EVALUATION OF EARLY VERSUS DELAYED LAPAROSCOPIC CHOLECYSTECTOMY IN ACUTE CHOLECYSTITIS: A PROSPECTIVE RANDOMISED STUDY

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ABSTRACT

Background: Laparoscopic cholecystectomy has revolutionised the treatment of this disorder significantly. Current trends are investigating the effectiveness of early intervention in this subset of patients.

Methods: After the institute's research evaluation committee approval, the study was conducted prospectively at department of General and laparoscopic surgery of Hayatabad Medical Complex Peshawar from June 2014 to June 2015. Preoperative clinical features, intraoperative findings and postoperative outcome was recorded. The data was analysed using IBM SPSS version 22.0.

Results: 100 patients, 54 in ELC group & 46 in DLC group with mean age 48.32 years ± 11.019 SD. The mean procedure time was 61.20 minutes ± 9.809 SD. Mean procedure time for ELC was 62.13 minutes ± 9.711 SD while 60.11 minutes ± 9.916 forDLC (between goups ANOVA; p = 0.307). Neither procedure was associated with statistically significant benefits in terms of LOS, complications or overall outcome (p = 0.58; OR= 0.944, 95% CI: 0.767-1.161).

Conclusions: For the management of acute cholecystitis, both early or delayed laparoscopic cholecystectomy are safe options with less complications and good overall outcome.

Keywords: Laparoscopy, Cholecystectomy, Early, Delayed intervention, Complications.

INTRODUCTION

The first successful laparoscopic cholecystectomy was performed by the French gynaecologist Mouret in 1987.[1] Gallbladder cholelithiasis is a relatively common condition which appears to constitute 5.9% to 21.9% of the Western societies while in Asia it is estimated to affect 3.1% to 10.7% of the population.[2] Almost 75% cases of gallstones are asymptomatic. Of those who experience an attack of acute cholecystitis (AC) due to gallstones, almost half of them experience a second attack during the same year, so that surgical intervention becomes essential in order to prevent the complications of the disease.[2]

Laparoscopic cholecystectomy (LC) is the standard surgical procedure for patients with gallstone disease. It is estimated to be performed at a rate of 139.7 per 100,000 population, more in females with a male to female ratio of 1:1.5 and this trend is noted to be increasing with time.[3] The procedure is more frequently performed in younger individuals than in the elderly and in 93.6% cases it is LC which is preferred and performed.[3,4,5]

Recently early laparoscopic cholecystectomy (ELC) during an attack of acute cholecystitis has been evaluated as a measure to rapidly counteract the disease process involving the biliary tree to take counter measures against the complications.[5] ELC was initially not favoured due to higher rates of conversion to open cholecystectomy (OC), difficulty due to inflamed pericholecystic tissues, bleeding due to tissue fragility, lost stones and bile leak from injury to common bile duct due to distortion of the anatomy.[6] However, more recently LC is increasingly being performed earlier and with lesser incidence of reported complications and good results postoperatively.[7]

The debate still continues as to whether favour early or delayed laparoscopic cholecystectomy (DLC).[8] We aimed to conduct this study in order to better analyse the postoperative outcome in both early and delayed operated patients by meaningfully distinguishing both groups on the basis of operative time, conversion rate, intraoperative complications and length of stay in a randomised manner.

METHODS

Study Design

After the institutes ethical and research evaluation committee's approval, the study was commenced from June 2014 to June 2015 at the Department of General and Laparoscopic Surgery Unit of Hayatabad Medical Complex Peshawar. Patients were randomly assigned to either early or delayed cholecystectomy group after obtaining their informed consent. A random number

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table was generated in Random Allocation Software-version 1.0. All patients were coded according to the random numbers for each group.

Diagnosis

Diagnosis of AC was made utilising clinical features (pyrexia, dyspepsia, RUQ pain, nausea, vomiting, RUQ tenderness), lab studies (total leucocyte count (TLC), liver function tests (LFTs) and ultrasound findings (thick walled, distended or both, pericholecystic fluid, positive Murphy's sign).

