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Gallbladder Ejection Fraction and Its Relationship to Sphincter of Oddi Dysfunction

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Theoretically, relative distal common bile duct obstruction due to sphincter of Oddi dysfunction may be a cause of poor gallbladder evacuation observed on quantitative cholescintigraphy. In this study, the relationship of sphincter of Oddi dysfunction to the gallbladder ejection fraction by quantitative cholescintigraphy was explored. Eighty-one patients with biliary-type pain and otherwise normal evaluations underwent quantitative cholescintigraphy, sphincter of Oddi manometry, and ERCP. Abnormalities of stimulated quantitative cholescintigraphy and/or sphincter of Oddi manometry were present in 70% of this study group. Manometric evidence of sphincter dysfunction was present in patients with similar frequency irrespective of the degree of gallbladder evacuation. In conclusion, abnormalities of quantitative cholescintigraphy and sphincter manometry appear to be independent factors, although frequent findings in this patient population.

KEY WORDS: gallbladder ejection fraction; quantitative cholescintigraphy; sphincter of Oddi dysfunction.

Cholescintigraphy has become a useful imaging technique for a variety of hepatobiliary disorders including acute cholecystitis, biliary obstruction, or bile leaks. In recent years cholescintigraphy has become increasingly utilized for the evaluation of patients with suspected chronic cholecystitis in whom ultrasound or oral cholecystography have been unrevealing. One such method is the stimulated quantitative cholescintiscan. The quantitative cholescintiscan combines standard hepatobiliary imaging principles with an agent, cholecystokinin-octapeptide (CCK-OP; Kinevac), to promote gallbladder emptying. A value representing the percent of gallbladder evacuation is determined and referred to as the gallbladder ejection fraction. Proponents of this nuclear medicine scan suggest that the gallbladder ejection fraction can identify the presence of chronic cholecystitis or cystic duct obstruction (1). However, other potential causes of poor gallbladder evacuation or emptying by quantitative cholescintigraphy must be considered. These include relative distal common bile duct obstruction secondary to sphincter of Oddi dysfunction, common duct stone(s), stricture(s), or tumor(s). Obesity, diabetes, sex hormones, and anticholinergics and narcotic analgesics may also adversely effect gallbladder evacuation through nonobstructive mechanisms.

Although the incidence and pathophysiology of sphincter of Oddi dysfunction/dyskinesia in patients with gallbladder *in situ* is not known, there is substantial evidence that it does exist in this setting (2, 3). In this study, the relationship of sphincter of Oddi dysfunction (SOD) to gallbladder ejection fraction (gb-EF) by quantitative cholescintigraphy was explored.

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MATERIALS AND METHODS

During the time period of July 1988 through November 1990, 81 patients with gallbladder *in situ* and "biliary-type" right upper quadrant pain (usually with right subscapular or shoulder radiation) were studied. All patients had otherwise previous normal evaluations including liver chemistries, ultrasound (and/or oral cholecystography), and esophagogastroduodenoscopy. All patients underwent evaluation of the gallbladder and biliary tree with quantitative iminodiactetic acid scanning (HIDA or DISIDA). Each patient also underwent endoscopic retrograde cholangiopancreatography (ERCP) and attempted sphincter of Oddi manometry (SOM). Diagnostic ERCPs were negative for ductal stones, strictures, or tumors. Patients were not on any medications or hormones known to affect gallbladder evacuation. All studies were prospectively interpreted, although retrospectively tallied for purposes of this review. The study group was comprised of 68 females and 13 males ages 16–73. Mean age was 42.5 years.

Biliary scintigraphic imaging was performed on patients following an overnight fast in a fashion previously described by Fink-Bennett et al (1). The radiopharmaceutical agent used was technetium-99m diisopropyl iminodiacetic acid (DISIDA) or [^{99m}Tc] disofenin (HIDA). Following maximum gallbladder visualization, 0.02 μg/kg of intravenous CCK-OP (Kinevac, Squibb Diagnostics, Princeton, New Jersey) was administered over 3 min. Imaging was then maintained for 20 min with corrected gb-EFs being determined by the percent reduction of nuclide within the gallbladder region of interest (over prestimulated values). An abnormal ejection fraction was defined as less than 35% reduction in the gallbladder nuclide counts at any point during the post-Kinevac scanning period. This value and technique is consistent with other previously published studies (4, 5). Scans were interpreted by nuclear radiologists blinded to the patients' histories.

ERCP and sphincter of Oddi manometry were performed by experienced endoscopists. Manometry of the biliary and/or pancreatic sphincter(s) was performed and evaluated in standard fashion using the station pull-back technique (6–8). Mean basal sphincter pressures during two to three pull-throughs were averaged to determine whether sphincter dysfunction was present. As is our institution's practice, two independent endoscopists evaluated each tracing with a consensus interpretation being provided. Basal pressures greater than 40 mm Hg were considered abnormal. Phasic wave pressure, frequency, or sphincter response to CCK-OP were not examined as they are generally not believed to be reliable indicators of sphincter dyskinesia (7). No patient had previous biliary surgery or prior sphincter ablative procedures.

RESULTS

All patients had successful cholangiography performed in addition to the scintigraphic studies. Intraductal stones, tumors, and/or strictures were not identified. The results are displayed in Table 1.

TABLE 1.

