Basrah Journal Of Surgery

Bas J Surg, December, 23, 2017

LAPAROSCOPIC VERSUS OPEN REPAIR OF PERFORATED PEPTIC ULCER

Abutalib B Alluaibi[®], Ali Y Al-Wajeeh^{\$} & Mansour Amin Mohammed^{*}

[®]MB,ChB, FIBMS, General Surgeon, Al-Mawanee General Hospital, Basrah. ^{\$}MB,ChB, CABS, General Surgeon, Al-Mawanee General Hospital, Basrah. *MB,ChB, DS, CABS, MRCS, Lecturer, Dept. of Surgery, College of Medicine, Basrah, IRAQ.

Abstract

Peptic ulcer is the most common GIT disorder with a prevalence of 2%, peaking around the age of 70 years. Laparoscopic repair of perforated peptic ulcer began to evolve and replace the ordinary upper laparotomy. We studied 47 patients suffering from perforated duodenal or gastric ulcer in Al-Mawanee General Hospital in Basrah in the period 2014-2017, the patients were categorized into 2 groups: 1st group(24 patients) managed laparoscopically and the 2nd group (23 patients) managed by open approach. Perforation found to occur more with duodenal ulcer (29 pt. 61.70%) and more in male patients (26 pt. 55.33%). The peak perforation seen in age group >60 years and the commonest risk factors was the NSAIDs usage. Operative time was insignificantly longer in laparoscopic approach. However, the laparoscopic approach has less post operative pain and less overall complications (4 pt. 16.6% vs. 8 pt. 34.7%).

In conclusion, laparoscopic repair of perforated peptic ulcer is a feasible operation and considered promising with less postoperative pain, less postoperative complications and better cosmetic results.

Introduction

Deptic ulcer is the most common GIT disorder with a prevalence of 2% and lifetime cumulative prevalence of 10%, peaking around the age of 70 years¹. Etiology of peptic ulcer basically is due imbalance between: increase aggression (H.pylori infection, increase acid secretion, bile, NSAIDs), decrease defense (decrease blood flow and mucus barrier) & decrease repair (decrease restitution and decrease proliferation)^{2,3}. However, in general, the most common two causes of peptic ulcer are: H.pylori infection & NSAIDs. Where the H.pylori infection causes peptic ulcer by both increasing acid secretion and compromise mucosal defense, NSAIDs causes peptic ulcer by only compromising mucosal defense. Actually, it's found that 20% of the patients who are older than 60 years and presented with perforated peptic ulcer, they were taking NSAIDs at time of presentation⁴. Peptic ulcer disease usually occurs in the 1st part duodenum curvature However, it can occur at distal esophagus,

Mickel's Diverticulum and in the stomas following gastric surgery⁵. Perforated peptic ulcer usually presented as an acute abdomen. Initially, gastric and/or duodenal secretions produce chemical peritonitis. Soon, and after hours it changes into bacterial peritonitis. Usually, patient can often give the exact time of onset of pain which starts in the epigastric region then becomes generalized⁵. Despite that "air under diaphragm" on Chest x-ray is the most dependant radiological finding practically, still it's just seen in 70-80% of cases and its absence doesn't exclude the presence of perforation. Actually, the most sensitive imaging tool is the CT-scan, but due to its cost, it's not routinely done⁶. Once perforated peptic ulcer is diagnosed, immediate surgical intervention would be mandatory. However, still non-operative management can be applied perforation has been sealed (should this seal proved radiologically) or patient has no clinical features of peritonitis⁷. The surgical options for perforated Duodenal

ulcer are: simple patch closure, batch closure with HSV, Patch closure with (Vagotomy & Drainage).

Perforated gastric ulcer has higher mortality due to older age and delay seeking medical attention. surgical options are: Batch closure with biopsy, Local excision with closure, Distal gastrectomy, Trunal vagotomy with drainage, biopsy and closure (all gastric ulcer should be biopsied if not excised, even the prepyloric ulcers)⁴.

