

Longitudinal changes in health and symptoms following laparoscopic cholecystectomy

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Abstract

Background: Spinal anaesthesia is a common technique for day case

Aim: To investigate the progress of recovery up to 6 months following laparoscopic cholecystectomy concerning patients' perception of their health, symptom occurrence, degree of distress caused by each symptom and if gender differences exist in relation to these variables.

Results: Patients' perception of health improved, mainly caused by increased physical well-being, between day 7 and 1 month. Symptom occurrence and symptom distress decreased rapidly during the first post-operative week. Pain and loss of appetite were further resolved at 1 month. However, 30% of the patients had at least one distressful symptom at 6 months which calls for further investigation.

Conclusion: Post-operative distressful symptoms last longer than generally thought.

Keywords: Laparoscopic cholecystectomy; Day case; Post-operative symptoms.

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Introduction

Laparoscopic cholecystectomy (LC) is one of the most common surgical procedures in the western world. Approximately 50,000 cholecystectomies are performed every year in England and 500,000 in the United States [1]. Gallstone disease typically affects fertile women aged 40-60 years who are slightly overweight [2]. LC is a treatment intended to relieve pain and other symptoms of gallstones. Pain disappears in most patients after surgery. However, some patients are not relieved of their symptoms and, in some cases, the onset of new symptoms has been reported [3].

Investigations into long term outcome following LC have earlier focused on persistent symptoms of gallbladder disease such as pain, dyspeptic symptoms and gastrointestinal related quality of life [4-11]. Resolution of abdominal pain ranges from 57% to 88%, and failure to achieve pain relief is the major reason for poor long term results after LC [11]. Although biliary pain is specific for gallstones, 80% of the patients report other abdominal symptoms [12-14]. A pain history of long duration, constipation and abdominal bloating is related to poor outcome after LC [12-14]. In an earlier qualitative study [15] we investigated patients' experiences during the first post-operative week following LC. Post-operative pain varied to a great extent and several patients had a relapse of pain on the third day lasting up to 1 week. Moreover, bloating was a problem. However, how distressing the experienced symptoms are in the long-term perspective is scarcely investigated.

Improvement in gastrointestinal symptoms and health related quality of life following cholecystectomy has been reported [6, 7, 9-11, 13]. Further, patients' perception of subjective health after LC has also been reported to improve after a followup of on average 17.1 months [5], or remain unchanged three months following surgery [10]. Gender differences exist among healthy individuals but whether men and women manifest different symptoms in the short term and the

long term during their postoperative recovery following LC has not been clearly established.

The present study focuses on the long term outcome following LC. The primary aim was to investigate the progress of recovery for up to 6 months with special reference to patients' perception of their health, symptom occurrence, and degree of distress caused by each symptom. A secondary aim was to examine whether gender differences exist in relation to these variables.

Methods

Patients

The study was conducted at the outpatient surgery department at a university hospital setting in Sweden. During the period of May 2002 to September 2005 patients who fulfilled the following inclusion criteria were consecutively invited to participate: ultrasonography documented cholelithiasis, scheduled for LC, physical status class I-II according to American Society of Anaesthesiologists, 20-70 years old, and able to understand and speak Swedish. Moreover, the patients needed support from an adult carer at home for the first night following LC. Exclusion criteria for patients undergoing LC in day surgery were immunodeficiency, HIV, previous upper gastrointestinal tract surgery and proven malignancy.

We randomized 100 patients to undergo LC either as outpatients (n=50) or inpatients (n=50). Seventy-seven patients finally received surgery and treatment according to protocol, and of these a total of 73 patients responded to questionnaires about symptom occurrence, symptom distress and subjective health during the whole 6 months study period. Details regarding patient selection and drop-outs are published in a previous paper comparing short-term outcome after in- and outpatient surgery, respectively [16]. As only minor

differences were found between the outpatient and the inpatient groups, these are treated as one single group in this report.

Data collection

Sociodemographic and medical data

A questionnaire designed for this study was used for the collection of background data such as age, sex, marital status and work. Medical data, physical status, body mass index (BMI) and sick leave were collected from the patients' medical records.

Health Index (HI)

The HI first published by Nordström et al. [17], consists of 10 items concerning energy, temper, fatigue, loneliness, sleep, vertigo, bowel function, pain frequency, mobility and general health. For each statement, the participants were asked to rate their health status during the previous week on a four-graded Likert scale, ranging from 1 to 4. The scores are summarized to form a HI ranging from 10 to 40. The higher the score, the better the self-rated health.

