Practice and Yield of Early CT Scan in Acute Pancreatitis: A Dutch Observational Multicenter Study

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Abstract

Background: Early computed tomography (CT) (within 4 full days after symptom onset) may be performed to distinguish acute pancreatitis (AP) from other intra-abdominal conditions or to identify early pancreatic necrosis. We analyzed practice and yield of early CT in patients with an established clinical diagnosis of AP in a Dutch cohort (EARL study). *Methods:* Multicenter observational study. Etiology, disease course, CT timing, Balthazar CT score, and clinical management were evaluated. *Results:* First documented hospital admissions of 166 patients were analyzed. Etiology was biliary (42.8%), unknown (20.5%), alcoholic (18.1%), post-endoscopic retrograde cholangiopancreatography (11.4%), and miscellaneous (7.2%). In 89.2% (148/166), the disease course was mild. Out of 18 patients with severe AP, 11 eventually developed (peri)pancreatic necrosis. At least one CT (range 1–12) was performed in 47% (78/166) of all patients and in 62.8% (49/78) it was acquired within 4 full days after symp-tom onset. Practice, timing, and Balthazar CT score of early CTs were not significantly different between mild and severe AP. None of the early CTs showed necrosis and no alternative diagnoses were established. In 89.8% (44/49), clinical management was not altered after early CT. In 10.2% (5/49), prophylactic antibiotics were started, but in absence of necrosis. *Conclusions:* A CT scan was frequently acquired early in the course of AP, but its yield was low and had no implications with regard to clinical management. It seems prudent that clinicians should be more restrictive in the use of early CT, in particular in mild AP, to prevent unnecessary radiation exposure and to save costs.

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Introduction

The clinical course of acute pancreatitis (AP) is in most cases mild and the treatment is mainly supportive [1–6]. Many patients with AP do not require a computed tomography (CT) at admission or at any time during hospitalization [7–10]. The diagnosis of AP is usually based on compatible clinical features (e.g. upper abdominal pain, nausea and vomiting) and elevations in amylase

and/or lipase greater than three times the upper limit of normal [7, 9, 11–13]. If in doubt (e.g. insufficient elevation of serum amylase/lipase), the diagnosis of AP is best evaluated by a CT scan. A contrast-enhanced CT in the early course of AP may also be indicated to exclude alternative diagnoses such as e.g. a bowel perforation. However, there is no consensus whether to perform a CT in the early course of AP as a prognostic indicator [4, 9, 11, 14–23]. Scientific proof that development of pancreatic necrosis occurs as early as within 96 h after symptom onset is disputable [15]. Importantly, an early CT might underestimate the amount of pancreatic necrosis, and such misconception is associated with a worse prognosis [4, 9, 11, 12, 24]. We analyzed the practice and yield (alternative diagnoses and/or early (peri)pancreatic necrosis) of an early CT scan (within 4 full days after symptom onset) in a convenient cohort of patients with an established clinical diagnosis of AP or recurrent AP.

Materials and Methods

Study Population

In August 2003 an observational prospective multicenter (2 academic and 16 community hospitals) cohort study in the province of Northern Holland was initiated (the EARL study). All patients with AP, recurrent AP and/or chronic pancreatitis who were admitted in the hospital or attended the outpatient clinic were ask for their participation. Patient inclusion stopped in May 2006. A total of 512 patients were entered in the study database. Approximately two thirds of patients had AP or recurrent AP and one third of patients suffered from chronic pancreatitis. The time period during which an individual hospital contributed to the inclusion of patients differed as centers joined the study along the way.

For the present study, we included those patients with a confirmed diagnosis of AP or recurrent AP in whom at least one documented hospital admission during the study period was available. Only the first documented hospital admission of each patient was studied. AP was defined as a clinical disease entity with acute epigastric pain combined with a serum amylase and/or lipase value of more than three times the upper limit of normal, and in the absence of any feature of chronic pancreatitis. Disease severity (mild and severe AP) was defined according to the Atlanta criteria [25]. Because this was an observational study, the Acute Physiology and Chronic Health Evaluation (APACHE II) score, Glasgow score and the serum C-reactive protein (CRP) level at 48 h after disease onset, could not be included as they were not available in all cases.