Recently, there has been a decline in performing acid reducing procedures in the management of perforated peptic ulcer due to the evolution of PPI and unfamiliarity of surgeons with these operations. Thus, the principle procedure done in most of cases is simple patch closure +/- omental patch (with biopsy if it's a gastric ulcer)8. In the new era of minimal invasive surgery, and due to improved technical laparoscopic skills, laparoscopic repair of perforated peptic ulcer began to evolve and replace the ordinary upper laparotomy. Laparoscopic repair of perforated peptic ulcer described for the 1st time in 1990 for a perforated duodenal ulcer. It has not only allowed the identification of perforation, but allowed also acceptable peritoneal lavage and closure of perforation, which can be added to the well known advantages of laparoscopic approach (decrease postoperative pain, decrease risk of complication wound "like wound infection and wound dehiscence or hernia", in addition to early return to daily activity and finally the better cosmetic outcome⁹. Despite the fact that studies reported the feasibility laparoscopic omental patch repair of perforated peptic ulcer, still it can be technically challenging for surgeons as it involves steep learning curve and needs advanced laparoscopic suturing skills¹⁰. At present, no evidence is available that

At present, no evidence is available that supports the superiority of laparoscopic repair of perforated peptic ulcer over the laparotomy approach. Many metaanalysis studies has been done all over the world to assess the superiority of either approaches. however, since 2010, there has been increase trend toward laparoscopic approach in many countries like singapore¹⁰.

This study aimed to compare between laparoscopic and open approach for the repair of perforated peptic ulcer and to find which approach is superior and has better results.

Patients and methods

This is a prospective study done in Al-Mawanee General Hospital from April 2014 to April 2017. In this study, 47 patients suffering from perforated duodenal or gastric ulcer were included. Certain parameters were considered during taking the History regarding the demography and etiology of the peptic ulcer, these are: sex, age, smoking, alcohol intake and NSAIDs intake. All the patients had presented with history of epigastric pain or generalized abdominal pain with features of peritonitis (tenderness, rebound tenderness, abdominal guarding or boardrigidity). General investigations were done for patients in form of complete blood picture, blood sugar and urea. ECG for patients older than 40 years, or with any history of hypertension or ischemic heart diseases . Diagnosis was ascertained by Chest x-ray in an erect position (which revealed air under diaphragm in all cases. serological test to check for the presence of H. pylori done to all patients. all patients were admitted to the ward, Intravenous lines were inserted and IV fluid (Ringer's lactate) was started with antibiotic cover in form of intravenous Cephatriaxone vial(1gm twice daily) and intravenous Metronidazole vial(500mg three times daily). Esmoprazole infusion also was started and in cases with intolerable pain, analgesia in form of Tramadol ampoule was given. Based on lottery method, patients were randomized into two groups. We used equal number of cards marked with:

- OA (for patients who were to undergo open repair of perforate peptic ulcer).
- LA (for patients who were to undergo laparoscopic repair of perforated peptic ulcer).

Written consents were taken from patients whether to undergo open, laparoscopic, or conversion from laparoscopic to open approach.

The group of patient underwent open approach, were proceeded for surgery under general anesthesia, through an upper midline incision (sometimes wound extended slightly through umbilicus). If there is gastric or duodenal secretions in the peritoneal cavity, a saline wash of about 500-1000 ml and suction was performed. The perforated ulcer was to be identified. If it was a gastric ulcer, multiple biopsies were taken from the edges of perforated ulcer or excision of ulcer and then modified Graham patch was done (2-3 stitches of 2/0 vicryl suture were used to close the perforation followed by a viable omental patch being fixed with the same stitches). Two drains were inserted if wash was done (pelvic and subhepatic) and one drain is applied if there was no soiling and no wash was done(usually being put subhepatic). closure of incision in layers and patient kept on cephatriaxone vial 1gm twice daily, metronidazole vial 500mg three times daily, esmoprazole infusion 80mg daily, IV fluid and analgesia. Patient kept nill by mouth until positive bowel sound started, drains were removed when they were empty. Stitches removed in the 8th post operative day if there were no complications. **Patients** underwent laparoscopic approach were also preceded for surgery under general anesthesia, CO2

