Prediction of Pancreatic Necrosis by Dynamic Pancreatography

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Parenchymal necrosis has recently been recognized as the principal determinant of the incidence of secondary infection in acute pancreatitis. Because secondary infection of pancreatic necrosis accounts for more than 80% of all deaths from acute pancreatitis, a method for determining the presence or absence of parenchymal necrosis would offer considerable prognostic and therapeutic information. Thirty seven patients with unequivocal acute pancreatitis and five normal controls were prospectively studied with intravenous bolus, contrast-enhanced computed tomography (dynamic pancreatography). In the absence of pancreatic necrosis, there were no significant differences in parenchymal enhancement between any of the following patient groups: controls (5), uncomplicated pancreatitis (20), pancreatic abscess (7), or peripancreatic necrosis (4) ($p < 0.05$). On the other hand, pancreatic parenchymal enhancement was significantly reduced or absent in all six patients with segmental or diffuse pancreatic necrosis ($p < 0.05$). Postcontrast pancreatic parenchymal enhancement was also found to be inversely correlated with the number of Ranson signs ($p < 0.001$). Dynamic pancreatography offers prognostic information and is a safe and reliable technique for predicting the presence or absence of pancreatic parenchymal necrosis.

DESPITE SIGNIFICANT ADVANCES in supportive and resuscitative care, the overall mortality rate from acute pancreatitis has remained remarkably constant at 10% to 12% for the past 40 years.[1,2] Today few patients succumb from the consequences of hypovolemia in the early phase of acute pancreatitis. Rather 80% of current deaths from acute pancreatitis can be attributed to infectious complications that occur later in the course of the disease.[3,4]

For some time it has been recognized that the incidence of infectious complications in acute pancreatitis was directly related to the clinical severity of the attack.[5] More recently, however, a link has been established between the severity of clinical presentation and pancreatic histology; in particular, the presence or absence of pancreatic necrosis.[6,7] Because of these observations, increasing attention has been paid to pancreatic parenchymal necrosis, not only as a principal determinant of the severity of an episode of acute pancreatitis, but also as a primary risk factor for pancreatic infection.[8]

Due to the pivotal role that the development of pancreatic necrosis plays with regard to clinical decision making in patients with severe acute pancreatitis, considerable efforts are being made to find a safe, reliable, and minimally invasive technique for detecting the presence of parenchymal necrosis. The present report describes our experiences with a noninvasive technique for measuring the integrity of the pancreatic microcirculation by parenchymal contrast enhancement, using commonly available equipment and materials.

Patients and Methods

Pancreatic parenchymal enhancement was prospectively studied in thirty seven patients with unequivocal acute pancreatitis. The diagnosis of acute pancreatitis was established in each patient by a combination of typical pain patterns, abdominal tenderness or guarding, leukocytosis, an elevated serum amylase or lipase, and a noncontrast CT scan demonstrating either swelling of the gland or extrapancreatic extensions of inflammation. A number of other patients, originally diagnosed as having probable acute pancreatitis, were excluded from further study by these stringent criteria. In this group of 37 patients, there were 21 male and 16 female patients with an average age of 41.3 years. The underlying pancreatitis was

Presented at the 109th Annual Meeting of the American Surgical Association, Colorado Springs, Colorado, April 10–12, 1989.

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Accepted for publication: April 17, 1989.

TABLE 1. *Average Aortic and Pancreatic Parenchymal Densities (Hounsfield Units)*

Patient Groups	# Pts.	Ranson Signs	Before Intravenous Contrast				After Intravenous Contrast		
			Aorta	Head	Body	Tail	Aorta	Pancreas	Pancreas:Aorta*
Controls	5	N/A	49	50	48	42	131	92	70%
I Uncomplicated pancreatitis	20	1.1	42	41	39	36	137	88	64%
II Pancreatic abscess	7	3.6	41	42	41	37	126	71	56%
III Peripancreatic necrosis	4	5.5	39	47	41	40	123	79	64%
IV Pancreatic necrosis (<50%)	2	4.0	36	37	33	29	118	54	46%†
V Pancreatic necrosis (>50%)	4	6.0	38	40	36	34	139	28‡	20%‡
Total (Avg)	42		(41)	(43)	(40)	(36)	(129)		

* Significant inverse correlation with number of Ranson signs ($p < 0.001$).

† Significantly different from controls ($p < 0.05$).

‡ Significantly different from all other groups ($p < 0.05$).

judged to be due to alcohol in 18, gallstones in 14, hyperlipidemia in 2, and drug reaction in 1. The pancreatitis was idiopathic in two cases. Five patients (three male, two female, average age 45.2 years), without known pancreatic disease, and who were undergoing computed tomography for other purposes, served as controls.

After giving informed consent, each of the 42 patients underwent dynamic pancreatography using either the Picker 1200 (Cleveland, OH) or the General Electric 9800 (Milwaukee, WI) computed tomographic scanners. Dynamic pancreatograms were initially performed within 48 hours of admission and were repeated as clinically indicated. Each study was preceded by routine CT scanning of the abdomen, using oral contrast and 10 mm sections to locate the pancreas in a cranial-caudal plane. Preliminary scanning also served to demonstrate any extrapancreatic collections or extensions of the inflammatory process, and to eliminate the presence of other intra-abdominal pathologic conditions. When possible precontrast density (Hounsfield units) was measured in each segment of the pancreas.

