

## **Review Article**

# **Perforated Peptic Ulcer-Current Management-Narrative review article.**

### **Abstract**

Perforated peptic ulcer is a complication of peptic ulcer disease with its incidence being stable despite the introduction of proton pump inhibitors. This condition is seen in older patients with comorbidities and early diagnosis improves the mortality of this condition. The treatment of perforated peptic ulcer is performed by closure of the perforated peptic ulcer, and this procedure can be performed by open or laparoscopic surgery. The current trend over the last few years has been the use of laparoscopic surgery in the management of perforated peptic ulcer and we have conducted this narrative review article to investigate the current trend in management of this condition.

Keywords-Perforated peptic ulcer perforated duodenal ulcer, laparoscopic surgery, open surgery, helicobacter pylori.

### **Introduction**

Perforated peptic ulcer is a complication of peptic ulcer disease which presents with generalized abdominal pain and generalized peritonitis on examination of the abdomen. This condition is associated with a risk of developing sepsis and death. The risk factors for developing perforated peptic ulcer include, socio-economic development, cigarette smoking, helicobacter pylori infection and use of non-steroidal anti-inflammatory drug. Perforated peptic ulcer is seen in older patients in the western population and in younger patients in Asia and Africa. The perioperative mortality from perforated peptic ulcer was also higher in Africa.(1–7)

The clinical presentation of perforated peptic ulcer is a sudden onset of severe upper abdominal pain which becomes generalized, and it is associated with nausea and vomiting. Patients who present late will have signs of tachycardia and tachypnea with the development of sepsis and death. Perforated peptic ulcer accounts for 10% of cases of peptic ulcer disease and up to 70% of deaths from peptic ulcer diseases. (8,9)

The use of proton pump inhibitors in the management of peptic ulcer disease has seen a decrease in the complication like perforated peptic ulcer and this was confirmed by a population study that was conducted by hermannsson et al.(10)

The trend of peptic ulcer disease has seen a decrease in the incidence in male patients when compared to female patients. There has been a slight increase in female patients who have presented with perforated peptic ulcer. The most common site is the first part of the duodenum followed by the

pylorus. Gastric ulcers are commonly seen in older patients when compared to duodenal ulcers which is seen in younger patients.(11–13)

The incidence of perforated peptic ulcer has been decreasing over the past forty years and is seen in older patients. This condition is also seen in patients with co-morbidities and those who have an American Society of Anesthesia score of 4 to 5 are associated with a higher mortality. The incidence of perforated peptic ulcer has been gradually decreasing over the last decade with decrease in smoking has been associated with this.(14–17)

The World Society of Emergency Surgeons (WSES) guidelines on perforated peptic ulcer recommends the use of chest and abdominal x-ray as the initial imaging of choice with computerized tomography being reserved for cases where the diagnosis is uncertain. The treatment of perforated peptic ulcer is performed by surgical closure which can be done by laparoscopic or open surgical methods.(18)

The Surgical treatment of perforated peptic ulcer can be divided into simple closure of the perforated peptic ulcer and definitive surgery which involves partial gastrectomy and vagotomy. Simple closure of the perforated peptic ulcer is the preferred option as it is associated with reduced morbidity and mortality when compared with definitive surgery.(19,20)

The introduction of laparoscopic closure of perforated peptic ulcer has been associated with improved post operative outcome and mortality as this was shown by Johnson et al who conducted a retrospective cohort study on this.(21)

The management of perforated peptic ulcer has been undergoing a change in the trend of management with laparoscopic closure of perforated gastric ulcer being the preferred treatment option and open surgical closure of the perforated gastric ulcer being reserved for patients who present with sepsis and signs of shock. We have conducted this review article to investigate the various management options. We conducted a literature review using PUBMED, Cochrane database of clinical reviews and Google scholar looking for clinical trial, observational studies, cohort studies, systemic reviews, and meta-analysis from 1985 to 2022. We used the following keywords, “perforated peptic ulcer”, “perforated duodenal ulcer”, “laparoscopic surgery”, “open surgery” and, “*helicobacter pylori*”. All articles were in English language only. Further articles were obtained by manual cross referencing of the literature. Case reports and studies with less than 10 patients and editorials were excluded.

