Journal of Gastroenterology and Hepatology
JGHF
doi:10.1111/jgh.13384

REVIEW

Extra-pancreatic necrosis alone: Contours of an emerging entity

Vishal Sharma, Surinder S Rana and Deepak K Bhasin

Department of Gastroenterology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Key words
acute pancreatitis, computed tomography, endosonography, necrosectomy, pancreatic necrosis.

Accepted for publication 15 March 2016.

Correspondence
Dr Surinder Rana, Associate Professor, Department of Gastroenterology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh 160012, India.
Email: drsurinderrana@gmail.com

Abstract

Acute pancreatitis is of two morphologic types: interstitial edematous pancreatitis that is not associated with any tissue necrosis and necrotizing pancreatitis wherein the pancreatic parenchyma with or without varying amount of extra-pancreatic tissue/fat undergoes necrosis. Necrotizing pancreatitis has a worse outcome compared with interstitial pancreatitis because of increased severity related to a heightened systemic response and cytokine storm associated with tissue necrosis. Increasingly, an entity of extra-pancreatic necrosis (EPN) alone, wherein the pancreatic parenchyma is normal on an enhanced computed tomographic scan but the peri-pancreatic tissues undergo necrosis, is being recognized. Available data suggest that the outcomes in patients with EPN alone are between the excellent prognosis of patients with interstitial and adverse prognosis of patients with necrotizing pancreatitis. The extent of EPN also seems to determine the outcome. This review summarizes the currently available literature on this entity and various radiological scores that have been suggested to determine the presence and stage of EPN.

Introduction

Acute pancreatitis is a disease of varying severity and is recognized primarily to be of two morphological types: interstitial edematous pancreatitis and necrotizing pancreatitis. The important distinction between these two entities is the absence or presence of pancreatic parenchymal necrosis.[1] Pancreatic necrosis is an important determinant of prognosis in acute pancreatitis, and its presence increases the risk of morbidity and mortality.[1] Necrotizing pancreatitis, as per the revised Atlanta classification, encompasses an entire spectrum of patients with combined pancreatic parenchymal and peri-pancreatic necrosis as also patients with either of these two phenomena alone. Many recent reports, however, seem to suggest that the entity of peri-pancreatic necrosis alone (extra-pancreatic necrosis [EPN] alone) has prognosis that is better than pancreatic parenchymal necrosis but worse than interstitial pancreatitis.[2–5] This has led to suggestions that EPN alone be considered as a distinctive third group while classifying acute pancreatitis. The present review summarizes the available literature about this entity and presents the current evidence comparing the outcome of patients with EPN alone with that of patients with interstitial and necrotizing pancreatitis (pancreatic with or without extra-pancreatic tissue/fat necrosis).

Defining extra-pancreatic necrosis alone. Possibly, the first description of this entity was reported in 1989 by Howard and Wagner who reported their surgical and pancreatographic findings in 13 patients who had survived an episode of acute severe pancreatitis. The authors reported clear delineation of necrotic retroperitoneal tissue and thereby suggested that late necrosectomy may be easier. The authors expected the pancreas to be completely necrosed in such an extensive and severe disease, but to their surprise, the pancreatography revealed normal pancreatic duct suggesting viable pancreatic parenchyma.[6] Angelini *et al*. had previously reported a dichotomy in outcomes of patients with acute necrotizing pancreatitis with some of them developing overt endocrine insufficiency while others having a normal endocrine function as well as normal pancreatographic findings.[7] In 1994, Madry *et al*. also reported patients of acute pancreatitis (AP) having retroperitoneal tissue necrosis with viable pancreatic parenchyma. Some of these patients also had colonic necrosis presumably because of extension of peri-pancreatic necrosis. This subset of patients with EPN alone had low mortality.[8] However, the term EPN alone was used by Sakorafas *et al*. in 1999 for a distinctive group of patients who had a better prognosis than patients with combined parenchymal and EPN.[9]

Pancreatic necrosis is defined on the basis of lack of enhancement of pancreatic parenchyma on a contrast enhanced computed tomographic (CECT) scan. This non-enhancement may involve the pancreatic parenchyma focally or diffusely.[1,3] EPN has been variably defined. Singh *et al*. defined it to be present when there is normally enhancing pancreas on computed tomographic examination with evidence of extra (peri) pancreatic collections, which may be liquid or heterogeneous, and thought it to represent necrosis of extra-pancreatic fat and tissues.[2] Others have described EPN to be any peri-pancreatic changes that are more than mere fat stranding (Fig. 1).[3,4] When the EPN extends into the para-colic gutters or into the pelvis, it has been termed as extensive EPN (Fig. 2).[4]

Pathophysiology. The genesis of AP is related to activation of inflammatory cascade that is precipitated by intracellular

