Abstract

Background and Aim: The postcholecystectomy syndrome includes a heterogeneous group of diseases, usually presenting as abdominal symptoms following gallbladder removal. The clinical management of these patients is frequently without an evidence-based approach. Method: We evaluated 80 patients with postcholecystectomy problems consecutively admitted during a period of 36 months. The liver function tests (LFTs) assessment and transabdominal ultrasound (TUS) were followed by endoscopic ultrasound (EUS). Endoscopic retrograde cholangio-pancreatography (ERCP) was then performed depending on the results. With knowledge of the final diagnosis, the probable evaluation and outcomes were reassessed assuming that ERCP would have been performed as the initial procedure. Final diagnosis was confirmed by a combination of imaging findings, as well as clinical follow-up of 6 months. Results: In 53 patients biliary or pancreatic diseases were diagnosed: common bile duct stones, chronic pancreatitis, pancreatic cancer, papillary tumors, cholangiocarcinoma, insufficient cholecystectomy or sphincter of Oddi dysfunction. The other 27 patients had non-biliary symptoms (dyspepsia, IBS, etc.) and were consequently managed according to the symptoms. The sensitivity and specificity of EUS were high in the subgroup of patients with biliary or pancreatic symptoms (96.2% and 88.9%) and helped to indicate subsequent ERCP. Conclusion: An algorithmic approach which used EUS for the initial evaluation of the patients with postcholecystectomy problems decreased the number of ERCPs by 51%, having as a consequence a decreased morbidity and mortality in this group of patients.

Key words


Introduction

Postcholecystectomy syndrome (PCS) includes a heterogeneous group of diseases, usually manifested by the presence of abdominal symptoms following gallbladder removal. Although this term is used widely in the medical literature, it is rather inaccurate, because it encompasses a large number of biliary and non-biliary disorders. The symptoms occur within a few weeks of surgery in one half of the patients and months to years later in the remainder. The symptoms are nonspecific and vary with the underlying etiology, but most often include right upper quadrant or epigastric pain that tends to occur following meals and to be sharp in character, jaundice or dyspeptic symptoms [1-5]. These patients are initially assessed by transabdominal ultrasound (TUS) or computed tomography, followed by endoscopic retrograde cholangiopancreatography (ERCP) as the gold standard [6-8].

The aim of our study was to prospectively assess the role of a clinical algorithm that included liver function tests (LFTs) and transabdominal ultrasound (TUS), followed by endoscopic ultrasound (EUS), for the evaluation of late PCS.

Methods

We included 80 patients with postcholecystectomy problems consecutively admitted during a period of 36 months. Clinical symptoms included abdominal pain, rigors, jaundice or dyspepsia. The interval from cholecystectomy ranged from 1 to 60 months. The liver function tests (LFTs) analysed were serum bilirubin and serum alkaline phosphatase. A diameter of the common bile duct (CBD) of less than 10 mm was considered normal and greater than or equal to 10 mm was considered abnormal. Direct evidence of a stone in the bile duct was considered as a true positive test result, irrespective of the size of CBD.
TUS was the initial imaging test. It was performed on fasting patients in a supine and right anterior oblique position. A 3.5-5 MHz sector probe was used (ProSound 5000; Aloka Co, Ltd, Tokyo, Japan) and the diameter of the CBD was measured at the level of the right hepatic artery using electronic callipers. EUS procedures were performed by an experienced gastroenterologist with a linear echoendoscope (GF-UCT 140 AL5; Olympus Optical Co, Ltd, Tokyo, Japan) coupled with the corresponding ultrasonography system (ProSound 5000; Aloka Co, Ltd, Tokyo, Japan). ERCP was performed with a diagnostic (JF Q140; Olympus Optical Co, Ltd, Tokyo, Japan) or therapeutic (TJF Q140; Olympus Optical Co, Ltd, Tokyo, Japan) endoscope, according to usual protocols.

Endoscopic retrograde cholangiopancreatography was then performed as a function of the results. With knowledge of the final diagnosis, the probable evaluation and outcome were reassessed assuming that ERCP would have been performed as the initial procedure. Final diagnosis was confirmed by a combination of imaging findings, cytology and/or histology after EUS-guided fine needle aspiration procedures (EUS-FNA) or direct biopsies obtained during subsequent surgery, as well as clinical follow-up of minimum 6 months.

During EUS or ERCP, patients were placed in the left lateral decubitus position, and sedation with midazolam and/or propofol was applied.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated for each of the tests (LFTs, TUS and EUS) by comparing the results with the final diagnosis.