Inclusion Criteria

The ELC group comprised of patients diagnosed with cholecystitis after presentation. These patients were put on analgesics, intravenous fluids & antibiotics andwere enlisted for a ELC during the first 72 hours of their admission.

The DLC group patients once diagnosed as having AC were treated conservatively (with analgesia, antibiotics & fluids) during the admission until their acute episode was subsided. They were dated for an elective LC after 4 to 6 weeks after admission.

Exclusion Criteria

All patients with clear cut indications for OC such as previous upper abdominal surgery, common bile duct (CBD) stones, pancreatitis, history of liver disease (hepatitis B or C) or any coagulation disorder were excluded from the study. Moreover, those patients who either did not consent for inclusion in the study groups were also excluded.

Operative Procedure

The operative procedure was performed by the senior consultant surgeon from the authors (Z.A) in order to standardise the operative procedure and minimise any confounders associated with individual expertise.

The procedure was performed under General anaesthesia using endotracheal intubation in supine position. Nasogastric tube was passed to decompress the stomach. Direct trocar insertion with elevation of the rectus sheath using 2 towel clips method was used to create the pneumoperitoneum with CO2 gas. Intraabdominal pressure was kept between 8 to 12 mm Hg.Four laparoscopic ports were made.10mm port at umbilicus was made for telescope. Another 10mm port made in the epigastrium was for dissection, suction and specimen retrieval. Two 5mm ports, one in right upper quadrant and another in right flank at the level of umbilicus,were used for grasping forceps. Adhesions if present were cleared first to expose the gallbladder. Distended gallbladder when encountered was decompressed with suction needle to allow better grasping. Calot's triangle was ascertained and dissection started by taking small bands and strands of tissue staying close to the gallbladder. Curved dissector was used to isolate the Cystic duct and artery which were then clipped and divided separately. Gallbladder was dissected off its bed using monopolar cautery hook. After completion of dissection, gallbladder was extracted through epigastric port. Retrieval bag was used for extraction of gallbladder where necessary. Haemostasis was secured and after a thorough saline lavage, a drain was placed in sub-hepatic regionin all patients and the ports closed. Whenindicated, conversiontoOC was performed through a right subcostal incision.

Postoperative Care

Postoperatively, all patients received broad spectrum antibiotics, analgesics and proton pump inhibitors (PPIs). All patients were discharged after conducting a thorough physical examination for any complications.

Outcome Measures

Procedure time, intraoperative complications, conversion to OC, postoperative length of stay and frequency of postoperative complications were recorded. Complications were promptly treated and patients were closely followed up for two weeks. Any late arising complications were also identified and managed accordingly.

Data Analysis

Data was analysed using the IBM SPSS version 22.0. Frequencies and percentages were presented in the form of tables and charts. Tests of significance (Chi-Square Correlation, ANOVA, Binary Logistic Regression and Bivariate Correlation) were performed and results presented.

RESULTS

100 patients were included in the study with 54 patients in ELC group while 46 in DLC.Table 2 The mean age was 48.32 years ± 11.019 SD. Overall there were 21 males & 79 females.Table 1. In ELC group there were 10 (18.5%) male patients while 44 (81.5%) females. In the DLC group there were 11 (23.9%) males and 35 (76.1%) female patients. (Figure 1)

The overal mean duration of symptoms was 10.9 months ± 8.912 SD. 55% patients presented within 10 months of the appearance of initial symptoms.Table 1 84% patients presented with acute complaints of RUQ pain, 36% with nausea, 9% with vomiting, 8% with fever and 41% with dyspepsia syndrome.