Recurrent AP was defined as more than one attack of AP in the time period before inclusion and/or during the observation period.

Hospital records and nursing reports were reviewed and study items were recorded in a study database. The following data were retrieved from the database: demographic data, etiological factors, hospitalization time, department of admission, timing (after the onset of symptoms) of CT scan, Balthazar CT score, development of organ failure, presence of local complications (pseudocyst, abscess, pancreatic necrosis) and management change (e.g. start of prophylactic antibiotics or fine-needle aspiration) after early CT. The etiology was assessed after a review of hospital and outpatient charts regarding reported alcohol consumption and drug use (both retrieved from hospital charts and study questionnaires), laboratory results (e.g. liver function tests, triglycerides, calcium) and imaging investigations (e.g. ultrasound, CT, magnetic resonance cholangiopancreatography, endoscopic retrograde cholangiopancreatography and endoscopic ultrasound).

The yield of early CT was defined as the detection of alternative diagnoses and/or local complications, including early (peri)pancreatic necrosis. A CT was considered 'early' if it was performed within the first 4 full days after symptom onset (days 0–4). Day 0 was designated the day of symptom onset. The Balthazar CT scores (grades A–E) were derived from the actual reports of the attending radiologists [26]. Generally, CT images were acquired using intravenous injection with slices of at least 5 mm and included scanning of the pelvis in the majority of cases. CT scans of patients with severe AP were reviewed by an expert radiologist from a tertiary referral hospital. This re-evaluation was done in order to prevent misclassification of local complications, e.g. especially the development of pancreatic or peripancreatic necrosis. The radiologist re-evaluated (blinded for the results of the original report) the presence of local complications according to the Atlanta criteria and the interval between the onset of symptoms and the complications.

The study protocol was approved by all local ethics committees and informed consent was obtained from all patients.

Statistical Analysis

In this observational study, descriptive statistics were used. The analysis was performed for mild and severe AP admissions separately. Categorical data were reported as proportions, quantitative data as medians with ranges. For non-normally distributed data the Mann-Whitney U test was used for group comparisons. To assess the associations between the severity of AP course on the one hand and frequency of use, yield and management implications following CT scanning on the other hand, Pearson's χ^2 test was used. To minimize low cell frequencies, data were meaningfully dichotomized. In case of remaining low cell frequencies <5, either the Yates's correction for continuity was applied (for n = 3 or n = 4) or Fisher's exact test was performed (n ≤ 2). Statistical significance was defined as a p value <0.05. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) Version 12.0.1 (SPSS, Inc., Chicago, Ill., USA).

Results

Etiology, Disease Course and Hospital Stay

From the original EARL pancreatitis study database, a total of 176 patients with AP or recurrent AP were identified of whom at least one fully documented record of a hospital admittance was available. Ten patients were excluded because of failure to meet the inclusion criteria.

Ultimately, 166 patients with a completed review of a hospital admission were analyzed. Nineteen patients had more than one documented hospital admission during the study period. As previously mentioned, only the first documented hospital admission of each patient was considered for the present analysis. The baseline characteristics of the study population are presented in table 1. The proportions of male and female patients were the same and the median age was 50 years (range 18–95). One quarter of patients suffered from recurrent attacks of AP. The most common etiological factor were a biliary cause (43%) followed by an unknown etiology. Importantly, this latter group consisted of 19 patients with an idiopathic pancreatitis, but also of 15 patients in whom the diagnostic work-up to identify an etiological cause was incomplete (e.g. pancreas divisum not excluded). Alcoholic AP was the third most common cause (18.1%). In 89.2% (148/166) the disease course was mild. Of those 18 severe AP patients, 8 were diagnosed as severe at its early stage (within the first 2 weeks after onset of symptoms of the disease). The most common local complication during admissions for severe AP was the development of pancreatic necrosis. Table 1 lists also the local complications established after re-evaluation of the CT scans by the expert radiologist. This expert re-evaluation of CT images showed no major discrepancies. Two patients developed within the first 2 weeks organ failure. Out of 18 patients with severe AP, 11 developed pancreatic necrosis and/or peripancreatic necrosis. Four patients developed pancreatic necrosis or peripancreatic necrosis within the first 2 weeks after onset of symptoms (range 5–14 days). Among patients with abscesses, 2 developed an abscess within the first 2 weeks after onset of symptoms (days 9 and 12) and according to the Atlanta criteria these should be considered as infected post-necrotic fluid collections. Finally, 1 patient developed two pseudocysts after 41 days.

