Sonographic Evaluation of Resting Gallbladder Volume and Postprandial Emptying in Patients with Gallstones

Soad M. A. Kishk[1]
Reda M. A. Darweesh[1]
Wylie J. Dodds[2]
Thomas L. Lawson[2]
Edward T. Stewart[2]
Mark K. Kern[2]
Effat H. Hassanein[1]

We investigated fasting gallbladder volume and gallbladder emptying in response to a fatty meal in 20 patients with asymptomatic gallstones and compared the results with findings from healthy controls. Compared with control subjects without gallstones, the majority of patients with gallstones exhibited a higher resting gallbladder volume, less fractional emptying after a fatty meal, and a higher postmeal residual volume. These abnormalities all appeared to stem from an abnormally high resting gallbladder volume. Whether the increased gallbladder volume and decreased postprandial fractional emptying in the gallstone patients represents a primary or secondary abnormality remains to be determined.

The results suggest that in some patients decreased gallbladder contractility may contribute to gallstone development or proliferation.

Although gallstones are common in adults, the factors that contribute to their pathophysiology remain incompletely understood. Findings from previous studies, particularly recent studies using hepatobiliary scintigraphy, suggest that abnormal gallbladder motor function may contribute to the development of gallstones in some patients with cholelithiasis [1–7]. Results from recent studies validate the utility of sonography for measuring gallbladder volume [8–10]. In this study we used sonography to evaluate fasting gallbladder volume and gallbladder emptying in response to a fatty meal in patients with gallstones and compared the results with those obtained from normal subjects.

Subjects and Methods

During a 1-year period from August 1985 through July 1986 we determined fasting gallbladder volume and volume changes in response to a fatty meal in 40 consenting adult subjects. Twenty of the subjects were healthy asymptomatic volunteers: 11 men and nine women with a mean age of 45 ± 8 years (range, 24–66). The other subjects were random patients with one or several gallstones that occupied less than 25% of the gallbladder lumen. This group consisted of 11 men and nine women with a mean age of 45 ± 8 years (range, 18–69). Thus, the control and patient groups were comparable in age and gender distribution. Of the 20 patients with cholelithiasis, 15 were without any symptoms suggestive of biliary disease. Their gallstones were discovered incidentally during abdominal sonography or CT done for reasons unrelated to suspected biliary tract disease. The other five patients with gallstones were examined for symptoms, such as epigastric fullness, abdominal bloating, or fatty-food intolerance, considered by their referring physicians to be suggestive of gallstones. None of these patients had symptoms suggestive of biliary colic. The patients were without a history of diabetes, vagotomy, or other conditions believed to be associated with abnormal gallbladder emptying. In all cses the common duct appeared normal on sonography.

Each subject fasted a minimum of 4 hr before the sonographic examination. For sonography we used a real-time sonographic unit with a 3.5- and 5.0-MHz transducer (GE/RT 3600 General Electric Medical Systems, Waukesha, WI). We obtained multiple longitudinal and transverse images of the gallbladder immediately before the subject ingested a fatty meal and at 5, 15, 30, 45, and 60 min after the meal. The fatty meal consisted of Lipomul (Mead

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[1] Department of Radiology, Alexandria University, Alexandria, Egypt.

[2] Department of Radiology, Medical College of Wisconsin, Milwaukee County Medical Complex, 8700 W. Wisconsin Ave., Milwaukee, WI 53226. Address reprint requests to W. J. Dodds.

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Johnson Laboratories, Evansville, IN) given in a volume of 0.7 ml/kg, followed by 100 ml of water.

As described previously [10], we measured gallbladder volume by the ellipsoid method wherein volume = 0.52 (W × H × L), where W = gallbladder width, H = height, and L = axial length. Measurement of gallbladder length was made from longitudinal sections through the long axis of the gallbladder, while width and height were measured from transverse sections through the middle of the gallbladder. All measurements were made in duplicate, and the averaged values were used in the calculation. Changes in gallbladder volume after the fatty meal were analyzed as changes in absolute volume and also as percentage changes by using the premeal value as the index value. Fractional gallbladder emptying was then calculated by dividing the minimal postprandial volume by the initial preprandial volume × 100. For statistical analysis the data were evaluated by an analysis of variance and by the Student's paired or unpaired t test.