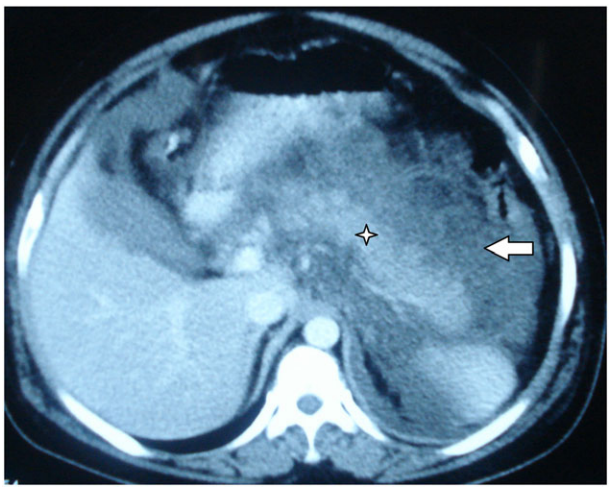

Figure 1 Extra-pancreatic necrosis alone: abdominal computed tomography showing areas of extra-pancreatic necrosis (arrow) and normal enhancing pancreas (star).

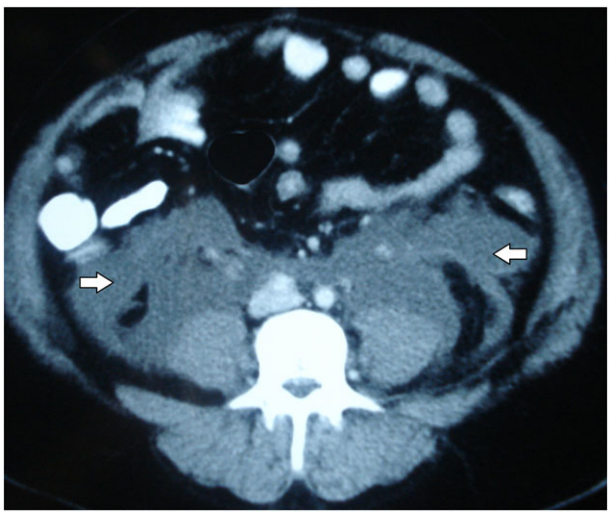

Figure 2 Extensive extra-pancreatic necrosis: computed tomography showing extra-pancreatic necrosis extending into the para-colic gutters bilaterally (arrows).

pancreatic pro-enzyme activation This premature pancreatic enzyme activation is believed to be a consequence of co-localization of digestive enzymes and lysosomal contents.[10] The EPN, which occurs in most patients with pancreatic necrosis as well as in the absence of any detectable parenchymal necrosis, is possibly because of necrosis of peri-pancreatic fat/tissues by the leaking pancreatic enzymes.[10,11] This fat necrosis releases the adipocytokines into the blood, and therefore, determination of blood levels of adipocytokines may predict the presence and extent of EPN. Studies that report an increase in the levels of adipocytokines in patients with EPN lend support to this proposed phenomenon. Some of the adipocytokines such as resistin and vistafin have been found to be more specific for visceral adipose tissue, and their serum levels have been demonstrated to correlate with peri-pancreatic necrosis.[12–14] In a report of 23 patients, resistin levels in serum were found to correlate with clinical severity as determined by Ranson's and Acute Physiology and Chronic Health Evaluation (APACHE-II) scores.[14] Patients with higher Schroder score on computed tomography (CT) had higher resistin and leptin levels vis-à-vis those with lower Schroder CT score. Of the three markers evaluated, namely, adiponectin, leptin, and resistin, serum resistin levels correlated best with the extent of EPN.[14] The Schroder score is a scoring system based on the evaluation of extra-pancreatic findings in AP and is described in detail later.[15] In another report on 50 patients with AP, the same group reconfirmed their previous findings.[12,13] The authors reported that serum resistin levels correlated with the extent of EPN as well as with clinical severity and mortality.[12] The same group also evaluated serum vistafin, a novel adipocytokine, in the same cohort of patients and demonstrated that serum vistafin levels correlate with clinical severity, extent of EPN, and mortality in acute pancreatitis. Interestingly, the authors found that admission serum vistafin levels were better than serum C-reactive protein in predicting end points.[13] The results of the aforementioned studies suggest that the necrosis of visceral fat plays an important role in pathophysiology of EPN. Obesity is a well-recognized predictor of severe pancreatitis although it remains to be determined if it is an important adverse prognostic factor in EPN alone also.[16]

