OBSTRUCTIVE JAUNDICE CAUSED BY PANCREATIC HEAD MALIGNANCIES ARE THERE PREDICTIVE FACTORS FOR SUCCESSFUL ENDOSCOPIC BILIARY STENTING?

Deriban G¹, Andreevski B¹, Mishevski J¹, Krstevski M¹, Trajkovska M¹, Popova R¹, Joksimovic N¹, Serafimoski V¹,²

¹University Gastroenterohepatology Clinic, Medical Faculty, Skopje, R. Macedonia
²Macedonian Academy of Sciences and Arts, Skopje, R. Macedonia

Abstract: Endoscopic retrograde cholangiopancreatography provides precise imaging of malignant biliopancreatic strictures and allows palliative treatment with endoscopic stenting.

Initial successful biliary stenting can be achieved in about 69–100% of patients with pancreatic head malignancies. Preliminary data from our Clinic reported a much lower success rate of endoscopic biliary stenting in obstructive jaundice caused by pancreatic head malignancies. These findings may be because patients are referred at more advanced stages, which could contribute to the lower success rate of biliary stenting.

We aimed to determine the success rate of endoscopic biliary stenting prospectively in 50 patients with pancreatic head malignancies and to assess if clinical, laboratory and ultrasound findings can be predictive of success and safety in biliary stenting.

Initial successful biliary stenting was achieved in 70% of our patients. No major complications (perforation, severe pancreatitis, massive bleeding, death) were noted. We were able to identify factors predictive of a lower success rate which were associated with a more advanced disease and a longer delay before treatment.

Based on our results, we conclude that ERCP should be offered without delay as a primary treatment option for all patients with unresectable pancreatic head malignancy and as a possible treatment option in patients with resectable malignancy who are poor candidates for surgery.

Key words: Pancreatic head malignancy, obstructive jaundice, endoscopic biliary stenting.
Background and aims

Endoscopic retrograde cholangiopancreatography provides precise imaging of malignant biliopancreatic strictures and allows palliative treatment with endoscopic stenting. [1–5]

According to data from literature, successful biliary stenting can be achieved in 69–100% of patients with pancreatic head malignancies [6, 19–22]. The success rate of this procedure at our Clinic is, according to preliminary data, lower. Our assumption is that the lower success rate of biliary stenting is due to the advanced stages of disease at which patients are referred to our clinic.

The aim of our study was prospectively to evaluate 50 patients with pancreatic head malignancies, to determine the success rate of endoscopic biliary stenting and to see if clinical, laboratory, ultrasound [7] and ERCP findings have a predictive value for success in biliary stenting [8].

Further objectives are:

To determine the length and grade (complete, incomplete) of strictures.

To document stent characteristics.

To determine the success rate of percutaneous biliary drainage and subsequent percutaneous stenting in patients in whom the endoscopic approach has failed.

To document the number of patients treated surgically following an endoscopic or percutaneous biliary approach.

Patients and methods

Fifty patients with pancreatic head malignancies and biliary obstruction were prospectively included in our study and their clinical, laboratory, ultrasound and ERCP findings were evaluated.

Clinical symptoms: The duration from jaundice occurrence to endoscopic treatment was assessed. Based on their answers, patients were divided in 5 groups: no jaundice noticed, jaundice noticed within one week before ERCP, jaundice noticed within two weeks before ERCP, jaundice noticed within one month, jaundice noticed more than one month before ERCP.

Lab parameters: Cholestatic parameters and prothrombin time were assessed.

Based on the cholestatic parameters, patients were divided into five groups: bilirubin within normal range (elevated alkaline phosphatase and GGT), bilirubin up to 50 mmol/l, bilirubin up to 100 mmol/l, bilirubin up to 200 mmol/l and bilirubin over 200 mmol/l.
Based on the prothrombin time (PT) at hospital admission, patients were divided into 3 groups: normal prothrombin time, prothrombin time up to 20 seconds, prothrombin time over 20 seconds.

*Ultrasound examination:* Patients were divided into three groups based on the bile duct dilation proximal of the pancreatic head malignancy: Dilated bile ducts up to 10 mm, dilated bile ducts up to 15 mm and dilation exceeding 15 mm.

With regard to tumour diameter, patients were divided into four groups: suspected pancreatic head tumour, pancreatic head tumour up to 2 cm, pancreatic head tumour up to 4 cm and pancreatic head tumour exceeding 4 cm.

