

# Comparison between endoscopic and surgical intervention in acute pancreatitis and pancreatic cancer

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## 1.0. COMPARISON BETWEEN ENDOSCOPIC AND SURGICAL INTERVENTION IN ACUTE PANCREATITIS

### 1.1. Introduction

Gallstones and alcohol abuse have been shown to be the major causes of acute pancreatitis and are responsible for 80% of all cases.<sup>1</sup>

The course of acute pancreatitis varies and there are several prognostic criteria to evaluate its outcome. Acute pancreatitis might progress to vascular thrombosis with concomitant vascular rupture resulting in haemorrhagic and necrotic pancreatitis. The clinical syndrome of the disease includes pancreatic abscess, pseudocyst, extension of necrosis to adjacent structures, as well as systematic complications such as respiratory failure, disseminated intravascular coagulation, fat necrosis in the retroperitoneal space, profound loss of fluids in the third space and hypovolemic shock.<sup>2</sup>

Successful medical management of acute pancreatitis ranges from 70-80% of patients. Complications develop in the rest and mortality raises to 15-50%. Many authors have proposed early surgical treatment of these patients, although it has not been proved, in randomized trials that prognosis is improved. It has also been considered early endoscopic sphincterotomy and removal of bile duct stones. This method seems to improve mortality in selected patients with poor early prognostic signs.<sup>3</sup>

Details of surgical and endoscopic therapy in acute pancreatitis are analyzed below, in order to define not only selection criteria for each method but also the most appropriate method for each particular patient.

### 1.2. Emergency surgical treatment

Urgent surgical approach in cases of gallstone pancreatitis intends to avoid not only deterioration of the disease but to prevent recurrences as well. The usefulness of this approach has been questioned by many authors due to high mortality and complications. It is well known that most of the cases respond to medical management and surgical operations with doubtful results should be avoided.

The diagnosis of choledocholithiasis in patients with acute pancreatitis is rather difficult. During the acute phase of the disease abdominal ultrasonography may visualize only 60% of gallstones.<sup>4</sup> Computed tomography is less sensitive and less specific for the diagnosis of gallstones. The use of radio-isotopes is of no value. Blood tests give more reliable results.<sup>5</sup> On admission serum bilirubin >3 mg/dl has 83-85% sensitivity for the diagnosis of choledocholithiasis.<sup>6</sup> Recently the use of magnetic resonance imaging and particularly magnetic resonance cholangiopancreatography (MRCP) has greatly improved diagnostic accuracy with non-invasive methods. Although the MRCP images do not have the quality and sensitivity of the ERCP ones, they are of great benefit because the method carries no risk and there is no need for contrast injection. The sensitivity and specificity of MRCP reaches 80%. The gold standard for the diagnosis of a stone in the common bile duct, is endoscopic cholangiography. It is approximately 98% sensitive and specific for choledocholithiasis, but it has the disadvantage of being an invasive method with accompanying morbidity and mortality. The ability for direct

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intervention immediately after diagnosis and stone extraction is the principle advantage of this technique.

There is still a debate for patients with severe acute pancreatitis according to Ranson's or Glasgow criteria, as they are expected mostly to gain benefit from surgical treatment than conservative management. Common bile duct stones are found in 30-60% of patients who die from gallstone pancreatitis, but the stones are not always impacted in the papilla or the distal common part (channel) of the common bile duct and pancreatic duct. Evaluation of surgical literature regarding surgical management of acute pancreatitis is difficult because patients in relevant studies have not been allocated in groups according to disease severity and consequently comparison of results is being done by historical data and not with control groups.<sup>7</sup> Due to Acosta et al there was one death in 46 patients (2%) in the patients' group who underwent an operation, compared with 14 deaths in 86 patients (16%) in the group who were treated conservatively.<sup>8</sup> Stone et al in a randomized prospective trial report 1/36 (2,8%) deaths following surgical treatment and 2/29 (6%) postoperative ones when the operation was held during the first ten days.<sup>9</sup> Severity of acute pancreatitis had not been considered when patients were randomized in study groups. Ranson having had disappointing results with urgent surgical management, strongly advised conservative treatment for his patients. In this study patients were separated according to severity but comparison of groups was not appropriate, as patients who underwent a surgical procedure had 5,4 risk factors, compared to those who were treated conservatively with 3,5 ones respectively. This problem seems to exist in other series as well.<sup>10</sup> Kelly and Wagner found a high percentage of mortality (48%) in patients with severe pancreatitis who were operated urgently, compared to 11% of those who underwent a Scheduled operation. Nevertheless in patients with few Ranson's criteria mortality was 3,3% and 0% after an urgent and scheduled surgical operation respectively.<sup>11</sup>

