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Quality of Life After Surgery in Candidates of Laparoscopic and Open Cholecystectomy: A Comparison Study

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Abstract

Background: Nowadays quality of life (QOL) is an important part of health and measuring health-related QOL after surgery is necessary for decision-making by patients and surgeons. To assess post cholecystectomy QOL, documentation of high quality care has been subjected to extended discussions, and the use of patient-reported outcome satisfaction for quality improvement has been advocated for several years.

Objectives: The aim of this study was to compare quality of life after surgery in candidates of laparoscopic and open cholecystectomy.

Patients and Methods: This study was an optional part of a longitudinal study for comparison of quality of life in candidates of laparoscopic (LC) and open cholecystectomy (OC). One hundred consecutive cases of hospitalized patients, aged 20 to 65 years, at two hospitals of Karaj, Iran (Imam Khomeini and Alborz), were recruited in the study from May to December 2011. Patients were divided to two groups based on the order of admission and the surgeons' and patients' preference. Patients were evaluated with the medical outcomes study 36-item short-form health survey (SF-36). Quality of life was measured at three points of time (the baseline was two and four weeks after surgery) using this health questionnaire. Differences between baseline time periods of two and four weeks were compared by independent-samples t-test and within groups the time periods were compared by the paired-sample t-test.

Results: Two weeks after the operation, in the LC group, the QOL scores decreased significantly in physical functioning, physical status, body pain and emotional status (for all of them $P \leq 0.01$), whereas, in the OC group all the aspect of QOL decreased (for all of them $P < 0.01$), with the exception of body pain ($P = 0.982$) and social functioning ($P = 0.502$). Four weeks after the operation, the QOL scores of the LC group, in every aspect increased and became significantly higher than the preoperative baseline ($P < 0.001$ for all parameters); while in the OC group only in the aspects of body pain ($P < 0.001$), general health ($P = 0.003$), and social functioning ($P < 0.001$) exceeded the preoperative level. Between-group analysis indicated that the LC group had significantly better outcome scores after four weeks compared to the OC group, in all aspects ($P < 0.05$ for all of them) with the exception of general health ($P = 0.052$). The results of the repeated measures analysis showed that there was a significant difference between the two groups during the three follow-up periods in the aspect of physical status ($P = 0.008$), vitality ($P = 0.015$), general health ($P = 0.048$) and emotional status ($P = 0.003$).

Conclusions: Quality of life is an important factor affecting medical and surgical treatment, as well as decision-making. Improvement of short-term quality of life after laparoscopic cholecystectomy in comparison to open cholecystectomy proves the obvious superiority of LC over OC.

Keywords: Quality of Life, Cholecystectomy, Laparoscopy, Laparotomy

1. Background

Gallbladder diseases are very common in industrialized countries. Complicated gallstone disease is the most frequent biliary disorder for which surgical management is regularly required. Therefore, cholecystectomy is a common abdominal surgical intervention (1). Symptomatic cholecystolithiasis are managed with three techniques including open, small-incision and laparoscopic surgery (2). Nowadays, laparoscopic surgery is usually preferred over open laparotomy. Nearly 750000 cases of cholecystectomies are treated by the laparoscopic method, each year in the United States (1, 3, 4). As laparoscopic cholecystectomy gained more acceptance as the approach of choice for gallbladder disease in the early 1990s, more practice

decreased the operation time significantly from several hours to around 60 minutes or less, also covesation rate of laparoscopic cholesystectomy to open proceedure hase reduce to around 5%. These advances are due to rapid technological advances in the laparoscopic approach (5). Despite numerous cholecystectomy surgeries performed daily globally, little evidence exists on the assessment of postsurgical quality of life (QOL) in patients.

