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Gallbladder and Sphincter of Oddi Disorders

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The concept that motor disorders of the gallbladder, cystic duct, and sphincter of Oddi can cause painful syndromes is attractive and popular, at least in the United States. However, the results of commonly performed ablative treatments (eg, cholecystectomy and sphincterotomy) are not uniformly good. The predictive value of tests that are often used to diagnose dysfunction (eg, dynamic gallbladder scintigraphy and sphincter manometry) is controversial. Evaluation and management of these patients is made difficult by the fluctuating symptoms and the placebo effect of invasive interventions. A recent stringent study has shown that sphincterotomy is no better than sham treatment in patients with post-cholecystectomy pain and little or no objective abnormalities on investigation, so that the old concept of sphincter of Oddi dysfunction type III is discarded. Endoscopic retrograde cholangiopancreatography approaches are no longer appropriate in that context. There is a pressing need for similar prospective studies to provide better guidance for clinicians dealing with these patients. We need to clarify the indications for cholecystectomy in patients with functional gallbladder disorder and the relevance of sphincter dysfunction in patients with some evidence for biliary obstruction (previously sphincter of Oddi dysfunction type II, now called "functional biliary sphincter disorder") and with idiopathic acute recurrent pancreatitis.

Keywords: Cholecystectomy; Biliary Pain; Post-Cholecystectomy Pain; Sphincter Manometry; Sphincterotomy; Idiopathic Pancreatitis; Endoscopic Retrograde Cholangiopancreatography.

Functional disorders of the gallbladder (GB) and the sphincter of Oddi (SO) are controversial topics. They have gone by a variety of names, including acalculous biliary pain, biliary dyskinesia, GB dysmotility, and SO (or ampullary) stenosis. This articles builds on the Rome III consensus,[1] recognizing that the evidence base is slim. This articles does not cover the anatomy and physiology, which are well described elsewhere.

Biliary Pain

The concept that disordered function of the GB and SO can cause pain is based mainly on the fact that many patients have biliary-type pain in the absence of recognized organic causes, and that some apparently are cured by removal of the GB or ablation of the sphincter.

E1. Diagnostic Criteria for Biliary Pain

Pain located in the epigastrium and/or right upper quadrant and all of the following:

1. Builds up to a steady level and lasting 30 minutes or longer
2. Occurring at different intervals (not daily)
3. Severe enough to interrupt daily activities or lead to an emergency department visit
4. Not significantly (<20%) related to bowel movements
5. Not significantly (<20%) relieved by postural change or acid suppression

Supportive Criteria

The pain may be associated with:

1. Nausea and vomiting
2. Radiation to the back and/or right infrascapular region
3. Waking from sleep

This definition for biliary pain differs from Rome III only in quantitating "not significantly" to mean <20%. We included the Rome III criterion that pains should be "not daily" although this is not evidence-based. Further studies are needed.

Functional Gallbladder Disorder

Definition

In conformity with the Rome consensus that defines functional gastrointestinal disorders as symptom complexes

Abbreviations used in this paper: CCK-CS, cholecystokinin-stimulated cholescintigraphy; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; FGBD, functional gallbladder disorder; GB, gallbladder; GBEF, gallbladder ejection fraction; MRCP, magnetic resonance cholangiopancreatography; SO, sphincter of Oddi; SOD, sphincter of Oddi dysfunction.

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not explained by a clearly identified mechanism or by a structural alteration, we use the term *functional gallbladder disorder* (FGBD) to describe patients with biliary pain and an intact GB without stones or sludge.

E1a. Diagnostic Criteria for Functional Gallbladder Disorder

1. Biliary pain
2. Absence of gallstones or other structural pathology

Supportive Criteria

1. Low ejection fraction on gallbladder scintigraphy
2. Normal liver enzymes, conjugated bilirubin, and amylase/lipase

Since the diagnosis is primarily one of exclusion, the prevalence depends on the rigor of investigation. Ultrasonography is the usual primary investigation, but endoscopic ultrasound (EUS) is more sensitive for detecting small stones and biliary sludge, and can also detect small tumors, and subtle changes of chronic pancreatitis.

