ISSN 1948-9366 (online)

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2024 November 27; 16(11): 3381-3642

Published by Baishideng Publishing Group Inc

WJGS

World Journal of Gastrointestinal Surgery

Contents

Monthly Volume 16 Number 11 November 27, 2024

Contents

World Journal of Gastrointestinal Surgery

Monthly Volume 16 Number 11 November 27, 2024

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Surgery*, Andrea Cavallaro, MD, PhD, Doctor, Research Assistant Professor, Researcher, Department of Surgery and Medical Surgical Specialties, University of Catania, Catania 95123, Italy. andreacavallaro@tiscali.it

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS*, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc*.

INDEXING/ABSTRACTING

The *WJGS* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJGS* as 1.8; JIF without journal self cites: 1.7; 5-year JIF: 1.9; JIF Rank: 126/292 in surgery; JIF Quartile: Q2; and 5-year JIF Quartile: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Zi-Hang Xu*; **Production Department Director:** *Xiang Li*; **Cover Editor:** *Jia-Ru Fan*.

NAME OF JOURNAL
World Journal of Gastrointestinal Surgery

ISSN
ISSN 1948-9366 (online)

LAUNCH DATE
November 30, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Peter Schemmer

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-9366/editorialboard.htm

PUBLICATION DATE
November 27, 2024

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Gastrointestinal Surgery

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Surg 2024 November 27; 16(11): 3413-3424

DOI: 10.4240/wjgs.v16.i11.3413

ISSN 1948-9366 (online)

MINIREVIEWS

Risk factors and prevention of pancreatic fistula after laparoscopic gastrectomy for gastric cancer

Shan-Shan Liu, Hong-Yu Xie, Hao-Dong Chang, Liang Wang, Su Yan

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B

Novelty: Grade B

Creativity or Innovation: Grade B

Scientific Significance: Grade A

P-Reviewer: Cui H

Received: April 16, 2024

Revised: August 6, 2024

Accepted: August 16, 2024

Published online: November 27, 2024

Processing time: 196 Days and 21.6 Hours

Shan-Shan Liu, Hong-Yu Xie, Hao-Dong Chang, Liang Wang, Su Yan, Department of Gastrointestinal Oncology Surgery, The Affiliated Hospital of Qinghai University, Xining 810000, Qinghai Province, China

Corresponding author: Su Yan, Professor, Chief Doctor, Department of Gastrointestinal Oncology Surgery, The Affiliated Hospital of Qinghai University, No. 29 Tongren Road, Xining 810000, Qinghai Province, China. yansuxining@outlook.com

Abstract

Following laparoscopic gastrectomy (LG), one of the critical complications that can arise is a pancreatic fistula (PF). The inability to promptly prevent, diagnose, and manage this condition can lead to severe complications and potentially be life-threatening for the patient. The incidence of PF post-LG in gastric cancer treatment is related to factors such as surgical approach, surgical instruments, characteristics of the pancreas itself, tumor stage, and the surgeon's experience. Currently, the diagnosis of postoperative PF is mainly based on the definition and diagnostic criteria consensus established by the International Study Group of Pancreatic Surgery. Gastrointestinal surgeons should be aware of the risk factors for PF, perform LG for gastric cancer with great care and precision, avoid pancreatic injury, and actively work to reduce the risk of postoperative PF.

Key Words: Gastric cancer; Laparoscopic surgery; Pancreatic fistula; Risk factors; Prevention

Core Tip: Pancreatic fistula after laparoscopic gastrectomy can lead to serious complications and even endanger the patient's life. Therefore, it is of great significance to detail the risk factors connected to the onset of postoperative pancreatic fistula and to actively prevent it in order to accelerate postoperative recovery of patients and promote clinical work.

Citation: Liu SS, Xie HY, Chang HD, Wang L, Yan S. Risk factors and prevention of pancreatic fistula after laparoscopic gastrectomy for gastric cancer. *World J Gastrointest Surg* 2024; 16(11): 3413-3424
URL: https://www.wjgnet.com/1948-9366/full/v16/i11/3413.htm
DOI: https://dx.doi.org/10.4240/wjgs.v16.i11.3413

INTRODUCTION

In recent years, with the continuous development of scientific technology, the surgical system has been significantly improved, and laparoscopic gastrectomy (LG) is the commonly accepted surgical practice for gastric cancer (GC) treatment. Compared with open gastrectomy (OG), LG has reduced the incidence of common complications such as bleeding and wound infection, but the prevalence of postoperative pancreatic fistula (POPF) has been climbing[1].

