Role of computed tomography in prediction of gastrointestinal fistula in patients with acute pancreatitis

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Abstract

Aim : **To identify computed tomography (CT) features that predict gastrointestinal fistula (GIF) in patients with acute pancreatitis (AP).**

Methods : **This retrospective study comprised 18 consecutive patients with AP and GIF from June 2017 to June 2018. The diagnosis of GIF was based on upper gastrointestinal endoscopy, colonoscopy or surgery. A cohort of 19 matched patients from a prospective database of AP served as control group. Measures of severity, and clinical outcome were evaluated. CT parameters were compared between the groups to assess the features that could predict the development of GIF.**

Results : **There was no difference between the two groups in terms of disease etiology, severity, drainage, and mortality. On univariate analysis, the CT features that were found to be significantly different between the two groups were the presence of bowel wall thickening (P=0.005), maximum thickness of the bowel wall (P=0.007), presence of air foci in extra pancreatic necrosis/ collection (P=0.013), discontinuity of the bowel wall (P=0.046) and the displacement/ compression of bowel by fluid collection (P=0.014). On multivariate analysis, all the above-mentioned CT findings except discontinuity of bowel wall were found to be statistically significant.**

Conclusion : **CT is helpful in predicting GIF in patients with AP.**
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Keywords : Acute pancreatitis, CT, Gastrointestinal fistula.

Introduction

Gastrointestinal fistula (GIF) is a well-recognized complication of acute pancreatitis (AP) (1,2). It may involve the stomach, duodenum, jejunum, ileum, and colon. Colonic and duodenal fistulas are the two most prevalent forms of GIF. Three mechanisms have been proposed for the development of GIF- (I) direct enzymatic action of the pancreatic juices on the adjacent bowel wall causing erosions, (II) intestinal necrosis secondary to vascular thrombosis in an inflamed/ infected area and (III) iatrogenic GIF (3,4). GIF may cause clinically severe consequences such as hemorrhage and exacerbation of infection (5-8). Colonic fistula is associated with higher mortality than those other forms of GIF (9). Clinically occurrence of diarrhea, GI bleed, prolonged sepsis and frank feculent drain output raise a suspicion for GIF. However, some of these features are non-specific. On CT, GIF is suspected when pancreatic or peripancreatic collections show air-foci. Again, this finding is not specific for GIF and may be seen more commonly with infection. No other imaging features on CT have been reported to predict GIF in AP. This study was aimed to investigate the CT findings of GIF in AP.

Materials and methods

This retrospective observational study was approved by our institutional ethics committee.

Patients

The medical records and imaging files of consecutive adult patients with AP and GIF admitted in the gastroenterology ward of a tertiary care referral center were evaluated. The study period was one year (from June 2017 to June 2018). The diagnosis of GIF was based on the findings of upper gastrointestinal endoscopy (UGIE), colonoscopy or surgery. The endoscopic (UGIE/ colonoscopy) features of GIF included direct visualization of a fistulous opening between the gastrointestinal tract and the collection (Figure 1). Additionally, in some patients, diagnosis was confirmed on CT scan or fluoroscopy performed following contrast injection via the percutaneous catheter that demonstrated the opacification of a bowel loop (Figure 2). Patients with following criteria were excluded from our study : CT scan after drainage of collection, patient who underwent non-contrast CT scan, known chronic liver parenchymal disease, inflammatory bowel disease or gastrointestinal tuberculosis, pregnancy or severe immune system disorders and those with chronic pancreatitis or known malignancy. A cohort of 19, age and severity [moderately severe and severe AP (SAP)] matched controls from a prospective database of 75 AP patients was selected for comparison.

Abdominal CT scan

CT scan evaluated in the study for the purpose of GIF prediction was the one acquired closest to the time of diagnosis of the fistula (before the diagnosis of fistula).

