Effectiveness of Laparoscopic Management of Perforated Duodenal Ulcer with Eradication of Helicobacter Pylori in Properly Selected Patients

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Abstract: Aim of the Work: To evaluate the effectiveness of laparoscopic repair of Perforated Duodenal Ulcer as regard its safety, postoperative pain, complications, hospital stay duration and recurrence after eradication of *H. Pylori*. **Patients and Methods:** From June 2008 till June 2012 twenty patients with sudden diffuse abdominal pain less than 24 hours duration secondary to perforated duodenal ulcer and free from comorbid disease were submitted to Urea Breath Test(UBT) to diagnose *H. Pylori* infection then laparoscopic exploration, peritoneal toilet and repair of the duodenal perforation by Cellan-Jones pedicled omental patch. This procedure was evaluated as regard safety, post-operative pain, complications and hospital stay duration. All patients with *H. Pylori* positive were submitted post-operatively to Clarithromycin triple therapy to eradicate *H. Pylori*. Levofloxacin Triple based therapy was used for the resistant cases. **Results:** All patients (20 patients) 16 males and 4 females were submitted to laparoscopic exploration, peritoneal toilet and Cellan-Jones pedicled omental patch repair of the perforated duodenal ulcer. The procedure was successful in all patients safely with post-operative pain score according to Visual Analog Scale (VAS) 6 in the 1st day post-operative decreasing to 4 after 48 hours post-operative. Wound infection was recorded in 3 patients (15%), chest infections in 2 patients (10%), with no mortality. Mean hospital stay was 5.5 days. There were 12 patients out of 20 (60%) *H. Pylori* positive by UBT, 10 patients were treated successfully by Clarithromycin Triple Therapy, while the other 2 necessitate Levofloxacin Triple Based Therapy. **Conclusion:** With new advent of minimal invasive surgery, laparoscopic repair of early perforated duodenal ulcer is recommended safely with minimal complications and with no mortality. Eradication of *H. Pylori* post-operatively is mandatory to eliminate recurrence of peptic ulcer disease.

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1. Introduction:

Duodenal ulcer perforation is a serious complication of peptic ulcer disease that occurs in 5 % to 10 % of duodenal ulcer patients and accounts for more than 70% of deaths associated with peptic ulcer disease [(1)]. The current peak age for perforated duodenal ulcer is 40 to 60 years [(2)], but the age of perforated peptic ulcer (PPU) patients is increasing especially the member of patients over 60 years old [(3)].

Non-steroidal anti-inflammatory (NSAIDS) are the most important risk factor for PPU [(4)]. The patients are at increased risk when using several NSAIDS at a time or a single NSAID at an increased dosage. Cocaine and psycho-stimulants were also noted for their destructive effects on gastric and duodenal mucosa [(5-6)]. Iatrogenic perforations were also described and may result from endoscopy [(7)].

Although the efficiency of histamine H_2 Blockers and Proton Pump Inhibitors (PPI), decrease the incidence of peptic ulcer disease and almost eliminate elective surgical management of peptic ulcer but the incidence of PPU has remained the same [(8,9)].

H. Pylori are now the recognized culprit of the majority of patients with duodenal and gastric ulcers and post eradication ulcer recurrence is uncommon [(10)]. More than 95% of patients suffering from duodenal ulcer and about 70-80% of patients with gastric ulcer are *H. Pylori* positive[(11, 12)].

Data regarding *H. pylori* infection in perforated peptic ulcers are conflicting, with different infection rates as noted by Reinbach 47% [(13)], Sebastian 83% [(14)] Sharma [(15)] 61 % while Chowdhary was 0 % [(16)]. Eradication of *H. Pylori* can prevent recurrent ulcer disease complications such as bleeding [(17-18)]. Eradication of *H. Pylori* prevents ulcer recurrence in patients with *H. Pylori* -associated perforated duodenal ulcer. Of 99 *H. Pylori* positive patients, 51 were assigned to an anti-helicobacter pylori therapy, and 48 to omeprazole alone. After one year, ulcer relapse was significantly lower in patients treated with an anti-helicobacter therapy (4.8 vs. 38.1 %) [(19)]. Urea Breath Test (UBT) identifies active *H. Pylori* infection by way of organism's urease activity with sensitivity and specificity typically exceeding 95% in most studies [(20)]. As UBT is quick and reliable test for *H. Pylori*, it can be used as screening test. A rapid