Two methods of intravenous contrast administration were studied. In the first 100 cc of iothalamate meglumine 60% was injected by pressure injector for 5 seconds, using two intravenous lines. Scanning was begun simultaneously with the onset of injection. In the second, 150 cc of contrast (200 cc for weight > 150 lbs) was given by pressure/injector at the rate of 2 to 5 cc/sec. Scanning was initiated 20 seconds after beginning the injection.

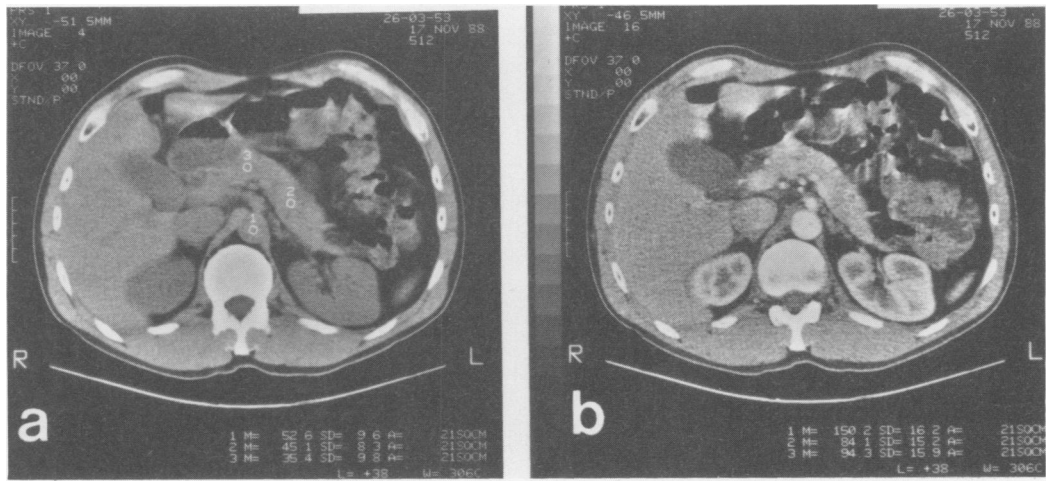
During the dynamic phase, scanning was restricted to the previously localized pancreas, using 5 mm sections at 5 mm intervals. Contrast density (Housefield units) was measured in three areas of the pancreas in each of the multiple tomographic sections, care being taken to avoid the contrast-filled splenic, superior mesenteric, and portal veins. Simultaneous contrast measurements were taken from the aorta in each tomogram to serve as a density reference for pancreatic tissue. Densities of any extrapancreatic collections or extensions of the pancreatic process were also noted.

Prospective predictions of the presence of pancreatic necrosis were based on whether the pancreatic parenchyma failed to be enhanced with dynamic pancreatography. Measurements of the presence or absence of pancreatic enhancement were compared to the individual hospital course. Patients were grouped into controls or one of five other clinical disease classifications (I Uncomplicated Acute Pancreatitis, II Pancreatic Abscess, III Peripancreatic Necrosis, IV Pancreatic Necrosis < 50%, and V Pancreatic Necrosis > 50%), using a combination of previously described clinicopathologic definitions[9] and the subsequent hospital course of each individual. Histomorphologic confirmation of the clinicopathologic classification was obtained in sixteen of the seventeen complicated cases.

In an effort to minimize differences between patients due to body geometry, plasma contrast concentration, cardiac output, or blood volume, pancreatic tissue density measurements after intravenous contrast administration were referenced to intra-aortic density by means of a pancreas: aorta ratio, thereby creating a form of internal control for each individual. The effect of time on postcontrast density measurements was minimized by averaging density values for the aorta and the pancreas in each patient. Data analysis was carried out by one way analysis of variance using Tukey's Multiple Pairwise test, and the Pearson Correlation Coefficient.

Results

The results of time–density measurements from dynamic pancreatography are shown in Table 1. In general, there was a tendency for precontrast density to fall with progression from the head of the pancreas to the tail, the average density decreasing from 43 HU in the head to 36



FIGS. 1A and B. Dynamic pancreatogram in a control patient. (A) Precontrast density is 52.6 HU in the aorta (1M), 45.1 HU in the tail of the pancreas (2M), and 35.4 HU in the body of the pancreas (3M). (B) During the dynamic phase, note the rise in corresponding aortic and pancreatic densities and the overall enhancement of the pancreatic parenchyma. (pancreas:aorta ratio, 60%)

HU in the tail. There were no significant differences in precontrast pancreatic parenchymal density between any of the patient groups ($p > 0.05$), reinforcing previous observations that routine computed tomography cannot differentiate parenchymal necrosis from pancreatic edema.

When intravenous contrast was given, there was an approximate threefold increase in aortic density, whereas only a twofold increase occurred in average pancreatic density. In the five control patients (group I), pancreatic parenchymal enhancement was prompt, equally distributed in all segments of the gland, and averaged 70% of aortic density (Fig. 1). In the absence of pancreatic necrosis (controls, groups I to III), there were no significant differences noted in either the average pancreatic parenchymal contrast density, or in segmental contrast density of the head, body or tail of the pancreas ($p > 0.05$) (Fig. 2). Postcontrast pancreatic parenchymal density was greater than 50 HU in controls, and in each case of uncomplicated acute pancreatitis (Fig. 3), pancreatic abscess (Fig. 4), and peripancreatic necrosis (Fig. 5). No patient with parenchymal enhancement > 50 HU was subsequently proved to have pancreatic necrosis.