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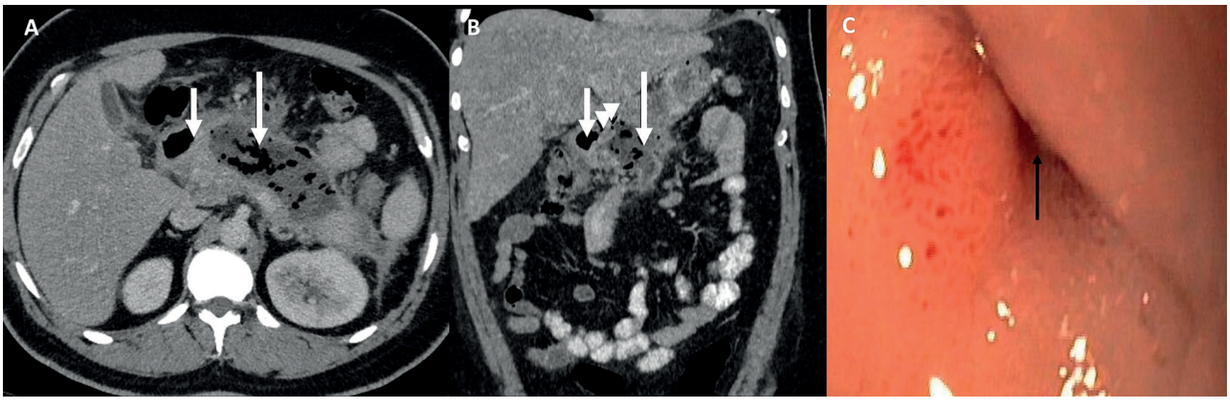

Figure 1. — A 42-year-old male with cysto-duodenal fistula. Axial (A) and coronal (B) CT images show a collection in the lesser sac with air-foci (arrow) adjacent to the first and second part of the duodenum that is thickened (short arrow) and small air foci along the fistulous tract (arrow heads). The corresponding endoscopic image is shown (arrow, C).

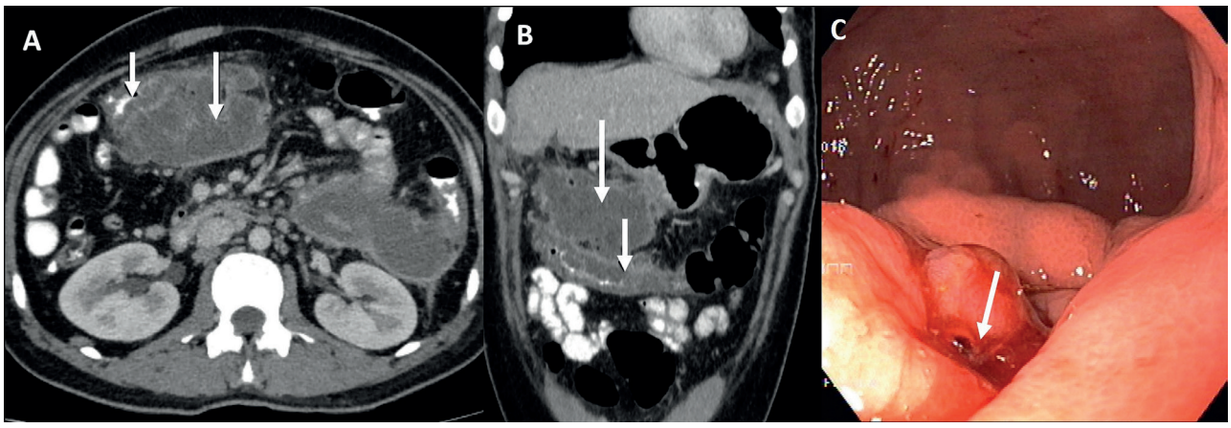

Figure 2. — A 38-year-old male with cystocolonic fistula at the level of transverse colon. Axial (A) and coronal (B) CT images show a collection in the transverse mesocolon (arrow) with marked mural thickening and displacement of the transverse colon (short arrow). The corresponding colonoscopic image is shown (arrow, C).

The scans were acquired on 64-, 128- or 256-detector row CT scanner (Siemens Medical Solutions, Erlangen, Germany or Philips Medical Solution, The Netherlands or GE Healthcare, USA). All patients underwent a contrast-enhanced CT scan following intravenous injection of non-ionic contrast agent (body weightX2 mL) at a rate of 3ml/second in the antecubital vein. CT scans were obtained 90 seconds after the onset of contrast injection. The imaging parameters were as follows : tube current, 200 mAs per section ; tube voltage, 120 kV ; field of view, 42 cm ; reconstruction thickness, 2 mm ; reconstruction increment, 1 mm ; and matrix, 512 × 512. The area scanned extended from the diaphragmatic domes to the ischium.

