

ORIGINAL PAPER

doi: 10.5455/medarh.2020.74.34-37

MED ARCH. 2020 FEB; 74(1): 34-37

RECEIVED: DEC 22, 2019 | ACCEPTED: FEB 14, 2020

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Early vs. Delayed Laparoscopic Cholecystectomy for Acute Cholecystitis - Single Center Experience

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ABSTRACT

Introduction: Laparoscopic cholecystectomy is now considered the procedure of choice that achieves a shorter recovery period after the surgery and reduction in the cost of treatment. **Aim:** The aim of the study is to prove which method: early or delayed laparoscopic cholecystectomy is the method of choice in the treatment of acute cholecystitis by examining: duration of hospitalization, conversion rate, duration of surgery, postoperative complications, and total cost. **Methods:** The study was conducted at the University Clinical Center of Republika Srpska as a retrospective-prospective study from May 1st 2013 until December 31st 2019. Patients diagnosed with acute cholecystitis were divided into two groups: Patients designated for early laparoscopic cholecystectomy within 72 hours of admission (group A—42 patients), Patients designated for initial conservative treatment followed by a delayed interval of 6-12 weeks until surgery (group B-42 patients). **Results:** In both groups, there were statistically significantly more female respondents. The results showed that the average cost of treatment in the early treated group was statistically significantly lower than the cost of treatment in the delayed treatment group. The patients in the early group had shorter hospitalization times (an average of 2.8 days and 5.6 days in the delayed group of patients), a smaller percentage of conversions (4.8% in the early and 16.7 in the delayed group of patients), the total cost of in the early group it was 1300.83 KM, while in the delayed group it was 1645.43 KM. **Conclusion:** Early laparoscopic cholecystectomy is a method to be preferred in surgical treatment.

Keywords: Acute cholecystitis, early laparoscopic cholecystectomy, delayed laparoscopic cholecystectomy.

1. INTRODUCTION

Acute cholecystitis is the most common acute disease in hepatobiliary surgery and one of the most common diseases in digestive tract surgery in general (1). With aging, the incidence increases from 4% in the third decade to 27% in the seventh decade of life (2). Biliary calculus is undoubtedly a disease of modern man. At least 20% of the human population is thought to have cholelithiasis, but in the most developed countries of the world, this percentage is higher. It is estimated that there are about 20 million people in the United States suffering from cholelithiasis. About 500 000 cholecystectomies are performed annually in the United States. The fact is that this disease is much more common in areas where the diet is irrational (fat-rich and high-calorie diet). The incidence of the disease increases with age. Women of childbearing age are more likely to suffer than men

(1.5-3.0 : 1). The most common occurrence of cholelithiasis in women is blamed on pregnancy (increased bile production, increased serum progesterone concentration that causes the bile stasis), but also the effect of estrogen, which increases the secretion and saturation of cholesterol and bile.

However, there are still several factors that are, to a greater or lesser extent, present acting on a genetically predisposed basis, that is, correlating with the individual characteristics of the patient.

There is a 4F formula that is attractive but does not explain the mechanism and occurrence of biliary calculus (female, forty, fat and fertile). It should also be known that almost 50% of biliary lithiasis is asymptomatic and is detected accidentally during some clinical trials or at autopsy. The classic classification of biliary stones into cholesterol, pigment and mixed ones has been outdated,

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since it is difficult to find pure forms that would fit into this strict division.

During the past few decades, studies have been conducted to develop less aggressive and less costly methods in the treatment of gallbladder calculus. Oral desaturation, contact dissolution, and extracorporeal nitrotripsy methods are limited by the structure, size, and number of concretions. These nonsurgical methods are inadequate for a large number of patients and cannot contribute to healing (3). Therefore, cholecystectomy remains as the method of choice in the treatment of gallbladder calculus. Open cholecystectomy has been the „gold standard“ for symptomatic cholelithiasis for a century. However, in the last two decades, the introduction of laparoscopic cholecystectomy has revolutionized the treatment of gallbladder calculus (4). The first laparoscopic cholecystectomy was performed by Flies in 1985, and the report was presented at the German Society of Surgeons in 1986. In September 1988, Reddick and Olsen developed the method currently in use (5). Laparoscopic cholecystectomy is now considered to be the procedure of choice that achieves a shorter recovery period and reduced treatment costs. In earlier years, acute cholecystitis was regarded as a relative contraindication for laparoscopic cholecystectomy because of inflammatory changes that impair tissue quality and make it difficult to accurately visualize anatomical structures. As technological advances have been accompanied by improvements in surgical performance, laparoscopy has become the „gold standard“ in the treatment of chronic cholecystitis with cholelithiasis, and over time the indications widen and acute gallbladder inflammation is also resolved by laparoscopy.

