**Name of Journal:** *World Journal of Gastrointestinal Surgery*

**Manuscript NO:** 89741

**Manuscript Type:** EDITORIAL

**How to identify early complications in patients undergoing distal gastrectomy?**

Tropeano G *et al*. Complications of distal gastrectomy

Giuseppe Tropeano, Maria Michela Chiarello, Valeria Fico, Giuseppe Brisinda

**Giuseppe Tropeano, Valeria Fico, Giuseppe Brisinda,** Emergency Surgery and Trauma Center, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome 00168, Italy

**Maria Michela Chiarello,** Department of Surgery, Azienda Sanitaria Provinciale di Cosenza, Cosenza 87100, Italy

**Giuseppe Brisinda,** Department of Medical and Surgical Sciences, Università Cattolica del Sacro Cuore, Rome 00168, Italy

**Author contributions:** Tropeano G, Chiarello MM, Fico V and Brisinda G designed the research; Fico V performed the research; Fico V and Chiarello MM analyzed the data; All the authors wrote, read and approved the final manuscript.

**Corresponding author: Giuseppe Brisinda, MD, Professor, Surgeon,** Emergency Surgery and Trauma Center, Fondazione Policlinico Universitario A Gemelli IRCCS, 8 Largo Agostino Gemelli, Rome 00168, Italy. gbrisin@tin.it

**Received:** November 12, 2023

**Revised:** February 5, 2024

**Accepted:** March 25, 2024

**Published online:**

**Abstract**

In this editorial we comment on the article by Zhang *et al* published in a recent issue of the W*orld Journal of Gastrointestinal Surgery*. Gastrectomy with appropriate lymph node dissection is still standard curative treatment in locally advanced gastric cancer. Several studies point out that gastric cancer surgery is a complex procedure that leads to a high risk of morbidity and mortality. Many factors can contribute to the onset of complications with consequent effects on prognosis and increased mortality. The complications can be divided in complications related to anastomosis, to motility and to surgical site infection. The study presented by Zhang B *et al* represent an interesting analysis on the possibility to prevent postoperative morbidity. The study was performed on 131 patients with distal gastric cancer who underwent gastrectomy with D2 lymph node dissection. Of these patients, 16% developed early postoperative complications. The univariate analysis showed that prealbumin level, hypertension, diabetes, history of abdominal surgery, R0 resection, and blood transfusion were factors influencing early postoperative complications after distal gastrectomy. Moreover, the inclusion of the above significant variables in the logistic regression analysis revealed that hypertension, diabetes, a history of abdominal surgery, and blood transfusion were independent predictors of postoperative complications. In conclusion, preoperative and intraoperative factors can be used to establish an early postoperative nomogram model. The results of the study presented by Zhang *et al* suggest that the prediction model can be used to guide the detection of postoperative complications and has clinical reference value.

**Key Words:** Gastric cancer; Gastrectomy; Lymph node dissection; Morbidity; Mortality; Surgical site infections

Tropeano G, Chiarello MM, Fico V, Brisinda G. How to identify early complications in patients undergoing distal gastrectomy? *World J Gastrointest Surg* 2024; In press

**Core Tip:** Surgical treatment is still the mainstay of curative gastric cancer treatment. The extent of lymphadenectomy is the only factor that can be influenced by the surgeon. Despite the therapeutic value of lymphadenectomy, mortality and complications are still high in gastric cancer surgery. The study presented by Zhang *et al* represent an interesting analysis on the possibility to prevent post-operative morbidity. The prediction model can be used to guide the detection of early postoperative complications.

**INTRODUCTION**

Gastric cancer (GC) represents a global health concern. With more than 1 million new cases every year, it is the fifth most commonly diagnosed cancer worldwide even if there are high incidence regions as East Asia, Eastern Europe, and South America. Although consistent decline in the incidence and mortality rate due to improved living conditions and screening programs in high-incidence areas, mortality rate for GC is still high, ranking as the third leading cause of cancer-related deaths[1]. Also, it is important to mention an increase in the incidence of GC in younger people, usually from high-income countries, indicating a change in the risk and epidemiology of the disease, which should be taken in consideration for future good clinical practice[2].

Early and advanced stage GC present morphological diversity resulting in a large number of classification systems. The staging system most often used for GC is the American Joint Committee on Cancer tumor-node-metastasis (TNM) system, which was last updated in 2017[3]. Staging of primary GC is dependent on the depth of penetration of the primary tumour (Table 1). Typically, GC doesn't spread to distant organs until it reaches the third stage, but it can affect nearby lymph nodes (LN) during the early stages, which holds significance for prognosis[4].

Surgery is the only potentially curative treatment for GC[5-10]. LN dissection is mandatory in the appropriate surgical treatment of GC due to its tendency to metastasize to the regional LNs. A gastrectomy with D2 lymphadenectomy represents the standard of care for the treatment of GC, according to the most current Japanese guidelines.