Pancreatic fistula (PF) refers to a condition where pancreatic fluid leaks into the abdominal cavity from the pancreatic duct, pancreatic-intestinal/stomach anastomosis, or pancreatic parenchyma. POPF involves an atypical communication between the pancreatic ductal lining and another epithelial surface, with the output of pancreatic enzyme-rich fluid[2]. POPF following gastrointestinal surgery involves the leakage of pancreatic fluid resulting from damage to the pancreatic tissue, which differs fundamentally from leakage occurring at the pancreatic-intestinal junction after a pancreatic resection. In 2005, an international study group introduced the definition of POPF[2] as the drainage of any measurable volume of fluid through drains (whether surgically or percutaneously placed) starting from the 3rd day after surgery, if the amylase content of the fluid exceeds three times the normal upper limit of serum amylase levels.

The incidence of PF was reported to be 2.2% after LG[3], whereas it was 1.0% after OG (P = 0.04). National clinical database records from Japan show that LG tends to result in more PFs compared to OG[4]. Compared to OG, LG shows a higher incidence of PF, as reported by a recent meta-analysis (risk ratio = 2.44; 95% confidence interval: 1.08-5.50)[5]. The rate of POPF was 11.8% when using the pancreas compression technique in LG, while it was 2.2% when using the pancreas compressionless (PCL) technique[6]. A multicenter prospective study showed that PF occurred in 20.7% of patients after laparoscopic radical gastrectomy (sample size n = 2089)[7]. Therefore, the rate of PF development post-LG for GC remains significant. Pratt *et al*[8] found that as PFs advance from grade A to grade C, there is a corresponding rise in total hospitalization costs, length of hospital stay, duration of intensive care unit care, and overall resource use. The presence of a PF significantly affects patient recovery and prognosis, requiring heightened vigilance from surgeons.

The occurrence of POPF after LG for GC is not only related to the surgical approach but also to factors such as surgical instruments, characteristics of the pancreas itself, tumor location, tumor stage, and the surgeon's proficiency. Pancreatic fluid leakage due to a PF after LG can initiate a series of escalating and severe complications. Consequently, identifying and mitigating the risk factors for POPF is essential for accelerating patient recovery after surgery and improving clinical outcomes. This study provided an in-depth analysis of the risk factors and prevention of PF following GC surgery. It reviewed and synthesized earlier research, outlined the limitations of those studies, and presented clinical recommendations for preventing PF after LG.

RISK FACTORS FOR PF

Anatomy and texture of the pancreas

The individual anatomical features of the pancreas may vary slightly, but the presence of specific structural anomalies greatly affects the risk of POPF following laparoscopic GC surgery. Several retrospective studies[9-13] have used preoperative computed tomography (CT) measurements to determine the potential for POPF in laparoscopic gastric resection. These metrics include the length from the pancreatic surface to the hepatic artery root, the maximum vertical distance from the upper edge of the pancreas to the left gastric artery root, the maximum vertical length from the pancreatic surface to the aorta, the angle between the line from the upper edge of the pancreas to the celiac artery and the aorta root, and the degree of anterior protrusion of the pancreatic head.

The anatomical structure of the pancreas was identified as an independent factor in predicting PF and/or postoperative complications according to these studies. In addition, Hayashi *et al*[14] discovered that measuring the pancreatic thickness at the anterior ventral segment of the splenic artery arch can serve as a specific predictor for the risk of POPF and intra-abdominal infections in individuals who have had LG. The above studies indicate that it is very important to identify the anatomical position and/or specific anatomical features of the pancreas using preoperative CT images to prevent the occurrence of POPF in laparoscopic GC surgery.

