Biliary Dyskinesia

James Toouli, MBBS, PhD, FRAS

Address
Professor of Surgery, Flinders University of South Australia, Flinders Medical Centre, Bedford, Park, South Australia 5042, Australia.
E-mail: jim.toouli@flinders.edu.au

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Opinion statement

- Biliary dyskinesia is a motility disorder that affects the gallbladder and sphincter of Oddi.
- The motility disorder of the gallbladder is called gallbladder dyskinesia. Patients with this condition present with biliary-type pain, and investigations show no evidence of gallstones in the gallbladder. The diagnosis is made by performing a gallbladder ejection fraction, which is a radionuclide investigation. An abnormal gallbladder ejection fraction has a value less than 40%. Patients with an abnormal gallbladder ejection fraction should undergo cholecystectomy. This procedure has been shown to be effective in curing the symptoms in over 90% of patients.
- Motility disorder of the sphincter of Oddi is called sphincter of Oddi dysfunction. This disorder is categorized as two distinct types—biliary sphincter of Oddi dysfunction and pancreatic sphincter of Oddi dysfunction.
- Typically, patients with biliary sphincter of Oddi dysfunction present with biliary-type pain on average 4 to 5 years after having undergone cholecystectomy. Sphincter of Oddi manometry is essential in making a diagnosis of abnormal motility of the sphincter. On manometry, diagnosis of a sphincter of Oddi stenosis should lead to division of the sphincter. Sphincterotomy results in long-term relief of symptoms in more than 80% of patients.
- Pancreatic sphincter of Oddi dysfunction clinically presents with recurrent episodes of pancreatitis of unknown cause. Having ruled out all of the common causes of pancreatitis, sphincter of Oddi manometry of the pancreatic duct sphincter should be performed. When manometric stenosis is diagnosed, these patients should undergo division of both the biliary and pancreatic duct sphincter. This treatment results in relief of symptoms in more than 80% of patients.

Introduction

Biliary dyskinesia is the term used to describe primary motility disorders of the gallbladder and sphincter of Oddi. These are uncommon disorders. However, in the patients in whom they present, the symptoms can be debilitating.

Gallbladder motility disorders are called gallbladder dyskinesia, and the patients who present with this condition have symptoms that are suggestive of gallstones [1]. However, investigations do not reveal evidence of stones. Once gallbladder dyskinesia has been diagnosed, there are few treatment options other than cholecystectomy, because pharmacotherapy does not provide relief. Motility disorders of the sphincter of Oddi most often present in patients 4 or 5 years after cholecystectomy usually performed for gallstones [2]. These patients present either with biliary type sphincter of Oddi dysfunction [3••] or pancreatic type sphincter of Oddi dysfunction [4,5].

Patients with biliary sphincter of Oddi dysfunction present with biliary type symptoms, often similar to symptoms of stones in the bile duct. Manometric studies of the sphincter of Oddi confirm the diagnosis of biliary sphincter of Oddi dysfunction [3••]. Treatment options consist of the division of the sphincter endoscopically, a number of smooth muscle relaxant medications, or injection of the sphincter with botulinum toxin type A (Botox;

Allergan, Inc., Irvine, CA). The only treatment that has stood the test of time and has provided long-term results has been division of the sphincter through an endoscopic approach. The other treatment options provide transient relief, but long-term results are disappointing.

Pancreatic sphincter of Oddi dysfunction clinically presents with recurrent episodes of acute pancreatitis when no other causes of pancreatitis are diagnosed [4,5]. Sphincter of Oddi manometry from the pancreatic duct sphincter is the best way to diagnose this condition. Following diagnosis, the most appropriate treatment is an operative approach, which divides both the biliary and pancreatic sphincter. Alternate therapies include endoscopic division of the pancreatic duct sphincter or insertion of a stent in the pancreatic duct. The available data supports the use of transduodenal division of the sphincter of Oddi over the other two approaches. The endoscopic division does show promise, and long-term results are required before a final judgment can be made.