A factor analysis performed by Nordström et al. [17] defined two factors – emotional well-being (EWB), consisting of four items (energy, temper, fatigue and loneliness) and physical well-being (PWB), consisting of five items (mobility, sleep, vertigo, bowel function and pain). The general health item was related to general well-being and was thus excluded from the specific subsets [17]. The HI has been tested for reliability in different patient populations with satisfactory results (Cronbach's α 0.77–0.85) [17, 18]. Data from a Stockholm population group showed a Cronbach's α of 0.74 [19]. The instrument also has been shown to have discriminant validity [17]. The patients responded to the HI pre-operatively and post-operatively at 1 week, 1 month and 6 months.

The Symptom, Frequency and Distress Questionnaire (SFD-LC)

The SFD-LC is a modified version of the Symptom, Frequency, Intensity and Distress Questionnaire (SFID-SCT), developed for patients undergoing stem cell transplantation [20]. Out of the original 23 symptoms, 18 symptoms were considered as relevant for LC patients and used in this study: nausea, vomiting, pain, shivers, fever, breathing difficulties, coughing, tiredness, sore mouth/throat, loss of appetite, diarrhoea, constipation, sleeping disturbances, reduced mobility, depression, anxiety, concentration difficulties and memory deficiencies. The excluded symptoms (loss of hair, mouth dryness, and changes of taste, skin changes, and changed body image) were specifically intended for stem cell transplantation and therefore omitted. In this way the validity of the instrument was weighed against scientific and clinical knowledge of post-operative symptoms following LC. For each symptom listed above, the respondents

were first asked if they perceived the symptom ('Yes' or 'No'). If they reported the symptom they were then asked how distressful they perceived each symptom to be (0 = 'No distress', 1 = 'A little distress', 2 = 'Much distress' and 3 = 'Very much distress'). The questionnaire was answered every evening during the first post-operative week, and after 1 month and 6 months following LC. The variable symptom distress is the total number of distress for each individual.

Pain Diary

A pain diary was designed for the study, where patients rated their experienced level of pain every evening on post-operative days 1 to 7, and after 1 month and 6 months, using a 100 mm visual analogue scale (VAS) [21].

Statistical methods and data management

To test differences between two unrelated groups, the Mann-Whitney U-test was used. Friedman's non-parametrical analysis of variance was used to analyze time dependent data, followed by Dunn's test for post hoc testing between consecutive time points. In order to evaluate hypotheses of variables in contingency tables, the Chi-square test was used or, in the case of small expected frequencies, Fisher's Exact Test. McNemar test was used to test differences in proportions between two dependant groups. Significance was accepted at $p < 0.05$, but for data on postoperative symptoms on an item level, multiple comparisons were made and therefore $p < 0.01$ was considered significant. Analyses were conducted using STATISTICA 7.0 (StatSoft Inc., Tulsa, OK) except for Dunn's test where GraphPad Prism 4.02 was used (GraphPad Software Inc., San Diego, CA).

Ethical approval

The ethics committee at the Karolinska University Hospital, Huddinge approved the study protocol (Reference number 434/00).

Results

Socio-demographic and medical data for the sample is presented in Table 1. No gender differences were found.

Perceived health

Subjective health was reported pre-operatively and at day 7, 1 month and 6 months following LC. A significant improvement over time was seen for the total HI score ($p < 0.001$), as well as for the PWB subscale score ($p < 0.001$) (Figure 1). The only significant improvement in health perception between consecutive time points was seen between day 7 and 1 month post-operatively for total HI and PWB, respectively ($p < 0.001$). During that time interval, the HI scores

Table 1 Socio-demographic and medical data for the sample of patients (n=73) undergoing laparoscopic cholecystectomy. Data are given in numbers (percent), or median (range). All gender differences were non significant.

