

# Prevention of post endoscopic retrograde cholangiopancreatography pancreatitis

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## Abstract

Post ERCP pancreatitis (PEP) is a common problem. Knowledge of patient and procedure related risk factors along with appropriate measures aimed at reduction of risk have been successful in reducing both the incidence and the severity. Prophylactic pancreatic duct stenting has definitely reduced the incidence and the severity of PEP in high risk patients. There are some emerging data on the use of non steroidal anti inflammatory agents though this is not widely adapted in practice. Key is to avoid procedures with marginal indications and use of non invasive/less invasive procedures.

## Key words

ERCP, post ERCP Pancreatitis, pancreatic stents, post ERCP complications

## Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a commonly done procedure and yet one of the more challenging procedures done by endoscopists. Post ERCP pancreatitis (PEP) is one of the most common complications of ERCP. The reported rates of complications have been between 1-40%. The generally accepted background rate is about 5% and this includes a case mix of both low and high risk patients. The rates of PEP are variable depending on the rigor with which it is evaluated, patient population, type of procedures and to an extent on the operator. Several large clinical and experimental studies have enhanced our knowledge regarding the risk factors and this in turn has lead to further studies aimed at reduction of this risk.<sup>[1]</sup>

## Definition of post ERCP pancreatitis

To diagnose PEP the following criteria are used:

1. Abdominal pain (typically in the epigastric area with radiation to the back),

2. Greater than 3 fold elevation of amylase and or lipase,
3. Radiological imaging suggestive of pancreatitis.

To diagnose PEP ideally one has to have at least two of the above criteria. When amylase and lipase are routinely measured it is often seen that there is an elevation of the enzymes despite the patient being asymptomatic. It is also not uncommon to see patients with post procedural abdominal pain without any elevation of the enzymes. Radiological imaging thus is helpful when the diagnosis is equivocal. The severity of pancreatitis has also been standardized based on consensus guidelines and is based on the number of days of hospitalization and the interventions needed.<sup>[2]</sup>

## Mechanism for post ERCP pancreatitis

The exact mechanism for PEP is unclear. Like pancreatitis from other etiologies there needs to be an "initial trigger" event that sets off the inflammatory cascade leading to pancreatitis. The postulates for PEP include: thermal injury from sphincterotomy, mechanical obstruction to outflow of the pancreatic secretions as seen by papillary edema from attempted multiple cannulations, sphincterotomy etc., injury to the main duct or side branches from multiple passages of a guide wire, chemical injury from the contrast, possible microbiological injury due to introduction of duodenal flora into the pancreas etc.,

The relative risk or contribution of these factors are less clear and have formed a basis for intervention to reduce PEP. From the various multivariate analyses the risk factors are broadly classified as:

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1. Patient related
2. Procedure related
3. Physician related (case volume and technique).

Knowledge of these risk factors is important in reducing the risk of PEP by

1. Appropriate selection of patients by doing a careful risk: benefit analysis of doing ERCP and use of less/non invasive modalities
  2. identify patients who will need prophylactic intervention
  3. referral to an appropriate center for the procedure depending on the intervention needed and expertise of the endoscopist.
- It is also important to note that when multiple risk factors are present the total risk seems to be multiplicative rather than being simply additive.<sup>[1]</sup>

### Patient related risk factors

Based on the current data the following groups of patients are at a significant risk:

1. young age
2. females
3. suspected sphincter of Oddi (SO) dysfunction
4. history of prior PEP or recurrent pancreatitis,
5. Non elevation of bilirubin
6. absence of a stone in those suspected to have a bile duct stone. Non absence of a stone in those suspected, normal bilirubin and non dilated bile duct which are thought to be risk factors and might in fact be surrogate markers for suspected sphincter of oddi dysfunction.<sup>[1,3-5]</sup>

### Procedure related risk factors

There are several procedural risk factors identified and include:

1. repeated cannulation attempts or multiple cannulations of the pancreatic duct. This causes papillary edema and possible outflow obstruction of the pancreatic duct.
2. Pancreatic sphincterotomy (including minor papilla) and not biliary sphincterotomy.
3. Injection of contrast into the pancreatic duct.<sup>[6]</sup> Though acinarization of the pancreas should be avoided it has been shown to be a risk factor only in univariate analysis and not on multivariate analysis. Also the risk of PEP seems to increase with the degree of ductal opacification. SO manometry itself especially with the use of an aspiration catheter is not a significant risk factor. Precut sphincterotomy especially when done at a non tertiary center/low case volume endoscopist appears to have a higher risk.<sup>[1,7]</sup>

### Prevention of PEP

Since the data suggest that the risk of pancreatitis is no different between diagnostic and therapeutic procedures and since non invasive imaging modalities such as magnetic resonance pancreatography can provide information regarding ductal imaging, diagnostic ERCP should be generally avoided. The risk seems to be the highest in whom the procedure is needed the least.

