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PATIENT SELECTION FOR CHOLECYSTECTOMY
the value of sonography

PATIENTEN SELECTIE VOOR
CHOLECYSTECTOMIE
de waarde van echografie

Proefschrift

Ter verkrijging van de graad van doctor
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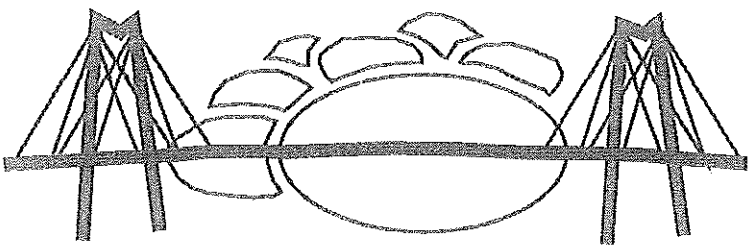
CHAPTER 1

INTRODUCTION



Introduction

In the western world, more than 10 % of adults have gallstones. The incidence is increasing with age in both sexes. Women are affected more commonly than men with nearly 40 % of women in their 9th decade having stones. It is estimated that more than 25 million Americans have gallstones, with 1 million new cases discovered each year [8]. In 10 to 15 % of the gallstones patients, the presence of these stones give rise to symptoms. Without treatment, symptoms will nearly always remain in these patients. Spontaneous passing of the gallbladder stone is seen in less than 5% of the patients [42]. Annually approximately 500,000 to 700,000 cholecystectomies are performed in the United States. The annual cost of caring for patients with gallstone disease is estimated at more than $5 billion [15].

Stages of gallbladder stone disease

Prior to a decision on the appropriate therapeutic approach, the following stages of gallstone disease can be defined [32]:

Asymptomatic gallbladder stones: Lack of symptoms and laboratory findings. Dyspeptic symptoms may be present.

Uncomplicated symptomatic gallbladder stones: acute biliary pain (conventionally misnamed colic) involving one or more episodes of abdominal pain (usually epigastric or right upper quadrant) lasting more than 15 minutes but less than 5 hours (without signs or symptoms of complicated symptomatic disease).

Complicated symptomatic disease: prolonged biliary pain lasting more than 5 hours with or without fewer and/or acute cholecystitis, cholangitis or pancreatitis.

Asymptomatic or silent gallstones appear to carry a low risk of developing symptoms with time [33]. Prophylactic cholecystectomy for silent gallstones was shown to cause a decrease in survival and led to more costs than expectant management. Therefore consensus exists that silent gallstones in patients without co-morbidity, should not be treated [13, 34].

For patients with complicated symptomatic disease there is little doubt that symptoms are caused by gallstones. For the patients with uncomplicated symptomatic gallstones this will be more difficult.

Symptoms and gallbladder stones

The relation between gallstones and symptoms is unclear, only a part of the patients with gallstones will get upper abdominal symptoms. Severe pain in the right upper quadrant (RUQ) of the abdomen, vomiting, RUQ pain provoked by fatty food, fever (≥38° C), and jaundice predict the presence of gallstones on sonography [4]. With the exception of jaundice, however, these symptoms are not specific for gallstones. Therefore the determination whether patient's symptoms are attributable to gallstones can not be based on the selectivity of the abdominal symptoms solely [4]. Thijs et al. described upper abdominal pain as the symptom most closely related to gallstone disease [41]. In our prospective studies on pain relief after cholecystectomy (chapter 5 and 6), relief of upper abdominal pain was used as the sign related to the symptomatology of gallbladder stones. Upper abdominal pain included all reported upper abdominal pain independent of severity and duration, except upper abdominal pain that only occurred after fatty food intake.

Jorgensen found that the predictive value of abdominal pain and discomfort as regards stones in the gallbladder is very poor (0 to 25%) in a random population. In subjects with gallstones, the prevalence of upper right quadrant pain during the last 12 months was equal to that in subjects with a normal gallbladder, whereas in cholecystectomized subjects the prevalence of pain was significantly higher [24].

In contrast to the belief of many clinicians, intolerance to greasy food is of no assistance in distinguishing patients in the gallstone group from those with normal studies [9].

Complaints like non-specific dyspepsia ('flatulent dyspepsia') is less clearly relieved by cholecystectomy. Janzon et al found that current or previous history of epigastric pain and/or heartburn was as common in women with as in women without gallstones. In women with a history of cholecystectomy, dyspeptic symptoms were twice as common as in the two other groups [22]. In a meta-analysis on the recent literature on gallstone disease we found that biliary pain, defined as a steady upper abdominal pain lasting ≥1 hour is a clinical sign consistently and significantly associated with gallstones on sonography [5].

So it is difficult to define the symptoms specific for gallstones and thereby to distinguish between symptomatic and asymptomatic gallstones [24].

Diagnosis of gallbladder stones

Computed tomography, ERCP and MRI have essentially no role as primary imaging modality for the detection of gallstones but have important roles in the evaluation of associated complications like pancreatitis and degree of biliary obstruction. Approximately 15 to 25% of gallstones contain enough calcium to be visible on plain films. Oral cystography was introduced in 1924 and remained the mainstay in radiographic diagnosis gallstone disease for decades. It has largely been replaced by sonography for evaluation of cholelithiasis and its associated complications, most notable acute cholecystitis. Hepatobiliary scintigraphy is also sensitive and specific in diagnosing acute cholecystitis [15].

Sonography is used as a diagnostic tool for detecting gallstones. Beside the presence of gallstones, the sonographic examination gives a wide range of additional information including the gallbladder size and wall thickness, the size of the stones and the presence of echogenic bile or stone impaction.

Therapy

Since 1882, the standard treatment for symptomatic gallbladder stones has been open cholecystectomy which can be done as an elective or an acute procedure. Elective cholecystectomy has a lower mortality rate (0.16% versus 1.8%) and morbidity (2.6% versus 11.2%) compared with acute cholecystectomy [19].

Since the early 1990th, laparoscopic cholecystectomy (LC) is considered to be the standard procedure for symptomatic gallbladder stones [2, 3, 6, 10, 16, 20, 26, 27, 30]. The advantages of LC over OC are reduction of operative trauma and postoperative pain, shorter hospital stay and an earlier return to work [16, 18].

Conversion of LC to OC

Of all LC, 1-17% need to be converted to an open cholecystectomy (OC) [1, 11, 12, 18, 20, 21, 27, 30, 38, 44, 46]. Patients are preoperatively informed that if intraoperative complications, such as uncontrollable bleeding or unclear anatomy, arise, conversion to open surgery will be necessary. It would be helpful to establish criteria that could assess the risk for conversion preoperatively. This would not only be useful for informing the patient, but could also aid in the selection of patients for ambulatory care or short stay. In addition, a more experienced surgical team could be assembled when the risk for conversion appears considerable.

Table 1: Predictive (sonographic) signs for conversion found in literature.

							Stone			Gall-bladder		
	Conv. Rate (%)	Age	♂	Acute chole-cystitis	Thick. Gall-bladder wall *	Comm bile duct diam.	No.	Size ≥20 mm	Im-pac-tion	Con-trac-ted	Dis-ten-ded	Echo-genic bile
Liu [29]	15.8	s	ns	ns	s							
Schrenk [38]	4.3	ns	ns		s (>5.0)					ns	ns	
Urbano [43]	6.0				s (>7.0)							
Velden v.d. [44]	17.2			s	s		ns		s	ns	s	ns
McLoughlin [31]	10.4				ns					ns		
Hutchinson [20]	8.6	ns	s		s	s	ns		ns		ns	ns
Jansen [21]	3.5	s			s (>4.0)	s		s		s		
Alponat [1]	7.4			s	s (≥3.5)	ns	ns	ns				
Fried [12]	5.4	s	s	s	s							

s = significant
ns = not significant
* = in mm

In a retrospective study, chapter 2, we looked for sonographic signs that could predict conversion. In several retro- and prospective studies, sonographic signs like gallbladder distention, stone impaction and thickened gallbladder wall were found to be related to conversion (table 1).

These studies involved both patients with acute and chronic cholecystitis. Including acute cholecystitis is undesirable since conversion rates are higher in this condition [1, 7, 12, 21, 38, 44]. The sonographic signs like thickened gallbladder wall found in these patients will not be independent predictors for conversion but will be linked to acute cholecystitis. Because we were primarily interested in the value of sonography for elective surgery in gallstone patients, we excluded patients with acute cholecystitis in our prospective study (chapter 3). The aim of that prospective study was to determine whether sonography could be helpful in predicting conversion in gallbladder stone patients without clinical signs of acute cholecystitis.

Post cholecystectomy symptoms

It is expected that patients with biliary pain or related symptoms will be relieved of pain after cholecystectomy. However of all patients who had a cholecystectomy, 12 to 47% had no relief of pain during a follow-up period of 24 to 120 months [14, 17, 25, 36, 37, 40, 45]. The outcome of surgery in patients with gallstone disease, without signs of cholestasis and/or cholecystitis is difficult to predict [4, 23, 37]. It seems useful to know in advance which patients are at risk for persistent complaints, so patients can be better informed about the possible outcome. And even more important to select patients who will have a low chance of pain relief after LC, in whom the search for the right diagnosis can then be continued. Sonography allows, in addition to detecting gallstones, assessment of the size of the gallbladder, wall thickness, the size of the stones and presence of echogenic bile or stone impaction. No prospective study has been reported to our knowledge relating sonographic findings of the gallbladder with the outcome of cholecystectomy. In a retrospective study, Gui et al. found thick-walled gallbladder on ultrasound to be associated with pain-free outcome after cholecystectomy [17]. Ros described that multiple stones, and those which were small or of dissimilar size, were associated with biliary pain [35]. In chapter 4 we describe a retrospective study and chapter 5 a prospective study on the relation between preoperative sonographic signs of the gallbladder and relief of upper abdominal pain after laparoscopic cholecystectomy.

In chapter 6 we discuss the benefit of these sonographic signs of the gallbladder for the prediction of clinical outcome after cholecystectomy when preoperative symptoms are taken into account.

Importance of patient selection for cholecystectomy

Since the introduction of the LC, the number of cholecystectomies has increased by 30 to 55 % in a period of 3 to 5 years [28, 39]. Assuming that there is a constant number of patients with symptomatic gallbladder stones in the overall population and an increasing number of cholecystectomies, the absolute number of patients, who will not benefit from cholecystectomy will increase as well. This implies the quest for selection.

Purpose of this thesis

The purpose of this thesis was to demonstrate in patients with gallbladder stones, the value of sonography in predicting conversion of LC to OC and in predicting relief of upper abdominal pain after cholecystectomy.

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CHAPTER 2

CAN SONOGRAPHIC SIGNS PREDICT CONVERSION OF LAPAROSCOPIC TO OPEN CHOLECYSTECTOMY?

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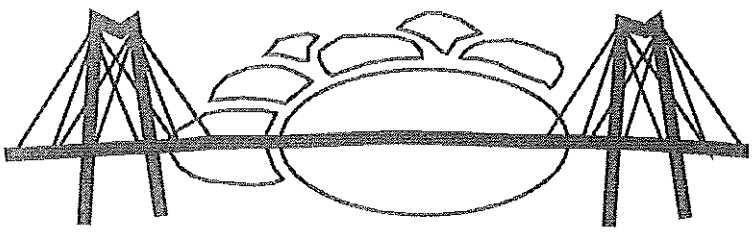

This chapter is adapted from:
Surg Endosc 1998, 12: 1232-1235.

Abstract

BACKGROUND: The aim of this study was determine whether sonographic signs can predict the risk for conversion of laparoscopic (LC) to open cholecystectomy (OC).

METHODS: All 346 patients who underwent LC at our institution between the first of January 1, 1993 and March 1, 1996, were studied retrospectively. Patients who had no sonographic examination during 6 months prior to surgery and patients treated by inexperienced surgeons were excluded from the study. Patient characteristics and sonographic parameters were evaluated by univariate and multivariate analysis, using conversion to OC as a dependent variable.

RESULTS: In 23 of 134 patients (17.2%), LC was converted to OC. In the univariate analysis, gallbladder distention (>4.5cm, Relative Risk [RR] 3.5; 95% Confidence Intervals [CI] 1.7-5.3), stone impaction (RR 2.4; 95% CI 1.1-5.1), thickened gallbladder wall (RR 2.4; 95% CI 1.2-5.1) and acute cholecystitis (RR 2.6; 95% CI 1.1-6.7) were able to predict the need for conversion. Logistic regression defined only the sonographic sign of distention of the gallbladder as a predictor of conversion.

CONCLUSIONS: Gallbladder distention as a sonographic sign is associated with a high relative risk for conversion. The predictive value of sonographic signs for conversion requires further assessment in a prospective study.

Key words

Gallstones - Laparoscopy - Cholecystectomy - Sonography

Introduction

Laparoscopic cholecystectomy (LC) is the standard procedure for the treatment of symptomatic gallbladder stones. However of all LC, 1-13% require conversion to an open cholecystectomy (OC) [2, 3, 6-8, 11]. Patients are informed preoperatively that if intraoperative complications, such as uncontrollable bleeding or unclear anatomy, arise, conversion to open surgery will be necessary. It would be helpful to establish criteria that could assess the risk for conversion preoperatively. This would not only be useful for informing the patient, but also aid in the selection of patients for ambulatory care or short stay. In addition, a more experienced surgical team could be assembled when the risk for conversion appears considerable.
The purpose of this study is to determine whether sonographic signs can predict the need for conversion of LC to OC.

Materials and methods

We reviewed the medical records of 372 patients, who were consecutively admitted for cholecystectomy at the Department of Surgery of the University Hospital of Rotterdam between January 1, 1993 and March 1, 1996. Twenty-six patients were initially scheduled for OC and 346 for LC. Sonographic examinations done within 6 months prior to surgery at our hospital were available in 197 of the 346 patients scheduled for LC. A total of 134 of the 197 were treated by an experienced surgical team. We then reevaluated the sonographic examinations of these 134 LC patients. We also recorded patient characteristics, including age, sex and body mass index (BMI, body weight/length^2).

Surgical procedure

Operations were performed either by surgeons or residents. LC was carried out using a standard four-trocars approach.
The surgical reports of the LC group were evaluated for conversion and its causes. Indications for conversion were divided into the following groups: infiltrates, perforation, inability to define anatomy, adhesions, bleeding, contracted gallbladder, and stone impaction. The surgical team was considered "experienced" when the surgeon and first assistant together had

performed > 50 LC. Surgical teams with experience ≤50 LC were regarded as "inexperienced". Although a heterogeneous group of surgeons performed the laparoscopic cholecystectomy, there was consensus on the indications for conversion. These indications included inability to obtain adequate exposure of Cabot's triangle, bleeding that could not be controlled laparoscopically, and extensive intraperitoneal adhesions.

Sonographic examination

All patients were examined in a fasting state with a 3.5-MHz scanner according to the following standardized protocol: Patients were positioned in a supine position and on their left side; when stone impaction was suspected, they were placed in an upright position. The diameter of the gallbladder was calculated as the maximum diameter perpendicular to the longitudinal axis. The sonographic examinations were performed either by radiologists or senior residents.

The most recent sonography performed within 6 months before surgery was reevaluated independently by two radiologists who had no prior knowledge of the surgical outcome . The opinion of a third radiologist was solicited when the first two did not agree. The following parameters were assessed: gallbladder size (normal or contracted- i.e., collapsed gallbladder filled with stones only-- or distended gallbladder - i.e., diameter of ≥4.5 cm), wall thickness, number and size of stones, echogenic bile and impaction of stones in the cystic duct.

Statistical analysis

The results were entered in a data base and evaluated using univariate and multivariate analysis. For univariate analysis, continuous variables were dichotomized or divided into thirds; in the latter case, the first was used as a reference. For variables scored on the three-point scale, the first category was used as a reference. In the univariate analysis, the 95% confidence intervals (CI) for the risk ratios (RR) were calculated according to Woolf [10]. The variables introduced in the logistic regression were those identified by univariate analysis. Prognostic variables were selected on the basis of maximum likelihood ratio.

Variables were included if they substantially improved the log likelihood ($p<0.10$). The Statistical Package for the Social Sciences (SPSS Inc. Chicago, IL, USA) was used for statistical computations.

