Pancreatology xxx (2016) 1–6

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Original article

# Endotherapy is effective for pancreatic ductal disruption: A dual center experience

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ARTICLE INFO

*Article history:*
Available online xxx

*Keywords:*
Endoscopic retrograde cholangiopancreatography
Pancreatic ducts
Pancreatic fistula
Pancreatic pseudocyst
Pancreatitis
Pancreatic duct stent

ABSTRACT

*Background and study aims:* Pancreatic duct (PD) disruptions occur as a result of different etiologies and can be managed medically, endoscopically, or surgically. The aim of this study was to provide an evaluation on the efficacy of endotherapy for treatment of PD disruption in a large cohort of patients and identify factors that predict successful treatment outcome.
*Patients and methods:* We retrospectively evaluated consecutive patients who underwent endoscopic retrograde pancreatography (ERP) for transpapillary pancreatic stent placement for PD disruption from 2008 to 2013 at two tertiary referral institutions. PD disruption was defined as extravasation of contrast from the pancreatic duct as seen on ERP. Therapeutic success was defined by resolution of PD leak on ERP, clinical, and/or imaging evaluation.
*Results:* We evaluated 107 patients (58% male, mean age 53 years) with PD disruption. Etiologies of PD disruption were acute pancreatitis (36%), post-operative (31%), chronic pancreatitis (29%), and trauma (4%). PD disruption was successfully bridged by a stent in 45 (44%) patients. Two patients developed post-sphincterotomy bleeding, two had stent migration, and two patients died as a result of post-ERP related complications. Placement of a PD stent was successful in 103/107 (96%) patients. Therapeutic success was achieved in 80/107 (75%) patients. Non-acute pancreatitis etiologies and absence of complete duct disruption were independent predictors of therapeutic success.
*Conclusions:* Endoscopic therapy using a transpapillary stent for PD disruption is safe and effective. Absence of complete duct disruption and non-AP etiologies determine a favorable endoscopic outcome.


## Introduction

Pancreatic duct (PD) disruption can occur as a consequence of several different types of injuries to the pancreatic duct, including acute pancreatitis (AP), chronic pancreatitis (CP), abdominal trauma, and pancreatic surgery. PD disruptions are generally classified as either being internal when the PD communicates with the peritoneal/pleural cavity or external when the PD communicates with the skin. Clinically, they may resolve spontaneously, or present with clinical features of an ongoing pancreatic leak, most commonly as a pancreatic fluid collection (PFC). Diagnostically, endoscopic retrograde pancreatography (ERP) has the highest accuracy to identify injury to the PD [1–3].

Patients with PD disruptions require prolonged hospital stay and an overall increased health care utilization as compared to patients who sustain pancreatic injury without ductal disruption [4,5]. They are initially managed with supportive care by a combination of different measures [6–9]. Supportive management has been associated with a 50–60% success rate for resolution of PD disruption; for patients who remain refractory, surgery was traditionally the only option. Although surgical management of PD

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http://dx.doi.org/10.1016/j.pan.2015.12.176
1424-3903/

disruptions has a success rate of nearly 90%, it is associated with a significant mortality of up to 10% [10].

Over the last 20–30 years, endoscopic therapy has become the preferred approach for treatment of most PD disruptions refractory to conservative management. Specifically, endoscopic placement of a PD stent and/or pancreatic sphincterotomy can facilitate transpapillary drainage of pancreatic secretions and divert them into the duodenum. Although several cohort studies have examined the success of transpapillary treatment of PD disruption [11–16], most of these studies have been limited by relatively small sample sizes and/or cohorts accumulated from single institutions. The success rates from these reports have been variable, being approximately 60% in the largest studies reported thus far [11,12].

The primary aim of this study was to provide an updated evaluation of the efficacy of transpapillary treatment of PD disruption and examine predictors of successful outcome in a large cohort of patients gathered retrospectively from two independent institutions. Our secondary aim was to assess the recurrence rate of PD disruption after endoscopic treatment as obtained from follow-up data.

## Patients and methods

Endoscopic databases were retrospectively reviewed to identify patients with PD disruption managed endoscopically at Thomas Jefferson University Hospital (TJUH) and the University of Pittsburgh Medical Center (UPMC) from 2008 to 2013. PD disruption was defined as extravasation of contrast from the PD as documented on ERP. The institutional review board at both institutions approved the study prior to its initiation.

The study population consisted of patients with symptomatic internal PD disruption who had failed conservative therapy, including percutaneous drainage and pancreas rest, and were referred for endoscopic transpapillary drainage. The time from initial clinical suspicion of PD disruption to transpapillary therapy was documented. Patients with necrotizing acute pancreatitis were excluded from this study.

