic and peripancreatic tissue.^{13,14} The correlation of a positive CT-FNA and surgery for bacteriologic status is greater than 90% in patients with PI.

However, when to perform CT-FNA in AP patients still is a matter of debate. Recently, an European survey publication about management of severe AP demonstrates a wide variation in the medical care of these patients.¹⁵ Several clinical studies have shown that PI generally occurs after the second or third week of AP attack, although PI may be an early complication (first week).^{4,13,16} In most studies, the indication for FNA is in the presence of symptoms related to infection but these symptoms usually are similar to the symptoms of the systemic inflammatory response syndrome (SIRS). CT-FNA is a safe

procedure and the mean time to perform it is around 10 to 14 days after AP onset.^{17,18}

Different clinical criteria have been used in making the decision to indicate CT-FNA, but the time and frequency has not been clearly defined.^{15,19,20} In a retrospective study, the criteria of rectal temperature $> 38.5^{\circ}\text{C}$, base excess of $> 4\text{mmol/l}$ and hematocrit $< 35\%$ had a sensitivity of 83% to detect PI, but only 25% of patients with documented PI had the above mentioned criteria.²¹ The Bern's criteria for suspicion of infection are fever, leukocytosis, and new onset of OF but in this study the time to perform CT-FNA was not determined.²⁰ In light of the above and since clinical findings can not differentiate between SIRS and sepsis in severe AP in addition to trying to defined the best time to start to suspect PI,²² we used as clinical criteria for suspicion of pancreatic infection (SPI) the presence, recurrence or persistence of fever $\geq 38^{\circ}\text{C}$ for more than 48 hours, leukocytosis ($\geq 12,000\text{ mm}^3$) and OF as defined by the Atlanta criteria²³ applying these criteria on or after the seventh day of onset of AP attack. Any positive criteria were an indication to perform a CT-FNA.

PATIENTS AND METHODS

This study was prospectively conducted at the University Hospital "Dr. José E. González" from January 2000 to April 2003. We included all patients with diagnosis of AP directly admitted to our institution. The AP diagnosis was based on clinical symptoms and a 3-fold elevation of serum amylase and/or lipase levels or a compatible CT scan image.

On admission, all patients were treated medically with intravenous fluids, withholding oral intake and providing pain relief.

The AP severity was determined according to Ranson's score (mild and severe, < 3 points and ≥ 3 points, respectively). Antibiotic prophylaxis with a quinolone plus metronidazole or imipenem was provided in cases of severe AP or positive criteria for SPI. In patients with severe acute biliary pancreatitis and suspicion of stone impacted or cholangitis an endoscopic retrograde cholangiography with

biliary sphincterotomy was done. We applied the SPI criteria starting at the seventh day from the beginning of the first AP clinical symptom and after ruling out other potential sources of infection. CT-FNA was performed by a single radiologist, obtaining samples from pancreatic and/or peripancreatic inflammatory tissue, as well as fluid collections if present. Specimens were sent for Gram stain and cultures for aerobic/anaerobic and fungus microorganisms. In the case of negative results and persistent SPI criteria for more than 72 hours, a CT-FNA was repeated. PI was defined as a positive CT-FNA for bacterial or fungal stain and/or a positive culture. Once PI was established, surgical necrosectomy was recommended. At the time of surgery samples for bacterial culture were taken from the pancreatic and peripancreatic tissue or fluid collections.

We excluded patients with pancreatic abscess CT scan criteria.⁹ We also studied the following variables: age, gender, etiology, SPI criteria to indicate a CT-FNA, Ranson and Balthazar CT scores, time from AP onset to hospital admission and to CT-FNA indication, CT-FNA complications, Gram stain and culture results, length of hospital stay (LOS), time from diagnosis of PI to surgery and mortality.

The computer program SPSS software version 11.5 (SPSS Inc, Chicago IL) was used for statistical analysis. The categorical variables are expressed as a mean and standard deviation and range. The continuous variables

are expressed as percentages. The Student's t Test, Chi-square or Fisher exact test were used for comparisons. The significance level was set at a *p* value of < 0.05. Sensitivity, specificity, positive and negative predictive values for the SPI criteria is reported.

