Cholecystokinin Cholescintigraphic Findings in the Cystic Duct Syndrome

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Fourteen patients with a cystic duct syndrome (CDS) underwent cholecystokinin (CCK) cholescintigraphy. All patients presented with persistent postprandial right upper quadrant pain and biliary colic. None of the patients had an abnormal oral cholecystography, gallbladder (GB) ultrasound exam or upper GI series. Each patient (NPO after 12 a.m.) received 5 mCi of technetium-99m disofenin. When the GB maximally filled, 0.02 μg/kg CCK was administered (3 min) intravenously. Background corrected gallbladder ejection fractions (GBEFs) were determined every 5 min × 4 by ratioing the pre-CCK GB counts minus post-CCK GB counts to pre-CCK GB counts. GBEFs were: 12% (3 patients), 17% (2), 0%, 1.3%, 3%, 4%, 6%, 11%, 14%, 18.5%, and 22% (1 each). All patients underwent a surgical exploration and all had macro- or microscopically abnormal cystic ducts (five fibrotic, seven elongated and narrow, two kinked) with (12 patients) or without (2 patients) concomitant chronic cholecystitis. No patient with a partially occluded cystic duct with or without concomitant chronic cholecystitis had an ejection fraction that exceeded 22%. In an appropriate clinical setting, a low EF response to CCK should alert the physician to the presence of either chronic acalculous cholecystitis, CDS, or the combination of both.

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The term, the "cystic duct syndrome" (CDS) (noncalculous partial cystic duct obstruction), was originally proposed by Cozzolino et al. in 1963 (*1*). It describes a condition that is clinically characterized by recurrent right upper quadrant pain and biliary colic. Oral cholecystograms, upper gastrointestinal (GI) series, gallbladder (GB) sonography, and routine blood chemistries are normal. If performed, cholecystokinin (CCK) cholecystograms have been reported as demonstrating impaired gallbladder contraction and/or a reproduction of the patient's right upper quadrant pain (*2*). It is caused by a partial mechanical obstruction (fibrosis, kinking, adhesions) of the cystic duct. Its recognition is important, for if undiagnosed, patients with impaired gallbladder evacuation are inappropriately treated (if at all) and forced to endure continuous postprandial pain. In some individuals, symptoms are so severe that anorexia nervosa develops. European and/or South American synonyms for the CDS include the cystic syndrome, biliary infundibulo-cervico-cystic dyskinesia, mechanical dyskinesia, gallbladder siphopathy, and/or the cystic-cholecystic syndrome (*3*).

To determine if cholecystokinin cholescintigraphy can aid in the early detection and/or recognition of the CDS, we retrospectively analyzed the maximal gallbladder ejection fraction response (MGBEFR) to CCK in 14 patients with a noncalculous partial cystic duct obstruction.

MATERIALS AND METHODS

Fourteen female patients (ages 14–72 yr) presented with postprandial right upper quadrant pain and biliary colic. None of the patients had an abnormal oral cholecystogram gallbladder ultrasound examination, and/or upper GI series.

After an overnight fast, each patient received 5 mCi of technetium-99m (^{99m}Tc) disofenin intravenously.

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TABLE 1
Cholecystokinin Functional Cholescintigraphic Findings in Patients with Partial Cystic Duct Obstruction — The Cystic Duct Syndrome (CDS)