Results

The median time between the sonographic examination and the cholecystectomy was 55 days (0-180 days). The mean age was 50.7 years (18-80), and the male/female ratio was 1:2.8. The mean BMI was 27.1 kg/m^2 (17.8-42.9). No significant differences were found for patient characteristics and indications for LC between the groups of patients with and without a sonographic examination 6 months prior to surgery and between the groups of patients treated by an inexperienced and experienced team of surgeons.
The indications for the 134 LC are listed in Table 1, together with the median time between sonography and surgery for each indication. Symptomatic gallbladder stones (n=116) was the most frequent indication.

Table 1. Indications for laparoscopic cholecystectomy (LC), number of conversions, median time between sonography (US) and LC, and percentage of patients who had LC within 3 days after sonography

Indications for LC	No. LC	No. conversions		Median time between US and LC (days)		No. of patients treated within 3 days after US	
Symptomatic gallbladder stones	116	16	(13.8%)	57	(1-178)	5	(4.3%)
Acute cholecystitis	11	4	(36.3%)	2	(0-15)	7	(64%)
Cholecystitis in the past	5	2		65	(12-180)	-	
Biliary pancreatitis	1	-		7	(-)	-	
Partial gallbladder in situ	1	1		25	(-)	-	
Total	134	23	(17.2%)	55	(0-180)	12	(9%)

In the evaluated group, we found a relationship between time of sonography to surgery and the acuteness of illness. The more acute the indication, the more recent the sonographic examination. In 23 of 134 patients (17.2%), LC was converted to OC. The indications for conversion included infiltration or perforation of the gallbladder (n=11), inability to define bile duct anatomy (n=3), abdominal adhesions (n=4), bleeding (n=3), contracted gallbladders (n=1) and stone impaction in the cystic duct (n=1). Compared to symptomatic gallbladder stones, acute cholecystitis was correlated with a higher risk for conversion (RR 2.6; 95% CI 1.1-6.7). The results of the univariate analysis for sonographic parameters in predicting conversion are shown in Table 2.

Table 2. Number of laparoscopic cholecystectomies (LC), number of conversions, risk ratio (RR) and 95% confidence intervals (CI) for sonographic items

		Number of LC	Number of Conversions	RR	95% CI
Gallbladder size	Normal (< 4.5 cm)	112	16	1	
	Contracted	9	1	0.8	0.1-5.3
	Distended (≥4.5 cm)	12	6	3.5[a]	1.7-7.1
Thickness of wall (mm)	≤ 2	98	14	1	
	≥ 3	23	8	2.4[a]	1.2-5.1
Number of stones	≤ 9	96	16	1	
	≥ 10	26	5	1.2	0.5-2.9
Diameter of stones (mm)	≥ 6	86	12	1	
	≤ 5	29	7	1.7	0.8-4.0
Echogenic bile	no	100	15	1	
	yes	21	6	1.9	0.8-4.3
Stone impaction	no	94	13	1	
	yes	24	8	2.4[a]	1.1-5.1
Total		134	23 (17.2%)		

[a] = $p < 0.05$

Sonographic signs associated with a significantly increased risk for conversion were distention of the gallbladder, thickness of the gallbladder wall of ≥3 mm, and stone impaction. Controlling for other variables in the multivariate analysis, gallbladder distention (odds ratio 4.4; 95% CI 1.4-15.1) was the only independent predictor of conversion. The relations between conversion rates of acute cholecystitis and gallbladder distention are shown in Table 3. Of the patients with a distended gallbladder on the preoperative sonography (n=12) who were converted to an open procedure (n=6), the indications for conversion were infiltrate or perforation of the gallbladder (n=3), abdominal adhesions (n=2) and contracted gallbladders (n=1).
For patients treated by an inexperienced surgical team, the conversion rate was 34.9% (22 of 63).

Table 3. The differences in conversion of LC to OC for patients with acute (n=11) or elective indication for LC (n=122) and the presence or absence of a distended gallbladder on sonography

	Sonographic finding			
Indication for LC	distended No. (conversion)	nondistended No. (conversion)	RR (95% CI)	*p*
Acute cholecystitis	4 (2)	7 (2)	1.8 (0.4-8.3)	NS
Elective	8 (4)	114 (15)	3.8 (1.7-9.1)	< 0.05

RR = relative risks, 95% CI = 95% confidence intervals

Discussion

Since its introduction in 1989, LC has been regarded as the procedure of choice in the treatment of symptomatic gallbladder stones [1, 7, 8]. The advantages of LC over OC are reduction of operative trauma and postoperative pain, shorter hospital stay, and an earlier return to work [5, 6]. Some of the planned LC have to be converted to OC. It would be useful to know in advance which ones would require conversion, since it would allow the surgeon to prepare for a more difficult operation. In such cases, an experienced laparoscopic surgeon could be scheduled to minimize the risk

of conversion. Furthermore, the patients can be forewarned of the possible surgical outcome and the duration of their hospital stay.

In our patient population, we noted that the majority (93%) of patients with gallbladder stones had an LC. For the 7% of initially planned OC, previous surgery and acute cholecystitis were the main indications. The conversion rate of LC to OC was rather high (17.2%) in our series. One possible explanation for this is that our institution is a tertiary referral and teaching hospital that treats patients with complicated disease. There is a low threshold to convert the laparoscopic approach to open surgery. Our policy is to convert to OC in every case in which the safety of LC is in doubt. These indications include inability to obtain adequate exposure of Cabot's triangle, bleeding that could not be controlled laparoscopically, and extensive intraperitoneal adhesions. This policy has resulted in zero bile duct lesions in these 346 patients. For patients treated by an inexperienced surgical team the risk for conversion was even higher (34.9%). Sonographic findings were comparable for patients treated by the inexperienced and experienced teams. Because we were primarily interested in the value of sonography, we excluded all patients who had been treated by an inexperienced surgical team. The high risk for conversion was mainly due to the inexperience of the team.

In the literature, the percentage of planned LC as part of the overall number of cholecystectomies is not always indicated clearly and ranges from 75% and 95% [4]. The percentage found for those to be converted varies from 1 to 13% [2, 3, 6-8, 11]. These differences depend on preoperative selection criteria which are not always clear. If preoperative selection is used, the number of planned OC will be high and the number of conversions of LC to OC lower. If all cholecystectomies were initially scheduled as LC, the conversion rate to OC will be high.

We realize that gallbladder size is not synonymous with raised pressure inside the gallbladder lumen. Moreover, gallbladder size depends on body constitution. Probably the best way to detect a "hydropic" gallbladder is to carefully palpate the gallbladder sonographically and assess the change of its form during compression. This finding, however, is impossible to determine in a retrospective study. We therefore chose for the more objective finding of a diameter of $\geq$4.5 cm as the sign of a distended, "hydropic" gallbladder.

We found that apart from gallbladder wall thickening, gallbladder distention and stone impaction significantly increased the risk for conversion (univariate analysis). The multivariate analysis revealed that gallbladder distention as an independent predictor of conversion. Until now only a thickened gallbladder wall seen on sonography was found to be predictive for conversion [3, 7, 9, 11]. Acute cholecystitis as indication for LC was also found to be a predictor of conversion. As can be seen in Table 3, in patients with no acute cholecystitis as an indication for LC, the finding of a distended gallbladder substantially increased their risk for conversion. One possible explanation for conversion in these patients is that intermittent gallbladder distention leads to more adhesions and scarring.

Gai and Thiele [4] argued that some of the positive sonographic criteria we found should be regarded as contraindications for LC. In our opinion, however, the presence of these findings should not be considered a reason to plan an OC.

One of the pitfalls of a retrospective study is the occurrence of selection bias. In this study, selection bias may occur when sonographic signs are only sought in those at high risk for conversion, for example, patients with acute cholecystitis. As we have already stated, patients with an acute indication for LC were more likely to have had a recent sonographic examination. If a distended gallbladder is only found in cases of clinically well-recognized acute illness, a spurious relation between distended gallbladder and conversion might occur. Despite the small numbers in this study, the finding of a distended gallbladder predicted conversion in both acute and non-acute patients (Table 3). A prospective study should be done to evaluate this finding further.

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CHAPTER 3

CAN SONOGRAPHY PREDICT CONVERSION OF LAPAROSCOPIC TO OPEN CHOLECYSTECTOMY? A prospective study.

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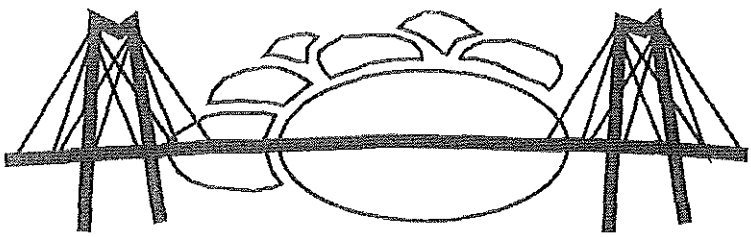

Submitted for publication

Abstract

Background: Laparoscopic cholecystectomies (LC) have to be converted to open surgery if intraoperative complications arise. The aim of this prospective study was to determine whether sonographic signs could predict the risk for conversion.

Methods: General practitioners referred 233 patients, who had recent symptoms suggestive of gallbladder stones, for abdominal sonography. Preoperative sonographic parameters were evaluated by univariate and multivariate analysis using conversion as the dependent variable.

Results: Eight of the 80 planned LC were converted to an open cholecystectomy (OC) (10%). Distended gallbladder on sonography was the only single sonographic sign that had a significant higher risk for conversion (RR 4.5, 95% CI 1.0-20). Also the finding of at least two of the other sonographic signs (i.e. contracted gallbladder, thickened gallbladder wall of ≥3 mm, grit, echogenic bile, or impaction of stones in the cystic duct or gallbladder neck), had a significant higher risk for conversion (RR 3.4, 95% CI 1.0-12.3).

Conclusion: This prospective study showed that distended gallbladder or the presence of at least two other sonographic signs (i.e. contracted, thickened gallbladder wall of ≥3 mm, grit, echogenic bile, or impaction of stones) were able to predict conversion of LC to OC.

Key words

Gallstones - Laparoscopy - Cholecystectomy - Sonography - Conversion - Prospective Study

Introduction

Laparoscopic cholecystectomy (LC) is considered as the standard procedure for the treatment of symptomatic gallbladder stones [2, 5, 9, 11, 13, 14, 16]. However of all LC, 1-17% needs to be converted to an open cholecystectomy (OC) [1, 6, 7, 10-12, 14, 16-19]. Patients are preoperatively informed that if intraoperative complications, such as uncontrollable bleeding or unclear anatomy, arise conversion to open surgery will take place. In a retrospective study we found that sonographic signs like gallbladder distension, stone impaction and thickened gallbladder wall could predict conversion [18]. In several retro- and prospective studies, similar sonographic signs were found to be related to conversion [1, 3, 7, 11, 12, 15, 17]. These studies involved both patients with acute and chronic cholecystitis. Combining these two conditions is undesirable since conversion rates are higher in acute cholecystitis [1, 3, 7, 12, 17, 18]. The sonographic signs like thickened gallbladder wall found in these patients will not be independent predictors for conversion but will be linked to acute cholecystitis. We therefore excluded patients with acute cholecystitis. The aim of this prospective study was to determine whether sonography could be helpful in predicting conversion in gallbladder stone patients without clinical signs of acute cholecystitis.

Materials and methods

Study design

Four hundred family doctors, practising in the Rotterdam area of the Netherlands, were asked to participate in the study. Two hundred forty seven agreed to participate in the study. All patients 18 years and older, who presented with recent abdominal pain and were considered by the GP to have symptomatic gallbladder stones, were entered into this prospective study. Patients who were suspected of acute cholecystitis or other acute abdominal illnesses were excluded. All patients were asked for written informed consent. The research ethics committee of the University Hospital Rotterdam approved the study protocol.

Sonographic examination

The sonographic examinations were performed either by radiologists, senior radiological residents or experienced radiology technicians, who were blinded to the medical history of the patients. All patients were examined in a fasting state with a 3.5 MHz scanner according to the following standardised protocol: Patients were placed in a supine position and on their left side. When stone impaction was suspected, they were placed in an upright position.

The following parameters were assessed: gallbladder size (normal, contracted, defined as collapsed gallbladder filled with stones, or distended gallbladder, defined as diameter of $\geq$4.5 cm), thickened gallbladder wall of $\geq$3 mm, number and size of stones, echogenic bile, and impaction of stones in the cystic duct. The diameter of the gallbladder was calculated as the maximum diameter perpendicular to the longitudinal axis.

Surgical procedure

Operations were performed either by surgeons or surgical residents in experienced centers. LC was carried out using a standard four-trocar approach. A questionnaire on the operation technique (primary open cholecystectomy, LC or conversion) and complications was completed after surgery.

Although a heterogeneous group of surgeons performed the laparoscopic cholecystectomy, there was consensus on the indications for conversion. These indications were inability to acquire adequate exposure of Calot's triangle, bleeding that could not be controlled laparoscopically and extensive intraperitoneal adhesions, interfering with gallbladder surgery.

Statistical Analysis

Conversion of LC to OC was categorised as an absolute endpoint. Sonographic findings were compared with the presence or absence of conversion using the chi-square test with Yates correction. Crude relative risks (RR) were calculated with 95% confidence intervals (CI) around the RR. Variables significant at $p<0.05$ were considered to be individually but not independently predictive of conversion.

Variables ($p<0.25$) were analysed using logistic regression to assess the relationship to conversion.
The Statistical Package for the Social Sciences 7.5 (SPSS Inc. Chicago, IL, USA) was used for statistical computations.

Results

Two hundred and thirty three patients completed a written informed consent. Gallstones were present in 107 patients (45%). Cholecystectomy was planned in 85 of the 107 gallbladder stone patients (primary open cholecystectomy n=5 , LC n=80). The indication for primary open cholecystectomy was suspected adhesions in all patients.

Table 1. Indications for conversion and sonographic signs of the gallbladder (GB)

Case	Indication	GB-Size	Stones	GB-Wall (mm)	Impaction	Grit	Sludge	Prev. surgery
170	Bleeding	hydropic	2 - 5	≥ 3	no	yes	yes	no
1089	No good exposure of Calot's triangle	normal	2 - 5	≥ 3	yes	no	no	no
1169	No good view because adiposity	normal	2 - 5	≥ 3	yes	no	no	no
1551	Technical difficulty	contracted	2 - 5	≥ 3	yes	no	no	no
3226	Intraperit. adhesions	contracted	> 10	< 3	no	no	no	no
3207	Fibrosis, no good view	normal	> 10	< 3	no	yes	yes	no
3161	Missing CBD	normal	2 - 5	< 3	no	no	no	yes[1]
1240	Thick. wall, infiltration	normal	2 - 5	≥ 3	yes	no	no	yes[2]

[1] = sterilisation, [2] = no answer CBD = common bile duct

The conversion rate was 10% (8/80). The indications for conversion and the sonographic signs found in these patients are listed in table 1.
Between the group of patients with and without a conversion, no significant differences were found in age (39.3 versus 43.5 years, p=0.260), sex (75% F versus 83% F, p=0.625), BMI (29.1 versus 26.6 kg/m^2 , p=0.105) and previous surgery.

Table 2. Number of laparoscopic cholecystectomies (LC), number of conversions, risk ratio (RR) and 95% confidence intervals (CI) for sonographic items

			Conversion			
		LC	No.	(%)	RR (95% CI)	
Gallbladder size	Normal (<4.5 cm)	63	4	(6)	1	
	Contracted	9	2	(22)	3.5	(0.8-16.4)
	Distended (≥5.5 cm)	7	2	(29)	4.5	(1.0-20.0)
Number of stones	0	3	0			
	1	16	0			
	2-5	36	5	(14)	ns	
	6-10	5	0			
	>10	20	3	(15)		
Thickness of wall	≥ 3 mm	30	4	(13)	1.7	(0.5-6.2)
	< 3 mm	50	4	(8)	1	
Grit	yes	29	3	(10)	1.1	(0.3-4.1)
	no	51	5	(10)	1	
Sludge	yes	13	2	(15)	1.7	(0.4-7.6)
	no	67	6	(9)	1	
Impaction	yes	28	4	(14)	1.9	(0.5-6.8)
	no	52	4	(8)	1	
No. of sonographic signs	0 or 1	68	5	(7)	1	
	≥ 2	12	3	(25)	3.4	(1.0-12.3)
Total		80	8	(10)		

ns = non significant, RR = relative risks, CI = 95% confidence interval

The time between the start of pain until the first sonography was within 24 hours for 62 %, and within 48 hours for 95 % of the patients. The time from sonography until the operation was for 8 % of the patients the same day, 42% was operated within two weeks, 99% within one year.
The time between the visit to the GP and sonography had no influence to the conversion rate (p=0.22). The time between sonography and surgery had also no significant influence on the conversion rate (p=0.73).
The relation between conversion and sonographic signs are listed in table 2. Distended gallbladder on sonography was the only single sonographic sign that had a significant higher risk for conversion (RR 4.5, 95% CI 1.0-20). Also the finding of at least two of the other sonographic signs (i.e. contracted gallbladder, thickened gallbladder wall of ≥3 mm, grit, echogenic bile, or impaction of stones in the cystic duct or gallbladder neck), had a significant higher risk for conversion (RR 3.4, 95% CI 1.0-12.3).