Finally in a more recent study<sup>12</sup> the authors concluded that pancreatic necrosis has been recognized as a principle determinant of survival in acute pancreatitis. It occurs in 20% of patients, however even when accompanied by organ failure, it is not an absolute indication for surgery.

After the above results surgeons believe that is wise avoiding emergency surgical procedures in patients suffering severe acute pancreatitis. Whenever safer extraction of common bile duct stones is feasible, an open operation with its complications should be avoided.

### ***1.3. Urgent endoscopic treatment***

Endoscopic retrograde cholangio-pancreatography and endoscopic sphincterotomy were initially used in isolated cases of gallstone pancreatitis, around 1980. The fear of additional complications resulting from endoscopy (bleeding, cholangitis, deterioration of pancreatitis, retroperitoneal perforation) did not prove to be an efficient suspending factor. The majority of the authors were really impressed by the fast improvement of their patients and the normalization of their biochemical parameters. Despite the promising results the ensuing reports were not complete, regarding their design, patients' selection, the time ERCP was performed related to the onset of symptoms, disease severity and precise recording of the complications.<sup>13,14</sup>

The group from Leicester reported the first article with the first designed, prospective, randomized, controlled trial comparing ERCP and endoscopic sphincterotomy, with conservative management in patients with acute pancreatitis. One hundred and twenty one patients suffering from gallstone pancreatitis were included in the above study. Early (within 72 hours) ERCP and endoscopic sphincterotomy was performed in 59 patients and medical treatment was offered in 62. The evaluation of disease severity was made according to the modified Glasgow criteria. ERCP and endoscopic sphincterotomy were successful in 80% of patients with severe pancreatitis and in 94% of those who presented with moderate severity pancreatitis. Injection of contrast into the pancreatic duct and multiple probing of the ampulla were avoided. Stones in the bile duct were found in 63% of patients with severe pancreatitis and in 26% of those with moderate severity pancreatitis. Bile duct's diameter was larger in the group of patients with severe disease.<sup>15</sup>

This study had the following conclusions:

1. ERCP and endoscopic sphincterotomy can be performed with safety from experienced endoscopists, in patients with acute pancreatitis.
2. Compared with traditional medical treatment, there has been considerable reduction of severe complications in acute pancreatitis after endoscopic sphincterotomy and stone removal, especially in patients with severe disease (12% morbidity compared with 61%).
3. Mortality has also been decreased among those with severe disease, who underwent ERCP and endoscopic sphincterotomy.
4. Endoscopic sphincterotomy in patients with severe

pancreatitis shortened the total duration of hospitalization by 50% (mean: 9,5 days vs 17 days of the conservative treatment group).