	Total	Males (n=19)	Females (n=54)
Age, years	45 (22-67)	48 (25-58)	44 (22-67)
Marital status married-cohabiting : single	59 (81) : 14 (19)	16 (84) : 3 (16)	43 (80) : 11 (20)
Education elementary school : high school/uni- versity	17 (22) : 56(78)	4 (21) : 15 (79)	13 (24) : 41 (76)
Work status, working/studying : sick leave/ pension	63 (86) : 10 (14)	19 (100) : 0 (0)	45 (83) : 9 (17)
BMI (body mass index) kg/m²	26 (21-41)	27 (22-35)	26 (21-41)
Duration of disease, months	14.5 (1-420)	12 (2-78)	12 (1-420)

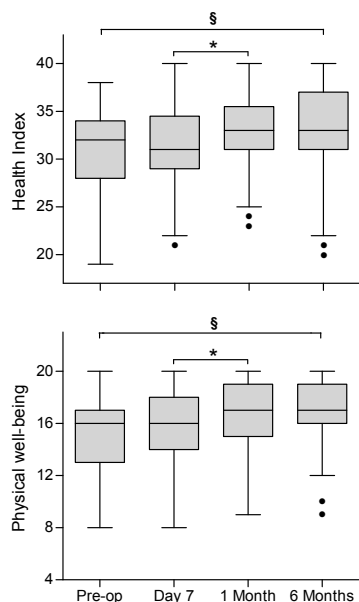


Figure 1 Changes in Health Index and the subscale Physical well-being over four different time points preoperatively (Pre-op), and post-operatively at day 7, 1 month, and 6 months, respectively, in 73 patients after laparoscopic cholecystectomy. Significant changes over time by Friedman's ANOVA are denoted by §, $p < 0.001$. Significant differences between consecutive time points by post-hoc Dunn's test are denoted by *, $p < 0.001$. Data are presented as median (line), 25-75% (grey box), non-outliers (whiskers) and extremes (●).

improved in 42 patients, deteriorated in 10 patients, and did not change in 21 patients. When comparing HI measured on an item level pre-operatively, and at 6 months, a greater proportion of patients reported a significant improvement with regard to pain frequency ($p < 0.001$) and bowel function ($p = 0.041$) (Table 2).

Females reported significantly lower scores on the total HI day 7 (30.7 vs 32.7; $p = 0.042$) and on the PWB subscale compared with men (15.4 vs 16.5; $p = 0.038$). No other significant differences were found between the gender groups at any of the measured time points.

Symptom occurrence

In total, the 73 patients reported 527 symptoms (median 7, range 1–15) on the first postoperative day. After 6 months, the corresponding figure was 163 symptoms (median 1, range 0–13). At that time 18 patients (25%) had 1–2 symptoms and 25 (34%) had three or more symptoms. Females reported a significantly higher

frequency of symptoms on day 1 (7.7 vs 5.9; $p = 0.032$) and day 7 (2.4 vs 0.9; $p < 0.001$) in comparison to males. No significant gender differences were seen at the other time points regarding the number of symptoms.

The occurrence of each symptom over time is presented in Figure 2. The three most frequently reported symptoms on the first post-operative day were pain (68%), reduced mobility (67%), and tiredness (67%). These symptoms were also most frequently reported on day 7. Fifteen of the 18 symptoms (pain, reduced mobility, tiredness, nausea, loss of appetite, constipation, coughing, sleeping disturbances, difficulty to concentrate, sore mouth/throat, depression, anxiety, shivers, breathing difficulties, and vomiting) were significantly less frequently reported on post-operative day 7 in comparison to the first post-operative day.

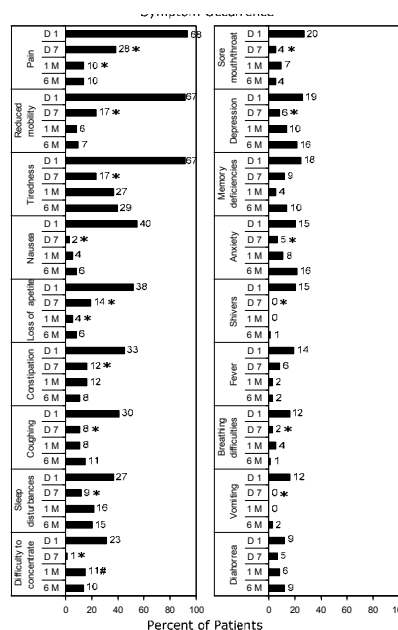


Figure 2 Symptom occurrence. The bars show the percent of patients reporting ongoing symptoms at post-operative day 1 (D1), day 7 (D7), 1 month (1M), and 6 months (6M) following laparoscopic cholecystectomy ($n = 73$). Numbers present the actual number of patients. Significant differences between consecutive time points are denoted by * $p < 0.01$.

