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World Journal of Gastrointestinal Surgery (*World J Gastrointest Surg*, *WJGS*, online ISSN 1948-9366, DOI: 10.4240) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJGS covers topics concerning micro-invasive surgery; laparoscopy; hepatic, biliary, pancreatic and splenic surgery; surgical nutrition; portal hypertension, as well as associated subjects. The current columns of *WJGS* include editorial, frontier, diagnostic advances, therapeutics advances, field of vision, mini-reviews, review, topic highlight, medical ethics, original articles, case report, clinical case conference (Clinicopathological conference), and autobiography. Priority publication will be given to articles concerning diagnosis and treatment of gastrointestinal surgery diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

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REVIEW

Perforated peptic ulcer - an update

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Abstract

Peptic ulcer disease (PUD) affects 4 million people worldwide annually. The incidence of PUD has been estimated at around 1.5% to 3%. Perforated peptic ulcer (PPU) is a serious complication of PUD and patients with PPU often present with acute abdomen that carries high risk for morbidity and mortality. The lifetime prevalence of perforation in patients with PUD is about 5%. PPU carries a mortality ranging from 1.3% to 20%. Thirty-day mortality rate reaching 20% and 90-d mortality rate of up to 30% have been reported. In this review we have summarized the current evidence on PPU to update readers. This literature review includes the most updated information such as common causes, clinical features, diagnostic methods, non-operative and operative management, post-operative complications and different scoring systems of PPU. With the advancement of medical technology, PUD can now be treated with medications instead of elective surgery. The classic triad of sudden onset of abdominal pain, tachycardia and abdominal rigidity is the hallmark of PPU. Erect chest radiograph may miss 15% of cases with air under the diaphragm in patients with bowel perforation. Early diagnosis, prompt resuscitation and urgent surgical intervention are essential to improve outcomes. Exploratory laparotomy and omental patch repair remains the gold standard. Laparoscopic surgery should be considered when expertise is available. Gastrectomy is recommended in patients with large or malignant ulcer.

Key words: Peptic ulcer; Perforation; Laparoscopy; Surgery

Core tip: The classic triad of sudden onset of abdominal pain, tachycardia and abdominal rigidity is the hallmark of perforated peptic ulcer. Early diagnosis, prompt resuscitation and urgent surgical intervention are essential to improve outcomes. Exploratory laparotomy and omental patch repair remains the gold standard and laparoscopic surgery should be considered when expertise is available. Gastrectomy is recommended in patients with large or malignant ulcer to enhance outcomes; however the outcomes of patients treated with gastric resections remain inferior.

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INTRODUCTION

Peptic ulcer disease (PUD) results from an imbalance between stomach acid-pepsin and mucosal defense barriers. It affects 4 million people worldwide annually[1]. The incidence of PUD has been estimated at around 1.5% to 3%[2]. A systematic review of seven studies from developed countries estimated that the annual incidence rates of PUD were 0.10%-0.19% for physician-diagnosed PUD and 0.03%-0.17% when based on hospitalization data[3]. Although 10%-20% of patients with PUD will experience complications, only 2%-14% of the ulcers will perforate causing an acute illness[4,5]. Perforation is a serious complication of PUD and patients with perforated peptic ulcer (PPU) often present with acute abdomen that carries high risk for morbidity and mortality[6]. The lifetime prevalence of perforation in patients with PUD is about 5%[7]. PPU carries a mortality ranging from 1.3% to 20%[8-10]. Thirty-day mortality rate reaching 20% and 90-d mortality rate of up to 30% have been reported[11,12]. In this review we have summarized the current evidence on PPU and we hope our review will assist surgeons updated with evidence based practice.

AETIOLOGY

Although previous studies have indicated that seasonal variation did influence the incidence of PPU, other studies have failed to prove such a pattern[13-16]. In developing world, patients tend to be young male smokers while in developed countries; patients tend to be elderly with multiple co-morbidities and associated use of non-steroidal anti-inflammatory drugs (NSAIDs) or steroid[17,18]. NSAIDs, *Helicobacter pylori* (*H. pylori*), physiological stress, smoking, corticosteroids and previous history of PUD are risks factors for PPU[1,19-27]. In the presence of risk factors, recurrence of ulcer is common despite initial successful treatment. A systematic review of 93 studies has shown that the average long-term recurrence of perforation was 12.2% (95%CI: 2.5-21.9)[5].

NSAIDs

NSAIDs are widely used for its analgesic, anti-inflammatory and anti-pyretic effects. NSAID use is known to increase the risk of PPU[28,29]. About a quarter of chronic NSAID users will develop PUD and 2%-4% will bleed or perforate[30-33]. Drug interaction with steroids and selective serotonin reuptake inhibitors also increases the risks of PUD. Selective cyclo-oxygenase-2 inhibitors are less associated with PUD. A study in western Denmark showed that the standardized hospitalization rates for PPU reduced from 17 per 100000 population in 1996 to 12 per 100000 population in 2004 (HR 0.71; 95%CI: 0.57-0.88) after the introduction of selective cyclo-oxygenase-2 inhibitors into clinical practice[34].

H. pylori

H. pylori remain one of the commonest infections worldwide. The prevalence of *H. pylori* has decreased in developed countries due to improved hygiene and reduced transmission in early childhood. The mean prevalence of *H. pylori* in patients with PPU varies between studies due to different diagnostic methods and geographical variations. Recent studies using histopathological methods of *H. pylori* detection have shown that *H. pylori* prevalence in patients with perforated duodenal ulcers ranges from 50%-80%[22,35]. A randomized controlled trial in 2008 involving 65 patients who underwent simple closure of a perforated duodenal ulcer showed one year ulcer recurrence rate of 6.1% in *H. pylori* treated patients as opposed to 29.6% in the control group[36]. Recurrent PUD mainly occurs in patients with *H. pylori* infection suggesting that *H. pylori* play an important role in the development of PUD and its complications[22,37]. The risk of recurrent *H. pylori* infection is significantly reduced with proton pump inhibitor therapy, but proton pump inhibitors have only a modest efficacy for reduction in ulcers with NSAID users.

Smoking

Tobacco is thought to inhibit pancreatic bicarbonate secretion, leading to increased acidity in duodenum[38,39]. It also inhibits the healing of duodenal ulcers. A meta-analysis has indicated that 23% of PUD could be associated with smoking[40]. However, in some studies, there was no difference in tobacco use between patients with non-*H. pylori*, non-NSAID duodenal ulcers and those with *H. pylori* related ulcers, indicating a limited role of smoking[41]. This is in agreement with previous studies, which indicated that smoking did not increase the risk of ulcer recurrence once the *H. pylori* had been eradicated[42,43].

Others

A study involving 72 patients investigated the genetic differences between *H. pylori*-positive and negative duodenal ulcer patients. *DQA1*0102* allele were significantly more common in *H. pylori* negative patients[44]. This study indicated that genotypes might influence the ability of the host to resist *H. pylori* infection. A study involving 228 patients indicated that steroid use prior to hospital admission was associated with two fold increase in 30 d mortality amongst patients admitted for PPU[45]. Other risk factors may include excessive alcohol consumption and excessive acid production such as gastrinomas and Zollinger-Ellison syndrome (ZES)[18,46,47]. Alcohol consumption is known to damage gastric mucosa and stimulate *gastrin* secretion. Despite these acute effects, there is no evidence that alcohol causes PUD. ZES

is caused by a gastrin secreting tumor of the pancreas that stimulates the parietal cells in stomach to increase the acidity, resulting in gastrointestinal mucosal ulceration. Over 90% of patients with ZES develop peptic ulcers and typically these ulcers are refractory to proton pump inhibitor therapy. ZES should be suspected in patients with multiple or refractory peptic ulcers, jejunal ulcers, family history of PUD and associated diarrhea. All patients with ZES should be screened for Multiple Endocrine Neoplasia 1 (MEN1) syndrome.

CLINICAL FEATURES

In 1843 Edward Crisp stated that "the symptoms are so typical, I hardly believe that it is possible that anyone can fail in making a diagnosis"[48].

Symptoms of PUD include abdominal pain, upper abdominal discomfort, bloatedness and feeling of fullness. When PUD worsen and eventually perforate, gastric juice and gas enters the peritoneal cavity leading to chemical peritonitis. Sudden onset of abdominal pain or acute deterioration of the ongoing abdominal pain is typical of PPU. Typically the pain never completely subsides despite usual premedical remedies and forces the patient to seek medical attention. The chemical peritonitis due to efflux of gastroduodenal contents and severe pain lead to tachycardia. The classic triad of sudden onset of abdominal pain, tachycardia and abdominal rigidity is the hallmark of PPU.

The clinical manifestation can be divided into three phases[49]. In the initial phase within 2 h of onset, epigastric pain, tachycardia and cool extremities are characteristic. In the second phase (within 2 to 12 h), pain becomes generalized and is worse on movement. Typical signs such as abdominal rigidity and right lower quadrant tenderness (as a result of fluid tracking along the right paracolic gutter) may be seen. In the third phase (more than 12 h), abdominal distension, pyrexia and hypotension with acute circulatory collapse may be evident.

A study involving 84 patients with PPU reported that the commonest presenting symptoms were sudden onset of severe epigastric pain (97.6%), abdominal distention (76.2%) and vomiting (36.9%)[50]. Abdominal tenderness and classical signs of peritonitis could be elicited in 88.1% and 66.7% of the patients with PPU in this study. Other symptoms also included nausea (35.7%), severe dyspepsia (33.3%), constipation (29.8%) and fever (21.4%)[50]. In our experience of managing 332 patients with PPU, the most common presenting symptom was acute onset of abdominal pain (61.7%)[51]. A recent study in Taiwan has shown that patients with PPU were more likely to present to emergency room on weekends and this needs to be validated[52].

Tachycardia and abdominal tenderness with rigidity are common clinical signs. Severe pain, systemic inflammatory response from chemical peritonitis and fluid deficit either due to poor intake or vomiting or pyrexia leads to compensatory tachycardia. In patients who delay seeking medical attention, hypotension ensues due to total body water deficit. If uninterrupted; this progresses to mental obtundation and acute kidney injury. This leads to a state where patient becomes physiologically unfit for operative intervention which is absolutely necessary. Hence it is important to establish prompt confirmatory diagnosis.

DIAGNOSIS

An urgent erect chest X-ray and serum amylase/lipase is basic essential test in a patient with acute upper abdominal pain. In modern era it is not prudent to perform an exploratory laparotomy and establish a diagnosis of acute pancreatitis. Seventy-five percent of PPU have free air under diaphragm on erect chest X-ray[53]. In our experience of managing 332 patients, erect chest X-ray revealed free air in 59.8% of patients[51]. This variation could reflect the earlier presentation and easy access to healthcare locally. Sixty-one point seven percent of our patients presented within 24 h of onset of abdominal pain. In a patient with upper abdominal symptoms, free air on an erect chest X-ray establishes a diagnosis of PPU. In some patients, an abdominal X-ray may have been performed by emergency physician or primary medical team. It can show signs such as appearance of gas on both sides of the bowel wall (Rigler's sign), a large volume of free gas resulting in a large round black area (Football sign) and gas outlining soft tissue structures such as liver edge or falciform ligament. It is authors' practice not to perform an abdominal X-ray in patients with suspected PPU when chest X-ray does not show free air under the diaphragm. CT scan is recommended as it has a diagnostic accuracy as high as 98%[54]. Besides, CT scan can exclude acute pancreatitis that would not need surgical intervention. CT scan is performed in supine position and free air is usually seen anteriorly just below the anterior abdominal wall. The falciform ligament can sometimes be visible when air is present on both sides. In resource poor healthcare facilities, oral gastrografin can be used to diagnose PPU. Water-soluble contrast leaking into the peritoneal cavity can confirm the diagnosis of PPU. Absence of a leak does not exclude PPU as the perforation may have sealed off spontaneously[55]. Barium study is contraindicated in gastrointestinal perforation and should be avoided as a tool to diagnose PPU. We consider lateral decubitis abdominal radiographs as obsolete and do not recommend. The traditional practice of instilling air *via* the nasogastric tube and repeating the erect chest X-ray after few minutes is not recommended except in resource poor facilities. It takes time and a repeat negative chest X-ray does not rule out the diagnosis of PPU and still a CT scan would be warranted. Rarely a CT scan is performed even when an erect chest X-ray reveals free air under diaphragm. The utility of this CT scan is justified when clinical presentation is not specific to upper gastrointestinal pathology or a malignancy is suspected and patients' hemodynamics is not deranged. In patients with acute

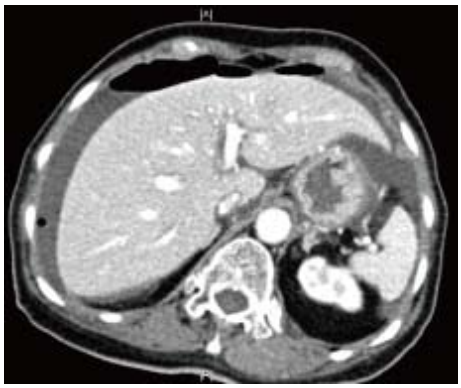

Figure 1 Computerized tomography scan shows free air under the diaphragm with peri-hepatic free fluid.

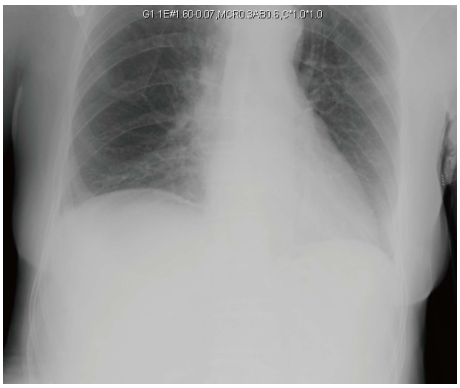

Figure 2 Erect chest X-ray image of the same patient with equivocal free air under the right hemidiaphragm.

kidney injury, a non-contrast CT scan is adequate to see free air. Oral contrast with CT scan is a useful tool and if free leak is seen, diagnosis is certain (Figures 1 and 2).

Laboratory tests are performed in PPU not to establish diagnosis but to rule out differential diagnosis and also to understand the insult to various organ systems. They are non-specific[56]. Serum amylase should be done at index presentation to emergency unit or after a normal chest X-ray. Raised serum amylase may be associated with PPU and it's usually raised less than four times its normal level[57]. Tests such as white cell count and C-reactive protein may be done as part of the investigation in PPU. Leukocytosis and raised C-reactive protein may be raised as a result of inflammation or infection[57]. Elevated creatinine, urea and metabolic acidosis reflects systemic inflammatory response syndrome (SIRS) and prerenal injury[58]. Serum gastrin levels are indicated in patients with history of recurrent ulcers or recalcitrant PUD and can help establish diagnosis of Zollinger Ellison syndrome. In patients with suspected parathyroid disorders, serum calcium levels are indicated.

MANAGEMENT

PPU is a surgical emergency associated with high mortality if left untreated. In general, all patients with PPU require prompt resuscitation, intravenous antibiotics, analgesia, proton pump inhibitory medications, naso-gastric tube, urinary catheter and surgical source control.

Drug treatment in PPU

Omeprazole and triple therapy for *H. pylori* eradication are useful adjuncts in treatment of PPU. Evidence has shown that omeprazole and triple therapy treatment reduces the recurrence rate significantly. Ulcer healing shown at 8-wk follow up with endoscopy was significantly higher in triple therapy eradication group[36]. Eighty-five point three percent of ulcers were healed in the triple therapy group as opposed to 48.4% in the omeprazole alone group. Several other studies from different countries have also proven triple therapy eradication after simple closure of PPU reduced the incidence of recurrent ulcer[37,59,60]. It is our practice to prescribe intravenous proton pump inhibitor for 72-96 h and start oral triple therapy immediately after. We perform urea breath test to establish *H. pylori* eradication after completion of medical treatment.

Non-operative management

Studies have shown that about 40%-80% of PPU will seal spontaneously with conservative management and overall morbidity and mortality are comparable[2,61,62]. Conservative management "Taylor method" consists of nasogastric suction, intravenous drip, antibiotics and repeated clinical assessment. A gastrograffin dye study is essential to confirm absence of leakage in patients selected for non-operative management. If patients are clinically stable and improving, especially with a sealed perforation, surgery may not be warranted. However, if they deteriorate, regardless of the presence and size of the leak, urgent operation is indicated. A Randomized controlled trial involving 83 patients compared the outcome of non-operative treatment with that of operative intervention in patients with PPU[61]. Cefuroxime, ampicillin and metronidazole were administered to all patients. Seventy-two point five percent (29/40) of patients in conservative group showed clinical improvement and were successfully managed without surgery. Covering with an appropriate antibiotic in patients with peritonitis is associated with an increased chance of resolution of the infection after primary surgery[63]. Another study looking at 82 patients who were treated conservatively also showed that 54% of the patients (44/82) showed clinical improvement and did not require a surgical intervention[64]. Study also suggests that patients do well without surgery if spontaneous sealing occurs[55]. A study has shown that about 40% of PPU had no evidence of leak on upper GI contrast studies, indicating that the perforation had sealed off spontaneously[65]. The mortality rate for non-operative management in patients with a sealed perforation was 3% as opposed to 6.2% where emergency surgery was performed for PPU[65]. This suggests that PPU with a sealed perforation can be managed conservatively. The advantages of conservative management include avoidance

of surgery, risks of general anaesthesia and post-operative complications. On the other hand, disadvantages include misdiagnosis and higher mortality rate if conservative management fails[61,66]. In clinical practice, non-operative management strategy is resource intensive and it requires a commitment of active regular clinical examination along with round the clock availability of a surgeon and if there is clinical deterioration, emergency surgery is warranted. The essential components of non-operative management of PPU can be grouped as "R"s: (1) Radiologically undetected leak; (2) Repeated clinical examination; (3) Repeated blood investigations; (4) Respiratory and renal support; (5) Resources for monitoring; and (6) Readiness to operate.

Operative management

Management of PPU is primarily surgical and different suture techniques for closure of the perforation are described. Johan Mikuliczradecki stated that "every doctor who is faced with a perforated ulcer of stomach or duodenum must consider opening the abdomen, sewing up the hole and averting a possible inflammation by a careful cleansing of the abdominal cavity"[4]. In 1992, Feliciano[67] also described 5 points of decision that surgeon needs to take into account. Those decisions include: (1) Is surgery indicated? (2) Is an omental patch sufficient or a definitive ulcer operation indicated? (3) Is the patient stable enough to undergo a definitive ulcer operation? (4) Which definitive ulcer operation should be done? (5) Should the availability of newer medical options influence the choice of operation? With the development of laparoscopic operation in the past few decades, a sixth decision point is proposed; and (6) Should the procedure be performed laparoscopically?[67,68]. Roscoe Graham described PPU to be not a local disease but a local manifestation of a constitutional disturbance[69]. There are many operative methods that could be used to treat PPU. Primary closure by interrupted sutures, closure by interrupted sutures covered with a pedicled omentum on top of the repair (Cellan-Jones repair) and plugging the perforation with a free omental plug (Graham patch) are the most common techniques.

VAGOTOMY

Vagus nerve plays an important role in the regulation of gastrin release and gastric acid secretion by stimulating parietal cells *via* cholinergic receptors[70]. Vagal stimulation also releases histamine and gastrin from enterochromaffin like cells and G-cells, which in turn, will stimulate the parietal cells to produce acid secretion. Vagotomy is a procedure that transects the vagal trunks (truncal vagotomy) or distal nerve fibers (highly selective vagotomy). Truncal vagotomy aims to reduce the gastric acid secretion, thus reducing the risks of recurrent PUD. Selective vagotomy, which spares the hepatic and celiac divisions of the vagal trunks, are associated with higher long-term recurrence rates[71]. Therefore, selective vagotomy is no longer performed. Studies have shown that the ulcer recurrence rate was as high as 42% in perforated duodenal ulcer patients who underwent simple omental patch repair[72,73]. Few prospective randomized studies also reported substantially less ulcer recurrence in patients who underwent vagotomy in addition to omental patch repair[37,74]. Nonetheless, vagotomy is now seldom performed for PPU due to the availability of medications such as histamine receptor antagonists, proton pump inhibitors and *H. pylori* eradication.

GASTRECTOMY

Rydiger did a partial gastrectomy for the management of PUD in 1880. Unfortunately, it was not successful[75]. A year later, Theodor Billroth performed a successful gastroduodenostomy in a 43-year-old woman with pyloric cancer. He was the first surgeon who did gastric resection for antral carcinoma[76]. Nowadays, emergency gastrectomy is reserved for a giant ulcer or a suspicion of malignancy when it is not safe to perform omental patch repair[77]. A retrospective study reported a mortality rate of 24% in 41 patients who underwent gastrectomy for perforated benign gastric ulcers[78]. A study comparing outcomes after gastrectomy and simple closure repair showed that there were no significant differences in patient recoveries[79]. Longer operating times, ventilation and postoperative blood transfusion are associated with increased mortality[80]. The larger size of perforation is associated with higher mortality and post-operative anastomotic leak[81]. In a study of 601 patients and including 62 patients treated with gastric resection, we have shown that serum albumin is the only preoperative factor predictive of mortality (OR 5.57) and outcomes of patients treated with gastric resection are inferior as compared to omental patch repair with mortality risk of 24.2%[82]. Gastric resections for acid reduction have become less favorable after proton pump inhibitors era and in our experience, up to 10% of PPU patients require gastric resection.

LAPAROSCOPIC REPAIR

Laparoscopic repair was first performed for a perforated duodenal ulcer in 1990[83]. Laparoscopic repair of PPU is believed to reduce the post-operative morbidity and mortality[84]. A recent systematic review of 3 randomized controlled trials with a total of 315 PPU patients compared laparoscopy with open surgery[85]. This study failed to demonstrate differences in abdominal septic complications, pulmonary complications, mortality and re-operation. However, the operative time was shorter in laparoscopic group in contrast with previous study[86]. A systematic review of 56 studies comparing laparoscopic *vs* open approach for PPU concluded that there was no consensus on the perfect operating techniques[87]. The overall conversion rate for laparoscopic surgery was 12.4% mainly due to the size of perforation. Ulcer size more than 9 mm is a significant risk factor for

conversion to open surgery[88]. The operating time was longer and recurrent leakage was higher in laparoscopic group. However, the laparoscopic group also showed less postoperative pain and a shorter hospital stay. Furthermore, the laparoscopic treatment is also associated with equivalent costs compared with the open surgery as it reduces duration of hospital stays[89]. The current evidence remains poor for choosing laparoscopic repair over open surgery for PPU. This review has suggested that patients with a Boey score of 3, age over 70 years and symptoms lasting longer than 24 h should have open surgical approach as these patients have higher morbidity and mortality. Laparoscopic repair of PPU has now been performed by trainee surgeons with acceptable results[90,91]. Our local experience also showed that strict selection such as Boey score of 0-1, ulcer size of less than 10 mm, ulcer located in pyloro-duodenal area, haemodynamic stable, no previous abdominal surgeries, not suspected malignant ulcer and excluding ASA 3 and above score were safe for training[92]. There were no conversions, complications or mortality.

Laparoscopic repair techniques mirror techniques of open surgery and in particular sutureless techniques are more prominently described. This may in part due to training in intra-corporeal knotting skills. Sutureless techniques involve gelatin sponge plug with fibrin glue sealing or endoscopic clipping[68]. A recent study has compared the effectiveness of a sutureless onlay omental patch with a sutured omental patch method[93]. Forty-three patients underwent laparoscopic repair of PPU with sutureless onlay omental patch and another 64 patients underwent laparoscopic repair of PPU with sutured omental patch. There were no leaks in either group. The operating time and length of stay were significantly shorter in sutureless onlay omental patch group. This study has indicated that both techniques are safe and effective for repair of PPU. Trainees can easily perform laparoscopic sutureless repair with limited experience in laparoscopic surgery. Laparoscopic gelatin sponge plug and fibrin glue sealing can be easily performed[94]. However, this technique has not been widely accepted as it has been reported to have a higher leak rate[95]. Endoscopic clipping of PPU is not widely practiced, as there are only few centers with technical expertise and experience is limited with reports showing high complications and mortality[96,97].

"Dilution with solution is the solution to pollution". Towards the end of surgery, some surgeons like to irrigate the peritoneal cavity with 6-10 litres and even up to 30 litres of warm saline although no evidence has been found in literature to support that irrigation can lower the risk of sepsis[98,99]. On the other hand, pneumoperitonuem induced during laparoscopic surgery may increase the risk of bacterial dissemination[100]. It also seems to be a surgeon's preference whether or not to leave a drain at the end of surgery[101]. There is no evidence to support that leaving a drain in can reduce the incidence of intra-abdominal collections[101,102]. On the contrary, it may lead to infection of drain site and increased risk of intestinal obstruction[102]. A questionnaire performed by Schein showed that eighty percent of the surgeons did not leave a drain in after surgery due to the reasons discussed above[63]. Nowadays, the tire test (watch for bubbles after submerging patch repair under water) and the dye test (to inject dye *via* nasogastric tube) to look for leakage after closure of PPU are rarely used (Figure 3).

SELF-EXPANDABLE METAL STENTS

Primary stenting and drainage may be used as new treatment option for PPU[103]. Eight patients with PPU were treated with self-expandable metal stents[103]. Two patients were treated with stenting due to postoperative leakage after initial surgical closure and six patients were treated with primary stenting. Seven out of 8 patients recovered without complications and were discharged 9-36 d after stenting. Another study involving 10 patients with PPU who were treated with stenting also showed good clinical results[104]. This study has indicated stent treatment as a minimal invasive alternative with fewer complications compared to surgical treatment. These studies indicate that patients with PPU may be treated with primary stenting and drainage where training and expertise is available. More data is required to prove the effectiveness of this method.

MARGINAL ULCER PERFORATION

Any form of gastroenteric reconstruction can lead to the development of ulcer at the margins of the gastrojejunal anastomosis, known as marginal ulcer. The incidence of marginal ulcer is around 1% to 16%[105,106]. The ulcer tends to develop on the jejunal side of the stoma since it is directly exposed to the gastric acid[107]. Local ischemia, NSAIDS, anastomotic tension, chronic irritation due to the suture material and duodenal reflux are implicated in the aetiopathogenesis of marginal ulcer[108]. Marginal ulcer can rarely lead to perforation[109]. The presentation of patients with marginal ulcer perforation should be similar to PPU, however it may not be so. The small bowel contents has increased bacterial load and will also neutralize the gastric acid. A prospective study has shown that 28% of patients with marginal ulcers were asymptomatic[110]. Operative management for marginal ulcer perforation includes anastomotic revision such as converting Billroth Ⅱ gastro-jejunostomy reconstruction into a Roux-en-Y. It can also be treated with simple omental patch repair[109,111]. In recent time, majority of the published studies describe marginal ulcer and its perforation following bariatric procedures. We have reported a series of nine patients with marginal ulcer perforation following previous gastric resections for benign and malignant diseases[112]. We have concluded that patients with marginal ulcer do not present with septic shock. Also, revision of Billroth Ⅱ gastro-jejunostomy to Roux-en-Y anastomosis is not mandatory and omental patch repair is sufficient[112].