Discussion

Since its introduction in 1989, LC has become the procedure of choice in the treatment of symptomatic gallbladder stones [2, 5, 9, 11, 14].
The advantages of LC over OC are reduction of operative trauma and postoperative pain, shorter hospital stay and an earlier return to work [9, 10]. Some of the planned LC have to be converted to OC. It seems useful to know in advance which ones would require conversion, since it would allow the surgeon to prepare for a more difficult operation. In such cases an experienced laparoscopic surgeon can be scheduled to minimise the risk of conversion. Furthermore the patients can be better informed about the possible surgical outcome and duration of their hospital stay.
In our patient population, we noted that the majority (94%) of patients with gallbladder stones had a LC. For the 6% of initially planned OC, suspected adhesions was the main indication not to treat the patients laparoscopically.
The rate of initially planned OC was similar when compared to the rate we found in our retrospective study dealing with patients treated between 1993 and 1996 (7%). The conversion rate in this study (10%), however, is lower compared to our earlier study (17.2%) [18]. A possible explanation could be that, in this study, patients with acute cholecystitis are excluded.

The clinical sign of acute cholecystitis is highly predictive for conversion [1, 7, 17, 18]. Because we were primarily interested in the value of sonography in chronic disease, we excluded patients with acute cholecystitis. In the participating institutions there is a low threshold to convert the laparoscopic approach to open surgery; the policy is to convert to OC in every case in which the safety of LC is in doubt. These indications include inability to obtain adequate exposure of Calot's triangle, bleeding that cannot be controlled laparoscopically, and extensive intraperitoneal adhesions. This policy has resulted in zero bile duct lesions in these 80 patients.

In literature the percentage of planned LC as part of the overall number of cholecystectomies is not always indicated clearly and ranges between 75% and 93% [8, 18]. The percentage found for those to be converted varies from 1 to 17% [1, 6, 7, 10-12, 14, 17-19]. These differences depend on preoperative selection criteria that are not always clear. If preoperative selection is used, the number of planned OC will be high and the number of conversions of LC to OC lower. If all cholecystectomies were initially scheduled as LC, the conversion rate to OC will be high.

We realise that gallbladder size is not synonymous with raised pressure inside the gallbladder lumen. Moreover gallbladder size depends on body constitution. Probably the best way to detect a "hydropic" gallbladder is to carefully palpate the gallbladder sonographically and assess the change of its form during compression. This finding, however, seemed to us impossible to determine objectively in a study with several radiologists in 9 institutions. We therefore chose the more objective finding of a diameter of 4.5 cm or more as the sign of a distended, "hydropic" gallbladder.

This prospective study showed that a distended gallbladder of ≥4.5 cm was the only single sonographic sign that was able to predict conversion of laparoscopic to open cholecystectomy. Also the finding of at least two of the other sonographic signs (i.e. contracted, thickened gallbladder wall of ≥3 mm, grit, echogenic bile, or impaction of stones in the cystic duct or gallbladder wall) was able to predict conversion. Corr et al. [3] described in a prospective study, that thickened gallbladder wall was associated with increased technical difficulty of the operation. Jansen et al [12] found in a recent prospective study on this subject that a stone at least 20 mm in diameter, a gallbladder wall thicker than 4 mm, a common bile duct wider

than 6 mm, and contracted gallbladder on ultrasound, significantly increased the risk of conversion. Another prospective study by Daradkeh et al. [4] showed that thickness of GB wall and CBD diameter were significant preoperative ultrasound findings of predicting difficulties encountered during LC. In several retrospective studies thickened gallbladder wall was also found to be predictive for conversion [1, 7, 11, 15, 17]. In an earlier retrospective study we found that beside thickness of the gallbladder wall of 3 mm and more, sonographic signs like distension of the gallbladder and stone impaction, significantly increased the risk for conversion [18].

The finding of the studies mentioned above, that thickened gallbladder wall was predictive for conversion, could not be confirmed by this study. An explanation could be that in this study patients with acute cholecystitis were excluded, something not always mentioned clearly in the studies mentioned above. An other explanation could be that the studies mentioned are all dealing with experiences of the early to mid 1990th . The participating surgeons will have gained more experience to finish a cholecystectomy laparoscopically.

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CHAPTER 4

CAN SONOGRAPHIC SIGNS PREDICT LONG-TERM RESULTS OF LAPAROSCOPIC CHOLECYSTECTOMY?

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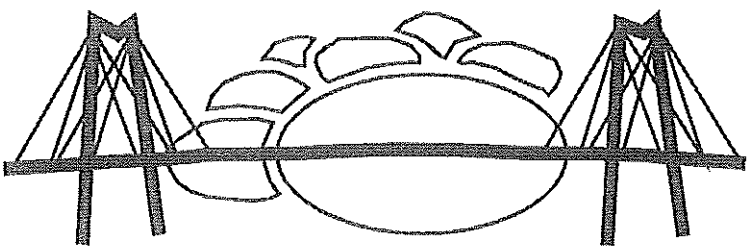

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Abstract

Background: To determine whether sonographic signs of the gallbladder can predict the long-term outcome of laparoscopic cholecystectomy (LC).

Methodology: All 346 patients, who underwent LC at our institution between January 1, 1993 and March 1, 1996, were interviewed using a structured questionnaire on the persistence of preoperative abdominal symptoms. Patients without a sonographic examination 6 months prior to surgery were excluded. Sonographic parameters, scored on the preoperative examination, were evaluated by univariate analysis using the relief of abdominal symptoms as a dependent variable.

Results: The response rate of correctly returned questionnaires was 68%. The follow-up ranged from 14 to 53 months. Fourteen percent (18/133) of all patients reported persistence of abdominal complaints after cholecystectomy. Grit in the gallbladder on the preoperative ultrasound examination was significantly associated with a higher relative risk (RR) for persistence of preoperative abdominal symptoms (RR 4.5, 95% confidence intervals (CI) 2.0-10.1). The presence of echogenic bile (RR 1.9, 95% CI 0.8-4.9), gallbladder distention (RR 1.9, 95% CI 0.6-5.7), and gallbladder wall thickening (RR 1.5, 95% CI 0.5-4.1) were associated with the persistence of symptoms. A contracted gallbladder (RR 0.6, 95% CI 0.4-1.1) and stone impaction (RR 0.44, 95% CI 0.1-1.8) were associated with the relief of abdominal symptoms. None of these sonografic signs reached significance. There was no difference in the postoperative symptoms rate between patients with a laparoscopic cholecystectomy and those who were converted to an open cholecystectomy.

Conclusion: This retrospective study showed that the sonographic sign of grit in the gallbladder is associated with a high relative risk for persistent abdominal symptoms after cholecystectomy. These findings will be re-evaluated in a prospective study to estimate the definitive clinical importance.

KEY WORDS

Gallstones, laparoscopy, cholecystectomy, sonography, postoperative symptoms, long-term follow-up.

Introduction

Laparoscopic cholecystectomy (LC) is the standard procedure for the treatment of symptomatic gallbladder stones. It is expected that patients with biliary colic or related complications will be relieved of preoperative symptoms after cholecystectomy. However of all the patients who had a cholecystectomy, 12 to 47% had no relief of symptoms in a follow-up period of 24 to 120 months [3, 7, 12]. The question is if the preoperative complaints in these patients were indeed caused by the gallstones. The association between gallstones and the spectrum of abdominal symptoms attributed to gallstones like flatulence and dyspepsia is uncertain. The outcome of surgery is therefore difficult to predict [5]. Sonography is used as a diagnostic tool for detecting gallstones. In addition to the presence of gallstones, the sonographic examination gives a wide range of additional information including the gallbladder size and wall thickness, the size of the stones and the presence of echogenic bile or stone impaction. No recent study has been found relating sonographic findings of the gallbladder with symptomatology of gallbladder stone disease. The purpose of this study was to determine whether sonographic signs could predict the long-term outcome of LC.

Methodology

All 346 consecutive patients, who underwent LC at the University Hospital Rotterdam, The Netherlands, between January 1, 1993 and March 1, 1996, were interviewed in June 1997 using a structured questionnaire on the persistence of preoperative abdominal symptoms. Patients without sonographic examination 6 months prior to surgery were excluded. We also included patient characteristics, including age, sex and Body Mass Index (BMI), (body weight/length^2).

Surgical procedure

Operations were performed either by surgeons or residents. LC was carried out using a standard 4-trocars approach.

Sonographic examination

All patients were examined in a fasting state with a 3.5 MHz scanner according to the following standardized protocol: Patients were placed in a supine position and on their left side; when stone impaction was suspected, they were placed in an upright position.

The diameter of the gallbladder was calculated as the maximum diameter perpendicular to the longitudinal axis. The sonographic examinations were performed either by radiologists or senior residents.

The most recent sonography performed within 6 months before surgery was re-evaluated independently by two radiologists, who had no prior knowledge of the surgical or long-term outcome. The opinion of a third radiologist was solicited when the first two did not agree. The following parameters were assessed: gallbladder size (normal or contracted - i.e., collapsed gallbladder filled with stones only- or distended gallbladder - i.e., diameter of ≥4.5 cm), wall thickness, size of stones, echogenic bile, impaction of stones in the cystic duct.

Statistical analysis

The results were entered in a database and evaluated using univariate analysis. For the analysis, continuous variables were dichotomized. For variables scored on a 3-point scale, the first category was used as a reference. In the univariate analysis, the 95% confidence intervals (CI) for the risk ratios (RR) were calculated according to Woolf [10]. The Statistical Package for the Social Sciences (SPSS Inc. Chicago, IL, USA) was used for statistical computations.

Results

Three hundred and forty-six patients were interviewed. In 197 patients, a sonographic examination was available made within 6 months prior to surgery. One hundred and fifty of the 197 patients (76%) returned their questionnaire. 133 questionnaires (68%) were completed correctly and could be used for analysis. The median time between the sonographic examination and the cholecystectomy in these 133 patients was 55 days (0-180 days). The median time between the LC and the questionnaire was 31 months (14-53

months). The mean age was 49.5 years (18-80) and the male/female ratio 1:2.8. No significant differences were found for patient characteristics (age, male/female ratio and BMI) and indications for LC (symptomatic gallbladder stones, acute cholecystitis, cholecystitis in the past and partial gallbladder in situ) between the groups of patients with and without a sonographic examination 6 months prior to surgery (χ^2=2.7, df=5, p=0.25) and between the groups of patients with and without a completed questionnaire (χ^2=4.8, df=5, p=0.41).

Fourteen percent of all patients (18/133) reported no relief of abdominal complaints after cholecystectomy. No significant differences were found between indication for LC and postoperative complaints (table 1).

Table 1. Indications for laparoscopic cholecystectomy (LC), number of patients with postoperative symptoms, and the relative risk of acute cholecystitis versus presumed symptomatic gallbladder stones

	No. LC	Complaints		RR	(95% CI)
Symptomatic gallbladder stones	108	14	(12%)	1	
Acute cholecystitis	16	3	(19%)	1.5	(0.47-4.5)
Cholecystitis in the past	6	1	(17%)		
Partial gallbladder in situ	1	-			
Total	133	18	(14%)		

Patient characteristics were not associated with a significantly higher risk for postoperative symptoms (female sex: n=98, symptoms 14%, male sex: n=35, symptoms 11%, RR 1.3, 95% CI 0.89-1.2; age < 60: n=99, symptoms 14%, age ≥60: n=34, symptoms 12%, RR 1.2; 95% CI 0.41-3.4). The results of the univariate analysis for sonographic parameters in predicting postoperative symptoms are shown in table 2. Sonographic sign of grit in the gallbladder was associated with a significantly increased relative risk for postoperative symptoms (RR 4.5, 95% CI 2.0-10.1).

In 34 of the 133 patients (25.6%) LC was converted to an open cholecystectomy.

There was also no significant difference in the postoperative symptoms rate between patients with a laparoscopic cholecystectomy (n=99, complaints 13 %) and those who were converted to an open cholecystectomy (n= 34, complaints 15 %, RR 1.2 95% CI 0.87-1.2).

Table 2. Number of laparoscopic cholecystectomies (LC), percentage of patients with post-operative symptoms, risk ratio (RR), and 95% confidence intervals (CI) for sonographic items

		Symptoms			
		No. LC	%	RR	95% CI
Gallbladder size	Normal (< 4.5 cm)	108	13	1	
	Contracted	12	8	0.6	0.4-1.1
	Distended (≥4.5 cm)	12	25	1.9	0.6-5.7
Thickness of wall (mm)	≤2	97	13	1	
	≥3	20	20	1.5	0.5-4.1
Diameter of stones (mm)	≥4	107	11	1	
	≤3	10	50	4.5[a]	2.0-10.1
Echogenic bile	no	97	12	1	
	yes	21	24	1.9	0.8-4.9
Stone impaction	no	89	15	2.3	0.5-9.1
	yes	27	6	1	
Total		133	14		

[a] = $p < 0.05$

Discussion

Since its introduction in 1989, LC is considered to be the procedure of choice in the treatment of symptomatic gallbladder stones [2, 4, 8]. However of all the patients who had a LC, 12 to 47% had no relief of symptoms in a follow-up period of 24 to 120 months [1, 3, 7, 11, 12]. The question is whether the gallstones caused the complaints in these patients. It is difficult to define the symptoms specific for gallstones and thereby distinguish between symptomatic and asymptomatic gallstones [6]. There is also no clear relation between pre- and postoperative complaints.

Gilliland and Traverso found in a patient group that had dyspepsia as an indication for cholecystectomy that postoperative symptoms were found more frequently compared to other indications (25% vs. 12%), but these numbers did not reach significance [3]. So also the relationship between gallstones and the spectrum of symptoms like flatulent dyspepsia is uncertain and therefore it is difficult to advise patients what the outcome of surgery is likely to be [5].

Since the introduction of the LC, the number of cholecystectomies has increased by 30 to 55 % in a period of 3 to 5 years [9, 13]. With the assumption that there is a constant number of patients with symptomatic gallbladder stones and an increasing number of cholecystectomies, the proportion of patients treated for asymptomatic stones will increase. And so the number of patients who will get no relief of symptoms after cholecystectomy will increase. This implies the quest for selection.

We found that sonographic signs like distention of the gallbladder, thickness of the gallbladder wall of 3 mm and more, and stone impaction, significantly increased the risk for conversion [14]. The purpose of this study was to determine whether these sonographic signs could also be helpful in predicting the long-term outcome of LC. No studies dealing with the relation of preoperative ultrasound and the persistence of complaints have been published before.

With a postoperative symptoms rate of 14% we are at the lower end of the 12 - 47 % found in literature. This might be due to the retrospective nature of this analysis.

It seems useful to know in advance which patients are at risk for postoperative complaints, so patients can be better informed about the possible outcome. And even more important, that patients who have a high risk of getting no relief of their complaints after LC, can be selected and the search for the right diagnosis can start earlier.

Our analysed patient group is probably a good sample of all patients treated in our hospital for gallstones because there were no differences in patient characteristics and indications for LC between the patients with and without an analyzable questionnaire and between the patients with and without an ultrasound 6 months before surgery. Patient characteristics and indications had no relation to postoperative symptoms.

