# Differential Gallbladder Contractility in Fundal Adenomyomatosis: Demonstration by Cholecystokinin Cholescintigraphy

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The cholecystokinin cholescintigraphic findings of fundal adenomyomatosis in a 29-yr-old male with severe post-prandial pain are presented. Planar cholescintigraphy demonstrated a trilobed gallbladder contour. Following the administration of 0.02 μg/kg of cholecystokinin at maximal gallbladder filling, fundal dyskinesia was observed. Regional gallbladder ejection fractions were: whole gallbladder, 43%; proximal two-thirds of the gallbladder, 70%; and gallbladder fundus, 32%. First harmonic Fourier phase and amplitude images demonstrated: (a) decreased fundal amplitude values, and (b) a phase shift of the pixels in the gallbladder fundus.

**A**denomyomatosis of the gallbladder is a benign noninflammatory condition of unknown etiology which is characterized by proliferation of the mucosa, thickening of the muscle wall, and intramural diverticula formation (Rokitansky-Aschoff sinuses). Jutras (1) classified adenomyomatosis along with cholesterolosis and neuromatosis under the broader category of hyperplastic cholecystoses, in order to emphasize their proliferative and degenerative nature. Three forms of the disease have been described, based upon the extent of the abnormality: diffuse, segmental, and localized (usually confined to the fundus). Adenomyomatosis occurs in men and women with equal frequency. Although the entity is recognized in approximately one-fourth of surgical specimens, it is preoperatively identified in only 5–10% of cases, based upon cholecystographic series (2).

The clinical implications and subsequent management of adenomyomatosis are controversial. Although frequently asymptomatic, the disease may be the cause of recurrent right upper quadrant pain, even in the absence of stones. Berk et al. (2) in their recent excellent literature review, concluded that the role of compart-

mentalization and abnormal emptying of the gallbladder in the production of symptoms has not been established. We report a case of fundal adenomyomatosis which was studied utilizing cholecystokinin cholescintigraphy. The patient's pain was clinically reproduced during the examination and was documented to coincide with abnormal emptying pattern of the fundal dyskinesia.

## Case Report

A 29-yr-old male presented with repeated attacks of severe right upper quadrant pain of seven years duration. The pain radiated to the right flank and back and was aggravated by heavy meals and fatty foods. The patient denied nausea, vomiting, jaundice, melena, or change in bowel habits.

A hepatobiliary scan was performed with 5 mCi of technetium-99m DISIDA, utilizing a large-field camera and an all-purpose, parallel hole collimator. Prompt gallbladder visualization was achieved at 15 min postinjection. Following maximal filling at 60 min, 0.02 μg/kg Sincalide* was intravenously infused over a 5-min interval. Serial scintigraphic and computer acquisition was obtained for 40 min at 1 frame per sec, with storage of the data in byte mode in a 64 × 64 computer matrix. Regions of interest were placed around the gallbladder, common hepatic duct, and common bile duct. Following background subtraction, a latent period (1 min), ejection period (18 min), ejection fraction (43%), and ejection rate (2.4 %/min) were calculated.

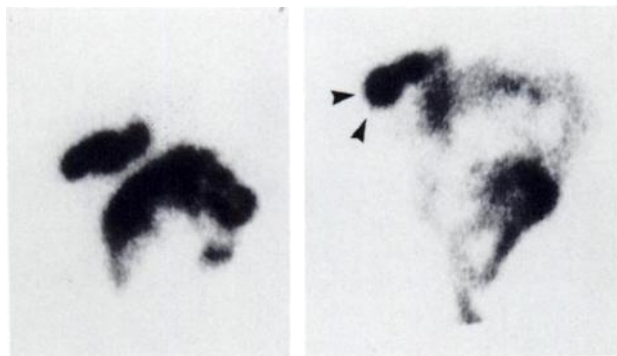Although a 43% ejection fraction is considered to be in the

**FIGURE 1**
Planar images of the gallbladder obtained at the beginning of contraction and at peak fundal dyskinesia, 11 min later. Note the tri-lobed contour of the gallbladder and fundal dyskinesia (arrowheads).