Which is the most appropriate lymphadenectomy to perform, to offer the best oncological outcome without increasing postoperative morbidity and mortality, is in fact controversial, due to the differences in results between East and West and between high and low volume centres[11]. This aspect is not of negligible importance, since LN metastasis, which can also appear in the early stages of the disease, is one of the most significant prognostic factors in these patients[7,12]. For this reason lymphadenectomy is recommended as the main step of a curative surgical treatment[6,13,14]. According to the TNM staging system[15], the N stage is classified into 5 levels based on the number of metastatic LNs (NX: Regional lymph LNs cannot be assessed; N0: No regional LNs metastasis; N1: Metastasis in 1-2 regional LNs; N2: Metastasis in 3-6 regional LNs; N3: Metastasis in 7 or more regional LNs; N3a, metastasis in 7-15 LNs; N3b, metastasis in > 15 LNs)[16].

However, the extent of lymphadenectomy has been a controversial topic for a long time with no worldwide consensus as yet. A minimum of 16 LNs has been recommended as an adequate number in radical gastrectomy for GC to ensure reliable N staging. Studies documented that the prognosis is influenced by the number of dissected metastatic LNs. The number of retrieved LNs is a prognostic factor for GC, but the optimal number of retrieved LNs still appears to be controversial. In patients with stage III GC, removal of more than 40 LNs during total gastrectomy has been recommended[17]. According to Lu *et al*[18] , however, the sampling of 21 LNs could represent a superior cut-off point for radical gastrectomy to better determine the prognosis of patients.

The classifications of LNs have been upgraded intermittently since their first publication in 1962. The regional LNs of the stomach are classified into stations numbered from 1 to 20 (Table 2).

The optimal extent of lymphadenectomy has been extensively discussed in the past years. Definitions regarding different types of dissection was made by the Japanese registry data, after mapping the likelihood site of LNs metastasis from each primary tumor location[8]. Multiple levels of dissection are described (Table 3)[19,20]. Moreover, it has been demonstrated that station 4d and 6 metastases were associated with 14v metastasis[21]. For these reasons, station 14v should be dissected during gastrectomy for distal cancer with apparent metastasis to the infra-pyloric LNs.

Since, as stated before, surgery is the cornerstone for treatment of GC, any deviation from the normal postoperative course should be promptly assessed and treated. Despite efforts to reduce postoperative complications for decades, the rate of postoperative complications after curative gastrectomy are still reported to be 10%-20% and severe complications are known to be about 5%-7%[11,22-24].

The complications can be divided in complications related to anastomosis, to motility and to surgical site infection. Mortality and complications are still high in GC surgery[23,25,26]. Infectious complications such as anastomotic leakage, intraabdominal abscess and pneumonia are serious complications which increase postoperative mortality rate[11,27-29].

**NOMOGRAM FOR PREDICTING EARLY POSTOPERATIVE COMPLICATIONS**

In a recent issue of the *World Journal of Gastrointestinal Surgery*, Zhang *et al*[30] published the interesting paper. The study presented by Zhang *et al*[30] represent an interesting analysis on the possibility to prevent post-operative morbidity. Although retrospective and short follow up of the cohort, the statistical analysis, based on numerous variables, pinpoints some independent predictors of postoperative complication such hypertension, diabetes, previous abdominal surgery and perioperative blood transfusions[30]. The subsequent calculated nomogram model can be used as a guide to identify patients prone to complications. The study was performed on 131 patients with distal GC who underwent gastrectomy with D2 LN dissection. Of them, 16% of the patients developed early postoperative complications. In these patients, at univariate analysis the authors documented that the factors influencing early postoperative complications after distal gastrectomy are prealbumin level, hypertension, diabetes, history of abdominal surgery, R0 resection, and blood transfusion. Furthermore, the same variables identified in the univariate analysis are independent factors of early postoperative complications after distal gastrectomy in the logistic regression analysis[30].

Surgical team’s attention could be focused, for instance, on predicting factors such as biomarkers which can be easily assessed. Among complications, the most fearsome is the anastomotic leakage considering the impact on postoperative course, oncological treatment and functional outcome[30]. Occurrence rates from 2% to 14% of all gastrectomy, usually 7 d after surgery[30]. C-reactive protein have already been tested to have high sensitivity for the detection of anastomotic leakage in different types of surgery[31-34]. Procalcitonin elevation was detected as a marker for surgical/infectious complications after esophagectomy or gastrectomy. The first study that prospectively and systematically analyzed procalcitonin as an early laboratory marker of anastomotic leakage concluded it was not superior to C-reactive protein as a predictor of anastomotic leakage[35].

In GC surgery, anastomotic leakage is a complication that occurs especially after total gastrectomy at the level of the esophago-jejunal anastomosis. An anastomotic leakage occurred in 4 our patients (2.1%), and was fatal in one case[11]. Other studies report an incidence of dehiscence in 8.6%[29] and 14.7% of patients[36]. The anastomotic leakage is responsible for an increase in the length of hospital stay, even lasting more than 40 d[37].

In relation to the reconstruction adopted, duodenal dehiscence result from the failure of the suture on the duodenal stump; this results in leakage of biliary-pancreatic secretion from the duodenal lumen into the abdominal cavity. Zhang *et al*[30] observed duodenal dehiscence in 19.1% of their cases. The incidence of duodenal dehiscence is on average around 3%[38], with mortality rate on average 11%[39].

