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EFFECTS OF CHOLECYSTECTOMY ON GASTRIC EMPTYING AND MYOELECTRICAL ACTIVITY IN MAN

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ABSTRACT

To investigate the effects of cholecystectomy on gastric motor function, 13 patients with symptomatic gallstones were studied before and 8–12 months after surgery. Twelve healthy subjects entered the study as control group. The cutaneous electrogastrography and ultrasound examination of gastric emptying were simultaneously performed at pre- and post-prandial states. The dominant gastric frequency and its coefficient of variation were not affected by surgery. After cholecystectomy, an increase in normal 3 cpm wave percentage and a decrease in power ratio were found ($P < 0.05$ and $P < 0.01$, respectively). Gastric emptying recorded after cholecystectomy was faster than before surgery (306.9 ± 15.9 min vs *336.9 ± 11.8 min, respectively; $P < 0.05$). Such changes were associated with the relief of symptoms, and the comparison between patients and controls showed a normalization of the gastric electrical activity and gastric emptying after surgery. In conclusion, in symptomatic patients, gallstones are associated with motor disfunctions, and cholecystectomy seems to induce a normalization of gastrointestinal motility.*

KEYWORDS: *Cholecystectomy, electrogastrography, gastric emptying, myoelectrical activity, ultrasound.*

INTRODUCTION

Cholecystectomy is an accepted surgical procedure for the complications of gallstones and biliary pain. Biliary pain is presumed to result from mechanical, inflammatory or chemical irritation of the gallbladder, but the basis for the other symptoms associated with gallstones remains incompletely understood (Johnson, 1971; Bouchier, 1983). Therefore, it is important to understand what symptoms are likely related to the presence of gallbladder disease and what effect cholecystectomy has on those symptoms. In gallstone patients with abdominal complaints, one of the key factors in clinical decision making is the recognition of symptoms caused by gallstone disease. However, these symptoms are so common in the general population that they might as well be "noise" when coinciding with the presence of gallstones (Diehl, 1992). Even though this relation has been disputed, cholecystectomy is frequently performed for dyspepsia only (Gilliland & Traverso, 1990).

The dyspeptic symptoms in lithiasic patients may be caused by concomitant alterations in the upper gastrointestinal tract. A delayed gastric emptying (GE) and an altered gastric electrical activity measured by electrogastrography (EGG), can be found in dyspeptic patients (Rothstein *et al*., 1993). Normal and altered myoelectrical activity can be recorded noninvasively by cutaneous electrodes (Abell & Malagelada, 1988; Geldof & Van der Schee, 1989), and cutaneous electrical activity has been shown to correlate with the signal derived from serosal electrodes (Familoni *et al*., 1991). The development of automated signal analysis (Fourier transform) has greatly expanded the possibilities of analysis and interpretation of cutaneous electrogastrography (Chen & McCallum, 1993). Gastric emptying is usually assessed by scintigraphy. However,

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ultrasonology has been recently introduced as an alternative noninvasive technique (Bolondi *et al.*, 1989) and may be particularly suitable for patients. Therefore, the aim of our study was to investigate and compare the gastric emptying time and the pattern of the electrogastrogram recorded noninvasively from abdominal surface before and after cholecystectomy.

MATERIALS AND METHODS

Patients. Thirteen patients (5 males and 8 females; mean age 44 years, range 22–66 years) with symptomatic gallstones and 12 healthy volunteers (5 males and 7 females, mean age 40 years, range 26–60 years) entered the study. It was approved by the Ethical Committee. Subjects provided a written informed consent before the start of the study. All patients showed gallstones at abdominal ultrasound and a normal liver function. No subject had history of neurologic, metabolic or systemic diseases. Data collection consisted of physician-derived data gathered at the preoperative, intraoperative, and follow-up sessions. Physicians were asked data regarding preoperative symptoms, indication for surgery, details of the operation, and postoperative symptoms at follow-up. Major pre-operative symptoms were: 1) biliary colic pain, and 2) non-pain symptoms (abdominal discomfort, vomiting, excessive gas, inability to tolerate fatty foods). According to the medical records, all patients were symptom-free after cholecystectomy.