Pt	Age	Sex	MGBEFR (%)	Clinical path correlation
1	42	F	17	Chronic GBD, fibrosis, distorted cystic duct
2	24	F	6	Normal GB, fibrotic cystic duct
3	29	F	0	Normal GB, long, narrowed cystic duct, kinked
4	18	F	12	Chronic GBD, long, narrowed cystic duct
5	47	F	1.3	Chronic GBD, long, narrowed cystic duct
6	74	F	3	Chronic GBD, fibrotic cystic duct
7	32	F	22	Chronic GBD, narrow cystic duct, with Aschoff-Rokitansky sinuses
8	31	F	17	Chronic GBD, bile stasis, fragmented yellow calculi, thickened, narrowed cystic duct
9	33	F	12.1	Chronic GBD, narrowed cystic duct with Aschoff-Rokitansky sinuses
10	22	F	4	Chronic GBD, chronic inflammation of cystic duct, narrowed lumen, Aschoff-Rokitansky sinuses and lymphocytes present
11	40	F	12	Chronic GBD, narrowed cystic duct, Aschoff-Rokitansky sinuses and lymphocytes present
12	30	F	11	Chronic GBD, narrowed cystic duct, Aschoff-Rokitansky sinuses and lymphocytes present
13	18	F	14	Chronic GBD, narrowed cystic duct, Aschoff-Rokitansky sinuses present
14	42	F	18.5	Chronic GBD, narrowed cystic duct, kinked, Aschoff-Rokitansky sinuses and lymphocytes present

Utilizing a large field-of-view gamma camera with a low-energy, medium resolution collimator, and a 20% window centered at 140 keV, anterior 500,000 ct hepatobiliary images were obtained every 10 min ×6, or until the gallbladder maximally filled (little to no activity within the major hepatic radicals, most within the gallbladder). An infusion of 0.02 μg/kg of sincalide was done over a 3-min duration. Following the CCK infusion, anterior post-CCK analog hepatobiliary images were obtained every 5 min ×4, as was the gallbladder's EF response to CCK. The post-CCK analog images were obtained for *set times*, not counts, and the time per image was determined from the number of seconds required to obtain a pre-CCK anterior 500k biliary scintiscan.

Gallbladder ejection fractions were determined from acquired serial 1-min images stored in a 64 × 64 matrix.* Acquisition was begun 1 min prior to, and continued for 20 min following, the administration of CCK. The EF determination was made by manually assigning regions of interest (ROI) over the gallbladder and an adjacent background area (background height equal to gallbladder length, background width 3–4 pixels) on the pre-CCK and 5, 10, 15, and 20 min post-CCK images. The total counts and the number of pixels within the ROI were determined, and the ejection fraction calculated according to the following formula:

$$\text{GBEF} = \frac{\text{Net pre-CCK GB cts-Net post}_i\text{-CCK GB cts}}{\text{Net pre-CCK GB cts}},$$

where i = the time post-CCK administration, and net GB cts = total GB cts minus the product of the background cts/pixel × the number of pixels within the GB as illustrated in the following equation.

$$\text{Net GB cts} = \text{total GB cts} - (\text{background cts/pixel} \times \text{No. of GB pixels}).$$

PATHOLOGIC EXAMINATION

Pathologic criteria of chronic cholecystitis and/or CDS included hypertrophy of the gallbladder wall (>1.5 - 2 mm), diffuse hypertrophy of the muscularis propria with or without a concomitant mononuclear cell infiltrate, the presence of Aschoff-Rokitansky sinuses and/or foamy macrophages filling the tips of mucosal folds, yellow papillary nodules, fibrosis of the cystic duct producing at least a 60–80% luminal narrowing and/or kinking, or adhesions of the cystic duct seen at operation.

RESULTS

Maximal GBEFS were: 12% (3 patients), 17% (2), and 0%, 1.3%, 3%, 4%, 6%, 11%, 14%, 18.5% and 22% (1 each). All patients had macro- or microscopically abnormal cystic ducts (five fibrotic, seven elongated and narrow, and two kinked); 12 had concomitant chronic cholecystitis, two had normal gallbladders (Table 1). No patient with a partially occluded cystic duct, with or without a concomitant chronic cholecystitis, had an EF that exceeded 22%. Normal maximal GBEF response to CCK was ≥ 35% (Figs. 1 and 2). Postoperatively all patients were clinically improved (i.e., without postprandial right upper quadrant pain and/or biliary colic. Duration of follow-up was 1.5 yr).

