Post-ERCP pancreatitis
A single center experience and an update on prevention strategies

Francesco D’Arpa, Roberta Tutino, Emanuele Onofrio Battaglia, Giuseppina Orlando, Giuseppe Salamone, Leo Licari, Gaspare Gulotta

Department of Surgical, Oncological and Oral Sciences, University of Palermo, General Surgery and Emergency Operative Unit, Policlinico Universitario “P. Giaccone”, Palermo, Italy

OBJECTIVES: Pancreatitis is one of the most frequent complications of ERCP; in unselected patients the incidence is 3.5%, reaching 25%, and is mild-moderate in 90%. A stratification of patients into low or high risk is important to provide adequate information to patients and to decide when to refer them to tertiary centers; moreover, many prophylactic measures have been proposed over years. Our aim was to select risk factors for PEP and compare them with current literature in order to propose adequate preventive strategies.

METHODS: It was analyzed the occurrence of Post-ERCP Pancreatitis in a series of 492 consecutives patients treated with ERCP by two expert interventional endoscopists. The possible risk factors were evidenced by a multivariate analysis, were states our proposals for Post-ERCP Pancreatitis prevention and compared them to the current literature.

RESULTS: We observed 14 PEP (2.8%). 6 mild, 4 moderates and 4 severe. The multivariate analysis evidenced as risk factors the high number of attempts of cannulation and the pancreatic injection of contrast medium and found a protective role for pre-cut sphincterotomy. Our mortality rate was 0.4%.

CONCLUSIONS: The guide-wire cannulation technique and, in selected cases, the pre-cut permit to minimize the number of cannulation attempts and to increase the success rate of primary cannulation; we promote their use to reduce PEP occurrence.

KEY WORDS: Endoscopic retrograde cholangiopancreatography, Pancreatitis

Introduction

ERCP recognizes nowadays a prevalent role in the treatment than in the diagnosis of pancreato-biliary diseases, thanks to the development of alternative diagnostic tools as MRCP and EUS that better follow the scope.

The procedure’s complications include bleeding, cholangitis, cholecystitis, perforation and pancreatitis and can lead to severe or fatal outcomes.

The post-ERCP pancreatitis (PEP) is the most frequent complication and its occurrence is nowadays difficult to manage. The diagnosis of pancreatitis according to Cotton’s criteria includes three main factors: clinical, laboratoristics and imaging. The upper quadrants abdominal pain is need. Biochemically an elevation of the amylase or lipase serum levels over three times the upper normal level (UNL) is the second element in diagnosing. The CT, MR or EUS can aid in the diagnosis. As proposed by Freeman in PEP these have to be present at 24 hours from the procedure determining a hospital admission or a prolongation of the planned.
CT examination to establish the grading of pancreatitis in accordance to Balthazar score must be used in uncertain diagnoses, to confirm the severity basing on clinical data, if there was an inefficient treatment, to confirm the failure of the therapy or if is planned an invasive attempt of treatment.

Were found patient related and procedure related risk factors for PEP.

We attempt to analyze the occurrence of this complication in our series comparing this to literature data to analyze the proposals for its prevention.

Methods

A retrospective study was carried out through the analysis of patients treated with ERCP for pancreato-biliary diseases by the General and Urgent Surgery Operative Unit of the Policlinico “Paolo Giaccone” of Palermo from January 2012 to November 2013 to evaluate the occurrence of PEP. All procedures were executed by two expert interventional endoscopists.

Patients’ anamnesis and admission diagnoses were analyzed. The elevation of serum amylase values more than 3 or 5 times the UNL at 4-6 hours post-ERCP, the occurrence of pain documented by clinical diaries and radiological investigation by CT scan were collected in all patients to evaluate the occurrence of PEP.

The presence of patients-related and procedure-related risk factors for PEP was analyzed.

Data were collected using frequencies and percentages and those about risk factors were then analyzed with a multivariate analysis using STATA software for the OLS regression and SPSS software for the binary logistic regression to evaluate the impact of the different risk factors proposed by the ESGE guidelines 2010 in our series. It was verified the relation between variables with the “correlate” command and all variable were found independents; the absence of multicollinearity between variable was tested with VIF and so could be performed the regression.

For the OLS regression it was done a linear regression that includes as variables: SOD; female gender; previous pancreatitis; younger age; non dilated bile ducts; absence of chronic pancreatitis; normal serum bilirubin; pre-cut; pancreatic injection of contrast; high number of attempts; Pte; biliary balloon extraction; failure to clear bile duct; then, it was done a STEPWISE regression (a normal linear regression) that permitted to evidence the relevant risk factors for our series.

It was done a test to understand which model was better for our database using the Fisher’s F and it was found preferable the STEPWISE regression.