All CT images were re-read by two radiologists with two years (GCD) and six years (PG) experience in reporting abdominal CT scans. The interval between the onset of pain and CT as well as the interval between the CT and diagnosis of GIF was recorded. The degree of pancreatic necrosis (<30% or >30%) was recorded. Modified CT severity index (MCTSI) was calculated. The presence and site of fluid collection was recorded. Air within pancreatic necrosis and peripancreatic fluid collection/ necrosis was documented (Figure 1). Following bowel findings were recorded : Bowel wall thickening (defined as thickness more than 5 mm in a collapsed loop and 3 mm in a distended loop) (Figure 2 and 3), degree of bowel thickening in mm (measured on a single wall from the mucosa to serosa), pattern of thickening (focal-defined as involving one region of the GI tract and diffuse defined as involvement of more than one region), pattern of enhancement (described relative to adjacent normal thickness bowel ; hypoenhancing, isoenhancing and hyperenhancing), discontinuity of the wall (defined as distinct defect in the wall at the site of thickening-either partial thickness or complete) and displacement or compression of the bowel loop by the fluid collection. Ascites and venous thrombosis were also recorded.

Clinical details and outcomes

Clinical details recorded in each group were as follows : etiology and severity (based on revised Atlanta

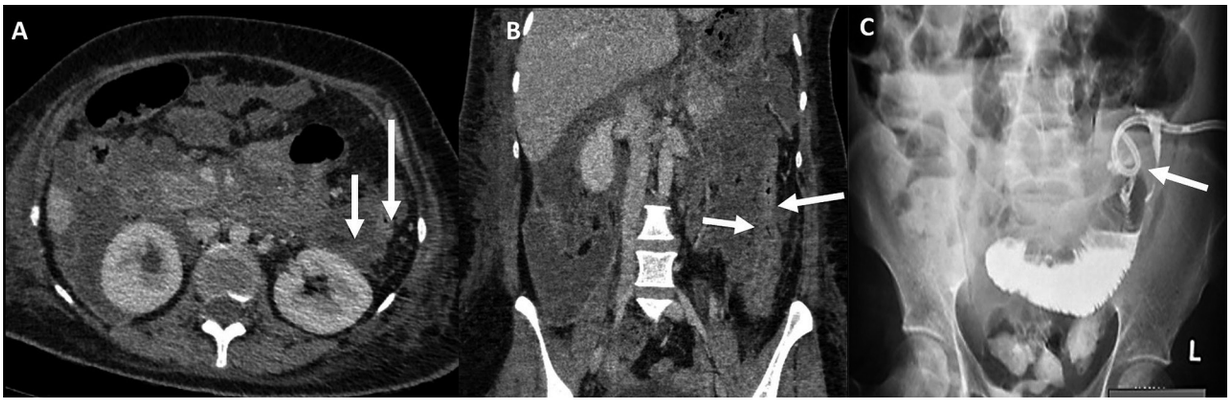

Figure 3. — A 30-year-old female with cystocolonic fistula at the level of descending colon. Axial (A) and coronal (B) CT images shows a collection in the left paracolic gutter (arrow) with long segment marked mural thickening and displacement of the descending colon (short arrow). Contrast injection through the percutaneous catheter opacified the descending colon confirming the location of fistula (arrow, C). The opacification of small bowel loop is secondary to the orally ingested contrast.