2. AIM

The aim of the study is to prove which method: early or delayed laparoscopic cholecystectomy is the method of choice in the treatment of acute cholecystitis by examining: duration of hospitalization, conversion rate, duration of surgery, postoperative complications, and total cost.

3. METHODS

The study was conducted at the University Clinical Center of Republika Srpska as a retrospective-prospective study from May 1st 2013 until December 31st 2019. Prior to the procedure, full consent of patients for surgery for both early and delayed cholecystectomy and consent for eventual conversion to open procedure were obtained. All patients underwent laparoscopic cholecystectomy. Patients diagnosed with acute cholecystitis were divided into two groups: Patients designated for early laparoscopic cholecystectomy within 72 hours of admission (group A-42 patients), Patients designated for initial conservative treatment followed by a delayed interval of 6-12 weeks until surgery (group B-42 patients). The criteria for inclusion in the experimental (group A) are: diagnosed acute cholecystitis, consent of the patient for surgery, persistence of symptoms (nausea, vomiting, pain) despite the conservative therapy, palpa-

tory sensitivity below right rib arch, maintaining high leukocyte values. The criteria for inclusion in the control group (group B) are in addition to the general conditions: significant reduction or complete absence of symptomatology by the conservative treatment, reduction of palpation sensitivity below right rib arch, decrease in leukocyte values. Criteria for establishing the diagnosis of acute cholecystitis are: acute pain in the upper abdomen followed by nausea and vomiting, leukocytosis greater than 10000 mm³, palpation sensitivity of the right chiphondrium with a positive Morphine sign longer than 6 hours, febrility higher than 38°C, positive ultrasonography of the gallbladder, presence of concurrence with thickening and edematous gallbladder wall and possibly pericholecystitis fluid. Initial treatment during the acute phase will be the same for both groups of patients. All should receive intravenous infusion (0.9% NaCl 1000 ml, Ringer 1000 ml), antibiotics (amoxicillin clavulonic acid 1.2g x 3), analgesics (ketoprofen 2x1), spasmolytics (hyoscine butylbromide 3x1) and IPP. Patients in group A underwent laparoscopic cholecystectomy within 72 hours of admission to hospital. released after rehabilitation of acute cholecystitis and commissioned for prolonged laparoscopic cholecystectomy after 6-12 weeks. The exclusion criteria for the search are:

Patients with symptoms lasting longer than 72 hours until confirmation of acute cholecystitis, patients with surgical icterus, choledocholithiasis verified ultrasonographically, malignancies, preoperatively diagnosed acute pancreatitis caused by biliary calculus, previous surgery with abdominal surgery, previous surgery who refused to undergo laparoscopic surgery. Both groups of patients will be monitored through the parameters set for this paper as follows:

- The duration of hospitalization will be measured from the moment of admission to the hospital until discharge to home, or receipt of a discharge letter.
- The conversion rate will be measured as a percentage of the total number of laparoscopies, if within 30 minutes of the start of the surgery, the elements of the Kalot triangle cannot be presented conversion to the open-method surgery will be made.
- The duration of the surgery will be measured from the introduction to the anesthesia to the placement of the last suture on the skin.
- Postoperative morbidity will be measured by evaluation of pain using a numerical (1-10) scale, amount and type of contents in the drain, the possible occurrence of febrility, infection at the port site.

The total cost price will be measured through:

- the price of the surgical interventions in the value recognized by the Health Insurance Fund of the Republika Srpska (HIF RS)
- Number of days of hospitalization according to HIF RS
- Any need for transfusions
- Additional antibiotics for the treatment of postoperative infections.