The logistic binary regression, even though the small number of cases analyzed, was conducted, too, for risk factors analysis. Data on hospital stay to assess the morbidity and mortality rates were finally collected.

Results

By the interventional endoscopy group of the General and Urgent Surgery O.U. of the Policlinico “P. Giaccone” of Palermo in the years 2012-2013 were executed 492 ERCP. The average age of patients treated was 70 years old with a standard deviation of 14 years. The diagnoses are summarized in Table I.

The Freeman’s criteria for the diagnosis of pancreatitis presented at 24 hours from procedure that occurred in our patients are summarized in Table II. We had 14 PEP accounting for 2.8 % of our patients. The admittance diagnoses in patients with PEP were lithiasis in 6 patients, malignancies of biliary tract in 6 patients and pancreatic neoplasms in 2 patients.

Presence of risk factors for PEP, according to ESGE guidelines 2010, presented by patients was analyzed with a univariate analysis and is reported in Tables III and IV. The multivariate analysis with the STEPWISE regression...
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TABLE IV

<table>
<thead>
<tr>
<th>Procedure-related risk factors</th>
<th>N.</th>
<th>%</th>
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<tbody>
<tr>
<td>Definite risk factors</td>
<td></td>
<td></td>
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<tr>
<td>Precut sphincterotomy</td>
<td>18</td>
<td>3.7</td>
</tr>
<tr>
<td>Pancreatic injection</td>
<td>114</td>
<td>23.2</td>
</tr>
<tr>
<td>Likely risk factors</td>
<td></td>
<td></td>
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<tr>
<td>High number of cannulation attempts</td>
<td>40</td>
<td>8.1</td>
</tr>
<tr>
<td>Pte</td>
<td>292</td>
<td>59.3</td>
</tr>
<tr>
<td>Biliary balloon sphincter dilation</td>
<td>6</td>
<td>1.2</td>
</tr>
<tr>
<td>Failure to clear bile duct stones</td>
<td>40</td>
<td>8.1</td>
</tr>
</tbody>
</table>

TABLE V

<table>
<thead>
<tr>
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</tr>
</tbody>
</table>

TABLE VI

<table>
<thead>
<tr>
<th>Cotton’s criteria</th>
<th>N. patient</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild pancreatitis: 2-3 days of hospital stay</td>
<td>6</td>
<td>42.8</td>
</tr>
<tr>
<td>Moderate pancreatitis: 4-10 days of hospital stay</td>
<td>4</td>
<td>28.6</td>
</tr>
<tr>
<td>Severe pancreatitis: More than 30 days</td>
<td>4</td>
<td>28.6</td>
</tr>
<tr>
<td>Tot.</td>
<td>14</td>
<td></td>
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biliary balloon sphincter dilatation, failure to clear bile duct stones. In June 2014 an update of these guidelines includes, as definitive procedure-related risk-factors: cannulation attempts duration > 10 minutes and pancreatic guide-wire passage ≥ 1, in addition to the pancreatic injection of contrast; moving pre-cut sphincterotomy to the likely, but not-definitive, risk-factors. In our multivariate analysis, using the STEPWISE regression, the only risk factor for PEP is the high number of cannulation attempts, while are favorable factors the pre-cut and failure to clear bile duct (Table V). The logistic binary regression, performed even though the small number of case, reveals, as only risk factor, the pancreatic injection of contrast (Table VI).

Four patients (10%) among those presenting high number of attempts and 8 patients (7%) among those presenting pancreatic injection of contrast have suffered PEP. Nobody of the patients in whom it was used pre-cut has showed PEP. Many prophylactic measures, as procedural tricks and various drugs were proposed over the years. Non-steroidal anti-inflammatory drugs (NSAIDs) can reduce the incidence of PEP. 100 mg of diclofenac or indomethacin administered rectally immediately before or after ERCP are recommended. Even if, Dobronte reports that indomethacin did not prove effective in preventing PEP and Li reports that NSAIDs effectively reduce the incidence of PEP but not that of moderate to severe pancreatitis. We didn’t use NSAID in the analyzed patients but their use seems to have found a large consensus, and being an easy and cost effect measure, we agree that it have to be enterprise. Zhao proposes pre-ERCP somatostatin in reducing the risk of PEP in high-risk patients, but not in low-risk ones; however in this regard there is no consensus. Cotton found a reduced risk for overall complications after prophylactic pancreatic stent (PS) placement but not specifically for pancreatitis. Masaki affirms that PS reduces the risk of PEP and is beneficial for patients with high risk. In high risk patients prophylactic PS is, also, recommended by ESGE guidelines 2014; although, Takenaka affirms that it is not apparent which group receives the most preventive effects from PS within the high risk group of PEP especially in the procedure-related group which is affected by intraoperative decision. However, Elmunzer reports that patients receiving Indomethacin alone appear to have a lower risk of PEP compared to those receiving a stent alone or a stent in combination with indomethacin. Failure of pancreatic stent placement is associated with high rates of PEP; we don’t use its and accord to Abu Dayyeh in that it seems not an ideal solution for PEP for multiple reasons: failure rate in stent placement > 65% PEP, adverse events, substantial costs and inconvenience to the patient. Trauma resulting from repeated attempts of biliary cannulation has been proven to be a risk factor for the development of PEP. High number of cannulation attempts is a risk factor also in our multivariate analysis. The number of cannulation attempts should be minimized. Injection of contrast medium into the pancreatic duct is an independent predictor of PEP and, if it occurs, the number of injections and the volume of contrast medium injected into the pancreatic duct should be kept as low as possible. Tse, in a large meta-analysis, reports that the guide wire cannulation technique reduces PEP facilitating selective biliary cannulation, limiting papillary trauma, and minimizing inadvertent contrast injection into the pancreatic duct or the papilla itself; he propose to put the guide wire in a sphincterotome as the most appropriate first-line primary cannulation technique in the era of therapeutic ERCP. The guide wire cannulation technique increases the success rate of primary cannulation when compared with the contrast assisted method and is recommended for deep biliary cannulation. We agree on this technique to reduce the number of cannulation attempts and use it several times.