## **Discussion**

### **Risk factors for developing perforated peptic ulcer.**

There are several factors that influence the development of perforated peptic ulcer, and they were analyzed by Akbulut et al in his case control study. Among the independent factors were, decreased body mass index, decreased hemoglobin levels, smoking and the use of non-steroidal anti-inflammatory drugs were associated with a higher risk of development of perforated peptic ulcer. These factors were also evaluated by Svanes et al and they came with the same conclusion. (22,23)

Egwuonwu et al retrospectively studied the role of non-steroidal anti-inflammatory drug use in patients who develop perforated peptic ulcer and concluded that both short term and long-term use of this drug is associated with a higher risk of development of perforated peptic ulcer. (24)

Suriya et al conducted a cohort study on the diagnostic indicators for perforated peptic ulcer and concluded that patients who present with severe upper abdominal pain, guarding and tenderness on abdominal examination and free air on plain abdominal x-ray were highly at risk of developing perforated gastric ulcer and should be used for early detection. (25)

Yamamoto et al performed a retrospective case control study on 136 patients with perforated peptic ulcer and concluded that risk factors like symptoms of upper abdominal pain, history of non-steroidal anti-inflammatory drug use, Helicobacter pylori infection and presence of anemia and leukocytosis were important factors in diagnosing perforated peptic ulcer. (26)

Unver et al conducted a retrospective study on the prognostic factors in peptic ulcer perforation and concluded that increasing age, presence of comorbidities like diabetes mellitus, hypertension and a high American Society of Anesthesia score were important risk factors for patients with perforated peptic ulcer. (27)

Laboratory blood investigations were evaluated by Mulder et al in predicting surgical outcomes in patients with perforated peptic ulcers. This study concluded that elevated serum creatinine was the strongest indicator of mortality in perforated peptic ulcer followed by abnormal hemoglobin and low platelets levels. (28)

Thorsen et al conducted a population-based study to look at what are the best predictors of mortality in perforated peptic ulcer, and they concluded that hypoalbuminemia was the strongest predictor of mortality, and this was followed by hyperbilirubinemia and elevated serum creatinine. (29)

### **Scoring Systems in predicting outcome in perforated peptic ulcer**

There are several scoring systems that are used to predict outcome in perforated peptic ulcer disease, the Boey score was the first that was used to predict mortality, it is divided into 3 components, delay in surgery for onset of symptoms of more than 24 hours, shock on admission and presence of comorbidities. The score ranges from 0 to 3, with an increase in score associated with increased mortality. The American Society of Anesthesia score which includes age, gender and various physiological parameters is also widely used to predict mortality in patients with perforated peptic ulcer. Both these scoring systems are the most applied in predicting outcome in perforated peptic ulcer but have variable accuracy. (30)

The peptic ulcer perforation score (PULP) was one of the newest scoring systems that was developed to predict mortality in perforated peptic ulcer. The score comprises eight variables that include, age over 65, active malignancy or acquired immunodeficiency, liver cirrhosis, steroid use, delayed presentation, shock, raised serum creatinine and American Society of Anesthesia score of more than 1. This score performs better than the Boey score. Patel et al also conducted a prospective observational study on the prognostic scoring systems in predicting 30-day mortality in perforated peptic ulcer disease and they concluded that the PULP scoring performed better than the Boey and ASA scoring systems.(31,32)

Koranne et al performed an observational study comparing the PULP score, ASA score and the Jabalpur score in predicting mortality in patients presenting with perforated peptic ulcer and the study concluded that the PULP score was good at predicting post operative complications.(33)

The conclusion from all these studies was that clinical scoring systems are useful in predicting mortality in perforated peptic ulcer disease.

