ORIGINAL ARTICLE

Preoperative Prediction Model of Outcome after Cholecystectomy for Symptomatic Gallstones

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The MULGO Group: Borly L, Andersen IB, Bardram L, Christensen E, Sehested A, Kehlet H, Matzen P, Rehfeld JF, Stage P, Toftdahl DB, Gernow A, Højgaard L. Preoperative prediction model of outcome after cholecystectomy for symptomatic gallstones. Scand J Gastroenterol 1999;34:1144–1152.

Background: After cholecystectomy for symptomatic gallstone disease 20%–30% of the patienrs continue to have abdominal pain. The aim of this study was to investigate whether preoperative variables could predict the symptomatic outcome after cholecystectomy. **Methods:** One hundred and two patients were referred to elective cholecystectomy in a prospective study. Median age was 45 years; range, 20–81 years. A preoperative questionnaire on pain, symptoms, and history was completed, and the questions on pain and symptoms were repeated 1 year postoperatively. Preoperative cholescintigraphy and sonography evaluated gallbladder motility, gallstones, and gallbladder volume. Preoperative variables in patients with or without postcholecystectomy pain were compared statistically, and significant variables were combined in a logistic regression model to predict the postoperative outcome. **Results:** Eighty patients completed all questionnaires. Twenty-one patients continued to have abdominal pain after the operation. Patients with pain 1 year after cholecystectomy were characterized by the preoperative presence of a high dyspepsia score, 'irritating' abdominal pain, and an introverted personality and by the absence of 'agonizing' pain and of symptoms coinciding with pain ($P < 0.000001$). In a constructed logistic regression model 15 of 18 predicted patients had postoperative pain (PVpos = 0.83). Of 62 patients predicted as having no pain postoperatively, 56 were pain-free (PVneg = 0.90). Overall accuracy was 89%. **Conclusion:** From this prospective study a model based on preoperative symptoms was developed to predict postcholecystectomy pain. Since intrastudy reclassification may give too optimistic results, the model should be validated in future studies.

Key words: Gallbladder stones; logistic regression model; prospective study; symptomatic outcome

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Treatment of symptomatic gallbladder stones with cholecystectomy is followed by cure or improvement of symptoms in about 90% of patients (1–4). However, in 20%–30% of patients significant pain and dyspeptic symptoms is still reported (1–9). The pathogenesis of gallstone disease may be multifactorial, including increased bile lithogenicity (10), augmented gallbladder volume, reduced gallbladder motility (11), imbalance of nucleating proteins (12), number of pregnancies and postoperative periods (13), and obesity and body composition (14). Previous studies have suggested that gallbladder motility and other physiologic characteristics may have a role in the outcome after cholecystectomy (15, 16). Other studies have compared pain and the presence of abdominal symptoms before and after cholecystectomy (1, 2, 5–7) but with variable rates of success due to different outcome factors (7). Few studies have identified preoperative factors that could predict the symptomatic outcome after surgery (8, 9). The presence of dyspepsia before operation seems related to continued postoperative dyspepsia (8), and psychologic vulnerability may be involved in overall postoperative outcome (17). Furthermore, it is unclear which abdominal symptoms are specifically caused by the gallstones (18), and how gallstones elicit pain (19).

This prospective study was a preoperative investigation of symptoms and gallbladder dynamics and a postoperative evaluation of outcome symptoms and pain after 1 year in patients referred for cholecystectomy owing to symptomatic gallstone disease. The aim was to investigate whether preoperative factors could predict symptomatic outcome after cholecystectomy.

Patients and Methods

Patients

One hundred and two patients referred for elective cholecystectomy owing to symptomatic gallstone disease were included in this 2-year prospective study. The first two were regarded as 'pilot patients' for the organization of the preoperative examinations and did not attend the post-operative follow-up. Patients were consecutively chosen among all those referred to cholecystectomy, following the department's standard criteria for operation for symptomatic gallstone disease (definition: presence of gallstones and socially disabling attacks of pain located in upper right abdominal quadrant). The presence of gallstones was determined by sonography. The following criteria had to be fulfilled to participate in the study: age more than 18 years, absence of pregnancy and lactation, ability to speak and write Danish, and informed consent.