Measuring health-related QOL after surgery is essential for decision making by patients and surgeons (6). To evaluate post-cholecystectomy QOL, documentation of high quality care has been performed, and attempts for quality improvement have been made for several years based on patient reports. Though, little research has been published investigating QOL after cholecystectomy; moreover, most current literature lacks systematic data on patient-centered outcomes (1). In evaluating treatment results, it is important to consider patients' satisfaction regarding their quality of life following surgical management (5). Quality of life cannot be directly estimated and observed, while its definition is clearly defined. The World Health Organization (WHO) defines "quality of life" as the determination of physical, mental and psychosocial condition of an individual. To characterize a patient's "quality of life," the term "Health-Related Quality of Life" (HRQOL) was introduced to clinical practice. There are several other factors, which, besides the entire operation, can have an influence on the quality of life of patients operated for uncomplicated cholecystolithiasis. These biases can significantly change the final results of QOL of these patients (7, 8). Factors influencing the quality of life can be divided to subjective (physical and mental condition, social situation, interpersonal relations and [quality and quantity of interpersonal contact]), and objective factors (the patient's general condition based on additional examinations, clinical condition, emotional and economic status, as well as the quality and number of social contacts). Studies dealing with the quality of life are performed using questionnaires, which can be divided to two groups. Generic questionnaires determine the patient's general condition, including psychosomatic and social spheres. Based on the study of Korolija et al., for evaluation of surgical effects, the following QOL instruments were recommended; for benign esophageal and gallbladder disease, the gastrointestinal quality of life index (GIQLI) or the quality of life in reflux and dyspepsia (QOLRAD) together with SF-36 or the PGWB; for obesity surgery, the Impact of weight on quality of life-lite (IWQOL-Lite) with the SF-36; for colorectal cancer, the FACT-C or the EORTCQLQ-C30/CR38; and for inguinal and renal surgery (5, 6).

2. Objectives

The aim of this study was to assess QOL after open or laparoscopic cholecystectomy, to gain a more clear insight that will allow better decision-making by patients and surgeons.

3. Patients and Methods

This study was an optional part of a longitudinal study to investigate quality of life in candidates for laparoscopic and open cholecystectomy. One hundred consecutive cases of hospitalized patients with cholecystolithiasis and chronic cholecystitis were recruited at our department. The sample size was calculated by the G*Power software with the use of the sample size formula (Equation 1):

$$\frac{2 \times (z_{1-\alpha} + z_{1-\beta})^2 \alpha^2}{d^2} \quad (1)$$

The expected power (1-β) for this study was 0.8. Inclusion criteria were as follows, having an age between 20 and 65 years and being elective candidates for cholecystectomy. Therefore, patients with acute cholecystitis, which were operated at the emergency department, or patients over 65 years old were excluded from the study. Convenient sampling was performed from May to December 2011 and continued until each group was composed of 50 individuals. Patients were divided to two groups based on the order of admission and the surgeons and patients' preference for LC or OC. Laparoscopy was performed for all patients by two surgeons in each hospital and patients in the open cholecystectomy group were operated on by two other surgeons with similar experience in surgery. The patients themselves or their close relatives were able to read and understand the questionnaires. Informed consent was obtained from all patients. Ninety-seven patients completed the questionnaires, including 49 cases with LC and 48 with OC. Three patients with incomplete follow-up were excluded from the study. There was no significant difference between these two groups regarding age, sex and preoperative quality of life in six subscales. No serious complications occurred in these patients after the operation. Quality of life was measured at three points (baseline, two weeks and four weeks after the operation) using the SF-36 health questionnaire. The SF-36 health questionnaire consists of eight subscales: physical functioning, role functioning, body pain, general health, vitality, social functioning, emotional status, and mental health. Taking into account these subscales, we could calculate component summary scores to reach a global measure for physical and mental functioning. The Physical Component Summary

(PCS) consists of the following subscales; physical functioning, role functioning, body pain, and general health. The mental component summary (MCS) comprises of the following subscales; vitality, social functioning, emotional status, and mental health. It is scored on a five point Likert scale with a range from zero (most negative) to four (most positive). Scores on all the subscales are transformed linearly to a possible range of 0 - 100; higher scores indicate more favorable physical functioning/psychological wellbeing. All of the patients were evaluated for four weeks. Patients were visited by surgeons every week after surgery for one month. Researchers visited the patients every week and evaluated their wellbeing and filled the questionnaire during the second and fourth week after surgery.

3.1. Statistical Analysis

Statistical analysis was performed using the SPSS software (Statistical Package for Social Sciences, V 11.5). Analysis of the data distribution was assessed by the Kolmogorove-Smirnove test. In order to show whether the variance of data in the two groups are equal or not, the Leven test was used. Mean and standard deviation were calculated for normal variables and median with interquartile range (IQR) described the non-normal variables. For normally distributed data, independent-sample t-test and paired-sample t-test were used; for non-normal variables, Mann Whitey U test and Wilcoxon test (nonparametric independent and two related sample comparison) was used to compare variables. univariate analysis was used to make adjustment for imbalances in baseline variables that are related to the outcome, such as social functioning and physical functioning. A Repeated Measures analysis with Greenhouse-Geisser test of within-subjects effects was used to determine if significant differences existed between and within groups for each aspect of QOL scores at follow-up periods. A P value of 0.05 was considered statistically significant.

