Immediate versus Delayed Laparoscopic Cholecystectomy after Endoscopic Retrograde Cholangiopancreatography in Choledocholithiasis

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ABSTRACT

**Background:** There would be less need for emergency open cholecystectomy and fewer problems if cholecystectomy was performed soon following endoscopic retrograde cholangiopancreatography (ERCP).

**Objective:** This study aimed to evaluate the advantages of immediate over delayed laparoscopic cholecystectomy among patients who had common bile duct stones post ERCP regarding outcome, safety and complications.

**Subjects and Methods:** At General Surgery Department of Zagazig University Hospitals, 60 patients with cholecystolithiasis after doing ERCP were divided into 2 groups. Group (A) for immediate laparoscopic cholecystectomy (LC) in same sitting after ERCP and Group (B) for delayed LC (4 weeks or more) after ERCP. Conversion rate, operative time, intra- and post-operative complications were assessed.

**Results:** The mean operative time was shorter in the immediate group (54.96 ± 14.21. min.) than in the delayed group (71.66 ± 24.72 min.), which represented a significant difference in favor of the immediate group. There was a statistically significant distinction in the incidence of complications after surgery where in delayed group five patients showed intraoperative bleeding and three patients converted to open cholecystectomy. Length of hospital stays also differed significantly between groups, 0.9 versus 1.95 for immediate LC group & delayed LC group, respectively.

**Conclusion:** Performing immediate LC post, ERCP in comparison to delayed LC after ERCP had better outcomes. It had the lower conversion rate, less operative time, shorter hospital stay, and less intra-operative and post-operative complications.

**Keywords:** Laparoscopic cholecystectomy, Immediate, Delayed, Endoscopic Retrograde cholangiopancreatography.

INTRODUCTION

Cholelithiasis is a major disease that demands surgical management and affect nearly 10% of adults. Choledocholithiasis affects roughly 10-20% of those who have gallbladder stones. Common bile duct (CBD) stones affect between 3 and 10% of people who have cholecystectomy. Liver function tests (LFTs) are performed to keep an eye on a bile duct stone. Although elevated levels of blood bilirubin and alkaline phosphatase are a reliable indicator of biliary obstruction, they lack the sensitivity and specificity needed to diagnose a common bile duct stone (1).

Endoscopic retrograde cholangiopancreatography (ERCP) is effective in the removal of about 90% of common bile duct stones. Treatment of stones in the common bile duct with medicines has been the subject of debate (2). For minor gallbladder issues, laparoscopic cholecystectomy (LC) is the go-to procedure. Simple cholecystectomy is effective for cholecytitis, cholelithiasis, and biliary colic. Stones in the common bile duct (CBD) can make any of these conditions more severe, but the best course of action is hotly contested. Treatment options for choledocholithiasis includes either simultaneous ERCP or laparoscopic cholecystectomy within the first 24 hours, or postponing the surgery by 4-8 weeks (3). The greatest risk of CBD stone extraction by ERCP before or after surgery are cholangitis and pancreatitis. The creation of laparoscopic cholecystectomy has reopened the controversy on the best treatment of cases with CBD stones or suspected CBD stones that undergo cholecystectomy (4). The strategy of treatment for gall bladder stones with secondary CBD stones is ERCP followed by laparoscopic cholecystectomy. Although immediate laparoscopic cholecystectomy is recommended there is no consensus about suitable gap between laparoscopic cholecystectomy and endoscopic retrograde cholangiopancreatography (ERCP) (5). There would be less need for open cholecystectomy and fewer problems during and after surgery if cholecystectomies were performed soon after ERCP (6). The goal of this study was to evaluate the advantages of immediate over delayed laparoscopic cholecystectomy in patients with common bile duct stones post ERCP regarding outcome, safety and complications.

SUBJECTS AND METHODS

Subjects:
In the Zagazig University Hospitals’ General Surgery Department, sixty patients with cholecystolithiasis after doing ERCP were studied in comparative randomized study.

Inclusion criteria: Patients with cholelithiasis after ERCP, and age between 18 to 70 years.

Exclusion criteria: Patients not fit for surgery, acute cholecystitis with biliary pancreatitis patients, patients who cannot undergo laparoscopic surgery due to medical conditions, and patients who underwent previous upper abdominal surgeries.
All patients were subjected to the following:

A. History taking: Full clinical history taking were obtained from each patient with special emphasis on the presenting symptoms.