If there is drainage near the dehiscence, the secretion is partially or totally conducted to the outside. The fistula is defined as "low flow rate”, if the secretion drained externally is < 200 mL/d, or “high flow rate”, if the secretion amounts to > 200 mL/d. This distinction has a prognostic value, as closure of the dehiscence can frequently be achieved with exclusive conservative treatment when the fistula has a low flow rate. Usually, mortality was almost zero if the fistula had a low flow rate, but around 40% if it had a high flow rate[38].

Clinically, duodenal dehiscence manifests itself more frequently between the 4th and 6th postoperative day with the change to a greenish shade of straw color, which normally has the serum collected in the sac connected to the peri-duodenal drainage. The biochemical test shows a concentration of amylase, lipase and bilirubin at least double that of serum. If the drainage has been removed before dehiscence occurs, the secretion collects in Morrison's lodge. Extensive effusions also reach the supra-hepatic site, the right parieto-colic shower and to a lesser extent the cable of Douglas and the folds of the mesentery. In this case the diagnosis is made after first performing an abdominal computed tomography (CT) scan, motivated by intermittent fever, and delayed intestinal canalization, and subsequently a percutaneous drainage.

An important cause of dehiscence is the excessive devascularization of the duodenal stump, which involves the failure of one or more points in an area of fragmented necrosis with consequent filtration of liquids. The problem typically manifests itself between the 5th and 6th postoperative day, probably in relation to the timing of the evolution of the necrosis and the resumption of peristalsis. The enzymes of the biliary-pancreatic secretion degrade the collagen on the lines of the anastomosis and aggravate the damage. Other possible causes of dehiscence are the accidental cauterization of the duodenal wall and the increased intraluminal pressure produced by the secretions that accumulate in case of prolonged duodenal hypokinesia.

The metabolic alterations caused by duodenal dehiscence can quickly lead to patient death. Initially, continuous fever occurs with possible peaks preceded by leukocytosis, tachycardia, persistent peristaltic silence, meteorism, diffuse or localized abdominal tenderness. If drainage of secretions to the outside is adequate, antibiotic treatment can control sepsis, but nutritional status must also be considered.

In some cases, the area of dehiscence adheres to the surgical wound; the enteric secretion forms a subcutaneous collection, which subsequently opens to the outside, creating the so-called "enterocutaneous fistula". More frequently, the secretion tends to be delimited by the tissue reaction in a collection varying in size between the right hemidiaphragm and the pelvic cavity, partially filtering outwards *via* drainage. Factors that prolong the duration of a fistula are malnutrition, epithelialization of the passage, a high flow rate, a short path, a previous exposure to radiation, distal obstruction of the duodenal lumen, age over 60 years and concomitant pathologies[38].

Treatment is subject to knowledge of the location and extent of the fistula. Ultrasound and/or CT allow you to locate the collections, position one or more 10-14 Fr percutaneous drains inside them and subsequently check their position to ensure optimal drainage. There are no randomized clinical trials demonstrating the superiority of conservative treatment or surgical treatment. However, experience indicates quite clearly that surgical treatment is initially contraindicated since acute tissue inflammation hinders the healing of a new suture. Conservative treatment should therefore be continued for no more than 6-8 wk, *i.e.* until the fistula no longer has any possibility of closing. At the same time, the resolution of acute inflammation will allow a safer surgical approach. This prolonged wait is justifiable in the case of a low-capacity fistula and in the absence of complications.

Another severe complication is pancreatic fistula. We have observed this complication only in a group of patients where more than 35 LNs had been removed[11]. This complication was found to be severe, as reported in the literature[40-42]. Many factors are held responsible for the onset of this fearful and often fatal complication. Among these, obesity, a pancreas with normal texture, intraoperative trauma, and the use of high-energy devices when performing LN dissection are considered the most important risk factors for the development of postoperative pancreatic fistula[40,41].

Other complications, although less serious, are gastrointestinal dysfunctions linked to the reconstruction of intestinal transit after distal gastrectomy and complications of the gallbladder and biliary tract, if the gallbladder is not removed during the gastrectomy operation.

Depending on the type of intestinal transit reconstruction after distal gastrectomy, such as Billroth-II gastrojejunostomy or Roux-en-Y, clinical syndromes of varying severity may occur. Billroth-II reconstruction exposes the patient to bile reflux and gastritis, with disabling symptoms and the risk of cancerization of the residual gastric stump. The operated stomach is considered as a pre-malignant condition and the greatest risk of cancerization occurs 15 years after the operation and especially in reconstruction according to Billroth-II. From a functional point of view, multiple studies in the literature recognize the Roux-en-Y gastrojejunostomy as having the best functional results[43,44]. These are confirmed in recent meta-analyses, so much so that this reconstruction modality has, for years, been the most widespread both after gastric resection and after total gastrectomy. The uniformly positive experience of using the Roux-en-Y jejunal loop for reconstruction after partial or total demolition of the stomach now tends to also replace the Billroth-II technique after gastric resection[45,46].

Another aspect to consider is that relating to biliary and gallbladder complications if the gallbladder is not removed during the distal gastrectomy operation. We always prefer to perform cholecystectomy during gastrectomy, both to avoid inflammatory complications of the gallbladder in the follow-up period and for an easier lymphadenectomy of the hepatoduodenal ligament. In patients with a radical resection, when a D2 lymphadenectomy is performed and the duodenum is excluded in the intestinal reconstruction, cholecystectomy, considered by some to be a non-essential measure, is necessary to avoid gallstone formation and its complications. In this setting, a prophylactic cholecystectomy is necessary for patients with a good cancer prognosis[47-49].