Experimental design. Patients were studied before and 8–12 months after traditional opening cholecystectomy. In patients and controls, all the examinations were made in the morning and patients were fasting for 12 h. The EGG recording times were usually 35 min and 360 min in pre- and postprandial states, respectively. The gastric emptying time was assessed in each patient by means of ultrasound examination. Simultaneously, the gastric emptying and electrical activity were recorded in 8 of 13 patients. A standard solid-liquid meal (513.1 cal; 63% carbohydrate, 23% protein, and 14% fat) including bread (100 g), butter (10 g), meat (100 g), an apple (150 g), and water (300 ml) was eaten by each patient in a normal sitting position.

EGG procedure. The stomach cutaneous projection was identified and drawn on the abdominal cutaneous surface under fluoroscopy after ingestion of radiopaque meal (Gastrografin *Schering*) the day before the examination. The map of the stomach and the costal arch of each patient were reproduced on a sheet of tissue-paper placed on the abdominal surface. By means of these sheets, the electrodes were located in the same position also after surgery. Cutaneous electrodes of the same type as used in electrocardiography were utilized (Red Dot 2249 *3M*, St.Paul, Minnesota). The location of the electrodes on the cutaneous surface, previously scrubbed by diethyl ether, is shown in Figure 1. The electrical activity was bipolarly recorded by means of the couples 1–4, 2–5, 3–6 (Mirizzi & Scafoglieri, 1983). The EGG signal was amplified by means of differential amplifiers (8811A Bioelectric Amplifier, *Hewlett Packard*), filtered and recorded on a paper chart (Reega Minhuit-TR, *Alvar*), and stored on a computer disk for a further analysis. Currently, a Vectra RS20 *Hewlett Packard* computer together with a 3852A Analogic–Digital Converter *Hewlett Packard* is used. Since the most significant EGG frequencies range from 0.6 to 15 cpm, a high- and low-pass filtering procedure was performed to eliminate cardiac and respiratory signals. This procedure cannot completely remove the respiratory signal, and a pneumogram was simultaneously recorded to distinguish between respiratory and pathological EGG signals. The frequency analysis of EGG recordings was performed by means of Running Spectra. The running spectral analysis (Van der Schee *et al.*, 1982) consists of power spectra calculated from successive partially overlapping data windows displayed as a function of time and it allows to perform both frequency and time analysis. The following para-

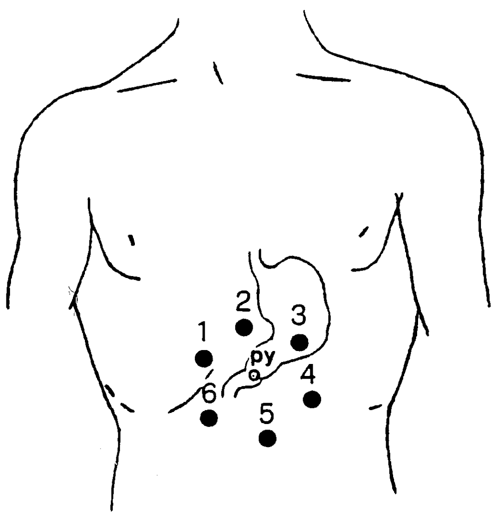

Fig. 1. SCHEMATIC REPRESENTATION OF THE LOCATION OF THE ELECTRODES ON THE ABDOMINAL SURFACE. The electrodes were circumferentially positioned around the cutaneous projection of the pylorus (py) as follow: bipolar distance 14 cm around the py a 0° (couple 3–6), 60° (couple 2–5) and 120° (couple 1–4). The couple 3–6 coincides with the antral axis.