B. Clinical Examination: Both general and local examination were performed to every patient including evaluations regarding post ERCP morbidities if present.

C. Imaging:

Pelvic-abdominal ultrasound examinations: (1) To check all solid organs status. (2) Gallbladder status; stones, wall thickness, pericholecystic or other collections if present or ultrasonographic signs of acute inflammation. (3) Biliary system; CBD diameter and/or stones and intrahepatic biliary radical dilatation.

MRCP for confirmation of complete clearance of their CBD from stones in whom serum bilirubin, ALP and GGT were elevated.

D. Laboratory investigations: Liver functions, kidney functions, CBC, coagulation profile, Glycemic profile.... etc.

Patients were scheduled to be operated upon into two groups:

Group (A) for immediate LC in same sitting after ERCP and Group (B) for delayed LC (4 weeks or more) after ERCP. Our primary outcome was to measure conversion rate to open procedure as it is the main index of operative difficulty of LC and secondary outcomes were the operative time, intra- and post-operative complications and hospital stay.

Operative Procedure:

After the patient had been put in the supine position and general anesthesia with endotracheal tube was given, the patient was fixed to the operating table then creation of an aseptic surgical field potential of switching to open procedure if such becomes necessary.

The following steps were conducted:

A- Establishment of pneumoperitoneum and insertion of first and second ports: After draping and taking places by surgical team Verses needle was introduced to induce pneumoperitoneum through an upper umbilical incision. First, insufflation of the abdomen was achieved to 12-15mmHg using carbon dioxide then 10 mm supra umbilical trocar was inserted. Using a camera connected to telescope 30º, the second 10 mm port was introduced under vision at the epigastrium below the xiphoid process just to the right of midline and an exploratory laparoscopy to the abdomen was done.

B- Exploratory laparoscopy: The first stage in the process is the diagnostic laparoscopy, which was performed meticulously with special focus on the umbilical region to rule out adhesions or damage to the omentum or intestine that might have occurred during port placement, and on the GB region to check for adhesions (Figure 1).

C- Insertion of the 3rd and 4th ports under direct vision: Two further 5 mm ports were placed after exploratory laparoscopy was completed: one in the right midclavicular line just below the right costal edge, and the other in the right anterior axillary line at the level of the umbilicus. Then the position of patient changed to reverse Trendelenburg position. Adhesions were broken up, and the gallbladder was withdrawn toward the right shoulder with the help of a lengthy device. Next, a grasper was inserted into the midclavicular port to secure the gallbladder's Hartmann's pouch. Therefore, the hepatocystic triangle is on display (Figure 1).

D- Hepatocystic triangle dissection and creation of critical view of safety: Opening of anterior & posterior peritoneal leaflets was done. The hepatocystic triangle was free of fibrous and fatty tissue, two tubular structures entered the base of the GB, and the bottom third of the GB was dissected away from the liver so that the cystic plate could be seen. These three conditions constitute the critical view of safety.

E- Clipping and division of cystic duct and artery: Once the critical view of safety was adequately achieved, the rest of the surgery proceeded with confidence. Both structures were carefully clipped proximally 2 clips and distally 1 and transected.

F- Dissection of gallbladder from liver: Dissection and separation of GB from CP and hemostasis were achieved by diathermy or Harmonic scalpel and deflation of the abdomen to 8 mmHg for 2 minutes so that any venous bleeding that may be tamponade by increased intra-abdominal pressure is not missed (15 mmHg).

G- Extraction of the gallbladder and placement of a drain: The GB was removed from the abdomen in a retrieval bag in some patients and by direct extraction with a claw forceps in the others. Irrigation and suction of the peritoneum and port site with normal saline.
Intraperitoneal (GB bed) tube drain No.18 was put in needed cases (Figure 2 & 3).

**H- Removal of trocars and wound closure:** All trocars were removed under direct visualization except the last one (umbilical port), which was lift until the abdomen was deflated completely and ovum forceps was inserted in this port, then the cannula was removed before the ovum to protect intestinal loops from prolapsing through port site causing incisional hernia. We used PDS suture number 1 for incisional hernia prevention, then fascial closure of trocar sites larger than 5 mm. All trocar sites were closed with subcuticular or interrupted sutures.