4. Results

A total of 100 patients, with cholecysthiasis and chronic cholecystitis, were enrolled in this study with mean age of 45.64 $\pm$ 8.63 (Rang: 20 - 63 years). The sample was made up of a greater number of females; 91 (91%) patients were females. Four (4%) patients were single and 96 (96%) were married. Regarding education statues, 65 (65%) of the patients were under diploma, 21 (21%) had diplomas and 14 (14%) had a high school diploma. Five (5%) patients were smokers. Ten percent of the patients had a history of heart disease, 17% had high blood pressure, 20% had a history of high blood fat, 24% had bone and joint problems, 3% had diabetes, and 24% had a history of dieting. Patients were divided to two groups on the basis of medical indications; the LC and OC group. Fifty patients, (five men (10.0%) and 45 (90%) women) underwent laparoscopic cholecystectomy (LC group) and 50 Patients (four men (8%) and 46 (92%) women) underwent laparotomy cholecystectomy (OC group). Groups were found to be similar for baseline characteristics, such as age (P value = 0.133), gender (P value = 0.727), marital status (P value = 0.558) and Body Mass Index (BMI) (P value = 0.122). Baseline characteristics for both groups are displayed in Table 1.

As shown in Table 2, two weeks after the operation, all aspects of QOL scores of the OC group was reduced significantly (for all of them, P $<$ 0.01), with the exception of bodily pain (P value = 0.982) and social functioning, compared with preoperative scores (P value = 0.502). Also in the LC group, during this period, their QOL scores decreased significantly only in the aspects of physical functioning (P value $<$ 00.1), physical status (P value $<$ 0.001), body pain (P value = 0.017), and emotional status (P value = 0.001); whereas no statistically significant differences were observed in the other aspects such as mental health (P value = 0.051), vitality (P value = 0.209), general health (P value = 0.562) and social functioning (P value = 0.144) in the LC group, after two weeks.

Four weeks after the operation, the QOL scores of the LC group improved significantly in every aspect as compared with the preoperative baseline (for all aspects, P $\leq$ 0.01); QOL scores had exceeded the preoperative level, especially in the aspect of emotional status and physical status (Table 2), while four weeks after the operation, in the OC group only the aspects of physical functioning (P value = 0.025), body pain (P value $<$ 0.001), general health (P value = 0.003), and social functioning (P value $<$ 0.001) had exceeded the preoperative level and all other aspects were still similar to the preoperative level (Table 2). All mean aspects of QOL scores at different time intervals are shown in Table 2. All aspects of QOL scores were found to be similar at baseline between the LC and OC groups with the exception of physical functioning (P value = 0.008) and social functioning (P value = 0.025). Two weeks after the operation, the scores of physical status (P value = 0.034), body pain (P value $<$ 0.001), vitality (P value = 0.016) and general health (P value = 0.002) in the OC group were significantly lower than the LC group (Table 2); similar results were found for physical (P value = 0.002) and social functioning (P value = 0.014) after adjustment for baseline scores. During this period the scores of mental health (P value = 0.126) and emotional status (P value = 0.504) in the two groups were similar (Table 2).

Between-group analysis at four weeks after the operation, indicated that the LC group had significantly better outcome scores for all aspects of QOL compared to the OC

Table 1. Patients' General Clinical Data [a,b]

Group	Patient (n = 100)	Mean Age, y	Gender		Marital status		BMI (X ± SD)
			Male	Female	Single	Married	
LC	50	43.02 ± 9.99	45 (90)	5 (10)	3 (6)	47 (94)	26.42 ± 4.59
OC	50	45.84 ± 8.57	46 (92)	4 (8)	1 (2.0)	49 (98)	27.74 ± 3.70

Abbreviations: LC, laparoscopic cholecystectomy; OC, open cholecystectomy.
[a] Data are presented as No. (%) or Mean ± SD.
[b] Compared with the OC group; No Significant difference in age, sex, marital status, BMI, independent sample t-test; P > 0.05.