insufflation done by direct trocar insertion and 3-4 ports were inserted depending on the feasibility and site of ulcer. the trocar positioned as following: Midline supra-umbilical(10mm, camera port), Right upper midclavicular(5mm, working port), Left upper midclavicular (5mm, working port), Epigastric port (optional 5mm liver retraction). Remaining steps are approximately the same as in open approach. However, sometimes the identification of perforated ulcer needs precise search because in some patients the perforation may be covered by fibrinous material or covered with liver or sometimes with even gall bladder that is not easy to be seen and need more efforts than usual to find the perforation. if perforation failed to be identified laparoscopically, the case converted to open and excluded from study (two patients accordingly were excluded from this study: one was gastric ulcer covered with fibrinous materials and the other was jejunal perforation). All patients were followed for the following Operative time. parameters: Postoperative pain (using Numeric Rating Scale NRS), Post-operative Hospital stay, Post-operative complications (Ileus. site, leakage from repair wound, infection, intra-abdominal abscess and pulmonary embolism). Data were collected, categorized into tables and analyzed using SPSS Protocol.

Results

In this study, 47 patients with perforated peptic ulcer were included as shown in figure 1, 24 patients (51%) were managed laparoscopically while 23 patients (49%) were managed by open approach





Figure 1: Percentage of laparoscopic perforated peptic ulcer repair and open perforated peptic ulcer repair (n = 47)

Table I, shows the site distribution of both types of ulcers. there was higher incidence of perforated duodenal ulcers (29 patients 61.70%) in compare with perforated gastric ulcers which were seen in (18 patients 38.30%). In general, sex distribution shows higher peptic ulcer perforation in males (26 patients 55.33%) compared with (21 patients 44.68%) in

females. However, this picture changed within each ulcer. As we see the ratio of male:female is 2:1 in perforated gastric ulcer, while (and despite the difference is little), perforation is seen more in female regarding perforated duodenal ulcer (15 patients) if compared with male patients (14 patients).

Table I: Site and gender distribution of gastric and duodenal

Gender & Ulcer site	Male	Female	Total
Duodenal ulcer	14	15	29 (61.70%)
Gastric ulcer	12	6	18 (38.30%)
Total	26 (55.33%)	21 (44.68%)	47 (100%)

Figure 2 shows age distribution among patient with perforated gastric and duodenal ulcers in this study. Peak of perforated gastric ulcers seen in patients who were older than 60 years old. while for the age groups of 30-39, 40-49, 50-59

years, the range is the same for perforated gastric ulcer. the picture of duodenal ulcer is different as the higher peak of cases found in the age group of 50-60 years, followed by the age group 30-39 years old.

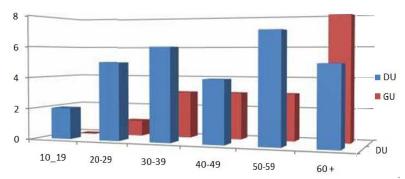


Figure 2: Age distribution of gastric and duodenal ulcer

Table II shows the risk factors for both gastric and duodenal ulcers perforation. Putting in mind that there is an intermingling of these risk factors where 2 or more risk factors may exist in same patient, however, our study showed that the use of NSAIDs was the most common risk factor causing perforated gastric or duodenal ulcer, followed by H. pylori infection. NSAIDs associated with more perforation in gastric ulcer, while H. pylori infection is associated with higher

rate of perforation in duodenal ulcer. The least identified risk factors is malignancy which was seen in a single case with perforated gastric ulcer and to a less extent alcohol intake which was seen more with perforated duodenal ulcer. Seven cases were not associated with any identified risk factor. All these results were considered with the p-value which is considered statistically significant when it is less than 0.05 (significant if p-value <0.05).