POPF is more likely to occur in a softer pancreas rather than a pancreas that has already undergone fibrosis. Yeo *et al*[15] identified that the incidence of PF in patients with a harder pancreatic texture was 0%, while it increased to 25% in subjects with a softer pancreatic texture. Miedema *et al*[16] and Yang *et al*[17] also confirmed these findings. Regarding pancreatic fibrosis, Gaujoux *et al*[18] uncovered that the absence of pancreatic fibrosis is a risk factor for POPF. Later, Lee *et al*[19] induced local fibrosis in the pancreatic section in a rat model and found that pancreatic fibrosis was increased by ethanol and octreotide injection into the pancreatic parenchyma. Unlike octreotide, ethanol causes local fibrosis. Therefore, it is expected that ethanol injection can eliminate PF after pancreatic surgery, but there is limited research in this area. Furthermore, fewer discussions have been made about pancreatic fibrosis, and the author argued that it was necessary to develop further analyses to explore these elements.

There is no dedicated research indicating that pancreatic fat infiltration directly causes PFs, but the added softness of the pancreatic tissue due to fat infiltration might contribute to the risk of developing fistulas. Mathur *et al*[20] observed that patients with post-surgical PFs were more likely to exhibit elevated pancreatic fat levels. Their study revealed a significant negative relationship between fat content and fibrosis ($P < 0.001$), implying that greater fat content correlates with a softer pancreas and less fibrosis. Evidence from several studies[18,21-23] suggests that pancreatic fat infiltration is related to the development of POPF. To assess pancreatic fat infiltration, researchers recommend employing CT imaging and carrying out necessary lymph node dissection to lower the chances of POPF[22,24]. By utilizing these predictive factors, surgeons can identify patients at high risk for developing PFs post-surgery earlier, thereby helping to lower the incidence of POPF and implement preventive strategies.

Analyses have investigated the risk factors for PF after LG, with a focus on the anatomy and texture of the pancreas. These studies indicate that certain anatomical features and pancreatic texture are independent predictors of POPF. Thus, before conducting surgical procedures, gastroenterologists assess the pancreas through CT scans. This procedure is an uncomplicated and trustworthy way to predict the occurrence of PF after LG. Achieving expertise in the structure of the abdomen, precisely detaching the pancreas from nearby structures, and safeguarding the pancreas from unintentional harm during surgery could prevent PFs. Surgeons should refrain from performing extensive lymph node dissection during pancreatic lymph node clearance to avoid complications like PF following LG for GC.

Patient's physical condition

Being obese is correlated with the onset of several diseases and increases the risk of PF after LG for GC. Multiple studies have identified that male patients, high body mass index, elevated triglycerides, and increased visceral fat area are risk factors for PF following gastrectomy surgery[1,12,25,26]. Male patients with a high body mass index, in particular, should be wary of LG. In patients with obesity, the unclear demarcation between the pancreas and surrounding adipose tissue makes lymph node dissection during surgery more difficult and increases the likelihood of pancreatic injury and PF.

Martiniuc *et al*[27] also examined the incidence and risk factors for PF post-D1 +/D2 gastrectomy among Eastern European patients. Their research identified cardiovascular complications as the sole independent predictor of POPF formation ($P = 0.024$). Thus, physicians should consider chronic comorbidities as significant factors in disease prevention and treatment.

Tumor location and tumor staging of GC

The location of the GC tumor impacts the risk of developing POPF. This is due to the possibility of suturing or resecting the pancreatic-gastric duct during a gastrectomy, which may cause the pancreatic duct to rupture or experience a sudden pressure spike, causing pancreatic fluid to leak into the surgical wound and form a PF. Tumors positioned on the back wall of the stomach or at the pylorus are more likely to interfere with the pancreatic duct and bile duct, owing to the anatomy of the stomach and its close connection to the pancreas, thereby increasing the risk of pancreatic injury and fluid leakage. In 2021, however, Martiniuc *et al*[27] concluded that the location of GC tumors (upper, middle, lower third of the stomach, $P = 0.608$) has no effect on the formation of POPF, which supports previous research outcomes[25,28]. The author maintains that the association between the location of GC tumors and POPF needs further examination.