Ethics

Before entering the study all patients were informed about the nature and purpose of the study, and all gave written informed consent. The study protocol was approved by the Ethical Committee for Copenhagen and was in accordance with the Helsinki II Declaration of 1975 as revised in 1983. The patient data file was approved by the Danish Data Protection Agency.

Study design

Before the operation a questionnaire, sonography, and dynamic cholescintigraphy were completed. One year after the operation a new questionnaire was completed.

Preoperative questionnaire

The preoperative questionnaire consisted of 121 questions on personal data and a visual analogue scale (VAS). The patients were asked to rate their pain intensity on a 100-mm scale with the boundaries of 'no pain' on the left and 'worst possible pain' on the right. Patients were requested to mark on the VAS where the pain is when it is worst.

The questions included a non-validated Danish version of the McGill Pain Questionnaire (MPQ). The original MPQ consists of a set of 78 pain descriptors segregated into 20 discrete categories (20). The patients were allowed to choose 1 descriptor from each of the 20 categories (in our study the number of descriptors had to be reduced from the 78 in the

Do your hands often shake or tremble?

Is your appetite always poor?

Do you suffer badly from frequent severe headaches?

Do you usually have great difficulty in falling asleep or staying asleep?

Do you often suddenly become frightened?

Do you often get spells of complete exhaustion or fatigue?

Do you often take tranquillizers or sleeping pills?

Do you often feel pain different places, such as your stomach or your back or your chest?

Do you suffer from nervous disorder?

Do you often have spells of severe dizziness?

Do sudden noises make you jump or shake badly?

Do you usually feel unhappy and depressed?

Does your work fall to pieces when the boss or a superior is watching you?

Does your heart often race like mad for no good reason?

Do you frequently feel faint?

Do you have difficulty in making friends?

Does it make you angry to have anyone tell you what to do?

Do you prefer to keep to yourself ?

Does every little thing get on your nerves and wear you out?

Do frightening thoughts keep coming back in your mind?

Are you extremely shy or sensitive?

Do people usually misunderstand you ?

Fig. 1. Twenty-two questions concerning psychosomatic and neurotic symptoms. Psychologic vulnerability was scored by counting the number of affirmative answers from 12 selected items merged with 10 indifferent items (20). The 12 selected items are shown in italics.

original version to 64, as there are fewer adjectives in Danish than in English). The main purpose of including the MPQ in this study was to look for possible preoperative descriptors that could predict the symptomatic outcome.

There were a further 16 questions on dyspeptic symptoms; a composite score based on yes (= 1) or no (= 0) answers to the 16 questions made up a ranking scale from 0 to 16—that is, the dyspepsia score. Zero represented no dyspepsia, and 16 represented maximal dyspepsia. The scale has not been validated.

The patients were asked whether they were bothered by dysphagia, globus, acid regurgitation, heartburn, nausea, vomiting, flatulence, eructation, borborygmus, diarrhoea, constipation, intermittent constipation and diarrhoea, abdominal distension, rapid satiety, incomplete defecation, and anorexia. In the next section patients were asked whether their dyspepsia coincided with their pain, whether their symptoms were felt as attacks or constant, the duration of symptoms (months or years), and the number of attacks (attacks/month). The final section aimed to measure psychologic vulnerability and consisted of 22 questions on psychosomatic and neurotic symptoms, with yes/no category answers. Psychologic vulnerability was scored by counting the number of affirmative answers to 12 selected items merged with 10 indifferent items (21). The 22 questions are shown in Fig. 1.

Postoperative questionnaire

One year after the operation a self-administered questionnaire was completed by the patients. The questionnaire had the same VAS for pain and questions on dyspepsia as the preoperative questionnaire.