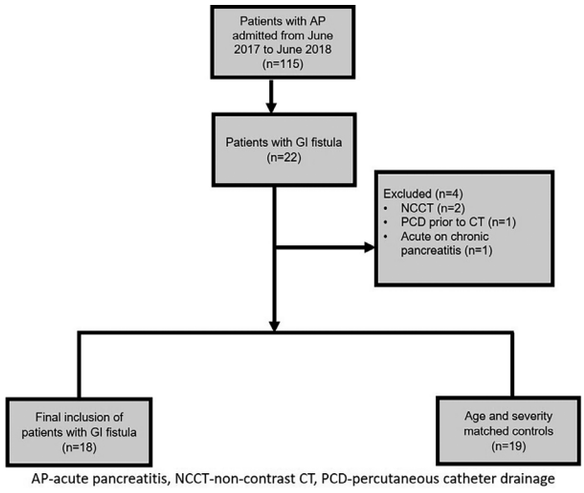

Figure 4. — Flowchart showing patient recruitment.

classification), infection of the pancreatic or peri-pancreatic necrosis, drainage, surgery, and mortality. The site of GIF was recorded as cysto-colonic, cysto-duodenal, cysto-gastric and cysto-jejunal.

All patients were managed according to standard recommendations that include fluid resuscitation, pain alleviation, support of the organ systems, and nutritional support (enteral or parenteral) (10). Antibiotics were employed for extra-pancreatic infections and suspected infected pancreatic or extra pancreatic necrosis. Infection of the necrotic collections was suspected based on patients' clinical condition. Infection was confirmed by culture of the drain fluid.

In hospital mortality were recorded. The patients who were discharged from the hospital were followed for a period of 3 months.

Statistical analyses

Statistical analysis was carried out using commercially available software (IBM Statistical Package for the Social Sciences Statistics, release 23 ; SPSS, Chicago, Ill). Distribution of categorical data was expressed as frequencies and percentages. The continuous data were expressed as mean or median with standard deviation. The comparison of categorical data was carried out by using Chi-square test or Fischer's exact test. The comparison of continuous data was carried out by using the Mann-Whitney U test or independent Student's T-test based on the distribution. Univariate analysis was done to identify the CT features predictive of GIF. Those factors that were found to be statistically significant (*P* value <0.05) were evaluated using multivariate analysis. Logistic regression analysis with forward LR method was used. All statistical analysis was carried out at 5% level of significance and a *P* value < 0.05 was considered significant.

Results

During the study period, 115 patients with moderately severe and severe AP were admitted. Among the 22 patients (19.13%) who fulfilled the inclusion criteria, 4 were excluded (2 patients had non-contrast CT scans, 1 patient had prior percutaneous drainage and 1 patient had acute on chronic pancreatitis). Finally, 18 patients comprised the GIF group (Figure 4). The median interval between onset of pain and CT scan was 24.5 days (±63.85 days). The median interval between CT scan and diagnosis of GIF was 7 days (range, 5-15 days). The most common site of GIF was colon (n=8), followed by duodenum (n=4), jejunum (n=3), stomach (n=2) and both duodenum and stomach (n=1). In the colon, the distribution of GIF was descending colon (n=5), splenic flexure (n=2) and transverse colon (n=1).

The GIF group and the control group were comparable in terms of age, gender distribution, etiology, severity and mortality. Majority of the patients in both the groups had severe disease with median MCTSI of 9.11 in the GIF group and 8.82 in the control group. Infected

Table 1. — **Baseline characteristics and outcome parameters in GIF group vs. control groups**

Parameters	GIF group (n=18)	Control group (n=19)	*P* value	Confidence interval	
				25%	75%
Mean age (years±SD)	38.61 (±15.355)	40.71 (±12.862)	0.921	-9.349	8.551
Gender (M/F)	15/3 (83.3% / 16.7%)	14/5 (73.7% / 26.3%)	0.45		
Mean modified CTSI (±SD)	9.11 (±1.023)	8.82 (±1.510)	0.131	-0.253	1.432
Severity (Atlanta) Mild Moderate Severe	 0 8 (44.4%) 10 (54.6%)	 0 5(26.3%) 14 (73.7%)	 0.35		
PCD	18 (100%)	19(100%)	0.851		
Etiology			0.652		
Alcohol	9 (50%)	13 (68.4%)			
Gall stones	7 (38.8%)	5 (26.3%)			
Others	2 (11.2%)	1 (5.3%)			
Mean length of hospital stay (days)	30.28	30.89	0.915	-12.34	11.11
ICU admission	13 (72.22%)	15 (78.9%)	0.814		
Mean length of ICU stay (days)	7.06	6.68	0.921	-7.30	8.04
Organ failure	13 (72.22%)	14 (73.7%)	0.891		
Multiorgan failure	5 (27.7%)	7 (36.8%)	0.081		
Mortality	5 (27.7%)	5 (22.7%)	0.714		
Surgery	10 (55%)	2 (9%)	0.001		
Site of fistula Colonic Duodenal Jejunal Gastric Gastric+duodenal	 8 4 3 2 1	-			