In the past, pre-cut sphincterotomy was considered a risk factor for PEP while recently this role was attributed most to the high number of attempts prior to pre-cut, than to the pre-cut itself. In a meta-analysis Navaneethan reports that precut sphincterotomy and persistent attempts at cannulation are comparable in terms of overall complication rates; early pre-cut prevent excessive and repetitive papillary trauma which may in turn increase the risk of PEP. Choudhary suggests that early pre-cut done within 5-10 min of failed cannulation decrease the odds of PEP without compromising cannulation rates or increasing other complications. We used it, in selected cases, without PEP occurrence and our data, in accordance with the recent literature, support this choice, finding it as a favorable factor.

**Conclusion**

In conclusion, the diffusion of MRCP and EUS as diagnostic tools and the strictly therapeutic intent for ERCP can prevent unnecessary procedures. Guide-wire cannulation technique and the early pre-cut can reduce the trauma to the papilla caused by high number of attempts and promote selective biliary cannulation reducing pancreatic duct contrast injection. The use of prophylactic drugs can reduce the inflammatory process. Even if PEP is an ineludible complication of the ERCP with these measures it seems to be possible to reduce the procedure’s complication rate.

Conflict of interest: Francesco D’Arpa and other co-authors have no conflict of interest.

**Riassunto**

La pancreatite rimane ad oggi la maggiore complicanza dell’ERCP nonostante numerose misure tese alla sua pre...
venzione siano state proposte negli anni. La sua incidenza è del 3,5% e raggiunge in alcune serie di casi anche il 25%; solitamente è lieve-moderata nel 90%.

La stratificazione dei pazienti in base al grado di rischio è necessaria per destinare i casi più complessi a centri di terzo livello presenti nel territorio; per far questo, un’analisi dei possibili fattori di rischio è stata originariamente proposta da Freeman ed è poi stata modificata dall’ESGE sulla base dei contributi dei singoli centri, con importanti modifiche.

Il presente studio analizza l’incidenza di pancreatite post-ERCP in un centro di terzo livello analizzando, sulla scorta dei fattori di rischio proposti, l’aderenza dei dati. Negli anni 2012-2013, 492 pazienti sono stati sottoposti ad ERCP da due esperti endoscopisti. Secondo le classificazioni di Freeman e Cotton sono state osservate 14 PEP (2.8%), di cui 6 lievi, 4 moderate e 4 severe. È stata condotta un’analisi multivariata che ha evidenziato come fattori di rischio l’elevato numero di tentativi di incannulamento della via biliare e l’iniezione di mezzo di contrasto nel dotto pancreatico; sono risultati fattori protettivi l’early pre-cut e il fallimento della procedura con la sua interruzione. Nella discussione sono state inoltre brevemente analizzate le varie misure profilattiche, quali il posizionamento di protesi pancreatiche e l’utilizzo dei FANS.

È interessante notare come i nostri risultati rafforzino gli ultimi orientamenti nel management dell’ERCP, circa l’utilizzo della tecnica di incannulamento filo-guidato e del pre-cut; questi infatti riducono il numero di tentativi di incannulamento ed il conseguente trauma alla papilla promuovendo un incannulamento biliare selettivo e prevenendo l’iniezione di mezzo di contrasto nel dotto pancreatico. Nonostante la pancreatite sia un’ineludibile complicanza dell’ERCP, reputiamo che questi accorgimenti tecnici possano essere utilizzati nel prevenire la sua insorgenza.

References


