Variability of contrast enhancement of pancreas on computed tomography in patients with acute pancreatitis and isolated extrapancreatic necrosis

P. Gupta[1], N. Verma[1], J. Samanta[2], H. Mandavdhare[2], V. Sharma[2], S. Kant Sinha[2], U. Dutta[2], R. Kochhar[2]

(1) Department of Radiodiagnosis and Imaging ; (2) Department of Gastroenterology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India 160012.

Abstract

***Background and study aim* : To evaluate the variability in the enhancement of pancreas on computed tomography (CT) in patients with acute pancreatitis (AP) and isolated extrapancreatic necrosis (EPN) and to investigate whether it affects the extrapancreatic findings and patient outcomes.**

***Patients and methods* : This retrospective study comprised of consecutive patients with isolated EPN evaluated between April 2017 and April 2019. A radiologist measured the pancreatic attenuation values (PAV) of head, body, and tail on a contrast enhanced CT. Using a cut-off PAV of 100HU, patients were divided into two groups. The extrapancreatic CT findings and outcome parameters were compared between the two groups.**

***Results* : Thirty patients (mean age, 42.13 years, 17 males) with isolated EPN were evaluated. The mean PAV in the head, body, and tail was 83.13 HU (range, 59-161), 84.17 HU (range, 60-160), and 82.23 HU (range, 53-137). The overall mean PAV was 83.12 HU (range, 58-152). There were six patients with overall mean PAV≥100 HU. The group with PAV≥100 HU had a higher number of patients with infected necrosis (66.6% vs. 14.2%, P=0.018). PAV had a significant association with length of hospitalization (P=0.045).**

***Conclusion* : There is significant variability in the pancreatic enhancement on CT among patients with AP and isolated EPN. Patients with PAV≥100 HU had a significantly longer hospital stay. This, however, may be related to a greater number of patients with infected necrosis in this group.** (Acta gastroenterol. belg., **2020**, 83, **593-597**).

Keywords : acute pancreatitis, computed tomography, extrapancreatic necrosis, enhancement.

Introduction

Extrapancreatic necrosis (EPN) without pancreatic necrosis (PN) has been recognized as a distinct clinical entity that has a better prognosis compared to patients with PN or combined PN/EPN (1). Over the last few years, several studies have reported variable clinical outcomes in patients with isolated EPN (1-6). Few studies have identified different outcomes in two types of EPN, limited and extensive (2, 5). However, none of the studies have reported the parenchymal enhancement characteristics in patients with isolated EPN. As the inflammatory cascade in necrotizing pancreatitis (whether PN/ EPN) is more severe compared to interstitial pancreatitis, pancreas even in patients with isolated EPN may be expected to have derangements in microcirculation and hence differences in enhancement. We hypothesize that in AP with isolated EPN, the pancreatic parenchyma has a spectrum of enhancement between necrosis (≤30 HU) at one end and normal pancreatic enhancement at the other end (100-150 HU) (7). In this retrospective study, we evaluated this variability in the enhancement of pancreas in patients with AP and isolated EPN. We also assessed the association between the pancreatic enhancement and the extrapancreatic CT findings and clinical outcomes.

Materials and methods

This was a retrospective study of consecutive patients with AP and isolated EPN evaluated by a gastroenterology unit of a tertiary care referral centre between April 2017 to April 2019. The institutional ethics committee approved the study. The diagnosis of AP was based on the revised Atlanta classification (8). The diagnosis of EPN was based on a contrast-enhanced CT performed between day 5 and 7 after pain onset. Isolated EPN was diagnosed when there were no non-enhancing areas in the pancreas, and there were changes in the peripancreatic fat that exceeded fat stranding (1). EPN was classified as limited or extensive based on the extension to paracolic gutters (2). The pancreatic enhancement was assessed quantitatively.

CT assessment

Contrast-enhanced CT scans were performed on multidetector-row CT scanners (64-, 128- or 256-detector row scanners, ACT, GE Healthcare ; Somatom Definition Flash, Siemens Healthcare ; Philips iCT, respectively). CT scans were acquired 65 seconds following intravenous injection of 80-100 ml of non-ionic contrast (Omnipaque ® 300mg/mL, GE Healthcare). The entire abdomen was scanned from the domes of the diaphragm to the pubic symphysis.