release ^{13}C urea tablets produces a result in 15 minutes is becoming available. The UBT also provides an accurate means of post-treatment testing [21], to evaluate proper eradication. UBT sensitivity is decreased by medications that reduce organism density or urease activity, including bismuth containing compounds, antibiotics and PPI's. It's currently recommended that bismuth and antibiotics be withheld for at least 28 days and a PPI for 7-14 days prior to the UBT [22-23].

Proper eradication of *H. Pylori* is essential to eliminate post-operative recurrence or bleeding either Primary or Salvage therapy for persistant *H. Pylori* infection. Primary treatment is either Clarithromycin-based Triple Therapy (PPI, Clarithromycin and Amoxicillin, or Metronidazole) for 14 days with eradication rates of 85 % or Bisthmus Quadruple therapy (PPI, Bisthmus, Metronidazole and Tetracyline) for 10-14 days with eradication rates of up to 90%. Salvage therapy for persistent *H. Pylori* infection should be made to avoid antibiotics that have been previously taken by the patients. Salvage therapy is either bisthmus-based quadruple therapy or Levofloxacin-based triple therapy (PPI, amoxicillin, and levofloxacin) for 10days with eradication rates up to 87%, provided antibiotic away from the primary therapy [24].

Boey score which seeks to predict mortality based on the presence of major medical illness (grade III or IV according to ASA score), preoperative shock (defined as systolic blood pressure less than 90 mmHg) and delayed presentation (duration of perforation longer than 24 hours). Hospital mortality proportion increased progressively with the number of prognostic variables, being 0%, 10%, 45.5% and 100% in patients with none, one, two or three of all three variables, respectively [25].

For most of the patients of PPU, only treatment is immediate surgical repair. The traditional management of perforated duodenal ulcer was Cellan-Jones Pedicled Omental Patch application described in 1929 [12]. It was not until 1937 that Graham published his results with a free omental graft [27]. Very often surgeons mention they used Graham patch, but they actually mean they used the pedicled omental patch described by Cellan-Jones [27]. Schein could not have outlined it any clearer "Do not stitch the perforation but plug it with viable omentum and patch a perforated ulcer if you can, if you cannot, then you must resect"[28].

With the advent of acid reducing medical treatment in form of proton pump inhibitor (PPI) and *H. Pylori* eradication post-operative, definitive acid reducing surgery is not recommended in PPU [12].

Laparoscopic treatment of PPU was first reported by Mouret *et al.* in 1989 [30], using fibrin glue and omental patch, followed soon after by Nathanson *et al.* [31], which describe the suture repair of the perforated duodenal ulcer. There are relative contraindications which include elderly patients, cardiac pathology, chronic respiratory insufficiency, cirrhosis, severe coagulopathy and delayed presentation (duration of perforation more than 24 hours).

2. Patients and Methods:

From June 2008 till June 2012 twenty patients with sudden diffuse abdominal pain less than 24 hours duration, were enrolled in the study. On examination all patients were vitally stable (patients with systolic blood pressure less than 90mmHg were excluded from the study) with tenderness all over the abdomen especially the epigastrium. X-ray of the abdomen and chest erect revealed air under the diaphragm (Figure1).