At one month, pain and loss of appetite were the only symptoms that were significantly less frequently reported in comparison to

Table 2 Health Index measured pre-operatively and at six months following laparoscopic cholecystectomy ($n = 73$). Data are given as numbers and percent of the patients' rating their symptoms as 'rather bad/very bad'.

Health Index 'Rather bad/very bad'	Pre-operatively n (%)	6 months post-operatively n (%)	p-values
Energy	9 (12)	5 (7)	ns
Temper	6 (8)	7 (5)	ns
Fatigue	33 (45)	24 (33)	ns
Loneliness	6 (8)	5 (7)	ns
Sleep	19 (26)	14 (19)	ns
Vertigos	10 (14)	4 (5)	ns
Bowel function	23 (32)	10 (14)	0.041
Pain	32 (43)	9 (12)	0.001
Mobility	3 (4)	1 (1)	ns
General health	11 (15)	9 (12)	ns

day 7, whereas difficulty when trying to concentrate was reported significantly more often. No other symptom reached a significant change in occurrence between one week and one month. After 6 months, no statistically significant differences in symptom occurrence were seen in comparison to one month.

Symptom distress

Fifty patients (68%) reported 'much/very much' distress of at least one symptom on the first post-operative day. The median number of distressful symptoms was 2, range 0–12. The number of patients reporting at least one much distressful symptom after 1 week, 1 month and 6 months were 13 (18%), 14 (19%), and 22 (30%), respectively, a difference that failed to reach significance. The frequency of 'much/very much' distress for each symptom over time is presented in Figure 3. The three most commonly distressing symptoms on the first post-operative day were pain (45%), reduced mobility (40%) and tiredness (36%). In 6 of the 18 symptoms (i.e. pain, reduced mobility, tiredness, nausea, loss of appetite, and constipation) 'much/very much' distress was significantly less frequently reported on post-operative day 7 in comparison to the first post-operative day.

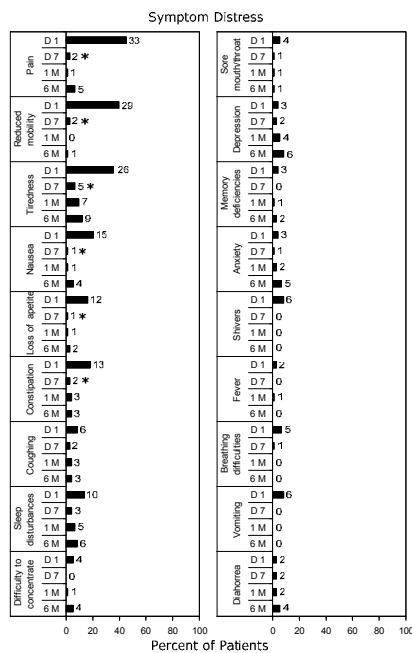


Figure 3 Symptom distress. The bars show the percent of patients reporting symptoms as 'much/very much' distressing at post-operative day 1 (D1), day 7 (D7), 1 month (1M), and 6 months (6M) following laparoscopic cholecystectomy (n=73). Numbers present the actual number of patients. Significant differences between consecutive time points are denoted by * $p < 0.01$.

At one month after surgery, tiredness was the most frequent distressing symptom reported by 10% of the patients. In comparison to 1 week after surgery, there were no differences with regard to the frequency of distressing symptoms. At 6 months after surgery, tiredness was still reported as the most frequent distressing symptom (12%), followed by sleeping disturbances (8%) and depression (8%), but in comparison to one month, no significant changes in the frequency of distressing symptoms were seen.

Table 3 presents the appearance and disappearance of distressful symptoms following LC. Data is dichotomized regarding symptom distress (low distress = no or little distress; high distress = much/very much distress) for all the 18 symptoms in the SFD-LC scale. The total number of reported distressful symptoms decreased significantly between day 1 and day 7 ($p < 0.001$), but increased again between 1 and 6 months ($p = 0.012$).

In comparison with males, females had a higher proportion of symptoms rated as distressing on post-operative days 1 and 7, when the sum of all 18 symptoms was analyzed (no data shown). However, the proportion of females presenting at least one distressful symptom did not reach significance compared with men at any of the measured time points.

Pain intensity

The highest VAS scores for pain were reported on the first post-operative day. A significant decrease was seen between day 1 and day 7 ($p < 0.001$), but at later time points no further differences in pain intensity reached significance (Figure 4). When comparing pain intensity (VAS) between females and males, no significant differences were found between the groups at any of the measured time points.