Table 2. Changes of the postoperative Quality of Life (QOL) (score, X ± SD)

QOL Score	Pre-Operative	Post-Operative Two Weeks Post Surgery	Post-Operative Four weeks Post Surgery	P Value (Repeated Measures ANOVA Test)
Physical Functioning				0.340
LC group	85.00 (63.70 - 95.00)	61.80 ± 20.09 [a]	95.00 (80.00 - 100.00) [b, a]	
OC group	64.50 ± 25.32	44.70 ± 19.75 [a]	68.10 ± 23.25 [c]	
Physical Status				0.008
LC group	75.00 (25.00 - 100.00) [d]	25.50(0.00 - 50.00) [e]	100.00 (75.00 - 100.00) [e, a]	
OC group	75.00 (18.75 - 100.00)	0.00 (0.00 - 25.00)	62.50 (0.00-100.00)	
Bodily Pain				0.124
LC group	52.75 ± 26.02 [d]	61.20 ± 16.96 [e, c]	87.50 (77.50-100.00) [e, a]	
OC group	46.70 ± 23.51	45.00 (35.00 - 57.50)	71.90 ± 17.52cc	
Vitality				0.015
LC group	59.00 ± 18.32 [d]	56.50 ± 12.09 [e]	66.100 ± 12.91 [e, a]	
OC group	58.90 ± 14.04	51.20 ± 9.23 [a]	58.90 ± 12.05	
General Health				0.048
LC group	60.83 ± 17.15 [d]	62.00 ± 12.47 [e]	69.42 ± 13.35 [a]	
OC group	58.42 ± 20.21	53.42 ± 14.64 [a]	63.75 ± 15.41 [a]	
Social Functioning				0.914
LC group	67.50 ± 24.87	62.25 ± 13.00 [b]	81.38 ± 14.68 [b,a]	
OC group	56.50 ± 23.45	54.00 ± 14.82	73.25 ± 13.60 [a]	
Emotional Status				0.003
LC group	66.67 (33.33 - 100) [d]	0.00 (0.00 - 66.67) [a]	100.00(100.00 - 100.00) [e, a]	
OC group	66.67(33.33-100.00)	0.00 (0.00-33.33) [a]	66.67 (25.00-100.00)	
Mental Health				0.209
LC group	67.52 ± 14.83 [d]	64.40 ± 11.26	71.04 ± 11.53 [e, c]	
OC group	66.40 ± 12.65	61.20 ± 9.40 [a]	66.32 ± 9.53	

[a] Compared with preoperative, P < 0.01.
[b] Compared with OC group after adjustment for baseline scores, P-value < 0.05.
[c] Compared with the preoperative period, P < 0.05.
[d] Compared with the OC group, P > 0.05.
[e] Compared with the OC group, P < 0.05.

group. As shown in Table 2, with the exception of general health (P value = 0.052), the scores of all the other aspects such as physical functioning (after adjustment for baseline score, P value = 0.001), physical status (P value < 0.001), body pain (P value < 0.001), vitality (P value = 0.005), social functioning (after adjustment for baseline score, P value

= 0.025), emotional status (P value < 0.001) and mental health (P value = 0.028) in the OC group were significantly lower than the LC group.

The results of the repeated measures analysis are illustrated in Table 2. According to the P values, the two groups were significantly different during follow-ups in the aspects of physical status (P value = 0.008), vitality (P value = 0.015), general health (P value = 0.048) and emotional status (P value = 0.003). Figure 1 displays changes in all aspect of QOL over time for the LC and OC groups. Also within group changes at two and four weeks after the operation are displayed in Table 3.

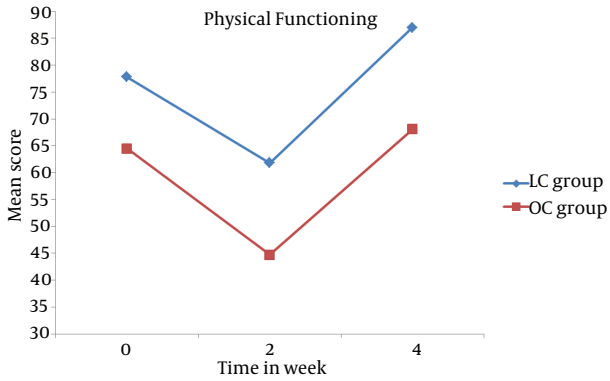

Figure 1. Mean Quality of Life Scores Over Time for the Laparoscopic and Open Cholecystectomy Groups

5. Discussion

Assessing patients' quality of life has become a major concern in the recent years. In this study QOL was compared between a laparoscopic and an open cholecystectomy group, before surgery and two and four weeks after surgery. The reason for choosing such a relatively short time period was to control and minimize the effect of time on patients' quality of life, since it could be changed with time because of factors such as medical advancements, changes in patients' knowledge and information level, usage of more utilities, and many other factors.