Others also found that sex did not affect symptomatic outcome but found that elderly (> 55 years) more commonly had an unsuccessful outcome [1].
This study showed that the finding of grit in the gallbladder on the preoperative sonography was strongly related to the persistence of preoperative complaints. A possible explanation for this could be that, in these patients, grit is also present in the biliary tree, which can give rise to recurrent complaints.
We expected to find significantly less persistence of preoperative symptoms in patients with sonographic signs like contracted gallbladder and stone impaction. This study could not confirm this hypothesis. This might be due to the fact that this was a retrospective study. Abdominal complaints due to other causes than gallstones might have disappeared by natural causes.
Conversion of the LC to an open procedure seemed to have no influence on the postoperative symptoms rate. Although a part of these conversions were done because of local problems such as adhesions, which makes symptomatic gallstone disease quite likely, the complaints rate in this group was not significantly lower. This could be due to the abdominal adhesions itself and to the longer scars needed for an open cholecystectomy.
One of the pitfalls of a retrospective study is the occurrence of selection bias. In this study selection bias may occur when patients still having complaints relatively more frequently return questionnaires. Because this will make the overall complaint rate higher, this does not seem likely to be the case with a complaints rate of 14%. Although only patients with presumed symptomatic gallbladder stones or related complications underwent LC, another problem with retrospective studies like this one is that an extensive preoperative questionnaire is not available. So it is not possible to make a good comparison between the pre- and postoperative complaints.
A prospective study with preoperative sonographic examinations of the gallbladder and pre- and postoperative questionnaires will be done to further evaluate and clarify the value of sonography in selecting patients for a cholecystectomy in order to reach nearly complete relief of symptoms.

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CHAPTER 5

CAN SONOGRAPHY PREDICT RELIEF OF UPPER ABDOMINAL PAIN AFTER LAPAROSCOPIC CHOLECYSTECTOMY?
A prospective study

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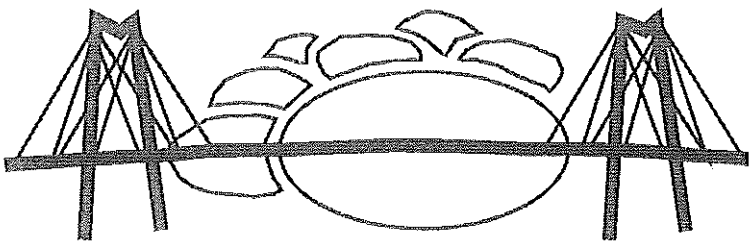

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Abstract

Background: Gallbladder stones are commonly found at sonography for upper abdominal pain. The purpose of this prospective study was to determine whether sonographic findings can predict relief of abdominal pain after cholecystectomy.

Methods: General practitioners referred 233 patients with symptoms suggestive of gallbladder stones for abdominal sonography. Preoperative sonographic parameters were evaluated by univariate and multivariate analysis using the relief of upper abdominal pain as the dependent variable.

Results: Gallbladder stones were present in 107 patients. Cholecystectomy was done in 85 of these patients. Follow up was available in 73 of the operated patients. In 65 of these patients, preoperative upper abdominal pain was present. After a median follow up after cholecystectomy of 14 months (range 11 to 34 months), 75% (49/65) of patients was free of upper abdominal pain.

In the univariate analysis, the presence of the sonographic signs of stone impaction in the gallbladder neck or cystic duct and/or thickened gallbladder wall was significantly related to relief of upper abdominal pain after cholecystectomy (odds ratio 4.0, 95% confidence interval 1.1 to 14.2). Grit in the gallbladder on sonography was significantly associated with pain persistence (OR 0.3, 95% CI 0.1 to 1.0). In the multivariable analysis none of these relations reached statistical significance. In 51% of the patients in our study, no thickened gallbladder wall or stone impaction was found. If these patients did not have a laparoscopic cholecystectomy, the upper abdominal pain rate in the operated group would fall from 25% to 12.5%.

Conclusion: This prospective study showed that sonographic signs of thickened gallbladder wall or impaction were associated with relief of upper abdominal pain after cholecystectomy. Grit found in the gallbladder on the preoperative sonography was associated with persistence of upper abdominal pain. Sonography appears therefore of value in the selection of patients with gallbladder stones for cholecystectomy.

Key words

Gallstones - laparoscopy - cholecystectomy - sonography - postoperative pain - long-term follow up - prospective study

Introduction

Laparoscopic cholecystectomy (LC) is the standard treatment of symptomatic gallbladder stones [1, 2, 4, 5, 7, 10, 13, 14, 16]. Severe upper abdominal pain is the symptom most closely related to gallstones [22]. It is expected that patients with severe upper abdominal pain or related symptoms will be relieved of pain after cholecystectomy. However of all patients who had cholecystectomy, 12 to 47% had no relief of symptoms during a follow-up period of 24 to 120 months [6, 8, 12, 18, 19, 21, 23]. The outcome of surgery in patients with gallstones, without signs of cholestasis and/or cholecystitis is difficult to predict [11, 19]. A method to predict outcome of cholecystectomy would be valuable for the patient. Sonography can, in addition to detecting gallstones, assess the size of the gallbladder, wall thickness, size of the stones and presence of echogenic bile or stone impaction. To our knowledge no prospective study has been reported relating findings of sonography of the gallbladder with outcome of cholecystectomy. In a retrospective study, Gui et al. found thick-walled gallbladder on ultrasound to be associated with pain-free outcome after cholecystectomy [8]. In a retrospective study, patients with grit (stones ≤3mm) in the gallbladder on preoperative sonographic examination had only a fifty-fifty chance of pain relief after cholecystectomy [23].

The purpose of this prospective study was to determine whether sonographic features of the gallbladder could predict relief of upper abdominal pain after laparoscopic cholecystectomy.

Materials and methods

Study design

Four hundred general practitioners (GP), practising in the Rotterdam area of the Netherlands, were asked to participate in the study. Two hundred forty seven (62%) agreed to participate. All consecutive patients aged 18 years and older who consulted a participating GP between January 1996 and June 1998 with abdominal symptoms and in whom the GP considered the possibility of gallbladder stones were eligible for the study. Patients suspected of acute cholecystitis or other acute abdominal illnesses were excluded.

All patients were asked for written informed consent (n=233). Consenting patients were referred to a primary diagnostic service centre or a radiology department of one of nine local hospitals for an ultrasound examination of the upper abdomen. Before sonography, the patient filled out a structured self-administered questionnaire on the presence or absence of 13 abdominal symptoms during the last month. The severity of these symptoms was recorded on a 4-point scale, anchored as absent, mild, severe, or very severe. Upper abdominal pain included all reported upper abdominal pain independent of severity and duration, except upper abdominal pain that only occurred after fatty food intake. One year after surgery, an identical questionnaire was sent to all patients. The research ethics committee of the University Hospital Rotterdam approved the study protocol.

Sonographic examination

The sonographic examinations were performed either by radiologists, senior radiological residents or experienced radiology technicians. All patients were examined in a fasting state with a 3.5 MHz scanner according to the following standardised protocol: Patients were placed in a supine position and on their left side. When stone impaction was suspected patients were placed in an upright position.

The following parameters were assessed: gallbladder size (normal, contracted, defined as collapsed gallbladder filled with stones, or distended gallbladder, defined as diameter of $\geq$4.5 cm), thickened gallbladder wall of $\geq$3 mm, number and size of stones (grit was defined as stones $\leq$3 mm), echogenic bile, and impaction of stones in the gallbladder neck or cystic duct. A combination of a thickened gallbladder wall or stone impaction, both as plausible indicators of symptomatic gallstones, was separately analysed. The diameter of the gallbladder was calculated as the maximum diameter perpendicular to the longitudinal axis. All items were scored on a structured form.

Statistical Analysis

Upper abdominal pain after cholecystectomy was the primary outcome parameter. The postoperative pain relief rate was defined as the relative number of patients in whom upper abdominal pain was absent

postoperatively, divided by the number of patients exhibiting the symptom preoperatively. The sonographic findings were compared with the presence or absence of postoperative pain using the chi-square test with Yates correction. Crude odds ratio's (OR) were calculated with 95% confidence intervals (CI). Variables significant at $p<0.05$ were considered to be predictive of symptomatic outcome with reference to postoperative pain.
Variables significant at $p<0.25$ were included in a multivariable logistic regression to assess the independent relationship to upper abdominal pain after cholecystectomy. Deletion of cases with missing data may cause bias and will increase variance [9]. For patients for whom one preoperative clinical characteristic was missing and for patients for whom one postoperative finding was missing, the most cited answer was imputed. Patients for whom more than one value was missing were excluded from the multivariable analysis.
The Statistical Package for the Social Sciences 7.5 (SPSS Inc. Chicago, IL, USA) was used for statistical computations.

Results

Gallbladder stones were present in 107 patients. Cholecystectomy was performed in 85 of these patients, of whom 73 patients had follow up. In 65 of these patients, the indication for cholecystectomy was upper abdominal pain. In 8 patients dyspepsia was the indication for cholecystectomy. Of these patients, one patient had no sonographic findings, two had wall thickness ≥3 mm and stone impaction, one had a contracted gallbladder and stone impaction. All others either had wall thickening (2), stone impaction (1), or grit (1). One patient with stone impaction was completely symptom free after cholecystectomy. In 12 patients follow up was not available; in all these patients the indication for cholecystectomy was upper abdominal pain.
Sixty-five operated patients suffered from preoperative upper abdominal pain. These patients had the following characteristics: male/female ratio 8/57, mean age 42.9 years (range 18 to 79). No significant differences were found between the groups of gallbladder stone patients with (n=65) and without (n=12) follow up after cholecystectomy, as far as mean age,

male/female ratio, distribution of sonographic signs, and time between sonography and cholecystectomy were concerned. More patients without follow up had fever and diarrhoea (75% versus 36%; p=0.003 and 67% versus 36%; p=0.04, respectively).

Table 1. Number of patients with a sonographic sign (n), percentage of patients with relief of upper abdominal pain, odds ratio (OR), with 95% confidence intervals (CI)

		n	Pain relief %	OR	95% CI
Gallbladder size#	Normal (< 4.5 cm)	51	74.5	1	
	Contracted	7	57.1	0.5	0.1 to 2.3
	Distended (≥4.5 cm)	7	100	§	ns
Thickness of wall (mm)	≤2	42	69.0	1	
	≥3	23	87.0	3.0[b]	0.8 to 11.9
Diameter of stones (mm)	≥4	42	83.3	1	
	≤3 (grit)	23	60.9	0.3[a]	0.1 to 1.0
Number of stones	1	15	73.4	1	
	> 1	50	76.0	1.2	0.3 to 4.3
Echogenic bile	no	53	73.6	1	
	yes	12	83.3	1.8	0.4 to 9.2
Stone impaction	no	45	68.9	1	
	yes	20	90.0	4.1[b]	0.8 to 2.0
Stone impaction and/or thickened wall ≥ 3 mm	no	33	63.6	1	
	yes	32	87.5	4.0[a]	1.1 to 14.2
Total		65	75.4		

#= A normal gallbladder size was taken as the reference category
§ = One cell was empty; no proper estimate af the odds ratio could be made
[a] = $p < 0.05$, [b] = $p < 0.25$, ns = not significant

The median time between the onset of upper abdominal pain and sonography was 1 day (range 1-15 days). In 63% of the patients the interval between sonography and surgery was less than one month. For 80% it was less than 2 months (range 0-405 days).

The median follow up after cholecystectomy was 14 months (range 11 to 34 months). Forty-nine out of sixty-five (75%) patients were free of upper abdominal pain.

In the (univariate) analysis, the presence of the sonographic signs of stone impaction and/or a thickened gallbladder wall was significantly related to relief of upper abdominal pain after cholecystectomy (OR 4.0, 95% CI 1.1 to 14.2) (table 1). Although all patients with gallbladder distention were free of upper abdominal pain after cholecystectomy, this relation did not reach the level of significance. A sonographic sign significantly associated with persistent pain was the presence of grit (0.3, 0.1 to 1.0). Of the patients with grit (n=23) only 3 patients had no stones greater than 3mm. In the multivariable analysis none of the relations mentioned above reached statistical significance (stone impaction: OR 2.9, 95% CI 0.56 to 15.4, p=0.20; thickened gallbladder wall: 2.3, 0.54 to 9.8, p=0.26; grit: 0.35, 0.10 to 1.2, p=0.09). In 51% of the patients in our study, no thickened gallbladder wall or stone impaction was found. If these patients would have had no LC, the postoperative upper abdominal pain rate would fall from 25% to 12.5% (table 1).

Discussion

This study showed that the presence of the sonographic signs of thickened gallbladder wall and/or stone impaction could be significantly related to relief of upper abdominal pain after cholecystectomy. Grit found on the preoperative sonography of the gallbladder was significantly associated with persistence of upper abdominal pain.

We assumed that in patients with gallbladder stones the presence of sonographic signs like contracted gallbladder and sludge were signs of a diseased gallbladder and that therefore patients with these sonographic signs would be symptom free after cholecystectomy.

Since its introduction in 1989, laparoscopic cholecystectomy has become the preferred treatment of symptomatic gallbladder stones [2, 4, 5, 7, 10, 14].

However of all the patients who had a laparoscopic cholecystectomy, 12 to 47% had no relief of symptoms in a follow-up period of 24 to 120 months [3, 6, 12, 17, 18, 23]. In this study the rate of persistence of upper abdominal pain was 25%.

Since the introduction of the LC, the number of cholecystectomies has increased by 30 to 55% in a period of 3 to 5 years [15, 20]. Assuming that there is a constant number of patients with symptomatic gallbladder stones in the overall population and an increasing number of cholecystectomies, the absolute number of patients, who will not benefit from cholecystectomy will increase as well. This implies the quest for selection.

It seems useful to know in advance which patients are at risk for persistent symptoms, so patients can be better informed about the possible outcome of surgery. And even more important, in patients who have a low probability of symptom relief after LC, other diagnoses can be searched for.

In this study most patients had a sonography shortly after the onset of upper abdominal pain (median time 1 day). This seems preferable because a relation between symptoms and sonographic findings can be made. Several findings during gallbladder sonography, like gallbladder wall thickening and stone impaction are probably reversible, and do not have to be present or are probably less prominent after some time.

In 51% of the patients in our study, no thickened gallbladder wall or stone impaction was found. If these patients would not have undergone LC, the upper abdominal pain rate in the operated group would fall from 25% to 12.5% (table 1). In order not to miss symptomatic stones in this subgroup a strategy could be to repeat sonography during a new episode of upper abdominal pain.

This study confirmed the finding of our retrospective study that the presence of grit in the gallbladder on the preoperative sonography is related to the persistence of preoperative upper abdominal pain [23]. A possible explanation for this could be that, in these patients, grit is also present in the bile tree, which can give rise to recurrent complaints. In this study grit was present in 35% (23/65) of the patients. We assume that, although not proven in this study, these patients could benefit from LC combined with an additional procedure like papillotomy or papil dilatation.

In conclusion: This prospective study showed that sonographic signs of thickened gallbladder wall and/or impaction were associated with relief of upper abdominal pain after cholecystectomy. Grit found in the gallbladder on the preoperative sonography was associated with persistence of upper abdominal pain. Sonography appears therefore of value in the selection of patients with gallbladder stones for cholecystectomy.

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CHAPTER 6

ARE SONOGRAPHIC FINDINGS USEFUL FOR THE PREDICTION OF CLINICAL OUTCOME AFTER CHOLECYSTECTOMY WHEN PREOPERATIVE SYMPTOMS ARE TAKEN INTO ACCOUNT

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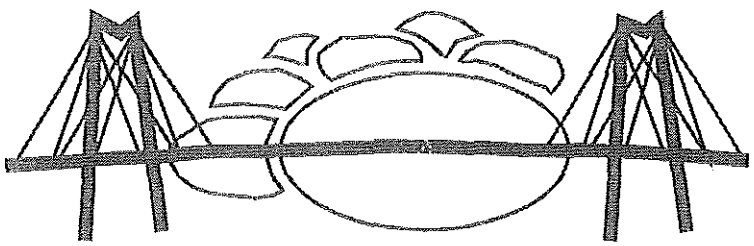

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Abstract

Context: Despite many efforts to predict the outcome of surgical treatment in patients with gallstones, it remains difficult to tell which abdominal symptoms will improve after cholecystectomy. Sonographic findings may help in predicting clinical outcome.

Objective: To evaluate the value of patient characteristics and preoperative symptoms in the prediction of clinical outcome after laparoscopic cholecystectomy for gallstone disease. To evaluate the additional value of sonographic findings, such as thickness of the gallbladder wall, stone impaction and stone size.

Design: A one-year, multi-center, follow-up study.

Setting: The departments of surgery and radiology of nine hospitals in the area of Rotterdam, The Netherlands

Patients: A total of 73 patients operated for gallstone disease.

Main outcome measures: Relief of upper abdominal pain and dyspepsia, one year after cholecystectomy.