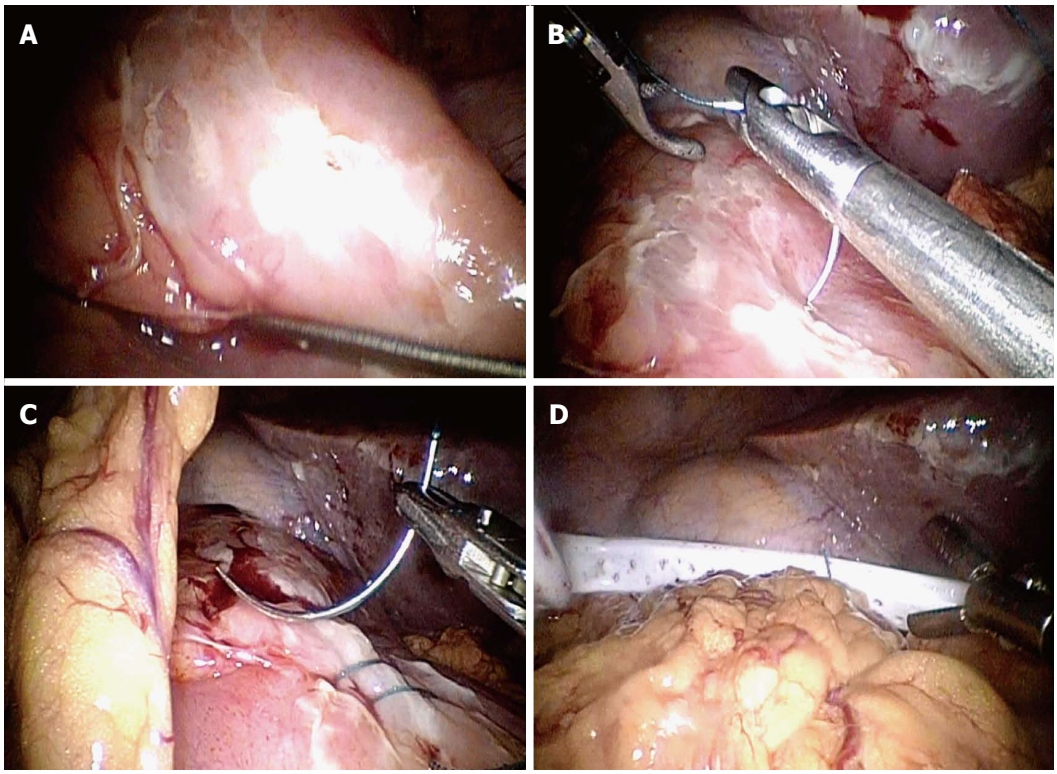

Figure 3 Shows laparoscopic omental patch repair. A: Anterior duodenal perforation; B: Laparoscopic suturing; C: Omental patch; D: Abdominal drain placement.

POST-OPERATIVE COMPLICATIONS

PPU treatment is associated with a significant post-operative morbidity and mortality regardless of whether laparoscopic or open repair is performed[113]. Post-operative mortality for PPU is estimated to be 6%-10%[114]. Age more than 60 years old, delayed treatment greater than 24 h, shock at presentation with systolic blood pressure less than 100 mmHg and concomitant diseases are the main risk factors influencing outcome[2,115]. Post-operative mortality in elderly is 3 to 5 times higher[116]. This may be due to the presence of medical comorbidities, delayed presentation, atypical presentation or delay of > 24 h in diagnosis[116].

Post-operative complications have been reported at around 30%[50,117]. Complications after surgical closure of PPU include surgical site infection, pneumonia, intra-abdominal collection/abscess, wound dehiscence, entero-cutaneous fistula, peritonitis, incisional hernia and ileus. A study has shown the commonest post-operative complications were surgical site infections (48%) and pneumonia (28%)[50]. However, this study only involved 25 patients and may not be representative. A more recent study involving 726 PPU patients between 2011 and 2013 in Denmark indicated the most common post-operative complications were post-operative leak (5.9%) and wound dehiscence (4.7%)[118]. Around 1 in every 5 patients underwent re-operation due to post-operative complications. This study also indicated that laparoscopic repair was associated with lower risk of re-operation than laparotomy or laparoscopic surgery converted to open surgery. Another study assessing postoperative complications in 96 patients reported that a total of 29 patients developed a total of 50 events of postoperative complications[119]. The most common complications were surgical site infection (32%), respiratory complications (30%), wound dehiscence (12%) and postoperative fistula (8%). Each additional complication was estimated to prolong hospital stay by 1.25 d. This study also reported that age > 40 years, larger size of perforation and history of shock significantly increased the rate of postoperative complications.

In our local study involving 332 patients who underwent surgery for PPU, post-operative complications included intra-abdominal collection (8.1%), leakage (2.1%) and re-operation (1.2%)[51]. Intra-abdominal abscess remains a serious postoperative complication after PPU surgery. Therefore, good surgical technique must be adopted to prevent this complication. Our low leak rates (2.1%) could be explained by early presentation, prompt diagnosis, early resuscitation and appropriate surgery. Our data on 30 d mortality was 7.2% which is comparable to a recent study from South Korea[120]. The lower mortality in our local study could be due to younger age (54.7), less co-morbidity (16.2%) and less patients with pre-operative shock (7.2%).

A recent study looked at the association of mortality with out of hours admission in patients with PPU[121]. A total of 726 patients who were surgically treated for PPU were included in this study. This study did not show statistically significance between 90-d mortality and out-of-hours admission in patients surgically treated for PPU.

In order to allocate resources appropriately and

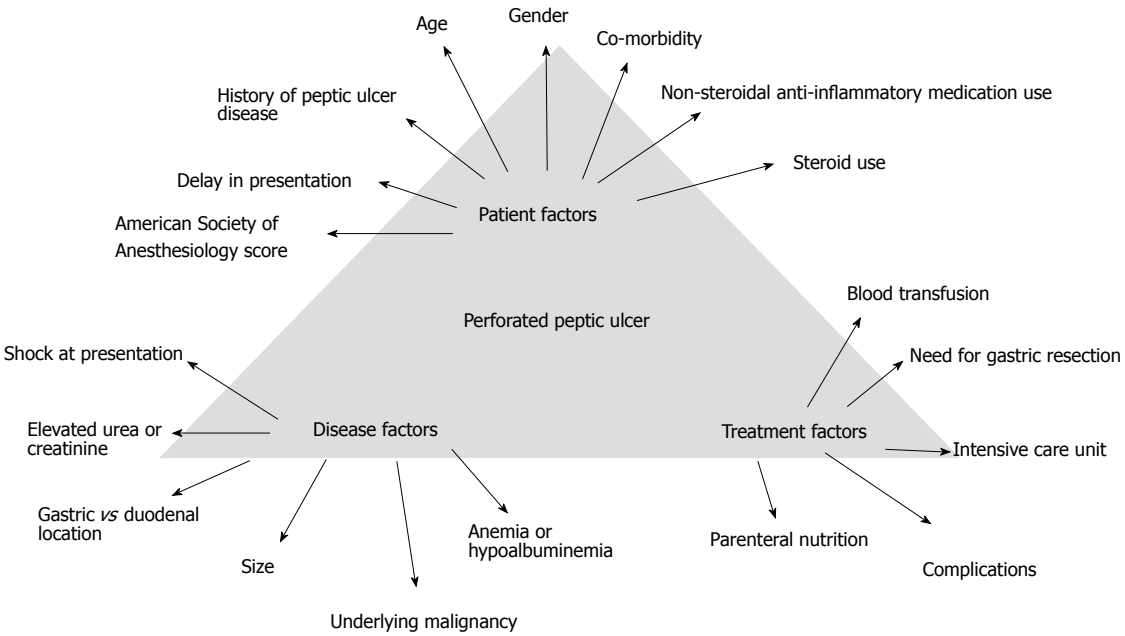

Figure 4 Determinants of outcomes in patients with perforated peptic ulcer.

provide optimal care, it is important to stratify patients into low and high risk of mortality. There are many scoring systems available to predict the mortality.

SCORING SYSTEMS TO PREDICT OUTCOMES IN PPU

About 11 different scoring systems used to predict outcome in PPU can be identified through the literature: the Boey score, the Americal Society of Anesthesiologists (ASA) score, the Sepsis score, the Charlson Comorbidity Index, the Mannheim Peritonitis Index (MPI), the Acute Physiology and Chronic Health Evaluation Ⅱ (APACHE Ⅱ), the Simplified Acute Physiology Score Ⅱ (SAPS Ⅱ), The Physiology and Operative Severity Score for the Enumeration of Mortality and Morbidity Physical Sub-score (POSSUM-phys score, the Mortality Probability Models Ⅱ (MPM Ⅱ), Peptic Ulcer Perforation (PULP) score, the Hacettepe score and the Jabalpur score[121]. Amongst these 11 scoring systems, the Boey score and ASA score are the most commonly validated systems[8,80,122-124]. Other scoring systems are not widely used due a lack of validation or their complexity in clinical use. We have validated ASA score, Boey's score, MPI and PULP score and found that all the four systems have moderate accuracy of predicting mortality with area under the receiver operator curve of 72%-77.2%[51]. In a recent study including 148 patients from two university affiliated hospitals in Singapore, Lee *et al*[125] has reported that in selected patients with presentation within 48 h and ulcer size < 2 cm, laparoscopic repair reduces length of hospital stay compared to open surgery in patients with MPI > 21.

A recent study was looking at 62 patients who underwent emergency surgery for PPU[126]. This study was investigating the correlation between the amount of peritoneal fluid and clinical parameters in patients with PPU. Using the methods described by Ishiguro *et al*[126], it was possible to predict the amount of accumulated intraperitoneal fluid by CT scan. This study has shown that the method of Ishiguro *et al*[126] was useful for predicting the amount of intraperitoneal fluid in patients with PPU. It is believed that it will be useful for predicting the severity of postoperative complications and also helpful for treatment decision-making (Figure 4).

MORTALITY

Mortality is a serious complication in PPU. As we mentioned before, PPU carries a mortality ranging from 1.3% to 20%[9,10]. Other studies have also reported 30-d mortality rate reaching 20% and 90-d mortality rate of up to 30%[11,12].

Significant risk factors that lead to death are presence of shock at admission, co-morbidities, resection surgery, female, elderly patients, a delay presentation of more than 24 h, metabolic acidosis, acute renal failure, hypoalbuminemia, being underweight and smokers[11,127-131]. The mortality rate is as high as 12%-47% in elderly patients undergoing PPU surgery[132-134]. Patients older than 65 year-old were associated with higher mortality rate when compared to younger patients (37.7% *vs* 1.4%)[131]. A study involving 96 patients with PPU also showed that there was a ninefold increase in postoperative complications in patients with comorbidities[119]. In another large population study, patients with diabetes had significantly increased 30-day mortality from PPU[135].

CONCLUSION

PUD can now be treated with medications instead of elective surgery. However, PUD may perforate and PPU carries a high mortality risk. The classic triad of sudden

onset of abdominal pain, tachycardia and abdominal rigidity is the hallmark of PPU. Erect chest radiograph may not establish the diagnosis and an index of suspicion is essential. Early diagnosis, prompt resuscitation and urgent surgical intervention are essential to improve outcomes. Non-operative management should be conducted by experienced teams with optimal resources and ideally under trial conditions. Exploratory laparotomy and omental patch repair remains the gold standard and laparoscopic surgery should be considered when expertise is available. Gastrectomy is recommended in patients with large or malignant ulcer to enhance outcomes; however the outcomes of patients treated with gastric resections remain inferior. Gelatin sponge plugs, fibrin glue sealants, self-expandable stents and endoscopic clipping techniques deserve to be tested in a controlled trial setting.

REFERENCES

1 **Zelickson MS**, Bronder CM, Johnson BL, Camunas JA, Smith DE, Rawlinson D, Von S, Stone HH, Taylor SM. Helicobacter pylori is not the predominant etiology for peptic ulcers requiring operation. *Am Surg* 2011; **77**: 1054-1060 [PMID: 21944523]

2 **Zittel TT**, Jehle EC, Becker HD. Surgical management of peptic ulcer disease today--indication, technique and outcome. *Langenbecks Arch Surg* 2000; **385**: 84-96 [PMID: 10796046 DOI: 10.1007/s004230050250]

3 **Sung JJ**, Kuipers EJ, El-Serag HB. Systematic review: the global incidence and prevalence of peptic ulcer disease. *Aliment Pharmacol Ther* 2009; **29**: 938-946 [PMID: 19220208 DOI: 10.1111/j.1365-2036.2009.03960.x]

4 **Bertleff MJ**, Lange JF. Perforated peptic ulcer disease: a review of history and treatment. *Dig Surg* 2010; **27**: 161-169 [PMID: 20571260 DOI: 10.1159/000264653]

5 **Lau JY**, Sung J, Hill C, Henderson C, Howden CW, Metz DC. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. *Digestion* 2011; **84**: 102-113 [PMID: 21494041 DOI: 10.1159/000323958]

6 **Bas G**, Eryilmaz R, Okan I, Sahin M. Risk factors of morbidity and mortality in patients with perforated peptic ulcer. *Acta Chir Belg* 2008; **108**: 424-427 [PMID: 18807594 DOI: 10.1080/00015458.2008.11680254]

7 **Vaira D**, Menegatti M, Miglioli M. What is the role of Helicobacter pylori in complicated ulcer disease? *Gastroenterology* 1997; **113**: S78-S84 [PMID: 9394765 DOI: 10.1016/S0016-5085(97)80017-0]

8 **Boey J**, Choi SK, Poon A, Alagaratnam TT. Risk stratification in perforated duodenal ulcers. A prospective validation of predictive factors. *Ann Surg* 1987; **205**: 22-26 [PMID: 3800459 DOI: 10.1097/00000658-198701000-00005]

9 **Hermansson M**, Staël von Holstein C, Zilling T. Surgical approach and prognostic factors after peptic ulcer perforation. *Eur J Surg* 1999; **165**: 566-572 [PMID: 10433141 DOI: 10.1080/11024159750006479]

10 **Rajesh V**, Chandra SS, Smile SR. Risk factors predicting operative mortality in perforated peptic ulcer disease. *Trop Gastroenterol* 2003; **24**: 148-150 [PMID: 14978992]

11 **Buck DL**, Møller MH. Influence of body mass index on mortality after surgery for perforated peptic ulcer. *Br J Surg* 2014; **101**: 993-999 [PMID: 24828155 DOI: 10.1002/bjs.9529]

12 **Søreide K**, Thorsen K, Søreide JA. Strategies to improve the outcome of emergency surgery for perforated peptic ulcer. *Br J Surg* 2014; **101**: e51-e64 [PMID: 24338777 DOI: 10.1002/bjs.9368]

13 **Gunshefski L**, Flancbaum L, Brolin RE, Frankel A. Changing patterns in perforated peptic ulcer disease. *Am Surg* 1990; **56**: 270-274 [PMID: 1973032]

14 **Janik J**, Chwirot P. Perforated peptic ulcer--time trends and patterns over 20 years. *Med Sci Monit* 2000; **6**: 369-372 [PMID: 11208340]

15 **Manfredini R**, De Giorgio R, Smolensky MH, Boari B, Salmi R, Fabbri D, Contato E, Serra M, Barbara G, Stanghellini V, Corinaldesi R, Gallerani M. Seasonal pattern of peptic ulcer hospitalizations: analysis of the hospital discharge data of the Emilia-Romagna region of Italy. *BMC Gastroenterol* 2010; **10**: 37 [PMID: 20398297 DOI: 10.1186/1471-230X-10-37]

16 **Svanes C**, Sothern RB, Sørbye H. Rhythmic patterns in incidence of peptic ulcer perforation over 5.5 decades in Norway. *Chronobiol Int* 1998; **15**: 241-264 [PMID: 9653578 DOI: 10.3109/07420529808998687]

17 **Windsor JA**, Hill AG. The management of perforated duodenal ulcer. *N Z Med J* 1995; **108**: 47-48 [PMID: 7885645]

18 **Kang JY**, Elders A, Majeed A, Maxwell JD, Bardhan KD. Recent trends in hospital admissions and mortality rates for peptic ulcer in Scotland 1982-2002. *Aliment Pharmacol Ther* 2006; **24**: 65-79 [PMID: 16803604 DOI: 10.1111/j.1365-2036.2006.02960.x]

19 **Chey WD**, Wong BC. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. *Am J Gastroenterol* 2007; **102**: 1808-1825 [PMID: 17608775 DOI: 10.1111/j.1572-0241.2007.01393.x]

20 **Fuccio L**, Minardi ME, Zagari RM, Grilli D, Magrini N, Bazzoli F. Meta-analysis: duration of first-line proton-pump inhibitor based triple therapy for Helicobacter pylori eradication. *Ann Intern Med* 2007; **147**: 553-562 [PMID: 17938394 DOI: 10.7326/0003-4819-147-8-200710160-00008]

21 **García Rodríguez LA**, Barreales Tolosa L. Risk of upper gastrointestinal complications among users of traditional NSAIDs and COXIBs in the general population. *Gastroenterology* 2007; **132**: 498-506 [PMID: 17258728 DOI: 10.1053/j.gastro.2006.12.007]

22 **Gisbert JP**, Pajares JM. Helicobacter pylori infection and perforated peptic ulcer prevalence of the infection and role of antimicrobial treatment. *Helicobacter* 2003; **8**: 159-167 [PMID: 12752726 DOI: 10.1046/j.1523-5378.2003.00139.x]

23 **Lewis JD**, Strom BL, Localio AR, Metz DC, Farrar JT, Weinrieb RM, Nessel L, Brensinger C, Kimmel SE. Moderate and high affinity serotonin reuptake inhibitors increase the risk of upper gastrointestinal toxicity. *Pharmacoepidemiol Drug Saf* 2008; **17**: 328-335 [PMID: 18188866 DOI: 10.1002/pds.1546]

24 **Malfertheiner P**, Dent J, Zeijlon L, Sipponen P, Veldhuyzen Van Zanten SJ, Burman CF, Lind T, Wrangstadh M, BayerdOrffer E, Lonovics J. Impact of Helicobacter pylori eradication on heartburn in patients with gastric or duodenal ulcer disease -- results from a randomized trial programme. *Aliment Pharmacol Ther* 2002; **16**: 1431-1442 [PMID: 12182742 DOI: 10.1046/j.1365-2036.2002.01285.x]

25 **Schubert ML**, Peura DA. Control of gastric acid secretion in health and disease. *Gastroenterology* 2008; **134**: 1842-1860 [PMID: 18474247 DOI: 10.1053/j.gastro.2008.05.021]

26 **Sonnenberg A**, Müller-Lissner SA, Vogel E, Schmid P, Gonvers JJ, Peter P, Strohmeyer G, Blum AL. Predictors of duodenal ulcer healing and relapse. *Gastroenterology* 1981; **81**: 1061-1067 [PMID: 7026344 DOI: 10.1016/S0016-5085(81)80012-1]

27 **Vergara M**, Catalán M, Gisbert JP, Calvet X. Meta-analysis: role of Helicobacter pylori eradication in the prevention of peptic ulcer in NSAID users. *Aliment Pharmacol Ther* 2005; **21**: 1411-1418 [PMID: 15948807 DOI: 10.1111/j.1365-2036.2005.02444.x]

28 **García Rodríguez LA**, Jick H. Risk of upper gastrointestinal bleeding and perforation associated with individual non-steroidal anti-inflammatory drugs. *Lancet* 1994; **343**: 769-772 [PMID: 7907735 DOI: 10.1016/S0140-6736(94)91843-0]

29 **Hernández-Díaz S**, Rodríguez LA. Association between nonsteroidal anti-inflammatory drugs and upper gastrointestinal tract bleeding/perforation: an overview of epidemiologic studies published in the 1990s. *Arch Intern Med* 2000; **160**: 2093-2099 [PMID: 10904451]

30 **Laine L**. Nonsteroidal anti-inflammatory drug gastropathy. *Gastrointest Endosc Clin N Am* 1996; **6**: 489-504 [PMID: 8803564]

31 **Larkai EN**, Smith JL, Lidsky MD, Graham DY. Gastroduodenal mucosa and dyspeptic symptoms in arthritic patients during chronic

nonsteroidal anti-inflammatory drug use. *Am J Gastroenterol* 1987; **82**: 1153-1158 [PMID: 3499815]
32 **Singh G**. Gastrointestinal complications of prescription and over-the-counter nonsteroidal anti-inflammatory drugs: a view from the ARAMIS database. Arthritis, Rheumatism, and Aging Medical Information System. *Am J Ther* 2000; **7**: 115-121 [PMID: 11319579 DOI: 10.1097/00045391-200007020-00008]
33 **Bombardier C**, Laine L, Reicin A, Shapiro D, Burgos-Vargas R, Davis B, Day R, Ferraz MB, Hawkey CJ, Hochberg MC, Kvien TK, Schnitzer TJ. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group. *N Engl J Med* 2000; **343**: 1520-1528, 2 p following 1528 [PMID: 11087881 DOI: 10.1056/NEJM200011233432103]
34 **Christensen S**, Riis A, Nørgaard M, Thomsen RW, Sørensen HT. Introduction of newer selective cyclo-oxygenase-2 inhibitors and rates of hospitalization with bleeding and perforated peptic ulcer. *Aliment Pharmacol Ther* 2007; **25**: 907-912 [PMID: 17402994 DOI: 10.1111/j.1365-2036.2007.03274.x]
35 **Reinbach DH**, Cruickshank G, McColl KE. Acute perforated duodenal ulcer is not associated with Helicobacter pylori infection. *Gut* 1993; **34**: 1344-1347 [PMID: 8244099 DOI: 10.1136/gut.34.10.1344]
36 **El-Nakeeb A**, Fikry A, Abd El-Hamed TM, Fouda el Y, El Awady S, Youssef T, Sherief D, Farid M. Effect of Helicobacter pylori eradication on ulcer recurrence after simple closure of perforated duodenal ulcer. *Int J Surg* 2009; **7**: 126-129 [PMID: 19138577 DOI: 10.1016/j.ijsu.2008.12.001]
37 **Ng EK**, Lam YH, Sung JJ, Yung MY, To KF, Chan AC, Lee DW, Law BK, Lau JY, Ling TK, Lau WY, Chung SC. Eradication of Helicobacter pylori prevents recurrence of ulcer after simple closure of duodenal ulcer perforation: randomized controlled trial. *Ann Surg* 2000; **231**: 153-158 [PMID: 10674604]
38 **Stabile BE**, Passaro E. Duodenal ulcer: a disease in evolution. *Curr Probl Surg* 1984; **21**: 1-79 [PMID: 6317293 DOI: 10.1097/00000658-200002000-00001]
39 **Nuhu A**, Madziga AG, Gali BM. Acute perforated duodenal ulcer in Maiduguri: experience with simple closure and Helicobacter pylori eradication. *West Afr J Med* 2009; **28**: 384-387 [PMID: 20486098 DOI: 10.4314/wajm.v28i6.55032]
40 **Kurata JH**, Nogawa AN. Meta-analysis of risk factors for peptic ulcer. Nonsteroidal antiinflammatory drugs, Helicobacter pylori, and smoking. *J Clin Gastroenterol* 1997; **24**: 2-17 [PMID: 9013343 DOI: 10.1097/00004836-199701000-00002]
41 **Xia HH**, Phung N, Kalantar JS, Talley NJ. Demographic and endoscopic characteristics of patients with Helicobacter pylori positive and negative peptic ulcer disease. *Med J Aust* 2000; **173**: 515-519 [PMID: 11194733]
42 **Borody TJ**, George LL, Brandl S, Andrews P, Jankiewicz E, Ostapowicz N. Smoking does not contribute to duodenal ulcer relapse after Helicobacter pylori eradication. *Am J Gastroenterol* 1992; **87**: 1390-1393 [PMID: 1415092]
43 **Chan FK**, Sung JJ, Lee YT, Leung WK, Chan LY, Yung MY, Chung SC. Does smoking predispose to peptic ulcer relapse after eradication of Helicobacter pylori? *Am J Gastroenterol* 1997; **92**: 442-445 [PMID: 9068465]
44 **Azuma T**, Konishi J, Ito Y, Hirai M, Tanaka Y, Ito S, Kato T, Kohli Y. Genetic differences between duodenal ulcer patients who were positive or negative for Helicobacter pylori. *J Clin Gastroenterol* 1995; **21** Suppl 1: S151-S154 [PMID: 8775009]
45 **Christensen S**, Riis A, Nørgaard M, Thomsen RW, Tønnesen EM, Larsson A, Sørensen HT. Perforated peptic ulcer: use of pre-admission oral glucocorticoids and 30-day mortality. *Aliment Pharmacol Ther* 2006; **23**: 45-52 [PMID: 16393279 DOI: 10.1111/j.1365-2036.2006.02722.x]
46 **Barazandeh F**, Yazdanbod A, Pourfarzi F, Sepanlou SG, Derakhshan MH, Malekzadeh R. Epidemiology of peptic ulcer disease: endoscopic results of a systematic investigation in iran. *Middle East J Dig Dis* 2012; **4**: 90-96 [PMID: 24829640]
47 **Kamada T**, Haruma K, Kusunoki H, Miyamoto M, Ito M, Kitadai Y, Yoshihara M, Chayama K, Tahara K, Kawamura Y. Significance of an exaggerated meal-stimulated gastrin response in pathogenesis of Helicobacter pylori-negative duodenal ulcer. *Dig Dis Sci* 2003; **48**: 644-651 [PMID: 12741450 DOI: 10.1016/S0016-5085(03)82254-0]
48 **Lau WY**, Leow CK. History of perforated duodenal and gastric ulcers. *World J Surg* 1997; **21**: 890-896 [PMID: 9327684 DOI: 10.1007/s002689900323]
49 **Silen W**. Cope's early diagnosis of the acute abdomen. New York: Oxford University Press, 1996 [DOI: 10.1097/01.sla.0000230276.84612.b4]
50 **Chalya PL**, Mabula JB, Koy M, McHembe MD, Jaka HM, Kabangila R, Chandika AB, Gilyoma JM. Clinical profile and outcome of surgical treatment of perforated peptic ulcers in Northwestern Tanzania: A tertiary hospital experience. *World J Emerg Surg* 2011; **6**: 31 [PMID: 21871104 DOI: 10.1186/1749-7922-6-31]
51 **Anbalakan K**, Chua D, Pandya GJ, Shelat VG. Five year experience in management of perforated peptic ulcer and validation of common mortality risk prediction models - are existing models sufficient? A retrospective cohort study. *Int J Surg* 2015; **14**: 38-44 [PMID: 25560748 DOI: 10.1016/j.ijsu.2014.12.022]
52 **Kao LT**, Tsai MC, Lin HC, Pai F, Lee CZ. Weekly pattern of emergency room admissions for peptic ulcers: a population-based study. *World J Gastroenterol* 2015; **21**: 3344-3350 [PMID: 25805943 DOI: 10.3748/wjg.v21.i11.3344]
53 **Grassi R**, Romano S, Pinto A, Romano L. Gastro-duodenal perforations: conventional plain film, US and CT findings in 166 consecutive patients. *Eur J Radiol* 2004; **50**: 30-36 [PMID: 15093233 DOI: 10.1016/j.ejrad.2003.11.012]
54 **Kim HC**, Yang DM, Kim SW, Park SJ. Gastrointestinal tract perforation: evaluation of MDCT according to perforation site and elapsed time. *Eur Radiol* 2014; **24**: 1386-1393 [PMID: 24623365 DOI: 10.1007/s00330-014-3115-z]
55 **Donovan AJ**, Berne TV, Donovan JA. Perforated duodenal ulcer: an alternative therapeutic plan. *Arch Surg* 1998; **133**: 1166-1171 [PMID: 9820345 DOI: 10.1001/archsurg.133.11.1166]
56 **Di Saverio S**, Bassi M, Smerieri N, Masetti M, Ferrara F, Fabbri C, Ansaloni L, Ghersi S, Serenari M, Coccolini F, Naidoo N, Sartelli M, Tugnoli G, Catena F, Cennamo V, Jovine E. Diagnosis and treatment of perforated or bleeding peptic ulcers: 2013 WSES position paper. *World J Emerg Surg* 2014; **9**: 45 [PMID: 25114715 DOI: 10.1186/1749-7922-9-45]
57 **Fakhry SM**, Watts DD, Luchette FA. Current diagnostic approaches lack sensitivity in the diagnosis of perforated blunt small bowel injury: analysis from 275,557 trauma admissions from the EAST multi-institutional HVI trial. *J Trauma* 2003; **54**: 295-306 [PMID: 12579055 DOI: 10.1097/01.TA.0000046256.80836.AA]
58 **Thorsen K**, Søreide JA, Søreide K. What is the best predictor of mortality in perforated peptic ulcer disease? A population-based, multivariable regression analysis including three clinical scoring systems. *J Gastrointest Surg* 2014; **18**: 1261-1268 [PMID: 24610235 DOI: 10.1007/s11605-014-2485-5]
59 **Kate V**, Ananthakrishnan N, Badrinath S. Effect of Helicobacter pylori eradication on the ulcer recurrence rate after simple closure of perforated duodenal ulcer: retrospective and prospective randomized controlled studies. *Br J Surg* 2001; **88**: 1054-1058 [PMID: 11488789 DOI: 10.1046/j.0007-1323.2001.01831.x]
60 **Tran TT**, Quandalle P. [Long term results of treatment by simple surgical closure of perforated gastroduodenal ulcer followed by eradication of Helicobacter pylori]. *Ann Chir* 2006; **131**: 502-503 [PMID: 16716245 DOI: 10.1016/j.anchir.2006.04.001]
61 **Crofts TJ**, Park KG, Steele RJ, Chung SS, Li AK. A randomized trial of nonoperative treatment for perforated peptic ulcer. *N Engl J Med* 1989; **320**: 970-973 [PMID: 2927479 DOI: 10.1056/NEJM198904133201504]
62 **Bucher P**, Oulhaci W, Morel P, Ris F, Huber O. Results of conservative treatment for perforated gastroduodenal ulcers in patients not eligible for surgical repair. *Swiss Med Wkly* 2007; **137**: 337-340 [PMID: 17629803]
63 **Schein M**. To drain or not to drain? The role of drainage in the contaminated and infected abdomen: an international and personal perspective. *World J Surg* 2008; **32**: 312-321 [PMID: 18080709 DOI: 10.1007/s00268-007-9277-y]
64 **Songne B**, Jean F, Foulatier O, Khalil H, Scotté M. [Non operative treatment for perforated peptic ulcer: results of a prospective study].