The images were assessed independently by two radiologists (PG and NV with six years and three years of experience in abdominal imaging, respectively) on Oxirix® viewer (Pixmeo, Geneva, Switzerland). The differences in the assignment of EPN were resolved in consensus. The pancreatic attenuation values (PAV)

Correspondence to : Dr. Pankaj Gupta, Assistant Professor, Department of Radiodiagnosis and Imaging, PGIMER, Chandigarh, India 160012.
E-mai l: Pankajgupta959@gmail.com

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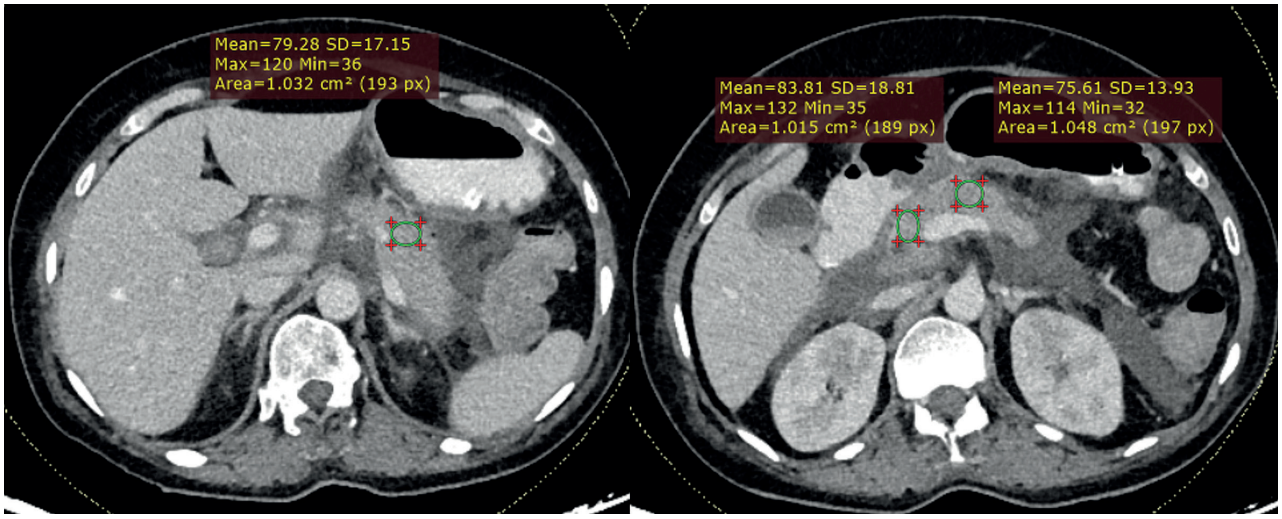

Figure 1. — Axial CT images in a 46-year-old patient with gallstone induced acute pancreatitis with isolated EPN. The pancreatic attenuation values were less than 100 HU in the head, body and tail (absolute values given by cursors).