**IV. Postoperative care and complications:**
All Patients were managed with current enhanced recovery protocols: (1) Shifted postoperatively to ordinary words under close observations. (2) The post-operative pain was managed by pain killers (Paracetamol, NSAID or opioids when needed). (3) Encouraged for early ambulation. (4) The patients were started on oral fluids by 6-8 h postoperatively. (5) The intravenous antibiotic ceftriaxone 1 gram per 12 hr was given in the 1st postoperative day. (6) Drains were removed if became minimal (< 30 ml in 24h).

**Ethical consent:**
Research ethics council of Zagazig University approved the study as long as all participants provided informed consent forms. Ethics guidelines for human experimentation were adhered to by the World Medical Association's Helsinki Declaration.

**Statistical analysis:**
In order to analyze the data acquired, Statistical Package of Social Sciences version 20 was used to execute it on a computer (SPSS). In order to convey the findings, tables and graphs were employed. The quantitative data were presented in the form of mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t test (T) was used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X²) were used to assess qualitatively independent data. The significance of a P value of 0.05 or less was determined.

**RESULTS**
The study was carried out on 60 patients who were divided into two equal group (30 patients in immediate group and 30 patients in delayed group). All 60 patients were followed up and analyzed statistically. Statistically, there was no discernible distinction between both groups in terms of age and gender (Table 1).

**Table (1): Age and gender of the both groups regarding**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Groups</th>
<th>Test</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Immediate LC Group</td>
<td>Delayed LC Group</td>
<td>t/χ²</td>
</tr>
<tr>
<td>Age (years):</td>
<td>N=30</td>
<td>N=30</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>40.6±9.29</td>
<td>44.66±9.5</td>
<td>1.67</td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>22 (73.3%)</td>
<td>24</td>
<td>0.37</td>
</tr>
<tr>
<td>Male</td>
<td>8 (26.7%)</td>
<td>6 (20.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Immediate group was significantly higher regarding all parameters of pre-OP lab than delay group (Table 2).
Table (2): Lab distribution between studied groups before operation

<table>
<thead>
<tr>
<th></th>
<th>Immediate Group</th>
<th>Delay Group</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T Bilirubin (μmol/L)</td>
<td>2.52±0.55</td>
<td>0.53±0.13</td>
<td>19.008</td>
<td>0.00**</td>
</tr>
<tr>
<td>D Bilirubin (μmol/L)</td>
<td>1.87±0.39</td>
<td>0.19±0.06</td>
<td>15.372</td>
<td>0.00**</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>207.4±41.46</td>
<td>53.23±12.8</td>
<td>19.450</td>
<td>0.00**</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>128.0±31.05</td>
<td>41.70±6.79</td>
<td>13.612</td>
<td>0.00**</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>191.0±8.03</td>
<td>49.43±11.97</td>
<td>15.583</td>
<td>0.00**</td>
</tr>
<tr>
<td>Amylase (U/L)</td>
<td>112.83±23.14</td>
<td>65.83±8.71</td>
<td>8.462</td>
<td>0.00**</td>
</tr>
</tbody>
</table>

There was a statistically significant decrease all parameters after operation (Table 3).

Table (3): The difference between the pre- and postoperative LFT in immediate group only

<table>
<thead>
<tr>
<th></th>
<th>Pre-operative LFT</th>
<th>Post-operative LFT</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALP (U/L)</td>
<td>207.4±41.46</td>
<td>133.5±31.16</td>
<td>0.00**</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>128.0±31.05</td>
<td>47.0±8.15</td>
<td>0.00**</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>191.0±8.03</td>
<td>83.5±14.80</td>
<td>0.00**</td>
</tr>
<tr>
<td>Amylase (U/L)</td>
<td>112.83±22.14</td>
<td>69.0±12.95</td>
<td>0.00**</td>
</tr>
</tbody>
</table>

The operative times for the two groups were significantly different. The delayed LC group had a longer mean operating time (Table 4).

Table (4): Operative time among groups

<table>
<thead>
<tr>
<th>Operative time (in minutes)</th>
<th>Immediate LC Group</th>
<th>Delayed LC Group</th>
<th>T</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>54.96±13.21</td>
<td>71.66±16.72</td>
<td>3.208</td>
<td>0.002*</td>
</tr>
</tbody>
</table>

The adhesion and difficult calot's dissection were statistically associated with delayed group (Table 5).