The average TLC was found to be 8974.4 cells/cmm ± 2178.057 SD. Similarly, mean bilirubin was 1.124 mg/dL ± 0.2471 SD, mean ALT was 44.79 U/L ± 5.867 SD, mean alkaline phosphastase was 206.34 U/L ± 9.808 SD.Table 1

Table 1: Quantitative variables

	Age	Duration of symptoms	TLC	Bilirubin	ALT	Alkaline Phos	Procedure Time	Length of Stay (LoS)
Mean	48.32	10.90	8974.40	1.12	44.79	206.34	61.20 min	3.31
Median	48.00	8.00	9125.00	1.10	45.00	205.00	60.00 min	3.00
Std. Deviation	11.019	8.91	2178.06	0.25	5.87	15.18	9.81	0.84

Table 2: Categorical variables & their significance

Clinical variable	Frequency (n)	Percentage (%)	P value
Gender			0.314
Male	21	21	
Female	79	79	
RUQ Pain	84	84	0.147
Nausea	36	36	0..201
Vomiting	09	09	0.022
Fever	08	08	0.011
Dyspepsia	41	41	0.441
Ultrasonography findings			
Distended GB	45	45	0.020
Thickened GB	47	47	0.055
Pericholecystic fluid	33	33	0.272
Murphy's Sign	83	83	0.380
Treatment Group			0.584
Early LC	54	54	
Delayed LC	46	46	
Intraoperative complications			
Dense Adhesions	21	21	
Bleed	12	12	
Postoperative Complications			
Pyrexia	17	17	
Wound infection	05	05	
Chest Infection	06	06	
Bile leak	02	02	
Bleeding	02	02	
Seroma	06	06	
Overall Outcome			
Favourable	78	78	
Unfavourable	22	22	

