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Biliary tract obstruction in chronic pancreatitis

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Abstract

Bile duct strictures are a common complication in patients with advanced chronic pancreatitis and have a variable clinical presentation ranging from an incidental finding to overt jaundice and cholangitis. The diagnosis is mostly made during investigations for abdominal pain but jaundice may be the initial clinical presentation. The jaundice is typically transient but may be recurrent with a small risk of secondary biliary cirrhosis in longstanding cases. The management of a bile duct stricture is conservative in patients in whom it is an incidental finding as the risk of secondary biliary cirrhosis is negligible. Initial conservative treatment is advised in patients who present with jaundice as most will resolve once the acute on chronic attack has subsided. A surgical biliary drainage is indicated when there is persistent jaundice for more than one month or if complicated by secondary gallstones or cholangitis. The biliary drainage procedure of choice is a choledocho-jejunostomy which may be combined with a pancreaticojejunostomy in patients who have associated pain. Since many patients with chronic pancreatitis have an inflammatory mass in the head of the pancreas, a Frey procedure is indicated but a resection should be performed when there is concern about a malignancy. Temporary endoscopic stenting is reserved for cholangitis while an expandable metal stent may be indicated in patients with severe co-morbid disease.

Incidence

The incidence of common bile duct stricture (CBDS) in chronic pancreatitis (CP) varies widely depending on the precise definition, diagnostic vigor, and demographics of any given series. The wide variation in the reported incidence, which ranges from 3% to 46% [1–8] (Table I), occurs because not all patients with biliary obstruction in CP present with jaundice. The jaundice may frequently be transient [9], and in an appreciable number of patients the bile duct stricture is discovered incidentally [10–14].

Pathogenesis

The anatomical relationship of the common bile duct (CBD) with the head of the pancreas is an important factor influencing the nature of the stenosis in CP. In up to 85% of people, the CBD traverses the pancreatic head and is adjacent posteriorly in the remainder [15]. The intrapancreatic portion of the CBD varies in length from 1.5 to 6 cm, which accounts for the variability of stricture lengths seen in clinical practice [16].

CBDS occurs as a consequence of recurrent acute inflammatory episodes which may ultimately result in a periductal fibrotic stricture [10]. This occurs more commonly in advanced CP, with the highest incidence in the calcific variant [9,17–21]. The development of a pseudocyst may also be a contributing factor, but is seldom the sole cause of a CBDS [22–24]. Resolution of the acute inflammatory process or a pseudocyst often results in relief of the jaundice, but a residual low-grade obstruction is common, as indicated by a persistently raised alkaline phosphatase (ALP) or a dilated CBD on ultrasonography. A pseudocyst, as the dominant cause of jaundice, is only implicated when this resolves with spontaneous resolution of the cyst or after cyst drainage [25].

Clinical presentation

The clinical course of a CBDS varies, and is characterized by exacerbations and remissions. Some
patients with biliary obstruction may be asymptomatic and have only modestly deranged liver function tests. This “incidental” presentation occurs in up to 17% of patients [13]. Although pain is the predominant clinical feature in most patients [2,3,8,13,26], it is doubtful that a CBDS per se is a major contributing factor. Jaundice is present in 30% [10] to 50% [13] of patients, and may be transient, recurrent, or persistent [26]. Transient jaundice is typically seen during acute exacerbations and recedes with resolution of the inflammatory process. Other biochemical markers of biliary obstruction, such as ALP and GGT, are slower to return to normal levels or may persist. Recurrent jaundice occurs with repeated exacerbations and may become persistent when associated with severe fibrosis and calcification. Cholangitis occurs in 10% of patients [27,28] and varies from subclinical episodes to overt septicemia [12]. Life-threatening cholangitis is seldom the first indication of the diagnosis [12,29].

Although several studies have reported a significant risk of development of secondary biliary cirrhosis [1,2,6,30], other series have not confirmed this finding [5,31–33]. Frey et al. [28] found that the average incidence of biliary cirrhosis associated with CBDS was 7.3% (Table II) [1,2,5,6,9,14,30–34], and in four of the studies [5,31–33] in their collected series no patients had biliary cirrhosis.