Table (5): Intraoperative adhesions among group

<table>
<thead>
<tr>
<th></th>
<th>Immediate LC Group</th>
<th>Delayed LC Group</th>
<th>t/χ²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=30</td>
<td>N=30</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adhesions according to Parkland Grading Scale:

- I: 14 (46.7%) 2 (6.7%)
- II: 11 (36.7%) 13 (43.3%)
- III: 4 (13.3%) 10 (33.3%)
- IV: 1 (3.3%) 5 (16.7%)
- V: 0 (0%) 0 (0%)

Intraoperative complications showed five patients in delayed group had intraoperative bleeding and three of them were converted to open. While, in immediate group no case had intraoperative bleeding. Regarding bile duct injury in both groups, no patient had bile duct injury (Table 6).

Table (6): Comparison between the studied groups regarding intraoperative complications.

<table>
<thead>
<tr>
<th>Intraoperative complications</th>
<th>Groups</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Immediate LC Group</td>
<td>Delayed LC Group</td>
</tr>
<tr>
<td>N=30</td>
<td>N=30</td>
<td></td>
</tr>
</tbody>
</table>

Regarding postoperative complications, there was no statistically significant difference between the two groups. Re-admission was not necessary for any patients in either cohort. Two patients in the group that had delayed LC experienced wound infection after surgery (Table 7).

Table (7): Comparison between the studied groups regarding postoperative complications

<table>
<thead>
<tr>
<th>Postoperative complications</th>
<th>Groups</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Immediate LC Group</td>
<td>Delayed LC Group</td>
</tr>
<tr>
<td>N=30</td>
<td>N=30</td>
<td></td>
</tr>
</tbody>
</table>

Bleeding

- No
  - 30 (100%) 0 (0%)
  - 30 (100%) 0 (0%)
  - 0.0 1.0

Bile leak

- No
  - 30 (100%) 0 (0%)
  - 30 (100%) 0 (0%)
  - 0.0 1.0

Jaundice

- No
  - 30 (100%)
  - 0 (0%)
  - 0.0 1.0

Pancreatitis

- No
  - 30 (100%)
  - 0 (0%)
  - 0.0 1.0

Cholangitis

- No
  - 30 (100%)
  - 0 (0%)
  - 0.0 1.0

Readmission

- No
  - 30 (100%)
  - 30 (100%)
  - 0.0 1.0

Wound infection

- No
  - 30 (100%)
  - 28 (93.3%)
  - 2 (6.7%)
  - 0.21 0.64

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When comparing the average length of hospital stays among the analysed groups, there was a statistically significant difference between the immediate and control groups (Figure 4).

Figure (4): Hospitalization duration analyses comparing different study groups

Two patients from the delayed group had a wound site infection at the site of umbilical port after the first week of follow up and managed by repeated dressings and removal of stitches with oral augmentin 1gm/12 hours for seven days. There were no other complications detected in all patients after 12 weeks (Table 8).

Table (8): Comparison between the studied groups regarding postoperative - follow up

<table>
<thead>
<tr>
<th>Follow up timing and parameters</th>
<th>Groups</th>
<th>Immediate LC Group</th>
<th>Delayed LC Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N=30</td>
<td>N=30</td>
</tr>
<tr>
<td>After 1 week</td>
<td>History</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Examination</td>
<td>NAD</td>
<td>2 patients developed port site infection</td>
</tr>
<tr>
<td></td>
<td>Laboratory</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Ultrasonography</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td>After 2 weeks</td>
<td>History</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Examination</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Laboratory</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Ultrasonography</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td>After 4 weeks</td>
<td>History</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Examination</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Laboratory</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Ultrasonography</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td>After 8 weeks</td>
<td>History</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Examination</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Laboratory</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Ultrasonography</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td>After 12 weeks</td>
<td>History</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Examination</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Laboratory</td>
<td>NAD</td>
<td>NAD</td>
</tr>
<tr>
<td></td>
<td>Ultrasonography</td>
<td>NAD</td>
<td>NAD</td>
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</tbody>
</table>

DISCUSSION

However, many surgeons still prefer delayed LC as the standard treatment for patients with gallstones and choledocholithiasis following ERCP, despite recent data suggesting that immediate interval LC has better outcomes. This is because surgeons believe that by waiting, the GB area can cool down and recover from the acute illness (7).