In addition, the location of the tumor determines the type of surgery surgeons may perform, which includes laparoscopic total gastrectomy, laparoscopic proximal gastrectomy, and laparoscopic distal gastrectomy. The incidence of POPF may vary depending on the surgical approach. Katai *et al*[29] were the pioneers in conducting a prospective study to assess the safety of proximal or total gastrectomy for clinical stage I GC. The study reported a 2% incidence of POPF. Two comparable studies[30,31] reported POPF rates of 12.0% for laparoscopic total gastrectomy and 3.4% for laparoscopic distal gastrectomy in advanced GC. A different study demonstrated that POPF occurs more frequently in patients who have had a total gastrectomy[32]. The higher incidence of POPF in total gastrectomy compared to distal gastrectomy might be due to pancreatic injury caused by the procedure, particularly when combined with lymph node dissection.

Moreover, advanced GC patients face a significant risk of developing low-grade PF, as lymph node dissection is essential during surgery, particularly in the upper pancreatic area. The intricate surgical techniques involved, including pancreatic compression and exposure of the portal and splenic veins, are anticipated to elevate the chances of intra-abdominal bleeding, fluid buildup, and PF[33]. Research by Martiniuc *et al*[27] showed that there is no link between the T staging of GC tumors and the occurrence of POPF, in line with earlier evidence[28,34]. On the flip side, research conducted by Katai *et al*[35] in Japan and Yu *et al*[32] has indicated that the incidence of POPF correlates with clinical T staging, evidenced by P values of 0.007 and < 0.001. This correlation suggests a higher incidence of POPF with advanced T stages. More exploration is warranted to delve into this issue.

In the final analysis, radical surgery remains the cornerstone of therapy for advanced GC[36]. A study[32] showed that the occurrence of POPF in patients with advanced GC is greater than that in those with early-stage disease (6.5% *vs* 1.1%). In the JLSSG0901 trial conducted in Japan[30], the incidence of POPF after LG treatment for advanced GC was 3.4%. The CLASS01 trial conducted in China[36] and the KLASS02 trial conducted in Korea[33] reported POPF incidences of 0.4% *vs* 0.0% and 1.9% *vs* 0.6%, respectively, following LG and OG treatments for advanced GC. Moreover, a review of past cases found that the overall rate of POPF after totally laparoscopic total gastrectomy for advanced GC patients was 13.0%[31]. The higher incidence of POPF in advanced GC, as compared to early GC, is related to the necessity for a more extensive lymph node dissection. Hence, surgeons are advised to proceed with increased caution when conducting surgery on patients with advanced GC.

Factors related to surgical injuries

Following the initial description of LG by Kitano *et al*[37] in 1994, its application in treating GC has become widespread, particularly for early GC. Laparoscopy delivers sharp and magnified visuals, allowing for careful lymph node dissection, especially in the regions of the lower pylorus and the upper pancreas[6]. Even though standard radical gastrectomy avoids direct surgical contact with the pancreas, lymph node dissection in the upper pancreatic area is intimately connected to it. Multiple studies have demonstrated that PF occurs more frequently after LG than after OG[3,9,38]. This increased incidence is attributed to the constraints of laparoscopic instruments and the presence of blind spots during surgery. The anatomy around the pancreas is intricate, and the precise removal of lymph nodes in the upper area necessitates advanced skills, which can easily result in pancreatic injury and the formation of a PF.

In LG, clamping the gauze or sponges are needed to compress the pancreas, which can cause blunt pancreatic injury. When performing lymph node dissection in the upper region of the pancreas, the pancreas is frequently and continuously compressed to maintain a clear view of the surgical field, considering its anatomical location. In 2017, Tsujiura *et al*[6] performed a PCL gastrectomy in which the assistant controlled the position of the pancreas by pulling the mesentery below the pancreas or the nerves around the aorta above the pancreas. The PCL technique, as opposed to the pancreas compression technique, in laparoscopic radical gastrectomy for GC markedly reduces the amylase concentration in drainage fluid on postoperative days 1 and 3 (P < 0.001 and P < 0.013, respectively) and decreases the incidence of severe PF (Figure 1A and 1B). This study delivers the first proof of the correlation between pancreatic compression and non-compression and amylase levels in postoperative drainage fluid, unveiling the potential mechanism of pancreatic injury.