The majority of cases, both mild and severe, were admitted to a community hospital, 68.2 and 55.6%, respectively. More than 90% of patients with mild AP were admitted to an internal medicine/gastroenterology department, whereas half of the cases with severe AP were managed at a surgical ward.

Practice and Yield of Early CT

A CT scan was performed in 47% (78/166) of all AP admissions. As expected, the proportion (40.5% (60/148) vs. 100% (18/18)) and the median number (1 vs. 3) of CT scans were significantly lower during mild AP admissions than during severe AP admissions. A CT scan was

Table 1. General characteristics of the study population (n = 166)

Male	83 (50)
Median age, years (range)	50 (18–95)
Acute pancreatitis	
First attack	126 (75.9)
Recurrent attacks	40 (24.1)
Etiology	
Biliary	71 (42.8)
Unknown[1]	34 (20.5)
Alcohol	30 (18.1)
Post-ERCP	19 (11.4)
Drugs	6 (3.6)
Tumor/obstruction	4 (2.4)
Pancreas divisum	1 (0.6)
Hypertriglyceridemia	1 (0.6)
Course of acute pancreatitis	
Mild	148 (89.2)
Severe	18 (10.8)
Organ failure	2 (11.1)
Necrosis[2]	11 (61.1)
Abscess	4 (22.2)
Pseudocyst	1 (5.6)

Figures in parentheses are percentages, unless indicated otherwise.
[1] Combination of 19 patients with idiopathic pancreatitis and 15 patients with an unknown cause, whereby the diagnostic work-up for an etiological factor was incomplete.
[2] Pancreatic necrosis and/or peripancreatic necrosis.

obtained at an early stage (within the first 4 full days after symptom onset) in 62.8% (49/78) of admissions: in 58.3% (35/60) of mild AP and in 77.8% (14/18) of severe AP admissions (table 2). Early CT during mild AP admissions was performed on days 0–2 in 48.6% (17/35) and on days 3–4 in 51.4% (18/35) of cases. During severe AP admissions this was 64.3% (9/14) and 35.7% (5/14), respectively. From the early CT scan results, the Balthazar scores were not significantly different between mild and severe AP: grades A–C in 91.4% (32/35) and 85.7% (12/14), respectively (table 2). Importantly, no early CT scan showed signs of necrosis or any other local complication of AP. Also, no alterative diagnoses were established. The etiology of AP was confirmed by early CT in 2 patients. However, this had already been documented by abdominal ultrasound in both cases; 1 patient was shown to have common bile duct stones and 1 patient had a pancreatic tumor. After early CT, the clinical management did not change in 89.8% (44/49) of admissions (table 2). Remark-

Table 2. Use and yield of early CT and observed management change during the hospital admissions for mild and severe AP

