SCIENTIFIC PAPER JSLS

# Routine Testing of Liver Function Before and After Elective Laparoscopic Cholecystectomy: Is It Necessary?

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## ABSTRACT

**Background and Objectives:** Liver function tests (LFTs) include alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), and bilirubin. The role of routine testing before and after laparoscopic cholecystectomy was evaluated in this study.

**Patients and Methods:** A total of 355 patients were retrospectively analyzed by examining the LFTs the day before, the day after, and 3 weeks after the surgery. The Wilcoxon signed-rank test and Student *t* test were performed to determine statistical significance.

**Results:** Alterations in the serum AST, ALT, and GGT were seen on the first postoperative day. Minor changes were seen in bilirubin and ALP. An overall disturbance in the LFTs was seen in more than two-thirds of the cases. Repeat LFTs performed after 3 weeks on follow-up were found to be within normal limits.

**Conclusion:** Mild-to-moderate elevation in preoperative LFTs may not be associated with any deleterious effect, and, in the absence of clinical indications, routine preoperative or postoperative liver function testing is unnecessary.

**Key Words:** Laparoscopy, Cholecystectomy, Hepatic dysfunction.

## INTRODUCTION

Since the introduction of the laparoscopic cholecystectomy in 1987, knowledge about the difficulties associated with the procedure and awareness of the potential complications have grown. Modernization of technical skills to overcome the difficulties and early detection of the complications and their timely management are keys to the success of this procedure. Although open cholecystectomy has largely been replaced by the laparoscopic technique, the potential for iatrogenic duct injuries is higher in the latter procedure.[1] The frequency and type of biliary injuries during laparoscopic cholecystectomy vary, and timely diagnosis and management is critical for the well-being of the patient.[2]

Among other techniques for the assessment of biliary injuries, biochemical testing of liver enzymes is a common clinical practice. The sensitivity of LFTs in detecting obstructions in bile flow has been found to be greater then 90%.[3] Any increase in their values is always a matter of concern for the clinician and warrants further investigation to determine the underlying pathology. AST and ALT are generally considered a measure of hepatocellular function. ALP levels are increased during obstruction of the biliary duct system; bilirubin levels can increase due to hemolysis or obstruction of the flow of bile. Very high levels of serum transaminases can also be suggestive of common bile duct (CBD) stones.[4]

With recent advances in minimal access surgery, laparoscopic cholecystectomy is entering an era where it is considered an outpatient procedure. Elevated LFTs are common soon after surgery. The elevation is usually transient, and the LFTs return to normal levels without any intervention.[5-7] Preoperative liver function tests were evaluated as one of the possible predictive factors for the conversion of a laparoscopic procedure to open cholecystectomy; it was found that impaired LFTs were not associated with an increased risk of conversion.[8,9] The aim of this study was to determine whether routine analysis of liver function is mandatory before and after laparoscopic cholecystectomy.

## PATIENTS AND METHODS

A total of 355 patients underwent laparoscopic cholecystectomy at Mid Western Regional Hospital, Ennis, between January 2001 and September 2005. Liver function

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Thanks to Dr Asim Iftikhar Syed for his help in the preparation of the final manuscript.

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DOI: 10.4293/108680811X13022985131291

tests were determined the day before surgery, the day after surgery, and at the follow-up after 3 weeks. An Olympus analyzer was used for the biochemical analysis of liver enzymes. The normal LFT ranges were different for males and females for AST, ALT, and GGT; therefore, the values were calculated separately. Similarly, the normal range of ALP was dependent on the age. There were no patients under the age of 16, so the adult range was used as a reference **(Table 1)**.

Out of 355 patients, 54 were excluded from the study. The exclusion criteria were emergency operations, procedures converted to open surgery, and patients requiring endoscopic retrograde cholangiopancreatography (ERCP) before surgery. This study was designed to appraise the effects of laparoscopic cholecystectomy on LFTs. We therefore excluded the cases converted to open surgery to minimize the possibility of bias. The need for preoperative ERCP was determined clinically by the presence of jaundice, radiological evidence of a dilated biliary duct system, and an obstructive pattern of liver function tests. Clinical jaundice in these cases was the trigger point to initiate the cascade of aforesaid investigations.