Subsequently, a study using a large animal model[39] and a retrospective study[40] both found that direct compression of the pancreas can cause blunt injury to the pancreas, leading to pancreatic fluid leakage. Pancreatic fluid is corrosive and can erode surrounding blood vessels and tissues when it flows into the abdominal cavity, causing more severe complications. Moreover, minimizing contact with the pancreas during lymph node dissection around the pancreatic area can avert postoperative pancreatic injury that might result in a PF. In 2021, Ebihara *et al*[41] introduced a novel technique in lymph node dissection for GC above the pancreas called the preemptive retropancreatic approach, which minimizes pressure on the pancreas when using multi-joint forceps during robotic distal gastrectomy. The authors reported the practicality of this technique in GC surgery.

The above studies suggest that the use of PCL in laparoscopic GC surgery is safer, can lower the risk of PF, and thereby reduce the inflammatory response and other postoperative complications that follow. Nevertheless, evidence supporting the use of non-pancreatic compression methods in LG to lower the rate of POPF is limited. The author advocates for multicenter, prospective, randomized controlled studies to validate this approach.

In addition, during the process of LG combined with lymph node dissection, frequent use of ultrasonic knife for continuous separation will inevitably cause thermal injury to the pancreas. The degree of thermal injury to the pancreas will also be higher[42]. Domestic scholars[7] found in a national prospective multicenter cohort study that patients using Liga Sure vessel sealing system were prone to PF. Therefore, the use of energy devices is another important cause of pancreatic injury.

The surgeon’s level of experience may ultimately play a role as a risk factor for POPF. Birkmeyer *et al*[43] concluded that surgeons with higher technical scores had fewer postoperative complications compared to those with lower technical scores. Casciani *et al*[44] analyzed the impact of surgeons’ personal experience on the outcomes of pancreaticoduodenectomy and found that surgeons with more experience had lower rates of POPF. Laparoscopic surgery is a technically advanced and steep learning curve procedure, and the proficiency of surgeons is an important factor affecting surgical outcomes. Therefore, efforts to improve surgeons’ surgical skills are crucial in reducing postoperative complications. However, research in this area is still limited, and further investigation is needed.

Surgical approach

The main determinant of PF occurrence after radical gastrectomy is the type of surgical approach used. The prevalence of POPF after OG is relatively low. This may be related to the fact that open surgery can provide a broader surgical field, allowing the surgeon to observe and handle the tissues around the pancreas more intuitively. Additionally, the direct touch and feel during open surgery help the surgeon to more accurately judge the texture and tension of the tissues. The general location of the tumor can be easily determined and completely resected. The pulsation of large arteries can also be easily felt, and bleeding vessels can be clamped between fingers to achieve hemostasis, thereby avoiding unnecessary damage. Nevertheless, in LG, the inability to palpate organs and the restricted surgical angle and field of view are inherent limitations of the laparoscope[45]. Accordingly, the prevalence of POPF grows.

Compared to LG, robotic gastrectomy (RG) can further minimize trauma to the pancreas, making it a viable and safe method for treating GC, and it can lessen the probability of POPF. The specific advantages are as follows. Firstly, in robotic surgery, the diameter of the surgical instruments is smaller, and the operation is more precise, allowing for more delicate protection of the pancreas and surrounding tissues. Secondly, during robotic surgery, smaller surgical incisions and more precise surgical instruments are used, and the robotic arm is employed for operation, which can minimize interference and trauma to the pancreas to the greatest extent. Compared to laparoscopic surgery, robotic surgery allows for more precise operations, protecting the pancreas and reducing damage to it.

A retrospective analysis by Japanese scholars[46] found that patients who underwent RG did not develop POPF, while POPF was observed in 4.7% of LG instances. Chinese researchers carried out a retrospective comparison[47] of the efficacy of robotic-assisted distal gastrectomy and laparoscopic-assisted distal gastrectomy combined with D2 lymph node dissection for advanced GC. They found that the robotic-assisted distal gastrectomy group had a lower incidence of POPF (2.8% *vs* 0.4%, P = 0.044) compared to the laparoscopic-assisted distal gastrectomy group. A randomized controlled trial[48] and a meta-analysis[49] both demonstrated that patients in the RG group exhibited a lower postoperative morbidity rate. However, Teranishi *et al*[50] reported that RG resulted in fewer cases of POPF compared to LG; however, this difference did not reach statistical significance (P = 0.12). This aligns with previous research findings[51-53].