Frequency of extra-pancreatic necrosis alone (Table 1). Multiple reports have described the occurrence of EPN alone, but the prevalence has been reported to vary. Interestingly, a large report from the Dutch pancreatitis group differs from some of the other reports on EPN by reporting that almost half of the patients with acute necrotizing pancreatitis have EPN alone.[3] However, most others have reported the frequency of EPN to be less than this study. Sakorafas *et al*. reported the frequency to be 19% among the 62 patients with necrotizing pancreatitis who underwent surgery.[9] Singh *et al*. reported that majority of their patients had interstitial pancreatitis while the frequency of EPN alone was 7.5%.[2] We reported EPN alone to be present in 22.5% of the patients with AP seen at a large tertiary care center in North India, but the study possibly had a referral bias as lesser number of patients had interstitial pancreatitis (10%).[4] A recent report from China reported EPN alone to constitute 6.3% of their patients of AP, but there was a selection bias as study included only those patients of necrotizing pancreatitis who underwent intervention.[5]

Prognosis of extra-pancreatic necrosis alone (Table 1). Sakorafas reported detailed clinical and imaging findings as well as outcomes in patients with EPN alone. They found that 12 patients (19%) with EPN alone had lower APACHE-II scores at admission, excellent outcomes as determined by need for repeated surgery, length of hospital stay, mortality, and long-term development of exocrine and endocrine dysfunction.[9] Lankisch *et al*. reported a large cohort of 228 patients with first attack of AP who underwent CECT within 72 h of admission. While the authors did not specifically deal with EPN alone, they did compare the patients who had evidence of

Table 1 Summary of major reports on patients with EPN alone

	Sakorafas *et al.*[9]	Singh *et al.*[2]	Bakker *et al.*[3]	Rana *et al.*[4]	Wang *et al.* 2016[5]
Total number	62	188	639	213	777
Distribution *N* (%)					
IP	NA	140 (74.5)	NA	21 (10)	443 (57)
EPN	12 (19.4)	14 (7.45)	315 (49)	48 (22.5)	49 (6.3)
NP	50 (80.6)	34 (18.0)	324 (51)	144 (67.5)	285 (36.7)
EPN cases	12	8	315	48	49
Age	55 (33–93)	46 ± 11	58 (44–72)	39.8† ± 13.2	42.3 ± 10.7
Gender (male)	10 (83%)	7 (88%)	184 (58%)	136† (63.8%)	29 (59.2)
Etiology	Gallstones (41%)	Alcohol (50%)	Gallstones (47%)	Alcohol† (47%)	Gallstone (42.9%)
APACHE-II	5.8 (0–19)	8 (5–13.5)	7 (5–10)	NA	8 (4–8.5)
BMI	26 ± 2	≥30: 4 (50%)	NA	NA	27.9 ± 3.3
Infected necrosis	9 (75%)	NA	51 (16%)	NA	10 (20.4%)
ICU	All	3 (38%)	NA	NA	23 (46.9%)
Intervention			57 (18%)	7 (14.6%)	NA
Surgery	All	NA	40 (13)	2 (4.2%)	NA
POF	NA	2 (25%)	66 (21%)	25 (52.1%)	6 (12.2%)
Mortality	1 (8%)	1 (13%)	29 (9%)	4 (8.3%)	1 (2.1%)
Remark	Only surgical patients	Provides details about eight nontransferred patients only	Multicenter report	Possible referral bias and low number of interstitial pancreatitis	Only includes patients who underwent an intervention

†Separate EPN alone data not provided for these parameters.

APACHE-II, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; EPN, extra-pancreatic necrosis; IP: interstitial pancreatitis; NP: necrotising pancreatitis; POF, persistent organ failure.

extra-pancreatic fluid collections (40%) with those not having any extra-pancreatic collections (60%). The authors reported an increased requirement of dialysis, artificial ventilation, pseudocyst formation, and surgery in the patients with extra-pancreatic fluid collections. The mortality was also higher in patients with extra-pancreatic fluid collection (15%) as compared with those without collection (1%). The authors also compared outcomes in patients with increasing degree of extra-pancreatic fluid collections and made three subgroups: anterior para-renal space collections alone, both anterior and posterior para-renal space involvement, and involvement of peri-splenic area along with anterior and posterior para-renal space. As the extent of extra-pancreatic involvement increased, the need for organ support and surgery also significantly increased.[11] Singh *et al*. reported data from 306 patients with AP and after exclusions studied 174 patients with interstitial pancreatitis, 34 patients with parenchymal pancreatic necrosis, and 14 patients with EPN alone. After excluding transferred patients, the authors compared 149 directly admitted patients of interstitial pancreatitis with eight patients of EPN alone and found that patients with EPN alone performed worse than interstitial group vis-à-vis need for intubation, dialysis, and vasopressor support.[2]