CTSI-computed tomography severity index, GIF-gastrointestinal fistula, PCD-percutaneous drainage, SD-standard deviation.

necrosis was recorded in 15 patients with GIF and 13 patients in the control group (*P*=0.605). All patients in the GIF group had percutaneous catheter drainage (PCD). Similarly, all the patients in the control group had PCD. This was explained by the fact both the groups had patients with moderately severe and severe disease and local complications were managed by percutaneous drainage. Additionally, endoscopic drainage (endoscopic ultrasound guided cystogastrostomy) was performed in three patients in GIF group and one patient in the control group. The patients in GIF group were subjected to surgery more frequently than the control group. The surgical procedures performed in patients with GIF included necrosectomy with hemicolectomy and ileostomy (n=5) and necrosectomy with ileostomy (n=1) in colonic fistulae. One patient underwent surgical exploration and was found to have multiple fistulae. The abdomen was frozen and hence no definitive resection could be performed. One patient with colonic fistula was managed conservatively and kept on follow up. Resection and anastomosis were performed in three patients with jejunal fistulae. All patients with cystogastric or cystoduodenal fistulae were managed by endoscopic stent placement. Table 1 shows the comparison of two groups in terms of baseline characteristics and outcome parameters. Table 2 shows the comparison of CT findings in the two groups.

On univariate analysis, the CT features that were found to be significantly different between the two groups were the presence of bowel wall thickening (*P*=0.005), maximum thickness of the wall bowel (*P*=0.007), presence of air foci in extra pancreatic necrosis/ collection (*P*=0.013), discontinuity of the bowel wall (*P*=0.046) and the displacement/ compression of bowel by fluid collection (*P*=0.014). On multivariate analysis, all the above-mentioned CT findings except discontinuity of bowel wall were found to be statistically significant. These results are highlighted in Table 3.

Discussion

GIF is a well recognized complication of late phase of AP with a reported incidence of 3 to 15% in different studies (8,9,11). SAP causes severe inflammatory changes that have the potential to erode contiguous viscera resulting in development of GIF (7). Little data is available to predict the risk of GIF in patients with SAP (9, 11). No studies have been published on the role of CT findings in predicting GIF in AP. We found no significant difference in the mean age, etiology, severity, mean MCTSI and mortality between patients with GIF and those without GIF. Jiang et al reported no significant difference in the overall mortality in patients with and without GIF,

Table 2. — **Comparison of CT findings in the GIF group vs. control groups**

Parameter		**GIF group (n=18)**	**Control group (n=19)**	***P* value**
Pancreatic necrosis	Absent	0	0	0.871
	<30%	10 (55.5%)	8 (42.2%)	
	>30%	8 (44.5%)	11 (57.8%)	
Collections		17 (94.4%)	19 (100%)	0.912
Predominant site of collection Lesser sac Paracolic gutter ● Right ● Left Pararenal space ● Right ● Left Pelvic		 10 (55.5%) 1 (5.6%) 3 (16.6%) 1 (5.6%) 2 (11.1%) 1 (5.6%)	 12 (63.2%) 0 2 (10.5%) 1 (5.3%) 2 (10.5%) 2 (10.5%)	0.652
Air foci in pancreatic necrosis		6 (33.3%)	3 (15.7%)	0.253
Air foci in peripancreatic collections		12 (66.6%)	6 (31.6%)	**0.013**
Positive culture of fluid collection		9/12 (75%)	6/6 (100%)	**0.058**
Bowel wall thickening		18 (100%)	12 (63.2%)	**0.005**
Maximum mural thickness, mm (mean±SD)		9.94 (±6.073)	4.95 (±4.962)	**0.007**
Pattern of thickening Focal Diffuse		 12 (66.6%) 6 (33.4%)	 10 (52.6%) 2 (10.5%)	0.150
Pattern of bowel wall enhancement Hypoenhancement Isoenhancement Hyperenhancement		 12 (66.6%) 5 (27.8%) 1 (5.6%)	 7 (36.8%) 2 (10.5%) 3 (15.7%)	0.243
Discontinuity of wall		3 (16.6%)	0	**0.046**
Compression of the bowel segment by collection		11 (61.1%)	5 (26.3%)	**0.025**
Ascites		10 (55.5%)	11 (57.8%)	0.821
Venous thrombosis		6 (33.3%)	8 (2.2%)	0.691

GIF-gastrointestinal fistula, SD-standard deviation.