RESULTS

Demographic data

We prospectively studied 372 patients with AP. We excluded three patients, two of them due to the presence of pancreatic abscesses on CT scan, as both patients were submitted to surgery and the diagnosis of pancreatic abscess was confirmed and the other patient with SPI criteria died before CT-FNA could be performed. A total of 369 patients were included, 151 male and 218 female (41%/59%). Their mean age was 40.8 years (range: 15-96 years). The most frequent etiologies were biliary in 242 patients (65.6%), alcohol in 61 (16.5%), hypertriglyceridemia in 30 (8.1%) and idiopathic in 27 (7.3%). The mean time from AP onset to hospital admission was three days.

Severe AP defined by Ranson's score was diagnosed in 96 patients (26%) and mild in 273 patients (74%). Severe AP was present in 54% of patients with SPI criteria and in 22% of patients with no SPI criteria (*p* < 0.001).

We performed a total of 98 ERCPs, of which 73 were performed within 72 hours from onset of AP. Eleven

TABLE 1
OVERALL POPULATION DEMOGRAPHIC DATA

	Overall Group		With SPI criteria		Without SPI	
Patients	369		48		321	
Sex (M/F)	151/218		30/18		121/200	
Age (yrs)	40.8 ± 18.4 (15-96)		37.4 ± 13.7 (17-70)		42.9 ± 19.2 (15-96)	
Ranson score	1.6 ± 1.5 (0-7)		2.8 ± 1.7 (1-7)		1.5 ± 1.4 (0-7)	
Ranson 3 or more (severe)	96	(26%)	26	(54%)	70	(22%)
Ranson 0 to 2 (mild)	273	(74%)	22	(46%)	251	(78%)
Etiology						
Biliary	242	(65.6%)	27	(56.2%)	215	(67%)
Alcoholic	61	(16.5%)	17	(35.4%)	43	(13.4%)
Hypertriglyceridemia	30	(8.1%)	2	(4.1%)	28	(8.7%)
Idiopathic	27	(7.3%)	1	(2%)	27	(8.4%)
Post-ERCP	6	(1.6%)	1	(2%)	5	(1.5%)
Miscellaneous	3	(0.8%)	0		3	(0.9%)
LOS (days)	13 ± 15 (1-137)		38.3 ± 30 (8-137)		9.7 ± 7 (1-59)	
Deaths	19	(5.14%)	12	(25%)	7	(2.18%)

patients with SPI criteria had an ERCP and six patients developed pancreatic infection.

The overall length of hospital stay (LOS) was 13 ± 15 days. In the SPI criteria the LOS was greater than in the non-SPI (38 ± 30 and 9 ± 7 days, respectively) ($p < 0.001$). The overall mortality was 19/369 patients (5.1%). Higher mortality was found in the group with SPI criteria compared to the non-SPI criteria, 12/48 (25%) versus 7/321 (2%) ($p < 0.001$). *Table 1* summarizes the demographic data of the overall group.

PATIENTS WITH NO SPI CRITERIA

A total of 321 patients, 121 male and 200 female with a mean age of 42.9 ± 19.2 years (range 15-96 years), did

not meet criteria for SPI. Mild and severe AP was found in 251 (78%) and 70 patients (21%), respectively.

Twenty-four patients developed OF; single (18 patients) and multiple (6 patients). The most frequent were pulmonary and renal failure; however, all of these patients recovered before the seventh day from the onset of AP.

Extrapancreatic infections were detected in 18 patients (5.6%). Fifteen patients had cholangitis, one patient had pneumonia, and one had infectious colitis and another patient bacterial endocarditis. Seven patients died and their mean time to death was 10 ± 11 days (range 3-36 days) from the onset of AP. Four of them died between the third and sixth day due to multi-systemic OF and two patients developed sudden death secondary to pul-

TABLE 2
DEMOGRAPHIC DATA, RANSON AND BALTHAZAR SCORE AND RESULTS IN PATIENTS WITH SPI

	PI (n = 28)	No PI (n = 20)	P
Gender M/F	18/10	12/8	NS
Age	41.2 ± 12.2	32 ± 11.3	0.02
Etiology			
Biliary	16	11	
Alcoholic	8	9	
Hypertriglyceridemia	2	0	
Post-ERCP	1	0	
Idiopathic	1	0	
Ranson score	3.5 ± 1.5	2.1 ± 1.6	0.02
Balthazar			
A	0	0	
B	2	0	
C	4	7	
D	5	9	
E	17	4	0.02
Mortality	11 (39%)	1 (5%)	0.03

TABLE 3
INDICATIONS FOR CT-FNA

CT-FNA indication	N = 48	PI (n = 28)	No PI (n = 20)
Fever	8	3	5
Fever + leukocytosis	19	11	8
Fever + leukocytosis + OF	14	11	3
Leukocytosis + OF	1	1	0
Fever + OF	5	2	3
CD	1	0	1

monary embolism on days 10 and 14, respectively. Another patient died on day 36 due to complications of a surgical tracheostomy. Late complications were observed in nine patients: two pancreatic pseudocysts, two with residual choledocholithiasis, three with pneumonia and two patients with upper gastrointestinal hemorrhage secondary to peptic disease. No clinical evidence of PI was detected during a mean follow up of one month after hospital discharge.