Sick leave

Sixty-three patients (86%) were employed, and 58 could return to their work within one week after surgery. Two women needed convalescence for one extra week, and two women and one man had two additional weeks of convalescence.

Discussion

This study focuses on the development of patients' perception of health, symptom occurrence, and symptom distress during the first 6 months following LC. Of 73 patients responding to questionnaires the first week after LC, all were successfully followed-up for 6 months.

The patients' perception of their health was unaffected 1 week after surgery compared to the pre-operative state, suggesting a very rapid recovery after LC for most patients. Thereafter, the perception of

Table 3 Appearance and disappearance of distressful symptoms over time following laparoscopic cholecystectomy. Data have been dichotomized to low (no/little distress) and high distress (much / very much distress), respectively for the 18 symptoms in the Symptom, Frequency and Distress Scale in all 73 patients.

Changes in level of distress	Day 1 vs Day 7	Day 7 vs 1 month	1 month vs 6 months
Constantly low distress	1124	1263	1235
Decreasing over Time (high to low)	165	18	24
Increasing over Time (low to high)	8	26	46
Constantly high Distress	17	7	9
Total opportunities	1314	1314	1314
	$p = <0.001$	ns	$p = 0.0012$

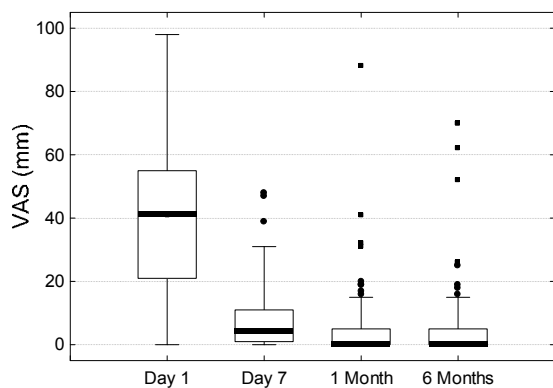


Figure 4 Pain score by Visual Analogue Scale (VAS, mm) among patients (n=73) following laparoscopic cholecystectomy. The bars show the 25-75 percentile, median scores = thick line, whiskers = non outlier range, filled circles = outliers and squares = extremes.

subjective health significantly improved over time, mainly related to an improvement in the physical well-being subscale between day 7 and 1 month post-operatively. Thus, the time course of health improvement after LC has, to some extent, been clarified for this healthy cohort of patients. Several patients were close to the maximum value of the HI, even before surgery, and thus could not improve further. This can have caused a ceiling effect that distorted the results. We think that it might be interesting to investigate patients in poorer health, i.e. those excluded from this study.

Other investigations only measured perceived health at one single postoperative time point for each patient, reporting health improvement after 1 year (n=257) [22], and 17 months (range 2-32 months, n=56) [5], respectively. It should be noted to the contrary, however, that Quintana et al [10] found no improvement in physical health three months after LC (n=509) and that Giurgu et al [23] reported that emergence of gastrointestinal symptoms 60 months after LC surgery are commonly reported. The vast majority of patients who reported persisting diarrhoea were women while men reported no change in bowel function [23]. A significantly improved bowel function was reported by our patients after 6 months compared with pre-operatively. One problem when comparing different studies is the utilization of different scoring systems for health or quality of life. We used the HI which measures subjective health, emotional and physical well-being, while other investigators used SF 36, a health related quality of life instrument [5, 10, 11, 24].

The patients reported a great number of symptoms on the first post-operative day, but most of them were resolved within the first post-operative week. After one month no further significant improvement in symptom occurrence was noted. Some symptoms were resolved, but new symptoms appeared, leaving the overall prevalence constant although highly dynamic. Weinert et al [11] reported that 6 months following cholecystectomy, out of 2481 patients, 41% had one or two symptoms and 15.5% of the patients had three or more symptoms. Our corresponding figures were somewhat inverted i.e. 25 and 34%, respectively. In line with our study, symptoms occurring de novo have been reported [6, 25, 26].

The most frequently reported post-operative symptoms were pain, reduced mobility and tiredness. The rapid decrease in pain-score during the first post-operative week suggest that this mainly refers to the surgical trauma rather than to symptoms of gallstone disease. Other investigators have reported persistence of abdominal pain ranging from 13% to 37% after cholecystectomy [14, 27]. Persistent abdominal pain is the leading cause of surgical treatment failure (15.2%) [11]. Moreover, unresolved pain is correlated with pre-operative bloating, and constipation [25]. In agreement with our results, reduced mobility after LC has been reported to be a problem

during the first few post-operative days [27]. As many as 23% of our patients reported this symptom on the seventh post-operative day, but only 10% after 1 and 6 months.