Table 3. — **Univariate and multivariate analysis of factors predictive of GIF on CT**

Parameter		Mean (SD) 25%	Confidence interval		Univariate analysis	Multivariate analysis
			75%			
Air in peripancreatic collection					*P*=0.013	***P*=0.020**
Bowel wall thickening					*P*=0.005	***P*=0.017**
Maximum mural thickness, mm (mean±SD)	GIF group	9.94 (±6.073)	1.368	8.612	*P*=0.007	***P*=0.035**
	Control group	4.95 (±4.962)				
Discontinuity of wall					*P*=0.046	*P*=0.999
Compression of the bowel segment by collection					*P*=0.014	***P*=0.023**

GIF-gastrointestinal fistula, SD-standard deviation.

however, they reported that patients with colonic fistula have a higher mortality (9). The higher mortality in this group of patients may be related to colectomy. Ileostomy should be preferred over colectomy for the management of colonic fistulae as studies have shown that the colonic fistulae may also heal spontaneously or with conservative measures such as PCD over time (9,11). However, in the study by Hua et al. there was no significant difference in the mortality between the two groups (11). Both Jiang et al. and Hua et al. reported a higher MCTSI in patients with GIF compared to those without GIF (9,11). No such difference was reported in the present study. This discrepancy may be explained by the fact by referral bias as most of the patients that present to our centre are those with SAP. Regarding the site of fistula, our results are in line with previous studies that found colonic fistula followed by duodenal fistula as the most common sites of GIF (9,11). Management of GIF includes PCD, continuous negative pressure irrigation, and surgery (ileostomy or colostomy). In the recent studies, there has been a trend towards non-surgical management. In the study by Jiang et al. all duodenal fistulas were managed non-surgically while surgical management was required for 61.1% colonic fistula (9). In the study by Hua et al.

fistula resolution was reported in 80.7% patients after PCD or control of infection (11). Ten patients underwent ileostomy or colostomy. Similar trend was seen in our patients. Surgery was performed in 7/8 patients with colonic fistula and all patients (n=3) with jejunal fistula while patients with gastric and duodenal fistula were managed non-surgically.

In the present study we found that the presence of bowel wall thickening, maximum thickness of the bowel wall, presence of air foci in extra pancreatic necrosis/ collection, and the displacement/ compression of bowel by fluid collection were the CT features predictive of GIF. Bowel wall thickening occurs secondary to the action of pancreatic enzymes that track through the mesentery and act on the bowel wall leading to inflammatory thickening. As it is one of the initial pathological mechanisms in development of GIF, its identification on CT is likely to be associated with a greater risk of development of GIF. On the same basis, a greater degree of mural thickening is likely to have a greater probability of development of GIF. Ji et al. in their observational study of 209 patients with AP who underwent magnetic resonance imaging evaluated the GI abnormalities (12). They found that 69% of the patients had at least one GI abnormality. GI mural thickening was reported in 45 patients. Gastric, duodenal, jejunal, ileal and colonic thickening was reported in 20%, 27%, 14%, 6% and 26% respectively. The authors did not report the detection of GIF.