In the study of Lien et al., ninety-nine patients were enrolled (male/female, 32:67, age 49.8 $\pm$ 13.7 years old). At baseline, patients performed inferiorly when compared to the general population in all SF-36 general health dimensions (P < 0.001). Postoperatively, the "physical status", "emotional status", and "body pain" dimensions of health were significantly improved. There were significant improvements in gastrointestinal quality of life index (GIQLI) "total" score as well as "physical well-being", "mental well-being", "gastrointestinal digestion", and "defecation" subscales scores. Serum direct bilirubin level and drainage tube indwelling were significant predictors for quality of life improvement following LC (9). In our study, four weeks after the operation, the QOL scores of the LC group improved significantly in every aspect, as compared with the preoperative baseline (P < 0.01).

Quality of Life assessments are increasingly being recognized as an integral factor in surgical decision-making (10). Therefore, surgeons should achieve their best to improve patient's QOL in addition to taking into account serious complications and even mortality. In a randomized controlled clinical trial that assessed QOL outcomes after endovascular versus open abdominal aortic aneurysm repair, Lottman et al. found that the endovascular group had significantly improved physical functioning, role limitations caused by physical problems, vitality and pain, one month after the operation (10). Research of Kuwabara and his colleagues revealed that LC had the advantage of fewer complications, shorter Length of Stay (LOS), and lower Total Charge (TCs) compared with OC (11). For this reason, on the premise of treatment, attenuating the tissue injury is an important measure for minimizing the adverse effects of the operation and reducing complications. Nowadays, the laparoscopic approach is preferred over open laparotomy. Globally, numerous cholecystectomies are performed daily; however, little evidence exists regarding assessment of post-surgical quality of life (QOL) following these interventions (11).

Matovic et al. found that QOL in patients that had undergone cholecystectomy after two and five postoperative weeks was significantly better in the laparoscopic group compared to the open laparotomy group (4).

The results showed that in the postoperative phase, after two weeks, many aspects were decreased in the two groups. However, after four weeks, all of the eight components of QOL were increased to better scores in the LC group. On the other hand, the scores that increased in the OC group were still lower than the LC group, and in some aspects, such as physical functioning, vitality and mental health, no significant change was observed before and after the operation. In a large-scale prospective cohort study conducted on a Taiwanese population, the gastrointestinal QOL index and short form-36 were used preoperatively and after three and six months, to assess 38 OC and 259 LC patients. The Health-related quality of life (HRQOL) of the cholecystectomy patients were significantly improved after three and six months postoperatively (P < 0.05). After three months from the operation, HRQOL improvement was more significant in patients that had undergone LC than OC (1).

Table 3. Within-Group Changes at Two and Four Weeks [a]

Measure	Time Period		Time Period	
	Baseline-2 Weeks	P Value [b]	Baseline-4 weeks	P Value [c]
Physical Functioning				
LC group	-16.00 (-22.14, -9.86)	< 0.001	9.20 (4.81,13.58)	< 0.001
OC group	-19.80 (-25.29, -14.13)	< 0.001	3.60 (-2.94, 10.14)	0.025
Physical Status				
LC group	-34.00 (-48.69, -19.31)	< 0.001	28.50 (18.15, 33.85)	< 0.001
OC group	-47.50 (-61.80, -33.20)	< 0.001	-2.00 (-19.74, 15.74)	0.760
Body Pain				
LC group	8.45 (1.61, 15.29)	0.017	30.40 (22.59, 38.21)	< 0.001
OC group	0.5 (-7.39, 8.39)	0.982	25.20 (17.17, 33.23)	< 0.001
Vitality				
LC group	-2.5 (-6.44, 1.45)	0.209	7.10 (3.40, 10.80)	< 0.001
OC group	-7.70 (-10.54, -4.85)	< 0.001	0.00 (-3.21, 3.21)	-
General Health				
LC group	1.17 (-2.85, 5.18)	0.562	8.58 (4.16, 13.00)	< 0.001
OC group	-5.00 (-8.67, -1.33)	0.009	5.33 (1.84, 8.82)	0.003
Social Functioning				
LC group	-5.25 (-12.36, 1.86)	0.144	13.77 (7.42, 20.13)	< 0.001
OC group	-2.50 (-9.92, 4.92)	0.502	16.75 (9.03, 24.67)	< 0.001
Emotional Status				
LC group	-29.33 (-44.48, -14.18)	0.001	34.00 (22.92, 45.07)	< 0.001
OC group	-40.00 (-53.67, -26.33)	< 0.001	0.67 (-17.33, 18.67)	0.889
Mental Health				
LC group	-3.12 (-6.25, 0.015)	0.051	3.52 (0.74, 6.29)	0.014
OC group	-5.20 (-7.54, -2.85)	< 0.001	-0.08 (-2.92, 2.76)	0.635