low-normal range in our laboratory (*3*), visual inspection of the planar images revealed a tri-lobed contour of the gallbladder with effective contraction occurring in the proximal two-thirds and focal dyskinesia appearing in the gallbladder fundus (Fig. 1). Separate regions of interest were drawn around these areas and background subtracted time-activity curves were generated for the whole gallbladder, the proximal two-thirds of the gallbladder, and the fundus. Ejection fractions for these regions were calculated and equaled 43% for the whole gallbladder, 70% for the proximal portion of the gallbladder, and 32% for the fundus. At the point of peak fundal dyskinesia, 56% of the ejected volume from the proximal gallbladder has travelled in a retrograde direction filling the gallbladder fundus. Clinically, the patient experienced his maximal discomfort during this time period.

First-harmonic Fourier analysis of the whole gallbladder time-activity curve was done after filtering with a seven-point spatial smooth, using a 0.15 coefficient. The resulting amplitude and phase images demonstrated: (a) decreased amplitude values in the fundal segment; and (b) fundal dyskinesia (phase shift) as compared with the proximal two-thirds of the gallbladder (Fig. 2).

Further workup of this patient included realtime sonography, which again demonstrated a tri-lobed contour of the gallbladder with focal wall thickening in the fundus and no evidence of cholelithiasis. An oral cholecystogram confirmed these findings and also revealed the presence of Rokitansky-Aschoff sinuses, consistent with fundal adenomyomatosis. Due to the severe recurrent symptomatology, an elective cholecystectomy was performed which resulted in immediate and permanent relief from all abdominal pain. The patient

remained completely symptom-free at a 10-mo clinical follow-up.

Pathologic examination of the surgical specimen revealed marked thickening of the gallbladder wall in the fundus with diffuse replacement of the submucosa by yellow-white adipose-like tissue. In addition, there were multiple disproportionately large vessels and hypertrophied nerves. Numerous Rokitansky-Aschoff sinuses were also present, many of which contained small intramural stones. There was no gross or microscopic evidence of superimposed acute inflammation.

Subsequently, a 61-yr-old female presented with similar sonographic and scintigraphic findings (whole gallbladder ejection fraction = 4%). At surgery there was evidence of chronic cholecystitis with numerous fibrinous adhesions to the gallbladder wall; pathologic examination confirmed the presence of fundal adenomyomatosis with numerous Rokitansky-Aschoff sinuses and small intramural stones. This patient also obtained complete relief following cholecystectomy, and remained asymptomatic at a 3-mo clinical follow-up.

Whole and regional gallbladder time-activity curves and Fourier analyses were also performed on gallbladders from ten additional patients from a prior series (*3*). All additional patients had no evidence of cholelithiasis on real-time sonography, performed with a 3.5-MHz transducer. Five of these patients were considered to be "normal" and had gallbladder ejection fractions of greater than 35% (mean = 60.4%, range = 38–89%). The other five patients had abnormal gallbladder ejection fractions of <35% (mean = 20.6%, range 9–34%) and each had pathologic evidence of chronic acalculous cholecystitis following cholecystectomy. None of these ten patients exhibited a similar contractile response to the patients reported herein.

## DISCUSSION

Jutras (*1*) classified adenomyomatosis, cholesterolosis, and neuromatosis under the generic term of hyperplastic cholecystoses in order to emphasize the proliferative and degenerative aspects of these diseases. He described a hyperfunctioning complex, consisting of hyperconcentration, hyperexcitability, and hyperexcretion. This clinical triad was attributed to hyperplasia of the mucosal, neural, and muscular elements within the gallbladder wall. Berk et al. (*2*), however, considered these findings to be of doubtful authenticity since their evidence was entirely anecdotal. Indeed, a wide variety of contractile responses have been reported in aden-