INDICATIONS FOR HOSPITALIZATION

Gallbladder dyskinesia and sphincter of Oddi dysfunction are painful conditions that may lead to hospitalization. Patients seek treatment because the pain is so severe. It is uncommon for evidence of peritonitis to be present. However, the pain may last for 24 to 48 hours. Consequently, it is prudent to treat patients with this condition by intravenous therapy and appropriate analgesia.

Treatment

Therapeutic options

Gallbladder dyskinesia

- Abdominal pain is the most common symptom associated with a motility disorder of the gallbladder. The pain is epigastric or in the right upper quadrant [1]. It occurs in episodes and is severe, often lasting for 2 to 3 hours or until it is relieved by analgesics. It may radiate to the back and under the tip of the right scapula. The pain may follow a fatty meal, and it may be associated with nausea and vomiting, although these are not diagnostic features.
- An objective diagnosis of gallbladder dyskinesia is made by evaluating the ability of the gallbladder to empty following a standard stimulus [6].
- ^{99m}Tc-labeled iminodiacetic acid is used to study the gallbladder, using a gamma camera and computer analysis. The gallbladder ejection fraction (GBEF) can be estimated by use of the following formula: GBEF (%) = Change in GB activity/Baseline GB activity X 100
- It has been shown that the normal gallbladder empties in excess of 50% of its volume in response to a standard meal or a 45-minute intravenous infusion of cholecystokinin octopeptide (CCK-OP; 20 ng/kg/h). In a patient with biliary-type pain, if the GBEF is lower than 40%, this is considered to be abnormal [7••].
- The most appropriate treatment for patients with identified gallbladder motility disorder is cholecystectomy because it permanently eliminates the organ that is producing the symptoms.
- The role of cholecystectomy was evaluated in 24 patients with abnormal CCK-OP GBEF. Patients were randomized prospectively to either cholecystectomy or follow-up. All but one of the patients who had a cholecystectomy were cured of biliary symptoms at 3 years after the operation. Histologic examination of the gallbladders removed at operation revealed features of chronic cholecystitis such as increased gallbladder wall thickness, fibrosis, and chronic inflammatory cells. None of the patients had gallstones. Those patients who did not have a cholecystectomy continued to experience symptoms, and three of these patients subsequently developed gallstones (7••).
- The approach for patients with suspected gallbladder motility disorder is to make the diagnosis using CCK-OP infusion scintigraphy. If the GBEF is abnormal, it is recommended to proceed to laparoscopic cholecystectomy.