Effective cannulation reduces papillary edema and need for repeated pancreatic duct injections. Though a papillotome has clearly shown to have a higher success at cannulation compared to a standard cannula there has been no reduction in PEP. However use of a guide wire along with a papillotome has shown to reduce PEP. Guide wire cannulation as opposed to contrast injection prior to deep cannulation appears to have a lower rate of PEP. In practice a combination of small injection of contrast along with guide wire cannulation probably is safe and effective.<sup>[8]</sup>

### Pancreatic duct stenting/mechanical prevention

Stenting of the pancreatic duct especially in high risk patients has shown to reduce the risk of PEP in several studies including meta analyses.<sup>[9-11]</sup> Stent placement likely preserves the pancreatic ductal outflow and thereby reduces PEP. Situations where prophylactic pancreatic stents are useful include:

1. SO manometry with or without sphincterotomy
2. Precut sphincterotomy
3. History of prior PEP/recurrent acute pancreatitis
4. prolonged cannulation
5. precut sphincterotomy for biliary access
6. ampullectomy
7. pancreatic duct wire cannulation as an aid to biliary cannulation
8. balloon dilation of the biliary sphincter etc.

Routine pancreatic duct stenting is not recommended.

Despite the advantage of reduction of PEP especially severe pancreatitis, pancreatic stenting has limitations. Endoscopists and assisting staff should be familiar with passage of small caliber wires into the pancreatic duct without damaging the side branches. One should be familiar with placement of either small caliber pigtail stents or modified straight stents. One should realize that risk of failed pancreatic duct stent placement after multiple attempts is worse than not placing a stent at all and one should weigh the risks of aborting an attempt versus a prolonged attempt at cannulation and placement of a prophylactic stent. Sometimes passage of a small length of the wire into the duct and anchoring with the help of a “knuckle or loop” is adequate for a straight stent placement.<sup>[12,13]</sup>

Despite evidence that pancreatic stenting reduces the severity of PEP; utility of prophylactic pancreatic stents among experts is variable.<sup>[14]</sup> The characteristics of the ideal stent are not clear. Data do suggest that smaller diameter stents cause less damage to the pancreatic duct.<sup>[15]</sup> Even short term stenting of the duct can cause significant ductal injury.<sup>[16]</sup> At least for now it is clear that short term stenting with a smaller caliber stent is preferable.<sup>[13]</sup> If a stent is placed one should ensure that there is a spontaneous dislodgement of the stent or else it should be removed endoscopically removed in 2 weeks.

### Chemoprevention of PEP

Chemoprevention of PEP is attractive since it does not require

any special expertise. Several agents including heparin, antibiotics, allopurinol, interleukin -10, platelet activating factors, low osmolar or non ionic contrast, etc., have been shown to be ineffective. Gabexate and somatostatin given over prolonged periods appear to be effective. These drugs are not routinely available in India. Recently diclofenac sodium given as a suppository prior to the procedure has been shown to be effective in a few studies including a meta analysis though this has not been widely adapted.<sup>[17,18]</sup> Another recent study has shown a combination of rectal diclofenac given prior to the procedure along with a somatostatin infusion for 6 hours post procedure was effective.<sup>[19]</sup> Larger studies are needed. Ideally the drug should be effective, easy to administer and safe without side effects. At the present time this does not appear to be the primary strategy for prevention.

## Conclusion

Clear understanding regarding the patient and procedure related risk factors helps in careful planning regarding risk stratification and taking measures to prevent PEP. Diagnostic ERCP should be avoided. Chemoprevention with diclofenac appears to be attractive but has not widely adapted in clinical practice. Prophylactic pancreatic stents have clearly reduced the risk and severity of post ERCP pancreatitis and should be placed in high risk patients.

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