*ERCP findings:* the procedure outcome was classified into 3 groups: successful stent insertion (SSI), failure of stent insertion after successful canulation (SC, SF) and unsuccessful canulation (CF). In the case of successful canulation, length and grade (incomplete, filiform, complete) of strictures were assessed.

Informed consent was obtained from all patients before the ERCP procedure. The expected benefit but also all possible risks and procedure-related complications were discussed in detail.

In order to avoid unsuccessful procedure outcomes due to insufficient experience, all ERCPs were carried out by endoscopists who have performed more than 400 ERCPs and perform at least 100 ERCPs per year.

*Exclusion criteria*

Patients were excluded from our study if:

Papilla was inaccessible due to malignant duodenal infiltration, or obstructive jaundice was caused by metastases from a primary non-biliopancreatic tumour.

*Results*

Our patient group consisted of 22 male and 28 female patients, with a male to female ratio of 0.9. The youngest patient was 38, the oldest 89, and the median age 66 years. Pancreatic head malignancy was found in 59% of all patients with malignant biliary obstruction (in whom ERCP was carried out at our clinic during 2011).

Successful stenting was achieved in 35 (70%) out of 50 patients. In 8 patients (16%) stenting failed after successful bile duct canulation and in the remaining 7 patients (14%) bile duct canulation failed. Taken together, canulation was successful in 86% (43 pts.) of our patients with pancreatic head malignancies.
Table 1

*Duration of jaundice in relation to successful stenting*

<table>
<thead>
<tr>
<th>Pancreas</th>
<th>Clinical symptom</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>SC, SF</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>CF</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

At the time of presentation all 50 patients had clinically visible jaundice. Jaundice was noticed within 2 weeks before ERCP in 40% (20 pts.) within 4 weeks in 52% (26 pts.) and more than 4 weeks before ERCP in 8% (4 pts.) The success rates of endoscopic biliary stenting were 80%, 69% and 25% respectively.

![Figure 1 – Duration of jaundice and successful stent insertion](image)

Table 2

*Successful stenting in relation to laboratory findings*

<table>
<thead>
<tr>
<th>Pancreas</th>
<th>Laboratory findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERCP Outcome</td>
<td>Prothrombin time in seconds</td>
</tr>
<tr>
<td></td>
<td>PT normal</td>
</tr>
<tr>
<td>SSI</td>
<td>18</td>
</tr>
<tr>
<td>SC, SF</td>
<td>6</td>
</tr>
<tr>
<td>CF</td>
<td>6</td>
</tr>
</tbody>
</table>

Thirty patients with pancreatic head malignancies had normal prothrombin time, stent insertion succeeded in 18 (60%) of these 30 patients. In 17 (80%) of 20 patients with prothrombin time in the range 13–20 sec. stent insertion succeeded. None of the patients had a prothrombin time longer than 20 sec.

None of our patients had normal bilirubin levels. Bilirubin below 50 mmol/l was noticed in 2 patients and below 100 mmol/l in another 2 patients; in all 4 patients stenting was successful. In 26 patients bilirubin was in the range 100–200 mmol/l, of them successful stenting was possible in 20 (77%). In 2 patients stenting failed following successful canulation and in 4 patients canulation was unsuccessful. Twenty patients had bilirubin levels exceeding 200 mmol/l, of them stenting succeeded in 11 (55%). In 6 patients stenting failed after canulation and in 3 patients canulation failed. Taken together, the success rates of stenting were 100%, 77% and 55% in patients with bilirubin levels below 100 mmol, 100–200 mmol/l and over 200 mmol/l respectively.
Successful stenting in relation to ultrasound findings

<table>
<thead>
<tr>
<th>Ultrasound findings</th>
<th>Proximal bile duct dilation</th>
<th>Diameter of pancreatic head tumour</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>dilation &lt; 10 mm</td>
<td>dilation &lt; 15 mm</td>
<td>dilation &gt; 15mm</td>
</tr>
<tr>
<td>ERCP Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSI</td>
<td>6</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>SC, SF</td>
<td>2</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>CF</td>
<td>0</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

In all patients with proximal bile duct dilation up to 10 mm canulation was possible and stent insertion was successful in 6 out of 8 patients (75%). Proximal bile duct dilation up to 15 mm was found in 28 patients. Of these 17 patients had successful stent insertion (60%) 6 patients (22%) stenting failure after successful canulation and in the remaining 5 patients (18%) canulation failed. In 14 patients proximal bile duct dilation exceeded 15 mm, twelve of them (86%) had successful stent insertion while in the remaining 2 canulation failed.