Definition of symptomatic outcome criteria

On the basis of the results 1 year after the operation the patients were categorized both in accordance with the presence of postoperative pain (+/−pain) and in accordance with the presence of postoperative abdominal symptoms (including pain) (+/−symptoms). The presence or absence of pain was determined from the pain VAS, and the presence of other abdominal symptoms from the questions on dyspepsia. In the postoperative questionnaire the patients were asked whether their symptoms had disappeared, partly diappeared, unchanged, or worse. If their symptoms had disappeared and the VAS = 0, they were classified as having no pain. If their symptoms had partly disappeared or were unchanged or worse, they were asked to answer the questions about pain and other abdominal symptoms. If they answered that they were without pain and the VAS = 0 but that they had other abdominal symptoms, these patients were classified as having no pain but still having symptoms. All patients with VAS >0 were classified as having pain.

Gallbladder sonography

The gallbladder volume was determined by sonography (Siemens Sonoline SL-2, Erlangen, Germany, with a 3.5-MHz mechanical sector scanner) with a modified Simpson method (22). The number of stones was noted.

Cholescintigraphy

After an overnight fast the patient was positioned supine under a gamma camera (Orbiter 2LC 7500, Siemens, Erlangen, Germany) with a 140-keV low-energy all-purpose parallel-hole collimator. The detector was placed anteriorly over the right hypochondrium to achieve visualization of the liver, gallbladder, bile duct, and upper small intestines. The camera was connected to a computer (Microdata, Siemens) that enabled simultaneous acquisition of data. Count rates were recorded continuously at one frame per min (cpm). Data acquisition was started at time zero during administration of a bolus injection of 100 MBq ^{99m}Tc EHIDA (sodium *N*-[*N*-1-(2,6-diethylphenyl)carbamoylmethyl]iminodiacetate; Amersham, UK). Recordings were made continuously for 60 min. At time 60 min cholecystokinin octapeptide (CCK-8) (Kinevac, Squibb, N.J., USA), 0.3 ng/min $\times$kg, was infused for 60 min by infusion pump (Ole Dich, Instrument Maker, Hvidovre, Denmark). Recordings and CCK-8 infusion was terminated at 120 min. When the data had been collected, images were replayed from the computer, and the time-activity curves for the gallbladder region, corrected for background and radioactive decay, were generated (23).

The maximum gallbladder ejection fraction from time 60 to time 120 min was calculated as

$$\text{(1) GB EF}_{\max}\% = \frac{\text{cpm}_{\max\ 60\ \pm 10\ \text{min}} - \text{cpm}_{\min\ 120\ \pm 10\ \text{min}} \cdot 100\%}{\text{cpm}_{\max\ 60\ \pm 10\ \text{min}}}$$

The 100-MBq technetium-99m EHIDA dose has an effective dose equivalent of 0.024 mSv/MBq, which gives an effective dose equivalent of 2.4 mSv.

Statistical analysis

Each of the descriptive variables was compared between the groups with different postoperative outcome by using the Mann–Whitney rank sum test (quantitative variables) or the Fisher exact probability test or chi-square test (qualitative variables). Variables showing some association ($P < 0.10$) with development of postoperative symptoms or pain were considered for inclusion in the logistic regression analysis, in which variables were combined in a model to predict, from the included preoperative variables, the 1-year postoperative status with regard to symptoms or pain. The final model was obtained by using the backward elimination technique until all included variables were significant ($P < 0.05$). In all the regression analyses and analyses based on the derived regression models, missing values were replaced by the grand mean value of the variable in question.

The number of missing values can be extracted from the information presented in Table I and Table II, which show the number of patients in whom each variable was available. The

Table I. Distribution of 1-year postoperative outcome in accordance with preoperative cholescintigraphy and sonography

	1-year postoperative dyspepsia including pain					1-year postoperative pain				
	Present	*n*	Absent	*n*	*P*	Present	*n*	Absent	*n*	*P*
Cholescintigraphy: GB motility										
Maximum ejection fraction (%)*	70 (10–99)	12	64 (6–97)	25	0.68	70 (17–99)	9	59 (6–97)	28	0.47
Non-visible GB (*n*)	10 (43%)	23	21 (45%)	47	1.00	6 (38%)	16	25 (46%)	54	0.58
Sonography										
GB volume (ml)*	21 (6–70)	24	23 (2–140)	42	0.83	20 (8–70)	16	23 (2–140)	50	0.84
More than four gallstones (*n*)	12 (50%)	24	20 (46%)	44	0.80	8 (47%)	17	24 (47%)	51	1.00

GB = gallbladder.
* Median and range.