**Table I**

**The table for the Boey score and outcomes.**

<b>Risk score</b>	<b>mortality</b>	<b>morbidity</b>
1	8%	47%
2	33%	75%
3	38%	77%

**Operative management of perforated peptic ulcer**

The operative management of perforated peptic ulcer can be divided into simple closure of the perforated peptic ulcer and definitive surgery which involves a partial gastrectomy and vagotomy. Most cases of perforated peptic ulcer are treated with simple closure of the perforated peptic ulcer with primary closure with interrupted sutures, primary closure with a pediculated omentopexy, the Graham free omental plug and the Cullen-Jones closure with pedicle omentoplasty. Definitive surgery is almost not performed as acid suppression can be achieved with proton pump inhibitors.(34–36)

A systemic review and meta-analysis were conducted by Demetriou et al comparing primary closure versus the graham patch omentopexy in the management of perforated peptic ulcer, and the results showed that there was no difference in the bile leakage rate, wound infection rates and outcomes. This study concluded that there was no difference in the outcome of both types of surgical repair. (37)

The surgical treatment of perforated gastric ulcer differs because of the risk of malignancy, and it involves excision of the ulcer and sending the specimen for histological assessment. If the biopsy result comes back as suspicious of malignancy than a definitive procedure like a partial gastrectomy can be done as an elective procedure.(38)

The emergence of laparoscopic surgery in the early nineties has influenced the surgical management of perforated peptic ulcer with the closure of the peptic ulcer and omental patch being performed laparoscopically.(39,40) The preliminary results by Matsuda et al showed that though the operative time was longer the outcome was similar with open surgical repair.(41)

A randomized control trial comparing laparoscopic repair for perforated peptic ulcer was conducted by Siu W et al. A total of 130 patients were included in the study and the results showed that the patients who underwent laparoscopic repair had decreased post operative wound infection, required less analgesia, and returned to work much earlier than those who underwent the open procedure. This study showed that laparoscopic repair was safe and feasible in the management of perforated peptic ulcer. A retrospective study by Siow et al also showed that laparoscopic repair of perforated peptic ulcer was associated with reduced post operative infection and shorter hospital stay.(42,43)

The LAMA trial which was a randomized clinical trial for laparoscopic versus open repair of perforated peptic ulcer where 109 patients with perforated peptic ulcer were included in this trial. The conclusions of the study showed that the laparoscopic repair was safe, feasible and associated with decreased post operative pain.(44)

A meta-analysis of randomized control trials by Tan et al on laparoscopic versus open repair for perforated peptic ulcer showed that laparoscopic repair was associated with reduced post operative wound infection, shorter nasogastric tube usage and less post operative pain.(45)

A systemic review comparing laparoscopic and open repair for perforated peptic ulcer by Lunevicious et al concluded that laparoscopic repair was associated with reduced post operative analgesia, reduced wound infection rate and reduced mortality. This study concluded that laparoscopic repair of perforated peptic ulcer should be offered for low-risk patients and open surgery be offered for high-risk patients.(46)

A multicentric retrospective study by Chung et al looking at the safety and efficacy of laparoscopic repair of perforated peptic ulcer concluded that laparoscopic repair was safe and associated with the same outcome as open surgical repair.(47)

Mirabella et al conducted a retrospective study on laparoscopic management of perforated peptic ulcer and they concluded that it was a viable alternative option in the surgical management of perforated peptic ulcer with morbidity and mortality related to the Boey score of the patient. Biertlieff et al also concluded that laparoscopic closure of perforated peptic ulcer can be the primary treatment of choice and that a presentation of more than 24 hours and a high Boey score are indications for conversion to an open laparotomy.(48,49)