Data analysis

The processing of the collected data will be performed with the use of Statistical Package for the Social Sciences (SPSS)—a statistical package for data processing and analysis. Quantitative data will be presented in tables. The results of the statistical analysis will be presented in the form of absolute and relative indicators and measures of central tendency and dispersion. In analyzing the results of statistical tests, $p < 0.05$ will be considered as statistically significant.

4. RESULTS

Based on the results of the chi-square test ($\chi^2=11.524$; $p=0.001$), it was concluded that in the early group of patients there were statistically significant ($p < 0.05$) more female than male respondents.

Based on the results of the chi-square test ($\chi^2=4.667$; $p=0.031$), it was concluded that in the delayed group of respondents there were statistically significantly ($p < 0.05$) more female respondents than male respondents.

The results of Pearson’s chi-square test ($\chi^2=0.933$; $p=0.334$) showed that there was no statistically significant difference between the early and the delayed group in terms of male and female patients (Table 1). Table 1 shows that the percentage of male respondents in the early group is similar to the percentage of male respondents in the delayed group.

		Group		Total	
		Early	Delayed		
Gender	Male	N	10	14	24
		%	23.8	33.3	28.6
	Female	N	32	28	60
		%	76.2	66.7	71.4
Total	N	42	42	84	
	%	100.0	100.0	100.0	

Table 1. Distribution of patients in early and delayed group by gender

Based on the Mann-Whitney U test ($U=79.500$; $p=0.000$), it was concluded that there was a statistically significant difference ($p < 0.05$) between the early and delayed groups relative to the number of hospitalization days (23.39 vs. 61.61). The likelihood that an early group respondent will be hospitalized is statistically significantly less than the probability that a delayed group respondent will be hospitalized. There was no statistically significant difference ($p > 0.05$) in the distribution of subjects versus conversion (Fisher’s exact test; $p=0.156$) between the early and delayed groups (Table 2). Based on the chi-square test ($\chi^2=34.381$; $p=0.000$), it was concluded that there was a statistically significant difference ($p < 0.05$) between the number of patients who had a conversion and the number of patients who did not have a conversion in the early group. Patients without conversion were more dominant than patients who had a conversion in the early group. Also, in the patients of the

delayed group, the patients without conversion were statistically significantly ($p < 0.05$) more dominant than those who had the conversion ($\chi^2=18.667$; $p=0.000$).

		Group		Total	
		Early	Delayed		
Conversion	No	N	40	35	75
		%	95.2	83.3	89.3
	Yes	N	2	7	9
		%	4.8	16.7	10.7
Total	N	42	42	84	
	%	100.0	100.0	100.0	

Table 2. Distribution of patients in the early and delayed group relative to conversion

Based on the results of Fisher’s exact test ($p=0.241$), it was concluded that there was no statistically significant difference ($p < 0.05$) between the early and delayed groups concerning biliary tract injury. The risk of bile duct injury was not statistically significant ($p < 0.05$) between the early and the delayed group (Table 3).

The results of the chi-square test ($\chi^2=30.657$; $p=0.000$) showed that the probability of bile duct injury was statistically significantly lower ($p < 0.05$) than the probability that injury would not occur in both the early and the delayed group.

		Group		Total	
		Early	Delayed		
BILE TRACT INJURIES	No	N	42	39	81
		%	100.0	92.9	96.4
	Yes	N	0	3	3
		%	0.0	7.1	3.6
Total	N	42	42	84	
	%	100.0	100.0	100.0	

Table 3. Distribution of early and delayed group subjects in relation to biliary tract injuries

There was no statistically significant difference ($p < 0.05$) between the early and the delayed group expressed as the mean bleeding rate in milliliters (48.8095 ± 70.47582 vs. 105.8333 ± 195.22319 ; $t= -1.781$; $p = 0.81$). Even so, the bleeding in the early group was less than in the delayed in this particular case—When looking at the incidence of bleeding, there was also no statistically significant difference ($p > 0.05$) between the early and the delayed group ($\chi^2=3.733$; $p=0.053$), although the results of the chi-square test was at the very limit.

In the early group of patients, there was no statistical significant difference ($p > 0.05$) between the number of patients who had to bleed and the number of subjects who had no bleeding ($\chi^2=2.381$; $p=0.123$).