Results: The relief rates for upper abdominal pain and dyspepsia were 75% and 49% respectively. Older patients had higher relief rates for upper abdominal pain (adjusted odds ratio 1.06, 95% confidence interval 1.0 to 1.13). Flatulence, severe acid regurgitation and bloating were associated with persistence of upper abdominal pain, with adjusted odds ratios of: 6.25 (95% CI 0.9 to 50), 5.0 (95% CI 1.16 to 20) and 7.1 (95% CI 1.39 to 33.3), respectively. Flatulence, severe acid regurgitation and belching predicted the persistence of dyspepsia (adjusted odds ratios 5.5 (1.27 to 25), 5.9 (1.41 to 25) and 3.7 (1.05 to 12.5), respectively. The presence of grit in the gallbladder (0.3; 0.1 to 1.0), wall thickness 3mm and/or stone impaction (4.0; 1.1 to 14.2) were each associated with upper abdominal pain relief but added little to the prognostic information of age and preoperative symptoms (multivariable analysis).

Conclusion: Flatulence, severe acid regurgitation, bloating and belching predict the persistence of upper abdominal pain and dyspepsia in patients cholecystectomized for symptomatic gallbladder stones. Sonographic findings do not add significantly to the predictive value of age and preoperative symptoms.

Introduction

The existence of gallstone-specific symptoms has been questioned [1,2]. The uncertainty around true clinical manifestations of gallstone disease is in sharp contrast with the unanimous recommendation that only symptomatic gallstones should be treated [3]. Although biliary pain defined as a severe, steady upper abdominal pain lasting more than 1 hour is related to gallstones [1,2,4,5] a causal relationship between other abdominal symptoms remains unclear. This makes it difficult to assess whether gallstones are truly symptomatic.

With the number of laparoscopic cholecystectomies increasing since the early 90's [6,7] several authors have felt the need grow to predict which patients will benefit from cholecystectomy and which ones will not. Many efforts have been put in the prediction of the clinical outcome after cholecystectomy but the prognosis of individual patients undergoing this procedure is still a matter of debate [8-11]. Sonography provides more information than just the presence or absence of gallstones. Gallbladder size, wall thickness, stone impaction, and the size of the stones can all be recorded. In principle, these characteristics might be related to clinical outcome of cholecystectomy [9,13]. If so, they can be used to predict the likely outcome of surgery in individual patients. In that case sonography might help the clinician to decide if cholecystectomy will be beneficial to a patient. The probability of symptom relief, however, is a joint function of findings on sonography and other associated information on the patient [12]. The aim of the prospective study reported in this paper was to evaluate the additional value of sonography, beyond patient characteristics and preoperative symptoms in predicting clinical outcome after cholecystectomy for gallstone disease.

Methods

Study Sample

Four hundred general practitioners (GPs) in the area of Rotterdam, the Netherlands, were invited to participate in the study, of which 247 (62%) accepted. All consecutive patients aged 18 years and older, who consulted a participating GP, between January 1996 and June 1998, with abdominal

symptoms and in whom the GP considered the possibility of gallbladder stones, were eligible for the study. Patients who were suspected of acute cholecystitis or other acute abdominal illnesses were excluded.
Eligible patients were asked for written informed consent. In all patients, a standardised clinical examination was performed to determine abdominal tenderness, location of the pain, weight and length. Patients were then referred to a GP diagnostic service or to the radiology department of one of nine local hospitals for a standardised ultrasonographic examination of the upper abdomen. The research ethics committee of the University Hospital Rotterdam approved the study protocol.

Clinical Examination
We distributed a structured self-administered questionnaire to record the presence or absence of 13 abdominal symptoms during the last month. These symptoms were: nausea, vomiting, feeling of distension (bloating), belching, acid regurgitation, constipation, diarrhea, flatulence, upper abdominal pain, upper abdominal pain after fatty food intake, upper abdominal pain lasting for more than one hour, jaundice, and fever ≥38°C. The severity of the symptoms was recorded on a 4-point scale: absent, mild, severe or very severe. Dyspepsia was defined as present whenever three or more dyspeptic symptoms (nausea, vomiting, bloating, belching, flatulence, and upper abdominal pain after fatty food intake) were quoted. Biliary pain was defined when the upper abdominal pain was severe and lasted more than one hour. One year after cholecystectomy a copy of the same questionnaire was sent by mail. Non-responders received a reminder by mail and a second reminder by telephone within one month.

Sonographic findings
Sonographic examinations were performed either by radiologists, senior radiological residents or experienced radiology technicians. All patients were examined in a fasting state with a 3.5 MHz scanner according to the following standardised protocol: Patients were placed in a supine position and on their left side. Whenever stone impaction was suspected, patients were placed in an upright position.

The following parameters were recorded: gallbladder size (normal, contracted or distended), wall thickness, number and size of stones, echogenic bile, and impaction of stones in the cystic duct or gallbladder neck. A contracted gallbladder was defined as a collapsed gallbladder filled with stones only. A gallbladder with a diameter of ≥4.5 cm was classified as distended. A gallbladder wall of ≥3 mm was classified as thickened and the presence of stones ≤3 mm were defined as grit. The diameter of the gallbladder was calculated as the maximum diameter perpendicular to the longitudinal axis. All items were scored on a structured form. Single sonographic findings and plausible combinations of two signs were analysed.

Statistical Analysis

Symptom relief rates after cholecystectomy were calculated for each symptom. The relief rate was defined as the number of patients in which the symptom had disappeared postoperatively, divided by the number of patients exhibiting the symptom preoperatively. For each symptom the de novo rate was calculated as the number of patients who developed the symptom for the first time postoperatively divided by the number of patients without the symptom preoperatively.

Associations were examined between age, sex, preoperative abdominal symptoms, and sonographic findings versus postcholecystectomy relief of upper abdominal pain, dyspepsia, and a symptom-free status. For this purpose the chi-square test statistic with Yates correction was used. Postcholecystectomy upper abdominal pain included all reported upper abdominal pain independent of severity and duration, except upper abdominal pain that only occurred after fatty food intake.

Multivariable Modelling

All symptoms that were univariately associated with one of the three endpoints at a significance level of $p<0.25$ were entered into a multivariable logistic regression model. One model each was built for post-cholecystectomy relief of upper abdominal pain, dyspepsia, and a symptom-free status. These three outcome measures were the respective dependent variables. Initially significant patient characteristics and

preoperative symptoms ($p<0.25$) were entered in the model. Then sonographic findings were added, testing for a significant improvement in the prognostic regression model. The general likelihood ratio test statistic was used for this purpose, using the chi-square distribution and the number of additional variables added as the degrees of freedom, with a level of significance of $p \leq 0.05$.

For each of the dependent variables, adjusted (prognostic) odds ratios (OR) with asymptotic 95% confidence intervals were calculated from the regression coefficients.

Deletion of cases with missing data may cause bias and will increase variance [15]. For 15 patients for whom one preoperative clinical characteristic was missing and 6 patients for whom one postoperative finding was missing, the most cited answer was imputed. Patients for whom more than one value was missing were excluded from the multivariable analysis. SPSS software was used to perform the analyses [14].

Results

In total 233 patients were referred for sonography of the upper abdomen. In this group 107 (46%) patients had gallbladder stones of whom 85 (79%) underwent cholecystectomy. Of these 73 (86%) patients responded to the follow-up questionnaire. The remaining 12 patients did not respond to the 2 reminders. They did not differ from the responding patients as far as age, sex, the presence of sonographic findings and time between sonography and cholecystectomy were concerned. The non-responders had more fever and diarrhea than the responders (75% versus 36%; $p=0.003$ and 67% versus 36%;$p=0.04$, respectively). The indication for cholecystectomy was upper abdominal pain in all 12 patients.

In sixty-five patients (89%) the indication for operation was upper abdominal pain. In 60 (92%) of these the pain occurred in episodes that lasted longer than 1 hour. In 45 (69%) upper abdominal pain was also provoked by fatty food intake. In 54 patients (83%) upper abdominal pain was accompanied by more than three dyspeptic symptoms. In only two patients the pain was not accompanied by dyspeptic symptoms.

Forty-four patients (60%) reported biliary pain, defined as an episode of severe upper abdominal pain lasting for more than one hour. In 40 (91%) of them biliary pain was accompanied by dyspepsia.
A total of 61 (94%) patients suffered preoperatively from dyspepsia. In 8 patients dyspeptic symptoms were the only indication for cholecystectomy.

After a median follow up of 14 months fifteen patients (21%) were completely symptom free. Sixteen patients (25%) still suffered from upper abdominal pain. In 12 of them (71%) upper abdominal pain was also provoked by fatty food intake; 16 patients (94%) suffered from more than 3 dyspeptic symptoms and 6 patients (35%) suffered from biliary pain. In total 41 patients had dyspeptic symptoms only; 7 of them (17%) had only upper abdominal pain after fatty food intake, and 16 patients (39%) reported more than three dyspeptic symptoms.

Table 1. Relief rates, persistence, and *de novo* rates of symptoms after cholecystectomy (n=73)

	Frequency preoperative	Symptom relief n (%)		No relief n (%)		*De novo* n (%)	
Biliary pain	44/73	38	(86)	6	(14)	0	
Upper abdominal pain	65/73	49	(75)	16	(25)	1	(13)
Dyspepsia	61/73	30	(49)	31	(51)	1	(8)
Belching	56/72	24	(43)	32	(57)	2	(13)
A feeling of distension (bloating)	56/72	33	(59)	23	(41)	5	(31)
Upper abdominal pain after fatty food intake	46/73	32	(70)	14	(30)	5	(19)
Nausea	58/70	39	(67)	19	(33)	2	(17)
Flatulence	47/73	18	(38)	29	(62)	10	(39)
Vomiting	39/71	35	(90)	4	(10)	4	(13)
Acid regurgitation	37/73	13	(35)	24	(65)	6	(17)
Diarrhea	26/73	6	(23)	20	(77)	12	(26)
Constipation	29/72	19	(66)	10	(34)	5	(12)

Table 1 shows the symptom relief rates and the de novo rates after cholecystectomy. Forty-nine of the patients with upper abdominal pain (75%) were relieved from their pain. In 31 (51%) of the patients with preoperative dyspepsia the dyspeptic symptoms persisted. In total 24 (65%) of the patients with preoperative acid regurgitation and 29 (62%) of the patients with preoperative flatulence were not relieved of these symptoms after cholecystectomy. Sonographic findings are presented in table 2. The median time between the onset of abdominal symptoms and sonography was 1 day (1-15).In 63% of the patients the interval between sonography and surgery was less than one month, for 80% it was less than 2 months (range 0-405 days).

Table 2. Preoperative sonographic findings in patients with gallstones (n=73) and their association with postoperative symptom relief

	Preoperative Sonographic findings n=73	Odds ratio for relief of upper abdominal pain (n=65) (95% CI)		Odds ratio for relief of dyspepsia (n=61) (95% CI)	
Gallbladder size:					
Normal (< 4.5 cm)	57 (78%)	1		1	
Contracted*	8 (11%)	0.5	(0.1 to 2.3)	0.8	(0.2 to 3.9)
Distended (≥ 4.5 cm)*	8 (11%)	§		1.4	(0.3 to 6.9)
Thickness of wall ≥ 3 mm	27 (37%)	**3.0**	**(0.8 to 11.9)**	0.7	(0.2 to 2.0)
Stones ≤ 3 mm (grit)	25 (34%)	**0.3**	**(0.1 to 1.0)**	1.2	(0.4 to 3.5)
Echogenic bile	13 (18%)	1.8	(0.4 to 9.2)	**4.0**	**(1.0 to 16.6)**
Stone impaction	24 (33%)	**4.1**	**(0.8 to 20.0)**	0.8	(0.3 to 2.3)
Wall thickness ≥ 3 mm and/or stone impaction	32 (44%)	**4.0**	**(1.1 to 14.2)**	1.1	(0.4 to 2.9)

* = A normal gallbladder size was taken as the reference category
§ = One cell was empty; no proper estimate af the odds ratio could be made
Bold = $p < 0.25$
95% CI = 95% confidence interval

Table 3. Prediction of outcome after cholecystectomy by preoperative symptoms and sonographic findings, a multivariable analysis

		Multivariable Odds Ratio	
	Crude Odds Ratio (95% CI)	without sonographic findings (95% CI)	including sonographic findings (95% CI)
Relief of upper abdominal pain (n=65)			
Age	1.05 (1.00 to 1.10)	1.06 (1.00 to 1.13)	1.04 (0.97 to 1.10)
Flatulence (yes/no)	0.18 (0.04 to 0.86)	0.16 (0.02 to 1.10)	0.21 (0.03 to 1.60)
Acid regurgitation (no, mild/severe, very severe)	0.12 (0.03 to 0.42)	0.20 (0.05 to 0.86)	0.11 (0.02 to 0.66)
Bloating (no, mild/severe, very severe)	0.12 (0.03 to 0.46)	0.14 (0.03 to 0.72)	0.13 (0.02 to 0.82)
Stones ≤ 3 mm (grit)	0.31 (0.10 to 0.99)		0.25 (0.04 to 1.48)
Stone impaction (yes/no) and/or wall thickness ≥ 3 mm	4.00 (1.13 to 14.2)		4.00 (0.70 to 23.7)
Relief of dyspepsia (n=61)			
Flatulence (yes/no)	0.26 (0.07 to 0.93)	0.18 (0.04 to 0.79)	0.21 (0.05 to 0.97)
Acid regurgitation (no, mild/severe, very severe)	0.19 (0.05 to 0.66)	0.17 (0.04 to0.71)	0.19 (0.04 to 0.78)
Belching (no, mild/severe, very severe)	0.31 (0.10 to 0.95)	0.27 (0.08 to 0.95)	0.21 (0.06 to 0.80)
Echogenic bile (yes/no)	4.00 (0.96 to 16.6)		3.90 (0.71 to 20.85)
Symptom free (n=73)			
Flatulence (yes/no)	0.19 (0.06 to 0.64)	0.23 (0.06 to 0.89)	
Dyspepsia	0.28 (0.07 to 1.04)	0.66 (0.14 to 3.08)	

95% CI = 95% confidence interval

Wall thickness ≥3mm and stone impaction were associated with relief of upper abdominal pain, whereas grit was inversely related. Of the 8 patients without preoperative upper abdominal pain, one patient had no sonographic findings, two had wall thickness ≥3 mm and stone impaction, one had a contracted gallbladder and stone impaction. All others either had wall thickening (2), stone impaction (1) or grit (1). One patient with stone impaction was completely symptom free after cholecystectomy.

Table 3 summarizes the findings on the prognostic value of preoperative findings for postoperative symptom relief. In the univariate analysis higher age, a wall thickness ≥3 mm and/or stone impaction on sonography were significantly associated with postoperative relief of upper abdominal pain (odds ratio >1). Flatulence, severe bloating, severe acid regurgitation and a stone diameter ≤3 mm (grit) on sonography, predicted the persistence of upper abdominal pain (odds ratio <1). None of the other symptoms tested showed a significant relation ($p \geq 0.25$) with upper abdominal pain relief. Comparable results were found for the postoperative relief of dyspepsia. Flatulence, severe acid regurgitation and severe belching were associated with persistence of dyspepsia, whereas the finding of echogenic bile on sonography predicted relief of dyspepsia.

In the multivariable analysis the sonographic findings did not add significantly to the predictive value of the abdominal symptoms (chi-square statistics 5.2, 2 df $p>0.5$, for relief of upper abdominal pain and 2.6, 1 df $p>0.05$ for relief of dyspepsia).

Table 4 presents the distribution of the abdominal symptoms, their association with symptom relief, the predicted symptom relief rates as calculated from the logistic regression model, and the observed symptom relief rates. In those patients with a high calculated probability of symptom relief, most patients also have a thickened gallbladder wall and/or stone impaction. In those patients with a low predicted relief rate for abdominal pain only few patients have these sonographic findings, but the patients in whom sonographic signs are found show higher symptom relief rates (70% (7 of 10) as opposed to 33% (6 of 18) in patients without sonographic findings). Echogenic bile did not add to the predictive value for relief of dyspepsia of the abdominal symptoms.