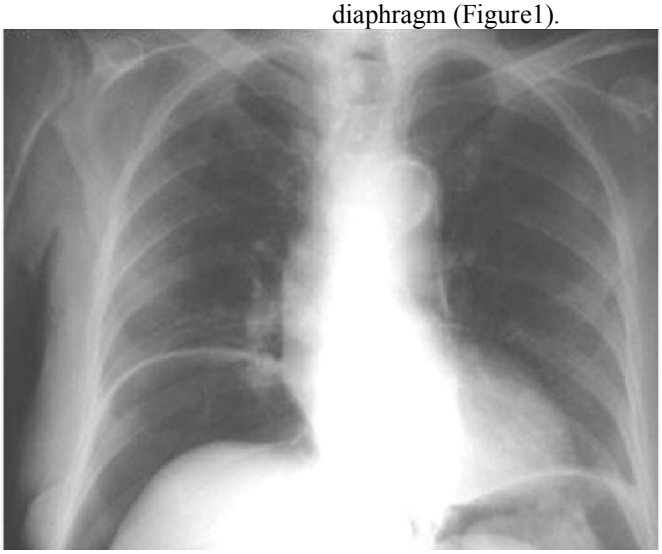

Figure 1. Chest X-ray revealed air under the diaphragm

ECG, CBC, Serum amylase, lipase, renal and liver function test, Na^+ , K^+ and Urea Breath Test(UBT) for diagnosis of H. pylori infection were done for all patients. 2gm Ceftriaxone, 500mg metronidazole and 40mg omeprazole were given through IV route after insertion of Nasogastric Tube (NGT) and proper resuscitation. All patients were transferred to Operating Room after general endotracheal intubation anesthesia, proper sterilization and draping, a 10mm endopath excel trocar with optic view technology with telescope was inserted under vision just above the umbilicus through which CO_2 insufflation was done with pressure 12 mmHg. Other ports inserted using the triangular concept to form a baseball diamond shape, as an angle 60° between the two working instrument tips with tangential approach to the working site (elevation angle 30°) and appropriate working distance. A 10mm working port inserted in the left hypochondrium 10cm from the midline. A 5mm port inserted in the right midclavicular line above the umbilicus and another 5mm port is placed in the epigastrium to the right of the falciform ligament 2cm below the right costal margin for liver retraction. The patient positioned in reverse trendelenburg position 15°. After liver retraction, use suction irrigation tube for suction and irrigation with saline exposing the duodenal perforation site then suction of the intra-peritoneal collections in the subphrenic spaces, paracolic gutters and pelvis. Start proper irrigation and suction 2-4 liters of warm normal saline. The perforation was closed with 3 interrupted 3/0 polygalactin sutures. The sutures were placed and kept without tying. An omental patch with intact blood supply was placed over the perforation, held in place by grasper in the epigastric port and the sutures were tied over the omental patch, completely sealing the perforation (Figure 2).