meters were evaluated for each patient: a) mean dominant frequency (DF): the frequency of the gastric peak was determined by the absolute peak value, and the mean frequency was computed by averaging the individual spectra; b) coefficient of variation (CV): it was introduced to specify the stability of the gastric electrical peak visible on the running spectra plot and was calculated as the percentage ratio of the frequency standard deviation to mean gastric frequency. While the percentage of normal slow waves specifies the normality of gastric electrical activity, the CV of the dominant frequency reflects subtle changes in the gastric slow waves; c) the percentage of normal slow waves (SW): it is defined as the percentage of time when a normal slow wave activity is observed during the EGG. The percentage of normal slow waves was determined by computing the percentage ratio between the number of normal spectra and total spectra. This parameter is a quantitative assessment of the regularity of gastric slow waves; d) power ratio (PR): it represents the changes in EGG power at a certain frequency at baseline and post-stimulus period and was calculated as the ratio between the EGG power at baseline and 30 min after the meal.

A rhythmic electrical activity ranging from 2.0 to 4.0 cpm was defined as normal gastric electrical activity. Tachygastria was considered to be present when the running spectrum had a dominant peak in the 4.0–9.0 cpm range, and bradygastria when the dominant peak was in the 0.5–2.0 cpm range (Chen & McCallum, 1993). A dysrhythmic episode had to be present at least for 2 minutes with absence of the normal gastric signal. As the signal/noise ratio of postprandial recordings was better than the preprandial ones, EGG parameters were calculated from postprandial EGGs only. The portions of EGG signal corresponding to ultrasound examinations were excluded from the analysis. Electrogastrograms were read in a blinded fashion, without knowledge of whether the tracing represented a baseline or follow-up study.

Gastric emptying study. The ultrasound examination of gastric emptying was performed by using a real-time apparatus (Sigma 20 – *Kontron Instrument*) equipped with a 3.5 MHz linear probe. The probe was positioned at the level of transpyloric plane to simultaneously visualize antrum, superior mesenteric vein, and aorta. The measurements of the antrum were always taken from the outer profile of the wall. The cross section of the gastric antrum, corresponding to the sagittal plane passing through the superior mesenteric vein, presents an elliptical shape. Its area can be calculated by measuring the longitudinal (L) and anteroposterior (AP) diameters and by using $\pi L \times AP/4$ formula (Bolondi *et al.*, 1985). Sonography was always performed by the same investigator, and the antrum areas were taken before (fasting area = FA) and 30 min after the start of meal, and subsequently at regular 30-min intervals for 360 min. The emptying curve was established by plotting the cross sectional area of the gastric antrum against time. In each patient, the emptying time (in minutes) was expressed as half emptying time (t½) corresponding to the time in which the cross-sectional area of the antrum had an intermediate value respect to the basal and the maximum values recorded after meal. t½ was calculated from the linear part of the emptying curve by using the linear regression analysis (Bolondi *et al.*, 1989), and the final time (FT) as corresponding to the time in which the cross sectional area of the antrum achieved the basal value.

Statistical analysis. Data were expressed as mean ± SD. Statistical analysis was performed by using a paired and unpaired non parametric test when appropriate. A P value less than 0.05 was considered to be statistically significant.

RESULTS

The gastric emptying parameters before and after cholecystectomy are shown in Table 1. The mean final times recorded before and after cholecystectomy were statistically different ($P < 0.05$). The final time recorded from patients was not different from that from controls. Gastric emptying time expressed as t½ was faster after surgery, but without a statistically significant difference. In the control group, t½ was 147.4 ± 10.9 min (control group value *vs* patient pre-operative value, P = NS; control group *vs* patient postoperative value, P = NS). Figure 2 shows the gastric emptying expressed as final time recorded from each patient

Table 1. Gastric emptying parameters recorded from patients (n = 13) and controls (n = 12).