Contrary to previous studies, we did not exclude patients with elevated preoperative LFTs. The rationale for including these patients was to assess the effects of pneumoperitoneum on patients with mild hepatic dysfunction. There was sonographic evidence of a normal biliary duct system and normal hepatic architecture in these patients.

### Statistical Analyses

The values of preoperative and postoperative LFTs the day after the surgery were determined. Changes in the postoperative LFTs were analyzed according to the percentage elevation with reference to the upper limit of the normal values. The mean and standard deviation of the pre- and postoperative LFT values were calculated, and the net change between the 2 was determined. Any alteration in the LFTs of patients with mild hepatic dysfunction was also examined separately. The Wilcoxon signed-rank test and the Student *t* test were performed. Statistical Package for Social Sciences (SPSS) version 14 was used for calculations.

## RESULTS

There were 301 patients with uncomplicated gallstone disease. The mean age was 48.41±15.17 years with a male to female ratio of 1 to 3. The usual $CO_2$ pressure during the surgery was 12mm Hg to 15mm Hg. Prophylaxis for deep venous thrombosis (DVT) and preoperative antibiotics were given to all patients. The same anesthesia protocol was used in all the cases. Opiates and NSAIDS were used postoperatively for analgesia. Gallbladder dissection was carried out with diathermy, and drains were used in select cases only.

The net change between the means of the preoperative and postoperative values of LFTs was calculated. Statistically significant differences were seen for the values of AST, ALT, GGT, and bilirubin. The difference in the preoperative and postoperative values of ALP was not significant **(Table 1)**.

In our study, the mean value for postoperative ALP was less than the preoperative value. A negative difference was observed, which suggests very little or no change in the postoperative value of this enzyme. This finding was commonly observed in patients with preoperatively elevated LFTs.

The alterations in postoperative LFTs were explored further by analyzing whether the values increased, decreased, or remained unchanged by using the Wilcoxon signed-rank test. A statistically significant difference was observed between the 2 values **(Table 2)**.

**Table 1.**
Differences in the Means and the Statistical Significance (*t* test)

| Enzyme[a] | Preoperative ± SD[a] | Postoperative ± SD[a] | Difference | Normal Range (M/F)[a] | P Value |
|---|---|---|---|---|---|
| AST | 25.39 ± 9.68 | 58.41 ± 54.04 | 33.02 | 10 to 37/31 | <0.05 |
| ALT | 28.03 ± 14.37 | 67.10 ± 66.33 | 39.13 | 10 to 37/31 | <0.05 |
| GGT | 43.26 ± 43.39 | 71.17 ± 93.28 | 27.91 | 11/7 to 52/34 | <0.05 |
| BIL | 10.34 ± 5.88 | 16.44 ± 10.45 | 6.10 | 5 to 17 | <0.05 |
| ALP | 83.93 ± 23.90 | 82.19 ± 33.87 | −1.81 | 34 to115 | 0.241 |

[a]ALT=alanine aminotransferase; AST=aspartate aminotransferase; GGT=gamma-glutamyl transpeptidase; ALP=alkaline phosphatase; BILI=bilirubin; SD=standard deviation; M/F=Male/Female.

The degree of alteration of individual enzymes varied and is described in **Table 3**. It is evident that the level of alteration is different for each enzyme and that most of the cases fall into the group that shows up to a 50% increase in the LFTs. This change can be labelled as mild elevation and is considered negligible by many. The next 2 groups that demonstrated elevations of up to 100% and 200% in the LFTs after surgery may cause some concern. The last group showed an increase of more than 200% from the preoperative value. This increase mostly involved the hepatocellular enzymes AST and ALT, along with GGT. Increased bilirubin levels were seen in a fraction of patients; alkaline phosphatase was not found to increase to such a high level in our study. No complication related to the procedure was observed in this series of consecutive patients.