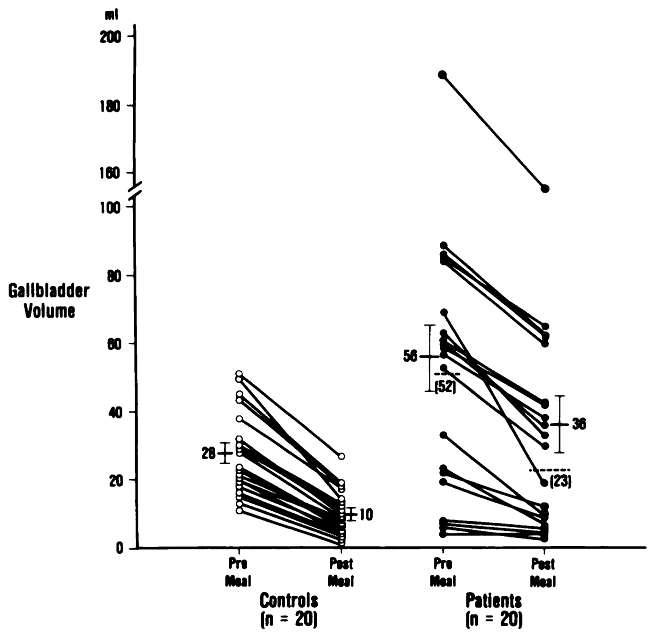


Fig. 1.—Gallbladder volume before and 60 min after a fatty meal in 20 control subjects and 20 patients with gallstones. Mean values ± 1 SE are shown for pre- and postmeal values of gallbladder volume. *Short broken lines* and underlying numbers in parenthesis on right represent index values of x̄ ± 2 SD for normal. Inspection indicates that 12 of 20 patients with gallstones had an initial gallbladder volume above the normal range. Eleven of the patients exhibited a residual postprandial volume above the normal range.