Ann Chir 2004; **129**: 578-582 [PMID: 15581818 DOI: 10.1016/j.anchir.2004.06.012]
65 **Berne TV**, Donovan AJ. Nonoperative treatment of perforated duodenal ulcer. *Arch Surg* 1989; **124**: 830-832 [PMID: 2742484 DOI: 10.1001/archsurg.1989.01410070084017]
66 **Truscott BM**, Withycombe JF. Perforated peptic ulcer; an assessment of the value of nonoperative treatment. *Lancet* 1950; **1**: 894-896 [PMID: 15416068]
67 **Feliciano DV**. Do perforated duodenal ulcers need an acid-decreasing surgical procedure now that omeprazole is available? *Surg Clin North Am* 1992; **72**: 369-380 [PMID: 1549799]
68 **Lagoo S**, McMahon RL, Kakihara M, Pappas TN, Eubanks S. The sixth decision regarding perforated duodenal ulcer. *JSLS* 2002; **6**: 359-368 [PMID: 12500837]
69 **Graham RR**. The surgeon's problem in duodenal ulcer. *Am J Surg* 1938; **40**: 102-107 [DOI: 10.1016/S0002-9610(38)90594-X]
70 **Debas HT**, Carvajal SH. Vagal regulation of acid secretion and gastrin release. *Yale J Biol Med* 1994; **67**: 145-151 [PMID: 7502523]
71 **Donahue PE**, Griffith C, Richter HM. A 50-year perspective upon selective gastric vagotomy. *Am J Surg* 1996; **172**: 9-12 [PMID: 8686811 DOI: 10.1016/S0002-9610(96)00046-3]
72 **Bornman PC**, Theodorou NA, Jeffery PC, Marks IN, Essel HP, Wright JP, Terblanche J. Simple closure of perforated duodenal ulcer: a prospective evaluation of a conservative management policy. *Br J Surg* 1990; **77**: 73-75 [PMID: 2302518 DOI: 10.1002/bjs.180077012]
73 **Raimes SA**, Devlin HB. Perforated duodenal ulcer. *Br J Surg* 1987; **74**: 81-82 [PMID: 2880633 DOI: 10.1002/bjs.1800740203]
74 **Hay JM**, Lacaine F, Kohlmann G, Fingerhut A. Immediate definitive surgery for perforated duodenal ulcer does not increase operative mortality: a prospective controlled trial. *World J Surg* 1988; **12**: 705-709 [PMID: 3072779 DOI: 10.1007/BF01655894]
75 **Pach R**, Orzel-Nowak A, Scully T. Ludwik Rydygier--contributor to modern surgery. *Gastric Cancer* 2008; **11**: 187-191 [PMID: 19132478 DOI: 10.1007/s10120-008-0482-7]
76 **Absolon KB**. The surgical school of Theodor BILLROTH. *Surgery* 1961; **50**: 697-715 [PMID: 14036553 DOI: 10.1007/978-3-319-13662-2_30]
77 **Hodnett RM**, Gonzalez F, Lee WC, Nance FC, Deboisblanc R. The need for definitive therapy in the management of perforated gastric ulcers. Review of 202 cases. *Ann Surg* 1989; **209**: 36-39 [PMID: 2910214]
78 **Lanng C**, Palnaes Hansen C, Christensen A, Thagaard CS, Lassen M, Klaerke A, Tønnesen H, Ostgaard SE. Perforated gastric ulcer. *Br J Surg* 1988; **75**: 758-759 [PMID: 3167522 DOI: 10.1002/bjs.1800750812]
79 **Kuwabara K**, Matsuda S, Fushimi K, Ishikawa KB, Horiguchi H, Fujimori K. Reappraising the surgical approach on the perforated gastroduodenal ulcer: should gastric resection be abandoned? *J Clin Med Res* 2011; **3**: 213-222 [PMID: 22383908 DOI: 10.4021/jocmr608w]
80 **Menekse E**, Kocer B, Topcu R, Olmez A, Tez M, Kayaalp C. A practical scoring system to predict mortality in patients with perforated peptic ulcer. *World J Emerg Surg* 2015; **10**: 7 [PMID: 25722739 DOI: 10.1186/s13017-015-0008-7]
81 **Gupta S**, Kaushik R, Sharma R, Attri A. The management of large perforations of duodenal ulcers. *BMC Surg* 2005; **5**: 15 [PMID: 15978134 DOI: 10.1186/1471-2482-5-15]
82 **Seow JG**, Lim YR, Shelat VG. Low serum albumin may predict the need for gastric resection in patients with perforated peptic ulcer. *Eur J Trauma Emerg Surg* 2016 Apr 13; Epub ahead of print [PMID: 27074924 DOI: 10.1007/s00068-016-0669-2]
83 **Mouret P**, François Y, Vignal J, Barth X, Lombard-Platet R. Laparoscopic treatment of perforated peptic ulcer. *Br J Surg* 1990; **77**: 1006 [PMID: 2145052 DOI: 10.1002/bjs.1800770916]
84 **Song KY**, Kim TH, Kim SN, Park CH. Laparoscopic repair of perforated duodenal ulcers: the simple "one-stitch" suture with omental patch technique. *Surg Endosc* 2008; **22**: 1632-1635 [PMID: 18030520 DOI: 10.1007/s00464-007-9670-5]
85 **Sanabria A**, Villegas MI, Morales Uribe CH. Laparoscopic repair for perforated peptic ulcer disease. *Cochrane Database Syst Rev* 2013; **2**: CD004778 [PMID: 23450555 DOI: 10.1002/14651858.CD004778.pub3]
86 **Bertleff MJ**, Halm JA, Bemelman WA, van der Ham AC, van der Harst E, Oei HI, Smulders JF, Steyerberg EW, Lange JF. Randomized clinical trial of laparoscopic versus open repair of the perforated peptic ulcer: the LAMA Trial. *World J Surg* 2009; **33**: 1368-1373 [PMID: 19430829 DOI: 10.1007/s00268-009-0054-y]
87 **Bertleff MJ**, Lange JF. Laparoscopic correction of perforated peptic ulcer: first choice? A review of literature. *Surg Endosc* 2010; **24**: 1231-1239 [PMID: 20033725 DOI: 10.1007/s00464-009-0765-z]
88 **Kim JH**, Chin HM, Bae YJ, Jun KH. Risk factors associated with conversion of laparoscopic simple closure in perforated duodenal ulcer. *Int J Surg* 2015; **15**: 40-44 [PMID: 25644542 DOI: 10.1016/j.ijsu.2015.01.028]
89 **Wright GP**, Davis AT, Koehler TJ, Scheeres DE. Cost-efficiency and outcomes in the treatment of perforated peptic ulcer disease: laparoscopic versus open approach. *Surgery* 2014; **156**: 1003-1007 [PMID: 25239359 DOI: 10.1016/j.surg.2014.06.047]
90 **Kuwabara K**, Matsuda S, Fushimi K, Ishikawa KB, Horiguchi H, Fujimori K. Community-based evaluation of laparoscopic versus open simple closure of perforated peptic ulcers. *World J Surg* 2011; **35**: 2485-2492 [PMID: 21915743 DOI: 10.1007/s00268-011-1252-y]
91 **Thorsen K**, Glomsaker TB, von Meer A, Søreide K, Søreide JA. Trends in diagnosis and surgical management of patients with perforated peptic ulcer. *J Gastrointest Surg* 2011; **15**: 1329-1335 [PMID: 21567292 DOI: 10.1007/s11605-011-1482-1]
92 **Shelat VG**, Ahmed S, Chia CL, Cheah YL. Strict Selection Criteria During Surgical Training Ensures Good Outcomes in Laparoscopic Omental Patch Repair (LOPR) for Perforated Peptic Ulcer (PPU). *Int Surg* 2015; **100**: 370-375 [PMID: 25692444 DOI: 10.9738/INTSURG-D-13-00241.1]
93 **Wang YC**, Hsieh CH, Lo HC, Su LT. Sutureless onlay omental patch for the laparoscopic repair of perforated peptic ulcers. *World J Surg* 2014; **38**: 1917-1921 [PMID: 24663480 DOI: 10.1007/s00268-014-2503-5]
94 **Lau WY**, Leung KL, Kwong KH, Davey IC, Robertson C, Dawson JJ, Chung SC, Li AK. A randomized study comparing laparoscopic versus open repair of perforated peptic ulcer using suture or sutureless technique. *Ann Surg* 1996; **224**: 131-138 [PMID: 8757375 DOI: 10.1097/00000658-199608000-00004]
95 **Lee FY**, Leung KL, Lai PB, Lau JW. Selection of patients for laparoscopic repair of perforated peptic ulcer. *Br J Surg* 2001; **88**: 133-136 [PMID: 11136326 DOI: 10.1046/j.1365-2168.2001.01642.x]
96 **Hashiba K**, Carvalho AM, Diniz G, Barbosa de Aridrade N, Guedes CA, Siqueira Filho L, Lima CA, Coehlo HE, de Oliveira RA. Experimental endoscopic repair of gastric perforations with an omental patch and clips. *Gastrointest Endosc* 2001; **54**: 500-504 [PMID: 11577318 DOI: 10.1067/mge.2001.118444]
97 **Ishiguro T**, Nagawa H. Inadvertent endoscopic application of a hemoclip to the splenic artery through a perforated gastric ulcer. *Gastrointest Endosc* 2001; **53**: 378-379 [PMID: 11231409 DOI: 10.1016/S0016-5107(01)70424-5]
98 **Whiteside OJ**, Tytherleigh MG, Thrush S, Farouk R, Galland RB. Intra-operative peritoneal lavage--who does it and why? *Ann R Coll Surg Engl* 2005; **87**: 255-258 [PMID: 16053685 DOI: 10.1308/1478708051847]
99 **Schein M**, Gecelter G, Freinkel W, Gerding H, Becker PJ. Peritoneal lavage in abdominal sepsis. A controlled clinical study. *Arch Surg* 1990; **125**: 1132-1135 [PMID: 2400306 DOI: 10.1001/archsurg.1990.01410210058008]
100 **Lau H**. Laparoscopic repair of perforated peptic ulcer: a meta-analysis. *Surg Endosc* 2004; **18**: 1013-1021 [PMID: 15136924 DOI: 10.1007/s00464-003-8266-y]
101 **Lunevicius R**, Morkevicius M. Management strategies, early results, benefits, and risk factors of laparoscopic repair of perforated peptic ulcer. *World J Surg* 2005; **29**: 1299-1310 [PMID: 16132404 DOI: 10.1007/s00268-005-7705-4]
102 **Pai D**, Sharma A, Kanungo R, Jagdish S, Gupta A. Role of abdominal drains in perforated duodenal ulcer patients: a prospective controlled study. *Aust N Z J Surg* 1999; **69**: 210-213 [PMID: 10075361 DOI: 10.1046/j.1440-1622.1999.01524.x]
103 **Bergström M**, Arroyo Vázquez JA, Park PO. Self-expandable

metal stents as a new treatment option for perforated duodenal ulcer. *Endoscopy* 2013; **45**: 222-225 [PMID: 23208777 DOI: 10.1055/s-0032-1325885]
104 **Bergström M**, Arroyo Vázquez J, Nsouli G, Park PO. [Good results of stent treatment in perforated duodenal ulcer]. *Lakartidningen* 2015; **112** [PMID: 26418934]
105 **Chung WC**, Jeon EJ, Lee KM, Paik CN, Jung SH, Oh JH, Kim JH, Jun KH, Chin HM. Incidence and clinical features of endoscopic ulcers developing after gastrectomy. *World J Gastroenterol* 2012; **18**: 3260-3266 [PMID: 22783050 DOI: 10.3748/wjg.v18.i25.3260]
106 **Sapala JA**, Wood MH, Sapala MA, Flake TM. Marginal ulcer after gastric bypass: a prospective 3-year study of 173 patients. *Obes Surg* 1998; **8**: 505-516 [PMID: 9819081 DOI: 10.1381/096089298765554061]
107 **Gumbs AA**, Duffy AJ, Bell RL. Incidence and management of marginal ulceration after laparoscopic Roux-Y gastric bypass. *Surg Obes Relat Dis* 2006; **2**: 460-463 [PMID: 16925381 DOI: 10.1016/j.soard.2006.04.233]
108 **MacLean LD**, Rhode BM, Nohr C, Katz S, McLean AP. Stomal ulcer after gastric bypass. *J Am Coll Surg* 1997; **185**: 1-7 [PMID: 9208953 DOI: 10.1016/S1072-7515(01)00873-0]
109 **Patel RA**, Brolin RE, Gandhi A. Revisional operations for marginal ulcer after Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2009; **5**: 317-322 [PMID: 19136312 DOI: 10.1016/j.soard.2008.10.011]
110 **Csendes A**, Burgos AM, Altuve J, Bonacic S. Incidence of marginal ulcer 1 month and 1 to 2 years after gastric bypass: a prospective consecutive endoscopic evaluation of 442 patients with morbid obesity. *Obes Surg* 2009; **19**: 135-138 [PMID: 18581192 DOI: 10.1007/s11695-008-9588-6]
111 **Wendling MR**, Linn JG, Keplinger KM, Mikami DJ, Perry KA, Melvin WS, Needleman BJ. Omental patch repair effectively treats perforated marginal ulcer following Roux-en-Y gastric bypass. *Surg Endosc* 2013; **27**: 384-389 [PMID: 22936436 DOI: 10.1007/s00464-012-2492-0]
112 **Natarajan SK**, Chua D, Anbalakan K, Shelat VG. Marginal ulcer perforation: a single center experience. *Eur J Trauma Emerg Surg* 2016 Sep 12; Epub ahead of print [PMID: 27619359 DOI: 10.1007/s00068-016-0723-0]
113 **Lunevicius R**, Morkevicius M. Systematic review comparing laparoscopic and open repair for perforated peptic ulcer. *Br J Surg* 2005; **92**: 1195-1207 [PMID: 16175515 DOI: 10.1002/bjs.5155]
114 **Imhof M**, Epstein S, Ohmann C, Röher HD. Duration of survival after peptic ulcer perforation. *World J Surg* 2008; **32**: 408-412 [PMID: 18172710 DOI: 10.1007/s00268-007-9370-2]
115 **Sarosi GA**, Jaiswal KR, Nwariaku FE, Asolati M, Fleming JB, Anthony T. Surgical therapy of peptic ulcers in the 21st century: more common than you think. *Am J Surg* 2005; **190**: 775-779 [PMID: 16226957 DOI: 10.1016/j.amjsurg.2005.07.019]
116 **Feliciano DV**, Bitondo CG, Burch JM, Mattox KL, Jordan GL, DeBakey ME. Emergency management of perforated peptic ulcers in the elderly patient. *Am J Surg* 1984; **148**: 764-767 [PMID: 6507748 DOI: 10.1016/0002-9610(84)90433-1]
117 **Lee FY**, Leung KL, Lai BS, Ng SS, Dexter S, Lau WY. Predicting mortality and morbidity of patients operated on for perforated peptic ulcers. *Arch Surg* 2001; **136**: 90-94 [PMID: 11146785 DOI: 10.1001/archsurg.136.1.90]
118 **Wilhelmsen M**, Møller MH, Rosenstock S. Surgical complications after open and laparoscopic surgery for perforated peptic ulcer in a nationwide cohort. *Br J Surg* 2015; **102**: 382-387 [PMID: 25605566 DOI: 10.1002/bjs.9753]
119 **Sharma SS**, Mamtani MR, Sharma MS, Kulkarni H. A prospective cohort study of postoperative complications in the management of perforated peptic ulcer. *BMC Surg* 2006; **6**: 8 [PMID: 16780583 DOI: 10.1186/1471-2482-6-8]
120 **Kim JM**, Jeong SH, Lee YJ, Park ST, Choi SK, Hong SC, Jung EJ, Ju YT, Jeong CY, Ha WS. Analysis of risk factors for postoperative morbidity in perforated peptic ulcer. *J Gastric Cancer* 2012; **12**: 26-35 [PMID: 22500261 DOI: 10.5230/jgc.2012.12.1.26]
121 **Knudsen NV**, Møller MH. Association of mortality with out-of-hours admission in patients with perforated peptic ulcer. *Acta Anaesthesiol Scand* 2015; **59**: 248-254 [PMID: 25495922 DOI: 10.1111/aas.12450]
122 **Thorsen K**, Søreide JA, Søreide K. Scoring systems for outcome prediction in patients with perforated peptic ulcer. *Scand J Trauma Resusc Emerg Med* 2013; **21**: 25 [PMID: 23574922 DOI: 10.1186/1757-7241-21-25]
123 **Fitz-Henry J**. The ASA classification and peri-operative risk. *Ann R Coll Surg Engl* 2011; **93**: 185-187 [PMID: 21477427 DOI: 10.1308/rcsann.2011.93.3.185a]
124 **Knaus WA**, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med* 1985; **13**: 818-829 [PMID: 3928249 DOI: 10.1097/00003465-198603000-00013]
125 **Lee DJ**, Ye M, Sun KH, Shelat VG, Koura A. Laparoscopic versus Open Omental Patch Repair for Early Presentation of Perforated Peptic Ulcer: Matched Retrospective Cohort Study. *Surg Res Pract* 2016; **2016**: 8605039 [PMID: 27722200 DOI: 10.1155/2016/8605039]
126 **Ishiguro T**, Kumagai Y, Baba H, Tajima Y, Imaizumi H, Suzuki O, Kuwabara K, Matsuzawa T, Sobajima J, Fukuchi M, Ishibashi K, Mochiki E, Ishida H. Predicting the amount of intraperitoneal fluid accumulation by computed tomography and its clinical use in patients with perforated peptic ulcer. *Int Surg* 2014; **99**: 824-829 [PMID: 25437594 DOI: 10.9738/INTSURG-D-14-00109.1]
127 **Noguiera C**, Silva AS, Santos JN, Silva AG, Ferreira J, Matos E, Vilaça H. Perforated peptic ulcer: main factors of morbidity and mortality. *World J Surg* 2003; **27**: 782-787 [PMID: 14509505 DOI: 10.1007/s00268-003-6645-0]
128 **Agrez MV**, Henry DA, Senthiselvan S, Duggan JM. Changing trends in perforated peptic ulcer during the past 45 years. *Aust N Z J Surg* 1992; **62**: 729-732 [PMID: 1520157 DOI: 10.1111/j.1445-2197.1992.tb07071.x]
129 **Svanes C**, Lie RT, Lie SA, Kvåle G, Svanes K, Søreide O. Survival after peptic ulcer perforation: a time trend analysis. *J Clin Epidemiol* 1996; **49**: 1363-1371 [PMID: 8970486 DOI: 10.1016/S0895-4356(96)00278-8]
130 **Walt R**, Katschinski B, Logan R, Ashley J, Langman M. Rising frequency of ulcer perforation in elderly people in the United Kingdom. *Lancet* 1986; **1**: 489-492 [PMID: 2869219 DOI: 10.1016/S0140-6736(86)92940-5]
131 **Kocer B**, Surmeli S, Solak C, Unal B, Bozkurt B, Yildirim O, Dolapci M, Cengiz O. Factors affecting mortality and morbidity in patients with peptic ulcer perforation. *J Gastroenterol Hepatol* 2007; **22**: 565-570 [PMID: 17376052 DOI: 10.1111/j.1440-1746.2006.04500.x]
132 **Blomgren LG**. Perforated peptic ulcer: long-term results after simple closure in the elderly. *World J Surg* 1997; **21**: 412-414 [PMID: 9143574 DOI: 10.1007/PL00012263]
133 **Svanes C**, Salvesen H, Stangeland L, Svanes K, Søreide O. Perforated peptic ulcer over 56 years. Time trends in patients and disease characteristics. *Gut* 1993; **34**: 1666-1671 [PMID: 8282252 DOI: 10.1136/gut.34.12.1666]
134 **Bulut OB**, Rasmussen C, Fischer A. Acute surgical treatment of complicated peptic ulcers with special reference to the elderly. *World J Surg* 1996; **20**: 574-577 [PMID: 8661633 DOI: 10.1007/s002689900089]
135 **Thomsen RW**, Riis A, Christensen S, Nørgaard M, Sørensen HT. Diabetes and 30-day mortality from peptic ulcer bleeding and perforation: a Danish population-based cohort study. *Diabetes Care* 2006; **29**: 805-810 [PMID: 16567819 DOI: 10.2337/diacare.29.04.06.dc05-1748]

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MINIREVIEWS

Practice, training and safety of laparoscopic surgery in low and middle-income countries

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Abstract

Surgical management of diseases is recognised as a major unmet need in low and middle-income countries (LMICs). Laparoscopic surgery has been present since the 1980s and offers the benefit of minimising the morbidity and potential mortality associated with laparotomies. Laparotomies are often carried out in LMICs for diagnosis and management, due to lack of radiological investigative and intervention options. The use of laparoscopy for diagnosis and treatment is globally variable, with high-income countries using laparoscopy routinely compared with LMICs. The specific advantages of minimally invasive surgery such as lower surgical site infections and earlier return to work are of great benefit for patients in LMICs, as time lost not working could result in a family not being able to sustain themselves. Laparoscopic surgery and training is not cheap. Cost is a major barrier to healthcare access for a significant population in LMICs. Therefore, cost is usually seen as a major barrier for laparoscopic surgery to be integrated into routine practice in LMICs. The aim of this review is to focus on the practice, training and safety of laparoscopic surgery in LMICs. In addition it highlights the barriers to progress in adopting laparoscopic surgery in LMICs and how to address them.

Key words: Laparoscopic surgery; Global surgery; Low and middle-income countries; Laparoscopic training; Patient safety; Laparoscopy; Minimally invasive surgery

Core tip: The rate of laparoscopic surgery in low and middle-income countries (LMICs) is gradually increasing. In this review we highlight the practice of laparoscopic surgery in LMICs from diagnostic procedures to complex resections. Training in laparoscopic surgery is inherently variable in LMICs, however innovative teaching methods with inexpensive materials have been developed. Safety data on laparoscopic surgery in LMICs is minimal and more research needs to be done. It is essential to establish safe practices that must be contextualized to serve the population in various LMICs.

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INTRODUCTION

Surgical management of diseases are now recognized as major unmet needs in low and middle-income countries (LMICs)[1]. These countries are defined by the World Bank as having a gross national income (GNI) per capita of $1045 or less for low-income countries and more than $1045 but less than $12736 for middle income countries[2]. High-income countries (HICs) by definition have a GNI per capita of more than or equal to $12736[2].

Laparoscopic surgery was first introduced in the 1980s and is the preferred approach to a number of surgical procedures in HICs[3]. There are growing numbers of global surgery initiatives that have acknowledged surgical need and volume will continue to rise in LMICs[4-6]. Laparoscopic surgery offers the benefit of minimizing the morbidity and potential mortality associated with laparotomies. Several studies have shown that laparoscopic surgery is feasible in LMICs with reports of laparoscopy reducing laparotomy rates from fourteen to six percent[7-11]. Particular advantages of minimally invasive procedures are lower surgical site infection rates, ileus, earlier return to work, better pain control and cosmesis[12,13]. Decreasing the length of stay in hospital is of paramount importance to patients in LMICs, where days lost working translates into lack of food for some families. Hence, laparoscopic surgery seems attuned to serve such communities.