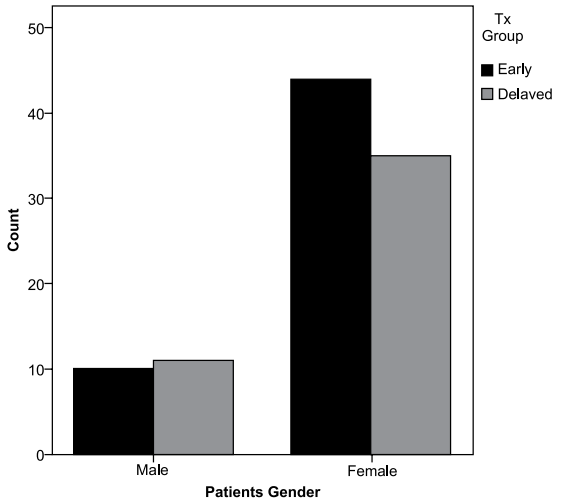

Figure 1: Gender distribution across the treatment groups

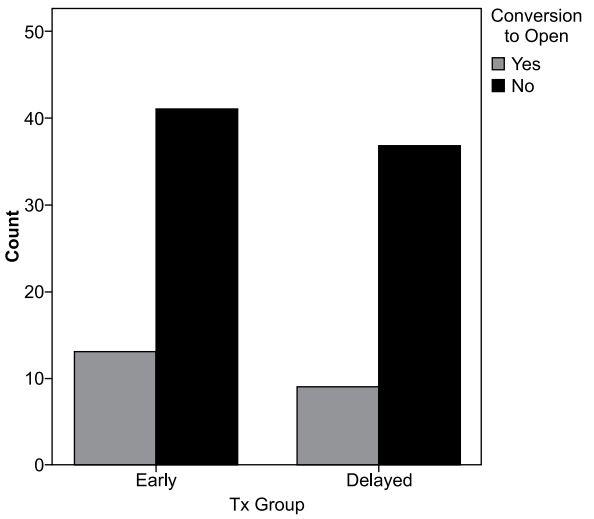

Figure 2: Conversion rate in Early versus Delayed treatment groups

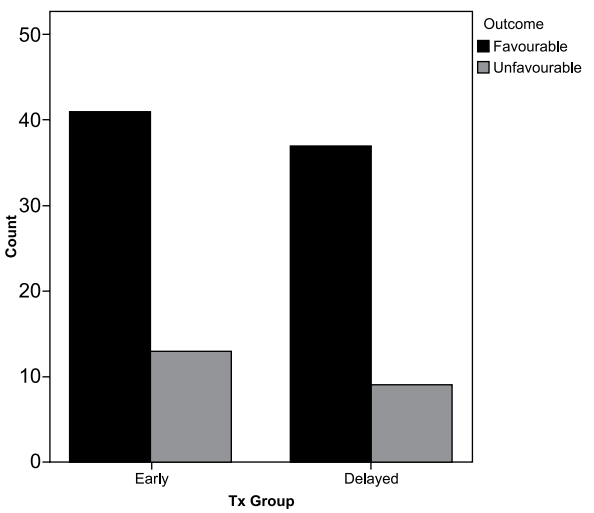

Figure 3: Treatment groups and outcome

On presentation ultrasound thickened GB was found in 45% patients, distended GB in 47% patients, 33% were found to have preicholecystic fluid collection while 83% had a positive Murphy's sign on probe compression. Table 2

The mean procedure time was 61.20 minutes ± 9.809 SD. Table 1 For the early cholecystectomy group the mean procedure time was 62.13 minutes ± 9.711 SD while for the delayed cholecystectomy group the mean procedure time was 60.11 minutes ± 9.916 (between goups ANOVA; p = 0.307) 22% cases were converted to open due to intraoperative complications, with 13 (59.1%) in the early treatment goup and 9 (40.9%) in the delayed treatment group. Though the conversion rate was not statistically significant (p = 0.635, OR: 1.23, 95% CI: 0.58-2.61), it appeared that the conversion to OC was higher in the ELC group. Figure 2

The mean total length of hospital stay (LOS) was 3.31 days ± 0.837 SD. Table 1 The mean LOS for the ELC group was 3.35 days ± 0.894 SD, while mean LOS for the DLC group was 3.26 days ± 0.773 SD (between groups ANOVA; p = 0.59).

The intraoperative complications included dense adhesions in 21% cases and bleeding in 12% cases. Postopertive complications included postoperative pyrexia in 17% cases, in which wound infection was noted in 6%, chest infection in 5%, bile leak in 2%, bleeding in 2% and subcutaneous seroma formation in 6% cases. All of the chest infection and seroma formation cases occurred in the OC group. Table 2.

Overall, ELC had 75.9% cases with favourable outcome while 24.1% cases with unfavourable outcome. The DLC group had 80.4% favourable outcome while 19.6% cases were in the unfavouable outcome group (p = 0.58; OR= 0.944, 95% CI: 0.767-1.161).Figure 3, Table 2.

The univariate analysis, multivariate analysis and binary logistic regression model between treatment group and outcome showed no significant association (OR: 1.304, 95% CI: 0.50-3.40) for early LC and unfavourable outcome (intraoperative complications, postoperative complications, length of stay) (p = 0.58). Table 2.

DISCUSSION

Gallstone disease is potentially a serious problem taking into account the gallstone associated pancreatitis and cholestatic jaundice due to biliary tree stones, cholangitis and acute cholecystitis and its sequelae.[9,10] Laparoscopic cholecystectomy has revolutionised the treatment of cholelithiasis as compared to the open cholecystectomy in terms of less morbidity and patient satisfaction. There is a trade-off between the expertise of a surgeon and the occurrence of complications, the most serious being the CBD injury.[11,12]

The original Tokyo guidelines (TG07)[13] and the revised[14] & updated Tokyo guidelines (TG13)[15] for the diagnosis and management of acute cholecystitis, cholangitis and gallstones are the landmark developments during the last decades which have combined the utilisation of clinical, radiologic and laboratory markers to improve upon the sensitivity and specificity of these parameters and improve outcomes for this subset of patients.[16,17] The comparison of early and delayed intervention of acute cholecystitis has been taken in numerous studies and it still continues to decide for the best choice of a procedure which could improve surgical outcomes.[7]