Robotic surgery has not yet been fully implemented for gastrectomy without compressing the pancreas. The observation angle of the rigid endoscope is limited, compelling the mechanical arm to compress the pancreas. Due to the lack of tactile feedback, the mechanical arm often applies considerable pressure to compress the pancreas[54], which may increase the occurrence of PF. Although robot-assisted surgery can overcome some of the disadvantages associated with laparoscopic surgery, there is still limited evidence regarding better clinical outcomes after robot-assisted surgery. The author argued that before further promoting robot-assisted surgery, more rigorous research is needed to explore its benefits for patients (Table 1 presents the rate of PF occurrence following gastric resection).

To conclude, the risk of POPF in patients who have had gastrectomy is determined by several factors. It is important for healthcare professionals to identify these risk factors early and take appropriate measures to reduce the likelihood of POPF in patients with GC.

DIAGNOSIS CRITERIA AND MANAGEMENT PRINCIPLES OF PF

Due to the different understanding of POPF, there are significant differences in the diagnostic criteria among various research centers. In 2005, the International Study Group of Pancreatic Surgery (ISGPS) issued a consensus on how to define and grade POPF[2]. A definitive definition of POPF was introduced: Drainage fluid with an amylase content greater than three times the upper limit of normal serum amylase, measured through surgical or percutaneous drains 3 days or more after the operation. The severity of PF is divided into 3 grades (Table 2), with higher grades indicating more severe fistula: Grade A PF: The most prevalent type, often referred to as “transient fistula.” It deviates slightly from the clinical pathway and has minimal clinical impact; Grade B PF (B-POPF): Deviates significantly from the clinical pathway, accompanied by abdominal pain, fever, and/or higher levels of leukocytes on the basis of Grade A PF. This type of PF can be stabilized with active treatment. If interventional surgery is required, it becomes a Grade C PF (C-POPF); and C-POPF: Severely deviates from the clinical pathway, often accompanied by sepsis and organ failure, with a possibility of postoperative mortality. The definition and diagnostic criteria for POPF provided by the 2005 consensus have been widely used domestically and internationally. However, some deficiencies in its application have gradually emerged in clinical practice.

In 2016, ISGPS made updates to address the deficiencies of this consensus (Table 3 and Figure 2)[55]. The consensus update adds a new requirement to the definition of POPF, which now includes “manifestation of specific clinical impacts and the need for active clinical management,” alongside the original criterion of “drainage fluid amylase levels surpassing three times the normal serum amylase upper limit 3 days or more postoperatively,” when compared to the 2005 version. Therefore, the condition is labeled clinically-relevant POPF to reflect its impact on clinical outcomes.

The term “Grade A PF” has been updated to “biochemical leakage,” indicating that it has no clinical impact and is not classified as a true PF. This change only requires a minor extension in the period for drainage tube removal without any need for special treatment. Further clarification was made on the diagnostic criteria for B-POPF and C-POPF. B-POPF refers to a PF that requires drainage tube placement for more than 3 weeks, or requires changes in postoperative treatment, or requires percutaneous or endoscopic drainage, or causes PF-related bleeding requiring blood transfusion and/or angiography, or causes mild infection without organ failure. C-POPF refers to a B-POPF that requires reoperation, or causes organ failure, or results in specific death. This update promotes the widespread application of the definition and diagnostic criteria for POPF developed by the ISGPS in the field of surgery.

Regarding the grading of POPF, the industry tends to use the Clavien-Dindo classification[56-58] (Table 4) instead of the classification standards established by ISGPS. Domestic scholars tend to recommend a modified version of the Clavien-Dindo classification[59].

PREVENTION OF PF

Firstly, by reviewing the preoperative CT images of the patient and evaluating certain specific structures of the pancreas, high-risk patients who may develop PF after surgery can be identified, which helps prevent the occurrence of PF.

Secondly, in recent years, obesity has become increasingly serious. Obesity is not only an independent disease but also an important risk factor for various chronic diseases such as cardiovascular disease, diabetes, and hypertension. Therefore, surgeons should promote health education to patients and their families as much as possible, emphasizing the importance of diet, exercise, and developing good lifestyle habits. For patients with chronic diseases such as respiratory and cardiovascular diseases, regular check-ups and proactive prevention are recommended.