Table II. Incidence of biliary cirrhosis in patients with common bile duct stenosis secondary to chronic pancreatitis (after Frey et al. [35]).

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. of patients</th>
<th>No. with biliary cirrhosis</th>
<th>No. with cholangitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warshaw et al. [30]</td>
<td>1976</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Scott [9]</td>
<td>1977</td>
<td>11</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Bradley &amp; Salam [31]</td>
<td>1977</td>
<td>13</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>Yadegar et al. [1]</td>
<td>1980</td>
<td>21</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Creaghe et al. [34]</td>
<td>1983</td>
<td>10</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>DaCunha et al. [32]</td>
<td>1984</td>
<td>24</td>
<td>–</td>
<td>3</td>
</tr>
<tr>
<td>Sugerman et al. [33]</td>
<td>1986</td>
<td>16</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Stabile et al. [2]</td>
<td>1987</td>
<td>40</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Stahl et al. [14]</td>
<td>1988</td>
<td>38</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>288</td>
<td>21 (7.3%)</td>
<td>27</td>
</tr>
</tbody>
</table>

Labetary investigations

Elevation of the ALP is the most frequently encountered abnormal laboratory test [2] and a persistent increase greater than 2-fold for more than 1 month has been proposed as a specific marker of a CBDS [11], although ALP levels may exceed 1000 IU. Transient hyperbilirubinemia is typically seen in CP and is the result of edema of the pancreas during an acute exacerbation, but may become persistent when there is established cicatrization of the distal CBD in more severe forms of the disease [26,35].

Radiology

The demonstration of pancreatic calcification on a plain abdominal roentgenogram may be the first clue to the diagnosis. Ultrasonography will demonstrate extrahepatic bile duct obstruction in 80% of cases [36], but a CT scan (Figure 1) is usually required to provide accurate delineation of the parenchymal and

Figure 1. CT scan showing chronic calcific pancreatitis. 1b. CT scan showing pancreatic calcification and common bile duct dilatation (arrow).
ductal morphological changes of the pancreas, including the presence of a pseudocyst [2, 36]. Typically, a smooth and tapering distal CBDS is seen on biliary imaging [7, 10, 12, 30, 35, 37]. Occasionally, other CBDS shapes, such as the “bent knee” and “hourglass” configurations have been described [7, 10, 12]. In an attempt to differentiate and characterize CBDS secondary to CP from those due to other causes, Caroli & Nora [38] classified the cholangiographic appearance of bile duct strictures into five types (Figure 2). Type I and type III are most commonly seen in CP [39, 40]. In 100 CP patients, Sarles & Sahel [10] showed a 60% incidence of type I stricture; a similar observation was made by Petrozza & Dutta [4]. In the latter series of 15 cholangiograms, the length of the strictured segment varied from 16 to 57 mm (mean 40.7 mm), while the maximal diameter of the dilated portion of the CBD ranged from 13 to 28 mm (mean 18.9 mm). Snapes et al. noted a CBD diameter ranging from 16 to 25 mm [37], and postulated that even partial stenosis of the CBD may elevate the biliary pressures sufficiently to dilate the proximal biliary system over time. Petrozza & Dutta [4] showed that a particular radiographic configuration of the stricture was not helpful in determining the nature of the underlying process, and therefore predict its natural history. As diagnostic investigations, ERCP (Figure 3a) and PTC have been superseded to a large extent by multislice CT scan and MRI/MRCP, which, in most instances, will provide adequate imaging of the biliary and pancreatic anatomy [41, 42] (Figure 3b).

**Cholestatic jaundice – carcinoma or pancreatitis?**

The differentiation from pancreatic cancer can be difficult, particularly in patients with pre-existing CP. Patients with alcohol-induced CP may be at higher risk of pancreatic malignancy, but the evidence is inconclusive. Lowenfels et al. [43] reported a 16-fold increase in risk, while Karlson et al. [44] failed to show any association in a Swedish Cohort study.