Furthermore, infectious complications may also be a risk factor for GC recurrence[50]. The severity of the complication may also be correlated to the timing of recurrence[51]. Complications in the postoperative period may also result in accelerated hepatic metastasis after GC resection[52]. Postoperative infectious complications were an independent prognostic factor for five-year overall survival after curative gastrectomy. In addition, inflammatory pathways associated with infectious complications have been reported to affect cancer recurrence and treatment. In a recent study of 6585 patients who underwent curative gastrectomy, 5-year survival was 86.0% in uncomplicated patients and 74.1% in patients with infectious complications. At univariate analysis, the authors documented that infectious complications have a statistically worse survival. It has also been documented that local recurrence, LNs recurrence and distant metastases are significantly associated with infectious complications[53]. In addition to these aspects, it must be considered that patients who experience postoperative infectious complications have a delay in adjuvant chemotherapy. Furthermore, the prolonged duration of hospitalization and the need for additional treatments, such as antibiotics or percutaneous drainage, reduce patient compliance with adjuvant chemotherapy.

**CONCLUSION**

In conclusion, the results of the study presented by Zhang *et al*[30] suggest that the prediction model can be used to guide the detection of early postoperative complications and has clinical reference value.

**REFERENCES**

1 **Li J**, Kuang XH, Zhang Y, Hu DM, Liu K. Global burden of gastric cancer in adolescents and young adults: estimates from GLOBOCAN 2020. *Public Health* 2022; **210**: 58-64 [PMID: 35870322 DOI: 10.1016/j.puhe.2022.06.010]

2 **Arnold M**, Park JY, Camargo MC, Lunet N, Forman D, Soerjomataram I. Is gastric cancer becoming a rare disease? A global assessment of predicted incidence trends to 2035. *Gut* 2020; **69**: 823-829 [PMID: 32001553 DOI: 10.1136/gutjnl-2019-320234]

3 **Komatsu S**, Otsuji E. Essential updates 2017/2018: Recent topics in the treatment and research of gastric cancer in Japan. *Ann Gastroenterol Surg* 2019; **3**: 581-591 [PMID: 31788646 DOI: 10.1002/ags3.12284]

4 **Mihmanli M**, Ilhan E, Idiz UO, Alemdar A, Demir U. Recent developments and innovations in gastric cancer. *World J Gastroenterol* 2016; **22**: 4307-4320 [PMID: 27158199 DOI: 10.3748/wjg.v22.i17.4307]

5 **Songun I**, Putter H, Kranenbarg EM, Sasako M, van de Velde CJ. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. *Lancet Oncol* 2010; **11**: 439-449 [PMID: 20409751 DOI: 10.1016/S1470-2045(10)70070-X]

6 **Sasako M**, Sano T, Yamamoto S, Kurokawa Y, Nashimoto A, Kurita A, Hiratsuka M, Tsujinaka T, Kinoshita T, Arai K, Yamamura Y, Okajima K; Japan Clinical Oncology Group. D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. *N Engl J Med* 2008; **359**: 453-462 [PMID: 18669424 DOI: 10.1056/NEJMoa0707035]

7 **Japanese Gastric Cancer Association**. Japanese gastric cancer treatment guidelines 2018 (5th edition). *Gastric Cancer* 2021; **24**: 1-21 [PMID: 32060757 DOI: 10.1007/s10120-020-01042-y]

8 **Brisinda G**, Chiarello MM, Fico V, Puccioni C, Crocco A, Bianchi V, Vanella S. Pattern of Distribution of Lymph Node Metastases in Individual Stations in Middle and Lower Gastric Carcinoma. *Cancers (Basel)* 2023; **15** [PMID: 37046800 DOI: 10.3390/cancers15072139]

9 **Rausei S**, Galli F, Lianos G, Rosa F, Cossu A, Biondi A, Martignoni F, Cananzi FCM, Fumagalli U, Alfieri S, Persiani R, Quagliuolo V, D'Ugo D, Rosati R. How Should We Measure the Quality of Lymphadenectomy for Gastric Cancer? Anatomical Versus Numerical Criterion. *J Gastrointest Cancer* 2020; **51**: 887-892 [PMID: 31691087 DOI: 10.1007/s12029-019-00321-x]

10 **Brenkman HJ**, Haverkamp L, Ruurda JP, van Hillegersberg R. Worldwide practice in gastric cancer surgery. *World J Gastroenterol* 2016; **22**: 4041-4048 [PMID: 27099448 DOI: 10.3748/wjg.v22.i15.4041]

11 **Brisinda G**, Chiarello MM, Crocco A, Adams NJ, Fransvea P, Vanella S. Postoperative mortality and morbidity after D2 lymphadenectomy for gastric cancer: A retrospective cohort study. *World J Gastroenterol* 2022; **28**: 381-398 [PMID: 35110956 DOI: 10.3748/wjg.v28.i3.381]