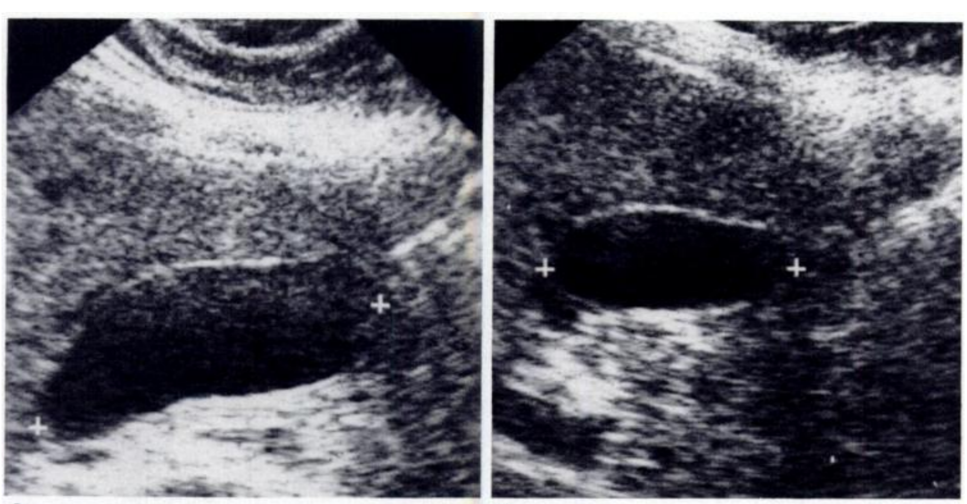
Results

Control Subjects

As a group, the 20 normal control subjects exhibited a fasting gallbladder volume of 28 ± 12 ml (range, 11–51 ml). Minimal residual gallbladder volume 60 min after the meal was 1–27 ml (Fig. 1). After ingestion of Lipomul, the gallbladder volume decreased significantly by 15 min, and the emptying became maximal at 45 or 60 min after the meal (Figs. 2 and 3). In the 20 control subjects, maximal gallbladder emptying occurred at 45 or 60 min. In 12 subjects, the fractional gallbladder emptying was greater at 60 min than at 45 min. For the other eight subjects, gallbladder emptying in six was the same at 60 min as at 45 min. In two subjects, both with a small residual volume of 3 or 4 ml, gallbladder emptying was maximal at 45 min. At 60 min, mean gallbladder emptying was 67 ± 3% (range, 47–91% ml) (Fig. 4). By 60 min after the fatty meal the absolute value for the decreases in gallbladder volume averaged 18 ± 7 ml (range 9–27 ml). During the 60 min after the meal, gallbladder emptying appeared nearly linear (Fig. 3) and had a slope of −0.3 ± 0.1 ml/min. None of the measured variables of gallbladder volume or emptying rate showed any correlation with the age or gender of the subjects.

Patients

An initial analysis revealed that the five gallstone patients with nonspecific symptoms suggestive of gallstones and 15



A B

Fig. 2.—Example of gallbladder emptying in response to a fatty meal in healthy control subject. Longitudinal sonograms of gallbladder before (*A*) and 60 min after (*B*) fatty meal. Gallbladder length indicated by electronic calipers. After the meal, the gallbladder exhibited a substantial decrease in volume.

patients without symptoms of cholelithiasis did not differ significantly with respect to gender, age, initial gallbladder volume, or fractional gallbladder emptying. Consequently, these subgroups of patients with cholelithiasis were analyzed as one group.

As a population, the 20 patients with cholelithiasis had a mean fasting gallbladder volume of 56 ± 10 ml (range, 4–189 ml) (Fig. 1). The fasting gallbladder volume in the patients was significantly greater than in controls ($p < .05$). Ten of the patients had a fasting gallbladder volume greater than 2 SD above the mean of normal (Fig. 1). In response to the fatty meal, the magnitude of absolute gallbladder emptying during a 60-min interval, 18 ± 11 ml, was comparable to that of control subjects, 18 ± 7 ml. Gallbladder emptying was maximal at 60 min. The rate of gallbladder emptying during the first 60 min after the Lipomul meal, −0.3 ± 0.2 ml/min, was virtually identical to that of the control subjects, −0.29 ± 0.1 ml/min. Compared with the control subjects, however, the patients exhibited a significantly lower fractional emptying (Fig. 4) and greater residual volume (Figs. 1 and 5). As shown in Figure 4, fractional emptying in the patients at 60 min averaged 36% in the patients, compared with 67% in the control subjects ($p < .05$). Fourteen of the patients exhibited feeble postprandial gallbladder emptying of <44%, which was below the range of normal. Residual gallbladder volume in the patient group was significantly greater than that of the control group ($p < .05$). Eleven patients had residual postprandial gallbladder volumes above the range of normal (Fig. 1).

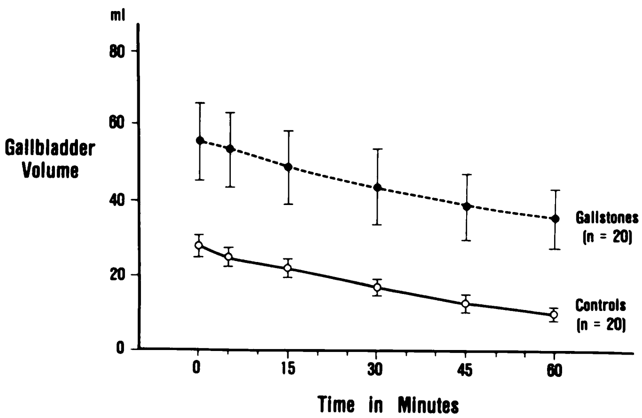


Fig. 3.—Pooled data for gallbladder volume during 60-min interval after fatty meal in 20 control subjects and 20 patients with gallstones. Data plotted as $\bar{x} \pm 1$ SE. For each time period, the patient population exhibited a significantly greater gallbladder volume than the control subjects ($P < .01$).