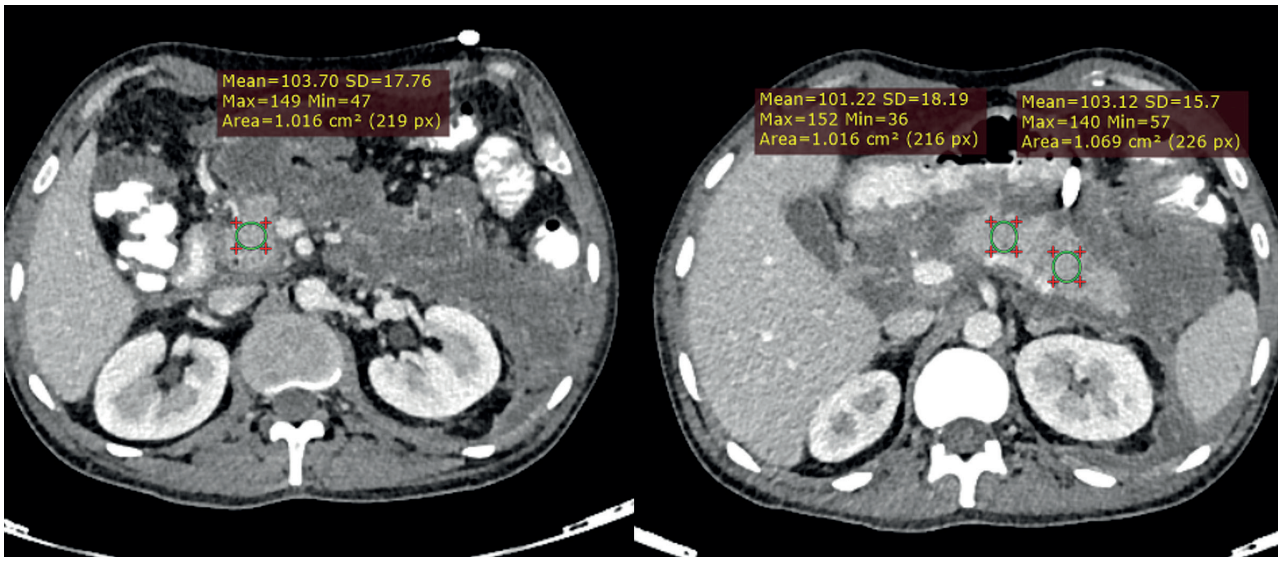

Figure 2. — Axial CT images in a 36-year-old patient with alcohol induced acute pancreatitis with isolated EPN. The pancreatic attenuation values were greater than 100 HU in the head, body and tail (absolute values given by cursors).

were obtained. Both the radiologists were blinded to the clinical outcome parameters. A region of interest of 1 cm^2 was placed in the head, body, and tail. The overall mean attenuation was calculated in each case by calculating the mean of these three values. A cut-off value of PAV of ≥100 HU was used to categorize patients into two groups (Figure 1 and 2). Modified CT severity index (MCTSI) was calculated. The extrapancreatic CT findings were also recorded. These included the maximum dimension of EPN, the extension of EPN to the paracolic gutters, and ascites. The patients were divided into two groups based on the size of the collection : <10 cm and ≥10 cm. This is based on the previous studies on EPN as well as our experience, showing that this size cut off allows accurate categorization of patients in terms of their clinical outcome. (2,3,9). The mean attenuation of the EPN was calculated by placing 1 cm^2 ROIs in the collection (one ROI for every 3 cm of the collection). Based on the CT attenuation of EPN, patients were divided into two groups : <20 HU and ≥20 HU. Infection in EPN was diagnosed based on the presence of air and culture results in patients who underwent drainage.

Clinical assessment and Patient management

Following clinical details were recorded in each group : etiology and severity (based on revised Atlanta classification), percutaneous drainage, surgery, duration of hospital stay, need for intensive care unit (ICU) admission, readmission, and mortality within 12 weeks after discharge from the hospital.

Standard recommendations were followed for patient management. These included pain alleviation, fluid

resuscitation, organ support, and nutritional support (enteral or parenteral). Antibiotics were used for suspected infected EPN and extra-pancreatic infections. Infection of EPN was suspected based on the worsening of patients' condition or by the presence of air within the collection on CT scan. Infection was confirmed by culture of the fluid aspirated in patients undergoing drainage/ surgery.

Statistical analyses

Statistical analysis was carried out using commercially available software (IBM Statistical Package for the Social Sciences Statistics, release 23 ; SPSS, Chicago, Ill). The categorical data were reported as frequencies and percentages. The continuous data were expressed as mean with range. The comparison of categorical data was carried out by using the Chi-square test or Fischer's exact test. The comparison of continuous data was carried out by using the independent Student's T-test or Mann-Whitney U test. All statistical analysis was carried out at 5% level of significance, and a *P*-value < 0.05 was considered significant.

Results

Demographics details and CT findings

During the study period, 125 patients with AP were evaluated. Thirty patients with isolated EPN were included in the study. The mean age was 42.13 years (range, 19-70 years). There were 17 males and 13 females. The etiology of AP was alcohol (n=14), followed by gallstone disease (n=7), endoscopic retrograde cholangiopancreatography (n=4), idiopathic (n=3), pancreas divisum (n=1) and hypertriglyceridemia (n=1). Mean MCTSI was 5.87 (range, 4-6). Majority of the patients (n=28) had an MCTSI of 6. Ten patients had moderately severe, and 20 patients had severe acute pancreatitis. Mean size of the EPN was 9.49 cm (range, 3-16 cm). Twelve patients had EPN≥10 cm. The extension of EPN to the paracolic gutters was seen in seven patients. Mean attenuation of EPN was 15.43 HU (range, 8-30 HU). Attenuation≥20 HU was recorded in five patients. Thirteen patients had ascites. Table 1 highlights the important demographic parameters and CT findings in the study group.

Pancreatic enhancement characteristics

Mean PAV in the head, body, and tail were 83.13 HU (range, 59-161), 84.17 HU (range, 60-160), and 82.23 HU (range, 53-137). The overall mean PAV was 83.12 HU (range, 58-152). There were six patients with an overall mean PAV≥100 HU (Figure 3).