Bakker *et al*. reported the findings of 639 patients with necrotizing pancreatitis and found that 49% ($n = 315$) of patients had EPN alone.[3] They also found that absence of parenchymal necrosis in patients with EPN alone seems to confer a better prognosis with respect to occurrence of persistent organ failure (POF), need for intervention, and mortality. Moreover, the authors observed that the presence of infected pancreatic necrosis seemed to confer a dismal outcome irrespective of presence or absence of parenchymal pancreatic necrosis.[3] We have previously reported 48 patients of EPN alone and found that the clinical course differed between interstitial pancreatitis, EPN alone, and combined pancreatic parenchymal and EPN groups. We found that the frequency of POF was higher in patients with EPN alone when compared with interstitial pancreatitis while the need for intervention, ascites, and pleural effusion was higher in the patients in the combined necrosis group as compared with patients with EPN alone.[4]

In a recent study of 334 patients of acute necrotizing pancreatitis of whom 49 (14.67%) had EPN alone, Wang *et al*. also reported the relatively good outcome associated with EPN alone vis-à-vis combined necrosis.[5] However, this study included only those patients who had an intervention and excluded patients who improved with conservative management.[5] Another report from Germany reported that 2% of their patients initially labeled as interstitial pancreatitis had EPN and therefore contributed to a relatively high mortality (5.5%) in this group. However, the study was limited by the fact that it was a retrospective study.[17]

The results of these studies suggest that EPN alone represents a distinct morphological category of acute pancreatitis. The prognosis of patients with EPN alone is better than patients with pancreatic necrosis or combined necrosis but worse than patients with interstitial pancreatitis and therefore deserves recognition as a distinctive clinical entity. On pooled analysis of the three reports that compared mortality between interstitial and EPN, alone the odds of mortality were found to be lower in interstitial pancreatitis (Fig. 3). Similarly, the odds of mortality were lower in EPN alone vis-à-vis necrotising pancreatitis (Fig. 4).

Radiological evaluation of extra-pancreatic necrosis (Table 2). Extra-pancreatic necrosis alone, as mentioned earlier, represents a subset of patients with AP who have well-enhancing pancreas on CECT scan but have evidence of extra-pancreatic fat/tissue necrosis. The extent of EPN is variable, and many CT

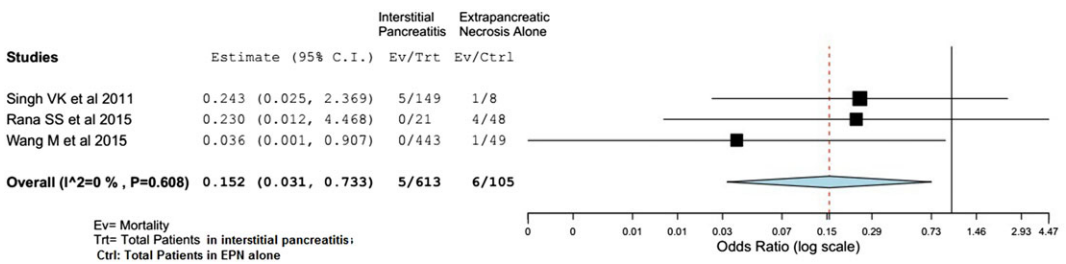

Figure 3 Forrest plot depicting odds of mortality in interstitial pancreatitis and extra-pancreatic necrosis alone.

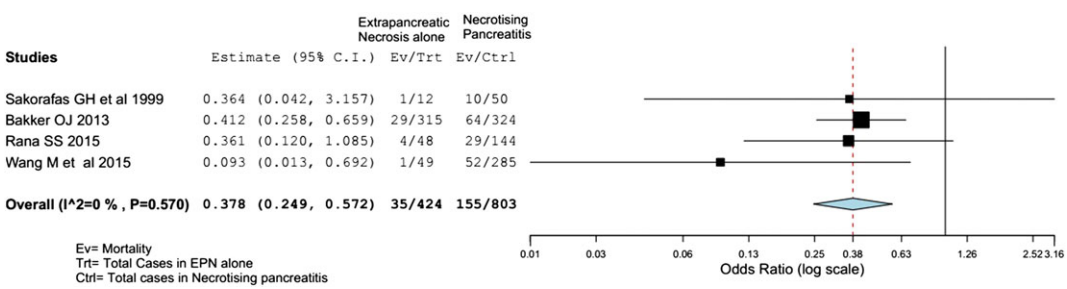

Figure 4 Forrest plot depicting odds of mortality in extra-pancreatic necrosis alone and necrotizing pancreatitis.