**FIGURE 2**
Amplitude and phase images from Fourier analysis. The amplitude image depicts diminished amplitude values within the fundus (curved arrow), indicative of decreased regional wall motion. The phase image and histogram, demonstrate a phase shift in the fundal pixels (arrows), consistent with fundal dyskinesia.
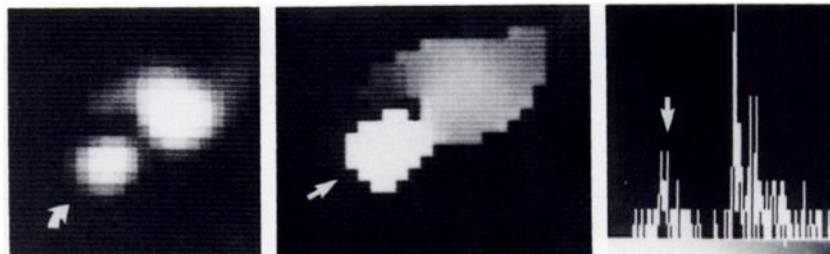
omyomatosis utilizing cholecystokinin cholecystography. These include: hypercontractility (*1*); poor concentration and excretion (*4*); absence of excretion with infundibular contraction and rounding of the gallbladder contour (*4,5*); and segmental wall motion abnormalities—septal thickening (*4*), fundal hypercontractility (*4*), and fundal dyskinesia (*6*).

Cholecystokinin cholescintigraphy is a relatively new technique which has been rigorously validated by Krishnamurthy et al. (*7,8*) and has several inherent advantages when compared with oral cholecystography and ultrasonography. Scintigraphy permits continuous physiologic monitoring of data, as opposed to the predefined filming intervals of oral cholecystography. The counts-based method of nuclear imaging also more accurately portrays volumetric changes than do "anatomic" imaging modalities which rely on less accurate geometric assumptions; the procedure yields a highly reproducible ejection fraction (mean error = 5%) (*7*). Additionally, the examination is easy to perform, results in a low radiation exposure, and has been shown to be independent of respiratory motion (*7*).

The technique has been used most frequently to investigate physiologic parameters of the gallbladder during emptying and filling (*9–12*). Several clinical laboratories (*13–16*), including our own (*3*), have also reported initially encouraging results in the preoperative assessment of acalculous biliary disease. These studies, performed primarily in chronically symptomatic patients, have utilized a decrease in the whole gallbladder ejection fraction as an indication for cholecystectomy. Few authors have commented specifically on the role of cholecystokinin cholescintigraphy in adenomyomatosis. Ram et al. (*17*) studied two patients with surgically proven adenomyomatosis who demonstrated poor contractility in response to cholecystokinin. Kramer et al. (*18*) reported three cases of compartmentalized gallbladders secondary to segmental adenomyomatosis, but did not have the opportunity to study the emptying dynamics of the distal compartment.

Cholescintigraphic detection of segmental gallbladder wall motion abnormalities has not previously been described. In our patient, the adenomyomatosis was confined to the fundus of the gallbladder, allowing a comparison with the 'normal' proximal portion. It is tempting to speculate on the exact role of the abnormal emptying pattern in the production of our patient's repeated episodes of severe post-prandial pain. Perhaps forceful retrograde distension of the noncompliant, fibrotic, gallbladder fundus was directly contributory, since clinically this coincided precisely with the period of maximal patient discomfort.

Fourier analysis (frequency-domain filtering) is a useful method for representing mathematical functions which are repetitive in time or space (e.g., cardiac cycle or gallbladder emptying or filling) (*19*). In this technique, the time-activity curves from each pixel of a dynamic study are fitted to a series of cosine waves of differing amplitudes and phase shifts. The sum of these values may then be displayed as functional images, portraying physiologic patterns of organ contractility. Each pixel in the amplitude image represents the magnitude of the cosine curve fitted to the data of the individual pixel; while in the phase image, each pixel is assigned the phase angle of its cosine wave fitted to the organ volume curve.

In summary, adenomyomatosis may cause focal wall motion abnormalities with or without an accompanying reduction in the whole gallbladder ejection fraction. Although the clinical implications and management of the disease are controversial, patients with chronic biliary tract symptomatology may benefit from cholecystectomy. Other entities which might manifest similar cholescintigraphic findings would include: compartmentalized gallbladders (*18*) and gallbladder duplications (*20*). Cholecystokinin cholescintigraphy may be a useful clinical tool in documenting abnormal emptying patterns in these patients.

## NOTE

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