**Results**

The study group comprised 32 males and 48 females, with age between 35 and 80 years (mean 56.15±6.3). The final diagnosis was of biliary or pancreatic diseases in 53 patients (Table 1). Twenty-four patients had common bile duct stones (30%), including four cases with non-dilated CBD (Fig. 1). The rest of the patients had chronic pancreatitis, pancreatic cancer (Fig. 2), papillary tumors, cholangiocarcinoma (Fig. 3), enlarged lymphnodes, cystic duct remnant, insufficient cholecystectomy or type 1 sphincter of Oddi dysfunction [2-7]. The other 27 patients were considered to have non-biliary symptoms (dyspepsia,
IBD, etc.) and were consequently followed-up or managed according to the cause of the symptoms.

Analysis of serum bilirubin was the most useful LFT parameter, but had a moderate overall performance with an accuracy of only 63% (Table II). Serum alkaline phosphatase was elevated in most of our patients, with a sensitivity of 89.3%, but had a poor specificity for bile duct disease in patients with postcholecystectomy pain, as well as low overall accuracy of 49.8%. TUS had an overall accuracy of 76.4%. If we correlated abnormal LFTs with TUS there was an increase in accuracy up to 90%.

Table II. Receiver operating characteristics of different tests used for the diagnosis of late postcholecystectomy syndrome

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Negative predictive value (%)</th>
<th>Positive predictive value (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>51.3</td>
<td>70.7</td>
<td>67.9</td>
<td>62.9</td>
<td>63</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>89.3</td>
<td>27.3</td>
<td>85.7</td>
<td>42.4</td>
<td>49.8</td>
</tr>
<tr>
<td>TUS</td>
<td>77.3</td>
<td>74</td>
<td>62.5</td>
<td>85.4</td>
<td>76.5</td>
</tr>
<tr>
<td>EUS</td>
<td>96.2</td>
<td>88.9</td>
<td>92.3</td>
<td>94.4</td>
<td>93.7</td>
</tr>
</tbody>
</table>

The sensitivity and specificity of EUS findings were high in the subgroup of patients with biliary or pancreatic symptoms (96.2% and 88.9%) and helped to decide subsequent ERCP. Moreover, EUS had a high NPV of 92.3% and PPV of 94.4%, with an overall accuracy of 93.7%. Based on EUS results we were able to avoid unnecessary ERCP in 41 patients, thus decreasing the number of ERCPs by 51%.

Discussion

Transabdominal US (TUS) is the first imaging procedure used for the initial evaluation of the patients with postcholecystectomy problems because it is a noninvasive, rapid method and presently widely accessible, being capable of differentiating between non-obstructive and obstructive jaundice [9]. Recent studies suggest that the level of obstruction can be correctly identified in up to 95% of patients, and the cause of obstruction can be established in up to 85% of patients, with a lower sensitivity for example for the diagnosis of choledocolithiasis (less than 50%) [10-13]. Improvement of the US devices determined recently an increased sensitivity and specificity for the detection of choledocolithiasis and other causes of CBD obstruction, including benign and malignant lesions [13, 14]. The distal part of the CBD, the papillary region and the retroperitoneum are difficult to examine by TUS due to the presence of gas in the overlying bowel. However, an abrupt change in the calibre of the bile duct from dilated to normal is highly suggestive for the presence of malignant obstruction, while gradual tapering is usually consistent with benign stenoses [14, 15]. The recent introduction of tissue harmonic imaging techniques allowed a better visualization of the common bile duct and its content, with a probable improvement in the quality of TUS diagnosis [16]. In our study, using the level of 10 mm CBD diameter for bile duct abnormalities, TUS alone had a moderate sensitivity, specificity and accuracy. The use of TUS resulted in 19 incorrect results, with 7 false-positive and 12 false-negative.