With regard to tumour diameter measured by ultrasound 12 patients had a "suspected" tumour (i.e. ultrasound could not clearly detect a tumor). In 10 (83.3%) of these 12 patients’ stent insertion succeeded while in the remaining 2 stent insertion failed after successful canulation. A clearly detectable tumour smaller than 2 cm was found in 14 patients. In 10 patients stent insertion succeeded (71%), 2 ended with stenting failure after canulation (14%) and in 2 canulation failed (14%). Eighteen patients had a tumour with a diameter from 2–4 cm, out of whom 9 patients were successfully stented (50%); in 6 patients stenting failed after canulation and in 3 patients canulation was unsuccessful. Six patients presented with tumours exceeding 4 cm but in all of them stenting succeeded (100% success rate).
Ten patients had a stricture length up to 2 cm. Of these, in 8 patients’ (80%) stent insertion was successful. In 29 patients the bile duct stricture measured from 2–4 cm. Successful stent insertion was possible in 23 patients (79%). In 3 patients the pancreatic head tumour caused strictures longer than 4 cm and in all of them stent insertion was successful.

Table 4

Successful stenting in relation to length and grade of the stricture

<table>
<thead>
<tr>
<th>Pancreas</th>
<th>ERCP findings</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stricture length</td>
<td>Grade of the stricture</td>
</tr>
<tr>
<td>ERCP Outcome</td>
<td>length &lt; 2 cm</td>
<td>length &lt; 4 cm</td>
</tr>
<tr>
<td>SSI</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td>SC, SF</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>CF</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Приложение, Одн. биол. мед. науки, XXXII/2 (2012), 59–71
With regard to stricture grade, one patient showed an incomplete stricture which was successfully stented. In 17 patients the stricture was filiform and stenting was possible in 15 (88%) of these 17 patients. Twenty-five patients showed complete strictures of which stenting was possible in 19 (76%).

![Bar chart showing successful stenting in relation to stricture grade](image)

**Figure 7 – Successful stenting in relation to stricture grade**

**Discussion**

Our study included patients with unresectable but also resectable pancreatic head malignancies. Complete surgical resection still remains the only possibility of curing pancreatic cancer, however only 10% of patients undergo curative surgery [9]. ERCP as palliative treatment was offered primarily to patients with unresectable pancreatic head malignancies. Unresectability was determined by CT. [10, 11] In patients with unresectable pancreatic malignancy biliary stent placement has now become the main and least invasive palliative modality with a lower morbidity than surgery, and perhaps may provide a survival benefit [12]. On the other hand studies with carefully selected patients with locally advanced diseases, in whom the operative risk was low, surgical by-pass resulted in significantly prolonged survival with fewer hospital readmissions compared to stented patients [13]. In patients with a potentially resectable malignancy ERCP was offered if patients were older, appeared to have malnutrition, had significant comorbid conditions, or a suboptimal performance status, making them poor candidates for surgery. Patients with resectable malignancies and a good overall condition were treated with ERCP only if the time frame for resection could not be determined [14–18].

In our study successful stenting was achieved in 70% of patients. These data are comparable with results of other studies. One study from the Netherlands in 2010 showed rates of initial successful stent placement of 83% in
academic centres and 69% in community hospitals [6]. Studies from Germany and Italy show successful endoscopic biliary decompression in 84% [19] and 86% [20] respectively. One study from California University San Francisco shows successful biliary decompression in 92% [21] while a study from Greece reports 100% success in endoscopic biliary stenting [22].

All inserted stents in our study were 10 french polyethylene plastic biliary stents. Although metal stents are proved to have longer patency they are considerably more expensive [23–27]. Bearing in mind the median survival time of patients with metastatic pancreatic cancer, which is only 3–4 months, plastic stents should be preferred in this group [28]. In the case of patients with longer life expectancy metal stents should be used [29]. In patients with preoperative biliary stenting, plastic stents or fully covered SEMS are recommended [30]. Unfortunately the costs of (covered) metal stents, which are 15–20 time more expensive than plastic stents, limited the use of them in our study.

In the group of 15 patients where stenting failed, 7 patients were treated with percutaneous biliary drainage, 4 were sent to surgery while 4 received no further treatment.