Sphincter of Oddi dysfunction

- The sphincter of Oddi is a smooth muscle structure approximately 1 cm in length that is situated at the junction of the bile duct, pancreatic duct, and duodenum. Its function has been characterized by manometric techniques that allow direct measurement of pressure changes using a small catheter directed into either the bile duct or the pancreatic duct [3,4].
- Clinically, patients who present with sphincter of Oddi dysfunction can be divided into two broad groups. The majority of patients have symptoms that are mainly referable to the biliary tract, whereas a smaller group present with symptoms that are referable to the pancreas.
- The majority of patients with sphincter of Oddi dysfunction are women who have had a cholecystectomy for treatment of symptomatic gallstones [2]. The operation usually results in improvement in symptoms, but pain recurs after 2 to 10 years [8••,9,10]. The pain is felt in the epigastrium or right upper quadrant, often radiates into the back, and may be associated with nausea and vomiting. It generally occurs in episodes that last for up to several hours or until relieved by analgesics. These episodes may occur at intervals of weeks or months. Some patients also describe discomfort in the upper abdomen, which is more frequent and may occur every day. In addition, symptoms consistent with irritable bowel syndrome may coexist with episodic biliary-type pain. Some patients are aware that their symptoms can be precipitated or aggravated by opioid analgesics, including codeine. Indeed, the first episode of pain may have been experienced following opiate medication, usually for an unrelated procedure.
- Physical examination during an acute episode of pain reveals a distressed afebrile patient who often moves on the examination couch in order to find the most comfortable position. Abdominal examination is usually noncontributory, other than revealing mild to moderate tenderness in the epigastrium or right upper quadrant. Signs of local or general peritonitis are not associated with this condition.
- Blood screens reveal a normal white blood cell count. However, about 10% to 20% of patients show increases in serum concentrations of liver transaminases, particularly in blood specimens that are taken 3 to 4 hours after the onset of pain. This is occasionally accompanied by increases in serum bilirubin and alkaline phosphatase. In a subgroup of patients, the serum amylase activity may be elevated either alone or in conjunction with changes in liver enzymes. This group of patients is often given the clinical label idiopathic recurrent pancreatitis.
- Initial treatment of patients presenting with the above-mentioned clinical symptoms is directed at relief of pain, which is usually achieved by administration of a systemic analgesic or hyoscine-*N*-butylbromide (Buscopan; Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO). Pethidine (meperidine) is thought to be the most appropriate analgesic in patients with suspected sphincter of Oddi dysfunction.
- Endoscopic sphincter of Oddi manometry [11] is the most objective of all available investigations for determining sphincter of Oddi motility characteristics (Fig. 1). Manometrically, the sphincter of Oddi is characterized by regular phasic contractions that are superimposed on a modest basal pressure (Fig. 2). The majority of the contractions are orientated in an antegrade direction, but simultaneous and retrograde contractions can be recorded in control subjects (Table 1).

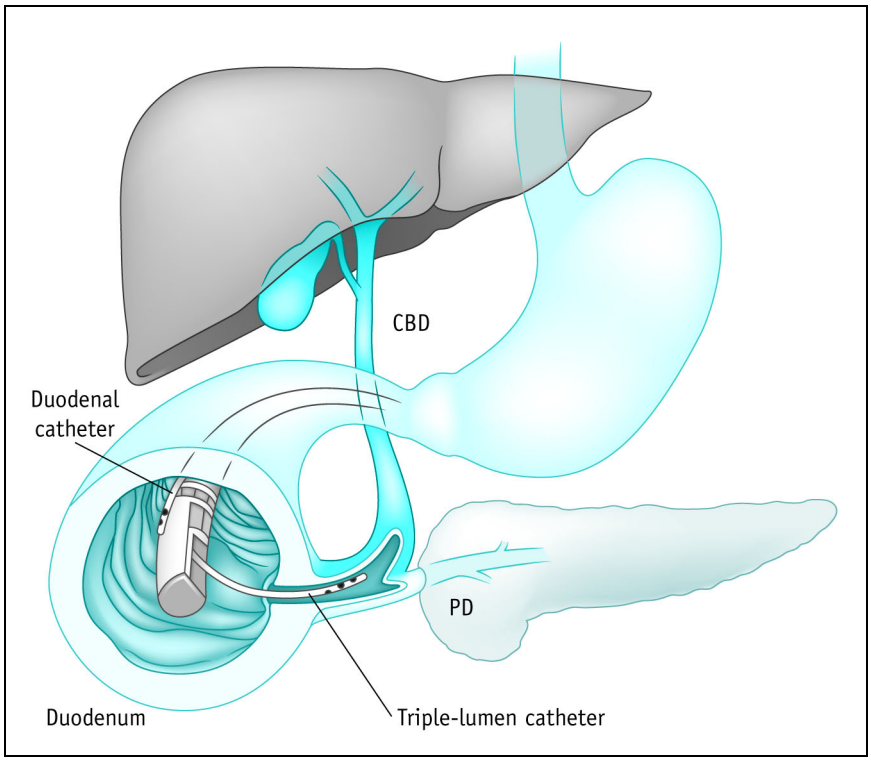

Figure 1. Endoscopic sphincter of Oddi manometry. The triple-lumen catheter is passed through the biopsy channel of a duodenoscope and inserted into either the bile duct or pancreatic duct so that the three ports record from the sphincter. CBD—common bile duct; PD—pancreatic duct.