Many retrospective, prospective, randomised and comparative cohort studies have taken into account LC for early or delayed intervention in AC patients with variable outcome results. A recent meta-analysis by Cao AM et al[18] has shown that early LC is clearly superior to delayed or routine LC in terms of the occurrence of intraoperative complications, wound infection, bleeding, LOS and bile duct injuries. They have determined that early LC without the duration of onset of symptoms in AC is superior.[18] However, they have confirmed that the definition for early intervention is variable and ranges in some studies for within 48 hours of onset of symptoms up to 7 days of presentation. This variability is mostly due to the different cohort characteristics in various studies. We tried to avoid falling such a discrepancy of early LC definition versus the definition of delayed LC. Therefore, we defined early LC as intervention performed strictly within 72 hours of onset of the acute symptoms and signs, compounded by laboratory data and ultrasonography findings.

In a 3 years prospective follow up study, Kum CK et al[6] assessed 530 cholecystectomies (424 routine, 54 early LCs) for benefits in terms of operative time, intraoperative and postoperative complications and found a significant incidence ($p<0.0001$) of these complications in the early LC groups as compared to routine LCs. They have concluded that the trade-off in terms of a significantly high rate of CBD injury is quite high in early LC as compared to routine LC. However, Ciftci F et al[19] in a large prospective study compared early LC to those which were converted to OC and found a significantly better outcome (follow up period; mean 27 months). They identified longer hospital stay for the OC group (mean: 3 days) and increased wound complications. Their demographic data was comparable to our study with mean age of 47.8 years and a higher proportion of female patients. This same study has pointed out that male gender, gallbladder wall thickness of > 1 cm, gangrenous cholecystitis and a pericholecystic collection on ultrasonography are the determinants of conversion to OC in early LC. Their conversion rate was 10.5% which was better than our study (22%).

In a retrospective analysis of a large cohort of patients (n=42,452) the optimal time definition was evaluated by Polo M et al[20], who concluded that adverse postoperative events (intensive care admission, reoperation and postoperative sepsis) were significantly lower ($p<0.001$) in those patients who underwent early LC between 1 and 3 days of admission as compared to those who were operated on the same day of admission or after the 5th day of admission ($p<0.001$).[20]

Kolla SB et al[21] in a prospective randomised trial has compared early LC with delayed LC and in concurrence to our study have found no difference in the conversion rate, procedure time, postoperative analgesia requirements and/or postoperative complications.[21] However, they recorded more blood loss and shorter LOS in the early LC group. These findings are in agreement with our study in terms of design of the study, the conversion and complication similarities in both early and late LC groups. They, however, in their early LC group operated within 24 hours of presentation which in the Polo M et al[20] study is a higher risk period for postoperative adverse events. The findings of Kolla SB et al[21] and hence the findings of our study are compounded by yet another systematic review of early versus delayed LC trials.[22] In this systematic review Lau H et al[22] has reported a significantly shorter hospital stay for the early LC group (weighted mean difference, -1.12; 95% confidence interval [CI], -1.42 to -0.99; $p < 0.001$) as compared to the delayed LC group.[22] However, they did not find any significant benefit of early LC over delayed LC in terms of operative time, rate of conversion to OC, rate of complications and bile leak due to CBD injury. They, however, have recommended early LC in order to reduce readmission rates for those patients who are listed for routine LC and to reduce total length of hospital stay.[22]

Our study is limited by shorter follow up period as in our set up the loss to follow is increasingly high due to multiple reasons ranging from patient's locality, lack of a digital registration system, patients' priority and transportation problems from far flung areas. Another limitation of our study is the lack of blinding and lack of a control group for both the early and delayed treatment groups. These limitations can however, be overcome by improving long-term patient follow up, conducting randomised study with blinding effects so as to minimise confounders and to introduce control groups.

CONCLUSION

For patients with gallstone disease early LC during an acute attack is as safe as a routine LC several weeks or months later. It is then better to perform early LC so as to relieve the patient of the disease and to shorten the duration of the suffering. This could also help in controlling the danger of gallstone associated complications for those patients who are sent home and to return for a routine LC.

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