

Incidence of Pancreatitis in Failed Versus Successful ERCP And the Possible Benefit of Pancreatic Duct Stenting in High Risk Cases. Prospective Randomized Study

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Abstract: Introduction: Pancreatitis is the most common complication after ERCP. The reported incidence ranges from 1% to 24%, depending on the study population, the endoscopic procedure, and disease definitions. Objectives: The study had two objectives. The first was to assess the incidence of post ERCP pancreatitis in cases of failed biliary access after manipulation of the pancreatic duct with multiple cannulations, dye injection and/or guide wire cannulation. The second objective was assess the benefit of pancreatic duct stenting in high risk cases especially those with failed biliary access and had pancreatic duct manipulation in cases with calcular obstructive jaundice. Methods: This is a prospective randomized study which included 50 patients presented with calcular obstructive jaundice, all patients diagnosed with malignant obstructive jaundice or had a previous attempt of ERCP were all excluded. Patients who had more than 10 attempts of CBD cannulation which ended with pancreatic duct cannulation were all randomized for pancreatic duct stenting using closed envelops. Results: A total of 50 cases were included in the study. The study included 28 females and 22 males with a mean age of 50 years. The indication of ERCP was due to calcular obstructive jaundice in all 50 (100%) patients. The overall incidence of post ERCP pancreatitis was 7/50 (14%), mild pancreatitis in 5 cases and moderate in 2 patients, none of the patients had severe pancreatitis. Females had an overall incidence of pancreatitis of 14.3% while males had an incidence of 13.4 %. Conclusions: Incidence of pancreatitis is more in cases with failed biliary drainage. Pancreatic duct stenting after manipulation of the pancreatic duct is safe and successful in decreasing the incidence of post ERCP pancreatitis whether it was successful or not to drain the biliary system.

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1. Introduction

Pancreatitis is the most common complication after ERCP. The reported incidence ranges from 1% to 24%, depending on the study population, the endoscopic procedure, and disease definitions^[1]. It was reported that young age, suspected sphincter of Oddi dysfunction (SOD), female sex, normal bilirubin, and a history of post-ERCP pancreatitis as having a significant association in at least 1 study. The procedure-related factors were: multiple pancreatic injections, pre-cut sphincterotomy, difficult cannulation, pancreatic sphincterotomy, and balloon biliary sphincter dilation. The patient factors that demonstrated a significant association with pancreatitis were suspected SOD, female sex, and a history of pancreatitis. The procedure-related variables that demonstrated a significant association were pre-cut sphincterotomy and pancreatic duct (PD) injection^[2]. Furthermore, it was demonstrated that multiple risk factors may act synergistically to substantially increase the risk of post-ERCP pancreatitis^[3]. Ampullary manipulation and the use of cautery or balloon sphincter dilation can lead to significant edema of the

pancreatic orifice. This, in turn, may cause impaired PD drainage. One strategy to minimize this problem is to place a temporary stent within the PD. Thus, there is no consensus in the literature about the indications for prophylactic PD stent placement and the technique for this procedure^[4].

Objectives:

The study had two objectives. The first was to assess the incidence of post ERCP pancreatitis in cases of failed biliary access after manipulation of the pancreatic duct with multiple cannulations, dye injection and/or guide wire cannulation. The second objective was assess the benefit of pancreatic duct stenting in high risk cases especially those with failed biliary access and had pancreatic duct manipulation in cases with calcular obstructive jaundice.

2. Methods:

This is a prospective randomized study which included 50 patients presented with calcular obstructive jaundice, all patients diagnosed with malignant obstructive jaundice or had a previous

attempt of ERCP were all excluded. Patients who had more than 10 attempts of CBD cannulation which ended with pancreatic duct cannulation were all randomized for pancreatic duct stenting using closed envelopes. Patients after the study were then categorized into the following groups; Group A: Successful cases of therapeutic ERCP with easy cannulation (less than 5 attempts) and no pancreatic duct cannulation by guide wire or dye injection. Groups B, C, D & E had manipulation of the pancreatic duct with dye injection and/or with guide wire cannulation several times (more than 5 up to 20 attempts) before access to the biliary system or termination of the procedure and deemed as a failure after 20 attempts of cannulation

Table 1: (shows the different groups of the study).