Comparison of PAV with CT findings

There were no significant differences in the age, gender, etiology, MCTSI, and severity of pancreatitis between the two groups. Similarly, there was no significant difference in the size of EPN and the number of patients with extension of EPN to the paracolic gutters in both the groups. Among patients with PAV<100 HU, ascites was recorded in 11 patients compared to two patients in the groups with PAV≥100 HU (P=0.580). EPN attenuation>20 HU was recorded in 2 (8.33%) patients in the group with PAV<100 HU compared to 3 (50%) patients in the group with PAV≥ 100 HU (P=0.014).

Table 1. — **Baseline characteristics in the two groups**

Parameters	PAV<100 HU (n=24)	PAV≥100 HU (n=6)	P value
Mean age (years)	40.88±13.456	47.17±7.387	0.283
Gender (M/F)	15/9	2/4	0.360
Severity (Atlanta) *Moderate* *Severe*	 9 (37.5%) 15 (62.5%)	 1 (16.6%) 5 (83.4%)	0.633
Modified CTSI	5.92 (4-6)	5.67 (4-6)	0.250
Infected necrosis	3 (14.2%)	4 (66.6%)	**0.016**
Size of EPN (cm)	9.5	9.4	**0.948**
Attenuation of EPN (HU)	14.7	18.3	**0.085**
Ascites	10 (41.6%)	3 (50%)	**0.713**

PAV : pancreatic attenuation value, M-male, F-female, CTSI-CT severity index, EPN-extrapancreatic necrosis, HU-Hounsfield unit, ICU-intensive care unit.

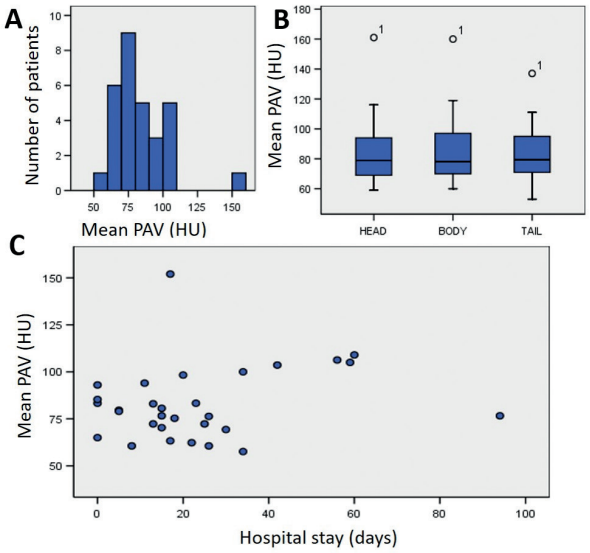

Figure 3. — A. Bar diagram shows the pancreatic attenuation values (PAV) in 30 patients with isolated EPN. B. Box plots show no significant difference in the PAV in the head, body and tail. C. Scatter plot shows the association between the PAV and length of hospital stay.

Comparison of PAV with clinical outcomes.

Infected necrosis was recorded in seven patients, 4/6 in the PAV≥100 HU group and 3/21 in the PAV<100 HU group (P=0.018). The mean length of hospital stay was 18.71±19.22 days in patients with mean PAV<100 HU compared with 42.33±19.58 days in patients with mean PAV ≥ 100 HU (P=0.012) (Figure 3). Readmission was required in 12.5% (3/21) patients in the mean PAV<100 group compared with 50% (3/6) patients in PAV>100 HU (P=0.040). There was no association of the mean

Table 2. — **Clinical outcomes in the two groups**

Parameters	PAV<100 HU (n=24)	PAV≥100 HU (n=6)	P value
Mean hospital stay (days)	18.71±19.22	42.33±19.58	**0.012**
Need for ICU stay	9 (37.5%)	3 (50%)	0.660
Mean ICU stay (days)	2.58	7.67	0.374
Readmission (%)	3 (12.5%)	3 (50%)	**0.040**
Need for drainage	14 (66.6%)	2 (33.3%)	0.272
Surgery	1 (4.2%)	0	1.00
Mortality	4 (16.6%)	0	0.283

PAV: pancreatic attenuation value, ICU-intensive care unit

PAV with the need for ICU admission, need for drainage, surgery, and mortality. The association of PAV with clinical outcomes is shown in Table 2.

