International Journal of Gastrointestinal Intervention

journal homepage: www.ijgii.org

Original Article

Usefulness of endoscopic pancreatography without contrast agents and efficacy of transpapillary intervention for pancreatic duct rupture in chronic pancreatitis: Our study of 321 cases in 11 years

Pankaj N. Desai^{1,*}, Chintan N. Patel¹, Mayank V. Kabrawala¹, Subhash K. Nandwani², Rajiv M. Mehta², Ritesh M. Prajapati², Nisharg B. Patel², Krishna K. Parekh³, and Neha D. Sheth³

ABSTRACT

Background: To assess the usefulness of endoscopic pancreatography without contrast agents and efficacy of transpapillary intervention for pancreatic duct (PD) rupture in chronic pancreatitis.

Methods: We retrospectively analyzed all cases of chronic pancreatitis with ductal rupture causing ascites, effusions and pseudocysts. We performed magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde pancreatography (ERP) without contrast. Results observed based on the possibility of wire crossing the leak or not and their resolutions were noted.

Results: We performed ERP in 1,324 patients. Ductal disruptions in 321/1,324 (24.2%). We divided cases into two groups. Group 1 involves disruptions causing ascites in 60 cases (18.7%) and effusions in 34 cases (10.6%), and group 2 involves pseudocysts in 227 cases (70.7%). In group 1, 82 patients (87.2%) experienced successful cannulation of PD. Leak crossed in 70 (74.5%) with complete resolution in all. Leak did not cross in 12 cases of which 8 (8.5%) installed stents resolved while four (4.3%) did not resolve. In group 2, 219 (96.5%) PD cannulated. Leak did not cross but stents put in cyst (176, 77.5%). Complete resolution occurred without infection. Leaks were crossed in 43 (18.9%); complete resolution, 14 (32.6%). Complete regression was not achieved in 19 (8.3%). Eight cysts were not resolved (3.5%). Transmural drainage was done. Infection was noted in 2 cases (0.9%). Sites of leak in pseudocysts were jenu & body, 167 (73.6%); tail, 60 (26.4%). We recorded pancreas divisum in 24/321 (7.5%). ERP failed in 20 (6.2%). Three were managed medically (1.3%), 5 with distal pancreatectomy (2.2%), 4 with lateral pancreatico jejunoanastomosis (1.8%), and 8 with transmural drainage (3.5%).

Conclusion: PD rupture in chronic pancreatitis can be managed transpapillary, without any contrast during ERP. In majority, endosonography aspiration and transmural drainage are needed only when transpapillary fails. Leak from tail responded better than those from proximal duct with ERP.

Copyright © 2021, Society of Gastrointestinal Intervention.

Keywords: Chronic pancreatitis; Endoscopic retrograde cholangiopancreatography; Pancreatic ducts; Retrospective studies

Introduction

The complications of chronic pancreatitis include pseudocysts, pancreatic ascites and effusions, duodenal obstruction and common bile duct, splenic vein thrombosis with left sided portal hypertension and pseudoaneurysm of splenic artery.

About 10% of chronic pancreatitis is complicated with pseudocysts. Ductal disruptions is the cause rather than pancreatic inflammation. There is always a ductal communication and hardly

any necrosis in them. Hence management strategies have to be different with respect to those complicating acute pancreatitis.

Pseudocysts tend to have a less robust fibrinous wall and allow pancreatic secretions to leak from the disrupted duct into the pseudocyst, and out into peritoneum. Conversely, pancreatic duct (PD) disruption without a pseudocyst will form a fistulous tract. Fistulas from anterior PD disruption allow for pancreatic secretions to empty directly into peritoneum leading to ascites. Posterior PD ruptures allow for fistula formation through the aor-

¹Department of Endoscopy & Endosonography, Surat Institute of Digestive Sciences (SIDS), Surat, India

²Department of Gastroenterology, Surat Institute of Digestive Sciences (SIDS), Surat, India

³Department of Clinical Research, Surat Institute of Digestive Sciences (SIDS), Surat, India

Received July 13, 2020; Revised December 9, 2020; Accepted December 28, 2020

* Corresponding author. Department of Endoscopy & Endosonography, Surat Institute of Digestive Sciences (SIDS), Majura Gate, Ring Road, Surat 395002, India.