Data was assembled on patient demographics, etiology of PD disruption, clinical manifestation of PD disruption, imaging findings prior to therapeutic ERP, ERP findings, procedural details, and adverse events. Therapeutic success was defined as resolution of PD disruption as evidenced by resolution of clinical signs and symptoms, resolution of pertinent imaging findings, and/or absence of contrast extravasation on follow up ERP. Therapeutic failure was defined as persistence of PD disruption despite adequate transpapillary therapy. For patients who did not achieve therapeutic success, subsequent management strategies were documented. For patients who did achieve therapeutic success, long term follow-up data was recorded by reviewing outpatient visits, imaging, emergency room visits, and hospitalizations in order to assess recurrence of PD disruption. Recurrence was defined by the development of a PFC on imaging and/or presence of contrast extravasation on ERP three months or more after documenting therapeutic success, as defined above.

All ERPs were done under the supervision of 9 experienced interventional endoscopists with monitored anesthesia care. All patients received antibiotics prior to undergoing the ERP. Upon deep cannulation of PD and identification of the pancreatic disruption, a guidewire was inserted into the PD for access and transpapillary therapy. PD stents were then placed for therapy of the ductal disruption, with stent diameters ranging between 3–5–7–10 French; the size and type of stent placed, as well as other transpapillary interventions including pancreatic sphincterotomy, PD stone extraction, and PD stricture dilatation was based upon the discretion of the endoscopist.

For all procedures, images were captured during the case for documentation and reviewed by the study investigators. PD disruption was defined as “complete” when there was lack of visualization of the PD proximal to the site of disruption and “partial” when there was visualization of the PD proximal to the site of disruption. A subset of patients underwent concurrent transmural drainage for large PFCs. Following index ERP, patients were scheduled to return for a repeat ERP in 4–8 weeks. At the subsequent endoscopic session, the PD stent was removed if the disruption resolved. If there was persistence of the pancreatic ductal disruption as evidenced by ongoing contrast extravasation, the pancreatic stent was replaced and exchanged at intervals of 4–8 weeks.

## Statistical analysis

Patients were classified according to whether endoscopic transpapillary treatment was successful or unsuccessful. Factors associated with PD stent success were then compared. Categorical variables were presented as percentages and continuous variables were presented as mean values with standard deviations. Chi-square testing was used for categorical variables and Wilcoxon rank-sum testing for continuous variables. To estimate the effect of relevant variables on endoscopic outcome, univariate analyses were followed by multivariate regression analysis using those variables found to be statistically significant on univariate analysis. A p-value of $<0.05$ was used to identify statistical significance.

## Results

### *Patient demographics and clinical characteristics*

A total of 125 patients were identified with evidence of PD disruption on ERP between 2008 and 2013. Of these patients, 18 had necrotizing pancreatitis and were excluded from the study, leaving 107 patients overall in the study cohort (38 from TJHU and 69 from UPMC). The mean age of the cohort was 53 years (SD 15) and the study population was predominantly male (58%).

The etiologies of PD disruption included AP in 39 patients (36%), post-operative in 33 patients (31%), CP in 31 patients (29%), and abdominal trauma in 4 patients (4%). Of PD disruptions due to AP, the etiologies included alcohol abuse in 12 cases (31%), idiopathic in 11 cases (28%), biliary in 7 cases (18%), and other etiologies in 9 cases (23%). PD disruptions as a result of surgery were due to distal pancreatectomy in 17 cases (52%), splenectomy or colon resection with consequent pancreatic tail injury in 8 cases (24%), enucleation in 4 cases (12%), extended pancreatectomy with celiac axis resection (Appleby procedure) in 3 cases (9%), and pancreatic necrosectomy in 1 case (3%). Of PD disruptions as a result of CP, etiologies included alcohol in 16 cases (52%), idiopathic in 12 cases (39%), and pancreatic divisum in 3 cases (10%). Of PD disruptions resulting from abdominal trauma, 3 cases were due to a fall and 1 was due to a motor vehicle accident.

Clinical manifestations of PD disruption included PFCs in 89 cases (83%), smoldering pancreatitis (ongoing symptoms with persistent pancreatic enzyme elevation and pancreatic inflammation on imaging for at least 10 days) in 14 cases (13%), pancreatic ascites in 7 cases (7%), and pancreatic pleural effusion in 5 cases (5%). Prior to index ERP, 35 patients received a somatostatin analog (33%), 51 patients had a percutaneous drain (48%), 31 patients received enteral nutrition through a nasojejunal feeding tube (29%), and 17 patients received nutrition through a parenteral route (16%).

Please cite this article in press as: Das R, et al., Endotherapy is effective for pancreatic ductal disruption: A dual center experience, Pancreatology (2016), http://dx.doi.org/10.1016/j.pan.2015.12.176