![Figure 2](image1.png)

*Figure 2. Cholangiographic appearance of bile duct strictures (as identified by Caroli & Nora) [38]. Type I: Long retropancreatic stenosis. Type II: Dilatation of the main bile duct, stricture of the sphincter of oddi. Type III: Hourglass stricture. Type IV: Symptomatic of either a cyst (a), or a cancer (b and c). Type V: Cancer of the pancreas.*

![Figure 3](image2.png)

*Figure 3. ERC demonstrating a smooth tapering biliary stricture in a patient with chronic calcific pancreatitis. 3b. MRCP showing dilated extrahepatic bile duct with smooth tapering stricture.*
entity of focal or segmental pancreatitis, which can be associated with groove pancreatitis, may also mimic carcinoma of the pancreas [45].

Warpnick et al. [46] devised a point score system to differentiate CP from carcinoma which showed that older patients with a higher and progressive rise in the serum bilirubin were more likely to have a pancreatic malignancy. A similar observation was made by Frey et al. [28].

While CT scan provides good visualization of the pancreas, differentiation between a carcinoma and CP may be difficult in the absence of other findings, such as metastases [47]. Cholangiographic features may be unreliable because of a wide variability of the cholangiographic appearances of the stricture [14], but complete obstruction is rare in CP. ERCP is still more accurate than MRCP in delineating main pancreatic and side duct morphology [11], which may assist in the differential diagnosis.

CA 19-9 is useful in establishing the diagnosis of pancreatic cancer [48], with a sensitivity of 80% to 85% and specificity of 85% to 90% [49,50]. Markedly elevated levels greater than 1000 U/ml increase the specificity for pancreatic cancer to 99% [49]. However, in patients with obstructive jaundice, elevated biliary pressures result in an exaggerated leakage of CA 19-9 into serum [51], with the resultant high levels seen in the absence of malignancy. Thus, CA 19-9 may be elevated in CP with biliary obstruction, although levels seldom exceed 100–120 U/ml [51]. In 20 patients with CP, Gentiloni et al. [52] reported a median CA 19-9 level of 30.4 U/ml with a range of 3 to 6123 U/ml. Other authors [53,54] have also reported levels in excess of 2000 U/ml. Caution should thus be exercised in the interpretation of CA 19-9 as a marker of differentiating carcinoma from pancreatitis, especially in patients with biliary obstruction.

Other tumor markers, such as CA 494 [55], pancreatic juice 90K [52], and pancreatic ductal cell telomerase activity [56] have been investigated to distinguish benign from malignant pancreatic disease, but their applicability has so far been limited. Del Maschio and co-workers [47] prospectively performed CA 19-9 assays, CT scan, ultrasound, and CT-guided fine needle aspiration biopsy of the pancreas in 81 consecutive patients with suspected CP or pancreatic neoplasm. The CT-guided aspiration yielded superior results with an accuracy of 94%.

Management

Management decisions are dictated largely by the clinical presentation and the morphological changes in the pancreas. Clinical factors to consider include the presence and severity of associated pain, the occurrence and duration of jaundice, and concern about an underlying malignancy. Surgical strategy will depend on whether there is an inflammatory mass in the head of the pancreas and the degree of bile duct and pancreatic duct dilatation.

The incidental finding of a CBDS with varying degrees of bile duct dilatation on imaging with or without a raised AP is well documented [10–12]. This particular group of patients may have either a normal or more typically a disproportionately elevated serum ALP level. The perceived risk of secondary biliary cirrhosis, especially if the ALP is markedly elevated, has prompted some authors to advocate prophylactic biliary drainage in these patients [11,12]. While Frey et al. [28] reported an overall incidence of 7.3% for secondary biliary cirrhosis, other authors have not noted this complication [5,13,31–33]. When adopting a conservative approach for asymptomatic or minimally symptomatic patients during a follow-up period of up to 4 years, Kalvaria et al. [13] found that no patients developed secondary biliary cirrhosis. A similar strategy and outcome has been reported by other authors [7,10,14,16,26]. These patients should therefore be treated conservatively and monitored with 6-monthly liver function tests and biliary ultrasound. As there is no reliable means of predicting progression to biliary cirrhosis, Yadegar and co-workers [1] have recommended serial liver biopsies at 6 and 12 months. However, the low risk of developing secondary cirrhosis in these patients does not justify routine or repeated liver biopsies, which may be difficult to interpret histologically. Similarly, the placement of stents is strongly discouraged, as this may cause secondary infections with clogging of the stents.