E-mail address: drp_desai@hotmail.com (P.N. Desai)

tic or esophageal hiatus or sometimes through the dome of the diaphragm leading to pleural effusion.

The ascites is typically exudative with high amylase activity. This is due to pancreatic fluid causing an inflammatory process leading to increased vasopermeability.

The mainstay of the management is diverting pancreatic fluid away from the leak to the small bowel with a pancreatic stent, while allowing the leak to heal. Adjunct treatment includes medical therapy to decrease pancreatic exocrine secretions and surgery. However, due to the low incidence of this condition, comparative studies with different treatment approaches are not available.^{1–4}

The mainstay of treatment was endotherapy. A transpapillary stent was placed from the major or minor papilla, decreasing intraductal pressure and diverting the pancreatic secretions to the small bowel thereby enhancing the healing of the ductal leak. Ideally, the stent should bridge the ductal disruption to have an optimal outcome.⁵ But there are cases where it is not possible to cross the disruption. In these cases, we placed the stent till the leak and healing occurred (48%–100% cases). Extrinsic cutaneous fistula may sometimes be blocked using fibrin or cyanoacrylate glue. But there is insufficient evidence backing their use routinely.⁶

Surgical management is reserved for failure of endoscopic intervention (or for cases where there has been complete disruption of the PD with no opacity proximal to the duct disruption on pancreatography).

There is limited evidence on the management of leaks complicating purely chronic pancreatitis. We were therefore prompted to explore the management of these ductal disruptions complicating

chronic pancreatitis transpapillary without contrast during endoscopic retrograde pancreatography (ERP).

The study was done to demonstrate the usefulness of endoscopic pancreatography without contrast agents and efficacy of transpapillary intervention for PD rupture in chronic pancreatitis.

Methods

We selected all cases of chronic pancreatitis presenting with pseudocysts, pleural effusions and pancreatic ascites from October 2008 to December 2019. The patients enrolled in our study had a combination of the following symptoms: recurrent or chronic abdominal pain, respiratory distress, fever, anorexia, weight loss. Their computed tomography (CT) scans and/or magnetic resonance cholangiopancreatography (MRCP) showed atrophied pancreas with dilatation of the main PD and/or dilated side branches, with or without parenchymal calcifications and having ascites, pseudocysts or pleural effusions with or without a demonstrable tract. Diagnostic fluid aspiration from these collections with an amylase content more than 1,000 IU/L was considered of pancreatic origin.

We excluded a few patients who had obstructing PD stones with leaks.

As a protocol, all patients with ascites and pleural effusions complicating chronic pancreatitis underwent therapeutic drainage to reduce fluid. Fluid amylase was explored to ascertain it is of pancreatic origin. No pseudocysts were aspirated. MRCP was performed in all cases. All patients were put on intravenous antibiotic-

Fig. 1. (A) Glide wire in PD across leak reaching the tail (arrow). No contrast injected. (B) A 5 Fr SPT stent in PD endoscopic view. (C) A 5 Fr SPT stent in PD fluoroscopic view reaching the tail bypassing the leak (arrow). PD, pancreatic duct; SPT, single pigtail.

Fig. 2. (A) Glide wire was seemed to be coiled in the communicating cyst not crossing across (arrow). (B) Endoscopic view of stent with cyst fluid drainage. (C) Fluoroscopic view of 5 Fr double pigtail stent with one end in the cyst and other in the duodenum (arrow).

ics (third-generation cephalosporin, with metronidazole).

ERP was also performed in all cases. In addition, we attempted to cannulate the PD from the major papilla. If PD could not be cannulated from major papilla, we looked for the minor papilla and attempted cannulating it, as it could sometimes be missing on MRCP.

We preferred a J-tip terumo wire (0.032 mm and 260 cm length) for cannulation and negotiation across the area of leak.

We divided the cases in two groups. Group 1 involved disruptions causing ascites and effusions and group 2 involved pseudocysts.

In group 1 if we crossed the site of leak, a pancreatic sphincterotomy was performed and a 5 Fr single pigtail (SPT) stent was placed bypassing the leak till the tail. In cases where the wire could not go across the leak, 5 Fr SPT stents were placed reaching the area of the leak (Fig. 1).

In group 2, if wire went across the site of leak, a 5 Fr SPT stent was placed till the tail. If we could not the wire could not go across the leak and it went into the cyst, we placed a 5 Fr double pigtail (DPT) stent into the cyst draining the cyst transpapillary (Fig. 2).