The EUS of the pancreatico-biliary system made significant advances, being able to visualize the extrahepatic biliary tree and the head of the pancreas from the second part of duodenum with great accuracy in the majority of patients [7]. The method is limited only in patients with duodenal stenoses or surgical anastomoses, as well as in the presence of previous biliary sphincterectomy or bile duct stents, which can induce artifacts due to the presence of air in the bile ducts [17]. Utility of EUS imaging was confirmed in different studies which assessed the specific role for the diagnosis of pancreatico-biliary diseases [18-20]. Small common bile duct stones (< 3-4 mm diameter) can be observed with an accuracy of up to 98%, slightly better than ERCP, even in the absence of posterior acoustic shadowing [18, 20]. In patients with pancreatic cancer, linear EUS allows the performance of fine needle aspiration biopsy, with cytological or microhistological examination. The procedure has a superior accuracy as compared with brush cytology performed during ERCP [21, 22]. Besides diagnosis, EUS also allows staging of pancreatic carcinoma, cholangiocarcinoma and ampullary tumors. It has a number of advantages over ERCP because duct cannulation is not required. The failure rate is lower, there is minimal risk of inducing acute pancreatitis and there is no radiation exposure. Nevertheless, EUS is not as widely available, it requires sedation, and has no therapeutic role in choledocholithiasis [23-28]. False-negative results may appear in case of intrahepatic or hilar lithiasis due to the limited penetration of ultrasound. In our cases there were three false-positive results and two false-negative. Again, it should be emphasized that the false-positive results were caused by small stones (< 4-5 mm), which either passed spontaneously before ERCP or were missed by ERCP due to contrast drowning. In this context the false positive results might have been probably misjudged, due to the continuous controversy on the best gold standard (EUS...
versus ERCP).

MRCP is able to demonstrate the level and presence of biliary obstruction with a sensitivity of 95% and a specificity of 97%, being less sensitive for detecting stones, especially less than 6 mm in size [29]. The major advantage is the noninvasiveness of the procedure. It does not require conscious sedation, intravenous contrast or radiation exposure, while diagnostic images can be obtained in the majority of patients, including those who have complex ileoenteric anastomoses. A recent meta-analysis demonstrated that, with respect to sensitivity, specificity and accuracy, there was no statistically significant difference between EUS and MRCP for the detection of cholelithiasis [30]. However, MRCP is known to produce false-positive results, especially at the distal end of the CBD due to a prominent or spasmotic papillary sphincter, while the specificity is lower than of EUS for pancreatic tumors and ampullary lesions [3]. Secretin-stimulated MRCP uses intravenous secretin to relax the sphincter of Oddi and stimulate the flow of pancreatic exocrine juice and bile, in order to better delineate pancreatic and bile duct [31]. Due to logistic reasons and limited availability during the study period, MRCP was not systematically done in our patients. Moreover, secretin is not yet available in Romania.

ERCP is probably the most accurate test whenever it is technically successful. It has a high sensitivity and specificity (100 and 95.2%), allowing the visualization of the papilla, pancreas and biliary system. Whenever pathology is found it permits tissue diagnosis and therapeutic interventions [27, 28, 32, 33]. However, ERCP is associated with a significant rate of complications. Acute pancreatitis is the most common complication, with an incidence of about 5% in low risk patients and 40% in high risk patients. Most patients experience mild pancreatitis, while severe diseases with pancreatic necrosis, multi-organ failure, prolonged hospitalization and death is seen in less than 1% of the patients [34-37]. In our study, the use of EUS for the evaluation of the patients with PCS significantly decreased the number of ERCPs by 51%, thus reducing the overall morbidity and mortality induced by an invasive procedure. After the initial evaluation, 7 patients were diagnosed with type 1 sphincter of Oddi dysfunction. Due to the high-risk of acute pancreatitis induced by sphincter of Oddi manometry, these patients were referred for ERCP with sphincterotomy directly since they were likely to have a clinical improvement regardless of manometric findings [38].

Based on our study we suggest the following algorithm in patients with postcholecystectomy syndrome: TUS should remain the first investigation in conjunction with LFTs. If the CBD size is < 10 mm and LFTs are normal, further EUS or ERCP is not recommended. If CBD stones are demonstrated during TUS, patients should immediately undergo ERCP, and EUS is not necessary. EUS should be performed in patients with a dilated CBD on TUS (≥ 10 mm) and/or elevated LFTs, without an identifiable cause. Its high sensitivity for detection of bile duct abnormalities can select patients appropriately for ERCP. Thus, ERCP should only be performed when an indication for endoscopic treatment is shown on either TUS or EUS (Fig. 4).

There are, however, limitations in our study. Due to the small sample size of patients, there is a considerable amount of uncertainty in the estimates of sensitivity, specificity and accuracy. A larger study population is necessary to be fully confident of the benefits of the suggested diagnostic algorithm. This could be accomplished in the setting of a large prospective, multicentric study. Another limitation consisted of the limited availability of MRCP, which precluded a direct comparison with EUS. Consequently, MRCP was not included in the proposed diagnostic algorithm.

In conclusion, an algorithmic approach which used EUS for the initial evaluation of the patients with postcholecystectomy problems decreased the number of ERCPs by 51%, having as a consequence a decreased morbidity and mortality in this group of patients.

Acknowledgment

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Conflicts of interest

None to declare.

References

Postcholecystectomy syndrome - an algorithmic approach