12 **Datta J**, McMillan MT, Ecker BL, Karakousis GC, Mamtani R, Plastaras JP, Giantonio BJ, Drebin JA, Dempsey DT, Fraker DL, Roses RE. Implications of Lymph Node Staging on Selection of Adjuvant Therapy for Gastric Cancer in the United States: A Propensity Score-matched Analysis. *Ann Surg* 2016; **263**: 298-305 [PMID: 26135687 DOI: 10.1097/SLA.0000000000001360]

13 **Songun I**, van de Velde CJ. How does extended lymphadenectomy influence practical care for patients with gastric cancer? *Nat Clin Pract Oncol* 2009; **6**: 66-67 [PMID: 19092798 DOI: 10.1038/ncponc1300]

14 **Zhu J**, Xue Z, Zhang S, Guo X, Zhai L, Shang S, Zhang Y, Lu H. Integrated analysis of the prognostic role of the lymph node ratio in node-positive gastric cancer: A meta-analysis. *Int J Surg* 2018; **57**: 76-83 [PMID: 30103072 DOI: 10.1016/j.ijsu.2018.08.002]

15 **Amin MB**, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, Meyer L, Gress DM, Byrd DR, Winchester DP. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. *CA Cancer J Clin* 2017; **67**: 93-99 [PMID: 28094848 DOI: 10.3322/caac.21388]

16 **Chiarello MM**, Fico V, Pepe G, Tropeano G, Adams NJ, Altieri G, Brisinda G. Early gastric cancer: A challenge in Western countries. *World J Gastroenterol* 2022; **28**: 693-703 [PMID: 35317273 DOI: 10.3748/wjg.v28.i7.693]

17 **Hayashi S**, Kanda M, Ito S, Mochizuki Y, Teramoto H, Ishigure K, Murai T, Asada T, Ishiyama A, Matsushita H, Tanaka C, Kobayashi D, Fujiwara M, Murotani K, Kodera Y. Number of retrieved lymph nodes is an independent prognostic factor after total gastrectomy for patients with stage III gastric cancer: propensity score matching analysis of a multi-institution dataset. *Gastric Cancer* 2019; **22**: 853-863 [PMID: 30483985 DOI: 10.1007/s10120-018-0902-2]

18 **Lu J**, Wang W, Zheng CH, Fang C, Li P, Xie JW, Wang JB, Lin JX, Chen QY, Cao LL, Lin M, Huang CM, Zhou ZW. Influence of Total Lymph Node Count on Staging and Survival After Gastrectomy for Gastric Cancer: An Analysis From a Two-Institution Database in China. *Ann Surg Oncol* 2017; **24**: 486-493 [PMID: 27619942 DOI: 10.1245/s10434-016-5494-7]

19 **Japanese Gastric Cancer Association**. Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer* 2011; **14**: 113-123 [PMID: 21573742 DOI: 10.1007/s10120-011-0042-4]

20 **Degiuli M**, De Manzoni G, Di Leo A, D'Ugo D, Galasso E, Marrelli D, Petrioli R, Polom K, Roviello F, Santullo F, Morino M. Gastric cancer: Current status of lymph node dissection. *World J Gastroenterol* 2016; **22**: 2875-2893 [PMID: 26973384 DOI: 10.3748/wjg.v22.i10.2875]

21 **Wu L**, Zhang C, Liang Y, Wang X, Ding X, Liang H. Risk factors for metastasis to No.14v lymph node and prognostic value of 14v status for gastric cancer patients after surgery. *Jpn J Clin Oncol* 2018; **48**: 335-342 [PMID: 29420744 DOI: 10.1093/jjco/hyy006]

22 **Hu Y**, Huang C, Sun Y, Su X, Cao H, Hu J, Xue Y, Suo J, Tao K, He X, Wei H, Ying M, Hu W, Du X, Chen P, Liu H, Zheng C, Liu F, Yu J, Li Z, Zhao G, Chen X, Wang K, Li P, Xing J, Li G. Morbidity and Mortality of Laparoscopic Versus Open D2 Distal Gastrectomy for Advanced Gastric Cancer: A Randomized Controlled Trial. *J Clin Oncol* 2016; **34**: 1350-1357 [PMID: 26903580 DOI: 10.1200/JCO.2015.63.7215]

23 **Bartlett EK**, Roses RE, Kelz RR, Drebin JA, Fraker DL, Karakousis GC. Morbidity and mortality after total gastrectomy for gastric malignancy using the American College of Surgeons National Surgical Quality Improvement Program database. *Surgery* 2014; **156**: 298-304 [PMID: 24947651 DOI: 10.1016/j.surg.2014.03.022]

24 **Fujiya K**, Kumamaru H, Fujiwara Y, Miyata H, Tsuburaya A, Kodera Y, Kitagawa Y, Konno H, Terashima M. Preoperative risk factors for postoperative intra-abdominal infectious complication after gastrectomy for gastric cancer using a Japanese web-based nationwide database. *Gastric Cancer* 2021; **24**: 205-213 [PMID: 32440807 DOI: 10.1007/s10120-020-01083-3]

25 **Xiao H**, Xiao Y, Quan H, Liu W, Pan S, Ouyang Y. Intra-abdominal infection after radical gastrectomy for gastric cancer: Incidence, pathogens, risk factors and outcomes. *Int J Surg* 2017; **48**: 195-200 [PMID: 28751223 DOI: 10.1016/j.ijsu.2017.07.081]