	Controls	Before cholecystectomy	After cholecystectomy
t½ (min)	147.4 ± 10.9	172.0 ± 21.0	143.0 ± 8.5.
FT (min)	310.0 ± 13.9	336.9 ± 11.8	306.9 ± 15.9 [b]
FA (cm^2)	5.5 ± 0.4	5.4 ± 0.3	6.2 ± 0.6

t½: half emptying time; FT: final emptying time; FA: fasting area of the antrum.
[b] difference before and after cholecystectomy ($P < 0.05$).

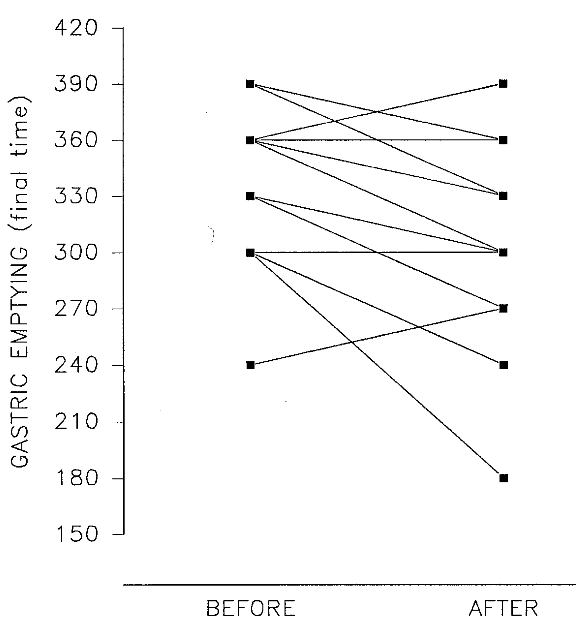

Fig. 2. Gastric emptying time, expressed as final time, recorded from each patient before and after cholecystectomy. After surgery, 9 of 13 patients show a decrease and 4 an increase in the emptying time.

before and after surgery. In 9 of 13 patients the gastric emptying was faster after cholecystectomy than before surgery. Figure 3 shows the mean gastric emptying profiles before and after cholecystectomy. Gastric emptying curves, expressed as area ratio from 0 to 360 min after the meal, showed similar profiles before and after cholecystectomy. Table 2 shows the EGG parameters recorded from patients and controls. No patient had clear episodes of gastric dysrhythmias before or after surgery. The dominant gastric frequency and instability coefficient of gastric frequency were not affected by cholecystectomy. An increase in 3 cpm wave percentage and a significant decrease in power ratio were found after surgery. Figure 4 shows the power ratio recorded from each patient before and after surgery. In all patients the power ratio was lower after cholecystectomy than before surgery. The comparison between patients and controls showed that 3cpm wave percentage from controls was higher than that from preoperative patients ($P < 0.05$), and power ratio from controls was statistically lower than that from preoperative patients ($P < 0.01$). As against, the EGG parameters recorded after cholecystectomy were similar to those obtained from controls (Table 2).