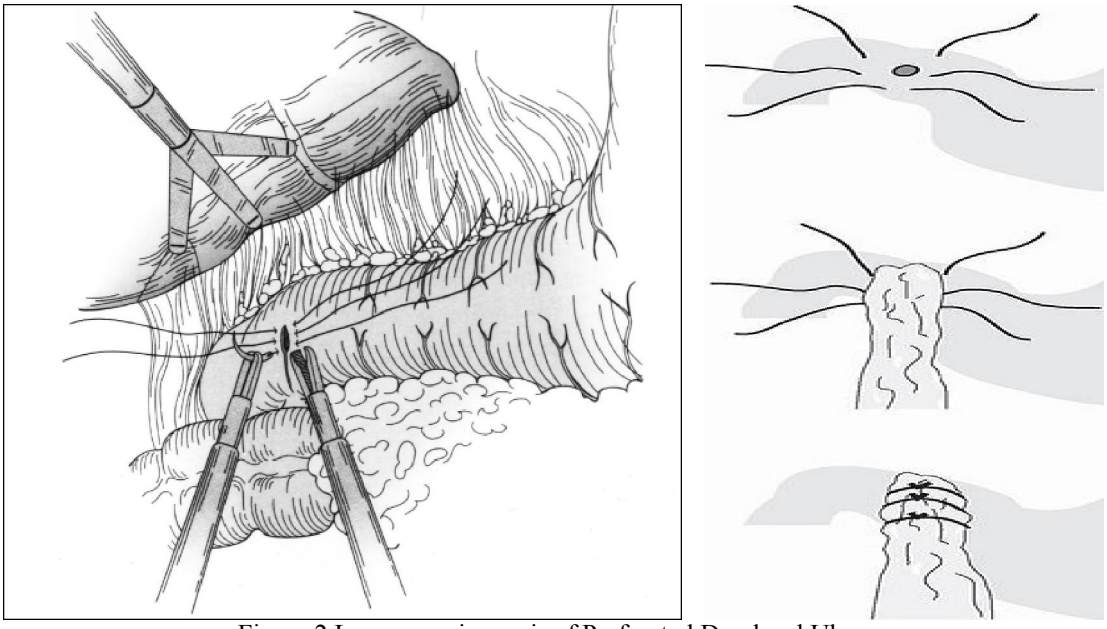

Figure 2 Laparoscopic repair of Perforated Duodenal Ulcer

Suction irrigation peritoneal lavage again with Normal Saline to ensure proper peritoneal toilet. Two closed tube drain were kept in the hepato-renal pouch and the pelvis. The 10mm port sites were closed under vision using suture passer with 1/0 polygalactin sutures.

After recovery the patients were transferred to the In-patient ward, kept in semi-sitting position, IV fluid, correction of electrolyte imbalance by giving the deficit and daily requirement of K, Na, Ca & Mg, continue the preoperative antibiotic and omeprazole. All patients started oral fluid two to three days post-operative depending on intestinal motility after removal of NGT.

All patients were discharged on 5^{th} to 7^{th} day post-operative. All patients with *H. Pylori* positive (12 patients) received Clarithromycin-based triple therapy (Omeprazole 20mg b.i.d. + Clarithromycin 500mg b.i.d. + Metronidazole 500mg b.i.d.) for two weeks then continue Omeprazole 20mg twice/day for 1.5 months. UBT is done after stoppage of all medications for 2 weeks with upper gastrointestinal endoscopy to ensure eradication of *H. Pylori* and healing of ulcer. Resistant *H. Pylori* was found in 2 out of 12 after primary treatment with eradication rate

83.3%, which necessitate salvage treatment by Levofloxacin triple therapy in form of PPI , amoxicillin 1 gm / 12 hours and levofloxacin 500 mg / 6 hours for 10 days. All patients were submitted to follow up upper GI endoscopy after 6months which revealed no recurrence.

3. Results:

There were twenty patients included in the study 16 males and 4 females (with ratio 4:1), 5 (20%) patients were NSAIDS users, 7(35%) were smokers and 12(60%) were UBT positive. Age range of the patient was from 22 to 60 years old. All patients included in the study were free from comorbid disease with ASA less than grade III, early presentation with onset of symptoms less than 24hours prior to admission and stable vitally with systolic blood pressure more than 90mmHg. All patients were submitted successfully to laparoscopic exploration, peritoneal toilet and closure of the perforated duodenal ulcer with Cellan-Jones omentoplasty. The median operating time was 115 minutes (range 90 to 140minutes). Median post-operative pain score according to visual analog scale was 6 in the first day with analgesics such as pethidine 100mg IM every 12hours and intravenous paracetamol 1gram every 8 hours. this score was reduced to 4 latter on necessitating intravenous paracetamol only. As regard Post-operative complications, wound infection occurred in 3 patients (15%), chest infection in 2 patients (10%).and no mortality. Mean hospital stay was 5.5 days. Oral feeding started on the 3rd post-operative day. All patients who were *H. Pylori* positive received Clarithromycin triple therapy for two weeks while the other patients received Omeprazole only which continued for 2 months for all patients. Eradication rate of *H. Pylori* by Clarithromycin triple therapy was (83.3%), 2 patients failed which required Levofloxacin triple therapy. Follow up upper GI endoscopy 2 and 6 months postoperatively revealed complete healing of the ulcer.

4. Discussion:

Laparoscopy found its way in repair of PPU by Mouret *et al.* 1989; using fibrin glue and omental patch [30], followed soon after by Nathanson *et al.,* 1990, using the suture repair [31]. There are relative contraindication to laparoscopic repair of PPU including delayed presentation (more than 24hours from the onset of symptoms), comorbid disease and shocked patients. PPU is a serious complication of peptic ulcer disease that occurs in 5 to 10 % of duodenal ulcer patients and accounts for more than 70 % of deaths associated with peptic ulcer disease [1]. NSAIDS and Corticosteroids are the most important risk factors for PPU [4].