Due to the small number of patients that participated in this study, there was no statistical difference regarding mortality (statistical error, type I). It must be pointed out that in one out of the three patients who died from the conservative treatment group, autopsy showed impaction of a stone in the ampulla of Vater. This fact strongly supports urgent ERCP and endoscopic sphincterotomy in gallstone pancreatitis. This study is considered to be the basis upon which patients suffering from acute pancreatitis, especially those with severe prognostic signs, should be treated with ERCP and endoscopic sphincterotomy. The high rate of coexisting cholangitis and acute pancreatitis due to impacted stone in the bile duct, supports the performance of ERCP and endoscopic sphincterotomy in order to decompress both the bile and the pancreatic ducts simultaneously. It has been observed that mortality after endoscopic treatment, is an independent factor from the patients' general condition and concomitant diseases as well. Consequently this method can be used in every patient. An additional argument for endoscopic treatment is that surgical management and general anaesthesia are not feasible in high risk patients with poor general condition. Similar results were given from the study by Fan ST et al from Hong Kong.<sup>16</sup>

However the above results seem to be different to those from a prospective multicenter study from Germany.<sup>17</sup> The authors randomly assigned 126 patients to early ERCP (within 72 hours after the onset of symptoms) and endoscopic papillotomy for the removal of stones in the common bile duct when appropriate, and 112 patients were assigned to conservative treatment. In the second group ERCP was performed within three weeks, if signs of biliary obstruction or sepsis developed.

The authors found that 14 patients in the invasive - treatment group and 7 in the conservative - treatment group died in a period of 3 months. Ten patients in the first and 4 in the second group died from acute biliary pancreatitis.

The overall rate of complications did not differ in the two groups, however patients in the first group presented with more severe ones.

The study concluded that early ERCP and endoscopic sphincterotomy were not beneficial in patients with acute biliary pancreatitis without concomitant obstructive jaundice.

## 1.4. Conclusions

The comparison between endoscopic and surgical treatment in patients with acute pancreatitis led to the following conclusions:

1. In patients with severe acute gallstone pancreatitis, the decision must be urgent ERCP, endoscopic sphincterotomy and retraction of stones especially in the presence of obstructive jaundice. Should this be not feasible, placing of an endoprosthesis or a nasobiliary drainage is sufficient as a temporary solution. When the patient is stabilized, radical treatment follows. Elective delayed cholecystectomy may ensue patient's stabilization, or it can not be performed in poorly conditioned elderly patients. The performance of prophylactic endoscopic sphincterotomy in patients without choledocholithiasis, although supported by many authors, is not totally acceptable.
2. Patients with moderate severity acute pancreatitis without complications, should initially be treated conservatively. Scheduled elective cholecystectomy with intraoperative cholangiography should be performed when the acute phase subsides. During the initial hospitalization bile duct stones should be extracted intraoperatively or by a postoperative endoscopic sphincterotomy.
3. Early surgery should not be considered in the treatment of acute pancreatitis, but only in the presence of complications (bleeding, abscesses, pseudocysts and infected necrosis).

## 2.0. SURGICAL VERSUS ENDOSCOPIC DRAINAGE OF OBSTRUCTIVE JAUNDICE, IN PATIENTS WITH UNRESECTABLE PANCREATIC CARCINOMA

### 2.1. Introduction

The great progress that has been made in interventional endoscopy over the past 20 years, has dramatically changed the traditional surgical drainage of malignant obstructive jaundice. The percutaneous transhepatic route was attempted as the first non-surgical drainage. However this method was accompanied by many complications, especially bleeding and bile leakage and consequently it did not have a wide acceptance.<sup>18</sup> The development of endoscopes with wide channels (4,2 mm) and of metal self-expandable stents made endoscopic drainage of malignant obstructive jaundice, feasible. This is an applicable and widespread method which can also be performed in well organized one day care centres.<sup>19</sup> Phy-

sicians must decide on the method of choice between surgical and endoscopic drainage of jaundice in patients with unresectable carcinoma of the pancreas.

## **2.2. Results of surgical and endoscopic drainage of malignant obstructive jaundice**

Surgical drainage of malignant obstructive jaundice due to occlusion of the lower bile duct can be performed by choledocho-duodenal, choledocho-jejunal or cholecysto-jejunal anastomosis. The latter has the disadvantage of the early recurrence of the jaundice, resulting from cystic duct's obstruction by the tumor.<sup>20</sup> Moreover anastomoses are considered to be difficult surgeries with all the consequent complications. Endoscopic drainage is relatively easy compared to surgery without the necessity of general anaesthesia. Recovering is quick and patients return to normal activities.