On the other hand, significant reductions in average and segmental parenchymal enhancement ($p < 0.05$) and in the pancreas:aorta density ratio ($p < 0.05$) occurred in all six patients with subsequently proved pancreatic necrosis (groups IV and V; positive predictive value 100%). In each of the patients with segmental or diffuse pancreatic necrosis, parenchymal density in the involved segment(s) was less than 40 HU (Figs. 6 and 7). Perhaps more im-

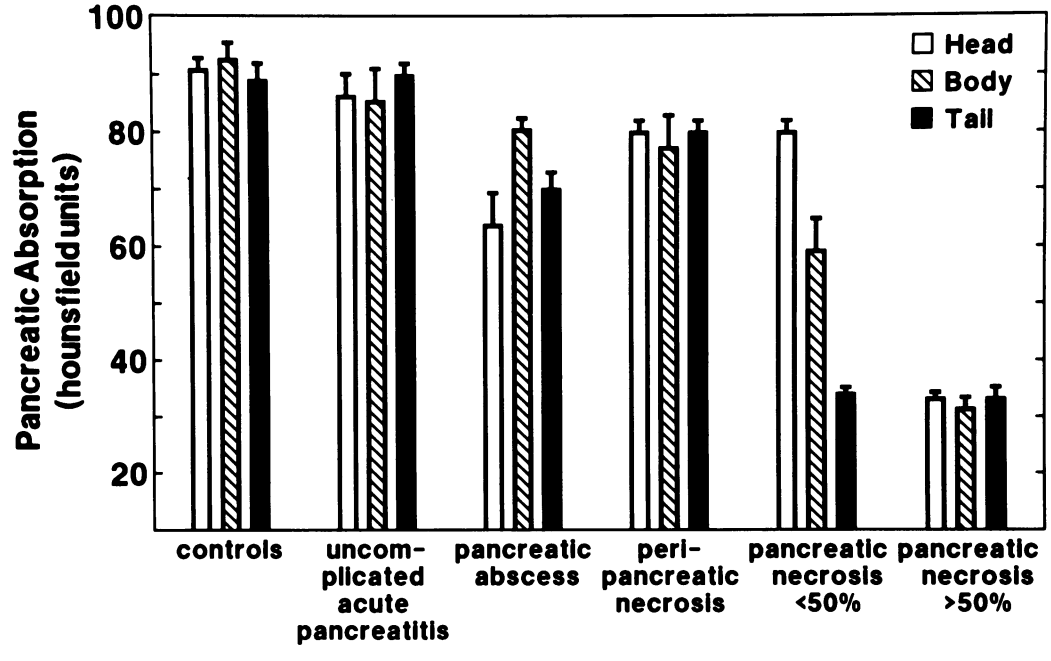
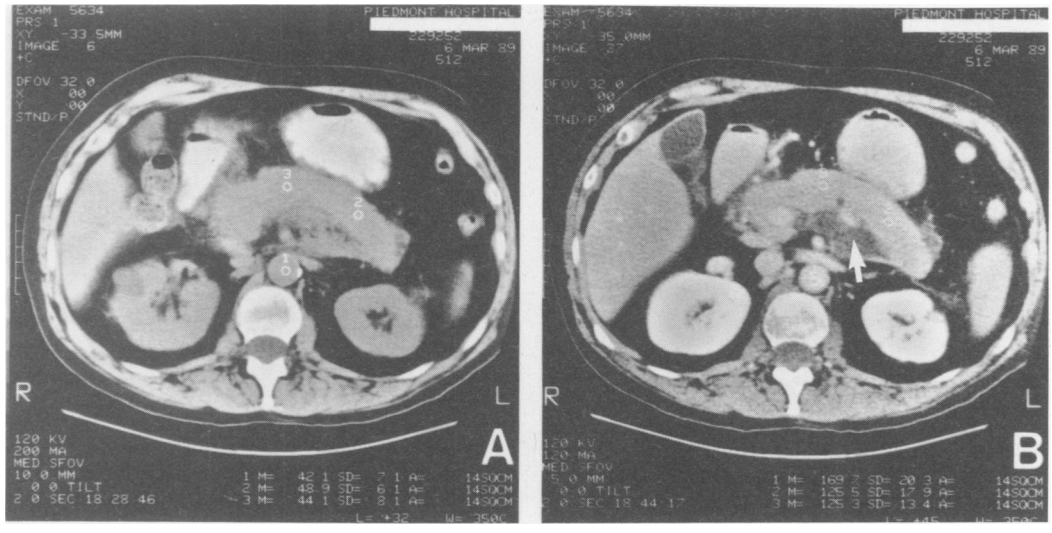


FIG. 2. Segmental pancreatic contrast densities in the control and study groups (average number of Hounsfield units + SEM).



FIGS. 3A and B. Uncomplicated acute pancreatitis. (A) Note marked swelling of the gland with bilateral pararenal space involvement. (Aortic density 42.1 HU, tail of pancreas 48.9 HU, body of pancreas 44.1HU) (B) Note uniform enhancement of pancreatic parenchyma during dynamic phase (125.5 HU, 125.3 HU), and delineation of retropancreatic inflammation (arrow) (pancreas: aorta ratio, 74%).

portantly the postcontrast pancreas:aorta ratio was less than 30% in each segment of pancreas subsequently proved to be necrotic by histology.