Table II. Distribution of 1-year postoperative outcome according to preoperative clinical variables

	1-year postoperative dyspepsia including pain					1-year postoperative pain				
	Present	*n*	Absent	*n*	*P*	Present	*n*	Absent	*n*	*P*
Preoperative variables (median and range)										
Pain intensity, VAS 0–100	87 (3–99)	27	86 (38–98)	45	0.83	86 (3–98)	18	88 (35–99)	54	0.67
Dyspepsia, score 0–16	6 (2–12)	24	4 (0–10)	45	0.0002	6 (2–12)	18	4 (0–11)	51	0.004
Psychic vulnerability, score 0–12	3 (0–10)	26	2 (0–8)	45	0.03	3 (1–10)	18	2 (0–8)	53	0.011
Duration of symptoms, years	3 (0.2–23)	29	1 (0.08–24)	48	0.1	3 (0.3–23)	20	1 (0.08–24)	57	0.06
Duration of attacks, h*	24 (0–192)	23	4 (0–122)	44	0.07	4 (0–192)	14	5 (0–122)	53	0.86
No. of attacks/month†	6 (0–20)	20	2 (0–48)	45	0.12	8 (0–20)	13	2 (0–48)	52	0.03
Preoperative variables (*n*)										
Acid regurgitation	16 (57%)	28	15 (31%)	48	0.03	13 (65%)	20	18 (32%)	56	0.02
Heartburn	12 (41%)	29	11 (23%)	48	0.12	10 (50%)	20	13 (23%)	57	0.04
Constipation	11 (39%)	28	8 (17%)	46	0.05	9 (47%)	19	10 (18%)	55	0.02
Early satiety	15 (54%)	28	8 (19%)	48	0.002	9 (45%)	20	15 (27%)	56	0.17
Trouble passing all stool	12 (41%)	29	9 (18%)	49	0.04	8 (40%)	20	13 (22%)	58	0.15
Repelled by food	11 (38%)	29	5 (10%)	48	0.007	7 (35%)	20	9 (16%)	57	0.11
Symptoms coincide with pain	17 (61%)	28	41 (89%)	46	0.007	10 (53%)	19	48 (87%)	55	0.003
Constant symptoms	7 (24%)	29	3 (6%)	48	0.04	7 (35%)	20	3 (5%)	57	0.002
Eating habits changed	20 (84%)	25	26 (55%)	47	0.04	14 (88%)	16	32 (57%)	56	0.04
Symptoms first as attacks, now constant	9 (47%)	19	4 (14%)	28	0.02	8 (57%)	14	5 (15%)	33	0.01
All activity stops due to symptoms	24 (96%)	25	34 (76%)	45	0.05	18 (100%)	18	40 (77%)	52	0.03
Problems at home since symptoms started	5 (18%)	28	2 (4%)	48	0.09	5 (26%)	19	2 (4%)	57	0.009
Lack of appetite	9 (44%)	27	8 (17%)	48	0.01	10 (53%)	19	10 (18%)	56	0.006
Strong headache	17 (59%)	29	12 (25%)	49	0.003	12 (60%)	20	17 (29%)	58	0.02
Sleeplessness	11 (39%)	28	13 (27%)	49	0.31	11 (55%)	20	13 (23%)	57	0.01
Often pains different places	20 (69%)	29	20 (42%)	48	0.03	14 (70%)	20	26 (46%)	57	0.07
Keep to yourself	8 (31%)	26	4 (9%)	45	0.02	8 (44%)	18	4 (8%)	53	0.001

* Only the 67 patients who had symptoms in attacks were analysed.
† The same as above, but two patients did not complete the question.

number of missing values replaced by the grand mean in the logistic regression analyses is presented directly below the results presented in Table III and Table IV.