PATIENTS WITH SPI CRITERIA

We found 48 (13%) patients, 30 male and 18 female, with one or multiple SPI criteria. The mean age was 37.4 years (range 17-70 years). Mild and severe AP was observed in 22/48 (46%) and 26/48 (54%) patients, respectively ($p = 0.56$).

Prophylactic antibiotic with quinolone plus metronidazole was used in 36 patients and 12 patients received imipenem. Antibiotic use was not longer than 14 days and the type and dose were adjusted depending on blood, CT-FNA or surgery culture results.

Table 2 summarizes the demographic data of patients with SPI criteria and PI.

Patients with PI were older than those without PI (41.2 ± 14.2 versus 32 ± 11.3 years, respectively; ($p = 0.02$) and had higher Ranson score (3.5 ± 1.5 versus 2.1 ± 1.6) ($p = 0.005$). The CT scan showed a C or higher Balthazar score in 46/48 patients (95.8%). Seventeen of 28 patients with PI had a Balthazar CT E score versus 4/20 patients without pancreatic infection ($p = 0.005$). Mortality rate was higher in infected than non-infected patients 11/28 (39%) versus 1/20 (5 %) ($p = 0.007$).

The SPI criteria were applied starting at the seventh day from the beginning of the first AP clinical symptom and any positive criteria was an indication for CT-FNA. Results of CT-FNA indications are shown in table 3.

Patients with fever, leukocytosis and OF had a higher probability of being infected (22/33 patients). One patient had poor clinical outcome after 12 days of medical treatment without criteria of SPI and a CT-FNA ruled out PI and he recovered but developed a pancreatic pseudocyst. We performed 53 CT-FNA in 48 patients, and no complications related to the procedure were detected. The mean time to perform the first CT-FNA was 10.7 ± 4.1 days (range 7-24 days).

Figure 1 summarizes the approach to patients according to the clinical scenario and CT-FNA results.

A diagnosis of PI by CT-FNA was made in 28/48 patients, positive Gram stain in 26 and negative gram stain but positive cultures in two patients. The PI diagnosis was made during the first two weeks of AP onset in 82% of patients. OF was present in 14/28 (50%) of patients at the time to diagnose PI. Patients with PI and OF versus PI without OF had a mortality of 42 % versus 32% ($p = 0.09$).

The mean time to CT-FNA in PI was 12.5 ± 7 days and without PI was 10.1 ± 3.9 days ($p = 0.43$). Five of 22 patients persisted with SPI criteria after a first negative CT-FNA, requiring a second CT-FNA and two of them were diagnosed with PI, one at day 20 (*Staphylococcus aureus*) and the other at day 40 (*Staphylococcus aureus* and *Acinetobacter* spp). Any of the 20 patients with negative FNA died or were diagnosed with PI during one month after hospital discharge.

Of 28 patients with a positive CT-FNA, 26 underwent surgical intervention, corroborating PI in 25 patients. The mean time from a positive CT-FNA to surgery was 36 hours. Two patients did not undergo surgery. One patient, who had AP after ERCP and a Balthazar-CT D score with a *Staphylococcus aureus*-positive culture, developed pulmonary failure but responded well to medical and antibiotic (imipenem) therapy. Another patient was a 38 year-old male diabetic with severe AP and Balthazar CT E score, who developed fever and leukocytosis on day 14 and had a negative CT-FNA. A second CT-FNA was indicated three days later because of persistent fever and leukocytosis, being positive for *Staphylococcus aureus*. He was treated with percutaneous pancreatic drainage and adjustments in antibiotic therapy which resulted in a good prognosis and was discharged in good condition 20 days later.