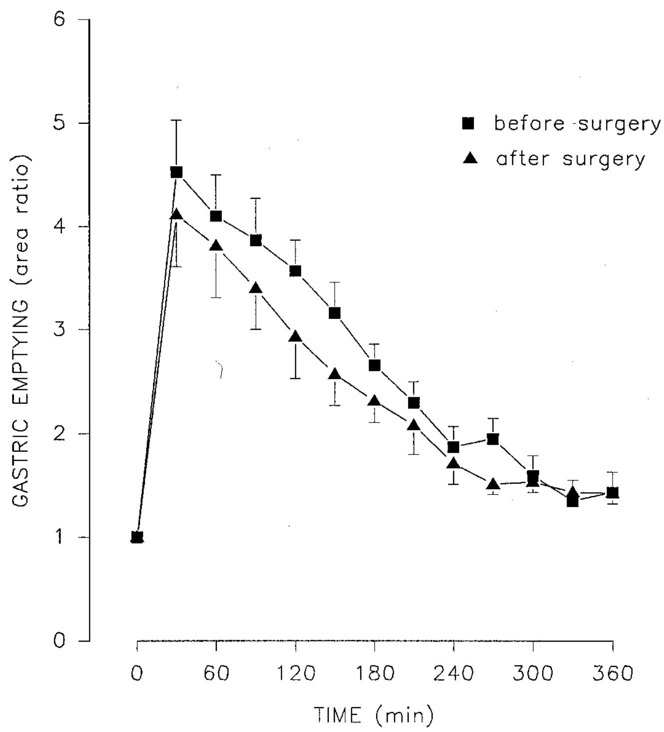

Fig. 3. Degree of dilatation of the gastric antrum obtained from 13 patients and expressed as ratio between values at different postprandial times and basal value (area ratio). Pre- and postcholecystectomy curves have similar profiles.

Table 2. EGG parameters recorded from patients ($n = 8$) and controls ($n = 12$)

	Controls	Before cholecystectomy	After cholecystectomy
SW (%)	79.9 ± 11.6	63.7 ± 12.7 [a]	76.0 ± 14.2 [b]
DF (cpm)	3.2 ± 0.3	3.0 ± 0.3	3.0 ± 0.5
CV (%)	30.0 ± 9.6	44.1 ± 14.5	39.3 ± 15.3
PR	1.9 ± 0.9	4.0 ± 2.7 [a]	1.4 ± 0.9 [b]

SW: 3 cpm wave percentage; DF: dominant frequency; CV: coefficient of variation; PR: power ratio.
[a] Difference between controls and patients before cholecystectomy.
[b] Difference before and after cholecystectomy; (for SW: $P < 0.05$, for PR: $P < 0.01$).

DISCUSSION

The gastric emptying after cholecystectomy was faster than before surgery when calculated as final time, and the mean post-operative values were similar to those recorded from controls. In addition, an increase in 3 cpm percentage and a decrease in power ratio were present after surgery. Such changes were associated with the disappearance of gastrointestinal symptoms.

The relationship between chronic gallbladder disease and a variety of less specific symptoms (dyspepsia, flatulence, gassiness, indigestion, postprandial bloating) and the effect of cholecystectomy on these symptoms is controversial. Nonpain symptoms or dyspepsia are common in patients with and without gallstones. For example, a prospective study (Price, 1963) on 142 women with an age range from 50 to 70 years, has found the incidence of dyspepsia (defined as various combinations of pyrosis, flatulence, fatty-food intolerance, nausea, and abdominal discomfort) to be approximately 50% in women with and without gallstones and has concluded that "the evidence indicates that the association of dyspepsia and gallstones is purely fortuitous". Others (Rhind & Watson, 1968; Johnson, 1971; Bates *et al*., 1991) have reported that gallstones are not only frequently associated with dyspepsia, but also that these symptoms are often relieved or cured by cholecystectomy. The mechanism whereby the removal of the gallbladder would relieve the flatulent dyspepsia is unclear. A study has shown a relationship between chronic cholecystitis and delayed gastric emptying, but no correlation with symptoms has been found (Watson & Love, 1987). Another study (Kingston & Windsor, 1975) has found no correlation of symptoms with a delayed gastric emptying, but a suggestive relationship with infected bile. In our study,