The logistic regression model was as follows:

$$(2)\ Y = b_0 + b_1 \times z_1 + \ldots\ldots + b_p \times z_p \quad \text{(equation 1)}$$

where Y is the logit—that is, $Y = \log_e (P/(1-P))$—P being the probability of pain with regard to symptoms 1 year after the operation (that is, $P = e^Y/(1+e^Y)$) (equation 2), b_0 is a constant, z_1–z_p are the scorings of the P variables, and b_1–b_p are the regression coefficients corresponding to each of the variables z_1–z_p. From the logistic regression model the probability (P) of symptoms with regard to pain 1 year after the operation for a given patient can be estimated from equation 2 by inserting Y from equation 1, using the obtained regression coefficients in the model and the variable scorings of the patient. The predicted odds ratio for the presence/absence of pain with regard to symptoms is given by the ratio $P/(1-P)$.

Results

Patients

One hundred patients entered the study. All completed the preoperative questionnaire, and cholecystectomy was performed in all. Twenty patients dropped out. The 20 dropouts

Table III. Logistic regression model to predict pain 1 year after cholecystectomy

Variable	Scoring	Coefficient	Standard error	*P* value
Pain agonizing	Yes, 1; No, 0	−3.629	1.207	0.0036
Introverted personality*	Yes, 1; No, 0	3.824	1.409	0.0083
Symptoms coinciding with pain	Yes, 1; No, 0	−2.546	0.980	0.01
Pain rasping	Yes, 1; No, 0	3.803	1.602	0.02
Dyspepsia score	0–12	0.304	0.143	0.04
Constant		−0.464	0.977	0.64

Model 2 = 46.59; d.f. = 5; $P < 0.000001$.
* Introverted personality covers the the question 'Do you prefer to keep to yourself?' from the 22 questions concerning psychosomatic and neurotic symptoms.

Table IV. Logistic regression model to predict dyspeptic symptoms 1 year after cholecystectomy

Variable	Scoring	Coefficient	Standard error	*P* value
Symptoms coinciding with pain	Yes, 1; No, 0	−2.667	0.794	0.0012
Strong headaches	Yes, 1; No, 0	1.559	0.651	0.0019
Dyspepsia score	0–12	0.310	0.151	0.043
Repelled by food	Yes, 1; No, 0	1.614	0.811	0.05
Constant		−0.919	0.805	0.26

Model 2 = 35.66; d.f. = 4; $P < 0.000001$.

consisted of 12 who had still not replied after 3 reminding letters with the postoperative questionnaire and 8 who chose to leave the study for different reasons. Eighty patients completed both the preoperative questionnaire and the postoperative questionnaire 1 year after surgery. These 80 patients were included in the study. There were 71 women and 9 men. The median age was 44 years, and the range 20–77 years. No significant differences were found between these patients and the 20 dropouts with regard to age and sex distribution.

Operation

Laparoscopic cholecystectomy was performed in 68 patients, and mini-cholecystectomy in 5. In seven the procedure was converted to open conventional cholecystectomy.

Symptomatic outcome 1 year after cholecystectomy

Of the 80 patients 30 (38%) had symptoms 1 year after the operation, whereas 50 had no symptoms in accordance with the definitions given above. Twenty-one (26%) had pain 1 year after the operation, whereas 59 had no pain.

In 50 (62%) patients all symptoms had completely disappeared, whereas 28 (35%) answered that their symptoms had partly disappeared. In one the symptoms were unchanged, and in one they were worse

Preoperative gallbladder motility and sonography.

As can be seen in Table I, the gallbladder (GB) motility as determined by cholescintigraphy did not differ between postoperative symptomatic and asymptomatic patients. Nor did the preoperative sonographic data with regard to GB volume and stone number show any differences between patients with and without pain and dyspepsia postoperatively (Table I).

Preoperative McGill Pain Questionnaire in relation to operative outcome

For the single pain-describing words 'splitting' ($P = 0.02$), 'rasping' ($P = 0.03$), and 'agonizing' ($P = 0.00049$) a highly significant difference was seen between the groups with and without pain after the operation.