Table 2 CT scores in use for acute pancreatitis

Score	Pancreatic Changes	Extra pancreatic changes	Components	Score range
			Others	
Balthazar	Grades A (normal pancreas) and B (pancreatic enlargement)	Grades C (fat stranding), D (single collection), and E (≥2 collections)	NA	Grades A–E
CTSI	Pancreatic changes: 1 (Balthazar A) and 2 (Balthazar B) Pancreatic necrosis: ≤30%: 2, 30–50%: 4, and >50%: 6	Extra-pancreatic changes: 2 (Balthazar C), 3 (Balthazar D), and 4 (Balthazar E)	NA	Scores 0–10
MCTSI	Pancreatic changes: 0 (Balthazar A) and 2 (Balthazar B and C) Pancreatic necrosis: ≤30%: 2 and >30%: 4	Four (extra-pancreatic changes in form of collections or fat necrosis)	Two points for features like pleural effusion, ascites, vascular complications, and colonic/bowel involvement	0–10
EPIC	Not used	Retroperitoneal inflammation: 1 if unilateral, 2 if bilateral	Pleural effusion: 1 unilateral, 2 bilateral Ascites: 1 one location, 2 points if >1 location Peritoneal fluid	0–7
MOP	None	Mesenteric edema	None	Grades 1–3
Renal rim grade	None	Grade 1: no changes Grade 2: renal rim present Grade 3: renal rim destroyed		
Schroder	None	Edema around part of pancreas: 1 Edema around entire pancreas: 2	Ascites: 1 Pleural effusion: 1	0–7
		Mesenteric fat edema:1 Peri-renal fat edema: 1	Dilated bowel loops (air fluid levels): 1	

CT, computed tomography; CTSI, CT severity index; EPIC, extra-pancreatic inflammation on CT; MCTSI, modified CTSI; MOP, mesenteric edema and peritoneal fluid.

scoring systems have attempted to quantify the extra-pancreatic involvement. The traditionally used Balthazar grading of AP predominantly focuses on pancreatic changes, but grades D and E represent single and two or more fluid collections, thereby also including extra-pancreatic changes in the overall assessment.[18] The CT severity index (CTSI) uses Balthazar grade along with the amount of pancreatic necrosis to stratify severity in acute pancreatitis.[19] Modified CTSI (MCTSI) as proposed by Mortele also utilizes changes like ascites, pleural effusion, and vascular complications apart from (peri) pancreatic changes and necrosis.[20] As is apparent, none of these scoring systems focuses completely on the EPN or its extent.

In contrast to the aforementioned scores, extra-pancreatic inflammation on CT (EPIC) score completely ignores pancreatic necrosis but is based on features suggestive of systemic and extra-pancreatic inflammation. The score consists of four components (pleural effusion, ascites, retroperitoneal inflammation, and mesenteric inflammation) and ranges from 0 to 7.[21] In the initial report, EPIC score out performed both Balthazar grading and CTSI in prediction of severity of AP as well as mortality.[21] Moreover, calculation of EPIC score does not necessarily require administration of intravenous contrast and, as against the scores based on pancreatic necrosis, can be determined within 24 h of admission. Other authors have also reported utility of EPIC score.[22–24]

In a study of 354 patients, 150 patients underwent CT on first day of admission and were assessed by clinical (APACHE-II and bedside index of severity in acute pancreatitis) and radiological scores (Balthazar, CTSI, MCTSI, EPIC, mesenteric edema and peritoneal fluid score, extra-pancreatic score, and pancreatic size index) for severity assessment. The study suggested that no additional value is added by early CT to the clinical scores for predicting severity or outcome in AP. Among the CT scores, the CTSI and Balthazar scores were shown to have highest accuracy for prediction of severity.[22] However, another report on 105 patients with AP who were assessed by clinical (bedside index of severity in acute pancreatitis and Systemic inflammatory response syndrome (SIRS) and radiological scores (CTSI, MCTSI, EPIC, and renal rim grade) reported EPIC scoring system to outperform other CT scores in prediction of severity and mortality. However, there was no additional benefit of doing a CT beyond the assessment provided by clinical scoring.[23]

Another study that evaluated role of multiple CT scores in predicting acute kidney injury in 145 patients of AP reported EPIC score to best predict occurrence of acute kidney injury vis-à-vis other scores (CTSI and Balthazar). Also, EPIC scoring system correlated best with the clinical severity assessment scores like Ranson's and APACHE-II.[24] Schroder score is a simple radiological score that scores extra-pancreatic changes (edema around a part or of entire pancreas, pleural effusion, ascites, peri-renal fat edema, mesenteric edema, and bowel paralysis). Schroder score gives 1 point for each of these parameters, and score of 4 or more (maximum 7) seems to predict severe AP.[15]