One unique feature was that we never used contrast during ERP. This idea was from lessons learnt from our early experience. In 7 cases of PD leak in our early practice (not included in this series), we used contrast to opacify the duct, find the leak and then do stenting. All had fever within 48 hours inspite of all aseptic precautions. Five developed severe sepsis and were treated with prolonged antibiotics and one even died. Since then, we adopted a policy of draining all effusions and ascites and never using contrast.

We used fluoroscopy and terumo wire effectively. We kept the MRCP film in front of us and negotiated the wire under fluoroscopic guidance based on where our wire was going and then completed the procedure. We could be sure of our wire in all cases with this technique.

We observed patients for 4 to 5 days with intravenous antibiotics and oral antibiotics on discharge (Cefixime 200 mg bid for 7

days) with proton pump inhibitor and supportive treatment. They were followed up after every fifteen days for three months to six months depending on their recovery and response. Follow-up was after six weeks to three months.

The stent was removed if collections dried up and we performed pancreatogram. If ducts were normal, no further stenting was done. If a dominant stricture was noted, then the patient was subjected to a stent exchange program with increasing diameter at about six months to a year and then given a stent free trial.

Amongst the 20 cases with failed cannulation, 12 were in the fistula group, 3 with leak responded after a prolonged medical management, 5 had distal leaks subjected to distal pancreatectomy, 4 patients underwent a lateral pancreaticojejunostomy, and 8 patients with pseudocysts were treated using endosonography (EUS) guided transmural drainage.

This retrospective study was exempted from review by the Ethics Committee of the Surat Institute of Digestive Sciences. The procedure and likely outcomes were discussed with the patients and the relatives and informed consent was taken.

Statistical analysis

We described categorical variables as frequency and percentages. We compared categorical variables using the chi-squared test. A P -value < 0.05 was considered statistically significant. We performed all statistical analyses using the SPSS (Statistical Package for Social Sciences) ver. 16.0 software (SPSS Inc., Chicago, IL, USA) (Table 1–4).

Results

We performed 1,324 ERP for chronic pancreatitis endotherapy in the period described. We found ductal disruptions in 321 of 1,324 (24.2%). We divided the cases in two groups for analysis based on our findings. Group 1 involves ductal obstruction causing ascites in 60 cases (18.7%) and effusions in 34 cases (10.6%) and group 2 involved pseudocysts in 227 cases (70.7%). ERP was possible in 301 (93.8%) and failed in 20 (6.2%). We recorded 12 ERP failure in group 1 and 8 in group 2.

In group 1, 82 patients (87.2%) had their PD cannulated. Area of leak could be crossed in 70 (74.5%) with resolution of the leak. Leak site was not crossed in 12 cases (14.6%). Amongst these, 8 (8.5%) cases had stents installed till the leak site till resolution ($P < 0.0001$), while four cases (4.3%) did not resolve with stents till leak. EUS drainage in form of pancreaticogastrostomy was

Table 1 Group 1: Pancreatic Duct Leak Causing Ascites and Effusion (94 Cases)

Variable	Number (%)	P -value
Successful cannulation	82 (87.2)	0.019
Leak crossed	70 (74.5)	< 0.0001
Leak resolution when crossed	70 (74.5)	< 0.0001
Leak not crossed	12 (14.6)	-
Leak resolution with stent till leak	8 (8.5)	< 0.0001
Total leak resolution	78 (83.0)	0.001

-, not available.

Table 2 Group 2: Pancreatic Duct Leak Causing Pseudocysts (227 Cases)

Variable	Number (%)	P -value
Successful cannulation	219 (96.5)	0.643
Leak crossed	43 (18.9)	< 0.0001
Leak resolution when crossed	14 (6.2)	< 0.0001
Stent in cyst	176 (77.5)	< 0.0001
Leak resolution with stent in cyst	176 (77.5)	< 0.0001
Total leak resolution	190 (83.7)	< 0.0001

Table 3 Comparison of Group 1 and Group 2

Variable	Group I	Group II	P -value
Successful cannulation	82 (87.2)	219 (96.5)	0.002
Leak crossed successfully	70 (74.5)	43 (18.9)	< 0.0001
Stent till leak	8 (8.5)	176 (77.5)	< 0.0001
Leak resolution	78 (83.0)	190 (83.7)	0.560

Values are presented as number (%).