Table 1. Sphincter of Oddi pressures

	Normal		Abnormal
	Median	Range	
Basal pressure (mm Hg)	15	3–35	>40
Amplitude (mm Hg)	135	95–195	>300
Frequency (n/min)	4	2–6	>7
Sequences			
Antegrade, %	80	12–100	
Simultaneous, %	13	0–50	
Retrograde, %	9	0–50	>50
CCK 20 ng/kg	inhibits		contracts

CCK—cholecystokinin.

- Manometric abnormalities have been identified in patients with clinically suspected sphincter of Oddi dysfunction [3••,10,12]. Using the manometric findings, sphincter of Oddi dysfunction has been divided into two major groups, irrespective of whether the symptoms are primarily biliary or pancreatic [3••]. This manometric division has allowed for targeting of specific therapy for patients in whom a diagnosis of sphincter of Oddi dysfunction is made. The two major groups are sphincter of Oddi stenosis and sphincter of Oddi dyskinesia (Table 2).

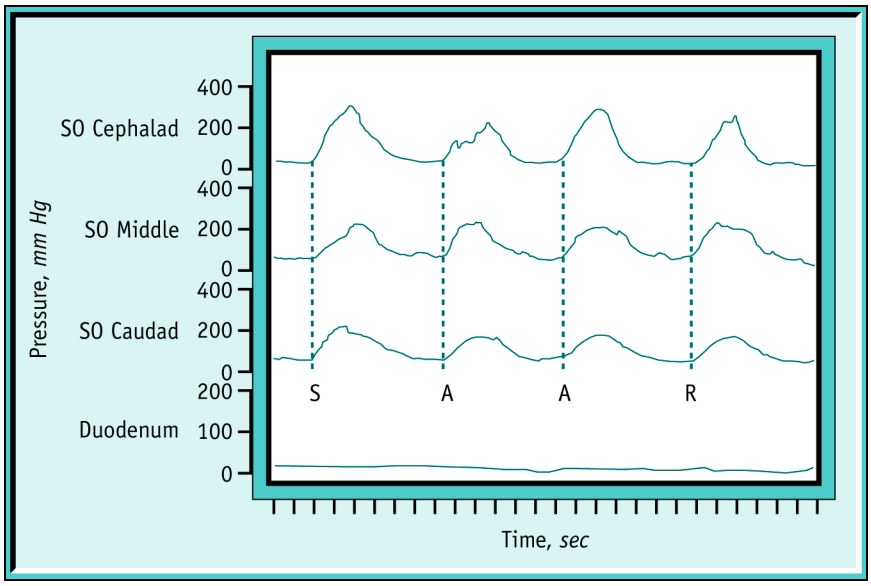

Figure 2. Manometric recording from the sphincter of Oddi. Prominent phasic contractions are superimposed on a modest basal pressure.

Table 2. Sphincter of Oddi dysfunction

Stenosis	Basal pressure > 40 mm Hg
Dyskinesia	Frequency > 7/min
	Intermittent rise in basal pressure
	Retrograde contractions > 50%
	Paradoxical CCK-OP response

CCK-OP—cholecystokinin octapeptide.

Sphincter of Oddi stenosis

Manometrically these patients have an abnormally elevated sphincter of Oddi basal pressure, which is defined as a basal pressure above 40 mm Hg (Fig. 3). Patients with manometric stenosis of the sphincter of Oddi and biliary symptoms are treated by endoscopic sphincterotomy (13••,14••). Potential complications of this procedure include hemorrhage, pancreatitis, and perforation of the duodenum. These complications are rare; however, they have been recognized in 3% of patients.

The finding of sphincter of Oddi stenosis may involve the pancreatic duct sphincter in patients with pancreatic sphincter of Oddi dysfunction. Treatment of these patients requires not only division of the bile duct portion of the sphincter of Oddi but also division of the septum between the bile duct and the pancreatic duct (15). This procedure is performed through an open operation requiring laparotomy. Potential complications include wound infection and pancreatitis. The incidence of the complications is approximately 3%.