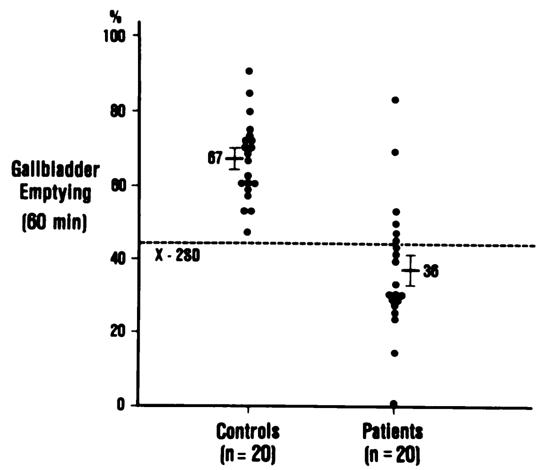
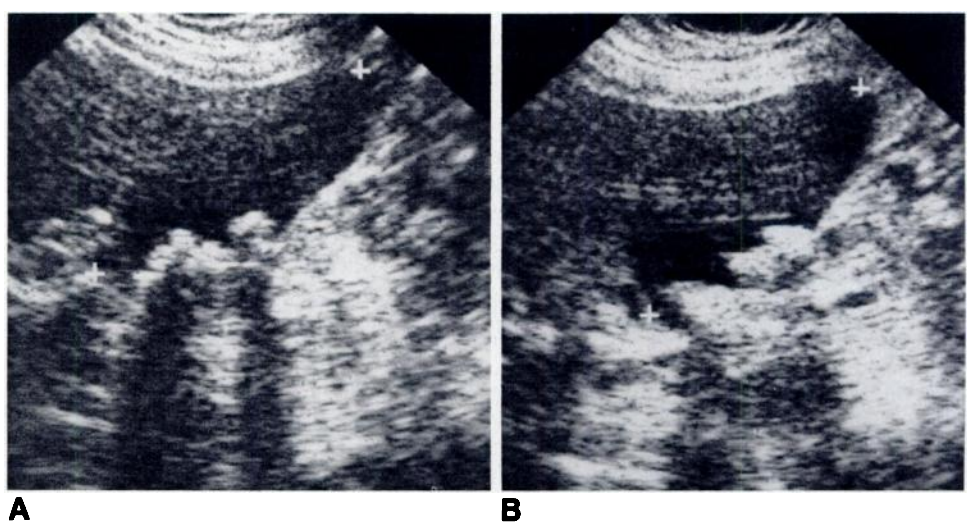


Fig. 4.—Fractional gallbladder emptying 60 min after a fatty meal in 20 healthy controls and 20 patients with gallstones. Averaged values given as $\bar{x} \pm 1$ SE. *Broken line* indicates index of $\bar{x} \pm 2$ SD for normal. Fourteen of the patients exhibited fractional gallbladder emptying that was below the normal range.



A B

Fig. 5.—Example of gallbladder emptying in response to a fatty meal in patient with asymptomatic gallstones. Gallstones are seen as multiple echogenic foci with posterior shadowing. Longitudinal sonograms of gallbladder before (*A*) and 60 min after (*B*) fatty meal. Some reverberation artifact is present. Gallbladder length indicated by electronic calipers. After the meal, the gallbladder exhibited only a minimal decrease in volume.

Discussion

Our aim in this study was to determine gallbladder volume during fasting and in response to a fatty meal in patients with uncomplicated gallstones and compare the results with those obtained from healthy control volunteers. The major study findings were that the gallbladder in a substantial subset of patients with gallstones exhibited (1) increased fasting volume, (2) decreased fractional emptying in response to a fatty meal, and (3) increased postprandial residual volume.

Three general methods are available for quantitating gallbladder emptying in humans: cholecystography [11, 12], cholecystoscintigraphy [2, 13], and cholecystosonography [8–10]. We elected cholecystosonography because this method is simple to use and does not require any radiation. Accurate approximations of gallbladder volume are derived from the sonographic images using either the ellipsoid or sum-of-cylinders method for calculation [8, 10]. Two important advantages of the sonographic method over scintigraphy are that sonography (1) accurately discriminates the presence or absence of gallstones and (2) determines fasting and residual postprandial gallbladder volume as well as fractional gallbladder emptying. Although scintigraphy yields superb curves for gallbladder emptying, this method does not provide any information about gallbladder volume.