	Mild AP (n = 35)	Severe AP (n = 14)	p value
Timing of early CT scan			0.32[1]
Day 0	7 (20%)	3 (21.4%)	
Day 1	5 (14.3%)	3 (21.4%)	
Day 2	5 (14.3%)	3 (21.4%)	
Day 3	8 (22.9%)	3 (21.4%)	
Day 4	10 (28.6%)	2 (14.3%)	
Balthazar CT score			0.62[2]
Grade A	3 (8.6%)	–	
Grade B	10 (28.6%)	3 (21.4%)	
Grade C	19 (54.3%)	9 (64.3%)	
Grade D	3 (8.6%)	2 (14.3%)	
Grade E	–	–	
Necrosis/abscess			n.a.[3]
Management change			0.66[4]
No change	31 (88.6%)	13 (92.9%)	
Start of antibiotics[5]	4 (11.4%)	1 (7.1%)	

[1] Calculated after dichotomization: group 1: days 0–2; group 2: days 3–4.
[2] Calculated after dichotomization: group 1: grades A–C; group 2: grades D–E.
[3] Not applicable.
[4] Calculated after dichotomization: group 1: no change; group 2: start antibiotics.
[5] Start of antibiotics on the day of early CT or 1 day after.

ably, the only change in management within 24 h after CT scanning was to start antibiotics, despite absence of necrosis on CT (mild AP 11.4% of cases, severe AP 7.1% of cases).

Discussion

This is an observational multicenter study reporting on the practice and yield of CT scans acquired within the first full 4 days of admission in patients with a clinically established diagnosis of AP. It shows that early CTs are often performed during admissions for mild and severe AP alike. In either group the yield of early CT was low and had no relevant clinical management consequences. This seems an important observation considering the serious concerns that were recently expressed about the role of diagnostic CT and radiation exposure [27]. It has been shown that in the United States there is an increase in CT use and in CT-derived radiation dose in the population. As a consequence, the estimated proportion of cancer at-tributable to the use of CT may have increased. From these worrying observations it becomes clear that physicians should be critical when ordering a CT scan. In patients presenting with severe abdominal pain, an early CT may be indicated to exclude an alternative serious abdominal condition, such as a bowel perforation [11, 12]. In the present study, no additional alternative diagnoses were made by early CT. It confirmed the etiologic diagnoses in 2 patients already established by prior abdominal ultrasound scanning which, although having a lesser sensitivity than CT, is most commonly performed in patients presenting with signs and symptoms of AP.

Another indication to perform an early CT is to confirm the presence of early pancreatic necrosis in patients with signs of organ failure or systemic inflammatory response syndrome (SIRS). In this study, the majority of patients (89.2%) developed mild AP according to the Atlanta criteria. This proportion of mild versus severe AP in our series is in accordance with existing literature data [1–5]. In the group of patients who ultimately developed severe AP, no pancreatic necrosis was detected on early CT. These findings contradict the concept of pancreatic necrosis developing very early in the course of the disease, or at least its detection by early CT. The scientific proof of the early presence and detection of pancreatic necrosis is poor [15]. Only one study claimed that in all patients with necrotizing pancreatitis, necrosis is present within 96 h after onset of symptoms [28]. However, in that study the existence of necrosis early in the course of the disease was not demonstrated with contrast CT scanning, but ascertained by the measurement of serum CRP. A CRP >120 mg/l was chosen as the criterion that determined the early presence of 'pancreatic necrosis'. Indeed, all patients who eventually developed necrotizing pancreatitis had a CRP >120 mg/l within 96 h after onset of the symptoms, but this is no proof that necrosis was actually present within 96 h after symptom onset. A further limitation of studies reporting on (early) pancreatic necrosis in AP is the lack of information about the time between the onset of symptoms and the time of CT scanning [8, 14, 15, 23]. In addition, study populations are often not comparable as a result of different definitions used for severe and necrotizing pancreatitis. Several studies have shown that pancreatic necrosis is present on the first CT in 11.8–15.9% of patients admitted for AP [8, 14, 23]. However, CT scans in these studies were all performed within 4 days of admission, not within 4 days after symptom onset. In patients with proven necrotizing pancreatitis, necrosis was identified in 15.5% of cases within 72 h after admission, again not after symptom onset [15]. Finally, a promising

new CT modality is the use of a perfusion CT. Tsuij et al. [29] showed that in the early stage of severe AP ischemic changes that ultimately lead to pancreatic necrosis can be detected by a perfusion CT.