In the delayed group, there was a statistically significant ($p < 0.05$) difference between the number of patients with bleeding and the number of patients with no bleeding ($\chi^2=16.095$; $p=0.000$). The probability of bleeding in the subjects of the delayed group was statistically significantly higher than the probability that no bleeding would occur (Table 4).

		Group		Total	
		Early	Delayed		
Bleeding	No	N	16	8	24
		%	38.1	19.0	28.6
	Yes	N	26	34	60
		%	61.9	81.0	71.4
Total	N	42	42	84	
	%	100.0	100.0	100.0	

Table 4. Bleeding frequency in the early and delayed group of patients

The results of the Mann-Whitney U test ($U=511.000$; $p=0.000$) showed that there was a statistically significant difference ($p<0.05$) between the early and delayed groups by a median grade of pain (33.67 vs. 51.33). The pain in the delayed group was statistically significantly higher than in the early group.

The results of the t-test ($t=6.712$; $p=0.000$) showed that there was a statistically significant difference ($p<0.05$) between the early and delayed groups in the mean duration of surgery (95.47 ± 11.41 vs. 73.69 ± 17.67). In the delayed group, the duration of surgery was statistically significantly ($p<0.05$) shorter than in the early group subjects. Based on the results of the Mann-Whitney U test ($U=674.000$; $p=0.025$), it was concluded that there was a statistically significant difference (47.45 vs. 37.55; $p<0.05$) between the early and delayed groups by the median number of hospitalization days after surgery. The number of days of hospitalization after the surgery in the delayed group is higher than the number of days of hospitalization after surgery in the early group. Based on the results of the Mann-Whitney U test ($U=299.000$; $p=0.025$), it was concluded significant difference ($p<0.05$) between the early and delayed group by median of total hospitalization days (28.62 vs. 56.37). The total number of hospitalization days in the delayed group subjects is higher than the total number of hospitalization days in the early group. The results of the t-test ($t=-3.100$; $p=0.003$) showed that the average cost of treatment in the early group was statistically significantly lower (1300.83 ± 291.58 vs. 1645.43 ± 658.76 Convertible Marks; $p<0.05$) from the treatment cost of the delayed group of subjects.

5. DISCUSSION

Acute cholecystitis is the most common acute disease in hepatobiliary surgery and one of the most common diseases in digestive surgery in general (1). In recent decades, studies have been conducted to develop less aggressive and less costly methods in the treatment of gallbladder calculus. Oral desaturation, contact dissolution, and extracorporeal nitrotripsy methods are limited by the structure, size, and several concretions. These nonsurgical methods are inadequate for a large number of patients and cannot contribute to healing (3). Therefore, cholecystectomy remains the method of choice in the treatment of gallbladder calculus. Open cholecystectomy has been the „gold standard“ for symptomatic cholelithiasis for a century. However, in the last two decades the introduction of laparoscopic cholecystectomy has revolutionized the treatment of gallbladder calculus

(4-6). The optimal way to treat acute cholecystitis, especially the choice of the time frame for surgical treatment, has been the subject of much debate, but lately there are more studies, meta-analyses, and guides suggesting early laparoscopic cholecystectomy in the treatment of acute cholecystitis. In a 2018 study by Kohg et al. results from Japan were published that included 465 patients, 288 of whom were wounded and 177 delayed cholecystectomy, had a conversion rate of 1.3% vs 10.7%, biliary tract injuries 0.3% vs 3.3% and surgery duration 105 min vs 124 min, all in favor of early laparoscopic cholecystectomy (7). In a 2017 study by Khalid et al, which included 188 patients, the conversion rate was (early 15.5% vs delayed 14.4%), surgery duration 64.32 min vs 58.24 min delayed (7). Goh et al., in a 2017 study that included 466 patients, the conversion rate was 8.6 vs 8.0% in favor of delayed surgery and 101.5 min in the early and 88.0 min in the delayed group (8). In our study, which included 84 patients, that is, 42 in the early and 42 in the delayed group, the percentage of conversions in the early group was 4.8%, while in the delayed group it was 16.7%. In the further comparison between the two groups, the duration of surgery in the early group was 95.47 min, while in the delayed one it was 73.7 min. There were no bile duct injuries in the early group, while in the delayed group it occurred in three patients, or 7.1%. In conclusion, we can say that the values of the measured parameters are in line with the above-mentioned world studies.