Ejection fraction	*Manometry*		
Normal (N = 41)	Normal	13	(43%)*
	Abnormal	17	(57%)*
		30	
	Failed	11	
Abnormal (N = 40)	Normal	18	(50%)*
	Abnormal	18	(50%)*
		36	
	Failed	4	

*Patients in group with successful manometry.

Of the 81 patients, 41 (50.6%) had a normal gb-EF (mean = 71.7%; range 42–99%). Sphincter of Oddi manometry was successful in 30 of these patients with a normal pattern of gallbladder evacuation. Thirteen of the 30 (43.3%) had normal sphincter of Oddi basal pressures, whereas 17 of 30 (56.7%) demonstrated abnormal basal sphincter pressures.

Forty patients (49.4%) had an abnormal ejection fraction on quantitative cholescintigraphy (mean = 9.9%; range 0–34%). Sphincter of Oddi manometry was successful in 36. Eighteen of these patients had normal sphincter manometry (18/36 = 50%), and an identical number had abnormal sphincter pressures.

Sphincter manometry was successful in 66 of the 81 patients (81.5%). Basal sphincter pressure abnormalities were frequent in this group of patients with "biliary-type" pain. Overall, 53% (35 of 66) of patients undergoing successful sphincter of Oddi manometry had evidence of abnormal sphincter pressures.

In manometry-successful patients, 80.3% (53/66) had a demonstrated abnormality of either gb-EF or sphincter of Oddi manometry. Including failed manometry patients, 70.3% (57/81) of this group demonstrated abnormalities of either quantitative scintigraphy or of the sphincter of Oddi.

No statistically significant differences were observed on comparison of the patients with normal or elevated sphincter pressures when compared to frequency of decreased gallbladder evacuation. The mean age of the patients with a normal gb-EF was 41.9 years versus 43.1 years for the group with an abnormal gb-EF.

DISCUSSION

The use of biliary or gallbladder scintigraphy in the assessment of biliary tract disease or sphincter of Oddi dysfunction is a new and promising area of

clinical interest. Currently, in the evaluation of acute cholecystitis, cholescintigraphy is widely accepted and employed. However, for the patient with suspected chronic acalculus cholecystitis, the available data on cholescintigraphy is not as clear (9, 10). Several recent studies have attempted to explore the relationship of the gallbladder ejection fraction (as determined by quantitative cholescintigraphy) with histological findings. Although techniques vary somewhat, the studies have shown a potential benefit and reproducibility to the quantitative gallbladder scan and ejection fraction as a means of detecting chronic acalculus cholcystitis or the cystic duct syndrome (4, 11, 12). Yap et al (11) in a prospective randomized study showed that patients with an abnormal gb-EF continued to have pain if untreated, whereas 92% had pain resolution with cholecystectomy. One nonresponder was found to have sphincter of Oddi dysfunction at follow-up manometry.

Sphincter of Oddi dysfunction is being increasingly recognized as a cause of postcholecystectomy pain (13). Several authors have noted the coexistence of SOD and abnormal gb-EF (2, 3, 14). It is suspected, but not proven, that physical obstruction of the bile ducts (stones, tumor, stricture) interfere with gallbladder evacuation. In this study, the relationship of the gb-EF to SOD was explored to determine if "functional" obstruction of the sphincter of Oddi would adversely effect or otherwise correlate with stimulated emptying of the gallbladder. A large percentage of the patients in this review were found to have evidence of sphincter dysfunction and/or a diminished gb-EF. At least one of these abnormalities was present in 70% of the patients. The ejection fraction, however, did not appear to correlate with manometric findings, and vice versa. In manometry-studied patients, evidence of SOD was found in 50% of patients with an abnormal gb-EF and 57% of those with a normal gb-EF. In patients with abnormal SOM, 51% had an abnormal gb-EF versus 58% with normal manometry.

If abnormalities on gb-EF via quantitative cholescintigraphy alone are utilized as an indication for cholecystectomy, a significant number of patients may not have pain relief due to residual SOD. Alternatively, if abnormal SOM is used as an indicator for sphincter ablative therapy in individuals with their gallbladder *in situ,* a portion of patients may not have symptom relief due to undetected gallbladder disease. Indeed, in a study that evaluated outcome of endoscopic sphincterotomy in patients with gallbladder *in situ* and abnormal SO basal pressure, Choudhry et al (2) found that only 50% of patients had good or excellent pain relief after 13 months of follow-up. Selective cholecystectomy in persons not responding to sphincterotomy increased the pain resolution rate to 77%.

In the search for subtle biliary tract disease, the cause(s) of biliary-type pain appears to be multifactorial. Careful assessment of the gallbladder, bile ducts, and sphincter of Oddi may be necessary. Quantitative cholescintigraphy and SOM should be considered. Additionally, the analysis of bile aspirated from the duodenum (not done in our study) may be of help in identifying patients with cholesterolosis or microcalculus gallbladder disease/ chronic cholecystitis. Exclusion of pancreatic disease may also be warranted in this patient population. Such thorough evaluations would result, it is hoped, in more accurate patient management.

With regards to quantitative cholescintigraphy, additional prospective trials with surgical controls and careful analysis of histological findings are needed to clarify the optimal technique and ejection fraction criteria for this promising technology. Although, as demonstrated by this study, the relationship of SOD and quantitative scintigraphy does not appear uniform in patients with their gallbladder *in situ,* additional studies employing quantitative biliary scintigraphy in postcholecystectomy patients appear to be encouraging (15–17).

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