There has been sporadic and marginal adoption of laparoscopic surgery in LMICs for various reasons. Some of the obstacles are intrinsically health care system related, others financially driven such as inadequately trained personnel and lack of equipment. The cost of initial set up and maintenance of laparoscopic surgery equipment has been reported in some studies as the main inhibitory factor for minimally invasive surgery being commonly used in LMICs[9,10]. Nevertheless, laparoscopic procedures are performed in a number of surgical specialties in LMICs such as general surgery, urology, paediatric surgery and gynaecology. Laparoscopic procedures such as hysterectomies, tubo-ovarian surgery, cholecystectomies, appendicectomies, herniorrhapies and diagnostic laparoscopies are well established and performed routinely mainly in private centres in LMICs[7,10,14,15]. The aim of this review is to highlight the practice, training and safety of laparoscopic surgery in LMICs.

PRACTICE OF LAPAROSCOPIC SURGERY

The benefits of laparoscopic surgery in LMICs are parallel to those of HICs. Diagnostic laparoscopy has the value of decreasing laparotomy rates. Furthermore, laparoscopy in certain LMICs has replaced radiological diagnosis due to the lack of radiologisits and radiological facilities. A study from Nigeria by Adisa *et al*[16] reported neoplastic lesions identified in 64 patients through diagnostic laparoscopy, which aided further management of their cancers in some cases with chemotherapy or palliative procedures. The study highlighted only six computed tomography (CT) scanners and three magnetic resonance imaging (MRI) scanners were serving a population of approximately 15 million in Southwestern Nigeria as at 2012[16].

The challenges of the adoption and use of new technology or ideas are common to any health care setting. The initial reservations of laparoscopic surgery not being "orthodox" surgery in LMICs are gradually disappearing. Interestingly, hierarchical surgical culture has been quoted as a hindrance for laparoscopic surgery being performed in some hospitals, as senior surgeons "did not feel comfortable with it" due to lack of engagement[17]. Some patient driven factors due to deficiencies in communication or education also contribute to the hurdles of the acceptance of laparoscopic surgery in LMICs[18,19].

Equipment donated by charitable organisations has enabled the practice of laparoscopic surgery in numerous LMICs. Minimally invasive procedures are being used in LMICs for both emergency and elective procedures. In many parts of Africa, laparoscopic surgery is much more common in private hospitals due to the availability of funding for equipment and maintenance. Diagnostic laparoscopy in particular has taken center stage in LMICs where radiological facilities are lacking. Udwadia[9] reported performing approximately 3000 diagnostic laparoscopies over an 18 year period with no mortalities and a complication rate of 0.1%. These procedures had been used for the evaluation of abdominal tuberculosis, peritoneal pathology and abdominal trauma[9]. Shehata *et al*[20] reported 36 successful laparoscopic inguinal hernia operations with no recurrences or conversions to open surgery in a paediatric cohort. Day case procedures in LMICs are feasible provided set discharge criteria are in place to ensure patient safety[18,19]. Laparoscopic appendicectomies have been performed with 87% of patients being discharged on the same day successfully from a cohort of thirty in India[21].

Studies on certain specialised laparoscopic procedures such as colorectal, endocrine and urological surgery are scarce. Laparoscopic colorectal surgery as a whole is not commonly performed in African countries[10], this may be a reflection of the low incidence of colorectal disease. An Egyptian study however has reported successful outcomes in 37 patients with colorectal cancer managed laparoscopically[22]. Laparoscopic urological procedures in sub-Saharan Africa are usually performed by visiting surgeons from HICs during voluntary work or by sponsored invitations.

Spinal and regional rather than general anaesthesia has been safely used in LMICs for laparoscopic surgery[9,23,24]. Insufflation with carbon dioxide alone is an expensive venture in LMICs. Therefore, the development

and use of "gasless" laparoscopy in LMICs has been revolutionary[25]. Inventive strategies such as insufflation with room air, extracorporeal knot tying and hand assisted techniques have evolved in LMICs[26,27]. Adisa *et al*[10] used tube drapes that can be autoclaved as camera covers. Such innovative measures make laparoscopic surgery more attainable in LMICs.

TRAINING IN LAPAROSCOPIC SURGERY

In certain LMICs, visiting surgeons and some nationals who have relocated from HICs work on the expansion and further development of laparoscopic surgery. Moreover, as part of their continuing professional development, some surgeons from LMICs travel to centres in the United States and Europe to gain more laparoscopic experience[28]. This also stimulates practice on box trainers where available on their return. Laparoscopy is not suited to the old surgical mantra of "see one, do one, teach one". Under this traditional model, some local surgeons in LMICs have acquired and developed laparoscopic abilities in an unstructured way. This has the potential for unsafe practices being learnt by surgeons in training.

The challenges for the surgeon of learning to decipher two to three dimensional images, hand eye co-ordination; past pointing and haptic feedback are universal. Learning and practicing outside the operating theatre is crucial for acquiring laparoscopic skills. The resource-limited environment in LMICs also hampers the progress of laparoscopic training, with the lack of expert trainers. Laparoscopy is not taught in postgraduate residency training programmes in several LMICs and hence simulated laboratories are not readily available due to equipment costs. Lack of animal laboratories or wet labs as aids to practice in a safe location also add to the training constraints. Nevertheless, innovative measures have been developed to counteract the simulation problem with low fidelity but effective trainers. Ingenious low technology and cost laparoscopic trainers have evolved from both LMICs and HICs. Low cost trainers vary in price in different countries ranging from $0 (if using already available materials) to $85[29,30]. For example, Mir *et al*[4] reused an empty dextrose solution cardboard box to make an inexpensive trainer. Home laparoscopic trainers have been made from recyclable materials such as storage and shoe boxes[29,31]. Simulation based training even with low cost equipment requires investing time and sustainability[32]. Locally sourced materials are key to the success of making low cost laparoscopic training tools.

Andreatta *et al*[33] developed a training programme in Ghana with laparoscopic exercises such as cutting or peeling a tangerine into as few pieces as methods to assist in learning dissection and haptic feedback[33] American surgeons have used validated training tools such as the McGill Inanimate System for Training and Evaluation of Laparoscopic Skills in Tanzania to assess the use of a low-cost laparoscopic box trainer, which they found to be effective when an expert trainer was present[29].

The recording of commonly performed procedures such as appendicectomies and cholecystectomies for teaching and training is significantly underutilized in both LMICs and HICs. This can allow nurses, medical students, surgical and anaesthetic trainees to understand the processes involved in these laparoscopic operations. Access to the Internet can also aid learning as a number of laparoscopic operations are freely available online. Curricular can facilitate learning of laparoscopic skills in LMICs using low cost trainers and these need to be developed.

Both surgeons and nurses need to be trained in the principles and practical aspects of laparoscopic surgery. Knowledge of the instruments is essential when performing laparoscopic surgery. The training and practice of laparoscopic surgery in LMICs, could be improved and made more widely available through postgraduate medical education. In Nigeria for example, a group of general surgeons have recently formed the Laparoscopic Surgery Society of Nigeria to assess the scope of practice, basic competency, proficiency, and outcomes of laparoscopic surgery, so as to develop training.

SAFETY OF LAPAROSCOPIC SURGERY

Variability in safety and quality exists with laparoscopic surgery in LMICs[34]. Although a number of studies have reported safely preforming laparoscopic surgery, studies on the early complication rates may however be under reported in the literature. Mortality associated with anaesthesia is a major concern in LMICs, with reports ranging from 1 in 100 to 500[35,36]. The direct relationship of anaesthetic risks during laparoscopic surgery in LMICs is scarce in the literature. This may be because in a number of LMICs, spinal rather than general anaesthetic is used for laparoscopic surgery. Furthermore, the numbers of laparoscopic cases in most units have not reached a level whereby complications directly related to laparoscopy are reported such as respiratory compromise secondary to a pneumothorax or pulmonary odema.

In a comparative study, Manning *et al*[37] reported major complications such as bile leaks and duodenal perforations in patients following laparoscopic cholecystectomy in a large patient series from Afghanistan. More advanced laparoscopic procedures are being undertaken in certain LMICs. Senthilnathan *et al*[38] reported long-term results of a 130 patients following a laparoscopic pancreaticoduodenectomy for pancreatic cancer. This included a 5-year actuarial survival of 29%, a mortality rate of 2% and a positive margin rate of 9%[38]. Adequate training is crucial for patient safety. The inability to easily recognise the complications associated with laparoscopic surgery is a potential safety concern. In LMICs, there are significant implications with morbidity and mortality risks that can be associated with laparoscopic surgery such as bile duct injury in laparoscopic cholecystectomies, as facilities such as

endoscopic retrograde cholangiopancreatography are lacking[39].

The use of reusable laparoscopic instruments has helped in reducing the financial load in LMICs compared with disposable instruments. Studies have reported instruments being used for over 10 years, as well as reusing disposable instruments[9,40]. However, safety data about such usage is unknown. Nonetheless, no short-term safety concerns or suboptimal function have been described post sterilization. The upkeep and repairs of laparoscopic equipment is a significant challenge in LMICs. Part of the problems with donated instruments and equipment is the unavailability of trained personnel to undertake servicing. To counteract this, the manufacture and maintenance of low-cost equipment should be part of the future projects for industries to cater for LMICs.

DISCUSSION

Laparoscopic surgery has been a paradigm shift in surgical practice. Global surgical diseases have been estimated at eleven percent, although this may be an underestimate[41-44]. Only four percent of surgical procedures are carried out in low-income countries[45]. Lower life expectancy and infant mortality, which could partly be related to surgical need in terms of trauma and obstetric care respectively, remain a major issue in LMICs[46,47]. Therefore, there is a rising trend to develop surgical treatment in LMICs[48-50] with laparoscopic surgery playing a central role.

Surgical cultures and behaviours have been narrated as having an impact on the introduction and progress of new technology. Therefore a mindshift towards laparoscopic surgery and other new surgical techniques needs to be encouraged in LMICs to challenge the status quo. The time taken for some laparoscopic procedures, because of the set up, is much longer than open surgery. Therefore in LMICs where demand for high output surgical procedures is great, the throughput ability of laparoscopic surgery may be questioned. The specialist "general surgeon" is fast disappearing in HICs due to sub-specialisation. In LMICs however, the general surgeon is still very necessary given the array of conditions he or she is required to treat. Controversially, the generalist laparoscopic surgeon may be too demanding to have among a personnel limited and population heavy setting that exists in many LMICs.

Inequalities in health with regards to access and affordability are wider in LMICs, where the more affluent are more likely to have their operations performed laparoscopically. The payment plans of health care services vary in LMICs. They may be self-financed, government subsidized or insurance based and this has the potential effect of influencing the choices in procedures carried out specifically with regards to cost such as in laparoscopic surgery. A number of units in LMICs have acquired their laparoscopic instruments through donations or following surgical missions from HICs. A way of accessing materials is for surgeons, healthcare service providers and governments to engage in the development process for laparoscopic surgery to be more accessible in LMICs.

Cost is a major barrier to healthcare access for a significant number of individuals in LMICs. The financial afflictions that face some LMICs may have been the result of war, conflict, corruption and other humanitarian crises. Thus, understanding the baseline operative capabilities in these countries is paramount before embarking on an improvement operation[51]. It is also key for surgical mission trips to endeavour to build, adapt and tailor practices that are sustainable for LMICs, rather than perform procedures with considerations only for the standards of HICs. The focus of these mission trips should be goal directed with long-term planning for continuous teaching, training and supervision of new initiatives.

The price of equipment is a major obstacle to laparoscopy being routine in LMICs. This was one of the initial factors hindering rapid uptake of laparoscopic surgery in a number of hospitals in HICs. Although some studies have reported diagnostic laparoscopy to be more cost effective in some African countries, others have reported laparoscopy costs to be similar to that of laparotomy[7-9]. Remarkably laparoscopic equipment per case has been reported to be as low as $20, with the cost of the procedures themselves ranging from approximately $55 to $300 in some LMICs[9,10,15]. Lowering the cost of the equipment, maintenance and surgery itself will increase the endorsement of laparoscopic surgery in LMICs. This could be achieved through collaborative work with governments and medical equipment suppliers.

Bal *et al*[18] have shown that day case laparoscopic procedures such as laparoscopic cholecystectomies are feasible in LMICs. Chauhan *et al*[19] on the other hand argue that day surgery is not cost effective in LMICs compared with HICs because of infrastructural constraints. The practice of day case surgery to negate the cost of hospital stay would be variable in LMICs. As patients sometimes have come from long distances and for safety reasons a period of in-patient observation may be necessary. However with the advent of global mobile phone technology, telephone and video based reviews and follow-ups may be the way forward to offset this problem.

The Fundamentals of Laparoscopic Skills, which involves web-based and technical skills training in the United States, is a good example of a method for standardizing skills. A low cost version of such a program would be appropriate in a resource-limited environment to provide education, training and accreditation. The training programmes should be structured to include lectures and workshops rather than just short-term courses. Global connectivity though technology can also facilitate teaching and training methods with the development of Google glasses, Face Time and Skype for example, to allow communication, consultation and feedback.

International organizations provide a lot of surgical

care in LMICs; therefore, cooperative efforts are crucial to the success of safe laparoscopic operations in LMICs. The benefit of experience from visiting or locally trained surgeons will provide insight into potential short and long-term problems with solutions, as well as the economic contingency measures. Centralization of laparoscopic surgery maybe better for infrastructure planning in the initial stages of service provision in LMICs. This may curtail the differences in the quality of health care delivery and integrate various concepts such as patient selection, safety, re-cycling of equipment and resource allocation. It could also help in training surgeons and nursing staff from different peripheral hospitals to a certain standard.

This review has a number of limitations that we acknowledge such as the difficultly in generalizing the differences between LMICs in terms of health care budgets and the surgical needs of the population. Therefore, some of the solutions we suggest may not be suitable for all LMICs. Most of the studies reported in the literature were retrospective, non-comparative with short-term follow-up periods. More research needs to be encouraged into data collection, formation of registries and reporting of outcomes of laparoscopic surgery in LMICs.

CONCLUSION

The management of surgical conditions in LMICs are now of great interest to health care funders and researchers in HICs. We believe laparoscopic surgery in LMICs offers the same advantages as in HICs - reduced surgical site infections, length of stay; and should be promoted as such. Social and economic change alongside with manufacturers and health ministries are the main drivers for cost effective healthcare in LMICs to enable deprived individuals access to surgical care. The global economic picture for better healthcare should include the manufacture of robust, durable and affordable surgical instruments that can be used by LMICs.

The realms of safety in surgery in certain LMICs still lies in the ability to obtain basic amenities such as clean water and electricity as well as having adequately trained medical, nursing and allied health professional staff. The culture of guidelines, regulation and monitoring also needs to be adopted in LMICs in line with accountability for complications. The trend of laparoscopic surgery is here to stay for a few years before robotic surgery or other means take over. It is therefore vital to establish safe practices that must be contextualized to serve the population in various LMICs.

REFERENCES

1 **Ozgediz D**, Riviello R. The "other" neglected diseases in global public health: surgical conditions in sub-Saharan Africa. *PLoS Med* 2008; **5**: e121 [PMID: 18532875 DOI: 10.1371/journal.pmed.0050121]

2 **Bank W**. Country and Lending Groups. 2016. [accessed 2016 Mar 25]. Available from: http://data.worldbank.org/about/country-and-lending-groups

3 **Lau WY**, Leow CK, Li AK. History of endoscopic and laparoscopic surgery. *World J Surg* 1997; **21**: 444-453 [PMID: 9143579 DOI: 10.1007/PL00012268]

4 **Mir IS**, Mohsin M, Malik A, Shah AQ, Majid T. A structured training module using an inexpensive endotrainer for improving the performance of trainee surgeons. *Trop Doct* 2008; **38**: 217-218 [PMID: 18820186 DOI: 10.1258/td.2008.070359]

5 **Weiser TG**, Haynes AB, Molina G, Lipsitz SR, Esquivel MM, Uribe-Leitz T, Fu R, Azad T, Chao TE, Berry WR, Gawande AA. Size and distribution of the global volume of surgery in 2012. *Bull World Health Organ* 2016; **94**: 201-209F [PMID: 26966331 DOI: 10.2471/BLT.15.159293]

6 **Weiser TG**, Regenbogen SE, Thompson KD, Haynes AB, Lipsitz SR, Berry WR, Gawande AA. An estimation of the global volume of surgery: a modelling strategy based on available data. *Lancet* 2008; **372**: 139-144 [PMID: 18582931 DOI: 10.1016/S0140-6736(08)60878-8]

7 **Bendinelli C**, Leal T, Moncade F, Dieng M, Toure CT, Miccoli P. Endoscopic surgery in Senegal. Benefits, costs and limits. *Surg Endosc* 2002; **16**: 1488-1492 [PMID: 11988789 DOI: 10.1007/s00464-001-9188-1]

8 **Ogbonna BC**, Obekpa PO, Momoh JT, Obafunwa JO, Nwana EJ. Laparoscopy in developing countries in the management of patients with an acute abdomen. *Br J Surg* 1992; **79**: 964-966 [PMID: 1422771 DOI: 10.1002/bjs.1800790937]

9 **Udwadia TE**. Diagnostic laparoscopy. *Surg Endosc* 2004; **18**: 6-10 [PMID: 12958680 DOI: 10.1007/s00464-002-8872-0]

10 **Adisa AO**, Lawal OO, Arowolo OA, Alatise OI. Local adaptations aid establishment of laparoscopic surgery in a semiurban Nigerian hospital. *Surg Endosc* 2013; **27**: 390-393 [PMID: 22806524 DOI: 10.1007/s00464-012-2463-5]

11 **Asbun HJ**, Berguer R, Altamirano R, Castellanos H. Successfully establishing laparoscopic surgery programs in developing countries. Clinical results and lessons learned. *Surg Endosc* 1996; **10**: 1000-1003 [PMID: 8864094 DOI: 10.1007/s004649900223]

12 **Agha R**, Muir G. Does laparoscopic surgery spell the end of the open surgeon? *J R Soc Med* 2003; **96**: 544-546 [PMID: 14594961 DOI: 10.1258/jrsm.96.11.544]

13 **Vellani Y**, Bhatti S, Shamsi G, Parpio Y, Ali TS. Evaluation of laparoscopic appendectomy vs. open appendectomy: a retrospective study at Aga Khan University Hospital, Karachi, Pakistan. *J Pak Med Assoc* 2009; **59**: 605-608 [PMID: 19750854]

14 **Ali R**, Khan MR, Pishori T, Tayeb M. Laparoscopic appendectomy for acute appendicitis: Is this a feasible option for developing countries? *Saudi J Gastroenterol* 2010; **16**: 25-29 [PMID: 20065570 DOI: 10.4103/1319-3767.58764]

15 **Esayas RS**, Shumey A, Selassie KG. Laparoscopic Surgery in a Governmental Teaching Hospital: An Initial Experience from Ayder Referral Hospital in Northern Ethiopia. *East Cent African J Surg* 2015; **20**: 49-54

16 **Adisa AO**, Lawal OO, Adesunkanmi AR, Adejuyigbe O. Impact of introduction of laparoscopic surgery on management of unresolved intra-abdominal malignancies in a West African hospital. *World J Surg* 2014; **38**: 2519-2524 [PMID: 24791947 DOI: 10.1007/s00268-014-2618-8]

17 **Choy I**, Kitto S, Adu-Aryee N, Okrainec A. Barriers to the uptake of laparoscopic surgery in a lower-middle-income country. *Surg Endosc* 2013; **27**: 4009-4015 [PMID: 23708726 DOI: 10.1007/s00464-013-3019-z]

18 **Bal S**, Reddy LG, Parshad R, Guleria R, Kashyap L. Feasibility and safety of day care laparoscopic cholecystectomy in a developing country. *Postgrad Med J* 2003; **79**: 284-288 [PMID: 12782776 DOI: 10.1136/pmj.79.931.284]

19 **Chauhan A**, Mehrotra M, Bhatia PK, Baj B, Gupta AK. Day care laparoscopic cholecystectomy: a feasibility study in a public health service hospital in a developing country. *World J Surg* 2006; **30**: 1690-1695 [PMID: 16902738 DOI: 10.1007/s00268-006-0023-7]

20 **Shehata SM**, El Attar AA, Attia MA, Hassan AM. Laparoscopic herniotomy in children: prospective assessment of tertiary center experience in a developing country. *Hernia* 2013; **17**: 229-234 [PMID:

23269403 DOI: 10.1007/s10029-012-1031-1]
21 **Hussain A**, Singh S, Ahi KS, Singh M. Status of Day Care Laparoscopic Appendectomy in Developing Countries. *Int Schol Res Not* 2014; **2014**: 5 [DOI: 10.1155/2014/502786]
22 **Amin AT**, Ahmed BM, Khallaf SM. Safety and feasibility of laparoscopic colo-rectal surgery for cancer at a tertiary center in a developing country: Egypt as an example. *J Egypt Natl Canc Inst* 2015; **27**: 91-95 [PMID: 25921235 DOI: 10.1016/j.jnci.2015.03.005]
23 **Bessa SS**, El-Sayes IA, El-Saiedi MK, Abdel-Baki NA, Abdel-Maksoud MM. Laparoscopic cholecystectomy under spinal versus general anesthesia: a prospective, randomized study. *J Laparoendosc Adv Surg Tech A* 2010; **20**: 515-520 [PMID: 20578922 DOI: 10.1089/lap.2010.0041]
24 **Olonisakin RP**, Sotunmbi PT, Afuwape OO, Ayandipo OO, Adigun TA. Regional anaesthetic technique for laparoscopic appendicectomy in Ibadan. *Afr J Med Med Sci* 2014; **43**: 219-223 [PMID: 26223139]
25 **Gnanaraj J**, Rhodes M. Laparoscopic surgery in middle- and low-income countries: gasless lift laparoscopic surgery. *Surg Endosc* 2016; **30**: 2151-2154 [PMID: 26275541]
26 **Nande AG**, Shrikhande SV, Rathod V, Adyanthaya K, Shrikhande VN. Modified technique of gasless laparoscopic cholecystectomy in a developing country: a 5-year experience. *Dig Surg* 2002; **19**: 366-371; discussion 372 [PMID: 12435907 DOI: 10.1159/000065836]
27 **Adisa AO**, Alatise OI, Arowolo OA, Lawal OO. Laparoscopic appendectomy in a Nigerian teaching hospital. *JSLS* 2012; **16**: 576-580 [PMID: 23484567 DOI: 10.4293/108680812X13462882737131]
28 **Ahmad JI**, Mishra RK. Minimal Access Surgery Educational Needs of Trainees from Africa: Perspectives from an Asian Training Institution. *West Afr J Med* 2015; **34**: 44-49 [PMID: 26902816]
29 **Beard JH**, Akoko L, Mwanga A, Mkony C, O'Sullivan P. Manual laparoscopic skills development using a low-cost trainer box in Tanzania. *J Surg Educ* 2014; **71**: 85-90 [PMID: 24411429 DOI: 10.1016/j.jsurg.2013.06.005]
30 **Long KL**, Spears C, Kenady DE, Roth JS. Implementation of a low-cost laparoscopic skills curriculum in a third-world setting. *J Surg Educ* 2014; **71**: 860-864 [PMID: 24931413 DOI: 10.1016/j.jsurg.2014.05.004]
31 **Alfa-Wali M**, Antoniou A. Eco-friendly laparoscopic home trainer. *Simul Healthc* 2011; **6**: 176-179 [PMID: 21646985 DOI: 10.1097/SIH.0b013e318208549b]
32 **Okrainec A**, Smith L, Azzie G. Surgical simulation in Africa: the feasibility and impact of a 3-day fundamentals of laparoscopic surgery course. *Surg Endosc* 2009; **23**: 2493-2498 [PMID: 19343438 DOI: 10.1007/s00464-009-0424-4]
33 **Andreatta P**, Perosky J, Klotz J, Gamble C, Ankobea F, Danso K, Dalton V. Pilot study outcomes from a resource-limited setting for a low-cost training program for laparoscopic surgical skills. *Int J Gynaecol Obstet* 2014; **125**: 186-188 [PMID: 24602775 DOI: 10.1016/j.ijgo.2013.10.030]
34 **Chao TE**, Mandigo M, Opoku-Anane J, Maine R. Systematic review of laparoscopic surgery in low- and middle-income countries: benefits, challenges, and strategies. *Surg Endosc* 2016; **30**: 1-10 [PMID: 25875087 DOI: 10.1007/s00464-015-4201-2]
35 **Hansen D**, Gausi SC, Merikebu M. Anaesthesia in Malawi: complications and deaths. *Trop Doct* 2000; **30**: 146-149 [PMID: 10902471]
36 **Ouro-Bang'na Maman AF**, Tomta K, Ahouangbévi S, Chobli M. Deaths associated with anaesthesia in Togo, West Africa. *Trop Doct* 2005; **35**: 220-222 [PMID: 16354475 DOI: 10.1258/00494750577493 8666]
37 **Manning RG**, Aziz AQ. Should laparoscopic cholecystectomy be practiced in the developing world?: the experience of the first training program in Afghanistan. *Ann Surg* 2009; **249**: 794-798 [PMID: 19387323 DOI: 10.1097/SLA.0b013e3181a3eaa9]
38 **Senthilnathan P**, Srivatsan Gurumurthy S, Gul SI, Sabnis S, Natesan AV, Palanisamy NV, Praveen Raj P, Subbiah R, Ramakrishnan P, Palanivelu C. Long-term results of laparoscopic pancreaticoduodenectomy for pancreatic and periampullary cancer-experience of 130 cases from a tertiary-care center in South India. *J Laparoendosc Adv Surg Tech A* 2015; **25**: 295-300 [PMID: 25789541 DOI: 10.1089/lap.2014.0502]
39 **Hofmeyr S**, Krige JE, Bornman PC, Beningfield SJ. A cost analysis of operative repair of major laparoscopic bile duct injuries. *S Afr Med J* 2015; **105**: 454-457 [PMID: 26716161 DOI: 10.7196/SAMJ.9038]
40 **Price R**, Sergelen O, Unursaikhan C. Improving surgical care in Mongolia: a model for sustainable development. *World J Surg* 2013; **37**: 1492-1499 [PMID: 22941237 DOI: 10.1007/s00268-012-1763-1]
41 **Chirdan LB**, Ameh EA. Untreated surgical conditions: time for global action. *Lancet* 2012; **380**: 1040-1041 [PMID: 22898075 DOI: 10.1016/S0140-6736(12)61305-1]
42 **McQueen KA**, Hyder JA, Taira BR, Semer N, Burkle FM, Casey KM. The provision of surgical care by international organizations in developing countries: a preliminary report. *World J Surg* 2010; **34**: 397-402 [PMID: 19685261 DOI: 10.1007/s00268-009-0181-5]
43 **Farmer PE**, Kim JY. Surgery and global health: a view from beyond the OR. *World J Surg* 2008; **32**: 533-536 [PMID: 18311574 DOI: 10.1007/s00268-008-9525-9]
44 **Holmberg S**, Nordberg E. Surgical rates in Africa. Variations and their possible explanations. *Trop Geogr Med* 1990; **42**: 352-358 [PMID: 2100078]
45 **Löfgren J**, Mulowooza J, Nordin P, Wladis A, Forsberg BC. Cost of surgery in a low-income setting in eastern Uganda. *Surgery* 2015; **157**: 983-991 [PMID: 25934080 DOI: 10.1016/j.surg.2015.01.026]
46 **Grimes CE**, Law RS, Borgstein ES, Mkandawire NC, Lavy CB. Systematic review of met and unmet need of surgical disease in rural sub-Saharan Africa. *World J Surg* 2012; **36**: 8-23 [PMID: 22057752 DOI: 10.1007/s00268-011-1330-1]
47 **Nanda K**, Lopez LM, Grimes DA, Peloggia A, Nanda G. Expectant care versus surgical treatment for miscarriage. *Cochrane Database Syst Rev* 2012; **(3)**: CD003518 [PMID: 22419288 DOI: 10.1002/14651858.CD003518.pub3]
48 **Meara JG**, Hagander L, Leather AJ. Surgery and global health: a Lancet Commission. *Lancet* 2014; **383**: 12-13 [PMID: 24332309 DOI: 10.1016/S0140-6736(13)62345-4]
49 **Dare AJ**, Grimes CE, Gillies R, Greenberg SL, Hagander L, Meara JG, Leather AJ. Global surgery: defining an emerging global health field. *Lancet* 2014; **384**: 2245-2247 [PMID: 24853601 DOI: 10.1016/S0140-6736(14)60237-3]
50 **Stuckler D**, King L, Robinson H, McKee M. WHO's budgetary allocations and burden of disease: a comparative analysis. *Lancet* 2008; **372**: 1563-1569 [PMID: 18984189 DOI: 10.1016/S0140-6736(08)61656-6]
51 **Bolkan HA**, Von Schreeb J, Samai MM, Bash-Taqi DA, Kamara TB, Salvesen Ø, Ystgaard B, Wibe A. Met and unmet needs for surgery in Sierra Leone: A comprehensive, retrospective, countrywide survey from all health care facilities performing operations in 2012. *Surgery* 2015; **157**: 992-1001 [PMID: 25934081 DOI: 10.1016/j.surg.2014.12.028]

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ORIGINAL ARTICLE

Prospective Study

Triple tube drainage for "difficult" gastroduodenal perforations: A prospective study

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Abstract

AIM

To prospectively study the outcome of difficult gastroduodenal perforations (GDPs) treated by triple tube drainage (TTD) in order to standardize the procedure.