Discussion

CT scan plays a vital role in imaging of patients with acute and chronic pancreatitis (9,10,11). It can also depict various abdominal and thoracic complications of acute pancreatitis (12,13). CT scan also predicts the severity of pancreatitis, and occurrence of various complications, such as gastrointestinal fistula (7,14,15). CT is not indicated for mild AP and in order to optimize radiation exposure a single-phase CT scan should be preferred (16).

The revised Atlanta classification divides AP morphologically into interstitial edematous and necrotizing pancreatitis (13). The latter is associated with significant morbidity and mortality. However, no distinction was made between PN with or without EPN and isolated EPN. Studies over the past few years have shown that EPN should be considered a separate clinical entity as it has a less severe clinical course and an outcome that is more favorable than PN (1-6). The site and size of EPN is highly correlated with the clinical outcomes in patients with AP with a performance better than MCTSI for certain outcomes (9). However, none of the published studies have evaluated the variability in the pancreatic parenchymal enhancement on CT in patients with EPN. In the present study, we found that patients with EPN show significant variability in the PAV and a higher PAV (≥100 HU) was associated with a higher frequency of infected necrosis and more extended hospital stay.

Healthy pancreas enhances homogeneously with CT attenuation between 100-150 HU (7). Variabilities in the pancreatic enhancement have been reported between normal subjects as well as in the same individual between different regions of pancreas. In a study by Delrue et al. comprising normal subjects, the enhancement differences in different parts of pancreas ranged between 2 and 21 HU using dual-energy CT and perfusion CT (PCT) (17). The authors attributed these differences to many physiological factors, including age, cardiac status, fatty infiltration, and BMI. Balthazar emphasized that regional variations of pancreatic enhancement are rare and of smaller amplitude (16). Balthazar also suggested differences in the enhancement of pancreas between normal individuals could be expected. However, these should not discourage from using the threshold enhancement values in clinical practice (18). The variability of pancreatic enhancement in the setting of EPN has not been studied previously. The variable PAV reported in our study could be attributed to several factors, both related to pancreatic injury and physiological factors. The changes at the level of pancreatic microcirculation in AP are well documented (19). Several studies have shown that a PCT may predict PN within 24 hours of the onset of AP (20, 21).

Among the outcome parameters, a significant association was found between the PAV and length of hospital stay. The hospital stay was significantly longer in patients with mean PAV≥100 HU. We also found infected necrosis to be more common in patients with mean PAV≥100 HU. The reason for these observations is not apparent. However, this could be due to reperfusion injury. The ischemia-reperfusion mechanism has been described in AP. However, its impact on pancreatic enhancement has not been studied (22,23). Additionally, significantly greater number of patients with mean PAV≥100 HU had infected necrosis. This could have contributed to the increased length of hospitalization. A prospective study evaluating all the potential factors that could affect pancreatic enhancement in patients with isolated EPN could clarify the reasons for our results.

The categorization of patients with isolated EPN into two groups based on PAV (with 100 HU as the cut-off) was based on the authors' experience and has not been described previously. We did statistical analysis using different cut-off values between 70 and 105 HU and found that with 100 HU as the cut-off, there was difference in few outcomes between the groups. However, we do acknowledge the fact that with a larger sample size, this cut-off value of PAV may change. Nevertheless, the novelty of this study lies in the proposal that there is a possibility of distinct subgroups even in the patients with isolated EPN based on the changes in the pancreas. Enhancement of pancreas could be used as a surrogate marker of changes in the pancreas in this setting. A study evaluating pancreatic PCT findings in patients with isolated EPN would be exciting and would lend strength to our results. Our results do suggest that this area is open to research that could utilize advanced imaging methods and could explain variability in the outcomes of patients with isolated EPN.

We acknowledge several limitations to our study. First, all the serial CT scans were not evaluated. It would be interesting to see the progression of changes in PAV during the course of AP. However, a study has reported that PN, as demonstrated by CT, remains stable in most patients (24). Second, the detailed co-morbidity profile of the patients was not available in this retrospective study. Co-morbid conditions, particularly cardiac diseases, can

lead to differences in pancreatic enhancement. Finally, the number of patients with PAV≥100 HU was small. This could be responsible for the lack of significant association with outcome variables other than the length of hospital stay.

In conclusion, this novel study suggests that there is significant variability in pancreatic enhancement among patients with isolated EPN. The association with clinical outcomes based on pancreatic attenuation values, however, needs more prospective studies and studies utilizing PCT in patients with isolated EPN will provide further insights into this exciting subject.

Conflict of interest

None

Financial Disclosure

None

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