Tartaglia et al assessed the safety of laparoscopic repair of perforated peptic ulcer retrospectively and they concluded that the procedure was safe, and they observed that patients with previous laparotomies, large peptic ulcer and posterior location of the peptic ulcer were all factors for conversion to open laparotomy.(50)

Laparoscopic repair of perforated peptic ulcer should be included for patients with low Boey score and that open repair is indicated for patients who present after 24 hours, are associated with hypotension,

shock and those who present with a large ulcer. The method of laparoscopic closure is also important with suture repair being the most common method.(51)

**Table II Comparison of the studies that compared laparoscopic and open repair of perforated peptic ulcer**

Study	year	N=number	Laparoscopic repair	Open repair	Study type
Lunevicious et al	2005	222	60	162	Retrospective study
Bertleff et al	2009	101	52	49	Randomized control trial
Matsuda et al	1995	15	11	4	Retrospective study
Critchley et al	2011	142	53	89	Prospective study
Tartaglia et al	2022	131	104	27	Retrospective study

### **Conservative treatment of perforated peptic ulcer**

Conservative treatment of perforated peptic ulcer involves treating the patient with fluid resuscitation and intravenous antibiotics and proton pump inhibitors and observing the patients' vital signs. It is normally indicated in high-risk patients like those with a Boey score of 3, an ASA score of 4 or 5 and

patients with multiple co-morbidities. The mortality is high in this patient and most studies have shown that this is a stop gap measure and is not widely practiced.(52–56)

## Conclusion

The treatment of perforated peptic ulcer has seen a change in the management with a trend towards laparoscopic surgery. The early diagnosis of this condition is important as this reduces morbidity and mortality. The introduction of laparoscopic closure of perforated peptic ulcer has seen an improvement of morbidity but it is not indicated in patients who present after 24 hours, Boey score of 3 and ASA score of 3 to 5. For these patients open laparotomy is the operation of choice. Prompt use of fluid resuscitation, intravenous antibiotics and proton pump inhibitors are important in the management of perforated peptic ulcer. The performance of laparoscopic closure of perforated peptic ulcer also depends on the experience of the operating surgeon and the availability of laparoscopic surgical services.

## References

1. Søreide K, Thorsen K, Harrison EM, Bingener J, Møller MH, Ohene-Yeboah M, et al. Perforated peptic ulcer. Vol. 386, *The Lancet*. Lancet Publishing Group; 2015. p. 1288–98.
2. Prabhu V, Shivani A. An overview of history, pathogenesis and treatment of perforated peptic ulcer disease with evaluation of prognostic scoring in adults. *Ann Med Health Sci Res*. 2014;4(1):22.
3. 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. Vol. 84, *Digestion*. 2011. p. 102–13.
4. Rosa F, Covino M, Fransvea P, Cozza V, Quero G, Fiorillo C, et al. Gastric emergencies in older adults: not always the same old story! A tertiary care emergency department observational cohort study. *BMJ Open*. 2022 Jan 25;12(1).
5. Peiffer S, Pelton M, Keeney L, Kwon EG, Ofosu-Okromah R, Acharya Y, et al. Risk factors of perioperative mortality from complicated peptic ulcer disease in Africa: Systematic review and meta-analysis. Vol. 7, *BMJ Open Gastroenterology*. BMJ Publishing Group; 2020.