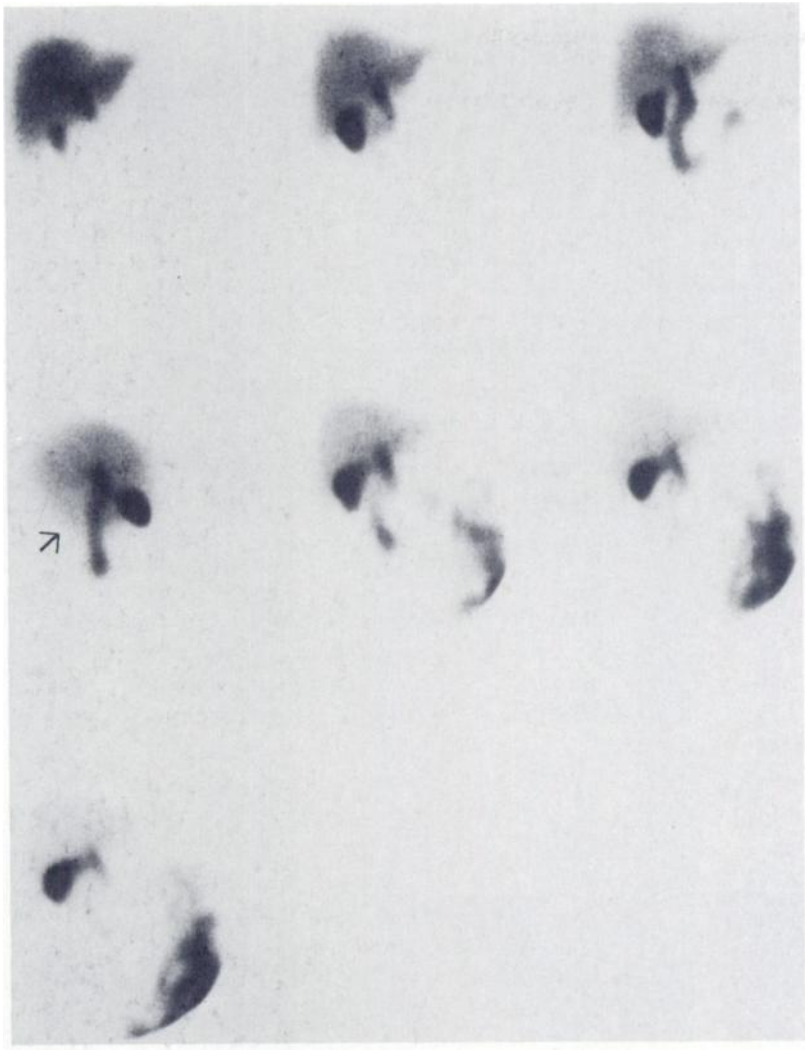


FIGURE 1A
Normal hepatobiliary scan in patient suspected of, but later not found to have, acalculous biliary disease. 500k anterior and lateral (arrow) images obtained every 10 min for 1 hr