Preoperative questionnaire variables outcome predictors

The postoperative outcome in accordance with preoperative clinical variables is shown in Table II. The preoperative pain intensity as measured with the VAS score was similar in those with and without postoperative symptoms. The preoperative dyspepsia score was significantly higher in patients with postoperative symptoms ($P = 0.0002$ in patients with dyspepsia including pain; $P = 0.004$ for pain alone). Psychologic vulnerability was also more prominent in patients with postoperative symptoms ($P = 0.03$ in patients with dyspepsia including pain; $P = 0.011$ for pain alone).

With regard to gallstone history patients with a longer history tended to do worse after operation. Those with dyspepsia including pain had longer attacks preoperatively ($P = 0.07$), and those with pain alone postoperatively had more attacks per month ($P = 0.03$) than those who were cured.

As can be seen in Table II, several preoperative clinical values differed significantly between those who were cured

Table V. Pocket chart for preoperative prediction of pain 1 year after cholecystectomy

Variable	Points to be added
Pain agonizing	
Yes	−36
No	0
Introverted personality	
Yes	38
No	0
Symptoms coinciding with pain	
Yes	−25
No	0
Pain rasping	
Yes	38
No	0
Dyspepsia score	
0	0
1	3
2	6
3	9
4	12
5	15
6	18
7	21
8	24
9	27
10	30
11	33
12	36
Constant	−5

Sum =
Y = Sum/10 =
Note only one number should be used for each variable.

Table VI. Pocket chart for preoperative prediction of dyspeptic symptoms 1 year after cholecystectomy

Variable	Points to be added
Symptoms coinciding with pain	
Yes	−27
No	0
Strong headaches	
Yes	16
No	0
Dyspepsia score	
0	0
1	3
2	6
3	9
4	12
5	16
6	19
7	22
8	25
9	28
10	31
11	34
12	37
Repelled by food	
Yes	16
No	0
Constant	−9

Sum =
Y = Sum/10 =
Note only one number should be used for each variable.

and those who were not. Significant differences were found in the following categories: dyspepsia (acid regurgitation, heartburn, constipation, early satiety, trouble passing stools), other gastrointestinal symptoms, behavioural aspects, and symptoms related to psychologic vulnerability.

Logistic regression analysis

The final logistic regression models for preoperative prediction of pain and dyspeptic symptoms 1 year after cholecystectomy are shown in Table III and Table IV, respectively. The fact that some patients had improved but still had pain or dyspepsia was not taken into consideration in the analysis.

In Table III it appears that introverted personality, 'rasping pain', and a high dyspepsia score were independently associated with the presence of pain 1 year postoperatively (positive coefficients), whereas agonizing pain and other symptoms coinciding with pain were associated with no 1-year postoperative pain (negative coefficients).

Table IV shows that strong headaches, a high dyspepsia score, and being repelled by food were associated with the presence of 1-year postoperative symptoms (positive coefficients), whereas symptoms coinciding with pain were associated with a symptom-free 1-year outcome (negative coefficient). These two models can be expressed as simple pocket charts (Table V and Table VI) from which an estimate of Y to one decimal can easily be obtained from the preoperative variables of any given patient by the simple addition of numbers. Using Table VII, the obtained value of Y can be transformed to the probability (likelihood) of experiencing pain or symptoms 1 year after cholecystectomy.

Example 1: estimation of the likelihood of 1-year postoperative pain in a patient with: agonizing pain, no introverted personality, no symptoms coinciding with pain, no rasping pain, and a dyspepsia score of 4. When Table V is used, Y becomes (−36 +0 +0 +0 +12 −5)/10 = −2.9. This corresponds to a 1-year postoperative pain likelihood of 5% (Table VII). Thus this patient would be expected to benefit from cholecystectomy.

Example 2: estimation of the likelihood of 1-year postoperative pain in a patient with no agonizing pain, an introverted personality, symptoms coinciding with pain, no rasping pain, and a dyspepsia score of 6. When Table V is used, Y becomes (0 +38 −25 +0 +18 −5)/10 = 2.6. This corresponds to a 1-year postoperative pain likelihood of about 93% (Table VII). Thus this patient would not be expected to benefit from cholecystectomy.

In the same manner the likelihood of 1-year postoperative symptoms can be estimated by using Tables VI and VII.