26 **Diers J**, Baum P, Wagner JC, Matthes H, Pietryga S, Baumann N, Uttinger K, Germer CT, Wiegering A. Hospital volume following major surgery for gastric cancer determines in-hospital mortality rate and failure to rescue: a nation-wide study based on German billing data (2009-2017). *Gastric Cancer* 2021; **24**: 959-969 [PMID: 33576929 DOI: 10.1007/s10120-021-01167-8]

27 **Sah BK**, Zhu ZG, Wang XY, Yang QM, Chen MM, Xiang M, Chen J, Yan M. Post-operative complications of gastric cancer surgery: female gender at high risk. *Eur J Cancer Care (Engl)* 2009; **18**: 202-208 [PMID: 19267738 DOI: 10.1111/j.1365-2354.2008.01036.x]

28 **Tokunaga M**, Kurokawa Y, Machida R, Sato Y, Takiguchi S, Doki Y, Yabusaki H, Watanabe M, Hato S, Nakamori M, Ito S, Yoshikawa T, Terashima M. Impact of postoperative complications on survival outcomes in patients with gastric cancer: exploratory analysis of a randomized controlled JCOG1001 trial. *Gastric Cancer* 2021; **24**: 214-223 [PMID: 32601909 DOI: 10.1007/s10120-020-01102-3]

29 **Pacelli F**, Papa V, Rosa F, Tortorelli AP, Sanchez AM, Covino M, Bossola M, Doglietto GB. Four hundred consecutive total gastrectomies for gastric cancer: a single-institution experience. *Arch Surg* 2008; **143**: 769-75; discussion 775 [PMID: 18711037 DOI: 10.1001/archsurg.143.8.769]

30 **Zhang B**, Zhu Q, Ji ZP. Nomogram for predicting early complications after distal gastrectomy. *World J Gastrointest Surg* 2023; **15**: 2500-2512 [PMID: 38111768 DOI: 10.4240/wjgs.v15.i11.2500]

31 **Chiarello MM**, Fransvea P, Cariati M, Adams NJ, Bianchi V, Brisinda G. Anastomotic leakage in colorectal cancer surgery. *Surg Oncol* 2022; **40**: 101708 [PMID: 35092916 DOI: 10.1016/j.suronc.2022.101708]

32 **Ji L**, Wang T, Tian L, Gao M. The early diagnostic value of C-reactive protein for anastomotic leakage post radical gastrectomy for esophagogastric junction carcinoma: A retrospective study of 97 patients. *Int J Surg* 2016; **27**: 182-186 [PMID: 26854957 DOI: 10.1016/j.ijsu.2016.02.021]

33 **Gozalichvili D**, Binquet C, Boisson C, Guiraud A, Facy O, Ortega-Deballon P. Early detection of anastomotic leak with C-reactive protein increases the chances of anastomotic salvage. *Colorectal Dis* 2023; **25**: 728-737 [PMID: 36323646 DOI: 10.1111/codi.16399]

34 **Kartik A**, Müller C, Acs M, Piso P, Starlinger P, Bachleitner-Hofmann T, Grotz TE. Early postoperative CRP predicts major complications following cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). *Pleura Peritoneum* 2023; **8**: 113-121 [PMID: 37662605 DOI: 10.1515/pp-2022-0203]

35 **Cananzi FCM**, Biondi A, Agnes A, Ruspi L, Sicoli F, De Pascale S, Fumagalli UR, D'Ugo D, Quagliuolo V, Persiani R; Italian Gastric Cancer Research Group (GIRCG). Optimal Predictors of Postoperative Complications After Gastrectomy: Results from the Procalcitonin and C-reactive Protein for the Early Diagnosis of Anastomotic Leakage in Esophagogastric Surgery (PEDALES) Study. *J Gastrointest Surg* 2023; **27**: 478-488 [PMID: 36509900 DOI: 10.1007/s11605-022-05547-y]

36 **Selby LV**, Rifkin MB, Yoon SS, Ariyan CE, Strong VE. Decreased length of stay and earlier oral feeding associated with standardized postoperative clinical care for total gastrectomies at a cancer center. *Surgery* 2016; **160**: 607-612 [PMID: 27316826 DOI: 10.1016/j.surg.2016.04.036]

37 **Sierzega M**, Choruz R, Pietruszka S, Kulig P, Kolodziejczyk P, Kulig J. Feasibility and outcomes of early oral feeding after total gastrectomy for cancer. *J Gastrointest Surg* 2015; **19**: 473-479 [PMID: 25519083 DOI: 10.1007/s11605-014-2720-0]

38 **Zizzo M**, Ugoletti L, Manzini L, Castro Ruiz C, Nita GE, Zanelli M, De Marco L, Besutti G, Scalzone R, Sassatelli R, Annessi V, Manenti A, Pedrazzoli C. Management of duodenal stump fistula after gastrectomy for malignant disease: a systematic review of the literature. *BMC Surg* 2019; **19**: 55 [PMID: 31138190 DOI: 10.1186/s12893-019-0520-x]

39 **Aurello P**, Sirimarco D, Magistri P, Petrucciani N, Berardi G, Amato S, Gasparrini M, D'Angelo F, Nigri G, Ramacciato G. Management of duodenal stump fistula after gastrectomy for gastric cancer: Systematic review. *World J Gastroenterol* 2015; **21**: 7571-7576 [PMID: 26140005 DOI: 10.3748/wjg.v21.i24.7571]