Table 4. Predictive value of preoperative symptoms on symptom relief and the additional value of sonographic findings

	N	Predicted probability of symptom relief (range based on age differences)		Observed probability of symptom relief	Symptom relief and sonographic findings: wall thickness < 3 mm, no stone impaction	Symptom relief and sonographic findings: wall thickness ≥3 mm, and/or stone impaction
Relief of upper abdominal pain (n=65)						
No flatulence, acid regurgitation or bloating	15	0.99	(0.97 to 1)	1.0	5/5	10/10
Flatulence	16	0.94	(0.83 to 0.99)	0.94	7/7	8/9
Acid regurgitation	1	0.99		1.0	1/1	-
Bloating	5	0.92	(0.83 to 0.98)	1.0	2/2	3/3
Flatulence and acid regurgitation	4	0.57	(0.38 to 0.83)		2/4	-
Flatulence and bloating	11	0.59	(0.36 to 0.88)	0.55	3/8	3/3
Acid regurgitation and bloating	3	0.55	(0.47 to 0.65)	0.33	-	1/3
Flatulence, acid regurgitation and bloating	10	0.31	(0.11 to 0.52)	0.40	1/6	3/4
Total	65			0.75	21/33	28/32

	N	Predicted probability of symptom relief (range based on age differences)		Observed probability of symptom relief	Echogenic bile: no	Echogenic bile: yes
Relief of dyspepsia (n =60)						
No symptoms	4	0.93		1.0	3/3	1/1
Flatulence	12	0.70		0.67	7/11	1/1
Acid regurgitation	1	0.69		1.0	1/1	-
Belching	7	0.78		0.71	2/4	3/3
Flatulence and acid regurgitation	4	0.29		0.25	1/4	-
Flatulence and belching	19	0.39		0.42	5/10	3/9
Acid regurgitation and belching	3	0.38		0.33	1/2	0/1
Flatulence, acid regurgitation and belching	10	0.10		0.10	1/9	0/1
Total	60			0.48	21/44	8/16

Discussion

In a follow-up study of cholecystectomized patients, the prognostic value of patients characteristics, preoperative abdominal symptoms and findings on sonography for postoperative symptom relief were evaluated. Older patients had higher relief rates for upper abdominal pain. Flatulence, severe acid regurgitation, bloating and belching were associated with persistence of upper abdominal pain and dyspepsia. Sonographic findings did not add significantly to the prognostic value of preoperative characteristics, when the latter had been incorporated into a logistic prediction model. In patients with a low likelihood of upper abdominal pain relief, wall thickness ≥3 mm or stone impaction were associated with higher relief rates for upper abdominal pain. This association did not reach statistical significance.

Biliary pain defined as a steady severe pain in the upper abdomen lasting ≥1 hour is suggested to be causally related to gallstone disease. In our study the relief rate for biliary pain was high (86%). In total 14 out of 44 patients (32%) with preoperative biliary pain still had upper abdominal pain 14 months after cholecystectomy. This finding indicates that biliary pain is not specifically caused by gallstones and that the indication for cholecystectomy should not solely be based on the presence of biliary pain.

Patients with flatulence and severe acid regurgitation and bloating or belching had low calculated relief rates. In these patients a finding of stone impaction or a thickened gallbladder wall at sonography increased the probability of symptom relief. As numbers were small, such an association could not reach statistical significance and larger patient groups are required to further explore this subgroup relation.

The variability in symptom relief rates as reported by others can be explained by differences in the methods for evaluation used, wording of questionnaires, varying duration of follow-up, patient case mix and differences in the strategies used for the analysis (symptom frequencies or symptom relief rates) [16]. Only few studies have performed a multivariable analysis. Gui et al [9] found fatty food intolerance, normal bowel habits, a body mass index <26 kg/m^2, and a thick-walled gallbladder to be predictive for a symptom free outcome after operation.

A clinical relevant discrimination between patients with and without symptoms after cholecystectomy could not be reached however. Only 15 patients in our sample were completely symptom free at follow-up. Patients without preoperative flatulence or dyspepsia were more frequently free of symptoms at follow-up. Sonographic findings did not have additional prognostic value. Ure et al [10] could not differentiate between patients with and without complaints after operation. Their model included 8 symptoms, age, sex and weight loss. Luman et al [11] found bloating, constipation and the use of psychiatric medication to be predictive of persisting complaints after operation. We confirmed that bloating was predictive for the persistence of symptoms. A relation between psychic vulnerability and persisting abdominal pain after cholecystectomy was also reported by Jørgenson et al [17] but could not be evaluated in our study. The Mulgo group reported that in a prospective study patients with abdominal pain 1 year after cholecystectomy were characterized by the preoperative presence of dyspeptic symptoms, 'irritating abdominal pain', and an introverted personality and by the absence of 'agonizing' pain and symptoms coinciding with pain [18]. In our study the severity of the pain was not related to a pain free outcome after cholecystectomy. The finding of dyspeptic symptoms predicting postoperative abdominal pain was confirmed in our study sample.

In a study on the diagnostic value of gastrointestinal symptoms for gallstones on ultrasound Farrell et al [19] reported that pain lasting for more than 1 hour, any radiating pain and the absence of flatulence were independent predictors of gallstones. This finding is in accordance with our finding that flatulence predicts the postoperative persistence of symptoms.

The influence of age on outcome of cholecystectomy was previously reported by Mort et al [20]. After adjustment for other patient characteristics, indication for operation, and comorbid conditions, older patients (≥60 years) experienced more symptomatic relief than did younger patients. A possible explanation is that older patients (and physicians?) may be more risk averse than younger patients and more likely to refuse surgery when offered, particularly when the likelihood of symptomatic relief is uncertain.

Preoperative findings in patients with gallstones allow the clinician to discriminate between patients with high and low relief rates for upper abdominal pain. With our multivariable model 57% of the patients (37 of 65) had a predicted probability for upper abdominal pain relief of more than 90%, the remaining 43% (28 of 65) had a probability of <60%. The question remains whether in case of such an almost fifty-fifty chance of symptom relief an operation is indicated. Based on our study, sonographic signs like gallbladder wall-thickening and stone impaction were not able to add further prognostic information that would allow a distinction between patients who will benefit from cholecystectomy and those who will not. Further studies with higher power should explore the association between sonographic findings with symptom relief in specific subgroups. To evaluate which symptoms actually improve due to the cholecystectomy a randomised controlled trial remains a necessity.

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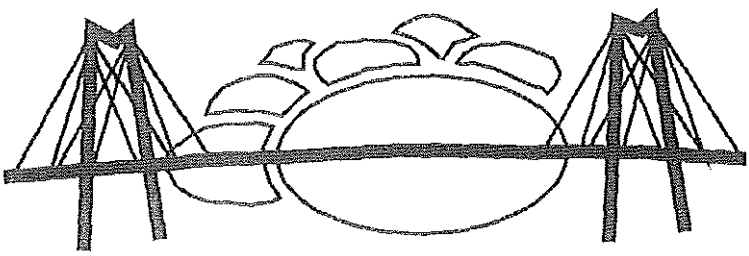
CHAPTER 7

SUMMARY AND CONCLUSIONS



Summary

Gallbladder stones are very commonly found at sonography for upper abdominal pain. Gallstones can also be found as a coincidental finding in patients without upper abdominal pain. The standard treatment for gallbladder stones is laparoscopic cholecystectomy (LC). Unfortunately, not all patients will be free of symptoms after cholecystectomy.
Not all patients with gallbladder stones can be treated laparoscopically; when intraoperative complications occur, conversion to an open cholecystectomy (OC) will be necessary.
In this thesis, the role of preoperative sonography of the gallbladder is discussed in relation to the prediction of conversion and in relation to the selection of patients who will benefit from cholecystectomy.

Chapter 1 give an overview of gallstone disease; described are the incidence of gallstones, symptoms, diagnosis, therapy, conversion, postcholecystectomy symptoms, importance of patient selection for cholecystectomy and the purpose of this thesis.

Chapter 2 presents the signs we found in our retrospective data of 346 patients, who underwent LC at our institution between January 1, 1993 and March 1, 1996, that could predict conversion of a laparoscopic cholecystectomy to an open cholecystectomy.
LC was converted to OC in 17.2%. Gallbladder distention, stone impaction, thickened gallbladder wall of ≥3mm and acute cholecystitis were able to predict conversion. Logistic regression defined only the sonographic sign of distention as a predictor of conversion.

Chapter 3 reports on the sonographic signs that could predict the risk for conversion of LC to OC. In this prospective study, called the 'Rijngast Study', general practitioners referred 233 patients, who had symptoms suggestive of gallbladder stones, for abdominal sonography shortly after the start of the symptoms. Eight of the 80 planned LC were converted to an OC (10%). Distention of the gallbladder is the only single sonographic sign that could significantly predict conversions (RR 4.5, 95% CI 1.0-20). Also patients with at least 2 of the other sonographic signs present (i.e. contracted gallbladder,

thickened gallbladder wall of ≥3 mm, grit, echogenic bile, or impaction of stones in the cystic duct), have a significant higher risk for conversion (RR 3.4, 95% CI 1.0-12.3).

Chapter 4 deals with the value of sonographic signs of the gallbladder in predicting the long-term outcome of laparoscopic cholecystectomy. The same patient group as discussed in chapter 2 was interviewed after cholecystectomy, using a structured questionnaire on the persistence of preoperative abdominal symptoms. The response rate of correctly returned questionnaires was 68%. This retrospective study showed that the sonographic sign of grit in the gallbladder is associated with a high relative risk for persistent abdominal symptoms after cholecystectomy.

Chapter 5 gives the results of the 'Rijngast Study' on the prediction of relief of abdominal pain after cholecystectomy. Of 233 patients referred by general practitioners, gallbladder stones were present in 107 patients. Cholecystectomy was done in 85 of these patients. One year follow up was available in 73 patients. In 65 of these patients, preoperative abdominal pain was present. The presence of the sonographic signs of stone impaction in the gallbladder neck or cystic duct and/or thickened gallbladder wall was significantly related to relief of upper abdominal pain after cholecystectomy (OR 4.0, 95% CI 1.1-14.2). Individually these signs did not reach the level of significance. Although all patients with gallbladder distention were free of upper abdominal pain after cholecystectomy, this relation did not reach the level of significance. Grit had a significantly relation with persistent pain (OR 0.3, 95% CI 0.1-1.0).
In 51% of the patients in our study, no thickened gallbladder wall or stone impaction was found. If these patients would not have had a LC, the upper abdominal pain rate in the operated group would fall from 25% to 12.5%. Sonography appears therefore of value in the selection of patients for cholecystectomy.

Chapter 6 discusses the surplus value of sonographic findings above patient characteristics and preoperative symptoms, in the prediction of clinical outcome after cholecystectomy for gallstone disease.

Flatulence, severe acid regurgitation, bloating and belching predict the persistence of upper abdominal pain and dyspepsia in patients cholecystectomized for gallstones. Increasing age predicts a higher chance for relief of upper abdominal pain. A possible explanation could be that in older patients the indication is made more precise because of age in this group of patients.
Sonographic findings did not add to the predictive value of age and preoperative symptoms when the latter had been incorporated into a logistic prediction model. But in patients in whom the predicted symptom relief rate -based on their preoperative symptoms (flatulence, severe acid regurgitation, bloating or belching) - is low (< 60%), a finding of stone impaction or a thickened gallbladder wall at sonography increased the probability of symptom relief. As numbers were small, such an association could not reach statistical significance and larger patient groups are required to further explore this subgroup relation.

Conclusions

With the use of sonographic signs of the gallbladder it is possible to select those patients who have an increased chance for conversion of laparoscopic cholecystectomy to an open procedure. It is also possible with the use of sonographic signs to select patient who have an increased chance for upper abdominal pain relief after cholecystectomy.
Conversion is seen in 10 % of the laparoscopic cholecystectomies. Especially in patients with a distended gallbladder or at least two sonographic signs like contracted gallbladder, thickened gallbladder wall, stone impaction, grit or sludge, there is a 3 times higher risk for conversion compared to patients without these signs (25% vs. 7%).
A quarter of the patients is not relieved of upper abdominal pain after a cholecystectomy. Patients without sonographic signs of stone impaction or thickened gallbladder wall of ≥3mm have a 3 times higher chance that the upper abdominal pain remains after cholecystectomy compared to patients with these sonographic signs (36% vs. 12%). Although sonographic findings did not add to the predictive value of age and preoperative symptoms, it can be used in patients in whom the predicted symptom relief rate based on their preoperative symptoms is low, to estimate the chance of symptom

relief. An association between sonographic signs like thickened gallbladder wall or stone impaction and symptom relief was found. As numbers were small, such an association could not reach statistical significance.

Treatment strategy for gallbladder stones (figure 1, flowchart)
Gallstones are frequently found on sonography for upper abdominal pain. Beside that, gallstones can also be found as an additional finding in patients with no upper abdominal pain.
Patients with abdominal symptoms and in whom the possibility of gallstones is considered, should get a sonography soon after the start of the complaints, preferably within 1 or 2 days. Beside the finding of possible gallbladder stones, also the sonographic signs of the gallbladder can than be related to present symptoms.
Based on literature, there is consensus that, patients with gallbladder stones but without symptoms, should not be treated.
In gallstone patients with flatulence, severe acid regurgitation, bloating and belching, with or without upper abdominal pain, one should be reluctant to do a cholecystectomy because there is an increased chance of persistence of upper abdominal pain and dyspepsia in these patients. Sonographic findings did not add to the predictive value of age and preoperative symptoms in our total patient group. However, it seems useful, especially in patients in whom the predicted symptom relief rate is low, to do a sonographic examination of the gallbladder shortly after the onset of symptoms. Not only to demonstrate the presence of a stone but also to look for sonographic signs of the gallbladder that can predict the probability of symptom relief. When sonography shows stone impaction and/or thickened gallbladder wall, one can consider cholecystectomy. A method to not to withhold patients with a negative sonography (i.e. no stone impaction or thickened gallbladder wall) a cholecystectomy would be, when an other episode of upper abdominal pain occurs, to do a new sonographic examination in the search for sonographic signs that make the chance for symptom relief higher.
For gallbladder stone patients with upper abdominal pain and no flatulence, severe acid regurgitation, bloating or belching, cholecystectomie seems indicated. Sonographic findings in these patients do not add to the

predictive value of preoperative symptoms in the prediction of pain relief after cholecystectomy.

To get relief of symptoms after cholecystectomy in patients with grit in the gallbladder, it will probably be necessary to do papillotomy or papil dilatation in addition to the cholecystectomy, to keep transport of grit out of the bile tree possible.

All patients with distention of the gallbladder or at least two of the sonographic signs should be informed about the increased chance for conversion of a laparoscopic cholecystectomy to an open procedure.