6. Bupicha JA, Gebresellassie HW, Alemayehu A. Pattern and outcome of perforated peptic ulcer disease patient in four teaching hospitals in Addis Ababa, Ethiopia: A prospective cohort multicenter study. *BMC Surg.* 2020 Jun 15;20(1).
7. Teshome H, Birega M, Taddese M. Perforated Peptic Ulcer Disease in a Tertiary Hospital, Addis Ababa, Ethiopia: Five Year Retrospective Study. *Ethiop J Health Sci.* 2020 May 1;30(3):363–70.
8. Chung KT, Shelat VG. Perforated peptic ulcer - an update. *World J Gastrointest Surg.* 2017;9(1):1.
9. Bertleff MJOE, Lange JF. Perforated peptic ulcer disease: A review of history and treatment. Vol. 27, *Digestive Surgery.* 2010. p. 161–9.
10. Hermansson M, Ekedahl A, Ranstam J, Zilling T. Decreasing incidence of peptic ulcer complications after the introduction of the proton pump inhibitors, a study of the Swedish population from 1974-2002. *BMC Gastroenterol.* 2009 Apr 20;9.
11. 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(12):1666-1671. doi:10.1136/gut.34.12.1666
12. Vijian K, Deva Tata M, Palayan K. Comparison of features and outcomes of perforated peptic ulcer between Malaysians and foreigners. *MJM.* 2016.Feb;71(1):12-16.
13. Wysocki A, Budzyński P, Kulawik J, Drozd W. Changes in the localization of perforated peptic ulcer and its relation to gender and age of the patients throughout the last 45 years. *World J Surg.* 2011 Apr;35(4):811–6.
14. Dadfar A, Edna TH. Epidemiology of perforating peptic ulcer: A population-based retrospective study over 40 years. *World J Gastroenterol.* 2020 Sep 1;26(35):5302–13.
15. Thorsen K, Søreide JA, Kvaløy JT, Glomsaker T, Søreide K. Epidemiology of perforated peptic ulcer: Age- and genderadjusted analysis of incidence and mortality. *World J Gastroenterol.* 2013;19(3):347–54.
16. Hut A, Tatar C, Yildirim D, Dönmez T, Ünal A, Kocakuşak A, et al. Is it possible to reduce the surgical mortality and morbidity of peptic ulcer perforations? *Turk J Surg.* 2017;33(4):267–73.
17. Testini M, Portincasa P, Piccinni G, Lissidini G, Pellegrini F, Greco L. Significant factors associated with fatal outcome in emergency open surgery for perforated peptic ulcer. *World J Gastroenterol* [Internet]. 2003;9(10). Available from: <http://www.wjgnet.com/1007-9327/9/2338.asp>
18. Tarasconi A, Coccolini F, Biffi WL, et al. Perforated and bleeding peptic ulcer: WSES guidelines. *World J Emerg Surg.* 2020;15:3. Published 2020 Jan 7. doi:10.1186/s13017-019-0283-9
19. Jordan PH, Morrow C. Perforated peptic ulcer. *Surgical Clinics of North America.* 1988;68(2):315–29.
20. Mouly C, Chati R, Scotté M, Regimbeau JM. Therapeutic management of perforated gastro-duodenal ulcer: Literature review. Vol. 150, *Journal of Visceral Surgery.* Elsevier Masson SAS; 2013. p. 333–40.