Distribution of estimated probabilities (likelihoods) of pain and symptoms 1 year postoperatively

For the patients who actually had pain 1 year postoperatively the median estimated 1-year postoperative like-

Table VII. Correspondence between Y (the logit) and *P* (the probability or more precisely the likelihood)

Y	*P*	
−6.0	0.00	
−5.0	0.01	
−4.0	0.02	Favourable outcome of cholecystectomy likely
−3.0	0.05	
−2.2	0.10	
−1.7	0.15	
−1.4	0.20	
−1.1	0.25	
−0.8	0.30	
−0.6	0.35	
−0.4	0.40	
−0.2	0.45	
0.0	0.50	—
0.2	0.55	
0.4	0.60	
0.6	0.65	
0.8	0.70	
1.1	0.75	
1.4	0.80	
1.7	0.85	
2.2	0.90	
3.0	0.95	
4.0	0.98	Unfavourable outcome of cholecystectomy likely
5.0	0.99	
6.0	1.00	

lihood of pain was 0.81 (range, 0.13–1.00). For the patients who did not have pain 1 year postoperatively the median estimated 1-year postoperative likelihood of pain was 0.05 (range, 0.00–0.90). Thus there was some overlap of the likelihoods between those with postoperative pain and those without. Considering a likelihood of 0.5 as the cut-off point between prediction of pain (>0.5) and no pain (<0.5), 71 of the 80 patients (88.7%) were correctly classified (15 of the 21 with pain and 56 of the 59 without pain) (sensitivity, 0.71; specificity, 0.95; PVpos = 0.83; PVneg = 0.90; kappa = 0.88). For the patients who actually had symptoms 1 year postoperatively the median estimated 1-year postoperative likelihood of symptoms was 0.68 (range, 0.10–0.99). For the patients who did not have symptoms 1 year postoperatively the median estimated 1-year postoperative likelihood of symptoms was 0.17 (range, 0.03–0.76). Thus there was more overlap of the likelihoods between those with postoperative symptoms and those without than for those with postoperative pain. When a likelihood of 0.5 is used as the cut-off point between the prediction of symptoms (>0.5) and no symptoms (<0.5), 63 of the 80 patients (78.7%) were correctly classified (18 of the 30 with symptoms and 45 of the 50 without symptoms) (sensitivity, 0.60; specificity, 0.90; PVpos = 0.78; PVneg = 0.79; kappa = 0.78).

Discussion

The introduction of the laparoscopic cholecystectomy technique has led to a reduction in hospital stay, morbidity, and convalescence. Because of the easiness of this procedure it is conceivable that the indications for surgical treatment for gallbladder stone disease will be widened, with a subsequent increased rate of cholecystectomy (24). A questionnaire showed that 17 of 19 specialists in gastroentrology have widened their indications for cholecystectomy since the introduction of laparoscopic cholecystectomy (25).

Because cholecystectomy may not increase life expectancy (26), and at least a subgroup of patients may not be cured by the operation, and because of a small risk of severe bile duct injury, the indications for cholecystectomy should be strict and well defined. In addition, further information about which patients may not be expected to improve after the operation should be obtained and evaluated.

Previous studies have suggested that the type of operation (open versus mini versus laparoscopic cholecystectomy) may not explain negative outcomes (2, 3, 27). The role of the type of cholecystectomy in late symptomatic outcome is debatable, and the small number of our patients undergoing open cholecystectomy precludes further analysis. Also, there seems to be no differences in outcome whether the operation was performed for well-defined acute cholecystitis or electively for 'symptomatic' gallstones (4). In contrast, psychic vulnerability (3, 17) and dyspeptic symptoms may be predictors of poorer outcome (9). A pain history of long duration may also be related to postoperative dissatisfaction (8).

Our results confirm the negative influence on outcome of a long duration of pain, occurrence of dyspepsia as a main complaint, and psychic vulnerability.

The preoperative pain intensity (preoperative VAS) was nearly identical in the different postoperative groups of patients. The best explanation is that pain was the main indication for cholecystectomy. It shows that patients with little pain were not cholecystectomized. A VAS only measures one dimension; that was the reason for including the MPQ. By means of the MPQ three important pain descriptors—splitting, rasping, and agonizing—were identified. These were shown to have predictive value for the postoperative outcome.