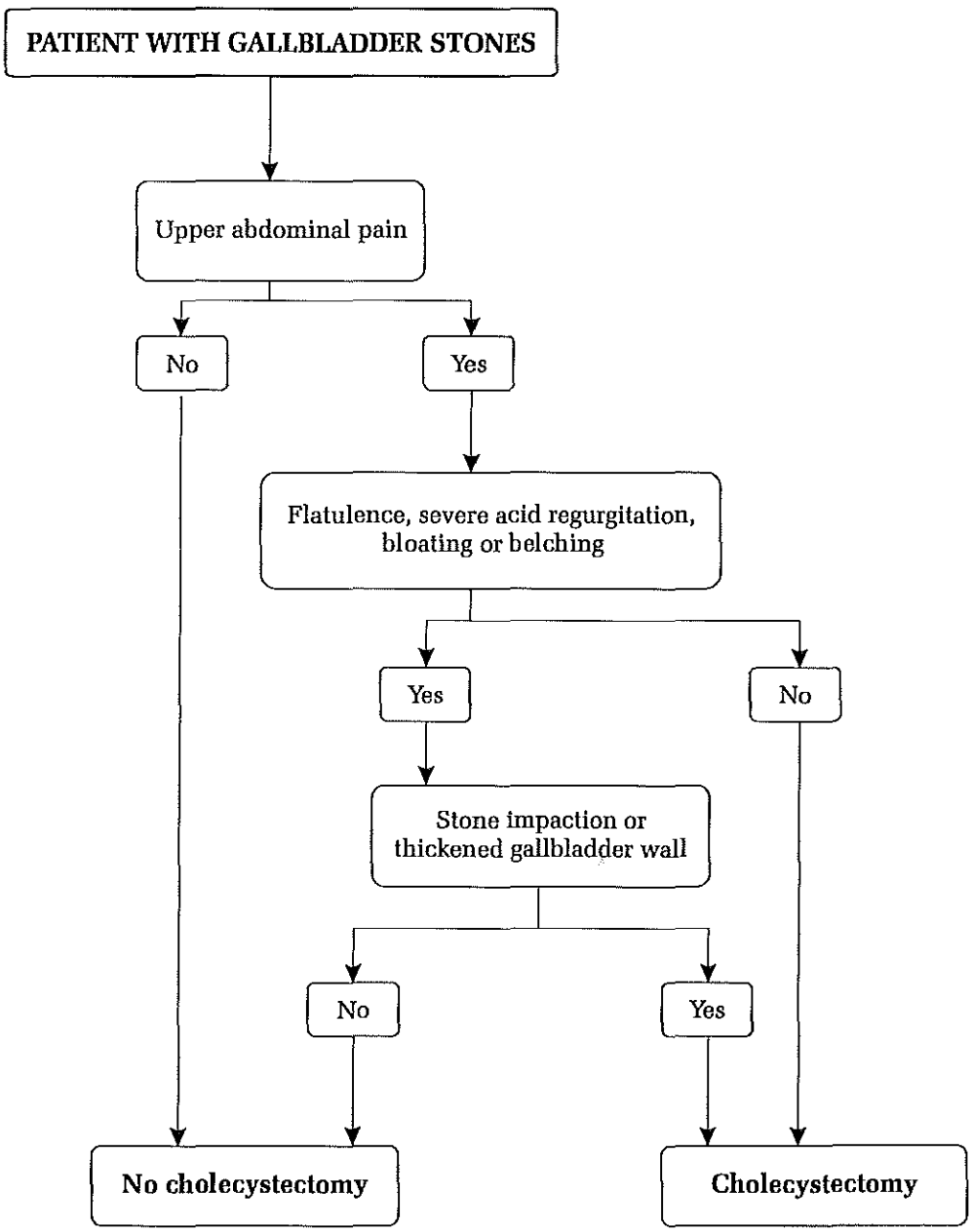
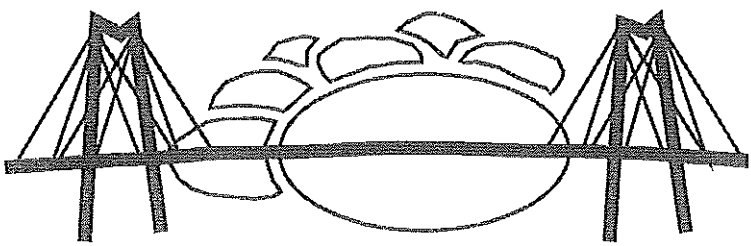


Figure 1. Flowchart of the decision for cholecystectomy based on clinical symptoms and sonographic findings of the gallbladder.

CHAPTER 8

SAMENVATTING EN CONCLUSIES



Samenvatting

Bij echografisch onderzoek voor bovenbuikspijn worden vaak galblaasstenen gevonden. Daarnaast kunnen bij patiënten zonder bovenbuikspijn galblaasstenen gevonden worden als nevenbevinding. De standaard behandeling voor galblaasstenen die tot klachten leiden, is een laparoscopische cholecystectomie (LC). Helaas zijn niet alle patiënten klachtenvrij na een cholecystectomie.
Het lukt niet om bij alle patiënten de cholecystectomie laparoscopisch uit te voeren. Wanneer er zich tijdens de operatie problemen voordoen zal er geconverteerd moeten worden naar een open cholecystectomie (OC).
In dit proefschrift wordt de rol van preoperatief echografisch onderzoek besproken in relatie met het kunnen voorspellen van conversie van de operatie van een laparoscopische tot een open cholecystectomie en met het kunnen voorspellen of patiënten al dan niet klachtenvrij zullen zijn na een cholecystectomie.

Hoofdstuk 1 geeft een overzicht van galsteenlijden; beschreven worden de incidentie van galstenen, symptomen, diagnose, therapie, conversie, postcholecystectomie symptomen, het belang van patiënten selectie voor cholecystectomie en het doel van dit proefschrift.

In *hoofdstuk 2* worden de tekenen gepresenteerd die conversie van een laparoscopische cholecystectomie naar een open cholecystectomie konden voorspellen. Het betreft gegevens uit onze retrospectieve studie over 346 patiënten, die tussen 1 januari 1993 en 1 maart 1996, een laparoscopische cholecystectomie hebben ondergaan.
Conversie vond plaats bij 17.2% van de patiënten. Hydrops van de galblaas, steenimpactie, galblaaswandverdikking ≥3mm en acute cholecystitis konden conversie voorspellen. Uit een logistisch regressie model kwam alleen het echografische teken van hydrops als voorspeller van conversie.

Hoofdstuk 3 behandelt de echografische beelden die de kans op conversie van een laparoscopisch tot open cholecystectomie kunnen voorspellen. In deze prospectieve studie, de 'Rijngast Studie' geheten, werden door

huisartsen, kort na het ontstaan van klachten, 233 patiënten, met voor galblaasstenen verdachte symptomen, ingestuurd voor een echografie van de buik. Bij 8 van de 80 geplande laparoscopische cholecystectomieën werd er geconverteerd tot een open cholecystectomie (10%). Hydrops van de galblaas is het enige losse echografische teken dat significant conversie kan voorspellen (RR 4.5, 95% CI 1.0-20). Ook het vinden van minimaal twee echografische afwijkingen, zoals samengevallen galblaas, steenimpactie, wandverdikking, gruis of sludge kan conversie voorspellen (RR 3.4, 95% CI 1-12.3).

Hoofdstuk 4 beschrijft de waarde van echografische tekenen van de galblaas bij het voorspellen van de lange termijn resultaten na een laparoscopische cholecystectomie. Dezelfde groep patiënten als in hoofdstuk 2, kreeg een gestructureerde enquête in te vullen over het nog aanwezig zijn van preoperatieve klachten. Het percentage correct ingevulde enquête formulieren bedroeg 68%. Deze retrospectieve studie liet zien dat het vinden van gruis in de galblaas bij echografisch onderzoek, geassocieerd is met een hoog relatief risico op het persisteren van buikklachten na een cholecystectomie.

Hoofdstuk 5 geeft de resultaten uit de 'Rijngast Studie' over het kunnen voorspellen van het verdwijnen van bovenbuikspijn na een cholecystectomie. Van de 233 patiënten die door de huisarts werden ingestuurd, werden er bij 107 patiënten galblaasstenen gevonden. Een cholecystectomie werd uitgevoerd bij 85 van deze patiënten. Van 73 patiënten was een 1 jaars follow-up aanwezig. Preoperatieve bovenbuikspijnen waren aanwezig bij 65 van deze patiënten. Het aanwezig zijn van galblaaswandverdikking van 3mm en/of een geïmpacteerde steen in de galblaas nek of ductus cysticus waren significant geassocieerd met het verdwijnen van bovenbuikspijn (OR 4.0, 95% CI 1.1-14.2). Individueel haalde deze tekenen niet het significante niveau. Ondanks dat bij alle patiënten met een hydropische galblaas de bovenbuikspijnen verdwenen waren 1 jaar na cholecystectomie, haalde ook deze relatie niet het significante niveau. Gruis had een significante relatie met het houden van bovenbuikspijn (OR 0.3, 95% CI 0.1-1.0).

Bij 51% van de patiënten in onze studie werd er echografisch geen verdikte galblaas wand of geïmpacteerde steen gevonden. Indien deze patiënten geen LC hadden ondergaan, dan zou het percentage patiënten met postoperatief bovenbuikspijn dalen van 25% tot 12.5%.
Echografie lijkt van waarde bij het selecteren van patiënten voor een cholecystectomie.

Hoofdstuk 6 behandelt de meerwaarde van echografisch kenmerken boven de waarde van patiënten karakteristieken en preoperatieve symptomen bij het voorspellen van het klinisch resultaat na cholecystectomy in verband met galstenen.
Flatulentie, opgeven van maagzuur, opboeren en het hebben van een opgeblazen gevoel, voorspellen het persisteren van pijn in de bovenbuik en dyspepsie bij patiënten die een cholecystectomie hebben ondergaan in verband met galstenen. Oplopende leeftijd voorspelt een hogere kans op het verdwijnen van pijn in de bovenbuik. Deze bevinding berust mogelijk op een nauwkeuriger indicatie stelling vanwege de leeftijd van deze groep patiënten.
In een logistisch regressie model droegen echografische bevindingen van de galblaas niet bij aan de voorspellende waarde van leeftijd en preoperatieve symptomen. Bij patiënten, die gezien hun klachten patroon, een lage kans hadden om klachten vrij te worden (<60%), hadden echografische bevindingen van wand verdikking en/of steenimpactie, wel waarde om de kans op het verdwijnen van klachten te voorspellen. Deze relatie haalde niet het significante niveau. De oorzaak hiervan ligt waarschijnlijk in het feit dat om te kleine patiënten aantallen gaat in deze subgroep. Nieuwe studies met een grotere patiënten aantallen moeten deze associatie tussen echografische afwijkingen van de galblaas en het klachtenvrij worden in specifieke subgroepen in kaart brengen.

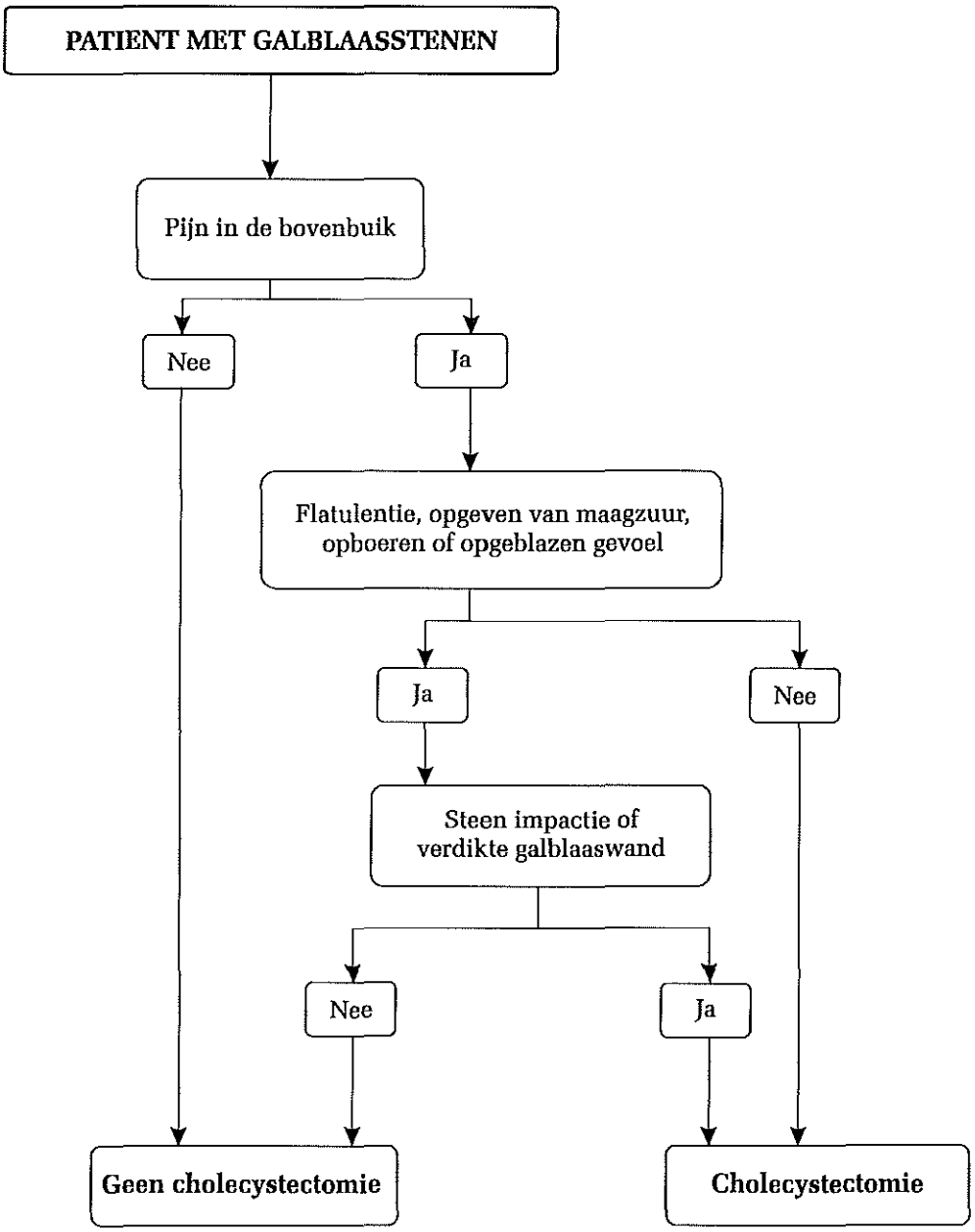
Conclusies

Door het toepassen van echografische criteria van de galblaas is het mogelijk aan te geven dat er een verhoogde kans bestaat op het moeten converteren

van een laparoscopische tot een open cholecystectomie en op het klachtenvrij worden na een cholecystectomie.
Laparoscopische cholecystectomieën worden in 10% geconverteerd tot een open procedure. Met name bij patiënten waarbij hydrops van de galblaas zichtbaar is of meerdere echografische kenmerken van de galblaas worden gezien zoals samengevallen galblaas, steenimpactie, galblaaswand-verdikking, gruis of sludge bestaat er een ruim 3 maal zo groot risico is op conversie in vergelijking met patiënten waarbij deze afwijkingen niet gevonden zijn (25% versus 7%).
Bij een kwart van de patiënten verdwijnt de bovenbuikspijn niet na een cholecystectomie. Patiënten zonder echografische afwijkingen aan de galblaas zoals steenimpactie en/of galblaaswandverdikking van 3mm hebben een 3 keer zo grote kans op het houden van klachten na een cholecystectomie dan patiënten met deze echografische afwijkingen (36% versus 12%). Hoewel de echografische bevindingen van de galblaas niet bijdragen aan de voorspellende waarde die de leeftijd en de preoperative symptomen van de patiënt hebben op het klachtenvrij worden, kan echografie met name bij patiënten, die gezien hun klachtenpatroon, een lage kans hebben op het klachtenvrij worden, de kans op het verdwijnen van klachten aan geven. Een associatie tussen echografische kenmerken van de galblaas zoals wandverdikking en steenimpactie werd bij deze groep patiënten wel gevonden echter deze relaties haalden niet het significante niveau. De oorzaak hiervan ligt waarschijnlijk in het feit dat om te kleine patiënten aantallen gaat het in deze subgroep.

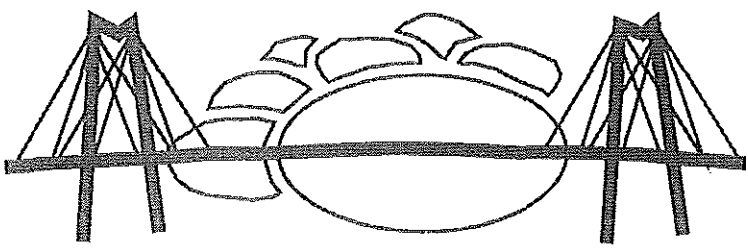
Behandeling strategie voor galblaasstenen (Figuur 1, stroomdiagram)
Bij echografisch onderzoek voor bovenbuikspijn worden vaak galblaasstenen gevonden. Daarnaast kunnen bij patiënten zonder bovenbuikspijn galblaasstenen gevonden worden als nevenbevinding.
Patiënten met voor galstenen verdachte bovenbuikpijn, moeten echografisch onderzocht worden, kort na het ontstaan van de klachten, bij voorkeur binnen 1 of 2 dagen. Dan kunnen, naast het aan tonen van eventuele galblaasstenen, de afwijkingen aan de galblaas gerelateerd worden aan de aanwezige klachten.