Table 4 Comparison of Leak Site vs Leak Resolution

Variable	Proximal duct	Tail	P -value
Successful leak resolution	160 (76.9)	100 (88.5)	0.012

Values are presented as number (%).

Fig. 3. Flow chart of methodology and results. PD, pancreatic duct; ERCP, endoscopic retrograde cholangiopancreatography.

required. Common sites of leak were proximal body in 41 cases (43.6%) and tail in 53 cases (56.4%).

In group 2, in 219 (96.5%) cases succeeded in cannulating the PD. Leak did not cross but stents were installed transpapillary into the cyst in 176 cases (77.5%). In all these, we had complete cyst resolution with no infection ($P < 0.0001$).

Leaks could be crossed in 43 cases (18.9%). Amongst these we achieved complete resolution in 14 cases (32.6%) ($P < 0.0001$). Complete regression was not achieved in 19 (8.3%) cases and EUS aspiration was needed for them. We did not resolve 8 cases (3.5%) and transmural drainage was needed. Infection was noted in 2 cases (0.9%) requiring EUS aspiration. Sites of leak in pseudocysts were jenu and body, 167 (73.6%); tail, 60 (26.4%).

We recorded pancreas divisum in 24 cases (7.5%). In these cases, we did the pancreatic endotherapy from the minor papilla.

ERP failed in 20 cases (6.2%). Group 1 contained 12 of these. Three cases (1.3%) were managed medically, five (2.2%) with a distal pancreatectomy and four (1.8%) with a lateral pancreatic jejunostomy. In Group 2, all the eight (3.5%) cases where ERP was not possible, were subjected to transmural drainage and were

treated successfully.

Comparing group 1 and 2, we found that cannulation success and leak resolution rates were similar and not statistically different. The major difference in both groups was that in group 1, we recorded more resolution when we traversed the leaks and placed stents while in group 2 the resolution was more when we placed stents in the cyst through transpapillary route.

In a subgroup analysis, we evaluated the effect of the leak site on the success of leak resolution and we found that the leak resolution in tail was better than leak from proximal duct in our series ($P = 0.012$).

The statistical analysis tables are listed below for each finding (Fig. 3).

Discussion

In our series, we had 321 patients with PD leak complicating chronic pancreatitis. Pseudocysts was the commonest form of leak occurring in 70.7%. Ascites was at 18.7% followed by effusions at 10.6%.

For better understanding and evaluation, we divided our cases in two Groups. Group 1 with leaks causing effusion and ascites in 82 cases (87.2%). Group 2 with pseudocysts in 219 cases (96.5%).

We defined technical success as being able to cannulate either major or minor papilla and placing a stent in the main pancreatic duct (MPD) in 93.8% patients. It was statistically similar in groups 1 and 2. We could not cannulate in 20 cases (6.2%).

In group 1, with fistulas, the leaks responded excellently when we traversed the leak and place a bridging stent. This was consistent with a study conducted by Varadarajulu et al⁷ in 2005, to identify predictors of outcome for PD disruption managed by endoscopic transpapillary stent insertion. They concluded that successful resolution of PD disruption by transpapillary stent insertion depends on the type of disruption and the ability to bridge the disrupted duct with a stent. In our study, in addition we found that in cases where we failed to bridge the leak but put stents till the leak also led to a reasonable healing of the fistula. This also is confirmed by study of Jang et al⁸ (2016), that partial disruption of MPD in cases of acute necrotizing pancreatitis responds well to transpapillary stenting. The rest could be managed by using EUS guided pancreatico gastrostomy. Surgery was required only when we failed to cannulate the PD during ERP.

In the group 2 (contrary to group 1), we observed that cases where we could bridge the leak did not experience complete resolution of the cyst. Though we had the duct covered, the fluid in the cyst did not drain out completely. Hence in this group, we had infections in the residual fluid in the cyst, needing EUS guide aspiration and non-collapsed cysts requiring transmural drainage. Meanwhile, cases where we could not cross the ductal obstructions and the wire went into the cyst and we placed transpapillary DPT stents in the cyst, they responded well.