21. Johnson CH, McLean RC, McCallum I, Perren D, Phillips AW. An evaluation of the epidemiology, management and outcomes for perforated peptic ulcers across the North of England over 15 years: A retrospective cohort study. *International Journal of Surgery*. 2019 Apr 1;64:24–32.
22. Akbulut S, Caliskan AR, Saritas H, Demyati K, Bilgic Y, Unsal S, et al. Analysis of risk factors affecting the development of peptic ulcer perforation: Case-control study. *Prz Gastroenterol*. 2021;16(1):23–8.
23. Svanes C. Trends in perforated peptic ulcer: Incidence, etiology, treatment, and prognosis. *World J Surg*. 2000 Mar;24(3):277–83.
24. Egwuonwu O, Chinedu O, Chianakwana G, Anyanwu S, Emegoakor C, Nzeako H. Changing pattern of perforated PUD: Are NSAIDs to be blamed? *Turk J Surg*. 2019;35(2):105–10.
25. Suriya C, Kasatpibal N, Kunaviktikul W, Kayee T. Diagnostic indicators for peptic ulcer perforation at a tertiary care hospital in Thailand. *Clin Exp Gastroenterol*. 2011 Dec 8;4(1):283–9.
26. Yamamoto K, Takahashi O, Arioka H, Kobayashi D. Evaluation of risk factors for perforated peptic ulcer. *BMC Gastroenterol*. 2018 Feb 15;18(1).
27. Unver M, Firat Ö, Ünalp ÖV, Uğuz A, Gümüş T, Sezer TÖ, et al. Prognostic factors in peptic ulcer perforations: A retrospective 14-year study. *Int Surg*. 2015 May 1;100(5):942–8.
28. Mulder WW, Arko-Cobbah E, Joubert G. Are admission laboratory values in isolation meaningful for predicting surgical outcome in patients with perforated peptic ulcers? *Surg Open Sci*. 2023 Jan 1;11:62–8.
29. 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. *Journal of Gastrointestinal Surgery*. 2014;18(7):1261–8.
30. Thorsen K, Søreide JA, Søreide K. Scoring systems for outcome prediction in patients with perforated peptic ulcer. Vol. 21, *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine*. 2013.
31. Søreide K, Thorsen K, Søreide JA. Strategies to improve the outcome of emergency surgery for perforated peptic ulcer. *Br J Surg*. 2014;101(1):e51–e64. doi:10.1002/bjs.9368
32. Patel S, Kalra D, Kacheriwala S, Shah M, Duttaroy D. Validation of prognostic scoring systems for predicting 30-day mortality in perforated Peptic Ulcer Disease. *Turk J Surg*. 2019;35(4):252–8.
33. Koranne A, Byakodi KG, Teggimani V, Kamat V V., Hiregoudar A. A Comparative Study between Peptic Ulcer Perforation Score, Mannheim Peritonitis Index, ASA Score, and Jabalpur Score in Predicting the Mortality in Perforated Peptic Ulcers. *The Surgery Journal*. 2022 Jul;08(03):e162–8.
34. Weledji EP. An Overview of Gastroduodenal Perforation. *Front Surg*. 2020;7:573901. Published 2020 Nov 9. doi:10.3389/fsurg.2020.573901
35. Critchley AC, Phillips AW, Bawa SM, Gallagher P V. Management of perforated peptic ulcer in a district general hospital. *Ann R Coll Surg Engl*. 2011 Nov;93(8):615–9.