METHODS

Patients presenting to a single surgical unit of a tertiary hospital with difficult GDPs (large, unfavourable local and systemic factors) were treated with TTD (gastrostomy, duodenostomy and feeding jejunostomy). Postoperative parameters were observed like time to return of bowel sounds, time to start enteral feeds, time to start oral feeds, daily output of all drains, time to clamping/removal of all drains, time for skin to heal, complications, hospital stay, and, mortality. Descriptive statistics were used.

RESULTS

Between December 2013 and April 2015, 20 patients undergoing TTD for GDP were included, with mean age of 44.6 ± 19.8 years and male:female ratio of 17:3. Mean pre-operative APACHE Ⅱ scores were 10.85 ± 3.55; most GDPs were prepyloric (9/20; 45%) or proximal duodenal (8/20; 40%) and mean size was 1.83 ± 0.59 cm (largest 2.5 cm). Median times of resumption of enteral feeding, removal of gastrostomy, removal of duodenostomy,

removal of feeding jejunostomy and oral feeding were 4 d (4-5 IQR), 13 (12-16.5 IQR), 16 (16.25-22.25 IQR), 18 (16.5-24 IQR) and 12 d (10.75-18.5 IQR) respectively. Median hospital stay was 22 d (19-26 IQR) while mortality was 4/20 (20%).

CONCLUSION

TTD for difficult GDP is feasible, easy in the emergency, and patients recover in two-three weeks. It obviates the need for technically demanding and riskier procedures.

Key words: Peptic ulcer; Perforation peritonitis; APACHE; Triple tube drainage; Duodenostomy

Core tip: Generalised peritonitis secondary to hollow viscous perforation is common in India, with poor outcomes in many patients. Gastroduodenal perforations (GDPs), commonly treated by pedicled omental patch repair, have high leak rates and consequent high mortality, especially with advancing age, large perforations, and other systemic insults. Described strategies for leakage like jejunal patches or grafts, or pyloric exclusion are actually fraught with more risk. To emphasize minimizing time and skill, the concept of damage control from trauma is extrapolated and triple tube drainage is proposed for sick and difficult GDP patients. This study is prospective and demonstrates the ease and utility of this procedure, in an attempt to standardize it.

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INTRODUCTION

Generalised peritonitis secondary to hollow viscous perforation continues to be one of the most common surgical emergencies in India. In fact, the most common cause of exploratory laparotomy in the emergency setting is intestinal perforation peritonitis[1,2]. In most Indian series, small bowel and gastroduodenal perforations are the predominant causes[1,3]. Gastroduodenal perforations (GDPs) in India occur in younger patients and have a worse outcome than in developed countries[1,3,4]. The most common and easily performed procedure for GDP is the pedicledomental patch repair[4,5].

The leak rates after patch repair are 8%-10% in Indian series, while the mortality rates are also high (10%-15%). Leakage leads to a significant increase in morbidity and mortality[1,5,6]. The factors reported to be associated with high leak rates and mortality in gastroduodenal perforations are advancing age, large perforation size (≥ 1.5 cm diameter), presence of malignancy or immunocompromised status, delay in treatment, pre-operative hypotension, and raised serum creatinine levels[4,7]. Up to 25% of GDPs are more than 1 cm in size; about 2%-3% are more than 2 cm. These are particularly predisposed to leakage[5,6]. In our hospital, almost 20% of patients of GDPs have two or more of these adverse factors.

Operative strategies to treat or prevent leakage have included jejunal serosal patch, jejunal or omental pedicle graft, pyloric exclusion with gastrojejunostomy, gastrectomyand vagotomy, and, novel techniques like myocutaneous flaps or gastric disconnection[5,6,8,9]. However, many authors now feel that adding more suture lines in these sick and septic patients is fraught with more risk and poorer results. These procedures need high degree of surgical expertise and may prolong operative time, and none of the above technique is immune to postoperative leak[6]. The emphasis should be on minimizing time and surgical skill.

The concept of damage control surgery for the treatment of complex pancreatico-duodenal injuries has led to the acceptance of diversion and decompression of all enteric secretions. This is mostly performed as "triple tube ostomy" or "triple tube drainage (TTD)". The components are tube gastrostomy, retrograde tube duodenostomy, and, feeding jejunostomy[10,11].

Duodenal decompression is also recommended for the protection of the duodenal stump after gastrectomy for malignancy[12]. Some authors have extrapolated the concept of damage control for GDPs, especially the large or "giant" subtypes and in re-operations after leakage. However, the reported experience of TTD for GDP is small, with only a few case series. There is only one study from India, despite the high prevalence of the condition here. The proponents of TTD feel it to be a significantly underutilized procedure[6,12-14].

This prospective observational study was performed as a pilot study in patients with difficult GDPs treated by triple tube drainage, to study outcomes and standardize this procedure.

MATERIALS AND METHODS

This prospective observational pilot study was conducted in the department of surgery of a teaching tertiary hospital in north India, from December 2013 to April 2015, after getting clearance from the institutional ethics committee. Patients undergoing triple tube drainage for difficult duodenal perforation were included in the study. Difficult gastroduodenal perforations, for the purpose of our study, were defined as cases with two or more of the following features: Perforation size ≥ 1.5 cm, late presentation (≥ 3 d), unfavorable systemic factors (APACHE Ⅱ score ≥ 10), unfavorable local factors (copious pus, friable bowel, indurated or friable margins), and, re-operated patients (leakage after omental patch repair).

The aim of the study was to observe the postoperative

Table 1 Mean/median hematological/laboratory parameters (n = 20)

Parameter	Mean/median ± SD	IQR (1st to 3rd)
Haemoglobin (g/dL)	11.76 ± 2.59	
Total leukocyte counts (/mm^3)	12550	4675 - 19425
Platelet (× 10^5/mm^3)	1.80 ± 1.05	
Blood urea (mg/dL)	47.15	39.75- 67.5
Serum creatinine (mg/dL)	1.49 ± 0.68	
Serum sodium (meq/L)	135.7 ± 7.70	
Serum potassium (meq/L)	4.33 ± 0.90	
pO_2 (mmHg)	93.8 ± 33.20	
pH	7.37 ± 0.07	

IQR: Inter quartile range.

course and outcome of patients undergoing triple tube drainage for difficult gastroduodenal perforations. The primary outcome variables were: Time to oral feeding, time to removal of drains, hospital stay, complications (leakage, surgical site infections, and respiratory complications), and, mortality. As a secondary objective, this was proposed as a pilot study to compare two techniques of duodenal decompression, namely T-tube duodenostomy and retrograde duodenostomy in terms of hospital stay and leak rate.

Flow of study

After a provisional diagnosis of gastroduodenal perforation peritonitis in the emergency room, the patients were admitted for investigations and treatment. Informed written consent was obtained from the patients. The relevant biochemical, haematological and radiological tests were performed; the APACHE Ⅱ score was recorded. After optimization, exploratory laparotomy was performed. Copious lavage with normal saline was followed by identification of perforation site, and assessment of suitability for patch repair. In patients who fulfilled the inclusion criteria for difficult gastroduodenal perforations, the gastroduodenal perforation was first repaired using the standard omental patch technique. This was followed by TTD, consisting of: (1) Gastric decompression using 12-14 Fr tube brought out as gastrostomy; (2) duodenal decompression by retrograde duodenostomy (RD) using 12-14 Fr tube brought out through the jejunum, 10 cm from duodeno-jejunal flexure; and (3) feeding jejunostomy (FJ) using 10-12 Fr tube introduced into jejunum 20 cm from duodeno-jejunal flexure.

All tubes were fixed internally to parietal peritoneum by double purse-string absorbable polygalactin (Vicryl) 2-0 sutures, and fixed externally using purse-string suture with silk No.1. Polydiaxanone sutures would offer less friction, but are more expensive. The feeding jejunostomy and gastrostomy tubes were pulled up till the parietal wall and bowel sutured to peritoneum to ensure a controlled fistula. A sub-hepatic drain (28-32 Fr) was placed near the duodenostomy tube to act as a sump drain.

The abdomen was closed using interrupted far-near technique with polypropylene No. 1 suture. Skin was sutured loosely with packs soaked in antiseptic solution.

Table 2 Pre-operative physiological profile

Parameters	Mean ± SD
Temperature (℃)	37.46 ± 0.87
Mean arterial pressure (mmHg)	78.40 ± 18.60
Pulse rate (beats/minute)	116.7 ± 20.63
Respiratory rate (/minute)	22.3 ± 2.77
Pre-op APACHE-II score	10.85 ± 3.55

Postoperative assessment

Patients were assessed on daily basis in the postoperative period using the following outcome parameters: time to return of bowel sounds, time to start enteral feeds, time to start oral feeds, daily output of all drains, time to clamping/removal of all drains, time for skin to heal, complications, hospital stay, and, mortality. All outcome parameters were analysed using descriptive statistics with SPSS software.

RESULTS

Between December 2013 and April 2015, 20 patients undergoing TTD for difficult gastroduodenal perforation were included in the study. Mean age of the patients was 44.6 ± 19.8 years (range: 10-73 years) with a male: female ratio of 17:3. Table 1 shows the mean/median hematological and laboratory parameters for the 20 patients.

Five patients (25%) were anaemic (Hb < 10 g/dL) at presentation, while five (25%) had total leukocyte counts within the normal range (4000/mm^3-11000/mm^3). Most had leukocytosis, while 4 (20%) had leucopenia. The slightly deranged mean renal functions reflect the state of prerenal/renal azotemia secondary to sepsis. Table 2 reflects the common physiological parameters and mean APACHE-II scores.

Intra-operative findings

Peritoneal contamination with more than 1.4 L of purulent fluid was present in all the cases. The perforation was prepyloric in 9 patients (45%), in the first part of duodenum (D1) in 8 (40%), present in the body of stomach in 2 (10%), and, in the duodenum distal to D1 in 1 (5%). Friable irreparable edges were noted in 11 (55%) perforations (excluding the 2 cases where the patients were re-explored after leak). The mean diameter of the perforations in our cases was 1.83 ± 0.59 cm (largest 2.5 cm).

Seven patients (35%) with perforation size of 0.5 cm were included, due to fulfillment of other inclusion criteria. All patients underwent TTD with the retrograde duodenostomy technique, as none were found suitable for T-tube duodenostomy. The reasons were: friable and edematous duodenal wall (8), and, dense adhesions around lateral duodenal wall (13).

Table 3 Postoperative course (n = 20)

Observations	Postoperative days (mean/median)	Standard deviation OR IQR (1st-3rd)
Time to return bowel sounds	3.53	± 0.91
Time to start feeding *via* FJ	4	4-5
Time to start oral feed	12	10.75-18.5
Time of clamping of Gastrostomy	9.87	± 3.75
Time of clamping of RD	13	± 4.18
Time of removal of Gastrostomy	13	12-16.5
Time of removal of RD	16	16.25-22.25
Time of removal of FJ	18	16.5-24
Total hospital Stay	22	19-26
Wound healing time	15.75	± 1.91

IQR: Inter quartile range; FJ: Feeding jejunostomy; RD: Retrograde duodenostomy.

Table 4 Postoperative outcomes/complications n (%)

Outcomes/complications	n = 20
Surgical site infection	9 (45)
Respiratory complications	4 (20)
Peritubal leakage	4 (20)
Peritubal excoriation	2 (10)
Burst abdomen	5 (25)
Bed sore	2 (10)
Postoperative leak	1 (5)
Mortality	4 (20)

Postoperative course

All patients were observed till discharge or death, in terms of parameters listed in Table 3.

The gastrostomy tube was accidentally pulled out in one patient, while the retrograde duodenostomy came out in two patients. These patients were excluded for the determination of time of removal of tubes.

The total hospital stay ranged from 17 to 139 d. Out of 20 patients included in the study, four (20%) died in the postoperative period. One patient underwent Whipple's procedure on postoperative day (POD) 29 for duodenal neuroendocrine tumor reported on histopathological examination of the perforation edge. Table 4 lists the various complications in the postoperative period.

DISCUSSION

Despite the proven advantages of TTD in pancreatico-duodenal trauma, it is an underused strategy for peptic perforations. This is despite the high morbidity (> 30% mortality; up to 50% leak rates) of certain types of peptic perforations. Less than 5 case series (largest about 40 patients) have been published on triple tube drainage for gastroduodenal perforations; most published data is retrospective. There is no standardization regarding postoperative management[6,11-14].

Though classical pedicled omental patch repair remains gold standard for the gastro-duodenal perforations[5,6], patients with difficult gastro-duodenal perforations are associated with poor outcome in terms of postoperative complications, postoperative leak, morbidity and mortality. Most authors have labeled large (> 1.5-2.5 cm) GDPs as difficult; however, we have included poor physiological performance also as "difficult" due to the known propensity for leak and mortality (vide infra). In our study, we have prospectively observed 20 cases of difficult gastroduodenal perforation undergoing triple tube drainage (Cellan-Jones omental patch repair with gastrostomy, retrograde duodenostomy and feeding jejunostomy) during December 2013-April 2015. Lal *et al*[6] compared 20 cases of controlled tube duodenostomy (primary repair of perforation with nasogastric tube or gastrostomy, retrograde duodenostomy and feeding jejunostomy) with 20 cases of classical omental patch repair over a period of 10 years. Fujikuni *et al*[13] studied 3 patients over 18 mo (between November 2009 and March 2011) undergoing triple-tube-ostomy for iatrogenic duodenal perforations. The higher number of patients in the present study could possibly be due to increased occurrence of difficult duodenal perforations in the study group or due to different inclusion criteria, which were not limited only to the size of perforation.

The higher mean age of patients in the present study is consistent with results of Svanes *et al*[15] who have shown that median age of the patients has increased from 38 years in 1935-44 to 60 years in 1985-90 for men and 55 to 69 years for women (Table 5). The authors have also observed that the relative incidence of duodenal perforation as has decreased, while pyloric and prepyloric perforations have increased from 1935-1990 in 1483 patients[15]. Male predominance in the cases is also consistent with available literature, which can be attributed to the higher incidence of smoking in males.

There is no clear-cut definition of giant gastroduodenal perforation in literature; it has varied from 1.5 to 3 cm[5,6,16]. Most authors would accept that a perforation of > 2 cm is fraught with more risk of leakage and mortality, and needs more specific intervention that just primary closure. Many of our patients are referred from far-off hospitals and present late; we have added physiological scoring (APACHE-Ⅱ) along with perforation size to improve the accuracy of the risk assessment. This has been shown to be consistent for prediction of outcome in GDPs[17,18].

In our view, the most crucial part of the procedure is the adequate decompression of the duodenal C-loop, as it is retroperitoneal in position and cannot be brought out as a stoma. The duodenum is also an unfriendly organ in terms of repair, as it lacks a proper serosal wall. Hence, in our mind, tube decompression of right side of the duodenal segment seemed like the most attractive option, as demonstrated by a few authors[11-14]. A T-tube, as used by Isik *et al*[12] seems ideal. Unfortunately, in our patients, extensive inflammation in the right upper quadrant precluded the use of this technique, and we used the retrograde duodenostomy inserted more

Table 5 Comparison between age, gender, and intra-operative findings

Study	Most common age group (yr)	Gender distribution (M:F)	Size of perforation	Site of perforation
Present study	46-70	5.6:1	1.83 ± 0.59	Prepyloric 45%, Duodenal 40%
Lal *et al*[6]	30-50	4:1	60% 2 to 3 cm; 40% > 3 cm	
Jani *et al*[16]	21-50	7.3:1	> 2 cm	
Menekse *et al*[17]	39-62	6.1:1	13% with > 1 cm	
Berleff *et al*[19]	40-50	3.7:1		
Chaudhary *et al*[20]	18-40	4.3:1	> 1 cm in 7.29%	Duodenal 69.7%, Gastric 30.2%

distally. The latter technique is limited by the maximum calibre possible though such a circuitous route, and is more prone to blockage and failure. We actively endeavoured to keep it patent with frequent flushes, and would prefer to perform T-tube decompression when possible.

Postoperative course

It is evident that a reliable inpatient protocol should be in place to manage these multiple tubes without complications. Unfortunately, due to the scant research on the subject, no clear guidelines are available. The prospective study which most closely resembles our design was conducted by Lal *et al*[6] at a nearby center. The postoperative course in the two studies has been compared. In present study, mean time of return of bowel sounds was 3.53 ± 0.91 d. Lal *et al*[6] observed that bowel sounds returned in 72 h, after which enteral feed could be attempted through the jejunostomy tube. It is consistent with other emergency procedures that small bowel peristalsis returns in 48-72 h. We clamped the gastrostomy and retrograde duodenostomy tubes at was 9.87 ± 3.75 d and 13 ± 4.18 d respectively, while it was 7 d and 9-10 d respectively in the Lal study. These tubes are safely removed once the patient resumes a normal oral diet 3-4 d later. The removal of tubes may vary by 24-72 h, at the discretion of the treating physician.

It would be needless to emphasize the importance of fluid and electrolyte balance during the recovery period. Our patients are thin-built and nutritionally poor; the high output from controlled fistulae can be the "tipping point" towards a poorer outcome. It is also imperative to ensure the patency of the tubes too, as any undrained collections could cause crippling sepsis. Since the entire assembly works as a proximal diversion of gastric, duodenal and pancreatic secretions (at least 2-2.5 L/d), patency is important (vide supra).

Damage control procedures are performed in the most critical patients. In the present study, median hospital stay was 22 d (17-139 d) while the mortality was 20%. The incidence of postoperative complications was also higher than similar series[6,15-17,19,20]. Poorer outcomes can be explained by the fact that all the patients included in our study had "difficult" gastroduodenal perforations in the truest sense, with higher predicted deaths.

We have thus shown in a prospective group of patients that TTD is feasible, easy to perform in the emergency setting, and is followed by two-three weeks of easy convalescence. The patients usually accept oral diet after the second week.

Limitations

Some limitations are evident in our study. A larger sample size over a longer duration would allow better recommendations to be put forward. We had hypothesized before the start of our study that TTD would be useful in both GDPs and also some very proximal jejunal perforations with tuberculous etiology. The latter are commonly seen in our scenario; and are difficult to treat due to high leak rate and an unmanageable short bowel if exteriorized. However, in the present study, we did not include such patients in order to enable comparison of "like with like". Also, a well-described technique of TTD, namely, T-tube decompression of the lateral wall of the duodenum, could not be evaluated as all our patients demonstrated intense fibrosis in that area. With a larger study duration and more number of patient, the next stimulus for research would be a more analytical study comparing the two types of TTD.

COMMENTS

Background

Generalised peritonitis secondary to hollow viscous perforation continues to be one of the most common surgical emergencies in India. In fact, the most common cause of exploratory laparotomy in the emergency setting is intestinal perforation peritonitis.

Research frontiers

Operative strategies to treat or prevent leakage have included jejunal serosal patch, jejunal or omental pedicle graft, pyloric exclusion with gastrojejunostomy, gastrectomyand vagotomy, and novel techniques like myocutaneous flaps or gastric disconnection.

Innovations and breakthroughs

In authors' mind, tube decompression of right side of the duodenal segment seemed like the most attractive option, as demonstrated by a few authors. A T-tube, as used by Isik *et al* seems ideal. Unfortunately, in the patients, extensive inflammation in the right upper quadrant precluded the use of this technique, and the authors used the retrograde duodenostomy inserted more distally. The latter technique is limited by the maximum calibre possible though such a circuitous route, and is more prone to blockage and failure. The authors actively endeavoured to keep it patent with frequent flushes, and would prefer to perform T-tube decompression when possible.

Peer-review

This is a very comprehensive review of the literature on NETs, also being very well written.

REFERENCES

1 **Agarwal N**, Saha S, Srivastava A, Chumber S, Dhar A, Garg S. Peritonitis: 10 years' experience in a single surgical unit. *Trop Gastroenterol* 2007; **28**: 117-120 [PMID: 18384000]

2 **Dian A,** Akhtar T, Jaskani S, Hanif M, Hassan H. An audit of patients undergoing midline emergency laparotomy. *JRMC* 2013; **17**: 52-53

3 **Jhobta RS**, Attri AK, Kaushik R, Sharma R, Jhobta A. Spectrum of perforation peritonitis in India--review of 504 consecutive cases. *World J Emerg Surg* 2006; **1**: 26 [PMID: 16953884 DOI: 10.1186/1749-7922-1-26]

4 **Gupta S**, Kaushik R. Peritonitis - the Eastern experience. *World J Emerg Surg* 2006; **1**: 13 [PMID: 16759427 DOI: 10.1186/1749-7922-1-13]

5 **Gupta S**, Kaushik R, Sharma R, Attri A. The management of large perforations of duodenal ulcers. *BMC Surg* 2005; **5**: 15 [PMID: 15978134 DOI: 10.1186/1471-2482-5-15]

6 **Lal P**, Vindal A, Hadke NS. Controlled tube duodenostomy in the management of giant duodenal ulcer perforation: a new technique for a surgically challenging condition. *Am J Surg* 2009; **198**: 319-323 [PMID: 19306982 DOI: 10.1016/j.amjsurg.2008.09.028]

7 **Møller MH**, Engebjerg MC, Adamsen S, Bendix J, Thomsen RW. The Peptic Ulcer Perforation (PULP) score: a predictor of mortality following peptic ulcer perforation. A cohort study. *Acta Anaesthesiol Scand* 2012; **56**: 655-662 [PMID: 22191386 DOI: 10.1111/j.1399-6576.2011.02609.x]

8 **Cranford CA**, Olson R, Bradley EL. Gastric disconnection in the management of perforated giant duodenal ulcer. *Am J Surg* 1988; **155**: 439-442 [PMID: 3344908 DOI: 10.1016/S0002-9610(88)80108-9]

9 **Chaudhary A**, Bose SM, Gupta NM, Wig JD, Khanna SK. Giant perforations of duodenal ulcer. *Indian J Gastroenterol* 1991; **10**: 14-15 [PMID: 2004794]

10 **Bhattacharjee HK**, Misra MC, Kumar S, Bansal VK. Duodenal perforation following blunt abdominal trauma. *J Emerg Trauma Shock* 2011; **4**: 514-517 [PMID: 22090749 DOI: 10.4103/0974-2700.86650]

11 **Crippa S**, Falconi M, Bettini R, Barugola G, Germenia S, Salvia R, Pederzoli P. Isolated blunt duodenal trauma: delayed diagnosis and favorable outcome with "quadruple tube" decompression. *JOP* 2007; **8**: 617-620 [PMID: 17873470]

12 **Isik B**, Yilmaz S, Kirimlioglu V, Sogutlu G, Yilmaz M, Katz D. A life-saving but inadequately discussed procedure: tube duodenostomy. Known and unknown aspects. *World J Surg* 2007; **31**: 1616-1624 [PMID: 17566821 DOI: 10.1007/s00268-007-9114-3]

13 **Fujikuni N**, Tanabe K, Yamamoto H, Suzuki T, Tokumoto N, Ohdan H. Triple-tube-ostomy: a novel technique for the surgical treatment of iatrogenic duodenal perforation. *Case Rep Gastroenterol* 2011; **5**: 672-679 [PMID: 22235196 DOI: 10.1159/000335742]

14 **Kutlu OC**, Garcia S, Dissanaike S. The successful use of simple tube duodenostomy in large duodenal perforations from varied etiologies. *Int J Surg Case Rep* 2013; **4**: 279-282 [PMID: 23357008 DOI: 10.1016/j.ijscr.2012.11.025]

15 **Svanes C**, Salvesen H, Stangeland L, Svanes K, Søreide O. Perforated peptic ulcer over 56 years. Time trends in patients and disease characteristics. *Gut* 1993; **34**: 1666-1671 [PMID: 8282252 DOI: 10.1136/gut.34.12.1666]

16 **Jani K**, Saxena AK, Vaghasia R. Omental plugging for large-sized duodenal peptic perforations: A prospective randomized study of 100 patients. *South Med J* 2006; **99**: 467-471 [PMID: 16711308 DOI: 10.1097/01.smj.0000203814.87306.cd]

17 **Menekse E**, Kocer B, Topcu R, Olmez A, Tez M, Kayaalp C. A practical scoring system to predict mortality in patients with perforated peptic ulcer. *World J Emerg Surg* 2015; **10**: 7 [PMID: 25722739 DOI: 10.1186/s13017-015-0008-7]

18 **Tassetti V**, Valvano L, Navez B, Mutter D, Scohy JJ, Evrard S, Marescaux J. [Perforated peptic ulcer and laparoscopic treatment]. *Minerva Chir* 1998; **53**: 777-780 [PMID: 9882965]

19 **Bertleff MJ**, Lange JF. Perforated peptic ulcer disease: a review of history and treatment. *Dig Surg* 2010; **27**: 161-169 [PMID: 20571260 DOI: 10.1159/000264653]

20 **Chaudhary V,** Mathur R. Clinical presentations, factors related with complications and mortality in peptic ulcer perforation in young adults: A tertiary level hospital study. *Int J Med Sci and Edu* 2014; **1:** 145-149

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Uncommon presentation of a common disease - Bouveret's syndrome: A case report and systematic literature review

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Abstract

AIM

To investigate and summarise the current evidence surrounding management of Bouveret's syndrome (BS).