Extra-pancreatic inflammation and changes have also been assessed using renal rim scoring. Mortele *et al*. described various renal and peri-renal changes associated with AP including renal parenchymal and vascular changes.[25] Imamura *et al*. described renal rim grading that described peri-renal changes on CT carried out within 24 h of admission. Grade 1 renal rim represented absence of any peri-renal changes, while grade 2 (Fig. 5)

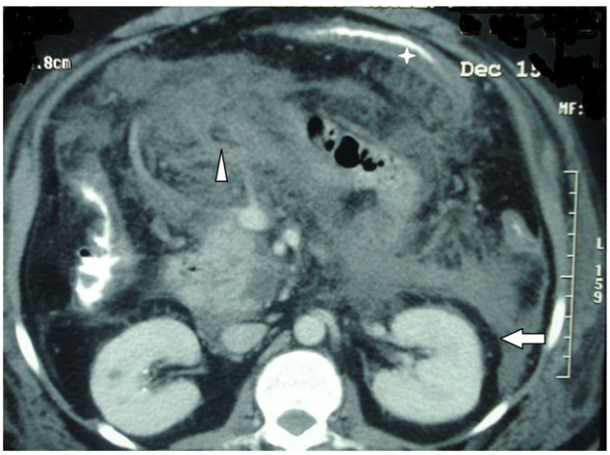

Figure 5 Extra-pancreatic computed tomography changes: abdominal computed tomography showing renal rim grade 2 (arrow), mesenteric edema (arrowhead), and mural thickening of colon (star).

represented presence of renal rim wherein extra-pancreatic changes involved the para-renal space, but the peri-nephric fat was preserved, and grade 3 renal rim represented loss of renal rim because of increased peri-nephric changes, and the EPN is seen to destroy the peri-renal fat and extend into the renal capsule. With increase in renal rim grade, the severity and mortality in patients with AP also increased.[26]

Others have used the presence of mesenteric edema and peritoneal fluid score to predict occurrence of severe acute pancreatitis.[27] Although the score is simple to perform, only few reports have compared it with other CT scores and clinical scores and need validation.[22] Occasional reports have also reported about involvement of gastric bare area, left adrenal, and retrocrural space as possible predictive markers of severe AP, but these simple parameters need validation before clinical applicability.[28,29]

We also subdivided EPN into limited and extensive EPN with extensive EPN being labeled when it involved para-colic gutters or pelvis and noted that this group of extensive EPN had higher occurrence of ascites, pleural effusion, and multi-organ failure. The frequency of mortality and need for intervention were also higher in the extensive EPN group.[4] Recently, volume of EPN has also been utilized for the purpose of prediction of outcome and severity in AP. In a retrospective study on 264 patients with AP, the CT films were assessed to determine the Balthazar grade, CTSI, and the volume of EPN, and these were correlated with severity and outcomes. EPN volume correlated well with duration of hospital stay, organ failure, need for intervention, and mortality. The optimal volume of EPN to predict severe pancreatitis was found to be 100 mL. Also, the area under receiver operating characteristic curve for prediction of organ failure or infection was highest for EPN volume when compared with CTSI, Balthazar grade, and C-reactive protein levels.[30] Recent reports also describe use of endoscopic ultrasound for detection of EPN (Figs 6 and 7), but the invasive nature of the technique may make routine applicability to all patients difficult. Endoscopic ultrasound also helps differentiate anechoic collections from the hetero-echoic EPN and may further classify the EPN seen on CT into two distinctive groups that seem to differ in outcome. Those with

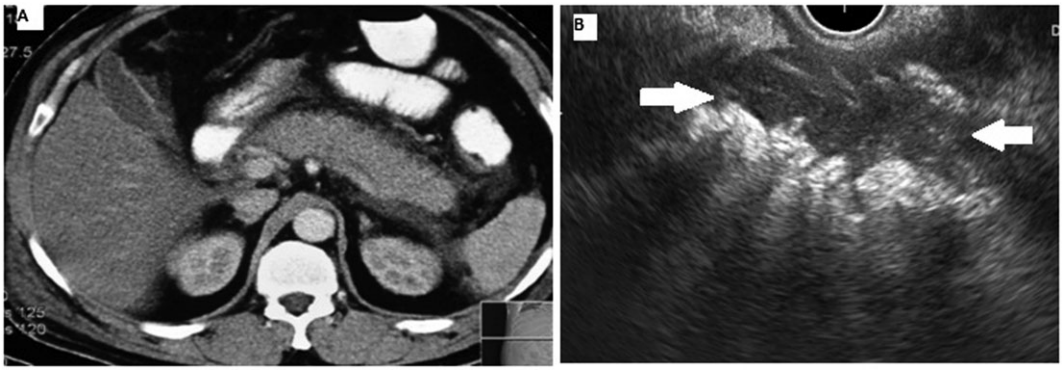

Figure 6 (a) Contrast enhanced computed tomographic scan showing extra-pancreatic necrosis and (b) endoscopic ultrasound showing heterogeneous echotextured peri-pancreatic area suggestive of extra-pancreatic necrosis (arrow).