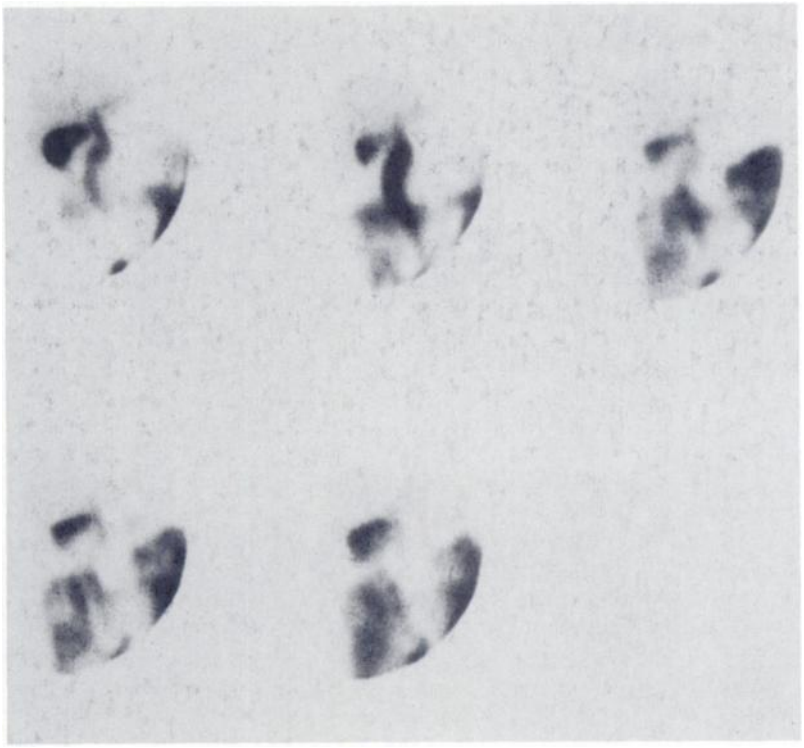


FIGURE 1B
Normal CCK Functional cholescintiscan. Pre-CCK and every 5 min post-CCK (set time not counts) anterior hepatobiliary scans X4. Note obvious decrease in amount of hepatolite within gallbladder post-CCK