The patient in whom surgery did not corroborate infection was a 52 year-old male with acute mild biliary pancreatitis and Balthazar CT E score who developed fever and leukocytosis without OF. The CT-FNA performed at day nine from the beginning of the AP symptoms was positive for Gram positive cocci and Gram negative rods. During surgery only necrotic tissue was detected and the Gram stain and cultures were negative; the patient did well and recovered after 30 days without local complications.

Monomicrobial infection was found in 18 of 28 patients (64%), and polymicrobial in 10/28 (36%). The most common isolated microorganism were *Staphylococcus* spp in 12 patients, *Enterococcus faecalis* in seven, *Pseudomonas aeruginosa* in four, *Escherichia coli* in three, *Acinetobacter* spp in three and *Streptococcus faecalis*, *Kleb-*

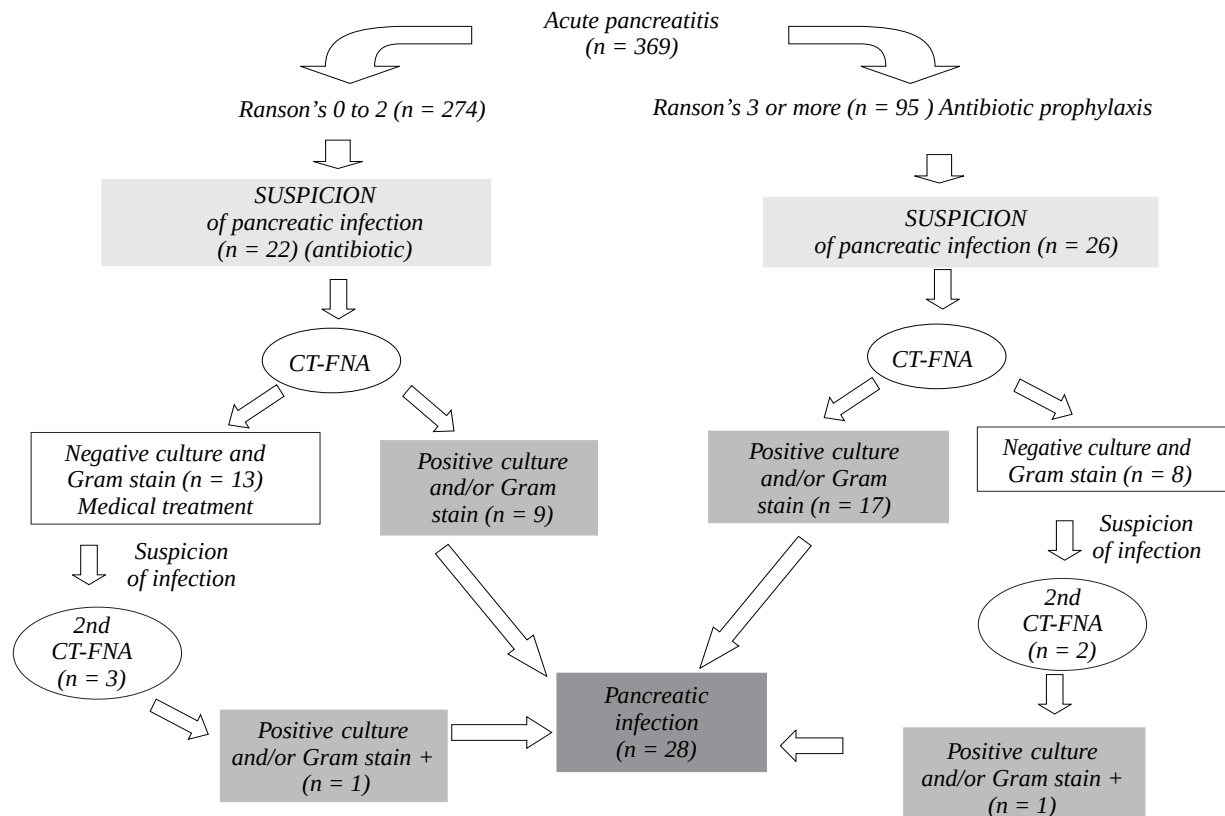


Figure 1.

siella pneumoniae, *Stenotrophomona* and *Enterobacter cloacae*, *Candida tropicalis* in one patient each.