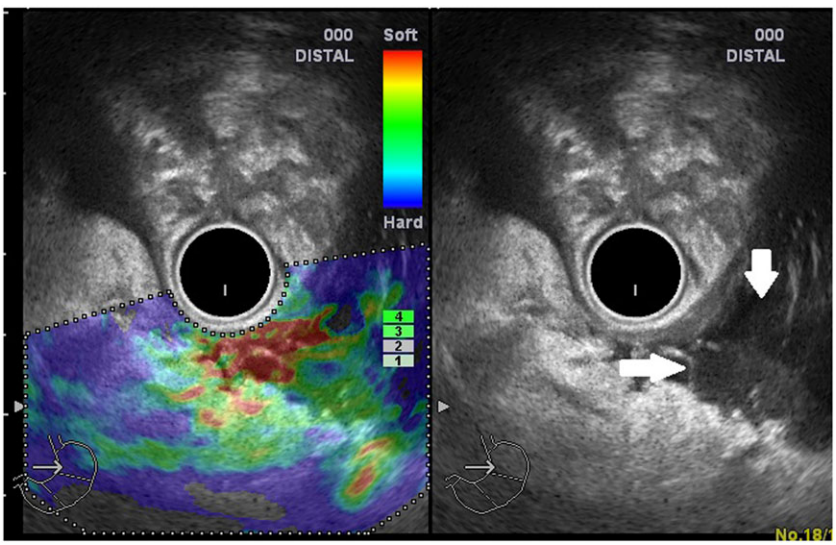

Figure 7 Endoscopic ultrasound elastography in extra-pancreatic necrosis. Extra-pancreatic necrosis is seen as soft region on elastography.

hetero-echoic collection seem to fare worse as compared with those with anechoic collection with higher frequency of POF and need for intervention.[31]

Conclusion

The currently available as well as emerging data about EPN alone seems to suggest that it may represent a separate clinical subgroup in AP, which may have an outcome that is worse than interstitial pancreatitis but better than pancreatic parenchymal necrosis group. EPN alone, as a group, seems to have higher severity estimation at the admission and can be diagnosed on CECT. Further research is needed to identify the mechanisms responsible for occurrence of EPN and whether the extent and the nature of EPN determine the clinical course and outcome in these patients.

References

1 Banks PA, Bollen TL, Dervenis C *et al.* Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013; **62**: 102–11.
2 Singh VK, Bollen TL, Wu BU *et al.* An assessment of the severity of interstitial pancreatitis. *Clin. Gastroenterol. Hepatol.* 2011; **9**: 1098–103.
3 Bakker OJ, van Santvoort H, Besselink MG *et al.* Dutch Pancreatitis Study Group. Extrapancreatic necrosis without pancreatic parenchymal necrosis: a separate entity in necrotising pancreatitis? *Gut* 2013; **62**: 1475–80.
4 Rana SS, Sharma V, Sharma RK, Chhabra P, Gupta R, Bhasin DK. Clinical significance of presence and extent of extrapancreatic necrosis in acute pancreatitis. *J. Gastroenterol. Hepatol.* 2015; **30**: 794–8.
5 Wang M, Wei A, Guo Q *et al.* Clinical outcomes of combined necrotizing pancreatitis versus extrapancreatic necrosis alone. *Pancreatology* 2016; **16**: 57–65.
6 Howard JM, Wagner SM. Pancreatography after recovery from massive pancreatic necrosis. *Ann. Surg.* 1989; **209**: 31–5.
7 Angelini G, Pederzoli P, Caliari S *et al.* Long-term outcome of acute necrohemorrhagic pancreatitis. A 4-year follow-up. *Digestion* 1984; **30**: 131–7.
8 Madry S, Fromm D. Infected retroperitoneal fat necrosis associated with acute pancreatitis. *J. Am. Coll. Surg.* 1994; **178**: 277–82.
9 Sakorafas GH, Tsiotos GG, Sarr MG. Extrapancreatic necrotizing pancreatitis with viable pancreas: a previously under-appreciated entity. *J. Am. Coll. Surg.* 1999; **188**: 643–8.