METHODS

A MEDLINE search was performed for the BS. The search was conducted independently by two clinicians (Yahya AL-Habbal and Matthew Ng) in April 2016. A case of BS is also described.

RESULTS

A total of 315 articles, published from 1967 to 2016, were found. For a clinically meaningful clinical review, articles published before 01/01/1990 and were excluded, leaving 235 unique articles to review. Twenty-seven articles were not available (neither by direct communication nor through inter-library transfer). These were also excluded. The final number of articles reviewed was 208. There were 161 case reports, 13 reviews, 23 images (radiological and clinical images), and 11 letters to editor. Female to male ratio was 1.82. Mean age was 74 years. Treatment modalities included laparotomy in the majority of cases, laparoscopic surgery, endoscopic surgery and shockwave lithotripsy.

CONCLUSION

There is limited evidence in the literature about the appropriate approach. We suggest an algorithm for management of BS.

Key words: Bouveret's syndrome; Biliary anomalies; Endoscopy; Digestive system; Duodenal obstruction diagnosis; Gallstones surgery; Gallstones complications; Duodenal obstruction etiology; Duodenal obstruction surgery; Intestinal fistula diagnosis; Humans

Core tip: Bouveret's syndrome is gastric outlet obstru-

ction secondary to an impacted gallstone in the duodenum or stomach. There is limited evidence surrounding management of this rare syndrome. Here we systematically review the published cases and recommend a treatment algorithm to clinicians facing this syndrome in future.

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INTRODUCTION

Bouveret's syndrome (BS) was first described by Beaussier in 1770, but reported in the literature first by Leon Bouveret in 1896, where he had two cases[1]. Leon Bouveret was actually an internist but supported surgery[2]. BS is gastric outlet obstruction secondary to a gallstone impacted in the duodenum or stomach.

We report a 39-year-old lady who presented with upper abdominal pain and vomiting. She was diagnosed with BS after scans and endoscopy. Her gallstone was successfully removed by gastroscopy. Though her symptoms continued, a literature review was sought to manage her according to the recent evidence. Almost all the case reports and limited case series were in favour of conservative management. She was managed expectantly, but represented with ongoing pain.

The patient underwent laparoscopic cholecystectomy. The fistula was dissected and closed laparoscopically. On intra-operative cholangiogram, she had more bile duct stones which were treated by laparoscopic bile duct exploration and stone extraction. She did well in the post-operative course.

MATERIALS AND METHODS

MEDLINE and PubMed searches were performed for the terms BS. The search was conducted in April 2016. Three hundred and fifteen articles, published between 1967 and 2016, were identified. For a clinically meaningful clinical review, articles published before 01/01/1990 and were excluded, leaving 235 unique articles to review. Twenty-seven articles were not available (neither by direct communication nor through inter-library transfer). The final number of articles reviewed was 208 (Figure 1A).

Data from retrieved articles were independently reviewed by the two authors (Yahya AL-Habbal and Matthew Ng) and data was extracted using a standardised collection tool. Data was analysed with descriptive statistics. In contrast to classic meta-analyses, statistical analysis was performed where the outcome was calculated as the percentages of an event (without comparison) in pseudo-cohorts of observed patients.

RESULTS

Articles comprised 161 case reports[3-163], 13 reviews[164-176], 23 images reports (radiological and clinical images[177-198] and 11 letters to the editor[199-209], as illustrated in (Figure 1F).

Articles were written in multiple languages. English articles constituted the main bulk of the literature (176 articles, 77%). The rest were Spanish (20 articles, 9%), Italian (7 articles, 3%) French (5 articles, 2%), and other languages (13%). These other languages include: Bulgaria, South Korean, Japanese, German, Romanian, Turkish, Hungarian, Ukrainian, and Czech. Articles not in English were translated to English using dependable medical dictionaries (Figure 1D and E).

A 39 years old lady presenting to the emergency department with two-week history of epigastric and right upper quadrant pain. The pain was constant, dull, and radiating to the back, she had acidity and reflux symptoms, nausea and vomiting. There was no history of jaundice, or weight loss.

On examination she was mildly dehydrated. Pulse rate was 92 beats/min and temperature was 37.3°. She was tender in the epigastrium and right upper quadrant, with a negative Murphy's sign.

Initial blood tests showed high white cells count 13.9 $\times$ 10^9. Her liver functions were deranged. Bilirubin was 14 IU/L, ALP 285 IU/L, ALT 335 IU/L, GGT 445 IU/L, and ALT 0f 205 IU/L. Her lipase was mildly raised at 455 IU/L (normal range < 45 IU/L).

With this mixed picture the initial differential diagnosis was cholangitis or pancreatitis, or Mirrizzi syndrome.

The patient was referred for an ultrasound (US) scan. The images were degraded by pneumobilia and, while difficult to characterize, demonstrated a contracted gallbladder without stones. Common bile duct was 10 mm with mild intrahepatic biliary tree dilatation (Figure 2). CT scan obtained to further characterize the gallbladder demonstrated large-volume pneumobilia, a fistula between the distal stomach and the collapsed gallbladder, and oral contrast in the region of the gallbladder neck.

There was an opacity in the stomach that was interpreted as hypo-dense gallstone in the stomach (Figures 3 and 4). At this point the diagnosis of cholecysto-gastric fistula secondary to gallstone disease with subsequent intermittent gastric outlet was made.

Upper GI endoscopy confirmed the presence of gallstone in the stomach and fistula orifice (Figure 5). The stone was successfully retrieved by snare (Figure 6). Patient's symptoms improved significantly and ultimately discharged home after 2 d. Her liver functions normalized before discharge. Given that there was no evidence of any further gallstones, and after reviewing the current evidence and practice, we decided to manage her expectantly.

Upon follow up, it was found that the patient was

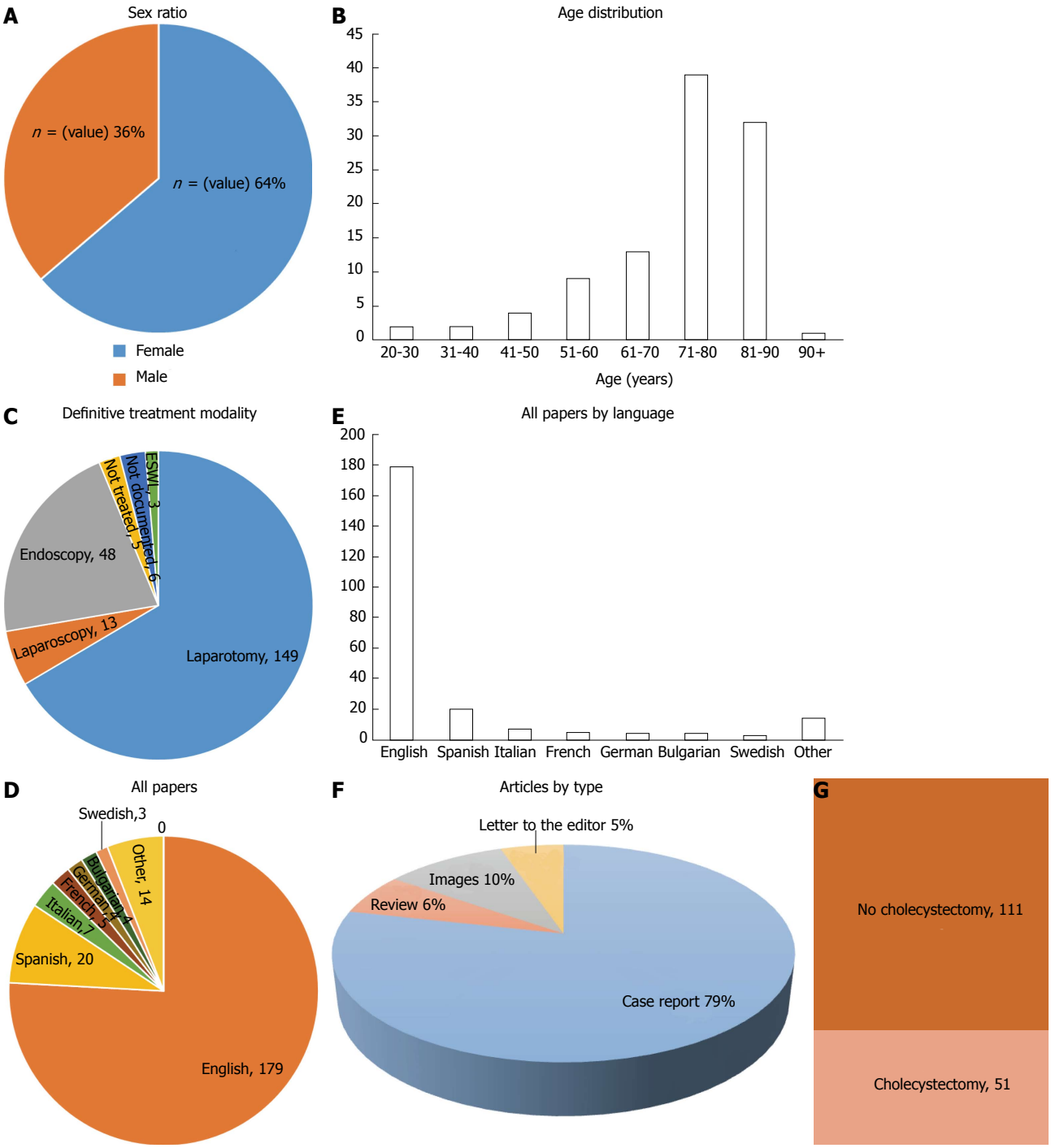

Figure 1 MEDLINE and PubMed searches were performed for the terms Bouveret's syndrome. A: Sixty-four percent of the identified cases in the literature were female; B: Bouveret's syndrome is more common in elderly patients, with the majority of cases occurring above 71 years of age; C: While some cases were successfully treated endoscopically, the majority of cases require open surgical management; D and E: Articles not in English were translated to English using dependable medical dictionaries; F: Results of the literatures; G: In patients receiving surgical stone retrieval, the majority did not receive a concurrent or delayed cholecystectomy.

still complaining of abdominal pain. An MRCP done at this point that showed more gallstones have fallen into the bile duct.

She underwent a laparoscopic cholecystectomy. The operation revealed adhesions between the gallbladder and distal stomach. No real fistular tract was seen, but dense adhesions were ligated by an Endoloop. Intra-operative cholangiogram confirmed bile duct stones. These were difficult to be retrieved by trans-cystic exploration. A laparoscopic bile duct exploration was performed. Several stones were successfully retrieved. Bile duct repaired primarily by 4/0 monofilament non-absorbable suture material. The postoperatrive course has been uneventful.

DISCUSSION

BS is a rare cause of gastric outlet obstruction caused

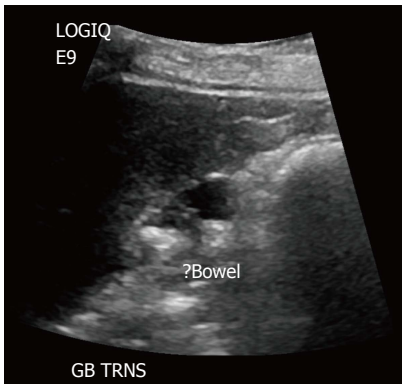

Figure 2 Common bile duct was 10 mm with mild intrahepatic biliary tree dilatation.

Figure 3 Coronal section of computed tomography scan.

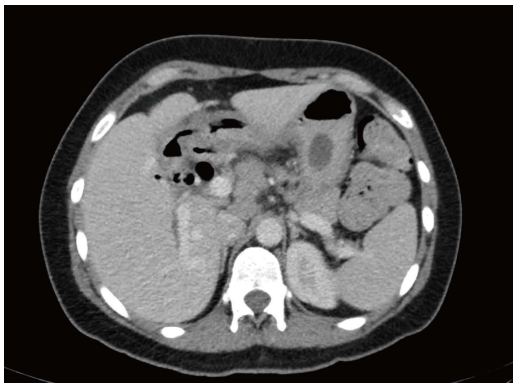

Figure 4 Cross section of computed tomography scan showing gallstone in the stomach and pneumobilia. The gallbladder is contracted and gas-filled.

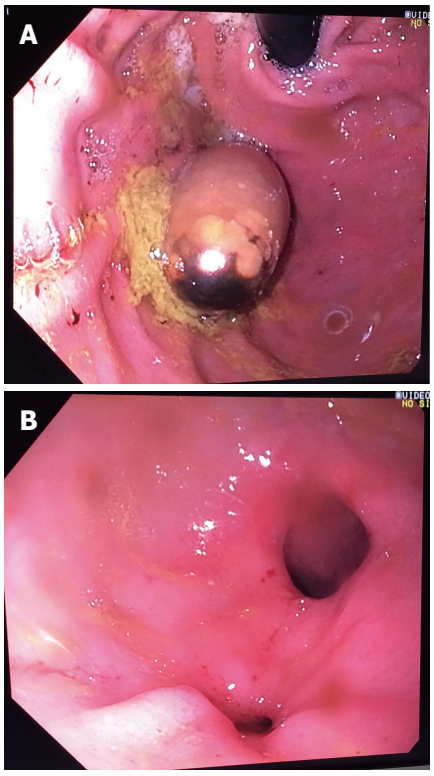

Figure 5 Upper gastrointestinal endoscopy confirmed the presence of gallstone in the stomach (A) and fistula orifice (B).

Figure 6 The stone was successfully retrieved by snare.

by gallstones. The stone(s) tend to migrate secondary to fistulation. The fistula can be cholecystogastric (less common) or more commonly, cholecystoduodenal. BS constitutes 1%-3% of cases of gall stone ileus which in turn complicates only 0.3%-4% cases of cholelithisasis[91,107]. BS can be associated with high mortality (up to 12%) mainly due to the frailty of patients[136]. The pathophysiology is usually caused by prolonged pressure, ischemia, and then fistulation and stone migration. The stone(s) then obstruct the gastric outlet or duodenum. A collection of small stones can produce the same picture[210]. Malignancy can also produce fistulation and stone migration. This has

been reported by Sharma *et al*[35] where the patient underwent laparotomy and stone extraction with gastro-jejunostomy to relieve the obstruction, while Shinoda *et al*[34] offered a curative cancer resection and fistula repair in a similar case of fistulating cancer.

In one interesting variant of BS, a patient presented with upper abdominal pain 10 years after Roux-en-Y Billroth Ⅱ resection for benign disease. A stone retrieved from the duodenum after laparotomy[64]. There have been a few cases in the literature where BS presented with pancreatitis[33,122]. The stone(s) can be lodged tightly in the duodenum causing necrosis and intra or extra-peritoneal perforation[109].

BS has been reported many times as a single case report. A few reports included more than one case[99,130,153,160,163,173,188]. These patients usually present with abdominal pain and vomiting as universally reported. There was one case in which the vomiting was severe to the point of causing Boerhaaves oesophageal rupture[63]. The diagnosis is usually late given the uncommon and vague nature of its symptoms. In about one-third of cases the diagnosis can be made by a plain abdominal film that demonstrates the classical Rigler's triad of a dilated stomach, pneumobilia, and a radio-opaque shadow in the region of the duodenum representing the ectopic gallstone[47,209-213]. There have been some reported cases of migrating stone into the mediastinum after relieving an obstructed duodenum of BS *via* endoscope[71]. Ultrasound can be helpful as indicated in some papers[184], but the study can be greatly degraded by the presence of gas in the biliary tree. Historical data shows that the diagnosis has only been made preoperatively in 50% of cases[80]. Due to the nearby inflammation, the gallbladder can be FDG/PET positive[178].

Spontaneous resolution can occur when the impacted stone falls back away from the pyloric orifice[16], but this can be associated with further bowel obstruction distal to the stomach and duodenum (gall stone ileus)[114,141]. On the other hand, the condition can be fatal due to the profound metabolic derangement[13], and later by sepsis and multi-organ failure[62].

In our review, the sex (female to male) ratio was (1.82), female being 64% and male being 36% (Figure 1A). Age distribution of these cases showed majority of cases being elderly patients above 60 years old with the average age of (74 ± 13), and minority less than 30 years old (Figure 1B).

There are multiple available treatment modalities. This includes laparotomy, laparoscopy, endoscopy and ESWL (Figure 1C). Majority of cases were treated with laparotomy and stone extraction through either an enterotomy or gastrotomy (146 cases, 71%). Successful laparoscopic treatment was also possible (13 cases, 6%). Some of patients had a radical procedure where the procedure was combined with cholecystectomy (51 cases, 25%), as illustrated in (Figure 1G). The advantages of doing cholecystectomy is not only removing the source of stones, but eliminating the theoretical carcinogenic risk of gastro-intestinal juices contacting the biliary tree[212]. Cholecystectomy has been described as a single procedure combined with fistula dissection and closure, or as a separate procedure done later on elective or semi-urgent basis (like our case).

With the recent advents in endoscopic technology, endoscopic treatment was tried in 160 cases (77%) and was successful in removing the stone in 46 cases of patients (29%). This was either through direct visualization and retrieval of the stone or combined with a lithotripsy method (laser, mechanical, shockwave). This is more than the reported 10% success rate in earlier narrative review of BS[168]. In recent years, therapeutic endoscopy has been more frequently and successfully used to extract the obstructing stone(s). This might be attributed to improved lithotripsy, better optical instruments and improved graspers and nets to extract gallstones.

Extracorporeal shock-wave lithotripsy (ESWL) has been described by Gemmel *et al*[115], Chick *et al*[181], Dumonceau *et al*[130] and Tanwar *et al*[23] which was successful combined with either endoscopy alone or laparotomy to remove stone fragments from distal bowels. Intracorporeal lithotripsy using water jet[6], or other mechanical methods[139], have been described.

It is estimated that up to 90% of patients will need some form of surgical intervention[173]. These interventions can vary but mainly depend on the patient's age and co-morbidities. The vast majority of these stones pass spontaneously without producing obstruction. Stones that obstruct the digestive tract are usually greater than 2-2.5 cm in diameter[175]. Cholecystostomy has been tried to treat associated cholecystitis but this has not been associated with a great deal of success[145]. Sometimes, to alleviate the obstruction and allow patients to eat and drink, an interim bypass procedure has been described[53]. Subtotal cholecystectomy and drain tube insertion is another option which is safe and successful[8,178].

A minority of cases in the literature were not treated due to either severely compromised patients or spontaneous resolution (5 cases, 2%). In addition, there were some reports where the treatment modality was not mentioned (6 cases, 3%).

After reviewing the (review) articles of BS, it was noted the majority of these reviews are more or less narrative reviews and not systematic, except three reviews[165,166,170]. A summary of these articles can be found in Table 1. There were issues with the previously done reviews being either limited to English language (thus excluding almost 15% of the literature) or incomplete not including all the papers. The limitation of our paper is the fact that we excluded 27 articles as we could not get them through multiple available channels. But almost all of these articles were published prior to 1995 and are case reports including single cases, or images for doctors.

Finally, the term pseudo BS has been used in the literature once to describe the condition of gall stones

Table 1 Review articles

Ref.	Year	No. articles	No. cases	Age (mean ± SD)	%Female	Endoscopy performed	Nonsurgical treatment success	Enterolithotomy	Cholecystectomy	Mortality/ major complications
Cappell *et al*[165]	2006	111	128	74.1 ± 11.1	65.10%	63%	18.00%	98/128 = 76.6%	40/98 = 40.8%	16/98 = 16.3%
Lowe *et al*[170]	2005	39	44	73 ± 13.5	68%	51%	13.60%	40/44 = 90.9%	36%	19%-24%
Frattaroli *et al*[166]	1997	79	79	68.6	65%	60%	14%	93%	Not reported	12%-33%

and gastric outlet obstruction due to external duodenal or pyloric compression (akin to Mirizzi's type I)[213].

In conclusion, with the current paucity of high level of scientific evidence about BS, the management remains highly arbitrary. Here we present a young patient with BS who failed conservative measures, and suggest a treatment algorithm for these patients. The management of this uncommon condition should be tailored to the patient's clinical presentation and morbidities. Perhaps a more radical treatment (which might include cholecystectomy) should be offered to young patients and patients with ongoing symptoms. Whenever possible, endoscopic approach should be offered first after immediate resuscitation, with stone extraction and lithotripsy as two options. If that fails, surgical management with enterolithotomy or gastrolithotomy depended on stone position. We do not recommend immediate cholecystectomy or fistula dissection as this can be associated with significant morbidity and mortality. Delayed cholecystectomy and fistula repair should be offered electively to patients with persistent symptoms or patients younger than 50 years old.

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COMMENTS

Background

Bouveret's syndrome (BS) is a rare complication of gallstone disease, where a gallstone erodes into the duodenum and causes gastric outlet obstruction following impaction in the stomach or duodenum. The stone must be removed to restore normal function of the gastrointestinal tract. This may be done *via* laparotomy or laparoscopic stone removal, or more recently, using lithotripsy with or without endoscopic retrieval to dislodge the stone.

Research frontiers

The literature surrounding BS is sparse and consists mainly of case reports and series. Reviews of these cases have been few and far between, with the most recent dating back to 2006. In this time, endoscopy, endoscopic interventions, and laparoscopy have improved, potentially offering new options for managing these patients.

Innovations and breakthroughs

In this study the authors systematically reviewed the published cases of BS from 1990 to the present. While laparotomy and laparoscopy were performed in a significant number of cases, endoscopic treatment has become much more successful with the advent of improved lithotripsy, improved endoscopic retrieval devices, and improved visualisation. Extracorporeal shockwave lithotripsy has also been successfully used in multiple cases.

Applications

They recommend that patients presenting with BS should be initially managed with attempted endoscopic retrieval, with or without lithotripsy, followed by open or laparoscopic surgical retrieval *via* enterotomy or gastrotomy if unsuccessful. In younger, healthier patients, a delayed cholecystectomy may be performed, however in older or multiply comorbid patients, this may be omitted from the treatment algorithm.

Terminology

BS is gastric obstruction due to an impacted gallstone in the duodenum or gastric outlet. Lithotripsy is the act of breaking a stone into multiple smaller pieces. This may be effected with extracorporeal shock waves, using a mechanical lithotripter, or a laser device.

Peer-review

In this systematic review, the authors have presented a thorough and critical analysis of the published cases of BS, and recommended an appropriate treatment algorithm for future cases.

REFERENCES

1 **Melamed JL**, Parker ML. Cholecystogastric fistula; report of a case. *J Am Med Assoc* 1956; **160**: 463-464 [PMID: 13286079 DOI: 10.1001/jama.1956.02960410039009a]
2 **Wickbom G**. [The man behind the syndrome: Leon Bouveret. The internist who supported surgery]. *Lakartidningen* 1993; **90**: 162, 165 [PMID: 8429751]
3 **Zoricić I**, Vukusić D, Rasić Z, Trajbar T, Sever M, Lojo N, Crvenković D. [Bile stone ileus with cholecystoduodenal fistula--Bouveret's syndrome]. *Acta Med Croatica* 2011; **65**: 63-66 [PMID: 21568076]
4 **Zafar A**, Ingham G, Jameel JK. "Bouveret's syndrome" presenting with acute pancreatitis a very rare and challenging variant of gallstone ileus. *Int J Surg Case Rep* 2013; **4**: 528-530 [PMID: 23570683 DOI: 10.1016/j.ijscr.2013.01.017]
5 **Yu K**, Yang J, Zhen J, Zhou X. Bouveret's syndrome: a rare cause of gastric outlet obstruction. *Chin Med J* (Engl) 2014; **127**: 3377 [PMID: 25269898]
6 **Yokoyama T**, Ashizawa T, Hibi K, Okada R, Suzuki Y, Takagi M, Shinohara Y, Sugimoto K, Aoki T. [A case of gastric outlet obstruction by gallstone (Bouveret's syndrome) treated by EHL]. *Nihon Shokakibyo Gakkai Zasshi* 2005; **102**: 1293-1298 [PMID: 16262161]
7 **Yau KK**, Siu WT, Tsui KK. Migrating gallstone: from Bouveret's syndrome to distal small bowel obstruction. *J Laparoendosc Adv Surg Tech A* 2006; **16**: 256-260 [PMID: 16796435 DOI: 10.1089/lap.2006.16.256]
8 **Yang D**, Wang Z, Duan ZJ, Jin S. Laparoscopic treatment of an upper gastrointestinal obstruction due to Bouveret's syndrome. *World J Gastroenterol* 2013; **19**: 6943-6946 [PMID: 24187475 DOI: 10.3748/wjg.v19.i40.6943]
9 **Wong CS**, Crotty JM, Naqvi SA. Pneumobilia: a case report and literature review on its surgical approaches. *J Surg Tech Case Rep* 2013; **5**: 27-31 [PMID: 24470847 DOI: 10.4103/2006-8808.118616]
10 **Wonaga A**, Fritz V, D'Alessandro M, Waldbaum C. [Bouveret