Elevated preoperative values of one or more enzymes were seen in 71 (23.5%) patients undergoing elective laparoscopic cholecystectomy. The rise in LFTs was not marked and in the absence of clinical jaundice and lack of radiological evidence of dilated biliary tree, intraoperative cholangiogram was deemed unnecessary. These patients responded in a diverse way to the effects of pneumoperitoneum. There was further deterioration of LFTs observed in some patients, whereas others exhibited some improvement or no change with reference to the preoperative values **(Table 4)**. The results at 3 weeks after the surgery were no different from results in the other group of patients.

Among the excluded patients who required ERCP before the procedure because of CBD stones had an obstructive pattern of liver enzymes. Procedures converted to open and patients with acute cholecystitis also had an inconsistent change in their LFTs and were not suitable for inclusion in this analysis. The reason for exclusion, as men-

**Table 2.**
Wilcoxon Signed-rank Test

| Enzyme[a] | Negative Ranks[b] | Positive Ranks[b] | Ties[b] | P Values |
|---|---|---|---|---|
| AST | 17 | 268 | 16 | 0.001 |
| ALT | 17 | 265 | 19 | 0.001 |
| GGT | 115 | 163 | 23 | 0.001 |
| BILI | 33 | 241 | 27 | 0.001 |
| ALP | 197 | 83 | 21 | 0.001 |

[a]ALT=alanine aminotransferase; AST=aspartate aminotransferase; GGT=gamma-glutamyl transpeptidase; ALP=alkaline phosphatase; BILI=bilirubin.

[b]Negative ranks=Decrease in postoperative values, Positive ranks=Increase in postoperative values, Ties=No change in postoperative values.

**Table 4.**
Preoperative Raised Liver Function Tests and Their Postoperative Changes

| Enzyme[a] | Raised Preoperatively (n)[b] | Deteriorated (n)[b] | Improved (n)[b] |
|---|---|---|---|
| AST | 18 (5.98) | 8 (2.65) | 10 (3.32) |
| ALT | 58 (19.26) | 46 (15.28) | 12 (3.98) |
| GGT | 71 (23.58) | 33 (10.96) | 38 (12.62) |
| BILI | 22 (7.30) | 8 (2.65) | 14 (4.65) |
| ALP | 27 (8.97) | 4 (1.32) | 23 (7.64) |

[a]ALT=alanine aminotransferase; AST=aspartate aminotransferase; GGT=gamma-glutamyl transpeptidase; ALP=alkaline phosphatase; BILI=bilirubin.

[b]n=number of cases, values in parenthesis are percentages.

**Table 3.**
Elevation in Postoperative Liver Function Tests According to the Degree of Alteration

| Enzyme[a] | Total Raised % | Raised up to 50%(n)[b] | Raised 51-100%(n)[b] | Raised 101-200%(n)[b] | Raised >200%(n) |
|---|---|---|---|---|---|
| AST | 74.5 | 108 (35.88) | 42 (13.95) | 42 (13.95) | 32 (10.63) |
| ALT | 78.8 | 89 (29.56) | 50 (16.61) | 54 (17.94) | 44 (14.61) |
| GGT | 52.5 | 47 (15.61) | 30 (9.96) | 30 (9.96) | 51 (16.94) |
| BILI | 30.7 | 60 (19.93) | 16 (5.31) | 10 (3.32) | 5 (1.66) |
| ALP | 11 | 24 (7.97) | 6 (1.99) | 3 (0.99) | 0 |

[a]ALT=alanine aminotransferase; AST=aspartate aminotransferase; GGT=gamma-glutamyl transpeptidase; ALP=alkaline phosphatase; BILI=bilirubin.

[b]n=number of cases, values in parenthesis are percentages.

tioned earlier, was the study design, which focused on elective laparoscopic procedures only.