The composite score, based on the 16 dyspepsia questions, provided useful predictive information.

We were not able to show any independent predictive value of preoperative gallbladder emptying. Gallbladder emptying has been related to gallstone formation (28), but it has not previously been investigated as a potential predictor of positive or negative outcome after cholecystectomy. Two studies claim that cholecystectomy alleviates acalculous biliary pain in patients with a reduced gallbladder ejection fraction (29, 30). Almost half of the patients (44%) in this study had a non-visible gallbladder on cholescintigraphy. This finding had no predictive value. Whether the cystic duct was closed or the function of the sphinter of Oddi was disturbed can be speculated on; none of the patients in this study had acute cholecystitis when the cholescintigraphy was performed, and there is evidence that the cystic duct reopens

after percutaneous gallbladder drainage in patients with acute cholecystitis (31). Accordingly, the most likely explanation is a disturbed function of the sphinter of Oddi, in accordance with studies showing increased bile reflux in some persons with gallstones (32, 33).

Increased gallbladder pressure is the main theory with regard to biliary pain, and in acute cholecystitis there is a correlation between volume and pressure (31). In this study gallbladder volume had no predictive value.

In one study abdominal symptoms differed in accordance with the number of gallbladder stones (34). This association was not found in this study. Because of the limited number of patients in our study the risk that some real differences between the defined groups may have been overlooked (a type-2 error risk) is not negligible. Our results therefore need to be substantiated in independent patients.

We have confirmed an association between psychic vulnerability and postcholecystectomy outcome (6, 14). The explanation for this is unknown, but some sort of visceral hyperalgesia, as in the irritable bowel syndrome (35), may be responsible and should be further explored.

Our study also confirms previous studies showing an overall high (90%) satisfaction rate after cholecystectomy but a relatively high occurrence of pain (30%) and dyspepsia (9). This may be partly explained by the dropouts, which probably mainly include those completely cured.

The aim of the present study was also to develop a logistic regression model for prediction of postoperative pain and dyspepsia. On the basis of the present data the developed prediction model had a high PVpos of 0.83 and high PVneg of 0.90. Overall, 89% of the patients could be classified correctly. However, it must be emphasized that the analysis focused on outcome in terms of pain and/or dyspepsia and not on the patient's statement with regard to being cured, improved, unchanged, or worse.

In the regression model we used the grand mean of the variable in question to replace missing values. The justification is that the grand mean is a neutral value that does not provide any artificial discriminative information—and therefore no bias—in the analysis but enables as many data as possible to be included in the analysis.

The number of variables tested statistically for potential inclusion in the logistic regression analyses was only about 10% of the total number of patients. The number of variables in the final logistic regression models was only 6% (Table III) and 5% (Table IV). This is accordance with the commonly accepted rules for inclusion of variables in regression models. Nevertheless, since any regression model will always be particularly well adapted to the patient data used for its development, the results of this study—in particular, the predictive value of the logistic regression models—need substantiation by confirmation in independent patients.

The indications for cholecystectomy are not well defined. Thus, in a consensus panel approach with two panels, one consisting entirely of surgeons and one consisting of a mix of relevant specialists, the panels were asked to rate a series of possible indications for cholecystectomy. For from one-third to half of all indications the panels were unable to reach agreement (36). In an audit of 252 cholecystectomized patients the appropriateness of cholecystectomy was rated. In 44% of the patients the surgical panel did not reach agreement. Most of the patients who would have been rated inappropriately had vague symptoms only (37). However, both the consensus panel approach and the audit approach were retrospective in nature. In contrast, the logistic regression model in our study is based on prospectively collected information.

The general applicability of the logistic regression model depends on its confirmation in future studies. When such confirmation has taken place, the model will be an important additional tool in determining the best treatment strategy in patients with symptomatic gallstones.

Acknowledgements

Grant support was provided by The Danish Medical Research Council. Karina E. Berg and Jette E. Mathisen are gratefully acknowledged for their expert secretarial assistance

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Received 15 March 1999
Accepted 12 July 1999