The application of the SPI criteria in our population shows that no patients in the non SPI criteria group had pancreatic infection detected during the study period. The sensitivity, specificity, PPV and NPV for the SPI criteria to detect PI using CT-FNA and surgery as the gold standard method to diagnose PI were 100%, 94% (CI 95% 92-97), 58% (CI 95% 44-72) and 100%. Considering that one patient's surgery did not corroborate the presence of PI and two patients were not treated with surgery, the SPI criteria had a sensitivity of 100%, a specificity of 93% (CI 95% 91-96), PPV of 52% (CI 95% 38-66), and NPV of 100% to detect PI.

DISCUSSION

Our study shows the utility of specific clinical criteria in order to decide to perform a CT-FNA in the diagnosis of PI at the borderline evolution time between symptoms related to SIRS and PI sepsis in patients with AP.

The hemodynamic profile of AP is usually hyperdynamic in the early state and most patients after 3 to 5

days of adequate medical treatment are controlled. Yet, patients with severe AP have an early toxic phase with distant organ dysfunction of various degrees and this event can last for 10 to 14 days. The PI can be an early event and these clinical symptoms are indistinguishable from SIRS. We determined that using specific clinical criteria on or after the seventh day of the AP attack would be a good approach in order to diagnose PI. The population of our study shares similar demographic data, pancreatitis etiology, pancreatitis severity and overall mortality when compared with several previous reports.^{17,24,25}

Severe AP was diagnosed in 26% of our patients. Half of the patients with positive SPI criteria can be considered as critically ill because they have OF at the time to indicate the CT-FNA. The AP severity by CT Balthazar score was C or higher in 92% of infected patients. One weak point of our study is that we do not have dynamic CT scans on admission or at 72 hours after onset of AP in order to determine the amount of pancreatic necrosis. The overall mortality was 5% and the mortality rate in the infected group was 39% and in the non infected group was 5%.

Different criteria have been published in regard to SPI. In a prospective study, Büchler et al., used as criteria for SPI those published in the consensus of OF and sepsis by the ACCP/SCCM²⁶ to indicate the need for pancreatic FNA. However, the timing to perform the procedure was not defined.²⁰

In our study, we defined as SPI using the following criteria: persistence, recurrence or new onset of fever $\geq 38^{\circ}\text{C}$ for more than 48 hours, leukocytosis $\geq 12,000\text{ mm}^3$ and OF as defined by the Atlanta criteria. These criteria were applied starting at the seventh day from the beginning of the first AP clinical symptoms. The presence of any criteria was an indication to perform a CT-FNA of pancreatic and/or peripancreatic tissue. These criteria were applied after ruling out extra pancreatic infection(s). If extrapancreatic infection was not considered the main cause of SPI criteria, then a CT-FNA was indicated. When the first CT-FNA was negative and SPI criteria persisted for more than 72 hours besides adequate medical treatment a new CT-FNA was performed. One of major determinants to indicate the CT-FNA in our study was the presence of OF as had been reported in other studies.^{21,26} The severity of AP defined by Ranson criteria or APACHE II score has not been useful to predict risk of pancreatic infection.²⁰

However, the extended pancreatic necrosis does correlate with increased risk of PI.²⁶ In our study, Ranson score shows not to be different in patients with or without SPI criteria, but patients with PI had a higher Ranson score ($p = 0.02$).

Also, we found PI only in the group who had the presence of SPI criteria. No patients in the non-SPI criteria developed clinical evidence of PI during one-month follow-up after hospital discharge. Is important to say that four patients died early because of multiple OF and these patients were not submitted to any procedure to rule out PI. Besides this, we considered them as non-infected patients. The mean time to diagnosed PI was 12 days since the beginning of AP symptoms and the surgery was performed during the first 36 hours of PI diagnosis. Another important point concerns the time to decide to perform a CT-FNA. The consensus of most experts recommends to wait until three weeks since the onset of AP attack before surgery be performed in patients with necrotizing pancreatitis, but it is a period of time when signs and symptoms of SIRS or sepsis might be superimposed and a clinical decision should be made. We know that early surgery carries a greater risk of complications in the non-infected patients, but in the infected patient surgery still is the gold standard of care. As other

authors, we think that surgery should be performed in patients with proven PI and the only way to be certain about this is to indicate a CT-FNA.^{17,27} Considering the existence of patients with organized sterile necrosis that may need surgery, Ashley and colleagues in a large single institution series of patients with AP found that only 8% of patients with sterile necrotizing pancreatitis needed surgery for symptomatic sterile organized necrosis.¹⁷