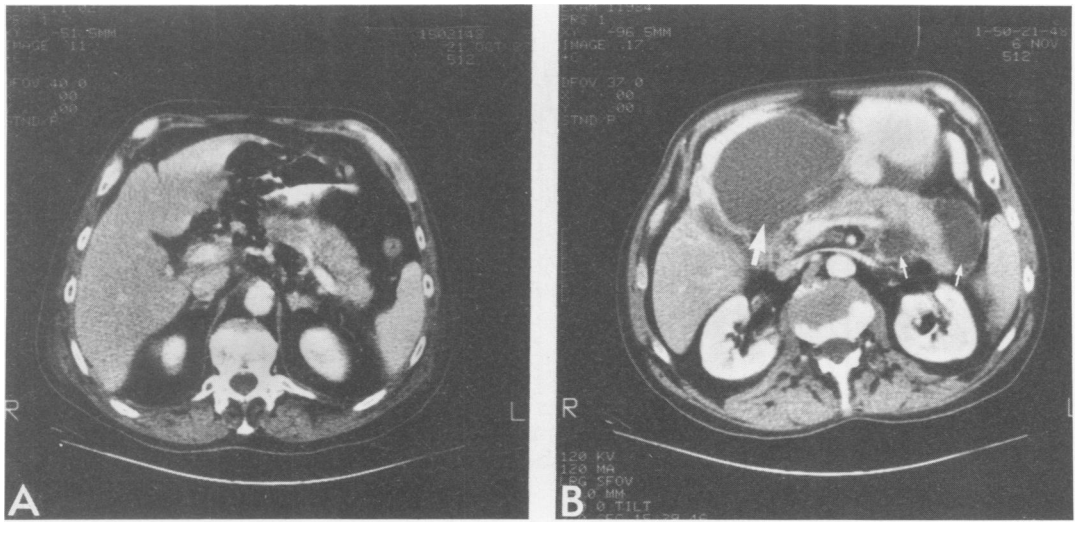
Of additional interest was the observation that average pancreatic parenchymal enhancement was correlated with the clinical severity of presentation; as the number of Ranson signs increased, postcontrast pancreatic parenchymal density decreased. The inverse correlation between Ranson's signs and the postinjection pancreas:aorta ratio was highly significant ($p < 0.001$).

There were no significant differences in postcontrast pancreas:aorta ratios between patients given the rapid intravenous bolus (5 seconds) and those given contrast during 40-to-80 second intervals.

No untoward reactions were noted in any of the 42 patients undergoing dynamic pancreatography. Despite prestudy concern no increases in serum creatinine occurred in any patient as a result of the large contrast load. However it is important to note that none of these patients underwent dynamic pancreatography in a volume-depleted state, and that similar results in regard to renal function might not be obtained if hypovolemia had been present.

Discussion

Recognition that pancreatic necrosis is the primary risk factor in the incidence of infectious complications in acute pancreatitis,[8] and that necrosis is also a principal determinant of overall outcome[6–8] has provided considerable impetus to the search for techniques capable of detecting parenchymal necrosis. Current methods for detection of pancreatic necrosis include meta-analysis of clinical features, various serum biochemical assays, and adaptations of pancreatic imaging techniques.



FIGS. 4A and B. Serial dynamic pancreatograms in a patient developing multiple pancreatic abscesses. (A) Only pancreatic swelling and pararenal involvement noted on first study (pancreas:aorta ratio, 64%). (B) Repeat study 2 weeks later shows three collections (arrows) that proved to be abscesses at surgery. Parenchymal enhancement remained uniform and normal (pancreas: aorta ratio, 63%).