Thirdly, laparoscopic GC surgery is favored for its less invasive approach, aesthetic appeal, and quick recovery time. However, there is an increasing occurrence of POPF, which is one of the significant complications post-surgery. The likelihood of developing a PF is largely dependent on the surgical technique used. Surgeons should fully evaluate the patient’s condition and the tumor site before performing the surgery and choose the appropriate surgical approach. Emerging robotic surgery applications are becoming more common in clinical practice, and the incidence of postoperative complications is reduced compared to laparoscopy. Therefore, robot-assisted surgery can be performed on patients when conditions permit. In addition, energy devices such as ultrasonic knives are essential surgical instruments in laparoscopic GC surgery, and surgeons should try to avoid direct contact between these energy devices and the pancreas during the operation, as they can cause thermal damage to the pancreas and induce PF. To conclude, reducing the prevalence of postoperative pancreatic injury-related complications is of great significance for accelerating postoperative recovery and reducing the psychological and economic burden on patients.

Table 1 Incidence of pancreatic fistula after gastric cancer surgery

Ref.	Year	Incidence %	Patient total	Surgical approach	Study type
Hiki *et al*[3]	2018	2.2	1067	LDG for GC	Multicenter prospective randomized controlled trial
		1.0	1067	ODG for GC	
Inaki *et al*[30]	2015	3.4	86	LG for AGC	Multicenter prospective randomized controlled trial
Nakauchi *et al*[31]	2016	13	92	TLTG for AGC	Single-center retrospective study
Yu *et al*[32]	2013	0.4	490	LDG/LPG for GC	Single-center retrospective study
		1.7	236	ODG/OPG for GC	
		3.8	79	LTG for GC	
		22.2	86	OTG for GC	
Lee *et al*[33]	2019	1.9	526	LDG for AGC	Multicenter prospective randomized controlled trial
		0.6	524	ODG for AGC	
Hu *et al*[36]	2016	0.4	519	LDG + D2 for AGC	Multicenter prospective randomized controlled trial
		0.0	520	ODG + D2 for AGC	
Obama *et al*[38]	2011	7.2	138	LG for GC	Single-center retrospective study
		2.1	95	OG for GC	
Ojima *et al*[46]	2019	4.7	639	LG for GC	Single-center retrospective study
		0.0	20	RG for GC	
Ye *et al*[47]	2020	2.8	285	LDG for AGC	Single-center retrospective study
		0.4	285	RDG for AGC	

AGC: Advanced gastric cancer; D2: Lymph node dissection; GC: Gastric cancer; LDG: Laparoscopic distal gastrectomy; LG: Laparoscopic gastrectomy; LPG: Laparoscopic proximal gastrectomy; LTG: Laparoscopic total gastrectomy; ODG: Open distal gastrectomy; OG: Open gastrectomy; OPG: Open proximal gastrectomy; OTG: Open total gastrectomy; RDG: Robotic distal gastrectomy; RG: Robotic gastrectomy; TLTG: Totally laparoscopic total gastrectomy.

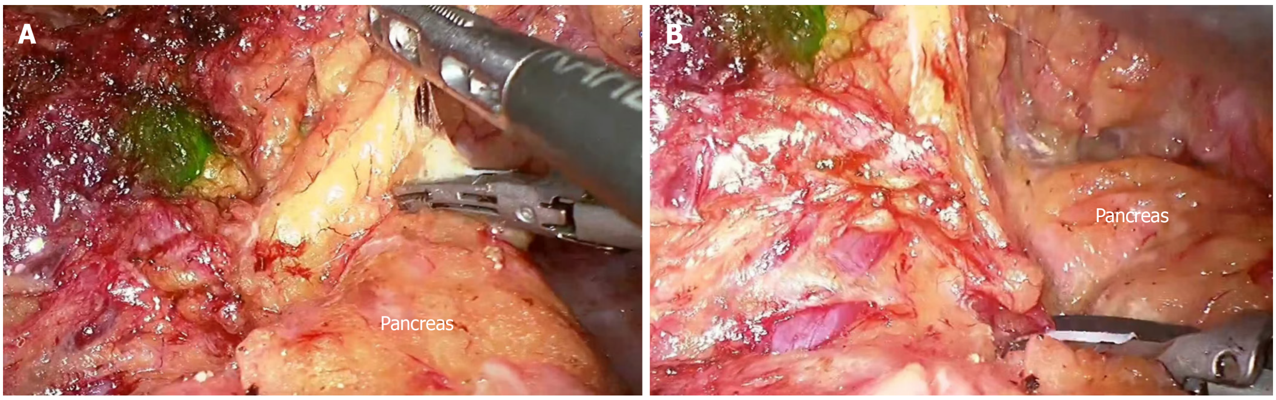

Figure 1 Laparoscopic gastric resection. A: Using pancreas compressionless technique; B: Using pancreas compression technique.