Prolonged jaundice was predictive of lower success rates of biliary stenting. The success rate dropped from 80% for patients jaundiced up to 14 days to 25% for patients with jaundice that had occurred more than one month before. Increased bilirubin levels were also associated with a lower success rate of biliary stenting. If the bilirubin level was below 100 the success rate was 100%, but if the bilirubin level was more than 200 mmol/l the success rate dropped to 55%. Proximal bile duct dilation exceeding 15mm was associated with higher success rates of stenting, suggesting that canulation is eased if the bile duct is more dilated. Incomplete and filiform strictures compared to complete strictures were associated with higher success rates in biliary stenting while stricture length showed no association with the success rate. The tumour diameter, measured by ultrasound, showed no association with the success rate of stenting. Although it could be expected that a bigger tumour mass in the pancreatic head causes more pronounced compression and lower success rates, this could not be shown in our results as the tumour mass can expand away from the bile duct.

No major complications were noticed in our patient group (major complications include perforation, severe bleeding, pancreatitis and death).

In our study we were able to identify factors predictive of lower success rates for biliary stenting. These factors showed that a more advanced disease, i.e. a longer delay from disease occurrence to ERCP, predicted a lower success rate of biliary stenting. Therefore it is important not only for patients with resectable but also for patients with an unresectable pancreatic head malignancy to receive treatment without delay.
Conclusion

The 70% success rate of biliary stenting in patients with pancreatic head malignancies in our study group is within the range of published data.

We were able to identify factors predictive of a lower success rate which were associated with a more advanced disease and a longer delay before treatment.

The safety of this procedure was good and no major complications occurred.

Based on our results we conclude that ERCP should be offered without delay as a primary treatment option for all patients with unresectable pancreatic head malignancy and as a possible treatment option in patients with resectable malignancy who are poor candidates for surgery.

REFERENCES


Резиме

Процена на предиктивни фактори за успехот на ендоскопското стентирање кај опструктивен иктерус предизвikan од малигном на главата на панкреасот

Дерiban G., Андреевски Б., Мишевски Ј., Крстевски М., Трајковска М., Попова Р., Јоксимович Н., Серафimoski V.

¹Универзитетска клиника за гастроенерохепатологија, Скопје, Р. Македонија
²Македонска академија на науки и уметности, Скопје Р. Македонија

Ендоскопската ретроградна холангиопанкреатографија (ЕРЦП) е метода која дава претцизен приказ на малигните билиопанкреатични стриктури и овозможува палиативна терапија со ендоскопско стентирање.

Според податоците од литература успехот на ендоскопското стентирање изнесува 69–100%. Успехот на ендоскопското стентирање кај пациенти со билопанкреатични малигноми третирани на Клиниката за гастро-ентерохепатологија според пределинварните резултати е много низок. Наша претпоставка е дека нискиот процент на успешно стентирање се должи на напреднатото стадиум на болеста во кој пациентите се јавуваат на нашата Клиника.

Цел на оваа проспективна студија е да се евалуира успехот и безбедноста на ендоскопското стентирање кај 50 пациенти со билијарна опструкција предизвикана од малигном на главата на панкреасот и да се процени
Обструктивен иктерус, предизвикан од малигном на главата на панкреасот, заснован на претпоставките дека е могуваа третераписка процедури (препаративни, лабораториски или ултрасонографски) за исходот на ендоскопското стентирање.

Во нашата студија успехот на ендоскопското билијарно стентирање кај пациентите со опстрективен иктерус предизвикан од малигном на главата на панкреасот изнесува 70%. Во текот на изведените интервенции не се регистрирани мажорни компликации (перфорација, тежок панкреатит, масивно крвосечење, смрт). Идентификувани се предиктивни фактори за понизок успех на ендоскопското стентирање кои истовремено укажуваат на напреднат стадиум на болеста.

Заклучокот од нашата студија е дека ЕРЦП како можна палијативна тераписка процедура треба да се понуди без одложување на сите иноперабилни или поради коморбидитетот имаат висок хируршки ризик.

Ключни зборови: малигном на панкреас, опстрективен иктерус, ендоскопско стентирање.

Corresponding Author:

Gjorgi Deriban
University Gastroenterohepatology Clinic
Medical Faculty, Skopje
R. Macedonia

E-mail: Deriban@sonet.com.mk

Приложение, Од. биол. наук, XXXII/2 (2012), 59-71
Successful stenting