After removing the stents at three to six months, there was no refilling of the cyst. This suggests that, ductal obstructions in chronic pancreatitis is partial. The cysts collapses partially at times, but the flow of pancreatic juice is established in the duct again. As we performed a pancreatic papillotomy in all cases, there was no probable recurrence. Moreover, we feel that placing of smaller diameter 5 Fr DPT stents prevented recurrence, because the disruption did not get very wide while placing the stent. However, there is always a risk of recurrence and we have to follow up the patient on a regular basis.

We assessed transpapillary stents after three months and removed if no stricture was found or exchanged to larger diameter stent if stricture was noted.

In our data, we found that there was a pancreas divisum in 24 cases (7.5%). This was diagnosed by MRCP in 15 cases (62.5%) only. The rest were found at primary ERP procedure. Our policy is, when we fail to cannulate MPD from the major papilla or the guide wire fails to cross the head in five attempts, we look for the minor papilla and try cannulating from it. In doing so, we managed to cannulate in 9 cases (37.5%).

In a subgroup analysis we found that leak resolution in tail

was better than leak from proximal duct in our series ($P = 0.012$).

In conclusion, PD leaks and collections following chronic pancreatitis are different from those due to acute pancreatitis and have to be dealt differently.

ERP without contrast (with transpapillary drainage) is very effective in managing these leaks and pseudocysts.

When transpapillary drainage fails, transmural drainage is required. EUS guided aspiration is useful in partially drained cysts after stenting. We needed surgery to repair persistent leaks. 5 Fr SPT or DPT stents are adequate for stenting. Leak from tail responded better than those from proximal duct with ERP in our series. We recommend further randomized studies to obtain verifiable evidence on management strategies in these very different subset of patients.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

ORCID

Pankaj N. Desai, <https://orcid.org/0000-0003-3931-5678>
 Chintan N. Patel, <https://orcid.org/0000-0003-2519-9493>
 Mayank V. Kabrawala, <https://orcid.org/0000-0003-4707-9695>
 Subhash K. Nandwani, <https://orcid.org/0000-0001-5648-6837>
 Rajiv M. Mehta, <https://orcid.org/0000-0003-3197-4337>
 Ritesh M. Prajapati, <https://orcid.org/0000-0002-8458-276X>
 Nisharg B. Patel, <https://orcid.org/0000-0002-1183-5826>
 Krishna K. Parekh, <https://orcid.org/0000-0003-2362-1785>
 Neha D. Sheth, <https://orcid.org/0000-0001-7935-2348>

References

1. Larsen M, Kozarek R. Management of pancreatic ductal leaks and fistulae. *J Gastroenterol Hepatol.* 2014;29:1360-70.
2. Dominguez-Munoz JE, Drewes AM, Lindkvist B, Ewald N, Czakó L, Rosendahl J, et al. Recommendations from the United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis. *Pancreatology.* 2018;18:847-54.
3. Tanaka T, Kuroki T, Kitasato A, Adachi T, Ono S, Hirabaru M, et al. Endoscopic transpapillary pancreatic stenting for internal pancreatic fistula with the disruption of the pancreatic ductal system. *Pancreatology.* 2013;13:621-4.
4. Kozarek RA, Ball TJ, Patterson DJ, Freeny PC, Ryan JA, Traverso LW. Endoscopic transpapillary therapy for disrupted pancreatic duct and peripancreatic fluid collections. *Gastroenterology.* 1991;100:1362-70.
5. Trevino JM, Tamhane A, Varadarajulu S. Successful stenting in ductal disruption favorably impacts treatment outcomes in patients undergoing transmural drainage of peripancreatic fluid collections. *J Gastroenterol Hepatol.* 2010;25:526-31.
6. Devière J, Bueso H, Baize M, Azar C, Love J, Moreno E, et al. Complete disruption of the main pancreatic duct: endoscopic management. *Gastrointest Endosc.* 1995;42:445-51.
7. Varadarajulu S, Noone TC, Tutuian R, Hawes RH, Cotton PB. Predictors of outcome in pancreatic duct disruption managed by endoscopic transpapillary stent placement. *Gastrointest Endosc.* 2005;61:568-75.
8. Jang JW, Kim MH, Oh D, Cho DH, Song TJ, Park DH, et al. Factors and outcomes associated with pancreatic duct disruption in patients with acute necrotizing pancreatitis. *Pancreatology.* 2016;16:958-65.