Group	Successful No PD manipulation	Successful + PD manipulation+stenting	Successful+PD manipulation+no stenting	Failed+PD manipulation+stenting	Failed+PD manipulation +no stenting
A					
B					
C					
D					
E					

There were 4 performing physicians that performed the procedure, randomization for pancreatic duct stenting was done during the procedure. All cases were monitored for the new onset of pancreatic-type abdominal pain associated with at least a threefold increase in serum amylase or lipase occurring within 24 hours after an ERCP, and the pain symptoms need to be severe enough to require admission to the hospital or to extend the length of stay of patients who are already hospitalized to diagnose as post ERCP pancreatitis. Patients in each group of groups B, C, D & E had a 50% chance of having a prophylactic pancreatic duct stent. All prophylactic stents used were 5fr pancreatic stents without an intraductal flange and were removed after one week-ten days if didn't fall off on its own.

3. Results:

A total of 50 cases were included in the study. The study included 28 females and 22 males with a mean age of 50 years. The indication of ERCP was due to calcular obstructive jaundice in all 50 (100%) patients. The overall incidence of post ERCP pancreatitis was 7/50 (14%), mild pancreatitis in 5 cases and moderate in 2 patients, none of the patients had severe pancreatitis. Females had an overall incidence of pancreatitis of 14.3% while males had an incidence of 13.4 %. Group A; 17 patients had an easy selective cannulation of the CBD with less than 5 trials for cannulation with no manipulation of the pancreatic duct followed by successful biliary drainage and had no pancreatitis (0%). In group B (failed ERCP with manipulated pancreatic duct) the incidence of post ERCP pancreatitis was 5/20 (25%), meanwhile in

group C (successful ERCP with manipulated pancreatic duct) the incidence of acute post ERCP pancreatitis was 2/20 (10%). So as to determine whether there is an increased incidence of post ERCP pancreatitis in failed cases (first objective) we compared groups A & C (successful ERCP) in which pancreatitis occurred in 2/30 (6.7%) with group B (failure of biliary drainage) where 5/20 (25%) had post ERCP pancreatitis. Furthermore we compared group A with group C as to determine the effect of pancreatic duct manipulation on the incidence of pancreatitis 0% Vs 6.7% respectively. We also compared groups B & C to assess the effect of failure of biliary drainage with manipulation of the pancreatic duct, we found that the incidence of pancreatitis in group B was 25% Vs 10% in group C. To answer to the second objective of the possible prophylactic effect of pancreatic duct stenting after a manipulation to the pancreatic duct we compared group C&E (had no pancreatic duct stenting whether the case was successful or not as of biliary drainage) and group B&D (had a prophylactic pancreatic duct stent whether the case was successful or not as of biliary drainage) the incidence of pancreatitis in the prophylactic pancreatic duct stent was 5%, while in the no stent group was 30%. The effect of PD stenting in prevention of post ERCP pancreatitis in failed cases was done by comparing groups BI (failed ERCP & no stent) & BII (failed ERCP & stent) the incidence of pancreatitis was 40% Vs 10% respectively.

4. Discussion:

In our study we tried to concentrate on the effect of failure of biliary drainage as an independent factor for the development of post ERCP pancreatitis in cases with calcular obstructive jaundice which is not sufficiently addressed in the literature and hence the question if in such cases the insertion of a prophylactic duct stent would be of any additional benefit even in cases of failure to drain. Pancreatitis remains the most frequent complication after ERCP. In high-risk patients, pancreatitis rates have historically been as high as 20%^[3,5-6]. More recently, however, therapeutic endoscopists have noted a significant decline in the frequency and severity of post-ERCP pancreatitis, principally because of the routine placement of temporary small-diameter plastic pancreatic duct stents. Indeed, severe pancreatitis complicating ERCP is now infrequently seen. To date, more than 30 studies have evaluated efficacy of stent placement in high-risk patients^[7]. In a meta-analysis of 5 prospective studies, Singh et al. demonstrated that pancreatic duct stenting reduced the frequency of post-ERCP pancreatitis nearly 3-fold, from 15.5% to 5.8%^[8]. There are both patient- and procedure-related risk factors for the development of post-ERCP pancreatitis^[9-18]. Biliary orifice balloon