To fully understand how persisting symptoms affect patients, one must not only consider the presence of symptoms, but also how distressing they are. Few studies have assessed the distress of symptoms in a longitudinal perspective following LC. Finan et al [5] investigated sixteen gastrointestinal symptoms after cholecystectomy where symptom distress of diarrhoea was rated to be 1.3 out of 4, not significantly different from pre-operative scores. In the present

study, pain, reduced mobility and tiredness were the most distressing symptoms the first post-operative week. Interestingly, at 1 and 6 months, numerous new symptoms appeared. We speculate that this might be because the patients' symptoms did not depend solely on gallstones. That 30% of the patients had at least one 'much' distressing symptom at 6 months should be distressing for the caregivers and calls for further investigations. However, it might also describe a normal variation of symptom distress in a relatively healthy cohort of persons. For example, through the entire measured period of 6 months, the most persistent distressing symptom was tiredness, reported to be 'much/very much' distressing by approximately 10% of the patients. In a Swedish normal population, severe tiredness is reported by 10% of the females and 5% of the males [28]. Thus, the reported tiredness 6 months after LC seems to be close to the population baseline.

Following LC, Swedish patients have the right to be on sick-leave for the first post-operative week without a doctor's certificate. In our study, this was sufficient for the majority of patients. Pain and medico-cultural traditions are the main factors responsible for prolonged convalescence after LC. To minimize pain and the duration of convalescence, a multi-modal analgesic treatment in combination with short, standardized instructions is recommend [29].

Studies focusing on gender differences in the recovery after LC are scarce, despite the fact that LC is relatively common also among men. In the present study, females reported significantly more symptoms on day 1 and day 7. The overall level of distress associated with these symptoms was also significantly higher in women on the first post-operative day. They also perceived poorer health and worse physical well-being one week after surgery than the male group. This is in accordance with Stefaniak et al [30], who reported that women perceive more post-operative complaints, indicating that they might recover differently from men.

We did not test for gender differences concerning symptom occurrence or distress for each of the 18 symptoms included in SFD-LC or for single items of HI. One important reason for this is that the statistical power of Fischer's exact test or the Chisquare test decreases rapidly when the prevalence of an investigated factor is low. With 19 and 54 subjects in the two groups, respectively, power is 80% to detect a difference in prevalence between 80 and 40% but only 12% to detect a difference between 20 and 10%. Although this is a small group of patients, the findings on the total occurrence of symptoms and prevalence of high distress at 6 months after LC are of clinical interest and should be further investigated in a larger study.

Conclusion

Patients' perception of health improved moderately but significantly over time, an effect mainly caused by increased physical well-being between day 7 and 1 month after LC. Both symptom occurrence and symptom distress decreased rapidly during the first postoperative

week. Only the symptoms of pain and loss of appetite were further resolved at 1 month and thereafter no changes in symptom occurrence were seen. However, 30% of the patients had at least one distressful symptom at 6 months. The occurrence of pain and bowel dysfunction had significantly decreased at 6 months compared with preoperatively.

Further research on persistent distress and gender differences, may lead to a more effective management of symptoms following LC.