40 **Washio M**, Yamashita K, Niihara M, Hosoda K, Hiki N. Postoperative pancreatic fistula after gastrectomy for gastric cancer. *Ann Gastroenterol Surg* 2020; **4**: 618-627 [PMID: 33319151 DOI: 10.1002/ags3.12398]

41 **Hiki N**, Honda M, Etoh T, Yoshida K, Kodera Y, Kakeji Y, Kumamaru H, Miyata H, Yamashita Y, Inomata M, Konno H, Seto Y, Kitano S. Higher incidence of pancreatic fistula in laparoscopic gastrectomy. Real-world evidence from a nationwide prospective cohort study. *Gastric Cancer* 2018; **21**: 162-170 [PMID: 28887712 DOI: 10.1007/s10120-017-0764-z]

42 **Sano T**, Sasako M, Mizusawa J, Yamamoto S, Katai H, Yoshikawa T, Nashimoto A, Ito S, Kaji M, Imamura H, Fukushima N, Fujitani K; Stomach Cancer Study Group of the Japan Clinical Oncology Group. Randomized Controlled Trial to Evaluate Splenectomy in Total Gastrectomy for Proximal Gastric Carcinoma. *Ann Surg* 2017; **265**: 277-283 [PMID: 27280511 DOI: 10.1097/SLA.0000000000001814]

43 **Davis JL**, Ripley RT. Postgastrectomy Syndromes and Nutritional Considerations Following Gastric Surgery. *Surg Clin North Am* 2017; **97**: 277-293 [PMID: 28325187 DOI: 10.1016/j.suc.2016.11.005]

44 **Inokuchi M**, Kojima K, Yamada H, Kato K, Hayashi M, Motoyama K, Sugihara K. Long-term outcomes of Roux-en-Y and Billroth-I reconstruction after laparoscopic distal gastrectomy. *Gastric Cancer* 2013; **16**: 67-73 [PMID: 22467062 DOI: 10.1007/s10120-012-0154-5]

45 **Yang D**, He L, Tong WH, Jia ZF, Su TR, Wang Q. Randomized controlled trial of uncut Roux-en-Y vs Billroth II reconstruction after distal gastrectomy for gastric cancer: Which technique is better for avoiding biliary reflux and gastritis? *World J Gastroenterol* 2017; **23**: 6350-6356 [PMID: 28974902 DOI: 10.3748/wjg.v23.i34.6350]

46 **Zong L**, Chen P. Billroth I vs. Billroth II vs. Roux-en-Y following distal gastrectomy: a meta-analysis based on 15 studies. *Hepatogastroenterology* 2011; **58**: 1413-1424 [PMID: 21937419 DOI: 10.5754/hge10567]

47 **Pitt HA**, Nakeeb A. Prevention of Gallstone Formation After Gastrectomy. *JAMA Surg* 2020; **155**: 712 [PMID: 32584943 DOI: 10.1001/jamasurg.2020.1527]

48 **Bencini L**, Marchet A, Alfieri S, Rosa F, Verlato G, Marrelli D, Roviello F, Pacelli F, Cristadoro L, Taddei A, Farsi M; Italian Research Group for Gastric Cancer (GIRCG). The Cholegas trial: long-term results of prophylactic cholecystectomy during gastrectomy for cancer-a randomized-controlled trial. *Gastric Cancer* 2019; **22**: 632-639 [PMID: 30244294 DOI: 10.1007/s10120-018-0879-x]

49 **Kimura J**, Kunisaki C, Takagawa R, Makino H, Ueda M, Ota M, Oba M, Kosaka T, Akiyama H, Endo I. Is Routine Prophylactic Cholecystectomy Necessary During Gastrectomy for Gastric Cancer? *World J Surg* 2017; **41**: 1047-1053 [PMID: 27896408 DOI: 10.1007/s00268-016-3831-4]

50 **Hayashi T**, Yoshikawa T, Aoyama T, Hasegawa S, Yamada T, Tsuchida K, Fujikawa H, Sato T, Ogata T, Cho H, Oshima T, Rino Y, Masuda M. Impact of infectious complications on gastric cancer recurrence. *Gastric Cancer* 2015; **18**: 368-374 [PMID: 24634097 DOI: 10.1007/s10120-014-0361-3]

51 **Lerut T**, Moons J, Coosemans W, Van Raemdonck D, De Leyn P, Decaluwé H, Decker G, Nafteux P. Postoperative complications after transthoracic esophagectomy for cancer of the esophagus and gastroesophageal junction are correlated with early cancer recurrence: role of systematic grading of complications using the modified Clavien classification. *Ann Surg* 2009; **250**: 798-807 [PMID: 19809297 DOI: 10.1097/SLA.0b013e3181bdd5a8]

52 **Ohtsuka T**, Kitajima Y, Takahashi T, Sato S, Miyoshi A, Kohya N, Kitahara K, Nakafusa Y, Miyazaki K. Infectious complications after gastric cancer surgery accelerate a rapid hepatic recurrence. *Hepatogastroenterology* 2009; **56**: 1277-1280 [PMID: 19950777]