syndrome: unusual cause of upper gastrointestinal bleeding]. *Acta Gastroenterol Latinoam* 2010; **40**: 159-161 [PMID: 20645566]
11 **Wittenburg H**, Mössner J, Caca K. Endoscopic treatment of duodenal obstruction due to a gallstone ("Bouveret's syndrome"). *Ann Hepatol* 2005; **4**: 132-134 [PMID: 16010248]
12 **Williams NE**, Gundara JS, Roser S, Samra JS. Disease spectrum and use of cholecystolithotomy in gallstone ileus transection. *Hepatobiliary Pancreat Dis Int* 2012; **11**: 553-557 [PMID: 23060405]
13 **Wight CO**, Seed M, Yeo WW, McCulloch TA. Gastric outflow obstruction caused by gall stones and leading to death by complex metabolic derangement. *J Clin Pathol* 1997; **50**: 963-965 [PMID: 9462252 DOI: 10.1136/jcp.50.11.963]
14 **Werner CR**, Graepler F, Glatzle J, Stüker D, Kratt T, Schmehl J, Bitzer M, Königsrainer A, Malek NP, Goetz M. Proximal duodenal obstruction--Bouveret's syndrome revisited. *Endoscopy* 2013; **45** Suppl 2 UCTN: E231-E232 [PMID: 23945924 DOI: 10.1055/s-0033-1344324]
15 **Warren DJ**, Peck RJ, Majeed AW. Bouveret's Syndrome: a Case Report. *J Radiol Case Rep* 2008; **2**: 14-17 [PMID: 22470599 DOI: 10.3941/jrcr.v2i4.60]
16 **Wagholikar GD**, Ibrarullah M. Bouveret's syndrome--an unusual cause of spontaneous resolution of gastric outlet obstruction. *Indian J Gastroenterol* 2004; **23**: 109-110 [PMID: 15250571]
17 **Vigneri S**, Scialabba A, Termini R, Fornaciari M, Ficano L, Pintacuda S. A temporary endoscopic solution that significantly improves the prognosis of Bouveret's syndrome. *Surg Endosc* 1991; **5**: 226-228 [PMID: 1805403 DOI: 10.1007/BF02653271]
18 **Venkatesh SK**, Thyagarajan MS, Gujral RB, Gupta A. Sonographic diagnosis of Bouveret's syndrome. *J Clin Ultrasound* 2003; **31**: 163-166 [PMID: 12594803 DOI: 10.1002/jcu.10149]
19 **Veloso N**, Silva JD, Pires S, Godinho R, Medeiros I, Gonçalves L, Viveiros C. Bouveret's syndrome. *Gastroenterol Hepatol* 2014; **37**: 523-524 [PMID: 25131318 DOI: 10.1016/j.gastrohep.2013.05.004]
20 **Van Dam J**, Steiger E, Sivak MV. Giant duodenal gallstone presenting as gastric outlet obstruction: Bouveret's syndrome. *J Clin Gastroenterol* 1992; **15**: 150-153 [PMID: 1401827 DOI: 10.1097/00004836-199209000-00014]
21 **Thomson WL**, Miranda S, Reddy A. An unusual presentation of cholecystoduodenal fistula: vomiting of gallstones. *BMJ Case Rep* 2012; **2012**: Epub ahead of print [PMID: 23166170 DOI: 10.1136/bcr-2012-007009]
22 **Thompson RJ**, Gidwani A, Caddy G, McKenna E, McCallion K. Endoscopically assisted minimally invasive surgery for gallstones. *Ir J Med Sci* 2009; **178**: 85-87 [PMID: 17973154 DOI: 10.1007/s11845-007-0096-9]
23 **Tanwar S**, Mawas A, Tutton M, O'Riordan D. Successful Endoscopic Management of Bouveret's Syndrome in a Patient with Cholecystoduodenocolic Fistulae. *Case Rep Gastroenterol* 2008; **2**: 346-350 [PMID: 21490867 DOI: 10.1159/000151581]
24 **Tan YM**, Yeo AW, Wong CY. Multiple giant duodenal gallstones causing gastric outlet obstruction: Bouveret's minefield revisited. *Hepatogastroenterology* 2003; **50**: 1975-1977 [PMID: 14696446]
25 **Stein PH**, Lee C, Sejpal DV. A Rock and a Hard Place: Successful Combined Endoscopic and Surgical Treatment of Bouveret's Syndrome. *Clin Gastroenterol Hepatol* 2015; **13**: A25-A26 [PMID: 26254202 DOI: 10.1016/j.cgh.2015.07.044]
26 **Solmaz Tuncer A**, Gürel S, Coşgun Z, Büber A, Cakmaz R, Hasdemir OA. A Rare Presentation of Xanthogranulomatous Cholecystitis as Bouveret's Syndrome. *Case Rep Radiol* 2012; **2012**: 402768 [PMID: 23346444 DOI: 10.1155/2012/402768]
27 **Smolilo D**, Bhandari M, Wilson TG, Brooke-Smith M, Watson DI. Bouveret's syndrome: gastric outlet obstruction caused by a gallstone. *ANZ J Surg* 2013; **83**: 996-997 [PMID: 24289055 DOI: 10.1111/ans.12227]
28 **Smith Z**, Totten J, Hughes A, Strote J. Delayed diagnosis of gastric outlet obstruction from bouveret syndrome in a young woman. *West J Emerg Med* 2015; **16**: 151-153 [PMID: 25671026 DOI: 10.5811/westjem.2014.10.23049]
29 **Singh AK**, Shirkhoda A, Lal N, Sagar P. Bouveret's syndrome: appearance on CT and upper gastrointestinal radiography before and after stone obturation. *AJR Am J Roentgenol* 2003; **181**: 828-830 [PMID: 12933489 DOI: 10.2214/ajr.181.3.1810828]
30 **Simůnek R**, Bohatá S, Kala Z. [Bouveret's syndrome--a rare case of proximal ileus of biliary etiology]. *Rozhl Chir* 2009; **88**: 119-122 [PMID: 19526942]
31 **Simpson J**, Lobo D. Gastrointestinal: Bouveret's syndrome. *J Gastroenterol Hepatol* 2014; **29**: 1339 [PMID: 25040616 DOI: 10.1111/jgh.12629]
32 **Simonek J**, Lischke R, Drábek J, Pafko P. [Bouveret's syndrome: biliary ileus manifested by acute upper gastrointestinal hemorrhage and impaired gastric emptying]. *Rozhl Chir* 2002; **81**: 259-261 [PMID: 12046431]
33 **Sica GS**, Sileri P, Gaspari AL. Laparoscopic treatment of Bouveret's syndrome presenting as acute pancreatitis. *JSLS* 2005; **9**: 472-475 [PMID: 16381370]
34 **Shinoda M**, Aiura K, Yamagishi Y, Masugi Y, Takano K, Maruyama S, Irino T, Takabayashi K, Hoshino Y, Nishiya S, Hibi T, Kawachi S, Tanabe M, Ueda M, Sakamoto M, Hibi T, Kitagawa Y. Bouveret's syndrome with a concomitant incidental T1 gallbladder cancer. *Clin J Gastroenterol* 2010; **3**: 248-253 [PMID: 26190330 DOI: 10.1007/s12328-010-0170-0]
35 **Sharma D**, Jakhetia A, Agarwal L, Baruah D, Rohtagi A, Kumar A. Carcinoma Gall Bladder with Bouveret's Syndrome: A Rare Cause of Gastric Outlet Obstruction. *Indian J Surg* 2010; **72**: 350-351 [PMID: 21938203 DOI: 10.1007/s12262-010-0145-x]
36 **Shah SK**, Walker PA, Fischer UM, Karanjawala BE, Khan SA. Bouveret syndrome. *J Gastrointest Surg* 2013; **17**: 1720-1721 [PMID: 23775095 DOI: 10.1007/s11605-013-2244-z]
37 **Sethi S**, Kochar R, Kothari S, Thosani N, Banerjee S. Good Vibrations: Successful Endoscopic Electrohydraulic Lithotripsy for Bouveret's Syndrome. *Dig Dis Sci* 2015; **60**: 2264-2266 [PMID: 25381652 DOI: 10.1007/s10620-014-3424-8]
38 **Schweiger F**, Shinder R. Duodenal obstruction by a gallstone (Bouveret's syndrome) managed by endoscopic stone extraction: a case report and review. *Can J Gastroenterol* 1997; **11**: 493-496 [PMID: 9347162]
39 **Sans M**, Feu F, Panés J, Piqué JM, Terés J. [Duodenal obstruction by biliary lithiasis (Bouveret's syndrome)]. *Gastroenterol Hepatol* 1996; **19**: 519-520 [PMID: 9044753]
40 **Sánchez Sánchez MR**, Bouzón Caamaño F, Carreño Villarreal G, Alonso Blanco RA, Galarraga Gay MA, Alvarez Obregón R. [Bouveret syndrome. A case-report]. *Rev Clin Esp* 2003; **203**: 399-400 [PMID: 12855123 DOI: 10.1016/S0014-2565(03)71303-4]
41 **Salah-Eldin AA**, Ibrahim MA, Alapati R, Muslah S, Schubert TT, Schuman BM. The Bouveret syndrome: an unusual cause of hematemesis. *Henry Ford Hosp Med J* 1990; **38**: 52-54 [PMID: 2228712]
42 **Sakarya A**, Erhan MY, Aydede H, Kara E, Ozkol M, Ilkgül O, Ozsoy Y. Gallstone ileus presenting as gastric outlet obstruction (Bouveret's syndrome): a case report. *Acta Chir Belg* 2006; **106**: 438-440 [PMID: 17017703 DOI: 10.1080/00015458.2006.11679926]
43 **Sağlam F**, Sivrikoz E, Alemdar A, Kamalı S, Arslan U, Güven H. Bouveret syndrome: A fatal diagnostic dilemma of gastric outlet obstruction. *Ulus Travma Acil Cerrahi Derg* 2015; **21**: 157-159 [PMID: 25904280 DOI: 10.5505/tjtes.2015.62558]
44 **Rossi D**, Khan U, McNatt S, Vaughan R. Bouveret syndrome: a case report. *W V Med J* 2010; **106**: 18-22 [PMID: 21744726]
45 **Rogart JN**, Perkal M, Nagar A. Successful Multimodality Endoscopic Treatment of Gastric Outlet Obstruction Caused by an Impacted Gallstone (Bouveret's Syndrome). *Diagn Ther Endosc* 2008; **2008**: 471512 [PMID: 18493330 DOI: 10.1155/2008/471512]
46 **Reinhardt SW**, Jin LX, Pitt SC, Earl TM, Chapman WC, Doyle MB. Bouveret's syndrome complicated by classic gallstone ileus: progression of disease or iatrogenic? *J Gastrointest Surg* 2013; **17**: 2020-2024 [PMID: 24018589 DOI: 10.1007/s11605-013-2301-7]
47 **Rehman A**, Hasan Z, Saeed A, Jamil K, Azeem Q, Zaidi A, Abduallah K, Rustam T. Bouveret's syndrome. *J Coll Physicians Surg Pak* 2008; **18**: 435-437 [PMID: 18760069]
48 **Rahelić V**, Zelić M, Grbas H, Depolo A, Kezele B. Bouveret's syndrome--case report. *Zentralbl Chir* 2009; **134**: 260-262 [PMID:

19536722 DOI: 10.1055/s-0028-1098694]
49 **Radonak J**, Vajó J, Jéger T, Stebnický M, Eperjesi O. [Recurrent acute hemorrhage in the duodenum as a symptom of Bouveret's syndrome]. *Rozhl Chir* 2000; **79**: 228-230 [PMID: 10967672]
50 **Qamrul Arfin SM**, Haqqi SA, Shaikh H, Wakani AJ. Bouveret' s syndrome: successful endoscopic treatment of gastric outlet obstruction caused by an impacted gallstone. *J Coll Physicians Surg Pak* 2012; **22**: 174-175 [PMID: 22414360]
51 **Puri V**, Lee RW, Amirlak BA, Lanspa SJ, Fitzgibbons RJ. Bouveret syndrome and gallstone ileus. *Surg Laparosc Endosc Percutan Tech* 2007; **17**: 328-330 [PMID: 17710061 DOI: 10.1097/SLE.0b013e31806c7dc2]
52 **Polistena A**, Santi F, Tiberi R, Bagarani M. Endoscopic treatment of Bouveret's syndrome. *Gastrointest Endosc* 2007; **65**: 704-706 [PMID: 17383468 DOI: 10.1016/j.gie.2006.12.022]
53 **Pissas A**, Mingat J, Massot C, Vincent J, Bouchet Y. [An usual observation of Bouveret syndrome (author's transl)]. *Sem Hop* 1981; **57**: 1740-1742 [PMID: 6272412]
54 **Pickhardt PJ**, Friedland JA, Hruza DS, Fisher AJ. Case report. CT, MR cholangiopancreatography, and endoscopy findings in Bouveret's syndrome. *AJR Am J Roentgenol* 2003; **180**: 1033-1035 [PMID: 12646450 DOI: 10.2214/ajr.180.4.1801033]
55 **Patel JC**, Lesur G, De Cervens T, Renier JF, Hardy C, Favas A, Gompel H, Dupuy P. [Antropyloric lithiasic obstruction. A variant of Bouveret's syndrome]. *Chirurgie* 1991; **117**: 417-419 [PMID: 1817840]
56 **Panov TA**, Kiossev KT, Losanoff JE. Bouveret's syndrome: a rare consequence of malignant cholecystoduodenal fistula. *Mil Med* 1994; **159**: 755-757 [PMID: 7724001]
57 **Palomeque-Jiménez A**, Calzado-Baeza S, Reyes-Moreno M. Bouveret syndrome: an infrequent presentation of gallstone ileus. *Rev Esp Enferm Dig* 2012; **104**: 324-325 [PMID: 22738704 DOI: 10.4321/S1130-01082012000600008]
58 **O'Neill C**, Colquhoun P, Schlachta CM, Etemad-Rezai R, Jayaraman S. Gastric outlet obstruction secondary to biliary calculi: 2 cases of Bouveret syndrome. *Can J Surg* 2009; **52**: E16-E18 [PMID: 19234638]
59 **O'Dwyer JC**, O'Dwyer HM, Lee MJ. Bouveret's syndrome: a rare complication of cholecystolithiasis. *Australas Radiol* 2005; **49**: 427-429 [PMID: 16174186 DOI: 10.1111/j.1440-1673.2005.01477.x]
60 **Nyui S**, Osanai H, Masuoka H, Ohba S, Ebata T, Yoshida Y. Gastric outlet syndrome caused by a gallstone: report of a case. *Surg Today* 1998; **28**: 412-415 [PMID: 9590708 DOI: 10.1007/s005950050152]
61 **Newton RC**, Loizides S, Penney N, Singh KK. Laparoscopic management of Bouveret syndrome. *BMJ Case Rep* 2015; **2015**: Epub ahead of print [PMID: 25903213 DOI: 10.1136/bcr-2015-209869]
62 **Nabais C**, Salústio R, Morujão I, Sousa FV, Porto E, Cardoso C, Fradique C. Gastric outlet obstruction in a patient with Bouveret' s syndrome: a case report. *BMC Res Notes* 2013; **6**: 195 [PMID: 23663702 DOI: 10.1186/1756-0500-6-195]
63 **Modi BP**, Owens C, Ashley SW, Colson YL. Bouveret meets Boerhaave. *Ann Thorac Surg* 2006; **81**: 1493-1495 [PMID: 16564302 DOI: 10.1016/j.athoracsur.2005.04.049]
64 **Mittal S**, Sutcliffe RP, Rohatgi A, Atkinson SW. A possible variant of Bouveret's syndrome presenting as a duodenal stump obstruction by a gallstone after Roux-en-Y gastrectomy: a case report. *J Med Case Rep* 2009; **3**: 7301 [PMID: 19830173 DOI: 10.1186/1752-1947-3-7301]
65 **Menon NJ**, Reid PJ, Ribeiro BF. Bouveret's syndrome: an unusual case of pyloroduodenal obstruction. *Hosp Med* 2002; **63**: 432-433 [PMID: 12187606 DOI: 10.12968/hosp.2002.63.7.1990]
66 **Melero MJ**, Heredia R, Lell A, Volpacchio M. [Bouveret syndrome (gastric or duodenal obstruction due to biliary lithiasis)]. *Medicina* (B Aires) 2010; **70**: 88 [PMID: 20228032]
67 **Matur R**, Yucel T, Gurdal SO, Akpinar A. [Bouveret'S syndrome: gastric outlet obstruction by a gallstone]. *Ulus Travma Derg* 2002; **8**: 179-182 [PMID: 12181765]
68 **Matincheva R**, Deredzhian S, Ivanov S. [Case of a biliodigestive fistula--a variant of Bouveret's syndrome]. *Vutr Boles* 1984; **23**: 60-64 [PMID: 6531875]
69 **Masson JW**, Fraser A, Wolf B, Duncan K, Brunt PW, Sinclair TS. Bouveret's syndrome: gallstone ileus causing gastric outlet obstruction. *Gastrointest Endosc* 1998; **47**: 104-105 [PMID: 9468440 DOI: 10.1016/S0016-5107(98)70308-6]
70 **Masannat YA**, Caplin S, Brown T. A rare complication of a common disease: Bouveret syndrome, a case report. *World J Gastroenterol* 2006; **12**: 2620-2621 [PMID: 16688813 DOI: 10.3748/wjg.v12.i16.2620]
71 **Martin-Cuesta L**, Marco de Lucas E, Pellon R, Sanchez E, Piedra T, Arnaiz J, Parra JA, Lopez-Calderon M. Migrating intrathoracic gallstone: imaging findings. *J Thorac Imaging* 2008; **23**: 272-274 [PMID: 19204473 DOI: 10.1097/RTI.0b013e3181833ee6]
72 **Marsdin EL**, Kreckler S, Alzein A, D'Costa H. Choledochal-duodenal fistula presenting as an upper GI bleed. *BMJ Case Rep* 2011; **2011**: Epub ahead of print [PMID: 22674938 DOI: 10.1136/bcr.05.2011.4275]
73 **Marschall J**, Hayton S. Bouveret's syndrome. *Am J Surg* 2004; **187**: 547-548 [PMID: 15041509 DOI: 10.1016/j.amjsurg.2003.12.031]
74 **Malvaux P**, Degolla R, De Saint-Hubert M, Farchakh E, Hauters P. Laparoscopic treatment of a gastric outlet obstruction caused by a gallstone (Bouveret's syndrome). *Surg Endosc* 2002; **16**: 1108-1109 [PMID: 11984680 DOI: 10.1007/s004640042033]
75 **Makker J**, Muthusamy VR, Watson R, Sedarat A. Electrohydraulic lithotripsy and removal of a gallstone obstructing the duodenum: Bouveret syndrome. *Gastrointest Endosc* 2015; **81**: 1021-1022 [PMID: 25805470 DOI: 10.1016/j.gie.2014.10.045]
76 **Maiss J**, Hochberger J, Hahn EG, Lederer R, Schneider HT, Muehldorfer S. Successful laserlithotripsy in Bouveret's syndrome using a new frequency doubled doublepulse Nd: YAG laser (FREDDY). *Scand J Gastroenterol* 2004; **39**: 791-794 [PMID: 15513369 DOI: 10.1080/00365520410005937]
77 **López-Martínez JA**, Delgado-Carlo MM, Palacio-Vélez F, Arenas-Espino G, Granja-Posada E, Senado-Lara I, García-Alvarado L. [Bouveret's syndrome. Case report]. *Cir Cir* 2004; **72**: 317-322 [PMID: 15469752]
78 **López Rosés L**, Toscano J, Iñiguez F, Santos E, Pérez Carnero A. [Successful endoscopic therapy in a case of Bouveret's syndrome]. *Rev Esp Enferm Dig* 1994; **85**: 483-485 [PMID: 8068428]
79 **Liao Z**, Li ZS, Ye P. Bouveret's syndrome. *Gastrointest Endosc* 2007; **65**: 703-704 [PMID: 17383467 DOI: 10.1016/j.gie.2006.06.054]
80 **Leopaldi E**, Ambrosiani N, Campanelli G. [Pyloric stenosis caused by gallstone (Bouveret's syndrome). Presentation of a further case]. *Minerva Chir* 1991; **46**: 405-409 [PMID: 1870742]
81 **Lenz P**, Domschke W, Domagk D. Bouveret's syndrome: unusual case with unusual therapeutic approach. *Clin Gastroenterol Hepatol* 2009; **7**: e72 [PMID: 19410019 DOI: 10.1016/j.cgh.2009.04.021]
82 **Lawther RE**, Diamond T. Bouveret's syndrome: gallstone ileus causing gastric outlet obstruction. *Ulster Med J* 2000; **69**: 69-70 [PMID: 10881651]
83 **Langhorst J**, Schumacher B, Deselaers T, Neuhaus H. Successful endoscopic therapy of a gastric outlet obstruction due to a gallstone with intracorporeal laser lithotripsy: a case of Bouveret's syndrome. *Gastrointest Endosc* 2000; **51**: 209-213 [PMID: 10650271 DOI: 10.1016/S0016-5107(00)70421-4]
84 **Kumar A**, Chaturvedi S, Agrawal S, Gautam A. Gallstone obstruction of the duodenum (Bouveret's syndrome). *Indian J Gastroenterol* 1995; **14**: 77-78 [PMID: 7797287]
85 **Kishi K**, Yamada K, Sugiyama T. Gastric outlet obstruction caused by a large gallstone in the duodenum (Bouveret's syndrome). *Clin Gastroenterol Hepatol* 2008; **6**: e11 [PMID: 18255345 DOI: 10.1016/j.cgh.2007.12.027]
86 **Khan AZ**, Escofet X, Miles WF, Singh KK. The Bouveret syndrome: an unusual complication of gallstone disease. *J R Soc Promot Health* 2002; **122**: 125-126 [PMID: 12134765 DOI: 10.1177/146642400212200216]
87 **Khalsa B**, Rudersdorf P, Dave D, Smith BR, Lall C. 63-year-old male with gastric outlet obstruction. *Case Rep Radiol* 2014; **2014**: 767165 [PMID: 25298900 DOI: 10.1155/2014/767165]
88 **Keller M**, Epp C, Meyenberger C, Sulz MC. Unspecific abdominal symptoms and pneumobilia: a rare case of gastrointestinal obstruction.

Case Rep Gastroenterol 2014; **8**: 216-220 [PMID: 25076865 DOI: 10.1159/000364818]
89 **Katsinelos P**, Dimiropoulos S, Tsolkas P, Baltagiannis S, Kapelidis P, Galanis I, Papaziogas B, Georgiadou E, Vasiliadis I. Successful treatment of duodenal bulb obstruction caused by a gallstone (Bouveret's syndrome) after endoscopic mechanical lithotripsy. *Surg Endosc* 2002; **16**: 1363 [PMID: 12073006 DOI: 10.1007/s00464-002-4200-y]
90 **Kasano Y**, Tanimura H, Yamaue H, Uchiyama K, Hayashido M, Hama T. Duodenal obstruction by gallstone: case report of Bouveret's syndrome. *Nihon Geka Hokan* 1997; **66**: 111-115 [PMID: 10363520]
91 **Kalwaniya DS**, Arya SV, Guha S, Kuppuswamy M, Chaggar JG, Ralte L, Chejera R, Sharma A. A rare presentation of gastric outlet obstruction (GOO) - The Bouveret's syndrome. *Ann Med Surg* (Lond) 2015; **4**: 67-71 [PMID: 25830020 DOI: 10.1016/j.amsu.2015.02.001]
92 **Joshi D**, Vosough A, Raymond TM, Fox C, Dhiman A. Bouveret's syndrome as an unusual cause of gastric outlet obstruction: a case report. *J Med Case Rep* 2007; **1**: 73 [PMID: 17760995 DOI: 10.1186/1752-1947-1-73]
93 **Jones TA**, Davis ME, Glantz AI. Bouveret's syndrome presenting as upper gastrointestinal hemorrhage without hematemesis. *Am Surg* 2001; **67**: 786-789 [PMID: 11510584]
94 **Jayakumar L**, Vernick J, Waheed U. Bouveret's syndrome: a rock in a hard place. *Am Surg* 2012; **78**: E404-E406 [PMID: 22964178]
95 **Jafferbhoy S**, Rustum Q, Shiwani M. Bouveret's syndrome: should we remove the gall bladder? *BMJ Case Rep* 2011; **2011**: Epub ahead of print [PMID: 22700609 DOI: 10.1136/bcr.02.2011.3891]
96 **Ivekovic H**, Deban O, Rustemovic N, Ostojic R, Skegro M. Freehand endoscopic lithotripsy for Bouveret's syndrome. *Acta Gastroenterol Belg* 2012; **75**: 375-376 [PMID: 23082717]
97 **Ivashchenko VV**, Skvortsov KK, Zhuravleva IuI, Skvortsov KK, Koĭko MA. [Successful treatment of Bouveret syndrome in elderly woman patient]. *Klin Khir* 2000; **(6)**: 60 [PMID: 11288293]
98 **Iuchtman M**, Sternberg A, Alfici R, Sternberg E, Fireman T. [Iatrogenic gallstone ileus as a new complication of Bouveret's syndrome]. *Harefuah* 1999; **136**: 122-124, 174 [PMID: 10914179]
99 **Iñíguez A**, Butte JM, Zúñiga JM, Crovari F, Llanos O. [Bouveret syndrome: report of four cases]. *Rev Med Chil* 2008; **136**: 163-168 [PMID: 18483669]
100 **Iancu C**, Bodea R, Al Hajjar N, Todea-Iancu D, Bălă O, Acalovschi I. Bouveret syndrome associated with acute gangrenous cholecystitis. *J Gastrointestin Liver Dis* 2008; **17**: 87-90 [PMID: 18392252]
101 **Hütter G**. [Bouveret syndrome. What is obstructing the duodenum?]. *MMW Fortschr Med* 2015; **157**: 5 [PMID: 25743492 DOI: 10.1007/s15006-015-2615-3]
102 **Hussain A**, Obaid S, El-Hasani S. Bouveret's syndrome: endoscopic or surgical treatment. *Updates Surg* 2013; **65**: 63-65 [PMID: 22238074 DOI: 10.1007/s13304-011-0131-2]
103 **Hürlimann R**, Enzler M, Binswanger RO, Meyenberger C. [Bouveret syndrome--a rare gallstone complication]. *Z Gastroenterol* 1995; **33**: 445-448 [PMID: 7483737]
104 **Huebner ES**, DuBois S, Lee SD, Saunders MD. Successful endoscopic treatment of Bouveret's syndrome with intracorporeal electrohydraulic lithotripsy. *Gastrointest Endosc* 2007; **66**: 183-184; discussion 184 [PMID: 17521642 DOI: 10.1016/j.gie.2007.01.024]
105 **Heyd RL**, Solinger MR, Howard AL, Rosser JC. Acute upper gastrointestinal hemorrhage caused by gallstone impaction in the duodenal bulb. *Dig Dis Sci* 1992; **37**: 452-455 [PMID: 1735369]
106 **Hernández Garcés HR**, Andrain Sierra Y, del Rio-Mendoza JR, Gutierrez Revatta E, Moutary I. [Bouveret Syndrome. First case diagnosed in Santa Maria del Socorro, Ica, Peru]. *Rev Gastroenterol Peru* 2014; **34**: 69-72 [PMID: 24721962]
107 **Heneghan HM**, Martin ST, Ryan RS, Waldron R. Bouveret's syndrome--a rare presentation of gallstone ileus. *Ir Med J* 2007; **100**: 504-505 [PMID: 17668686]
108 **Heinrich D**, Meier J, Wehrli H, Bühler H. Upper gastrointestinal hemorrhage preceding development of Bouveret's syndrome. *Am J Gastroenterol* 1993; **88**: 777-780 [PMID: 8480750]
109 **Harthun NL**, Long SM, Wilson W, Choudhury A. An unusual case of Bouveret's syndrome. *J Laparoendosc Adv Surg Tech A* 2002; **12**: 69-72 [PMID: 11905865 DOI: 10.1089/109264202753486975]
110 **Hameed K**, Ahmad A, Baghomian A. Bouveret's syndrome, an unusual cause of upper gastrointestinal bleeding. *QJM* 2010; **103**: 697-698 [PMID: 20176566 DOI: 10.1093/qjmed/hcq015]
111 **Goldstein EB**, Savel RH, Pachter HL, Cohen J, Shamamian P. Successful treatment of Bouveret syndrome using holmium: YAG laser lithotripsy. *Am Surg* 2005; **71**: 882-885 [PMID: 16468542]
112 **Giese A**, Zieren J, Winnekendonk G, Henning BF. Development of a duodenal gallstone ileus with gastric outlet obstruction (Bouveret syndrome) four months after successful treatment of symptomatic gallstone disease with cholecystitis and cholangitis: a case report. *J Med Case Rep* 2010; **4**: 376 [PMID: 21092262 DOI: 10.1186/1752-1947-4-376]
113 **George J**, Aufhauser DD, Raper SE. Bouveret's Syndrome Resulting in Gallstone Ileus. *J Gastrointest Surg* 2015; **19**: 1189-1191 [PMID: 25707814 DOI: 10.1007/s11605-015-2778-3]
114 **Gencosmanoglu R**, Inceoglu R, Baysal C, Akansel S, Tozun N. Bouveret's syndrome complicated by a distal gallstone ileus. *World J Gastroenterol* 2003; **9**: 2873-2875 [PMID: 14669357]
115 **Gemmel C**, Weickert U, Eickhoff A, Schilling D, Riemann JF. Successful treatment of gallstone ileus (Bouveret's syndrome) by using extracorporal shock wave lithotripsy and argon plasma coagulation. *Gastrointest Endosc* 2007; **65**: 173-175 [PMID: 17137860 DOI: 10.1016/j.gie.2006.05.025]
116 **Gan S**, Roy-Choudhury S, Agrawal S, Kumar H, Pallan A, Super P, Richardson M. More than meets the eye: subtle but important CT findings in Bouveret's syndrome. *AJR Am J Roentgenol* 2008; **191**: 182-185 [PMID: 18562743 DOI: 10.2214/ajr.07.3418]
117 **Gajendran M**, Muniraj T, Gelrud A. A challenging case of gastric outlet obstruction (Bouveret's syndrome): a case report. *J Med Case Rep* 2011; **5**: 497 [PMID: 21970809 DOI: 10.1186/1752-1947-5-497]
118 **Gaduputi V**, Tariq H, Rahnemai-Azar AA, Dev A, Farkas DT. Gallstone ileus with multiple stones: Where Rigler triad meets Bouveret's syndrome. *World J Gastrointest Surg* 2015; **7**: 394-397 [PMID: 26730285 DOI: 10.4240/wjgs.v7.i12.394]
119 **Foets TC**, Weusten BL, van Es HW, Boerma D. [An 84 year old man with gastric outlet obstruction]. *Ned Tijdschr Geneeskd* 2014; **158**: A7550 [PMID: 24867484]
120 **Finn H**, Bienia M. [Determination of gallstone ileus using emergency gastroscopy]. *Z Gesamte Inn Med* 1981; **36**: 85-87 [PMID: 7222856]
121 **Ferreira LE**, Topazian MD, Baron TH. Bouveret's syndrome: diagnosis and endoscopic treatment. *Clin Gastroenterol Hepatol* 2008; **6**: e15 [PMID: 18255348 DOI: 10.1016/j.cgh.2007.12.055]
122 **Fenchel RF**, Krige JE, Bornman PC. Bouveret's syndrome complicated by acute pancreatitis. *Dig Surg* 1999; **16**: 525-527 [PMID: 10805556]
123 **Fejes R**, Kurucsai G, Székely A, Luka F, Altorjay A, Madácsy L. Gallstone Ileus, Bouveret's Syndrome and Choledocholithiasis in a Patient with Billroth II Gastrectomy - A Case Report of Combined Endoscopic and Surgical Therapy. *Case Rep Gastroenterol* 2010; **4**: 71-78 [PMID: 21103231 DOI: 10.1159/000208993]
124 **Fedidat R**, Safadi W, Waksman I, Hadary A. Choledochoduodenal fistula: an unusual case of pneumobilia. *BMJ Case Rep* 2014; **2014**: Epub ahead of print [PMID: 25312898 DOI: 10.1136/bcr-2014-206798]
125 **Farman J**, Goldstein DJ, Sugalski MT, Moazami N, Amory S. Bouveret's syndrome: diagnosis by helical CT scan. *Clin Imaging* 1998; **22**: 240-242 [PMID: 9699044]
126 **Fancellu A**, Niolu P, Scanu AM, Feo CF, Ginesu GC, Barmina ML. A rare variant of gallstone ileus: Bouveret's syndrome. *J Gastrointest Surg* 2010; **14**: 753-755 [PMID: 19421821 DOI: 10.1007/s11605-009-0918-3]
127 **Ezberci F**, Kargi H, Ergin A. Gastric outlet obstruction by a gallstone (Bouveret's syndrome). *Surg Endosc* 2000; **14**: 372 [PMID: 10854523 DOI: 10.1007/s004640010050]
128 **Erlandson MD**, Kim AW, Richter HM, Myers JA. Roux-en-Y duodenojejunostomy in the treatment of Bouveret syndrome. *South Med J* 2009; **102**: 963-965 [PMID: 19668031 DOI: 10.1097/SMJ.0b013e3181b17dde]
129 **Englert ZP**, Love K, Marilley MD, Bower CE. Bouveret syndrome:

gallstone ileus of the duodenum. *Surg Laparosc Endosc Percutan Tech* 2012; **22**: e301-e303 [PMID: 23047413 DOI: 10.1097/SLE.0b013e318262ec13]
130 **Dumonceau JM**, Delhaye M, Devière J, Baize M, Cremer M. Endoscopic treatment of gastric outlet obstruction caused by a gallstone (Bouveret's syndrome) after extracorporeal shock-wave lithotripsy. *Endoscopy* 1997; **29**: 319-321 [PMID: 9255539 DOI: 10.1055/s-2007-1004197]
131 **Dugalić D**, Colović R, Savić M. [Duodenal obstruction caused by gallstones (Bouveret syndrome)]. *Acta Chir Iugosl* 1990; **37**: 75-82 [PMID: 2248014]
132 **Doycheva I**, Limaye A, Suman A, Forsmark CE, Sultan S. Bouveret's syndrome: case report and review of the literature. *Gastroenterol Res Pract* 2009; **2009**: 914951 [PMID: 19360112 DOI: 10.1155/2009/914951]
133 **Dimov R**, Deenichin G, Uchikov A, Molov V, Ivanov V, Stefanov Ch. [Bouveret' syndrome or secondary duodenal obstruction caused by gallstones. Case report]. *Khirurgiia* (Sofiia) 2005; **(4-5)**: 53-55 [PMID: 18693520]
134 **Dillon CK**, Ali A, Perry A. Laparoscopic management of gastric outlet obstruction. *ANZ J Surg* 2009; **79**: 663-664 [PMID: 19895535 DOI: 10.1111/j.1445-2197.2009.05034.x]
135 **Csermely L**, Tárnok F, Varga G, Tüske G. [Bouveret syndrome diagnosed by endoscopy]. *Orv Hetil* 1990; **131**: 2715-2717 [PMID: 2263363]
136 **Crespo Pérez L**, Angueira Lapeña T, Defarges Pons V, Foruny Olcina JR, Cano Ruiz A, Benita León V, Gónzalez Martín JA, Boixeda de Miquel D, Milicua Salamero JM. [A rare cause of gastric outlet obstruction: Bouveret's syndrome]. *Gastroenterol Hepatol* 2008; **31**: 646-651 [PMID: 19174082 DOI: 10.1016/s0210-5705(08)75813-8]
137 **Crans CA**, Cloney DJ. Bouveret's syndrome: an unusual twist on the classic cause. *South Med J* 1991; **84**: 1049-1051 [PMID: 1882261]
138 **Costil V**, Jullès MC, Zins M, Loriau J. Bouveret's syndrome. An unusual localization of gallstone ileus. *J Visc Surg* 2012; **149**: e284-e286 [PMID: 22633091 DOI: 10.1016/j.jviscsurg.2012.02.001]
139 **Cipolletta L**, Bianco MA, Cipolletta F, Meucci C, Prisco A, Rotondano G. Successful endoscopic treatment of Bouveret's syndrome by mechanical lithotripsy. *Dig Liver Dis* 2009; **41**: e29-e31 [PMID: 18406220 DOI: 10.1016/j.dld.2008.03.006]
140 **Chilovi F**, Farris P, Heinrich P. Bouveret's syndrome. *Gastrointest Endosc* 2002; **56**: 112 [PMID: 12085046]
141 **Charalambous CP**, Midwinter M, Bancewicz J. Unusual presentation of Bouveret's syndrome. *J Gastroenterol* 2002; **37**: 476-478 [PMID: 12108684 DOI: 10.1007/s005350200070]
142 **Carvalheiro J**, Mendes S, Sofia C. Bouveret's syndrome: a rare cause of abdominal pain in the elderly. *Asian J Endosc Surg* 2014; **7**: 93 [PMID: 24450355 DOI: 10.1111/ases.12073]
143 **Bruni R**, Bartolucci R, Biancari F, Cataldi C. [Bouveret's syndrome]. *G Chir* 1993; **14**: 439-441 [PMID: 8136238]
144 **Brice R**, Chivot C, Deguisne JB, Sabbagh C. [Hematemesis of unusual cause]. *Rev Med Interne* 2015; **36**: 365-366 [PMID: 25212968 DOI: 10.1016/j.revmed.2014.07.003]
145 **Brennan GB**, Rosenberg RD, Arora S. Bouveret syndrome. *Radiographics* 2004; **24**: 1171-1175 [PMID: 15256636 DOI: 10.1148/rg.244035222]
146 **Bonam R**, Vahora Z, Harvin G, Leland W. Bouveret's Syndrome with Severe Esophagitis and a Purulent Fistula. *ACG Case Rep J* 2014; **1**: 158-160 [PMID: 26157860 DOI: 10.14309/crj.2014.36]
147 **Bhama JK**, Ogren JW, Lee T, Fisher WE. Bouveret's syndrome. *Surgery* 2002; **132**: 104-105 [PMID: 12110804]
148 **Bernardin E**, Boati S, Bona D, Abraham M, Saino G, Bonavina L. [Bouveret's syndrome: a rare clinical variant of gallstone ileus]. *Chir Ital* 2005; **57**: 267-270 [PMID: 15916158]
149 **Baudet-Bourgarel A**, Boruchowicz A, Gambiez L, Paris JC. [Bouveret syndrome revealed by hematemesis]. *Gastroenterol Clin Biol* 1996; **20**: 112-113 [PMID: 8734318]
150 **Barranco B**, Eloubeidi MA, Canakis J, Johnson LF, Shore G, Wilcox CM. Bouveret's syndrome. *Gastrointest Endosc* 2002; **56**: 736 [PMID: 12397288 DOI: 10.1067/mge.2002.128697]
151 **Baharith H**, Khan K. Bouveret syndrome: when there are no options. *Can J Gastroenterol Hepatol* 2015; **29**: 17-18 [PMID: 25706571]
152 **Báez-García JJ**, Martínez-Hernández-Magro P, Iriarte-Gállego G. [Bouveret's syndrome; a case report]. *Rev Gastroenterol Mex* 2009; **74**: 118-121 [PMID: 19666294]
153 **Avén H**, Gözen M. [Bouveret syndrome--when gallstone causes duodenal obstruction. Unusual and very difficult diagnosis to make]. *Lakartidningen* 2014; **111**: 1843-1845 [PMID: 25759900]
154 **Arioli D**, Venturini I, Masetti M, Romagnoli E, Scarcelli A, Ballesini P, Borghi A, Barberini A, Spina V, De Santis M, Di Benedetto F, Gerunda GE, Zeneroli ML. Intermittent gastric outlet obstruction due to a gallstone migrated through a cholecysto-gastric fistula: a new variant of "Bouveret's syndrome". *World J Gastroenterol* 2008; **14**: 125-128 [PMID: 18176974]
155 **Ariche A**, Czeiger D, Gortzak Y, Shaked G, Shelef I, Levy I. Gastric outlet obstruction by gallstone: Bouveret syndrome. *Scand J Gastroenterol* 2000; **35**: 781-783 [PMID: 10972185]
156 **Apel D**, Jakobs R, Benz C, Martin WR, Riemann JF. Electrohydraulic lithotripsy treatment of gallstone after disimpaction of the stone from the duodenal bulb (Bouveret's syndrome). *Ital J Gastroenterol Hepatol* 1999; **31**: 876-879 [PMID: 10669997]
157 **Andersson EJ**, Kullman EP, Halldestam IR, Einarsson C, Borch K. Bouveret's syndrome followed by gallstone entrapment in the stomach: an uncommon cause of upper gastrointestinal bleeding and gastric retention. *Eur J Surg* 2000; **166**: 183-185 [PMID: 10724501 DOI: 10.1080/110241500750009582]
158 **Alsolaiman MM**, Reitz C, Nawras AT, Rodgers JB, Maliakkal BJ. Bouveret's syndrome complicated by distal gallstone ileus after laser lithotropsy using Holmium: YAG laser. *BMC Gastroenterol* 2002; **2**: 15 [PMID: 12086587]
159 **Algın O**, Ozmen E, Metin MR, Ersoy PE, Karaoğlanoğlu M. Bouveret syndrome: evaluation with multidetector computed tomography and contrast-enhanced magnetic resonance cholangiopancreatography. *Ulus Travma Acil Cerrahi Derg* 2013; **19**: 375-379 [PMID: 23884683 DOI: 10.5505/tjtes.2013.97254]
160 **Ah-Chong K**, Leong YP. Gastric outlet obstruction due to gall stones (Bouveret syndrome). *Postgrad Med J* 1987; **63**: 909-910 [PMID: 3447120]
161 **Afzal M**, Ghosh D, Leigh T. Mechanical lithotripsy for Bouveret' s syndrome. *Gut* 2007; **56**: 733-734; author reply 734 [PMID: 17440189 DOI: 10.1136/gut.2006.111591]
162 **Geron N**, Hazzan D, Shiloni E. Bouveret's syndrome as a rare complication of cholecystolithiasis: report of a case. *Surg Today* 2003; **33**: 66-68 [PMID: 12560912 DOI: 10.1007/s005950300013]
163 **Mengual-Ballester M**, Guillén-Paredes MP, Cases-Baldó MJ, García-García ML, Aguayo-Albasini JL. Gastrointestinal bleeding and bowel obstruction as a presentation of Bouveret syndrome. *Cir Cir* 2011; **79**: 557-559 [PMID: 22169375]
164 **Brezean I**, Aldoescu S, Catrina E, Fetche N, Marin I, Păcescu E. Gallstone ileus: analysis of eight cases and review of the literature. *Chirurgia* (Bucur) 2010; **105**: 355-359 [PMID: 20726301]
165 **Cappell MS**, Davis M. Characterization of Bouveret's syndrome: a comprehensive review of 128 cases. *Am J Gastroenterol* 2006; **101**: 2139-2146 [PMID: 16817848 DOI: 10.1111/j.1572-0241.2006.00645.x]
166 **Frattaroli FM**, Reggio D, Guadalaxara A, Illomei G, Lomanto D, Pappalardo G. Bouveret's syndrome: case report and review of the literature. *Hepatogastroenterology* 1997; **44**: 1019-1022 [PMID: 9261592]
167 **Kaushik N**, Moser AJ, Slivka A, Chandrupatala S, Martin JA. Gastric outlet obstruction caused by gallstones: case report and review of the literature. *Dig Dis Sci* 2005; **50**: 470-473 [PMID: 15810628]
168 **Koulaouzidis A**, Moschos J. Bouveret's syndrome. Narrative review. *Ann Hepatol* 2007; **6**: 89-91 [PMID: 17519830]
169 **Lee W**, Han SS, Lee SD, Kim YK, Kim SH, Woo SM, Lee WJ, Koh YW, Hong EK, Park SJ. Bouveret's syndrome: a case report and a review of the literature. *Korean J Hepatobiliary Pancreat Surg* 2012; **16**: 84-87 [PMID: 26388913 DOI: 10.14701/kjhbps.2012.16.2.84]
170 **Lowe AS**, Stephenson S, Kay CL, May J. Duodenal obstruction by gallstones (Bouveret's syndrome): a review of the literature. *Endoscopy* 2005; **37**: 82-87 [PMID: 15657864 DOI: 10.1055/

s-2004-826100]
171 **Mavroeidis VK**, Matthioudakis DI, Economou NK, Karanikas ID. Bouveret syndrome-the rarest variant of gallstone ileus: a case report and literature review. *Case Rep Surg* 2013; **2013**: 839370 [PMID: 23864977 DOI: 10.1155/2013/839370]
172 **Moschos J**, Pilpilidis I, Antonopoulos Z, Paikos D, Tzilves D, Kadis S, Katsos I, Tarpagos A. Complicated endoscopic management of Bouveret's syndrome. A case report and review. *Rom J Gastroenterol* 2005; **14**: 75-77 [PMID: 15800698]
173 **Nickel F**, Müller-Eschner MM, Chu J, von Tengg-Kobligk H, Müller-Stich BP. Bouveret's syndrome: presentation of two cases with review of the literature and development of a surgical treatment strategy. *BMC Surg* 2013; **13**: 33 [PMID: 24006869 DOI: 10.1186/1471-2482-13-33]
174 **Penkov N**. [Bouveret syndrome (review of literature and case report)]. *Khirurgiia* (Sofiia) 2003; **59**: 31-33 [PMID: 15641535]
175 **Qasaimeh GR**, Bakkar S, Jadallah K. Bouveret's Syndrome: An Overlooked Diagnosis. A Case Report and Review of Literature. *Int Surg* 2014; **99**: 819-823 [PMID: 25437593 DOI: 10.9738/INTSURG-D-14-00087.1]
176 **Rodriguez Romano D**, Moreno Gonzalez E, Jiménez Romero C, Selas PR, Manzanera Díaz M, Abradelo de Usera M, Hernández Ga Gallardo D. Duodenal obstruction by gallstones (Bouveret's syndrome). Presentation of a new case and literature review. *Hepatogastroenterology* 1997; **44**: 1351-1355 [PMID: 9356854]
177 **Antonini F**, Belfiori V, Macarri G. Bouveret's syndrome: a rare complication of gallstone disease. *Liver Int* 2013; **33**: 1132 [PMID: 23425023 DOI: 10.1111/liv.12123]
178 **Aras M**, Inanir S, Tuney D. Bouveret's syndrome on FDG PET/CT: a rare life-threatening complication of gallstone disease. *Rev Esp Med Nucl Imagen Mol* 2014; **33**: 125-126 [PMID: 24119548 DOI: 10.1016/j.remn.2013.08.004]
179 **Baloyiannis I**, Symeonidis D, Koukoulis G, Zachari E, Potamianos S, Tzovaras G. Complicated cholelithiasis: an unusual combination of acute pancreatitis and bouveret syndrome. *Case Rep Gastroenterol* 2012; **6**: 459-464 [PMID: 22855661 DOI: 10.1159/000341512]
180 **Calvo Espino P**, García Pavía A, Artés Caselles M, Sánchez Turrión V. [Bouveret syndrome: variant of gallstone ileus]. *Cir Esp* 2014; **92**: e3 [PMID: 24309166 DOI: 10.1016/j.ciresp.2013.02.007]
181 **Chick JF**, Chauhan NR, Mandell JC, de Souza DA, Bair RJ, Khurana B. Traffic jam in the duodenum: imaging and pathogenesis of Bouveret syndrome. *J Emerg Med* 2013; **45**: e135-e137 [PMID: 23880444 DOI: 10.1016/j.jemermed.2013.04.058]
182 **Djuric-Stefanovic A**, Pesko P, Saranovic D. Education and imaging. Hepatobiliary and pancreatic: Bouveret's syndrome. *J Gastroenterol Hepatol* 2011; **26**: 1216 [PMID: 21672022 DOI: 10.1111/j.1440-1746.2011.06792.x]
183 **Gijón-de-la-Santa L**, Camarero-Miguel A, Pérez-Retortillo JA, Ramia-Ángel JM. Bouveret's syndrome: evaluation with multidetector CT. *Rev Esp Enferm Dig* 2014; **106**: 283-284 [PMID: 25075660]
184 **Guntau J**, Oelckers M, Rathgeber T, Lock G. [Sonographic diagnosis of Bouveret's syndrome]. *Dtsch Med Wochenschr* 2007; **132**: 315-318 [PMID: 17286218 DOI: 10.1055/s-2007-959326]
185 **Gupta M**, Garg D. Bouveret's syndrome. *Indian J Gastroenterol* 2013; **32**: 351 [PMID: 22653366 DOI: 10.1007/s12664-012-0190-4]
186 **Herbener TE**, Basile V, Nakamoto D, Butler HE, Pickering SP. Abdominal case of the day. Bouveret's syndrome. *AJR Am J Roentgenol* 1997; **169**: 250, 252-253 [PMID: 9207534 DOI: 10.2214/ajr.169.1.9207534]
187 **Joshi RM**, Shetty TS, Singh R, Raja S, Satish R, Prabhu SV. Bouveret's syndrome. *Indian J Gastroenterol* 2009; **28**: 79 [PMID: 19696999 DOI: 10.1007/s12664-009-0028-x]
188 **Marco Doménech SF**, López Mut JV, Fernández Garcia P, San Miguel Moncín MM, Gil Sánchez S, Jornet Fayos J, Tudela Ortells X. [Bouveret's syndrome: the clinical and radiological findings]. *Rev Esp Enferm Dig* 1999; **91**: 144-148 [PMID: 10231306]
189 **McKee JD**, Tendler D, Chittani R. Image of the month. Bouveret's syndrome. *Gastroenterology* 1997; **112**: 682, 1059 [PMID: 10465623]
190 **Mullady DK**, Ahmad J. Clinical challenges and images in GI. Gallstone impacted in duodenum causing gastric outlet obstruction (Bouveret syndrome). *Gastroenterology* 2007; **133**: 1075, 1394 [PMID: 17919482 DOI: 10.1053/j.gastro.2007.08.056]
191 **Negi RS**, Chandra M, Kapur R. Bouveret syndrome: Primary demonstration of cholecystoduodenal fistula on MR and MRCP study. *Indian J Radiol Imaging* 2015; **25**: 31-34 [PMID: 25709163 DOI: 10.4103/0971-3026.150136]
192 **Ng SS**, Lai PB, Lee JF, Lau WY. Soft-tissue case 41. Bouveret's syndrome. *Can J Surg* 2001; **44**: 336, 364-365 [PMID: 11603745]
193 **Prachayakul V**, Aswakul P, Kachintorn U. Atypical clinical presentation of typical endoscopic finding of Bouveret's syndrome. *Endoscopy* 2011; **43** Suppl 2 UCTN: E55-E56 [PMID: 21287451 DOI: 10.1055/s-0030-1256059]
194 **Ramos Soria F**, Morales Coca C, Bustamante Maldonado E, Vida Mombiela F. [Bouveret syndrome]. *Med Clin* (Barc) 2008; **131**: 480 [PMID: 18928744]
195 **Rodgers AD**. Hepatobiliary and pancreatic: Bouveret's syndrome. *J Gastroent Hepat* 2003; **18**: 1210-1210 [DOI: 10.1046/j.1440-1746.2003.t01-1-03196.x]
196 **Sharma D**, Sood R, Tomar A, Jhobta A, Thakur S, Sood RG. Bouveret's Syndrome: 64-Slice CT Diagnosis and Surgical Management-A Case Report. *Case Rep Radiol* 2012; **2012**: 701216 [PMID: 23346445 DOI: 10.1155/2012/701216]
197 **Tüney D**, Cimşit C. Bouveret's syndrome: CT findings. *Eur Radiol* 2000; **10**: 1711-1712 [PMID: 11097393 DOI: 10.1007/s003300000444]
198 **Zippi M**, Di Stefano P, Manetti G, Febbraro I, Traversa G, Mazzone AM, De Felici I, Mattei E, Occhigrossi G. Bouveret's syndrome: description of a case. *Clin Ter* 2009; **160**: 367-369 [PMID: 19997682]
199 **Park SH**, Lee SW, Song TJ. Another new variant of Bouveret's syndrome. *World J Gastroenterol* 2009; **15**: 378-379 [PMID: 19140242]
200 **Qandeel H**, Tayyem R, Mahmud S. Bouveret's syndrome with cholecysto-colic fistula. *S Afr J Surg* 2010; **48**: 134 [PMID: 21542405]
201 **Mumoli N**, Cei M, Luschi R, Carmignani G, Orlandi F. Bouveret syndrome. *Emerg Med J* 2010; **27**: 525 [PMID: 20466830 DOI: 10.1136/emj.2008.068676]
202 **Gundling F**, Helmberger T, Schepp W. Duodenal perforation due to a gallstone in small intestinal gallstone ileus: "Bouveret's syndrome". *Turk J Gastroenterol* 2009; **20**: 232-233 [PMID: 19821210]
203 **Menéndez P**, Gambi D, Villarejo P, Cubo T, Padilla D, Martín J. [Biliary ileus as a consequence of a cholecystoduodenal fistula (Bouveret syndrome)]. *Rev Clin Esp* 2008; **208**: 321-322 [PMID: 18620667]
204 **Doody O**, Ward E, Buckley O, Hogan B, Torreggiani WC. Bouveret's syndrome variant. *Digestion* 2007; **75**: 126-127 [PMID: 17630474 DOI: 10.1159/000104975]
205 **Buchs NC**, Azagury D, Chilcott M, Nguyen-Tang T, Dumonceau JM, Morel P. Bouveret's syndrome: management and strategy of a rare cause of gastric outlet obstruction. *Digestion* 2007; **75**: 17-19 [PMID: 17429202 DOI: 10.1159/000101561]
206 **Rivera Irigoín R**, Ubiña Aznar E, García Fernández G, Navarro Jarabo JM, Fernández Pérez F, Sánchez Cantos A. [Successful treatment of Bouveret's syndrome with endoscopic mechanical lithotripsy]. *Rev Esp Enferm Dig* 2006; **98**: 790-792 [PMID: 17094729]
207 **Losanoff JE**, Richman BW, Jones JW. Endoscopic management of Bouveret's syndrome. *Surgery* 2003; **133**: 230; author reply 230-231 [PMID: 12605189 DOI: 10.1067/msy.2003.66]
208 **Ondrejka P**. Bouveret's syndrome treated by a combination of extracorporeal shock-wave lithotripsy (ESWL) and surgical intervention. *Endoscopy* 1999; **31**: 834 [PMID: 10604627]
209 **Kjossev KT**, Losanoff JE. Endoscopic management of Bouveret's syndrome. *Can J Gastroenterol* 1998; **12**: 168 [PMID: 9582539]
210 **Patel A**, Agarwal S. The yellow brick road of Bouveret syndrome. *Clin Gastroenterol Hepatol* 2014; **12**: A24 [PMID: 24703866 DOI: 10.1016/j.cgh.2014.03.028]
211 **Liew V**, Layani L, Speakman D. Bouveret's syndrome in Melbourne. *ANZ J Surg* 2002; **72**: 161-163 [PMID: 12074073]
212 **Zong KC**, You HB, Gong JP, Tu B. Diagnosis and management of choledochoduodenal fistula. *Am Surg* 2011; **77**: 348-350 [PMID:

21375850]
213 **Ha JP**, Tang CN, Li MK. Pseudo-Bouveret's syndrome. *Asian J Surg* 2004; **27**: 246-248 [PMID: 15564172 DOI: 10.1016/S1015-9584(09)60044-0]

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