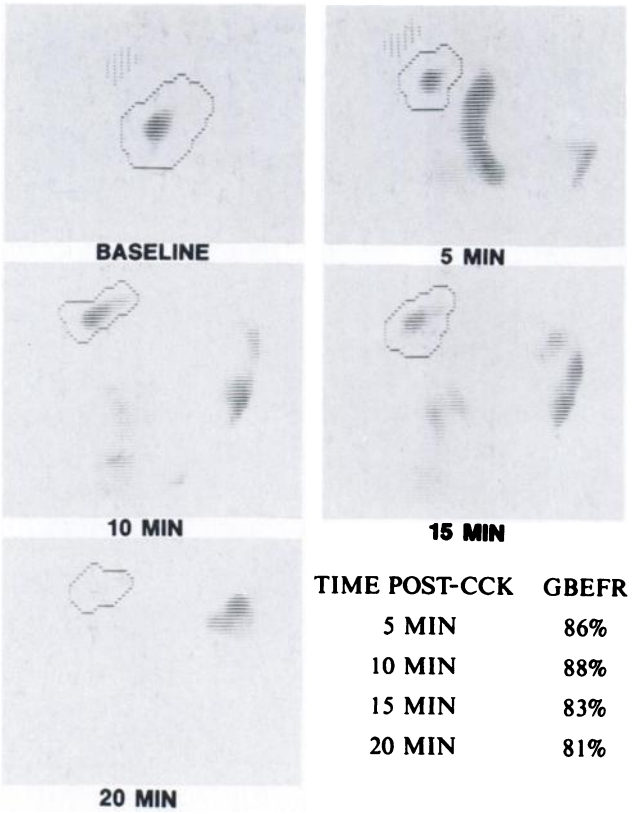


FIGURE 1C
Normal EF response to CCK

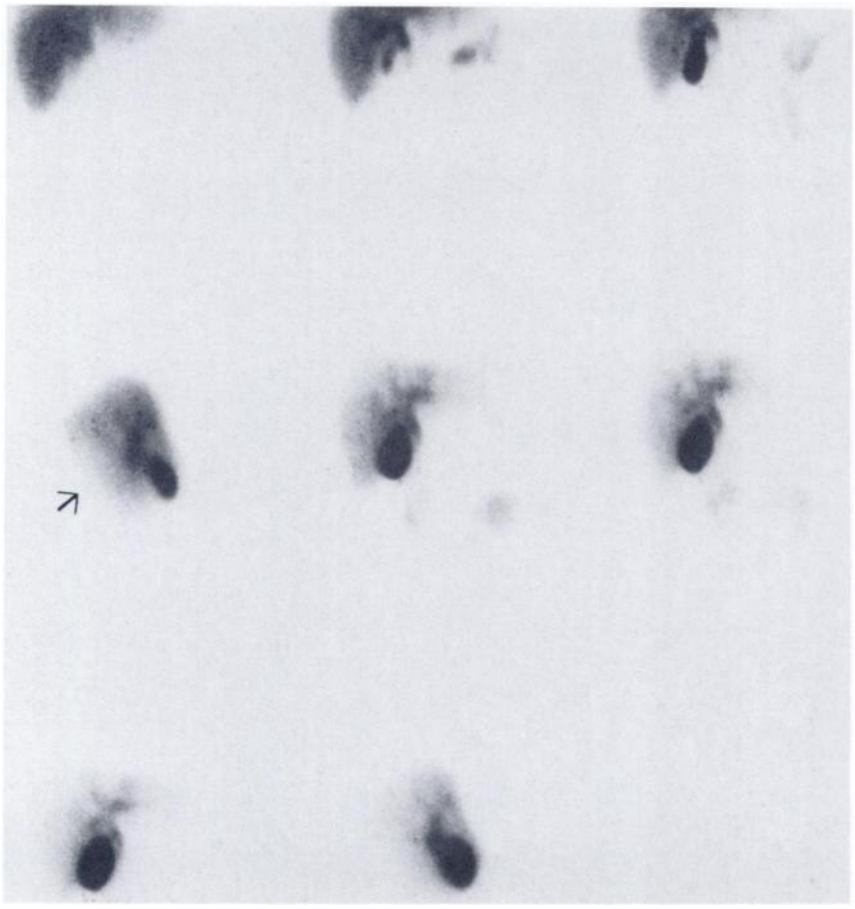


FIGURE 2A
Normal pre-CCK hepatobiliary scan of patient with CDS. 500k anterior and lateral (arrow) images obtained every 10 min for 1 hr