Even if the argument of timing (after symptom onset versus after admission) is put aside, it remains questionable if the finding of early pancreatic necrosis would have led to a change in management anyway. Clinical management in patients with early organ failure and SIRS, irrespective of the presence of necrosis, would be primarily supportive, such as fluid resuscitation and mechanical ventilation [4, 30]. Notably, early death (≤2 weeks after admission) results primarily from multisystem organ failure, whereas late death occurs mainly from complications in patients with infected necrotic tissue [31–33]. In particular, organ failure or SIRS within 7 days of onset of AP is associated with a high early mortality [34]. The urge and clinical relevance to detect pancreatic necrosis in the early course of AP seems less important. Secondly, at present, there is only weak evidence to start prophylactic antibiotics in case of pancreatic necrosis [35]. From this point of view, it is rather surprising that in this series in 10.2% (5/49) of patients, prophylactic antibiotics were started in the absence of necrosis. In fact, according to guidelines, only infected pancreatic necrosis as proven by fine-needle aspiration would prompt for antibiotic therapy. Definite management by either surgical or endoscopic necrosectomy will not likely be performed early in the course of the disease, but if at all possible postponed to the third or fourth week of the disease course, at which time there is a much clearer demarcation between viable and necrotic tissue [30, 36, 37].

It has also been suggested to use early CT scanning as a prognostic indicator of the severity of AP [26, 38]. However, such indication is disputable [4, 9, 11, 14–20]. At present, several prognostic indicators are available, but none being perfect [4, 7, 12, 39]. Ongoing clinical assessment coupled with the use of a multifactor scoring system and imaging studies probably is the best way to predict disease severity [11]. However, a serum CRP level >150 mg/l at 48 h after disease onset is a simple and cheap indicator of severity and a good alternative for an early CT [17, 18].

A potential limitation of this observational study is that physicians may have behaved differently with regard to clinical management after a patient consented to participate in the study. The results of this study do not support this concern as the use of CT clearly was not according to internationally established guidelines. Moreover, patients from this report were a selection of all patients with (recurrent) acute and/or chronic pancreatitis patients that were included in the study. The specific aim of this study, in particular practice and yield of CT, was not specifically stated other than the remark that clinical management would be monitored.

Although the absolute number of patients with severe AP (n = 18) in the present study was relatively low, the proportion in relation to patients with mild AP, 89.2 and 10.8%, respectively, is in accordance to what is reported in the literature [1–6].

It is important to note that the Balthazar score and the assessment of local complications (e.g. pseudocysts, abscesses) were based on reports from local radiologists as they were also used by the attending physicians in the clinical management of these patients. Considering our study aim, such an approach provides a fairer assessment of the real-world impact of early CT than an expert CT review would have provided. Re-evaluation by an expert radiologist of the CT scans from the severe AP patients was performed to confirm adequate classification of local complications by the attending radiologists.

Multiple surveys have shown that compliance of practitioners to published (evidence-based) guidelines of the different national and international scientific societies on the management of AP is suboptimal [8, 40–45]. Unfortunately, the results of the present study support these observations. Implementation strategies are urgently needed to increase the actual compliance to these guidelines [45].

In summary, in this observational multicenter study, a CT scan was frequently acquired early in the course of AP, but its yield was low and had no implications with regard to clinical management. An early CT scan should only be obtained when there is clinical doubt about the diagnosis of AP and other life-threatening conditions must be excluded. For demonstration of pancreatic necrosis, one should preferably postpone imaging beyond the fourth day after the onset of symptoms in the presence of additional circumstantial evidence of a predicted severe disease outcome (e.g. CRP >150). Given the outcome of this study, it seems prudent that clinicians should be more restrictive, especially in mild AP, in the use of early CT to prevent unnecessary radiation exposure and save costs.

Addendum 1

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