[a] All values are expressed as mean values with 95% CI.
[b] At two-weeks compared with preoperative status.
[c] At four-weeks compared with preoperative status.

In a randomized study, 157 patients with uncomplicated symptomatic gallstones, confirmed by ultrasound, were categorized randomly to two groups: 85 for mini-laparotomy cholecystectomy and 72 for LC. The study was prospective and randomized yet not blinded or consecutive. The study groups were similar considering patients' age, gender, body mass index, American association of anesthesiology physical fitness classification, and the operating surgeon. Patients were reevaluated four weeks after the operation using the SF-36 quality of life questionnaire. The SF-36 questionnaire did not identify statistically significant differences between the study groups in general health perceptions, physical functioning, emotional well-being, social functioning, energy, body pain, and role functioning/emotional score. Only the role functioning/physical score was slightly higher in the LC group (P = 0.038) (12). These results are similar with that of the present study.

Obviously, laparoscopic surgery is associated with less perioperative trauma to the abdominal wall compared to open surgery (13). Based on the study of Dowson and his colleagues about QOL in laparoscopic and open surgery, there was no difference in preoperative HRQOL scores between the surgical groups, yet the postoperative EQ-5D questionnaire and SF-36 scores were significantly higher in the laparoscopic group (EQ-5D questionnaire P = 0.005, SF-36 P = 0.007). This study presents unique prospective data demonstrating that laparoscopic surgery confers HRQOL

benefits for patients in the early recovery period following colorectal surgery, compared with open surgery (14).

Braga et al. measured quality of life after one, two and four years postoperatively. Only three subscales ("general health", "physical functioning" and "social functioning") of the SF-36 were used for the analysis. Two of the three subscales ("physical functioning" and "social functioning") scored significantly better in the laparoscopic group (15). Based on the results of this study, the LC group had better scores in many aspects. Hiki et al. performed one QOL measurement after six weeks on patients that had undergone open and laparoscopic colorectal surgeries and reported a difference in four of eight aspects of the SF-36 including: "pain", "social functioning", "role limitations due to physical health" and "role limitations due to emotional problems"(16). This result was consistent with our study. Based on several studies CL has many advantages over laparotomy. In our study patients in the CL group improved significantly in every aspect as compared with the preoperative baseline that is similar with the study of Zapf and his colleagues (17). They showed that physical functioning worsened from before surgery (31.7 ± 6.2) to one week after the operation (27.5 ± 5.9, $P < 0.001$), but surpassed preoperative levels at three weeks (33.5 ± 3.4, $P < 0.01$). Return to daily activities occurred at 6.3 ± 4.7 days and work at 11.1 ± 9.0 days. Fatigue increased from before the surgery (15.8 ± 6.2) to the first post-operative week (20.7 ± 6.6, $P < 0.0001$) before improving at week three (14.0 ± 5.8, $P < 0.01$). Quality of life was significantly affected in the first 24 hours after LC yet returned to baseline at week three (17, 18). Generally it can be concluded that the laparoscopic approach is the procedure of choice for cholecystectomy especially for older and comorbid patients, when there is no local or anesthesiological contraindications.

Limitations of our study include: first, this study collected data for LC surgery patients who had been at two different medical centers, under the supervision of two surgeons, each of whom had performed the highest volume of LC surgery procedures in his respective hospital during the previous years. Secondly, the patients were divided to two groups based on the order of admission and on the patients' preference for LC or OC.

Therefore, we recommend future studies with a randomized sample and one surgeon and other instruments for evaluation of patients' satisfaction.

Footnotes

Authors' Contribution: Leila Sadati and Pazouki drafted the manuscript. Tamannaie drafted the manuscript and collected the data. Pishgahroudsari conducted the analysis. Golchini and Montazeri directed the conception and inclusion of items in this survey, gave guidance in analysis and critically reviewed the manuscript.

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