Vanuit de literatuur bestaat er consensus dat patiënten met galblaasstenen zonder klachten geen behandeling behoeven.
Bij galblaassteen patiënten met klachten van flatulentie, opgeven van maagzuur, opboeren en het hebben van een opgeblazen gevoel, al dan niet met pijn in de bovenbuik, zal men terughoudend moeten zijn een cholecystectomie uit te voeren in verband met het verhoogde risico op persisteren van pijn in de bovenbuik en dyspepsie. Hoewel echografische bevindingen van de galblaas voor de gehele patiënten groep niet bijdroegen aan de voorspellende waarde van preoperatieve symptomen lijkt het wenselijk om met name bij deze patiënten, die gezien hun klachten patroon, een lage kans op het klachten vrij worden, echografisch onderzoek uit te voeren recent na het ontstaan van de klachten om niet alleen galstenen aan te tonen maar om met name echografische afwijkingen van de galblaas op te sporen die de kans op het verdwijnen van klachten kunnen aangeven. Wanneer bij echografie van de galblaas steenimpactie en/of wandverdikking wordt gevonden kan overwogen worden een cholecystectomie te verrichten. Een methode om patiënten met een negatief echografisch onderzoek (geen steenimpactie of wandverdikking) niet ten onrechte een cholecystectomie te onthouden, zou zijn om het echografische onderzoek van de galblaas te herhalen in een nieuwe periode van klachten.
Bij galblaassteen patiënten met pijn in de bovenbuik zonder klachten van flatulentie, opgeven van maagzuur, opboeren of het hebben van een opgeblazen gevoel lijkt het geïndiceerd om een cholecystectomie uit te voeren. Echografische bevindingen van de galblaas dragen bij deze patiënten niet bij aan de voorspellende waarde van preoperative symptomen op het al dan niet houden van bovenbuikspijn.
Bij patiënten met gruis in de galblaas, zal het, om klachtenvrij te worden, waarschijnlijk nodig zijn om naast de cholecystectomie een extra behandeling toe doen in de vorm van een papillotomie of papil dilatatie, om passage van gruispartikels mogelijk te maken.
Alle patiënten met hydrops of meerdere echografische afwijkingen aan de galblaas moeten geïnformeerd worden dat er een gering verhoogde kans bestaat op het moeten converteren van de laparoscopische cholecystectomie tot een open procedure.



Figuur 1. Stroomdiagram voor de indicatie stelling van een cholecystectomie op basis van klachtenpatroon en echografische bevindingen van de galblaas.

MANUSCRIPTS BASED ON THE "RIJNGAST STUDY"



J.J. van der Velden, M.Y. Berger, H.J. Bonjer, K. Brakel, J.S. Laméris. Can sonographic signs predict conversion of laparoscopic to open cholecystectomy? *Surg Endoscop 1998; 12:1232-5*

J.J. van der Velden, M.Y. Berger, H. Pala, K. Brakel, H.J. Bonjer, J.S. Laméris. Can sonography predict conversion of laparoscopic to open cholecystectomy? A prospective study. *Submitted for publication*

J.J. van der Velden, M.Y. Berger, H.J. Bonjer, K. Brakel, J.S. Laméris. Can sonographic signs predict long-term results of laparoscopic cholecystectomy? *Hepatogastroenterol 1999; 46:3063-7*

J.J. van der Velden, M.Y. Berger, H.J. Bonjer, K. Brakel, A.M. Bohnen, J.S. Laméris. Can sonography predict relief of upper abdominal pain after laparoscopic cholecystectomy? A prospective study. *Submitted for publication*

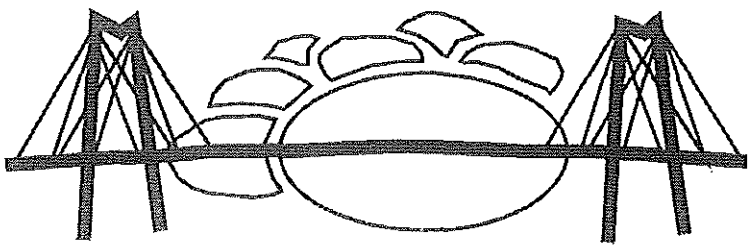
M.Y. Berger, J.J. van der Velden, J.G. Lijmer, H. de kort, A. Prins, A.M. Bohnen. Abdominal symptoms do they predict gallstones? A systematic review. *Scand J Gastroenterol; 2000:70-6.*

M.Y. Berger, J.J. van der Velden, J.S. Laméris, A.M. Bohnen, A. Prins, P.M.M. Bossuyt. Accuracy of a combination of abdominal symptoms and signs in the diagnosis of gallstones. *Submitted for publication*

M.Y. Berger, J.J. van der Velden, T.C. olde Hartman, H.J. Bonjer, A.M. Bohnen, A. Prins, P.M.M. Bossuyt. Abdominal symptoms, do they disappear after cholecystectomy? A systematic literature review and a controlled prospective study. *Submitted for publication*

M.Y. Berger, J.J. van der Velden, J.S. Laméris, A.M. Bohnen, H.J. Bonjer, A. Prins, P.M.M. Bossuyt. Are sonographic findings useful for the prediction of clinical outcome after cholecystectomy when pre-operative symptoms are taken into account? *Submitted for publication*

CO-AUTHORS



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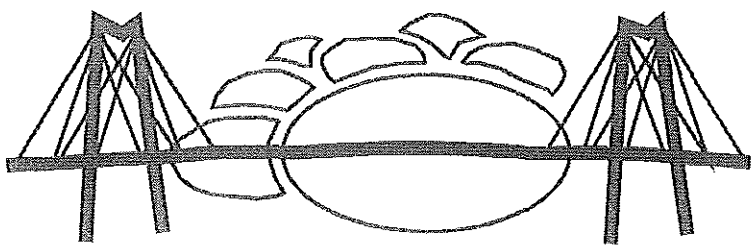
DANKWOORD



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De *'Rotterdam-Rijnmond Multicenter Gallstone study'*, (Rijngast) betrof een gezamenlijk project van de afdelingen Radiologie van het Academisch Ziekenhuis Rotterdam-Dijkzigt en het Huisartsen Instituut van de Erasmus Universiteit te Rotterdam. In deze studie werd samengewerkt met de huisartsen in het Rotterdam Rijnmond gebied, de afdelingen chirurgie en radiologie van het Dijkzigt Ziekenhuis, Haven Ziekenhuis, Holy Ziekenhuis, Schieland Ziekenhuis, St. Clara Ziekenhuis, St. Franciscus Gasthuis, IJsselland Ziekenhuis, Ikazia Ziekenhuis, en Zuider Ziekenhuis, en de afdeling echografie van de Stichting Trombosedienst en Artsenlaboratorium Rotterdam. Allen ben ik zeer erkentelijk voor de goede samenwerking.

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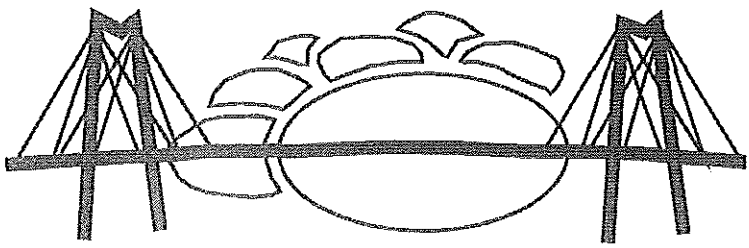
CURRICULUM VITAE



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Gehuwd met Annet Scheer, vader van Marieke, Daan en Nienke.

KLACHTENPROFIELLIJST

S.V.P. bij ieder symptoom **1 vakje** aankruisen
Heeft u de **afgelopen MAAND**, een of meerdere malen last gehad van:

	geen last	weinig last	vrij veel last	heel veel last
1. Misselijkheid	/__/	/__/	/__/	/__/
2. Braken	/__/	/__/	/__/	/__/
3. Opgeblazen gevoel	/__/	/__/	/__/	/__/

	geen last	weinig last	vrij veel last	heel veel last
4. Boeren/oprispingen	/__/	/__/	/__/	/__/
5. Brandend maagzuur	/__/	/__/	/__/	/__/
6. Krampende bovenbuikspijn rechts	/__/	/__/	/__/	/__/
7. Krampende bovenbuikspijn rechts, alleen na vet eten	/__/	/__/	/__/	/__/

	geen last	weinig last	vrij veel last	heel veel last
8. Bovenbuikspijn > 1 uur rechts	/__/	/__/	/__/	/__/
9. Obstipatie (verstopping)	/__/	/__/	/__/	/__/
10. Diarrhee (snelle stoelgang)	/__/	/__/	/__/	/__/

	geen last	weinig last	vrij veel last	heel veel last
11. Winderigheid	/__/	/__/	/__/	/__/
12. Ontkleurde ontlasting (stopverf)	/__/	/__/	/__/	/__/
13. Geelzucht	/__/	/__/	/__/	/__/

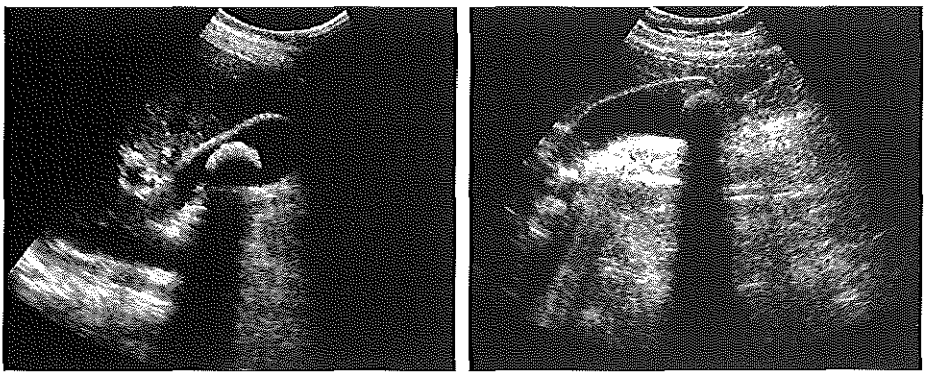


Figure 1a/b

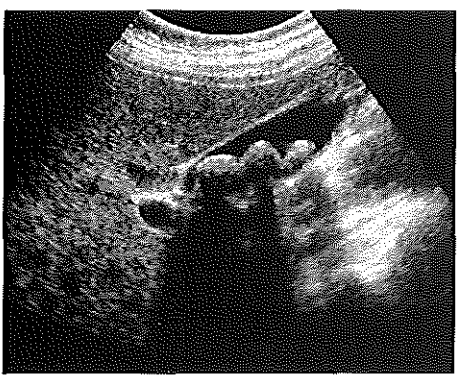


Figure 2

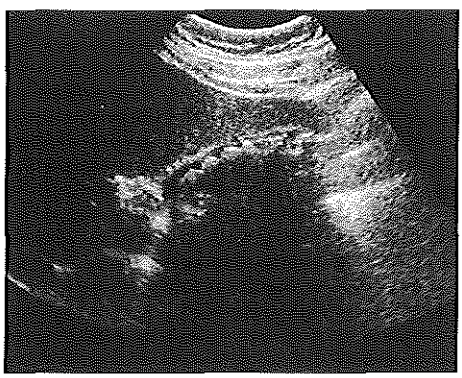
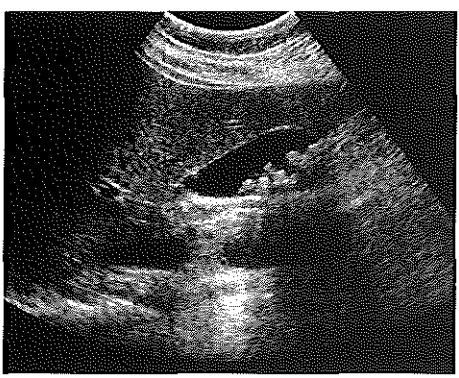


Figure 3



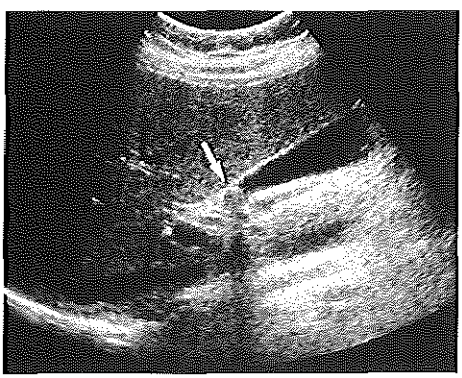


Figure 4 a/b

Figure 1a: Single stone.
Figure 1b: The stone falls in the gallbladder fundus in an upright position.
Figure 2: Multiple stones.
Figure 3: Contracted gallbladder, the gallbladder lumen containes only stones withoutnormal surrounding bile.
Figure 4 a: Stone impaction in the cystic duct or the gallbladder neck.
Figure 4 b: Impaction was considered present when stones (arrow) did not move with the change in patient position, especially in an upright position.

Sonographic signs of gallbladder stone disease

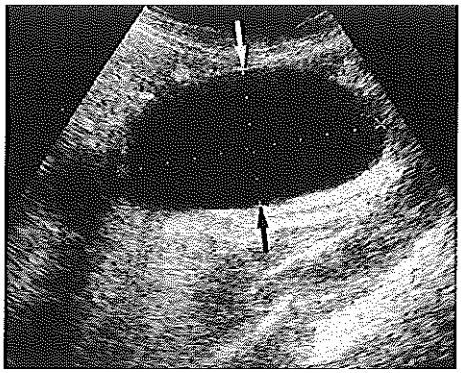


figure 5

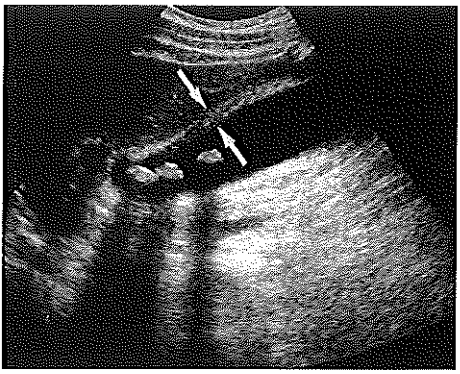
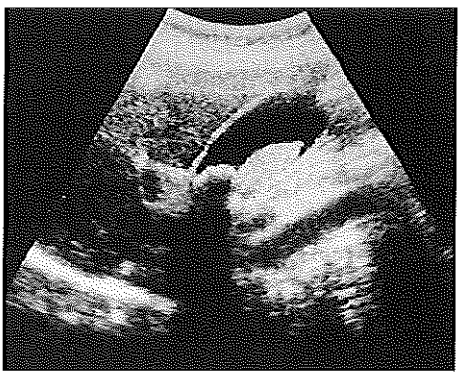


Figure 6



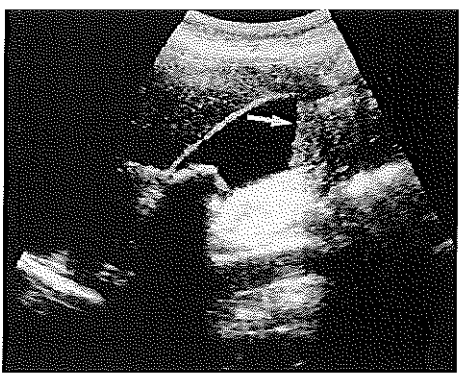


Figure7 a/b

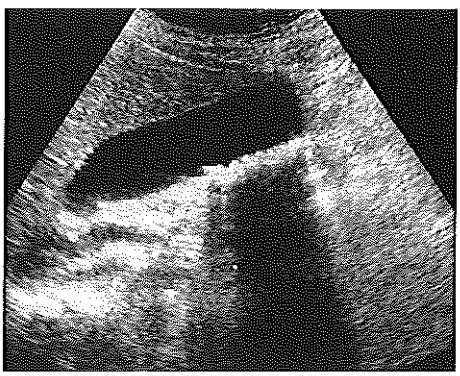


figure 8

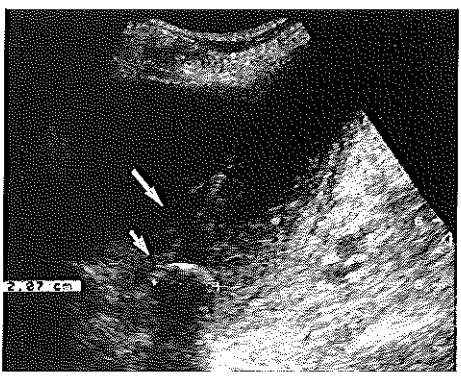


figure 9

Figure 5: Distended gallbladder or hydrops, diameter perpendicular to the longitudinal axis of ≥4.5 cm (arrows).
Figure 6: Thickened gallbladder wall of ≥3 mm (arrows)
Figure 7a: Gallstone in gallbladder neck and sludge.
Figure 7b: In an upright position the gallstone is impacted in the gallbladder neck and the sludge is lying on the bottom of the gallbladder. (arrow)
Figure 8: Grit, stones ≤3 mm.
Figure 9: Acute cholecystitis, thickened gallbladder wall, fluid arround the gallbladder (long arrow) and an impacted stone. (small arrow)