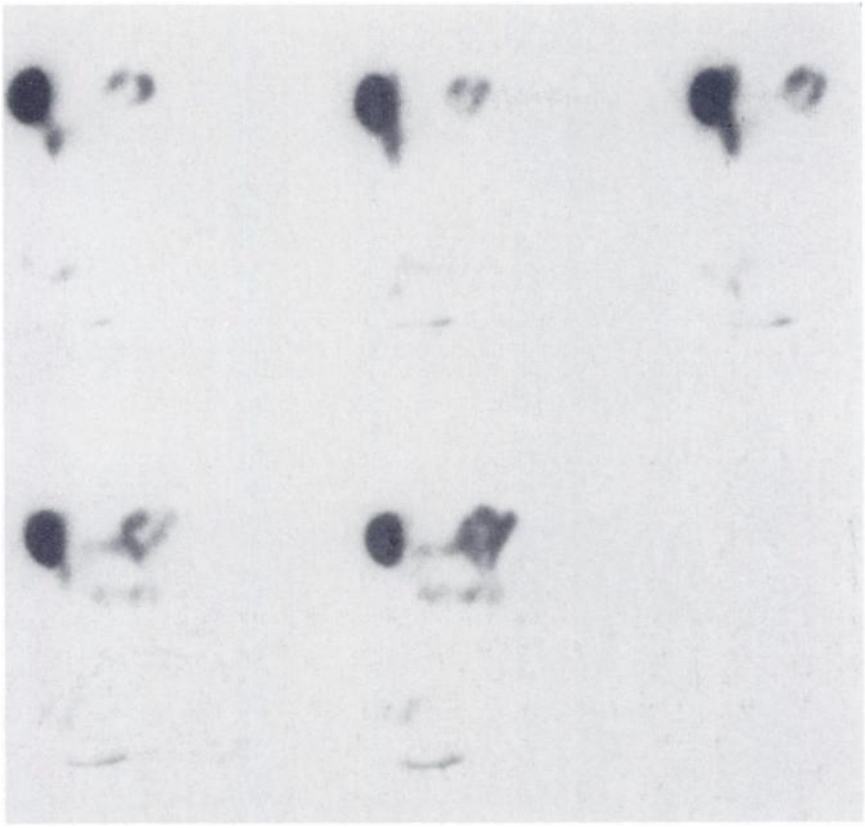
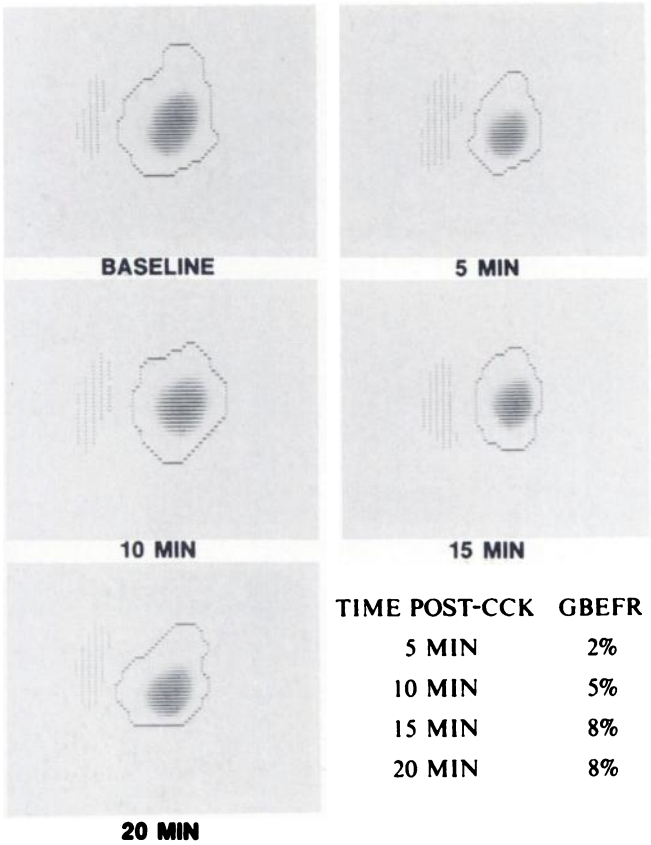


FIGURE 2B
Abnormal CCK functional cholescintiscan. Pre-CCK and every 5 min post-CCK (set time not counts) anterior hepatobiliary scans ×4. There is no visual evidence to suggest that the gallbladder has ejected >35% of its contents



TIME POST-CCK	GBEFR
5 MIN	2%
10 MIN	5%
15 MIN	8%
20 MIN	8%

FIGURE 2C
Abnormal EF response to CCK. Gallbladder has failed to eject ≥35% of its contents following the i.v. injection of CCK

DISCUSSION

The cystic duct syndrome (recurrent right upper quadrant pain and biliary colic) results from a partial noncalculous obstruction of the cystic duct. It often goes undiagnosed, as oral cholecystograms and biliary sonograms are normal. Cholesonography evaluates gallbladder morphology, oral cholecystograms morphology, and the gallbladder's ability to concentrate bile, but neither evaluates gallbladder emptying—the impairment of which represents the pathophysiology of CDS. Because surgeons are reluctant to operate on "normal functioning and morphologic gallbladders," CDS patients are forced to endure chronic pain.

In an appropriate clinical (recurrent postprandial epigastric pain and biliary colic) and laboratory (normal oral cholecystograms, upper GI, gallbladder ultrasound) setting, a low (≤ 35%) MGBEFR to CCK should alert the physician to the presence of CDS with or without an associated chronic acalculous cholecystitis.

FOOTNOTE

* MDS A^2, Medtronic/MDS, Ann Arbor, MI.

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