10 Lankisch PG, Apte M, Banks PA. Acute pancreatitis. *Lancet* 2015; **386**: 85–96.
11 Lankisch PG, Struckmann K, Lehnick D. Presence and extent of extrapancreatic fluid collections are indicators of severe acute pancreatitis. *Int. J. Pancreatol.* 1999; **26**: 131–6.
12 Schäffler A, Hamer O, Dickopf J *et al.* Admission resistin levels predict peripancreatic necrosis and clinical severity in acute pancreatitis. *Am. J. Gastroenterol.* 2010; **105**: 2474–84.
13 Schäffler A, Hamer OW, Dickopf J *et al.* Admission visfatin levels predict pancreatic and peripancreatic necrosis in acute pancreatitis and correlate with clinical severity. *Am. J. Gastroenterol.* 2011; **106**: 957–67.
14 Schäffler A, Landfried K, Völk M *et al.* Potential of adipocytokines in predicting peripancreatic necrosis and severity in acute pancreatitis: pilot study. *J. Gastroenterol. Hepatol.* 2007; **22**: 326–34.
15 Schröder T, Kivisaari L, Somer K, Standertskjöld-Nordenstam CG, Kivilaakso E, Lempinen M. Significance of extrapancreatic findings in computed tomography (CT) of acute pancreatitis. *Eur. J. Radiol.* 1985; **5**: 273–5.
16 Krishna SG, Hinton A, Oza V *et al.* Morbid obesity is associated with adverse clinical outcomes in acute pancreatitis: a propensity-matched study. *Am. J. Gastroenterol.* 2015; **110**: 1608–19.
17 Bruennler T, Hamer OW, Lang S *et al.* Outcome in a large unselected series of patients with acute pancreatitis. *Hepatogastroenterology* 2009; **56**: 871–6.
18 Balthazar EJ, Ranson JH, Naidich DP, Megibow AJ, Caccavale R, Cooper MM. Acute pancreatitis: prognostic value of CT. *Radiology* 1985; **156**: 767–72.
19 Balthazar EJ, Robinson DL, Megibow AJ, Ranson JH. Acute pancreatitis: value of CT in establishing prognosis. *Radiology* 1990; **174**: 331–6.
20 Mortele KJ, Wiesner W, Intriere L *et al.* A modified CT severity index for evaluating acute pancreatitis: improved correlation with patient outcome. *AJR Am. J. Roentgenol.* 2004; **183**: 1261–5.
21 De Waele JJ, Delrue L, Hoste EA, De Vos M, Duyck P, Colardyn FA. Extrapancreatic inflammation on abdominal computed tomography as an early predictor of disease severity in acute pancreatitis: evaluation of a new scoring system. *Pancreas* 2007; **34**: 185–90.
22 Bollen TL, Singh VK, Maurer R *et al.* A comparative evaluation of radiologic and clinical scoring systems in the early prediction of severity in acute pancreatitis. *Am. J. Gastroenterol.* 2012; **107**: 612–9.
23 Sharma V, Rana SS, Sharma RK, Kang M, Gupta R, Bhasin DK. A study of radiological scoring system evaluating extrapancreatic inflammation with conventional radiological and clinical scores in predicting outcomes in acute pancreatitis. *Ann Gastroenterol* 2015; **28**: 399–404.
24 Li Z, Zhang L, Huang Z, Yuan F, Zhang W, Song B. Correlation analysis of computed tomography imaging score with the presence of acute kidney injury in severe acute pancreatitis. *Abdom. Imaging* 2015; **40**: 1241–7.
25 Mortelé KJ, Mergo PJ, Taylor HM, Ernst MD, Ros PR. Renal and perirenal space involvement in acute pancreatitis: spiral CT findings. *Abdom. Imaging* 2000; **25**: 272–8.
26 Imamura Y, Hirota M, Ida S *et al.* Significance of renal rim grade on computed tomography in severity evaluation of acute pancreatitis. *Pancreas* 2010; **39**: 41–6.
27 King NK, Powell JJ, Redhead D, Siriwardena AK. A simplified method for computed tomographic estimation of prognosis in acute pancreatitis. *Scand. J. Gastroenterol.* 2003; **38**: 433–6.
28 Liu Z, Yan Z, Min P, Liang C, Wang Y. Gastric bare area and left adrenal gland involvement on abdominal computed tomography and their prognostic value in acute pancreatitis. *Eur Radio* 2008; **18**: 1611–6.
29 Xu H, Ebner L, Jiang S *et al.* Retrocrural space involvement on computed tomography as a predictor of mortality and disease severity in acute pancreatitis. *PLoS One* 2014; **9**: e107378.
30 Meyrignac O, Lagarde S, Bournet B *et al.* Acute pancreatitis: extrapancreatic necrosis volume as early predictor of severity. *Radiology* 2015; **276**: 119–28.
31 Rana SS, Bhasin DK, Sharma V, Sharma R. Prognostic significance of differentiating peri-pancreatic necrosis from fluid collection on endoscopic ultrasound in patients with presumed extra-pancreatic necrosis alone. *Gastrointest. Endosc.* 2015; **81** (5S): AB534–5.