dilation, difficult cannulation, performance of pancreatic sphincterotomy or precut sphincterotomy, and number of pancreatic duct injections were significant procedure-related risks for pancreatitis. In addition, it has been suggested that degree of pancreatic duct filling at ERCP^[20] and trainee involvement^[13] may be independent risk factors as well. In our study, we attempted to identify the incidence of the risk of developing pancreatitis in cases failed ERCP with failure of biliary drainage with multiple PD cannulation by a guide wire or repeated dye injection as an independent risk factor. As inclusion criteria, no patient had endoscopic therapy performed. We were able to assess degree of difficulty of cannulation (subjectively, by procedure time consumed before biliary access and the number of pancreatic duct injections or guide wire cannulation). Because of the potential risks and consequences of post-ERCP pancreatitis, considerable efforts have been made to define patient- and procedure-related factors that may be associated with an increased risk of this complication, along with determining interventions that can reduce post-ERCP pancreatitis. There have been numerous theories about the mechanisms of post-ERCP pancreatitis. The most widely accepted theory is that mechanical trauma to the papilla or pancreatic sphincter, caused during instrumentation, creates transient obstruction of outflow of pancreatic juice^[4]. In a prospective study of 1223 patients from a single referral center, pancreatitis occurred in only 3.3% of patients who required less than five attempts at cannulation; 9% when 6 to 20 cannulation attempts were required; and 14.9% when the cannulation was considered difficult, requiring more than 20 attempts^[16]. These data are more or less consistent with our study findings. Difficulty in cannulation, which can produce papillary trauma, has also proved to be an independent risk factor for procedural complications^[3,9,16,18]. This risk increases incrementally with the number of failed cannulations^[4]. This leads to the idea about determining the incidence of post ERCP pancreatitis in failed bile duct access after multiple attempts of cannulation during which there is a usual access to the pancreatic duct. This risk factor to our knowledge is not discussed nor studied thoroughly in any previous studies and the closest studied risk factor was difficult cannulation but it was not mentioned if bile duct access was eventually achieved or not and whether this makes a statistical difference. In our attempt to answer this question we found that the incidence of post ERCP pancreatitis in cases with failure of bile duct access and biliary drainage specially with a manipulated PD was 25% meanwhile in cases with successful biliary drainage the incidence was 6.7%. This is consistent with most studies as post ERCP pancreatitis has a reported incidence ranging

from 1.8% to 7.2% in most prospective series^[3,9,10,14,16,18,21]. However, The reported incidence can vary widely (up to 40%), depending on the criteria used to diagnose pancreatitis, the type and duration of patient follow-up, and case mix^[6]. This explains the difference in incidence of pancreatitis in different series as we think that the incidence of pancreatitis should be calculated or monitored according to each risk factor alone and then may be estimated for each case according to accumulation of multiple risk factors with its corresponding risk of post ERCP pancreatitis in each individual case. This is well demonstrated in our study as in cases that were easy with easy cannulation and bile duct access with no manipulation of the PD the incidence of post ERCP pancreatitis was 0% meanwhile in cases that were successful in biliary drainage but had manipulation of the PD the incidence of pancreatitis was 20%. The value of prophylactic PD stenting in the prevention of post ERCP pancreatitis in such failed cases with multiple manipulations of the PD was the second objective of our study. The incidence of pancreatitis in a manipulated PD without prophylactic PD stenting was 30% meanwhile the incidence in cases with a prophylactic PD stent was 5%. As numerous theories exist for the development of this complication, including mechanical trauma, hydrostatic, chemical, allergic, and enzymatic or thermal injury.^[19] However, papillary trauma is typically cited as to why pancreatic stent placement may be beneficial because poor pancreatic duct drainage may contribute to the onset of the inflammatory cascade.^[3,8,19] Potentially, with a widely patent pancreatic orifice, pancreatic duct drainage may be sufficient post-ERCP to obviate the need for stent placement^[7]. In a subgroup analysis the benefit of pancreatic duct stenting in cases with failed ERCP in preventing post ERCP pancreatitis, the incidence of pancreatitis was 10% in the stent group Vs 40% in the non-stent group. The value of PD stenting in successful biliary drainage but with manipulated PD the incidence of pancreatitis was 0% Vs 20% in cases with no stent. In summary, the incidence of post ERCP pancreatitis seems to be very low in cases with easy cannulation and no manipulation of the PD and seems to be highest in cases with failed biliary drainage with multiple trials of cannulation and with manipulation of the PD. The use of a prophylactic PD stent in cases with difficult cannulation and dye injection or guide wire cannulation of the PD imposes a clear benefit for the prevention of this complication and should be practiced and promoted specially if there is failure of ERCP in access of the bile duct and the inability of performing biliary drainage.

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