H. Pylori infection is now the recognized culprit of the majority of patients with duodenal and gastric ulcers. Ulcer recurrence is uncommon after proper *H. Pylori* eradication [10]. The increasing advent of more effective drugs for the treatment of the peptic ulcer disease (PPI) and greater understanding of the role of microbial infections (*H. Pylori*) and consequent antibiotic therapy are all factors that have progressively made elective surgery for uncomplicated peptic ulcer are very rare; it is now used only for complications [9,32].

In our study the median duration of surgery was 115 minutes (range from 90 to 140) which is larger than *Schirus et al.* [33] and Abdul Razaque *et al.* [34] which was average 75 minutes (range from 65 to 110), but shorter than Lau H [35] while Lunevicius, Morkevicius M which had claimed that laparoscopic repair with omental patch took up to 135 minutes [36]. Most of the times are taken in suction and irrigation for proper peritoneal lavage to avoid post-operative collection elsewhere.

In our study peritoneal irrigation is done with 2-4 liters of warm normal saline. Although irrigation with 6 to 10 liters of warm normal saline are often recommended [37- 40], others was using at least 30 liters [24].

The peritoneal cavity was drained in our study both pelvis and hepatorenal pouch, as recommended by other [25]. On the other hand, some authors do not advocate drainage of the peritoneal cavity [43].

In our study post-operative pain were 6 according to Visual Analog Scale (VAS) in the first 24hours which decreased to 4 after 48hours, Lau H advocate that post-operative pain was less after laparoscopic repair than open, and associated with lesser post-operative analgesic requirement [44]. According to Siu *et al.* pain was less in laparoscopic patients in day 1 and 3 post-operative [45].

Post-operative wound infection was 3 out of 20 (15%), while chest infection was 2 (10%). Lau H showed also lower wound infection in laparoscopic group than open, while Cochrane showed that there is no difference between the two groups [46].

All patients in our study were successfully operated laparoscopically as shown by Munro *et al.* [47], Issac *et al.* [48] and Urbano *et al.* [49] while conversion to open surgery in 3 patients out of 24 (13%) in Seelig *et al.* because of previous abdominal surgery [50], Lee *et al.* showed high conversion rate 46 out of 153 (30%) because of high Boey score but they emphasize that conversion did not affect the outcome [51].

The mean hospital stay was 5.5 days in our study like many other authors Lee *et al.* [37], Siuet *et*

al. [52] and Robertson *et al.* [53], while it extended to 9 day with seeling *et al.* [50].

In our study there were 12 patients, (60%) *H. Pylori* positive. They received post-operative Clarithromycin triple therapy for eradication of *H. Pylori* for two weeks. Ten patients out of 12 were successfully treated, with eradication rate 83.3% while the other persistant 2 required Levofloxacin triple therapy for another ten days. H. pylori eradication rate was consistent with William D.C and Benjamin C.Y. as regards the Primary and Salvage therapy [24].

In the past, it was unclear why ulcers recurred in some but not all patients after surgery for ulcer perforation [54]. Having a young age, smoking, and having a long interval after surgery, however, are associated with recurrence [54, 55]. Some authors advocated that *H. Pylori* were positive in 73.3% of cases with PPU, regardless previous use of NSAIDS [56]. Chu KM *et al.* showed that *H. Pylori* infection is detected in 77 patients out of 163 (47.2%) with recurrent duodenal ulceration in 29 patients (17.8%) after upper gastro-intestinal endoscopic examination which was performed at a mean interval of 74.5 months from the initial operation [57]. Multivariate analysis revealed male gender and positive. Pylori status to be independent factors associated with recurrent duodenal ulcer [44]. There is association between *H. Pylori* infection and perforated duodenal ulcers especially in a patient who is not taking NSAIDS. So, simple closure of the perforation followed by post-operative eradication therapy of *H. Pylori* is emphasized to prevent recurrence [58].

Conclusion:

With new advent of minimal invasive surgery, laparoscopic repair of early perforated duodenal ulcer is recommended safely with minimal complications and with no mortality. Eradication of *H. Pylori* post-operatively eliminates recurrence of peptic ulcer disease.

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