Table II: Risk factors associated with perforated gastric and duodenal ulcers

Risk Factor	GU	DU	TOTAL
NSAIDs	8	7	15
H.pylori	6	8	14
Smoking	8	4	12
Alcohol	1	2	3
Malignant ulcer	1	0	1
Non identified	2	5	7

Table III shows that the average of duration of surgery for open approach is shorter than that of laparoscopic approach (65.33±8.09 min. vs. 69.87±7.35 min.) respectively. However, this difference not found to be statistically significant. Regarding post-operative pain, although pain in the 1st post-operative 12 hours is less with laparoscopic approach in comparison with open approach [(7.96 Vs. 8.28) respectively, according to numeric rating scale of pain from 1-10], still this difference is insignificant. while

in the later 12 hours and 2nd 24 hours peaks, the pain is significantly less with laparoscopic approach than it was with open approach. (6.10Vs.8.35), (4.09Vs.7.14) respectively. The post-operative hospital stay for patient with laparoscopic approach found to be insignificantly shorter than hospital stay in open approach. All these results were considered with the p value which is considered statistically significant when it is less than 0.05 (significant if p value <0.05).

Table III: Difference in duration of operation, post-operative pain and postoperative hospital stay between open and laparoscopic approach.

Parameter		Open	Lap	P value
Duration of operation(Min.)		65.33±8.09	69.87±7.35	0.325
Post operative pain			7.96	0.534
	Second 12 hours	8.35	6.10	0.012
	2nd day		4.09	0.004
Hospital stay (Hrs.)		81.99±3.98	78.76±7.91	0.232

Table IV shows the difference in post operative complication between open and laparoscopic approach. It showed that the post-operative complications are more common in total with open approach (8 cases 34.7% vs. 4 cases 16.6%). The commonest complication is ileus which was seen significantly more with open approach (3vs.1) followed by wound infection which also was seen more with open approach (3vs.0). less commonly was the intra-abdominal

abscess which was seen more with laparoscopic approach, however this difference was insignificant. The least complications were the leakage and peritonitis which were more common with laparoscopic approach (1vs.0) and pulmonary embolism due to deep venous thrombosis which was seen more with open approach (1vs.0). Actually the difference of both of these last 2 complications were statistically insignificant.

Table IV: Postoperative complication in laparoscopic and open repair of perforated peptic ulcer NA= Not Applicable

Complication	Lap. (24 patients)	Open (23 patients)	P value
Ileus	1(4.1%)	3(13.1%)	0.011
Wound infection	0(0.0%)	3(13.0%)	NA
Intra abdominal abscess	2(8.4%)	1(4.3%)	0.345
Leakage	1(4.1%)	0(0.0%)	NA
Pulmonary embolism	0(0.0%)	1(4.3%)	NA
Total	4(16.6%)	8(34.7%)	0.009

Discussion

After dawning of laparoscopic surgery, enthusiasm to perform all the surgical procedures with minimally invasive technique began to rise and increase. management of perforated peptic ulcer was one of these operations which attracts surgeons to achieve it laparoscopically¹¹. In this study, and as shown in table I, the perforated duodenal ulcer found more than perforated gastric ulcer. actually this result doesn't mean that duodenal ulcer has higher risk of perforation than gastric, if not compared with the incidence of non-perforated duodenal and ulcer, as this result might be referred to the higher incidence of occurrence of duodenal ulcer itself more than the gastric ulcer in that area. In a study done by marietta j. bertleff et al.8, 60% of perforation seen in duodenal ulcer (usually1st part anteriorly). while the study done by Kenneth Thorsen et al¹¹ showed that the perforated gastric ulcer are more common(65%) than perforated duodenal ulcer(35%). This might depend on the area where the study done and on the patients selected in that study. The study showed higher incidence of perforation in male group with male:female =1.23, this is not so far from many studies showed relatively same ratio 12,13. This might be attributed to that the male patient are seeking medical care after repeated attacks of pain later than