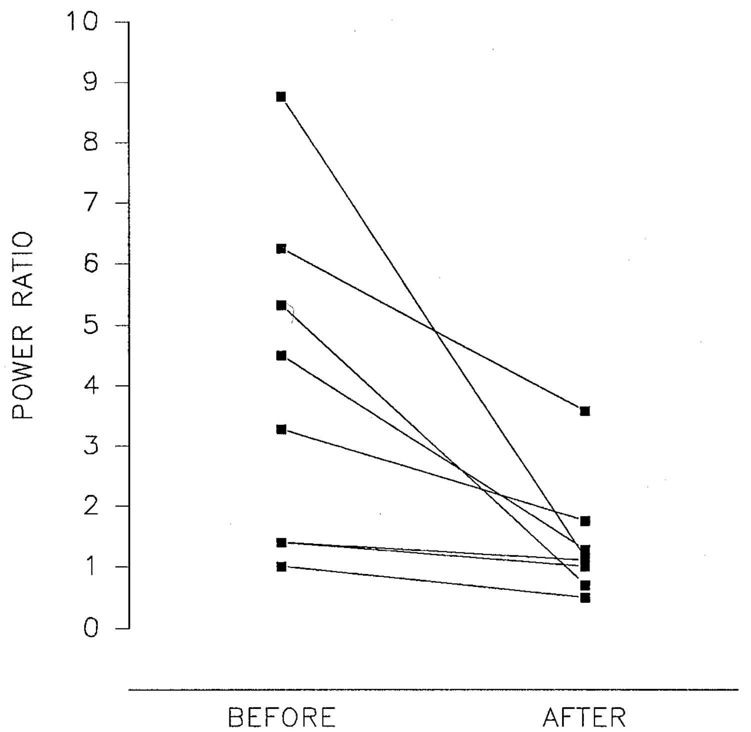

Fig. 4. POWER RATIO OBTAINED FROM EACH PATIENT BEFORE AND AFTER CHOLECYSTECTOMY. All patients ($n = 8$) show a clear reduction in power ratio after surgery.

patients were symptom-free after cholecystectomy, but 4 of 13 showed a gastric emptying time slower than before surgery. This comfirms the absence of correlation between symptoms and gastric emptying. The presence of gallstones or chronic cholecystitis or infected bile may cause an upper gastrointestinal dysmotility through multiple pathways such as the myogenic or hormonal control of the gastric functions. The motor events of the stomach are controlled by the myoelectrical activity (Szurszewski, 1981), called slow waves or electrical control activity (ECA) (Sarna, 1975). Slow waves propagate normally from proximal body to the distal antrum at a frequency of 3 cpm. When motor activity is present, the slow waves are accompanied by a second component referred as spike potential or electrical response activity (ERA) (Sarna, 1975). The cutaneous EGG is believed to detect normal and disturbed gastric slow waves (Smout *et al.*, 1980; Stoddard *et al*., 1981; Abell *et al*., 1985; Hamilton *et al*., 1986; Koch *et al*., 1987; Brujis *et al*., 1991). Our study has found the presence of a reduced 3 cpm percentage and an increased postprandial amplitude before surgery. The simultaneous EGG recording and gastric emptying time enabled us to demonstrate that the presence of such abnormalities in the gastric electrical activity is associated with a delayed gastric emptying time. In addition, the postoperative values of the gastric electrical activity and gastric emptying suggest a normalization of the motor activity in the stomach because, after surgery, the EGG and gastric emptying parameters correspond to those obtained from the control group.

Under normal conditions, food is the main stimulus for gallbladder emptying. Food entering the duodenum triggers the release of cholecystokinin (CCK) from the endocrine I cells in the duodenal mucosa. CCK causes gallbladder contraction, decreases the pressure of the sphincter of Oddi and, at gastric level, causes a delayed emptying (Ryan, 1987). After a solid meal, gallbladder bile is emptied up to 15% before the onset of gastric emptying, and refilling begins after expulsion of about 85% of solid gastric contents (Baxter *et al.*, 1985). The gallbladder emptying and filling are associated with the gastric emptying either in dyspeptic patients or controls (Marzio *et al*., 1996). It is possible to hypothesize that an alteration in one of these two processes can have some effects on the other. In lithiasic patients, alterations in the gallbladder motility have been described. Recently, the role of CCK and gallbladder emptying has been reexamined, and it has been reported that hypomotility may be due to an increased release of CCK (Katoaka & Syoji, 1985; Bailey *et al.*, 1992). This could explain the delayed gastric emptying found in patients with cholelithiasis before surgery.

Data concerning the CCK release and a more precise identification of symptoms are lacking in our study. Previously, other authors have wondered whether the association between dyspeptic symptoms and gallstones is casual or causal (Kraag *et al*., 1995). Further studies are necessary to investigate this matter and to predict who can benefit by the gallbladder removal.

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