We sent 26 patients to surgery and 20 had clear clinical signs of sepsis, of which four died. We might have used another treatment different than surgery in six patients who had no clear signs of either sepsis or organ failure at the time of positive CT-FNA. Maybe for patients without clinical signs of either sepsis or with “stable PI” others treatments rather than surgery could be used in order to delay surgery until the third week when pancreatic necrosis is more organized and better surgical results can be obtained.²⁸

In our study no patient had only leukocytosis as the sole criterion to indicate a CT-FNA. However, the presence of fever plus leukocytosis and/or organ failure determined the higher risk to be infected. One patient with clinical deterioration was sent to CT-FNA because of a high clinical suspicion of PI and no PI was detected. The PI was diagnosed with the first CT-FNA in 92% of patients. Two patients were diagnosed with PI after a second CT-FNA, one monomicrobial and other with polymicrobial infection. Pancreatic necrosis contamination after CT-FNA might be considered.

Most studies describe the overall usefulness of CT-FNA without regard to the number of procedures needed to obtain a diagnosis of PI. In Buchler's study, the first CT-FNA yielded a positive result of 44%.²⁰ Our overall 92% sensitivity for the first CT-FNA may be related to the time and use of more specific SPI criteria to indicate the FNA or to the performance of FNA by a single radiologist. Other studies have reported a higher number of FNA in order to diagnose PI.^{13,17} The sensitivity of the SPI criteria in our study was of 100%, we tried to explain this, because of a strict patient follow-up during the study or because all patients who were sent to surgery had a previous CT-FNA.

Early diagnosis of many medical diseases is expected to improve patient prognosis, yet in regard to patients with PI this issue still is unresolved. The definition of early PI does not exist. We propose the utilization of SPI criteria that could be useful to indicate a CT-FNA by trying to differentiate between patients with signs and symptoms related to SIRS versus sepsis secondary to PI.

Whether some of our patients with severe AP were already infected before FNA following the routine use of prophylactic antibiotic therapy to cure them, we cannot answer this question.

Actually, we do not have specific criteria to define patient without PI who will benefit from surgical debridement. The mortality rate reported in patients with infected pancreatic necrosis is 6% when surgical intervention from onset of AP was one month,²⁸ 24% when the mean time for surgery was 21 days²⁰ and as high as 60% when surgery is performed within the first two weeks.^{29,30}

In our study, the mean time for surgery was 12 days from the beginning of symptoms of AP and the mortality rate was 39%. The mortality rate with and without organ failure at the time of surgery was not different. Our increased mortality rate may be related to several factors such as time of surgery or different surgeons.

Only one patient without infection after a negative CT-FNA died. His death was related to a tracheostomy complication and no evidence of PI was detected.

We had two patients with diagnosis of PI who responded well to medical management. One patient had pulmonary failure at the time of diagnosing PI and his clinical status improved and surgery was not performed. The other patient did not have organ failure at the time of diagnosing infection and improved with medical treatment. The question of a false positive FNA, pancreatic contamination instead of a "real" pancreatic infection or a good response to medical treatment comes to mind.

Recently, a prospective study showed that the extension of pancreatic necrosis, persistence of organ failure and early surgical intervention are associated with a greater risk of morbidity and mortality. Therefore, it has been proposed to wait until the third week to perform surgery in patients with "stable" PI.^{25,31-34} However, until today no "stable" PI definition exists.

A better classification of different circumstances surrounding PI would be useful in our quest of trying to identify the subgroup of patients who may benefit from medical treatment until infected pancreatic necrosis becomes more organized and surgical intervention can lead to better outcomes.¹

In conclusion, we believe that the clinical criteria for SPI applied at or after the seventh day of the beginning of AP symptoms can be a useful tool to indicate a CT-FNA in differentiating between patients with SIRS and sepsis related to PI. Also, our approach can lead to better strategic plans in the management of these difficult ca-

ses. More clinical trials using these criteria are needed to measure the clinical impact of this approach.

Pros

1. To our knowledge this is the first prospective clinical trial which applied specific clinical criteria to indicate a CT-FNA trying to defined between SIRS and sepsis in AP. Our approach can help patients without PI by avoiding unnecessary surgical interventions.
2. The diagnosis of PI at early stage in patients severely ill can be helpful to planning new treatment modalities.

Disadvantages

1. Maybe the time to start to apply the SPI criteria was too early.
2. No dynamic CT scan was performed routinely at admission or at 72 hours from AP onset.
3. Several surgeons participated during the study.
4. High mortality rate in the PI group.

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