The presence of air within a pancreatic collection suggests infection. However, air is found in a minority of cases of confirmed infection (12%-22%) (13). The other important reason for gas within a pancreatic collection is GIF (14). In the present study, we found air within the pancreatic necrosis and peripancreatic fluid collections in 33.3% and 66.6% patients with GIF respectively compared to 13.6% and 27.27% patients respectively without GIF. However, the difference was statistically significant only for the presence of air within the peripancreatic collection. The percentage of patients without GIF showing air within the pancreatic necrosis or peripancreatic collection is like that reported in previous studies. There is no data on the frequency of air within pancreatic collections in GIF. Infection is a confounding factor as air in a necrotic collection is considered a sign of infection. Besides, representing direct communication with the GI tract, GIF also causes translocation of bacteria from GI tract into the collection and secondary infection. Thus, air in the setting of GIF may be multifactorial. In the present study, cultures of the fluid collection were positive in 75% of patients showing air in the peripancreatic collection. Displacement or compression of a bowel loop by fluid collection can predispose to GIF by inducing ischemia at the level of maximum compression as well as by the providing a route for spontaneous decompression of the contents of the collection.

There were a few limitations in the study. The sample size was rather small. However, as only a few patients with AP develop GIF, the reported patient cohort is still sizable for analysis of results. The retrospective nature of the study did not allow the comparison of all the clinical and outcome parameters between the two groups.

In conclusion, certain CT findings may predict the development of GIF in the setting of AP. However, prospective studies with inclusion of larger patient cohort are needed to validate the reported findings.

Conflict of interest

None of the authors declare any conflict of interest.

References

1. KOCHHAR R., JAIN K., GUPTA V., *et al*. Fistulization in the GI tract in acute pancreatitis. *Gastrointest Endosc.*, 2012, **75** : 436-440.
2. HO H.S., FREY C.F. Gastrointestinal and pancreatic complications associated with severe pancreatitis. *Arch Surg*., 1995, **130** : 817-822.
3. DOBERNECK R.C. Intestinal fistula complicating necrotizing pancreatitis. *Am J Surg*., 1989, **158** : 581-584.
4. MOHAMED S.R., SIRIWARDENA A.K. Understanding the colonic complications of pancreatitis. *Pancreatology*, 2008, 8 : 153-158.
5. TSIOTOS G.G., SMITH C.D., SARR M.G. Incidence and management of pancreatic and enteric fistulas after surgical management of severe necrotizing pancreatitis. *Arch Surg*., 1995, **130** : 48-52.
6. INOUE H., YAMADA R., TAKEI Y. Spontaneous fistulization of infected walled-off pancreatic necrosis into the duodenum and colon. *Dig Endosc.*, 2014, **26** : 293.
7. ALDRIDGE M.C., FRANCIS N.D., GLAZER G., DUDLEY H.A. Colonic complications of severe acute pancreatitis. *Br J Surg*., 1989, **76** : 362-367.
8. JIANG W., TONG Z., YANG D., *et al*. Gastrointestinal fistulas in acute pancreatitis with infected pancreatic or peripancreatic necrosis : a 4-year single-center experience. *Medicine* (Baltimore), 2016, **95** : e3318.
9. URAKAMI A., TSUNODA T., HAYASHI J., OKAYA Y., MIZUNO M. Spontaneous fistulization of a pancreatic pseudocyst into the colon and duodenum. *Gastrointest Endosc*., 2002, **55** : 949-951.
10. ARVANITAKIS M., DUMONCEAU J.M., ALBERT J., *et al*. Endoscopic management of acute necrotizing pancreatitis : European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. *Endoscopy*, 2018, **50** : 524-546.
11. HUA Z., SU Y., HUANG X., *et al*. Analysis of risk factors related to gastrointestinal fistula in patients with severe acute pancreatitis : a retrospective study of 344 cases in a single Chinese center. BMC Gastroenterol., 2017, **17** : 29.
12. JI Y.F., ZHANG X.M., MITCHELL D.G., *et al*. Gastrointestinal tract involvement in acute pancreatitis : initial findings and follow-up by magnetic resonance imaging. *Quant Imaging Med Surg*., 2017, **7** : 641-653.
13. VEGE S.S., FLETCHER J.G., TALUKDAR R., SARR M.G. Peripancreatic collections in acute pancreatitis : correlation between computerized tomography and operative findings. World J Gastroenterol., 2010 Sep. 14, **16**, 4291-4296.
14. BANSAL A., GUPTA P., SINGH H., *et al*. Gastrointestinal complications in acute and chronic pancreatitis. *JGH Open*, 2019. doi :10.1002/jgh3.12185.