Sphincter of Oddi dyskinesia

This group of disorders includes a number of other manometric abnormalities that have been described in patients with suspected sphincter of Oddi dysfunction. It includes rapid phasic contractions, excessive retrograde contractions, or a paradoxical response to cholecystokinin injection. At present, there is no specific therapy for this group of patients.

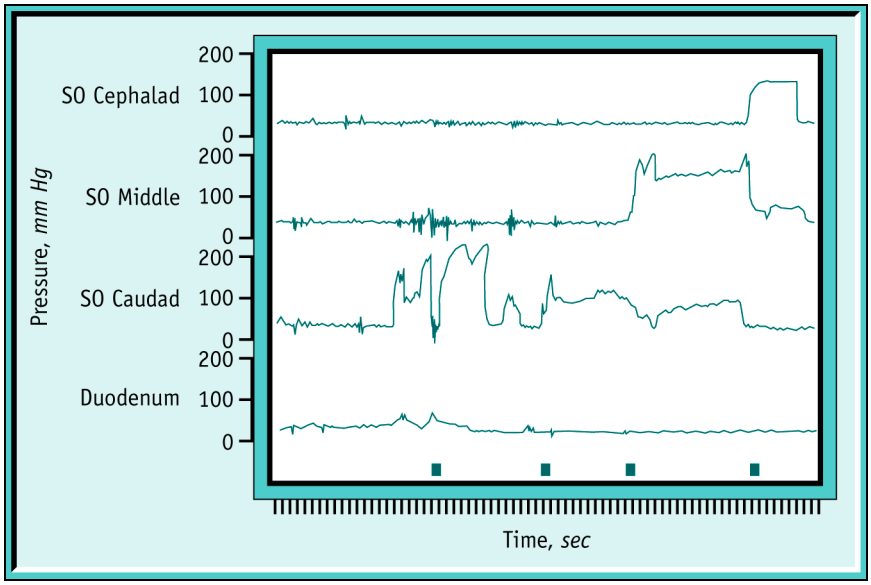

Figure 3. Manometric tracing illustrating sphincter of Oddi stenosis, which is characterized by a high basal pressure. The black squares illustrate a stepwise withdrawal of the triple-lumen catheter across a narrow stenosis.

Summary for treatment of sphincter of Oddi dysfunction

The options for management of sphincter of Oddi dysfunction are either division of the sphincter or pharmacotherapy.

Prospective clinical studies in Australia, the United States, and Europe have shown that patients with biliary-type symptoms and a manometric stenosis (*ie,* basal pressure > 40 mmg Hg) are either cured or else their symptoms are significantly improved following endoscopic sphincterotomy of the biliary sphincter of Oddi. The results of treatment are sustained on long-term follow-up of these patients.

In many patients with idiopathic recurrent pancreatitis, manometry reveals sphincter stenosis. Pancreatic duct stenosis may also be found in patients who have had a biliary sphincterotomy to treat recurrent pancreatitis. Thus, endoscopic sphincterotomy is often ineffective for recurrent pancreatitis, and treatment must include division of the pancreatic sphincter. This is achieved through a transduodenal approach at open operation, with division of the septum between the bile duct and pancreatic duct, which creates a wide opening for both ducts.

The results of this operation in producing symptomatic relief in patients with recurrent pancreatitis depend on the selection of patients. Approximately 80% of patients with an abnormally elevated basal pressure are improved by sphincteroplasty and pancreatic septoplasty.

The role of pharmacotherapy in the treatment of patients with sphincter of Oddi dysfunction is limited, because there are no drugs that are specific, long acting, and free of side effects. Buscopan may be helpful for acute episodes of pain. However, its action is short lived and it cannot be taken prophylactically. The calcium channel blocker nifedipine has also been used with some success in relieving pain, but it may be associated with cardiovascular side effects (16,17).

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