A CBDS is a common finding during investigations for pain in CP. Many authors concur that the pain is more likely to be pancreatic in origin [1,2,5,33,44] unless there are associated bile duct stones [13]. Although relief of pain after biliary diversion has been reported [30], a conservative approach should be adopted in the absence of associated jaundice [13]. In jaundiced patients, management will be determined whether jaundice is transient, recurrent, or persistent [32]. A conservative approach is warranted for transient jaundice, which is frequently self-limiting due to resolution of edema or a pseudocyst in the head [1,7,10–12,14,26,31,57]. Spontaneous resolution of jaundice occurs within 1 month in 20–50% of patients [4,7,9,11,31]. Early biliary drainage is indicated in the presence of choledocholithiasis and cholangitis.

Biliary decompression is recommended when jaundice persists for more than 1 month. The type of biliary drainage depends on the patient’s fitness and willingness to undergo surgery, the morphological changes in the pancreatic head, the biliary and pancreatic ductal systems, and the suspicion of malignancy. Options for biliary drainage include stenting and operative bypass.

Endoscopic biliary stenting has a high technical success rate and provides short-term resolution of
jaundice [58,59], but stent malfunctioning with clogging and septic complications is common (Table III) [58–66]. Farnbacher et al. [58] analyzed 31 patients following endoscopic plastic stent placement over a mean duration of 10 months and found that although the jaundice improved in all patients after insertion of the stent, complete regression of stenosis occurred in only 13%. Similar results were reported by Kahl et al. [59], who in addition found that their patients with pancreatic calcification did poorly with endoscopic biliary stenting. This finding was confirmed by Draganov et al. [67]. Deviere et al. [61] reported migration of the stent in 10 patients (40%) and blockage in 8 of 25 patients who were treated with a biliary endoprosthesis. Clogging of the stent occurred after a mean time of 6.5 months, and dislodgement 11 weeks after placement. Catalano and others [68], however, showed better long-term results with placement of multiple simultaneous biliary stents (4–5 stents per patient), even in the presence of calcification. They concluded that endoscopic intervention with multiple stents provided good long-term results and may obviate the need for surgical procedures. Nevertheless, close surveillance is important with judicious replacement of stents either at planned intervals or with early evidence of malfunctioning.

Although the role of self-expandable metal mesh stents for malignant biliary obstruction is well established [69–72], its use in benign strictures, including CP, is less clear and controversial. Deviere et al. [73] prospectively followed 20 patients with self-expanding metal stents for a mean period of 33 months. The stents remained patent and functional in all but two patients. They concluded that self-expanding metal stents could become an effective alternative to surgical biliary diversion. However, other smaller studies [74–77] have produced variable results, few of which could confirm the encouraging results of Deviere [73]. Currently, stenting is at best a temporizing procedure, particularly for cholangitis. As a definitive treatment, stenting should be reserved for patients with serious co-morbid disease or those unwilling to undergo surgery. However, indications for stenting may expand with the emergence of removable expandable [78,79] and bio-absorbable stents [80–82].

In a major review, Frey et al. [28] listed seven indications for surgical intervention for a CBDS in CP (Table IV). The authors are in full agreement with these proposed indications, except for the group of patients with a persistently raised ALP 3 times normal for more than 1 months. The choice of surgical procedure depends on the clinical presentation (associated pain or suspicion of malignancy), the presence of an inflammatory mass in the head, and main pancreatic duct anatomy. Careful radiological imaging is required to plan surgical strategy [13,28]. In the absence of pain, either a choledochoduodenostomy or a Roux-en-Y choledochojunostomy provides effective biliary drainage; these are the surgical procedures of choice [5,13,16,26–28,31,83]. While cholecystojejunostomy is easier to construct, it is a poor option, as the long-term failure rate is up to 23% [27] and compares unfavourably with choledochoduodenostomy and Roux-en-Y choledochojunostomy, which have failure rates of 2.5% and 2.1%, respectively. While choledochoduodenostomy is a simpler procedure [1–3,5,16,26,31], the reported higher incidence of “sump syndrome” [3,84] favours Roux-en-Y choledochojunostomy, particularly when an additional pancreatic duct or pseudocyst drainage is required.