The only change from Rome III is that normal liver and pancreatic enzymes have been moved to the supportive category. There can be other reasons for elevated liver enzymes, like fatty liver disease, that do not rule out GB dysfunction. We have also added a low ejection fraction on GB scintigraphy as supportive. It is not required for the diagnosis, nor is it specific for the diagnosis when abnormal.[2]

Epidemiology

Biliary pain is a common clinical problem, and cholecystectomy is a frequent operation. The number and proportion done for FGBD seems to be increasing in the United States, where case series now list it as the indication for cholecystectomy in 10%–20% of adults[2,3] and in 10%–50% of children.[4] FGBD is rarely diagnosed outside the United States.[5]

Pathophysiology

FGBD is often diagnosed by a low gallbladder ejection fraction (GBEF) at cholecystokinin-stimulated cholescintigraphy (CCK-CS). Although the relationship between GBEF and clinical outcome remains unclear, gallbladder dysmotility may still play a role in the pathogenesis of symptoms, by promoting gallbladder inflammation, which is commonly found. Microlithiasis is associated with a delayed ejection fraction on scintigraphy.[6] Investigators have found multiple defects in gallbladder contractility, including spontaneous activity and abnormal responses to both CCK and neural stimulation.[7] A vicious cycle of stasis and inflammation exists in the GB. Some patients may have intrinsic defects in contractility, and subtle defects in bile composition may also play a role. Studies have shown elevated sphincter of Oddi (SO) pressures in patients with GB dyskinesia, but without correlation between GBEF and SO pressure.[8] GB dysfunction may represent a more generalized dysmotility, as in irritable bowel syndrome and chronic constipation, and perhaps gastroparesis.[9] Experimental evidence has implicated several molecules that can link inflammation to motility, the most important of which may be prostaglandin E2 (PGE2).[10,11] Possible etiological mechanisms and outcomes in patients with "biliary dyskinesia" are illustrated in Figure 1.

Clinical Evaluation

GB stones should be excluded by ultrasound scanning (repeated if necessary), and complemented with EUS. Other tests may be needed to rule out peptic ulcer disease, subtle chronic pancreatitis, fatty liver disease, or musculoskeletal syndromes. Esophageal manometry, gastric emptying tests, and transit studies may be required if symptoms suggest alternative dysfunctional syndromes. Further management depends on the level of clinical suspicion. The diagnosis of FGBD may be made by exclusion if the pains are typical and

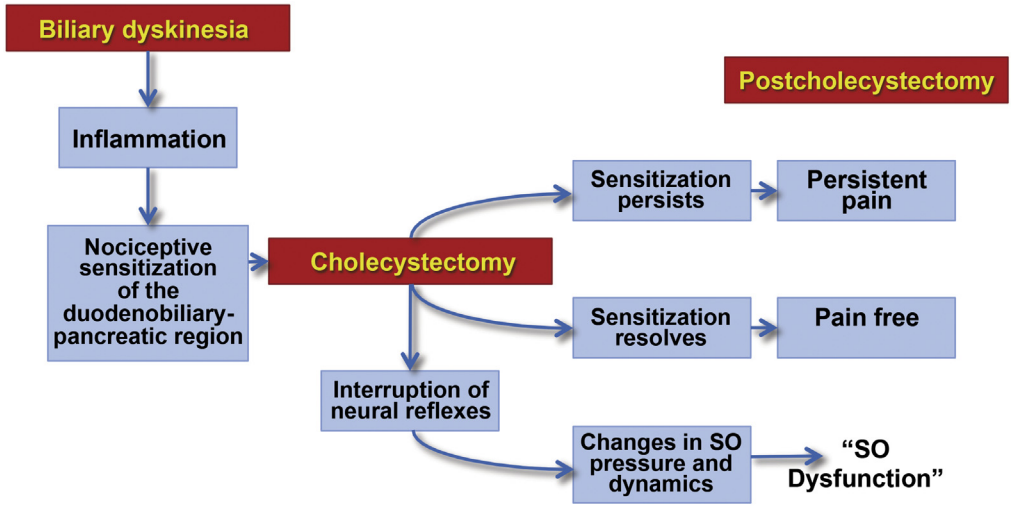

Figure 1. Potential etiological pathways and clinical outcomes in patients with "biliary dyskinesia"