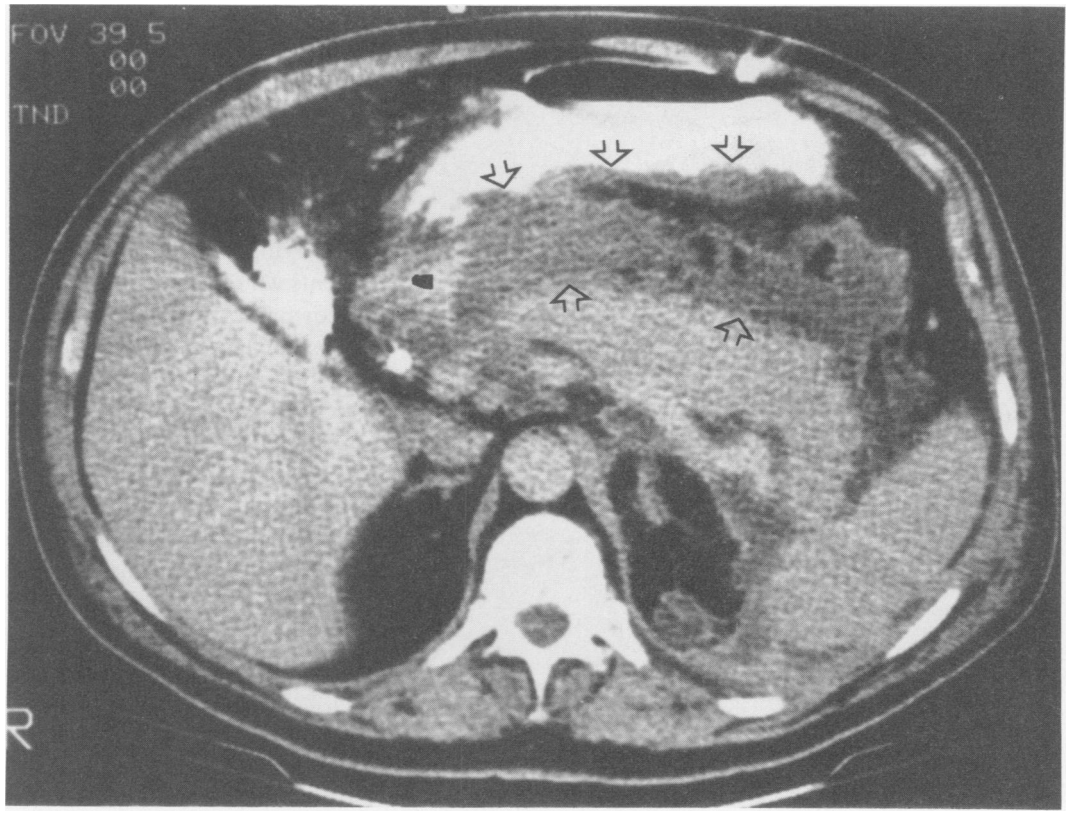
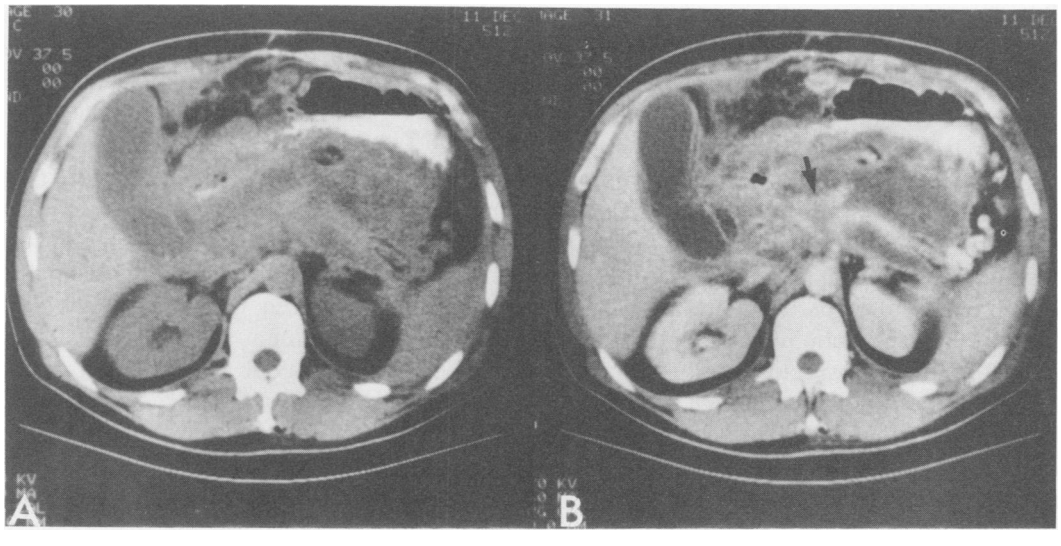


FIG. 5. Peripancreatic necrosis. Note well-enhanced pancreatic parenchyma (> 70 HU), but irregular borders of the gland. Extrapancreatic fat necrosis (arrows) is clearly seen.

In an extensive clinicopathologic analysis, Nordback and his coworkers found that the extent of pancreatic necrosis in glands resected for severe acute pancreatitis correlated poorly with fever > 38 C, abdominal distension, rebound, ileus, or even the presence of an abdominal mass.[10] In addition they were unable to correlate the degree of parenchymal necrosis with the leukocyte count, hematocrit, platelet count, blood glucose, or serum levels of Na, K, Ca, creatinine, bilirubin, triglycerides, or transaminases. Similarly Block and her coworkers found only a rough correlation between the number of Ranson signs and the presence of necrotizing pancreatitis.[11] Thirty-nine per cent of 93 patients undergoing pancreatic resection for necrotizing pancreatitis were initially classified as "mild" by Ranson criteria. Furthermore the histologic extent of pancreatic parenchymal necrosis cannot even



FIGS. 6A and B. Limited pancreatic necrosis. (A) Precontrast study is typical of a pancreatic "phlegmon." (B) After intravenous contrast, only the head and neck of the pancreas are enhanced (arrow). The nonenhanced body and tail of the pancreas were found to be necrotic at surgery.

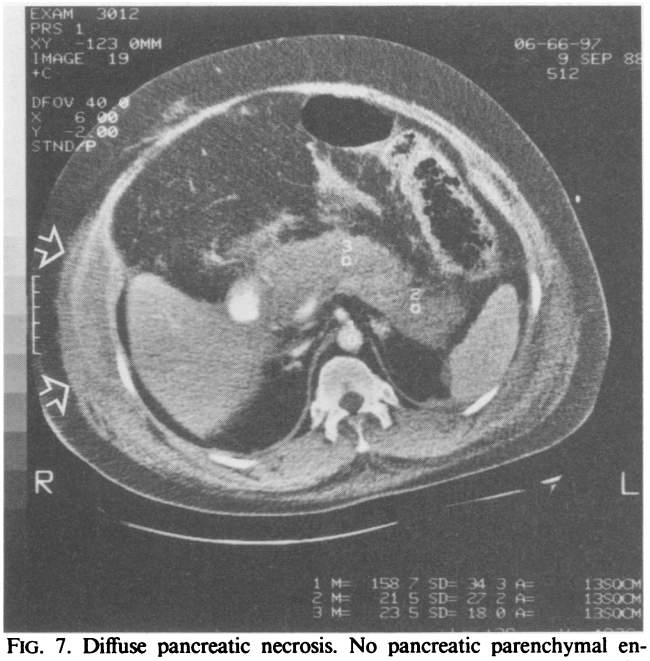


FIG. 7. Diffuse pancreatic necrosis. No pancreatic parenchymal enhancement occurred with dynamic pancreatography (pancreas:aorta ratio, 14%). Note the markedly thickened abdominal wall musculature (arrows). This patient also had Grey-Turners sign (flank ecchymosis).