During the past several decades, concepts about the development of gallstones have emphasized the contribution of "bad" bile that is supersaturated with cholesterol or has an abnormal ratio of cholesterol, bile acids, and phospholipid [14, 15]. Findings from recent studies, however, suggest that abnormal micellar formation, initiated by the presence of nidus material, such as mucus, or gallbladder stasis may contribute to the pathogenesis of gallstones in some patients [16–18]. To test the latter possibility we evaluated fasting gallbladder volume and postprandial gallbladder emptying in patients with uncomplicated cholelithiasis. Most patients in our study had no biliary tract symptoms. None had any evidence of acute cholecystitis, biliary colic, or common-duct stones.

To measure gallbladder emptying, we used a corn-oil fatty meal that has been tested as an effective method for inducing gallbladder emptying [10], The entry of fat into the duodenum and upper small bowel releases cholecystokinin from mucosal cells. Increased circulatory levels of cholecystokinin contract the gallbladder. The recent development of satisfactory immunoassay for cholecystokinin shows that a close correlation exists between the concentration of serum cholecystokinin and gallbladder volume [19–21]. Current evidence suggests that cholecystokinin contracts the gallbladder indirectly by acting on cholinergic excitatory nerves, but may also have a direct effect on gallbladder smooth muscle [22–25]. In addition, part of the immediate gallbladder contraction that occurs within a few minutes after the ingestion of a meal may be effected by neural reflexes independent of circulating cholecystokinin.

Compared with the control group, the patient group with gallstones exhibited greater resting gallbladder volume, less fractional emptying, and greater residual volume after a fatty meal. These findings all appear to stem from the larger initial gallbladder in the patients because the magnitudes of absolute gallbladder emptying and gallbladder emptying rates were comparable in patient and control groups. The larger initial gallbladder volume in the patients, therefore, accounts for the larger residual gallbladder volume and smaller degree of fractional emptying. The overall findings were similar in patients with the incidental finding of cholelithiasis compared with patients examined for nonspecific symptoms, judged by their clinicians to be suggestive of cholelithiasis. Nonspecific symptoms such as flatulence, bloating, and fatty-food intolerance, however, do not correlate with the presence or absence of gallstones.

Although our results indicate that a substantial subgroup of patients with uncomplicated gallstones has increased basal gallbladder volume and diminished postprandial gallbladder emptying, two important questions are not answered by the design of our study. First, the precise pathophysiology responsible for the abnormal gallbladder emptying shown in some patients was not established. In theory, diminished postprandial gallbladder emptying might be caused by (1) delayed gastric emptying, (2) impaired elaboration or release of cholecystokinin by intestinal mucosa, (3) impaired gallbladder innervation, (4) abnormal gallbladder smooth muscle, or (5) fibrosis of the gallbladder wall [26, 27]. The impaired postprandial gallbladder emptying that occurs in some patients with cholelithiasis may have a heterogeneous pathogenesis. Satisfactory clarification awaits further testing incorporating assessment of gastric emptying, circulating levels of cholecystokinin, and the effects of endogenous cholecystokinin.

A second critical unanswered question is whether the abnormal gallbladder emptying in some patients with cholelithiasis predates the gallstones and contributes to their development or is secondary to the presence of gallstones and possible inflammatory changes in the gallbladder. Several studies in animal models of gallstones, however, suggest that animals fed a lithogenic diet develop abnormal gallbladder motility before the development of gallstones [28–31]. The possibilities of a primary or secondary abnormality in gallbladder motor function are not mutually exclusive. Resolution of this issue, however, will depend on comprehensive longitudinal studies that evaluate patients with gallbladder sludge without stones and incorporate correlation of preoperative assessment of gallbladder contractility with the histologic findings from operative specimens.

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