36. Samuele Vaccari, Vito D'Andrea, Augusto Lauro, Roberto D'Intino, Eliana Gulotta, Maurizio Cervellera, et al. Laparoscopic repair for perforated peptic ulcer: our experience, a comparison with the open approach and a review of the literature. *Journal of Gastric Surgery*. 2021 May 26;2(2).
37. Demetriou G, Chapman M. Primary closure versus Graham patch omentopexy in perforated peptic ulcer: A systematic review and meta-analysis. Vol. 20, *Surgeon*. Elsevier Ltd; 2022. p. e61–7.
38. Wang A, Yerxa J, Agarwal S, Turner MC, Schroder V, Youngwirth LM, et al. Surgical management of peptic ulcer disease. *CurrProbl Surg*. 2020 Feb 1;57(2).
39. Pereira A, Santos Sousa H, Gonçalves D, et al. Surgery for Perforated Peptic Ulcer: Is Laparoscopy a New Paradigm?. *Minim Invasive Surg*. 2021;2021:8828091. Published 2021 May 12. doi:10.1155/2021/8828091
40. Soeratman A, Putranto A. The use of Laparoscopy In Treatment of Perforated Peptic Ulcer: A Literature Review A Literature Review. *The New Ropanasuri : Journal of Surgery [Internet]*. 2020 Dec 18;5(2):30–2. Available from: <https://scholarhub.ui.ac.id/nrjs/vol5/iss2/8/>
41. Matsuda M, Nishiyama M, Hanai T, Saeki S, Watanabe T. Laparoscopic omental patch repair for perforated peptic ulcer. *Ann Surg*. 1995;221(3):236-240. doi:10.1097/00000658-199503000-00004
42. Siu WT, Leong HT, Law BK, et al. Laparoscopic repair for perforated peptic ulcer: a randomized controlled trial. *Ann Surg*. 2002;235(3):313-319. doi:10.1097/00000658-200203000-00001
43. Siow SL, Mahendran HA, Wong CM, Hardin M, Luk TL. Laparoscopic versus open repair of perforated peptic ulcer: Improving outcomes utilizing a standardized technique. *Asian J Surg*. 2018 Mar 1;41(2):136–42.
44. Bertleff MJOE, Halm JA, Bemelman WA, Van Der Ham AC, Van Der Harst E, Oei HI, et al. Randomized clinical trial of laparoscopic versus open repair of the perforated peptic ulcer: The LAMA trial. *World J Surg*. 2009 Jul;33(7):1368–73.
45. Tan S, Wu G, Zhuang Q, Xi Q, Meng Q, Jiang Y, et al. Laparoscopic versus open repair for perforated peptic ulcer: A meta analysis of randomized controlled trials. Vol. 33, *International Journal of Surgery*. Elsevier Ltd; 2016. p. 124–32.
46. Lunevicius R, Morkevicius M. Systematic review comparing laparoscopic and open repair for perforated peptic ulcer. Vol. 92, *British Journal of Surgery*. 2005. p. 1195–207.
47. Kim CW, Kim JW, Yoon SN, Oh BY, Kang BM. Laparoscopic repair of perforated peptic ulcer: a multicenter, propensity score matching analysis. *BMC Surg*. 2022 Dec 1;22(1).
48. Mirabella A, Fiorentini T, Tutino R, Falco N, Fontana T, De Marco P, et al. Laparoscopy is an available alternative to open surgery in the treatment of perforated peptic ulcers: A retrospective multicenter study. *BMC Surg*. 2018 Sep 25;18(1).

49. Bertleff MJOE, Lange JF. Laparoscopic correction of perforated peptic ulcer: First choice? A review of literature. Vol. 24, *Surgical Endoscopy*. Springer New York; 2010. p. 1231–9.
50. Tartaglia D, Strambi S, Coccolini F, Mazzoni A, Miccoli M, Cremonini C, et al. Laparoscopic versus open repair of perforated peptic ulcers: analysis of outcomes and identification of predictive factors of conversion. *Updates Surg*. 2023 Apr 1;75(3):649–57.
51. Lunevicius R, Morkevicius M. Management strategies, early results, benefits, and risk factors of laparoscopic repair of perforated peptic ulcer. Vol. 29, *World Journal of Surgery*. 2005. p. 1299–310.
52. Gohil RK, Meher RK, Behera TK, Kujur S, Nayak MK, Rath BK. Combined conservative management and percutaneous peritoneal drainage as damage control approach in high-risk patients with perforated peptic ulcers. *Panacea Journal of Medical Sciences*. 2023 Apr 28;13(1):237–40.
53. Karabulut K, Dinçer M, Liman RK, Usta S. Non-operative management of perforated peptic ulcer: A single-center experience. *Ulusal Travmatoloji ve Acil Cerrahi Dergisi*. 2019;25(6):585–8.
54. Efendi R, Septarendra D. Profiles and Clinical Outcomes of Perforated Peptic Ulcer with Boey Score 3 Treated with External Drainage in Indonesia. *International Journal Of Scientific Advances*. 2022;3(1).
55. Kumar Mangtani J, Jain A. Non-surgical management of perforated peptic ulcer: An alternative method of definitive treatment. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)* e-ISSN [Internet]. 2017;16(11):57–60. Available from: [www.iosrjournals.org](http://www.iosrjournals.org)
56. Cao F, Li J, Li A, Fang Y, Wang YJ, Li F. Nonoperative management for perforated peptic ulcer: Who can benefit? *Asian J Surg*. 2014;37(3):148–53.