females, and hence: they might not receive anti-ulcer treatment at the proper time. Regarding age, duodenal ulcer perforation peaks in the 50-60 years while the gastric ulcer perforation peaks in the 60+ years. Actually this might referred to that the gastric ulcer patients are 10 years older than duodenal ulcer patients and incidence of peptic ulcer generally increased in elderly probably due to increase NSAID4. In study done in Manchester by Susan K L etal. 14, the peak age of perforation of both duodenal and gastric ulcer started in the 40-50 years old and remain steady for the older groups, while the study done by Kenneth Thorsen et al11, both gastric and duodenal ulcer peroration seen in higher incidence in those over 60 years old. As shown in table II, most common risk factor found to be NSAIDs followed by H. pylori infection. Actually, most of the studies showed that H. pylori infection is the most common risk factor for peptic ulcer disease^{15,16}. However, regarding perforated peptic ulcer, many studies showed that the commonest risk factor is NSAIDs¹⁷, other studies showed that H. pylori infection is the commonest risk factor¹⁸. This is difficult to be explained according to which pathology is more potent induce perforation if it exists. Actually, more than one factors might coexist at the same time. However this

might be explained on the base of which patients were selected and condition of patients included in the study. Most of the studies which showed higher incidence of NSAIDs, were done among old age patients(>60 years) in whom the use of NSAIDs is common due to osteoarthritic changes they have. While the studies which showed H. pylori infection as the commonest risk factor for perforation were done more between middle age patients (<60 years). Other risk factors comes in decreasing order (smoking, alcohol intake & malignancy). In many instances, smoking and alcohol intake found to coexist together with the previously mentioned causes and very difficult to tell really which one is the primary reason behind the ulcer and perforation. Malignant ulcer etiology only considered in gastric ulcers. Actually, malignant ulcers aren't considered peptic ulcer, but still it is a cause for perforation. Perforation from malignancy can result from obstruction and increase luminal pressure, or from some chemotherapeutic agents like darcabazine^{19,20}or sometimes from the overgrowth of the tumour itself. In our study the perforation was due to gastric lymphoma, In our study, the duration of surgery found to be more with the laparoscopic approach. Although this difference was not statically significant, It's not far from a study done by kariman et al. ¹⁷ which showed that laparoscopic repair of perforated peptic ulcer is significantly longer than in open repair. Actually, despite the fact that in many laparoscopic procedures it has advantage of being with shorter duration laparoscopic of operation, the management of perforated peptic ulcer has an exception. First of all, the operation is not a frequent operation that makes it familiar to the surgeon to perform with short duration laparoscopically. Second thing is that in many instances it takes long time to find the perforation as it is usually hidden under fibrinous material of peritonitis and

sometimes the perforation itself has begun to seal and this makes it so hard to be found. In addition to that, sometimes the process of peritoneal wash takes more time when done laparoscopically. some studies(like the one done by Williams K L et al.²¹) has showed shorter operative time with laparoscopic approach. This might be explained by high laparoscopic suturing skill for surgeons who performed these procedures. Post-operative pain as shown in the table III, found to be approximately the same in the 1st 24 hours while its less with laparoscopic approach in the 2nd day and then over. This attributed to the minimally invasive that characterize approach the laparoscopic approach. It is the most attractive advantage which makes the laparoscopic approach superior to the open approach. The result is close to other studies done by(S. Abdelaziem et al. & Karimian F.etal.) 17,22, which showed post operative pain laparoscopic repair of perforated peptic ulcer if compared with open approach. Although hospital stay for laparoscopic approach found to be less than for open approach. However, the difference found to be insignificant. This can be explained by the fact that the patient usually stayed until he has positive bowel motion, drains are empty and no complications appear. Actually this period, to a little extent is somewhat equal for both approaches. This is comparable to the study done in Norway²³. In addition to postoperative pain, Actually one cannot ignore the better cosmetic result for laparoscopic approach, as open approach for perforated peptic ulcer mandate an upper longitudinal incision which usually ends with ugly scar. while, on the contrary, laparoscopic approach has very good cosmetic results. The overall postoperative complications are significantly seen more frequently with open approach than with laparoscopic approach shown in table IV. Ileus for more than 6-7 days was found in three cases of open approach while it was seen in only one case with laparoscopic approach and difference found to be significant. This might be attributed to that the peritoneal incision and resultant more abdominal organs manipulation might add some to the delay in bowel motion. Same results seen in a study done by Sze Li Siow²⁴. However, and despite that Chunhua zhou et al. 10 agree with our explanation, their results were so different as they found both laparoscopic and open repair have the same rate of ileus. Intraabdominal abscess seen more with laparoscopic approach although the significant. difference is not this difference might be attributed to the ease of process of peritoneal wash and larger volume of normal saline that can be used with open approach while it's to a little bit more difficult with laparoscopic approach and can't be as effective as in open approach. this was comparable to many other studies which showed same results 10,17,25. Wound infection seen more frequent with open approach as seen in table IV. This is one of advantages of laparoscopic approach over the open approach, as long incision is more amenable infection. Also to open approach makes the wound vulnerable to be infected by intra-abdominal contents during exploration or during wash, not like laparoscopic approach where the trocars usually save the wound from infection.Biscione et al.26 demonstrated in a cohort study that laparoscopy is