be predicted by the macroscopic appearance of the gland at surgery.[6,10] Despite several observations that the presence of turbid or hemorrhagic ascitic fluid suggests necrotizing pancreatitis,[10,12] a disturbing number of false negatives and false positives effectively invalidates sole reliance on any of these clinical approaches for the detection of pancreatic necrosis in the individual patient.

Intensive efforts have also been directed toward finding a reliable serum test for detecting pancreatic necrosis. Poly-(C)-specific ribonuclease (RNAse) has been claimed to be highly sensitive for detecting necrosis of pancreatic cells.[13] However the biomechanical analysis has been cumbersome, the test invalidated by deteriorating renal function (a common occurrence in severe acute pancreatitis), and to date, confirmation from other laboratories has been lacking. In a retrospective clinicopathologic study of 35 patients undergoing pancreatic resection for severe acute pancreatitis, Büuchler and his coworkers monitored a number of serum acute-phase reactants and found that specifically abnormal levels of α 1-antitrypsin could have correctly identified parenchymal necrosis in 77% of patients, α-2 macroglobulin in 85%, and C-reactive protein in 95%.[14] In a prospective study from our institution, however, we found that although recommended "predictive" values of these acute-phase reactants were present in 30 of 45 consecutive patients with acute pancreatitis, 22 of the 30 patients with serum values "predictive" for pancreatic necrosis had uncomplicated hospital courses (unpublished data). Abnormal values of α 1 antitrypsin, α 2 macroglobulin, and C-reactive protein may, therefore, be overly sensitive for detection of pancreatic necrosis and cannot be used prospectively as indicators for surgery. The role of serum complement factors (C_3, C_4) in detecting pancreatic necrosis has also been controversial. Foulis et al.[15] observed persistently low levels of C_3 and C_4 in patients dying from necrotizing pancreatitis, while values in patients who recovered returned to normal. Buchler[14] and his coworkers reported persistent depression of C_3 and C_4 values in patients with pancreatic necrosis, with an overall detection rate of 74% and 79%, respectively. On the other hand, Whicher[16] and his colleagues could not demonstrate any correlation between serum complement values and clinical outcome from acute pancreatitis. We may conclude that, as yet, none of the serum tests for detection of pancreatic necrosis has demonstrated accuracy or clinical reliability sufficient for use in the individual patient.

A variety of imaging techniques for identifying pancreatic necrosis have been proposed. However both Indium 111-labeled leukocytes,[17] and abdominal sonography,[18,19] have proved incapable of distinguishing between pancreatic parenchymal necrosis and edema. Even though computed tomography reliably demonstrates extrapancreatic inflammation in acute pancreatitis, and is accurate in detecting fluid collections (abscesses and acute pseudocysts),[2,20,21] and although these extrapancreatic changes can be correlated with clinical severity and outcome,[2,20] noncontrast CT has not been capable of distinguishing between edema and necrosis within pancreatic tissue.[2,21-23] Results from the current study confirm these observations. Noncontrast high density parenchymal lesions may represent blood,[24] or fluid with a high protein content.[25] Low density lesions may represent fat,[23] fluid,[2,23,26], tissue edema,[21,27] or necrosis.[21,25,28] Because therapeutic options depend on the specific pathologic process in the gland and can range from continued observation to extensive retroperitoneal debridement and open packing, accurate characterization of the existing parenchymal pathology is of critical importance.

In 1983, Kivisaari[29] and her coworkers observed that pancreatic parenchyma failed to enhance after rapid intravenous contrast infusion in eight of eight patients with subsequently proved pancreatic necrosis. In a prospective study the next year, they identified 2 groups of patients with acute pancreatitis using intravenous bolus, contrast-enhanced CT, 10 patients with low parenchymal enhancement (<30 HU), and 10 patients with normal enhancement (< 40 HU). Necrotizing pancreatitis was demonstrated at surgery in each of the patients with low enhancement, while all ten patients with normal enhancement were treated supportively and recovered without complication.[30] Furthermore when patients were combined from the first and second studies, mean contrast

enhancement values for the 18 patients with necrotizing pancreatitis were significantly lower than the values for the 30 patients with presumptive acute edematous pancreatitis ($p < 0.01$).[30] The intravenous contrast bolus was well tolerated by all 48 patients.

The ability of intravenous bolus, contrast-enhanced CT scanning to detect pancreatic necrosis has been confirmed by other workers. Maier[22] has reported a sensitivity of 0.87 and a specificity of 1.0 for dynamic pancreatography in distinguishing between necrotizing pancreatitis in 63 patients undergoing surgery and 45 cases of "edematous pancreatitis" managed conservatively. No allergic reactions or deterioration in renal function occurred. As a result of failure of the pancreatic parenchyma to enhance, Larvin and his coworkers also correctly identified a group of eight patients with necrotizing pancreatitis from 31 patients with severe acute pancreatitis.[31] Finally Partanen et al.[32] reported significantly less contrast enhancement in 11 patients with necrotizing pancreatitis compared to 20 patients with non-nectrotizing acute pancreatitis. However we could not identify any previous reports studying dynamic pancreatography in normal controls, or in patients with complications of acute pancreatitis other than parenchymal necrosis.