References

1. NHS Institute for Innovation and Improvement, Focus on cholecystectomy – a guide for commissioners. 2006.
2. Anand, A.C., et al., Analysis of symptomatic patients after cholecystectomy: is the term post-cholecystectomy syndrome an anachronism? *Trop Gastroenterol*, 1995. **16(2)**:126–31.
3. Berger, M.Y., et al., Is biliary pain exclusively related to gallbladder stones? A controlled prospective study. *Br J Gen Pract*, 2004. **54(505)**:574–9.
4. Berger, M.Y., et al., Abdominal symptoms: do they predict gallstones? A systematic review. *Scand J Gastroenterol*, 2000. **35(1)**:70–6.
5. Finan, K.R., et al., Improvement in gastrointestinal symptoms and quality of life after cholecystectomy. *Am J Surg*, 2006. **192(2)**:196–202.
6. Gui, G.P., et al., Is cholecystectomy effective treatment for symptomatic gallstones? Clinical outcome after long-term follow-up. *Ann R Coll Surg Engl*, 1998. **80(1)**:25–32.
7. Mentis, B.B., et al., Gastrointestinal quality of life in patients with symptomatic or asymptomatic cholelithiasis before and after laparoscopic cholecystectomy. *Surg Endosc*, 2001. **15(11)**:1267–72.
8. Middelfart, H.V., et al., Pain and dyspepsia after elective and acute cholecystectomy. *Scand J Gastroenterol*, 1998. **33(1)**:10–4.
9. Niranjani, B., S. Chumber, and A.K. Kriplani, Symptomatic outcome after laparoscopic cholecystectomy. *Trop Gastroenterol*, 2000. **21(3)**:144–8.
10. Quintana, J.M., et al., Health-related quality of life and appropriateness of cholecystectomy. *Ann Surg*, 2005. **241**:110–118.
11. Weinert, C.R., et al., Relationship between persistence of abdominal symptoms and successful outcome after cholecystectomy. *Arch Intern Med*, 2000. **160(7)**:989–95.
12. Bates, T., et al., Influence of cholecystectomy on symptoms. *Br J Surg*, 1991. **78(8)**:964–7.
13. Borly, L., et al., Preoperative prediction model of outcome after cholecystectomy for symptomatic gallstones. *Scand J Gastroenterol*, 1999. **34(11)**:1144–52.
14. Luman, W., et al., Incidence of persistent symptoms after laparoscopic cholecystectomy: a prospective study. *Gut*, 1996. **39(6)**:863–6.
15. Barthelsson, C., et al., Patients' experiences of laparoscopic cholecystectomy in day surgery. *J Clin Nurs*, 2003. **12(2)**:253–9.
16. Barthelsson, C., et al., Outpatient versus inpatient laparoscopic cholecystectomy: a prospective randomized study of symptom occurrence, symptom distress and general state of health during the first post-operative week. *J Eval Clin Pract*, 2008.
17. Nordström, G., C. Nyman, and T. Theorell, Psychosocial adjustment and general state of health in patients with ileal conduit urinary diversion. *Scand J Urol Nephrol*, 1992. **26**:139–47.
18. Forsberg, C., The sense of well-being in a group of patients with gastro-intestinal cancer. 1996, Karolinska Institutet: Stockholm.
19. Forsberg, C. and H. Björvell, Swedish population norms for the GHRI, HI, and STAI-state. Quality of life research. *Scand J Caring Sci*, 1993. **2**:349–56.
20. Larsen, J., et al., Health-related quality of life in women with breast cancer undergoing autologous stem-cell transplantation. *Cancer Nurs*, 1996. **19(5)**:368–75.
21. Clarke, P.R.F. and G. Spear, Reliability and sensitivity in the self-assessment of well-being. *Bull Br Psychol Soc*, 1964. **17(55)**:18.
22. McMahon, A.J., et al., Symptomatic outcome 1 year after laparoscopic and minilaparotomy cholecystectomy: a randomized trial. *Br J Surg*, 1995. **82(10)**:1378–82.
23. Giurgiu, D.I., et al., Laparoscopic common bile duct exploration: long-term outcome. *Arch Surg*, 1999. **134(8)**:839–43; discussion 843–4.
24. Cristensen, T. and H. Kehlet, Postoperative fatigue. *World J Surg* 1993. **17**:220–5.
25. Ure, B.M., et al., Long-term results after laparoscopic cholecystectomy. *Br J Surg*, 1995. **82(2)**:267–70.
26. Vander Velpen, G.C., S.M. Shimi, and A. Cuschieri, Outcome after cholecystectomy for symptomatic gall stone disease and effect of surgical access: laparoscopic v open approach. *Gut*, 1993. **34(10)**:1448–51.
27. Young, J. and B. O'Connell, Recovery following laparoscopic cholecystectomy in either a 23 hour or an 8 hour facility. *J Qual Clin Pract*, 2001. **21(1–2)**: 2–7; discussion 8.
28. Folkhälsainstitutet, Hälsa på lika villkor. 2007: Östersund.
29. Bisgaard, T., H. Kehlet, and J. Rosenberg, Pain and convalescence after laparoscopic cholecystectomy. *Eur J Surg*, 2001. **167(2)**:84–96.
30. Stefaniak, T., et al., Psychological factors influencing results of cholecystectomy. *Scand J Gastroenterol*, 2004. **39(2)**: 127–32.