53 **Han WH**, Oh YJ, Eom BW, Yoon HM, Kim YW, Ryu KW. Prognostic impact of infectious complications after curative gastric cancer surgery. *Eur J Surg Oncol* 2020; **46**: 1233-1238 [PMID: 32362466 DOI: 10.1016/j.ejso.2020.04.032]

**Footnotes**

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** November 12, 2023

**First decision:** February 5, 2024

**Article in press:**

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** Italy

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Hori T, Japan **S-Editor:** Li L **L-Editor:** A **P-Editor:**

**Table 1 T staging system proposed by the Union for International Cancer Control and the American Joint Committee on Cancer**

|  |  |
| --- | --- |
| **T category definitions** |  |
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| Tis | Carcinoma *in situ*: Intraepithelial tumor without invasion of the lamina propria |
| T1 | Tumor invades lamina propria, muscularis mucosae, or submucosa |
| T1a | Tumor invades lamina propria or muscularis mucosae |
| T1b | Tumor invades submucosa |
| T2 | Tumor invades muscularis propria |
| T3 | Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures. T3 tumors also include those extending into the gastrocolic or gastrohepatic ligaments, or into the greater or lesser omentum, without perforation of the visceral peritoneum covering these structures |
| T4 | Tumor invades serosa (visceral peritoneum) or adjacent structures |
| T4a | Tumor invades serosa (visceral peritoneum) |
| T4b | Tumor invades adjacent structures such as spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum |

**Table 2 Anatomical definitions of lymph node stations**

|  |  |
| --- | --- |
| **Station** | **Definition** |
| 1 | Right paracardial lymph nodes, including those along the first branch of the ascending limb of the left gastric artery |
| 2 | Left paracardial lymph nodes including those along the esophago-cardiac branch of the left subphrenic artery |
| 3 | 3a Lesser curvature lymph nodes along the branches of the left gastric artery |
| 3b Lesser curvature lymph nodes along the 2nd branch and distal part of the right gastric artery |
| 4 | 4sa Left greater curvature lymph nodes along the short gastric arteries (perigastric area) |
| 4sb Left greater curvature lymph nodes along the left gastroepiploic artery (perigastric area) |
| 4d Right greater curvature lymph nodes along the 2nd branch and distal part of the right gastroepiploic artery |
| 5 | Suprapyloric lymph nodes along the 1st branch and proximal part of the right gastric artery |
| 6 | Infrapyloric lymph nodes along the first branch and proximal part of the right gastroepiploic artery down to the confluence of the right gastroepiploic vein and the anterior superior pancreatoduodenal vein |
| 7 | Lymph nodes along the trunk of left gastric artery between its root and the origin of its ascending branch |
| 8 | 8a Anterosuperior lymph nodes along the common hepatic artery |
| 8p Posterior lymph nodes along the common hepatic artery |
| 9 | Coeliac artery |
| 10 | Splenic hilar lymph nodes including those adjacent to the splenic artery distal to the pancreatic tail, and those on the roots of the short gastric arteries and those along the left gastroepiploic artery proximal to its 1st gastric branch |
| 11 | 11p Proximal splenic artery lymph nodes from its origin to halfway between its origin and the pancreatic tail end |
| 11d Distal splenic artery lymph nodes from halfway between its origin and the pancreatic tail end to the end of the pancreatic tail |
| 12 | 12a Hepatoduodenal ligament lymph nodes along the proper hepatic artery, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas |
| 12b Hepatoduodenal ligament lymph nodes along the bile duct, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas |
| 12p Hepatoduodenal ligament lymph nodes along the portal vein in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas |
| 13 | Lymph nodes on the posterior surface of the pancreatic head cranial to the duodenal papilla |
| 14 | Lymph nodes along the superior mesenteric vein |
| 15 | Lymph nodes along the middle colic vessels |
| 16 | 16a1 Paraaortic lymph nodes in the diaphragmatic aortic hiatus |
| 16a2 Paraaortic lymph nodes between the upper margin of the origin of the celiac artery and the lower border of the left renal vein |
| 16b1 Paraaortic lymph nodes between the lower border of the left renal vein and the upper border of the origin of the inferior mesenteric artery |
| 16b2 Paraaortic lymph nodes between the upper border of the origin of the inferior mesenteric artery and the aortic bifurcation |
| 17 | Lymph nodes on the anterior surface of the pancreatic head beneath the pancreatic sheath |
| 18 | Lymph nodes along the inferior border of the pancreatic body |
| 19 | Infradiaphragmatic lymph nodes predominantly along the subphrenic artery |
| 20 | Paraesophageal lymph nodes in the diaphragmatic esophageal hiatus |

**Table 3 Extent of systematic lymphadenectomy in distal gastrectomy**

|  |  |
| --- | --- |
| **Lymph nodes dissection** | **Lymph node station n** |
| D0 | Lymphadenectomy less than D1 |
| D1 | 1, 3, 4sb, 4d, 5, 6 and 7 |
| D1+ | 1, 3, 4sb, 4d, 5, 6, 7, 8a and 9 |
| D2 | 1, 3, 4sb, 4d, 5, 6, 7, 8a, 9, 11p and 12a |

D: Extent of lymph nodes dissection.