In this study we have demonstrated that dynamic pancreatography is capable of distinguishing between patients with parenchymal necrosis and those with uncomplicated acute pancreatitis. Furthermore it would appear that an accurate clinical distinction can be made between the various other complications of acute pancreatitis using dynamic pancreatography. Parenchymal necrosis is apparently not a prominent feature of uncomplicated acute pancreatitis, pancreatic abscess, or peripancreatic fat necrosis. This latter observation has far-reaching therapeutic implications because selection of an appropriate therapy is dependent on an accurate clinical diagnosis.

With the addition of the current report to the rapidly growing data base on dynamic pancreatography, it seems reasonable to suggest that this technique should be used early in the course of those patients with severe acute pancreatitis (three or more Ranson signs), and in those cases with prolonged or otherwise complicated clinical courses.

The technique of dynamic pancreatography and data analysis differs somewhat in the current study from previous reports. While the total contrast load is 100 to 200 cc in all dynamic studies, the rate of administration varies. In the Finnish studies,[29,32] the total contrast load was given over 7 to 8 seconds. Such rapid administration produces higher enhancement values, but also more rapid tissue diffusion of contrast. Because we did not observe any significant differences in pancreas:aorta ratios as a function of the rate of contrast injection, we, as well as others,[22,31] prefer administration of a larger amount of contrast over a longer time, resulting in a longer parenchymal phase for analysis.

Despite variations in contrast injection rate, decreased or absent parenchymal enhancement in patients with necrotizing pancreatitis has been observed by all previous investigators. Because this observation seems secure, objective guidelines for identification of parenchymal necrosis must be established. While we, as well as others,[22,29,32] have consistently observed postcontrast parenchymal density values of < 40 HU in patients with necrotizing pancreatitis, variations in blood volume, pancreatic blood flow, contrast load, and patient geometry may make interpretation of an absolute value problematic. To limit variables between patients, we have preferred to use a dimensionless number, the result of comparing pancreatic parenchymal enhancement to aortic enhancement (pancreas:aorta ratio) as a form of internal control.

How does dynamic pancreatography recognize parenchymal necrosis? After experimental intravenous bolus injection, contrast agents have been shown to spread rapidly throughout the extracellular space.[33] Diffusion of iothalamate meglumine from the pancreatic microcirculation is aided by its low molecular weight (809 Daltons), and by the increase in capillary permeability known to be associated with acute pancreatitis.[34] These observations account for the observed enhancement of pancreatic parenchyma in non-necrotizing acute pancreatitis.

On the other hand, necrotizing pancreatitis is characterized by a severe reduction in pancreatic blood flow and perfusion,[35] with capillary flow particularly affected.[36,37] The loss of capillary flow in necrotizing pancreatitis is primarily due to microvascular endothelial damage and resultant thrombosis of nutrient vessels.[38,39] Due to the absence of collateral circulation at this distal level, little (if any) contrast material is presented to the capillary for diffusion, with a corresponding failure of enhancement.

Data exist to support this hypothesis. Microangiographic studies in pigs with acute edematous pancreatitis demonstrate that normal intravenous contrast enhancement is associated with an intact microcirculation. When necrotizing pancreatitis is produced, however, contrast enhancement is significantly reduced, and marked capillary disruption along with thrombosis and poor filling is consistently observed.[40] That absence of parenchymal contrast enhancement in the presence of pancreatic necrosis is due to microcirculatory obstruction, and not to hypoperfusion secondary to hypovolemia, has been clearly demonstrated in a porcine model.[41] Even more persuasive, however, are recent observations in humans of a direct correlation between the extent of pancreatic microcirculatory disruption, the degree of necrotizing pancreatitis, and the failure of the pancreatic parenchyma to be enhanced.[42] In brief, enhancement of pancreatic parenchyma by contrast agents seem to depend on an intact

microcirculation. Parenthetically the principle of using parenchymal enhancement as a measure of microcirculatory flow may well have application in other fields of surgical interest, such as determining organ viability in transplantation or trauma, as well as in the diagnosis of mesenteric infarction.

If dynamic pancreatography proves to be capable of noninvasive prediction of pancreatic necrosis, how should this information be used? A thorough discussion of whether necrotizing pancreatitis should be resected as soon as it is recognized as advocated by some workers,[7,8,43] or whether noninfected pancreatic necrosis should be managed conservatively as suggested by others,[44–46] is beyond the scope of this paper. Indeed dynamic pancreatography may serve to resolve this conflict in the future. At the very least, however, because pancreatic necrosis is now known to be a principal determinant of complications and even of ultimate survival from acute pancreatitis, recognition of the development of pancreatic necrosis by dynamic pancreatography should alert the clinician to an escalation in risk and heighten anticipation of potential future complications.

Acknowledgments

The authors wish to thank Eyvin Rasmussen, M.D. and Stephen Wilkes, M.D. for suggestions and advice, and Lori Aiken, R.T., Pam Amatriain, R.T., Anne Marie Burke, R.T., Craig Henderson, R.T., Davida Krantz, R.T., Nancy Skinner, R.T., Rita Waller, R.T., and Tammy Williams-Smith, R.T. for excellent technical assistance.