Our study was intended to compare immediate versus delayed LC after ERCP as regards safety, operative time, conversion to open cholecystectomy, postoperative morbidity, hospital stay and outcomes of the same procedure in the two strategies of management of patients with cholecystolithiasis and choledocholithiasis. Our study included 60 patients who were divided into two groups: Immediate group 30 patients; 22 females (73.3%) and 8 males (26.7%) and their mean age was 40.6 ± 9.29 years. Delayed group 30 patients; 24 females (80.0%) and 6 males (20.0%) and their mean age was 44.66 ± 9.52 years. This finding is in agreement with Kent et al. (8) who studied an immediate (within 24 hours) LC group (1) compared to group (2), those who had delayed LC. Patients ranged in age from 12 to 90 years (median, 39 years), and 183 (72%) were female.

Concerning lab distribution of our study, immediate LC group was significantly higher regarding all parameters (T & D Bilirubin, ALP, AST, ALT and Amylase) than delay group regard pre-operative evaluation. In post-operative lab distribution, immediate LC group showed a significant decrease in the levels of ALP, AST, ALT and amylase (133.5, 47.0, 83.5 and 69.0, respectively) postoperatively versus (207.4, 128.0, 191.0 and 112.83, respectively) preoperatively. These findings are in concordance with Tokyo guidelines Mayumi et al. (9) and Kiriyma et al. (10). While, in contrast with Kent et al. (8) who reported an elevated total serum bilirubin (1.2 mg/ dL), but no significant difference between both groups.

In our study, the adhesion and difficult calot’s dissection were a statistically higher in delay LC group compared to immediate LC group. On other hand, Garancini et al. (11) noted that a higher risk of bile duct injury is connected with the formation of fibrosis in Calot’s triangle after the initial bout of inflammation after acute cholecystitis subsides, which has been considered the main cause for a technically challenging surgery.

Intra-operative complications in our study showed five patients in delayed group had intra-operative bleeding and three of them converted to open and in immediate group no case had intra-operative bleeding. Regarding bile duct injury in both groups no patient had bile duct injury. Tantia et al. (12) revealed that no major complications (bleeding, perforation, or pancreatitis) were encountered following ERCP.

The mean operative time in our study was shorter in immediate group (54.96 ± 14.21 min.) than in the delayed group (71.66 ± 24.72 min.). Trejo-Ávila et al.
(13) found that mean operative time among immediate LC was 98.7 ± 38.95 min with no significant difference with other group.

Our study revealed that 2 patients from the delayed group had a wound site infection at the site of umbilical port after the first week of follow up and managed by repeated dressings and removal of stitches with oral augmentin 1gm/12 hours for seven days. There were no other complications detected in all patients after 12 weeks. Tantia et al. (12) reported one patient had complication of minor bile leak from cystic duct stump, which was managed conservatively and was self-limiting among immediate LC patients. Other complications related to laparoscopy such as biloma, bile peritonitis, sepsis, multiple organ dysfunction syndromes, external biliary fistula, cholangitis and liver abscess are often associated with concomitant vascular injury or even haemobilia in rare cases (14).

Our study demonstrated statistically significant differences in length of hospital stays (LOS) between the groups was 0.9 versus 1.95 days for immediate LC group & delayed LC group respectively. This finding agrees with Tracy et al. (15) who concluded that performing a cholecystectomy right away significantly shortened recovery time after surgery. Also, Kent et al. (8) revealed that group 1 (immediate LC) had a significantly shorter hospital length of stay (2 ±1 day’s vs 3 ± 2 days), P ≤0.001). Similarly, Trejo-Ávila et al. (13) reported that patient’ stays were shorter overall in the group receiving immediate LC. (2 vs. 4 days, p<0.001).

Our study is in matched with Trejo-Ávila et al. (13) who concluded that laparoscopic cholecystectomy during the first 24 hours after endoscopic therapy of choledocholithiasis is safe and practical, without increased surgical morbidity, and associated with shorter hospital stays.

However, Ye et al. (16) stated that the best time to perform a laparoscopic cholecystectomy in individuals who undergo therapeutic ERCP for choledocholithiasis should be intermediate LC (within 2 months after admission). While early LC is associated with a measurable risk of complications. So, we strongly recommend immediate LC (≤ 24 hr.) after endoscopic retrograde cholangiopancreatography in choledocholithiasis treatment.

CONCLUSION
Performing immediate LC post, ERCP in comparison with delayed LC after ERCP had better outcomes. It had the lower conversion rate, less operative time, shorter hospital stay, and less intra-operative and post-operative complications. The comparison between the two groups revealed that immediate LC post ERCP had the upper hand of the advantages remembered above and the least disadvantages rather than the other group.

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Author contribution: Authors contributed equally in the study.

REFERENCES