## DISCUSSION

Laparoscopic cholecystectomy is considered the gold standard for the treatment of symptomatic gallstones. As with any surgical procedure, it is not 100% safe and free from complications. Retained stones and duct injuries are among the serious complications related to this procedure. Duct injuries are not easy to recognize during surgery and are usually detected postoperatively.[10]

Apart from the general assessment of liver function, LFTs are generally used postoperatively as an indicator of duct obstructions and iatrogenic injuries. The sensitivity of liver function tests in predicting biliary obstruction has been shown to be high. The predictive value of ALP has been accepted, and large values of this enzyme in particular raise the possibility of CBD stones.[11]

An elevation of the liver enzymes is not always suggestive of retained stones. In earlier studies, a change in liver function tests of up to 70% has been reported with no adverse clinical outcome.[12] This elevation has been attributed to increased pneumoperitoneum pressure during the procedure, which causes hepatic dysfunction. Further studies have also confirmed the negative effects of pneumoperitoneum pressure on cardiac function. They have demonstrated a decrease in cardiac output and stroke volume during laparoscopic cholecystectomy.[13,14] Decreases in gastrointestinal and hepatic perfusion have also been explained by the same principle.[15,16]

Disturbances in liver enzymes after laparoscopic cholecystectomy were first studied by Halevy et al in 1994.[12] The possible explanations included increased intraabdominal pressure, squeeze pressure effect on the liver, excessive use of diathermy, pulling on the gallbladder, or passage of microcalculi into the bile duct.[12] More work was performed to evaluate the causes of this alteration after laparoscopic procedures, and it was found that low pneumoperitoneum pressure was associated with fewer adverse effects on liver function.[17] The pneumoperitoneum pressure used for laparoscopic cholecystectomy is higher than the pressure in the portal venous system. This pressure impedes portal circulation and reduces portal flow up to 50%, which may cause depression of the hepatic reticular endothelial system.[6] This observation explains why the change in liver function tests is related to the duration and pressure used for the pneumoperitoneum.[5]

The assessment of preoperative LFTs is performed with the intent to diagnose hepatic dysfunction or biliary obstructions for timely and appropriate management. It was suggested that for patients exhibiting altered LFTs before the surgery, like patients with liver disease, laparoscopy might not be the right choice because it can further deteriorate hepatic function.[7] In contrast to this suggestion, a recent study of laparoscopic cholecystectomy in cirrhotic patients has confirmed that the procedure can be safely carried out in patients with Child Classes A and B cirrhosis of the liver with no significant increase in complications.[18]

Gallbladder surgery is not the only procedure associated with elevated postoperative LFTs. Other laparoscopic procedures like colorectal, gastric, or other abdominal surgery have also been associated with altered postoperative liver function tests.[5,6,19] Early elevation of LFTs soon after surgery should not cause major concern as they usually return to normal without intervention. In the case of laparoscopic cholecystectomy, close monitoring by performing serial biochemical analyses can be done when there is increased suspicion of an iatrogenic duct injury or slipped stone as indicated by elevated levels of alkaline phosphatase and bilirubin.[20]

In our study, the level of change of AST, ALT, and GGT was high. There were moderate changes in the postoperative bilirubin levels, and the level of ALP remained almost unchanged. Although the derangement in the level was more than 200% in a small number of patients but no adverse clinical event, directly related to this change, was noticed. With the exception of a negligible number of cases, all the values were found to have returned to normal at the follow-up after 3 weeks. This value, therefore, can safely be considered as a cut off point. This follow-up at 3 weeks after the surgery would only exclude complications in the early postoperative period. Longer follow-ups are required to determine late complications related to the procedure, which was beyond the scope of this study.

Previous studies on the same subject excluded patients with preoperative elevated LFTs from their analyses.[21] We did not exclude these patients just because of abnormal preoperative LFTs and did not find any negative impact upon the final outcome.

## CONCLUSION

Liver function tests include AST, ALT, GGT, ALP, and bilirubin. Raised values of AST, ALT, and GGT represent hepatocellular dysfunction. Any rise in the values of ALP

and bilirubin suggests obstructions to the flow of bile and may have clinical manifestations, warranting more investigations before surgery. Mild to moderate elevations in hepatocellular enzymes can be a benign observation and may not have any clinical features. High values of ALP and bilirubin are almost always associated with clinical signs and should be dealt with cautiously. In the absence of clinical signs and symptoms suggestive of an underlying pathology, the routine assessment of liver function before and after surgery seems unnecessary.

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