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Discussion

DR. CHARLES F. FREY (Sacramento, California): Dynamic pancreatography delineates the extent and site of pancreatic necrosis, information that is fundamental to the prognosis and clinical management of patients with acute pancreatitis.

Importantly this assessment of necrosis can be performed the day of hospital admission. In contrast many of the signs of severity of Ranson, Banks, and Imrie that we have come to rely on are not available until 48 hours after hospital admission, nor are their signs specific prognosticators of the presence or absence of necrosis or infection of the pancreas.

What are some of the applications of dynamic pancreatography? I will discuss three.

First, it facilitates the early diagnosis of infection. Approximately one half of the patients with significant amounts of necrosis will become infected. Further the greater the extent of pancreatic necrosis, the greater the likelihood of infection developing. Therefore dynamic pancreatography defines a group of patients at risk of developing infected pancreatic necrosis the day they enter the hospital. These patients require close follow-up. If infection is suspected, the area of necrosis can be aspirated under CT scan guidance, as advocated by Banks and Gerzoff and the returns gram stained and cultured. If infection is identified, almost every one agrees, operative debridement should be instituted promptly.

Second, dynamic pancreatography predicts pseudocysts. (Slide) This CT scan with IV bolus enhancement was performed on a woman with necrotizing pancreatitis involving the body of the pancreas but preserving the tail of the gland. As you can see on the CT scan, the tail is functioning. There is, however, no place for the fluid to go because the body of the pancreas is necrotic, so the fluid accumulates. We were able to predict in this woman on the day of admission that if she didn't develop infection of the necrotic portion of the pancreas, she would be at high risk of developing a pseudocyst, which she did 6 weeks later.

Third, dynamic pancreatography provides an opportunity to assess the value of different treatment protocols using patients with comparable degrees of pancreatic and peripancreatic necrosis. The CT scans with bolus enhancement of two patients show virtually total pancreatic necrosis. The first is this CT without enhancement (Slide), the second shows total, almost virtually total necrosis with enhancement.

This is another patient with almost total pancreatic necrosis.

We have been observing these patients with necrosis, even those with virtually total necrosis, and only operating if the clinical picture of hemodynamic or pulmonary failure or sepsis intervened or CT scan-guided aspiration of the area of necrosis demonstrated the presence of bacterial infection. We have not, nor have others, done well with this group of patients with more than 50% necrosis. Dynamic pancreatography provides an opportunity to identify this high-risk group of patients and evaluate new treatment protocols.

DR. JOHN H. C. RANSON (New York, New York): Dr. Bradley's report is, I believe, the first one in this country confirming the extensive observations in Finland and in Germany concerning the relationship between findings on contrast-enhanced CT and the presence of pancreatic necrosis.

In acute pancreatitis, tests can be used for predictive and also for diagnostic purposes. The prognostic signs that Dr. Bradley and Dr. Frey refer to were intended to identify, early in their disease, patients who have a high risk of life-threatening complications. Although they were not specifically intended to identify those with a high risk of local pancreatic complications, there is a relationship between these signs and late sepsis.

Computed tomography for the first time allows reasonably good noninvasive imaging of the anatomy of the pancreas and peripancreatic tissues. As we have reported in the past, early findings on CT help identify patients with a high risk of late pancreatic sepsis. They are usually not, however, diagnostic. In the present study, the addition of contrast enhancement to routine noncontrast CT identified six patients with pancreatic necrosis, but apparently did not help with the identification of 11 other patients who had abscesses or peripancreatic necrosis.

The assumption has been, and Dr. Bradley stated this, that it is the presence or absence of necrosis of the pancreas itself that determines the outcome of acute pancreatitis, and from my perspective, this may be the case, but it is still unproved. I think it may be the extent of pancreatic and peripancreatic necrosis and whether secondary infection supervenes that determines the outcome.

We are now reviewing a group of more than 80 patients with acute pancreatitis who underwent contrast-enhanced CT studies of the kind that you have heard about here. Six of this group were judged to have nonenhancement of 30% to 50% of the gland and three, or one half of this particular group, required operation for pancreatic sepsis. Three, however, recovered without any form of intervention at all. Eleven patients had nonenhancement of 50% or more of their gland and all of these patients required surgery, but nine required surgery for sepsis and two, as Charlie Frey has said, evolved to pseudocyst. They never became infected.

In terms of the sensitivity of contrast-enhanced CT in our patients, 14 of 20, or 70% of patients who required operation for sepsis or pseudocyst, had nonenhancement of 30% or more of their gland. Thus lack of pancreatic enhancement on contrast CT in our experience, as in that of Dr. Bradley, indicates a high probability of local complications, certainly if 50% or more of the gland does not enhance. However, as in Dr. Bradley's study, enhancement of the pancreas on contrast CT does not exclude the development of life-threatening late complications. In our study 17 patients developed infection of pancreatic or peripancreatic necrosis. Two of these patients, or 12%, died. Eleven had nonenhancement of the pancreas with a mortality rate of 9%, but the six who had enhancement had a mortality rate of 17%. Those patients who did not become infected did not die, despite the extensive nonenhancement.

Therefore, are you, Dr. Bradley, indeed willing to make therapeutic decisions based on the finding of nonenhancement of the pancreas that would not be dictated by the other clinical or radiographic findings?