associated with a reduction in the risk of surgical site infection by 60%-80% as compared with open diagnostic exploration of the abdominal cavity. Many other studies showed results^{17,27,28}. Leakage in our study has occurred in a single case of those who were managed by laparoscopic approach. In a study done by Leong H L et al.²⁹, the of leakage seen more with laparoscopic approach, but many other studies has showed higher incidence of leakage with open repair^{23,30}. This difference in rate of leakage between the two approaches and among the different studies can be attributed to many factors that affect the outcome of repair like the size of perforation and the suturing skill" especially for laparoscopic approach" which need highly skilled surgeon. Single case of pulmonary embolism has been seen with the open approach. occurrence might be presence of some risk factors of thrombotic phenomenon like old age, diabetes and relatively long hospital stay with immobility.

In conclusion, Laparoscopic repair of perforated peptic ulcer is a feasible procedure with good promising results. Laparoscopic repair of perforated peptic ulcer has less postoperative pain and better cosmetic result than open repair, with no significant difference regarding duration of operation and postoperative hospital stay. Laparoscopic repair significantly has lower overall postoperative complication than open repair.

References

- 1. Brock j, Sauaia A, Ahnen D.Process of care and outcomes for elderly patients hospitalized with peptic ulcer disease. JAMA.2001; 286:14-19.
- 2. Leong RW. Differences in peptic ulcer between the East and the West. *GastroenterolClinNorth America*. 2009;38:363-379.
- 3. Holle GE. Pathophysiology and modern treatment of ulcer disease. *Int J Mol Med.* 2010;25:483-491.
- 4. F.Charles Brunicardi. Yuko Kitagawa, Daniel T. Dempsey. Schwartz's Principal of surgery. McGraw. Hill puplisher. 10th edition. 2014;26:1035-1097.
- 5. Norman S.Williams, Christopher J. K. Bulstrode, P. Ronan O'Connell. Bailey & Love's short practice of surgery. Taylor & Francis. 26th Edition. 2013;63:1023-1057.
- Lauran M., Soran K L. Approach to perforated peptic ulcer. Int. Emerg. J. 2014; 12: 12-22.
- 7. Bucher P,Oulhaci W.Results of conservative treatment for perforated gastroduodenal ulcers in patients not eligible for surgical repair. Swiss med Wkly. 2007;137: 337-340.
- 8. Bertleff M J, Lange J F. Perforated peptic ulcer disease. a review of history and treatment. Dig Surg. 2010; 27: 161-169.
- 9. Hamed Alwadaani. Emergent laparoscopy in perforated peptic ulcer . Local experience from a tertiary center in Saudi Arabia. World journal of Emergency Surgery. 2013;10:1-14.
- 10. C.Zhou, W. Wang. An update meta-analysis of Laparoscopic Versus Open repair for perforated peptic ulcer. Scientific Reports. 2015; 5:13976.
- 11. Kenneth Thorsen, Jon Arne Søreide, Jan Terje Kvaløy, Tom Glomsaker, Kjetil Søreide. Epidemiology of perforated peptic ulcer: Age- and gender adjusted analysis of incidence and mortality. World J Gastroenterol. 2013; 19(3): 347-354.
- 12. A.I. Ugochukwu, O.C. Amub, M.A. Nzegwu, U.C. Dilibe. Acute perforated peptic ulcer: On clinical experience in an urban tertiary hospital in south east Nigeria. International Journal Of Surgery. 2013; 11: 223-227.