There have been only few reliable comparative results and reports coming from surgical centres differ substantially between them. Mortality ranges from 5-25%.<sup>21</sup> Series reporting small numbers of mortality, usually do not include severely ill patients or elderly ones with co-existing diseases. The same problem seems to exist in reports from endoscopy centres. This became evident early, in the first comparative results between endoscopic and surgical series.<sup>22</sup>

The first double blind randomized study comparing the results between surgical and endoscopic drainage of malignant obstructive jaundice began in 1987 in Middlesex Hospital in London. It included 200 patients and it lasted more than four years. In this study which included patients of all age and variable disease severity the two groups were comparable. The results showed less complications following endoscopic drainage (10%) versus surgical drainage (28%). Mortality in the endoscopic series was also less (7%) compared to the surgical one (17%). Benefits from endoscopic treatment did not however influence patients' survival. Survival curves were similar and mean survival was approximately five months.

Although it is well-known that 10Fr and 12Fr endoprostheses occlude after approximately five months, in only 18% from the endoscopy group a stent change was required. The majority of patients died without jaundice and the endoprosthesis was well functioning.<sup>23</sup> Self-expandable metallic stents partly solved the problem of stent's obstruction due to their larger diameter (10mm). Therefore compared to plastic stents (3-3,5 mm diameter) they occlude with more difficulty and last longer. Consequently after the use of metallic stents, the number

of patients, who need an endoprosthesis change, has been drastically reduced. However one should consider their high cost. Unsuccessful efforts have been made to manufacture plastic endoprostheses coated with antibiotics or other substances which protect from obstruction.

In another multicenter trial from the U.K.,<sup>24</sup> 52 patients with malignant jaundice were randomized to receive either an endoscopically placed biliary endoprosthesis or conventional surgical by pass. Patients treated with endoscopic drainage had a significantly shorter initial hospital stay, compared to those treated surgically. Moreover, overall survival in the two groups was similar.

The same as the above results were found in two other randomized studies by Andersen J.R. et al. and Bornman Ph. et al,<sup>25,26</sup> who suggested that palliation of obstructive jaundice in malignant bile duct obstruction with endoscopically placed stent, is as effective as operative by pass.

## **2.3. Conclusion**

There is still a debate regarding surgical or endoscopic drainage of malignant jaundice in patients with unresectable pancreatic carcinoma. Endoscopic drainage is the method of choice due to low cost, short hospital stay and small percentage of complications and mortality. Disadvantages of the method are stents' occlusion, where new admission and endoscopic intervention are needed, as well as potential infiltration and duodenal obstruction where surgery with gastroenteroanastomosis are clearly indicated. Surgical drainage is not always feasible in severely ill patients, it is accompanied by a high percentage of complications and mortality and long duration of hospitalization. On the other hand recurrence of jaundice and duodenal obstruction are negligible and rarely surgery is required. The method of drainage does not influence patients' survival.

Patients with malignant obstructive jaundice due to pancreatic carcinoma, can be classified into four groups:

- A. Patients with resectable tumors, good general condition who can potentially be cured after surgical removal of the tumor. Surgical resection is indicated.
- B. Patients with unresectable neoplasms, good general condition, younger than 70ys old, with obstructive duodenal signs and expected survival longer than 6 months. Surgical by-pass of jaundice and gastroenteroanastomosis is indicated.
- C. Patients with unresectable tumors, poor general condition, older than 70ys old, without duodenal infil-

tration and obstruction, and expected survival less than 6 months. Endoscopic drainage is indicated.

- D. Patients with unresectable neoplasms, poor general condition and expected survival less than 2 months. No treatment is indicated.

Staging of patients and selection of the most appropriate treatment, necessitates the need for a full preoperative investigation. Care must be taken so that patients will not suffer from unnecessary operations, or they will not be denied radical ones which offer the chance of long survival, better quality of life or even cure.

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