The length of the total hospitalization is also one of the important parameters in my study for which the worldwide studies cite the following data. In one large study from 2014, de Maestral et al. included 14,220 patients, in which they recorded a shorter duration of hospitalization in the early group by 1.9 days compared to the delayed one (9). Minutolo et al included 92 patients, the duration of total hospitalization in the early group was 4 days shorter than the delayed group of patients (3). In a 2015 study, which included 502 patients, divided into 209 early and 233 delayed surgeries, Pisano et al. reported results for shorter hospitalization in the early group by 2.5 days and no differences in postoperative complications (10). Like the coworkers, in a June 2018 study, they analyzed 86 patients divided into early and delayed groups of patients through hospitalization days (4 vs 7 days), cost (9,349 vs 12,361 Canadian dollars), and equal postoperative morbidity in both groups (11). In our study, the total length of hospitalization was 2.8 vs 5.6 days. Our study concluded that there were more female subjects in both the early and the delayed group. In the early group, the percentage of female respondents was 76.19% versus 23.81% of male respondents. These results are correlated with most other studies, where this sex ratio ranges from 4 : 1 to 3 : 1.5 in favor of the female sex. The most common occurrence of cholelithiasis in women is blamed on pregnancy (increased bile production and increased serum progesterone concentration that causes the biliary tract), as well as the effect of estrogen, which increases the secretion and saturation of cholesterol and bile. There are a number of other factors that are more or less present by acting on a genetically predisposed basis,

that is, correlating with the individual characteristics of the patient. Formula 4F is attractive and partly explains the mechanism and occurrence of biliary calculosis (female–female, forty–forties, fat–obesity, fertile–fertility). One of the important parameters in the monitoring between the two groups of patients is the injury of the biliary tract. In a 2016 study by Roulin et al., The overall morbidity rate between the two patient groups was 14% vs 39% in favor of the early surgery group (12).

In a 2018 study of 72 patients, Jee and colleagues found results in perioperative complications of 7.78% vs 11.76% in favor of an early patient group (13). In our study, we did not have any bile duct injury in the early group of patients, while in the delayed group of patients this was happened in three cases, of which two patients had a complete section of the main bile duct and one thermal injury of the main bile duct. All of these patients were dealt with by a new surgery, exclusively open surgery, which involves one of the most difficult types of biliary tract reconstruction, which implies a significant prolongation of the hospitalization of patients, a longer stay at ICU. All of these parameters support a significant benefit of early over delayed laparoscopic cholecystectomy. An important parameter in our study was the total cost of treatment cost between the wound and the delayed group of patients, for which the following studies are reported by world studies. Gutt et al., 2013 Long Term Collaborators, Heidelberg, Germany, which included 618 patients, reported the results of a total cost of cost between the wound and the deferred group of 2,919€ vs 4,262€ in favor of the early patient group (6). A group of Italian surgeons from the University of Catania, Italy, published the results of their 2014 study, in which the cost of the total cost of treatment in the early group was 4,171€ and in the delayed group it was 6,041€ (3). A 2016 study by Roulin et al., Lausanne, Switzerland, which included 86 patients, 42 in the early and 44 in the delayed group, also confirmed a significant advantage in the early group of patients over the delayed overall cost of treatment (13). The total cost of treatment in our study was 1300 KM in the early and 1645 KM in the delayed group of patients. In conclusion, we can say that our results also favor the early versus the delayed group of patients according to the criterion of the total cost of treatment of patients.

6. CONCLUSION

Patients in the early group had shorter hospitalizations and a lower conversion rate. Postoperative complications are more pronounced in the delayed compared to the early group of patients. Early laparoscopic cholecystectomy is a method to be preferred in surgery.

- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms
- **Author's Contribution:** Each author gave substantial contribution to the conception or design of the work and in the acquisition, analy-

sis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

- **Conflicts of interest:** There are no conflicts of interest.
- **Financial support and sponsorship:** Nil.

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