- 13. Nuhu A, Madziga AG, Gail BM. Acute perforated duodenal ulcer in Maiduguri. Internet J Surg 2009;21:1-16.
- 14. Susan K L. Mariana Smith, Johan D.O. Incidence of perforated duodenal and gastric ulcer in Manchester. Br. J. of Emerg. 2014; 4:23-33.
- 15. Gufran Kadhim, Hishamuddin Omar, Ahmad Ismail. Risk Factors Associated with Peptic Ulcer Disease. J Bioengineer & Biomedical Sci. 2015; 5:1.
- 16. Murtaza Mustafa1, Jayaram Menon, R K.Muiandy, R.Fredie, A.Fariz. Risk
- Factors, Diagnosis, and Management of Peptic ulcer Disease. IOSR Journal
- of Dental and Medical Sciences. 2015; 14: 40-46.
- 17. karimian F. Aminian A, Lebaschi A H, Perforated Peptic Ulcer, Comparison Between Laparoscopic and Open Repair. Shiraz emedical journal. 2010;10: 20-26.
- 18. Juliana M Karl, Juan G F. Peptic ulcer disease: what are the causative factors?. Nor. GE Journal. 2014; 13:24-29.
- 19. Salomone Di Saverio, Marco Bassi, Nazareno Smerieri, Michele Masetti, Francesco Ferrara, Carlo Fabbri, Luca Ansaloni, Stefania Ghersi, Diagnosis and treatment of perforated or bleeding peptic ulcers.WSES.2014;12:1-20.
- 20. Oosting SF, Peters FT, Hospers GA, Mulder NH: A patient with metastatic melanoma presenting with gastrointestinal perforation after dacarbazine infusion: a case report. J Med Case Reports. 2010, 4 (1): 10.
- 21. Williams K L, Susan Bush. comparative study between laparoscopic and open repair of perforated ulcer disease. Int. Journal of Surg. 2015; 3(15): 45-53.
- 22. S. Abdelaziem, Mohamed S. Hashish, Ahmed Nafea Suliman. Laparoscopic repair of perforated peptic ulcer. Surg Sci. 2015; 6: 80-90.
- 23. Heinz J., Sally L. K, Mao K. Lee. Perforated Peptic Ulcer and Minimally invasive Surgery. Nor. Journal of Surgery. 2012;13:22-29.
- 24. Sze Li Siow, Hans Alexander Mahendran ,Chee Ming Wong , Mark Hardin , Tien Loong Luk. Laparoscopic versus open repair of perforated peptic ulcer: Improving outcomes utilizing a standardized technique. Asian Journal Of Surgery. 2016; 3: 1-9.
- 25. Daniel Jin Keat Lee, Ma Dong Ye, Keith Haozhe Sun, Vishalkumar G Shelat. Laparoscopic Versus Open Omental patch Repair for early presentation of perforated peptic ulcer. Matched retrospective cohort study. Surg Research& Practice. 2016; 2016;1-7.
- 26. Biscione FM, Couto RC, Pedrosa TM, Neto MC. Factors influencing the risk of surgical site infection following diagnostic exploration of the abdominal cavity. J Infect. 2007; 55: 317-323.
- 27. K. Anbalakan, D. Chua, G.J. Pandya, V.G. Shelat. 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. Journal of Surg. 2015; 14: 38-44.
- 28. P N Sreeramulu, T S Venkatachalapathy, C S Supreet. A comparative study of laparoscopic Vs open surgery for the management of duodenal ulcer perforation. World journal of lap.surgery. 2013; 6(1): 11-14.
- 29. Leong H L, Lau D S. Comparative study between open repair and laparoscopic repair of peptic ulcer perforation. Asian ann. journal. 2014; 22:27-36.
- 30. Ahmed A. Ibrahim, Backeet Turkeye, Mohammad M.Alkatary. Laparoscopic and open repair of perforated peptic ulcer. Int Surg J. 2017;4(6):2022-2024.