In the presence of jaundice and an inflammatory mass, a modified Frey [85] operation is preferred.

### Table III. Sustained clinical benefit of endoscopic plastic biliary stent drainage in biliary stenosis in chronic pancreatitis.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. of patients</th>
<th>Initial technical success (%)</th>
<th>Patients (%) with improvement of cholestasis*</th>
<th>Mean follow-up months*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huibregts et al. [60]*</td>
<td>1984</td>
<td>52</td>
<td>–</td>
<td>33</td>
<td>32</td>
</tr>
<tr>
<td>Deviere et al. [61]</td>
<td>1990</td>
<td>25</td>
<td>100</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Barthe et al. [62]</td>
<td>1994</td>
<td>19</td>
<td>100</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Smiths et al. [63]</td>
<td>1996</td>
<td>58</td>
<td>100</td>
<td>28</td>
<td>46</td>
</tr>
<tr>
<td>Born et al. [64]</td>
<td>1998</td>
<td>18</td>
<td>100</td>
<td>17</td>
<td>23</td>
</tr>
<tr>
<td>Kiehn et al. [65]</td>
<td>2000</td>
<td>14</td>
<td>100</td>
<td>16</td>
<td>52</td>
</tr>
<tr>
<td>Vitale et al. [66]</td>
<td>2000</td>
<td>25</td>
<td>100</td>
<td>80</td>
<td>32</td>
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<tr>
<td>Farnbacher et al. [58]</td>
<td>2003</td>
<td>31</td>
<td>94</td>
<td>32</td>
<td>28</td>
</tr>
<tr>
<td>Kahl et al. [59]</td>
<td>2003</td>
<td>61</td>
<td>100</td>
<td>26</td>
<td>40</td>
</tr>
</tbody>
</table>

* After stent extraction.

### Table IV. Indications for biliary drainage (Frey et al. [28])

1. Symptomatic cholangitis or infected bile.
2. Biliary cirrhosis (biopsy proven).
3. CBD stones in association with common bile duct stricture.
4. Inability to rule out cancer of the pancreas.
5. Progression of the common bile duct stricture based on radiological assessment of increased dilatation of the common and intrahepatic bile ducts.
6. Persistent jaundice for over a month.
7. Persistently elevated alkaline phosphatase (>3 x normal levels >1 month).
The coring out of the pancreatic head may decompress the intrapancreatic portion of the CBD [86], but if there is any doubt, and in particular when the bile duct is grossly dilated, it is advisable to add a side-to-side Roux-en-Y choledochojejunostomy. An alternative to the Frey operation is the Beger duodenal preserving resection of the head [87], but if there is concern about malignancy it is strongly recommended to proceed to standard or pylorus preserving pancreato-duodenectomy, which will avoid the risk of tumor seeding.

**Conclusion**

CBDS associated with CP usually indicates advanced disease and is mostly found with chronic calcific pancreatitis. The natural history depends on the severity of the fibrosis and calcification and the frequency of the superimposed acute inflammatory exacerbations. The clinical presentation varies from an incidental discovery to persistent jaundice and, more rarely, overt cholangitis. Minimally symptomatic patients should be treated conservatively with careful monitoring of liver functions at 6-month intervals (Figure 4). A conservative approach is also recommended for patients who present with jaundice, since this may resolve after resolution of an acute inflammatory episode. Biliary intervention is indicated when there is persistent jaundice for longer than a month or when frequent relapses occur, thus avoiding the risk of secondary biliary cirrhosis and cholangitis.

The preferred surgical biliary drainage is a choledochojejunostomy and in patients who also have pain and an inflammatory mass in the head, the authors prefer the addition of a Frey procedure. When there is concern about an underlying malignancy, the preferred operation is a pancreaticoduodenectomy.
Biliary stenting should be restricted to patients who present with overt cholangitis or patients who are unfit for surgical intervention. In future, the role of stenting as definitive treatment may be extended with the development of removable expandable stents.

**References**