Fourthly, regarding the pharmacological prevention of PF, multiple studies have shown that specific drugs (such as octreotide/antibiotics, *etc.*) can prevent POPF, most of which are related to the prevention of PF after pancreatic resection/pancreaticoduodenectomy, while data on pharmacological prevention after LG are relatively lacking. Additionally, PF formation after gastrectomy is commonly related to tumor stage and local invasion, making preoperative chemotherapy and nutritional support viable treatment options. A study found that patients receiving preoperative chemotherapy showed a diminished incidence of PF[60]. American scholar Fuentes *et al*[61] retrospectively analyzed patients with esophagogastric junction tumors and found that compared to surgery alone, neoadjuvant chemotherapy did not significantly increase the risk of intraoperative complications and postoperative mortality. During that year, Kosaka *et al*[62] observed that the incidence rate of POPF was elevated in patients subjected to neoadjuvant chemotherapy relative to those who underwent surgical procedures alone (P = 0.011). Currently, there is insufficient

Table 2 Key parameters for postoperative pancreatic fistula grading[2]

Grade	A	B	C
Clinical conditions	Well	Often well	Appearing/bad
Specific treatment[1]	No	Yes/no	Yes
US/CT (if obtained)	Negative	Negative/positive	Positive
Persistent drainage > 3 weeks[2]	No	Usually yes	Yes
Reoperation	No	No	Yes
Death related to POPF	No	No	Possibly yes
Possibly yes	No	Yes	Yes
Sepsis	No	No	Yes
Readmission	No	Yes/no	Yes/no

[1]Partial (peripheral) or total parenteral nutrition, antibiotics, enteral nutrition, somatostatin analogs, and/or minimal invasive drainage.
[2]With or without a drain *in situ*.
CT: Computed tomographic scan; POPF: Postoperative pancreatic fistula; US: Ultrasonography.

Table 3 Revised 2016 International Study Group of Pancreatic Surgery classification and grading of postoperative pancreatic fistula: Checklist for clinical use[55]

Event	BL	Grade B POPF[1]	Grade C POPF[1]
Increased amylase activity > 3 times upper limit institutional normal serum value	Yes	Yes	Yes
Persisting peripancreatic drainage > 3 weeks	No	Yes	Yes
Clinically relevant change in management of POPF[2]	No	Yes	Yes
POPF percutaneous or endoscopic specific interventions for collections	No	Yes	Yes
Angiographic procedures for POPF related bleeding	No	Yes	Yes
Reoperation for POPF	No	No	Yes
Signs of infection related to POPF	No	Yes, without organ failure	Yes, with organ failure
POPF related organ failure[3]	No	No	Yes
POPF-related death	No	No	Yes

[1]A clinically relevant postoperative pancreatic fistula is defined as a drain output of any measurable volume of fluid with an amylase level greater than 3 times the upper Institutional normal serum amylase level, associated with a clinically relevant development/condition related directly to the postoperative pancreatic fistula.
[2]Suggests prolongation of hospital or intensive care unit stay, including use of therapeutic agents specifically employed for fistula management or its consequences (of these: somatostatin analogs, total parenteral nutrition/total enteral nutrition, blood product transfusion, or other medications).
[3]Postoperative organ failure is defined as the need for re-intubation, hemodialysis, and/or inotropic agents > 24 h for respiratory, renal, or cardiac insufficiency, respectively.
BL: Biochemical leak; POPF: Postoperative pancreatic fistula.

research on the role of preoperative chemoradiotherapy in reducing the incidence of POPF. Future large-scale investigations should aim to clarify the impact of chemoradiotherapy on the development of PF after LG for GC.

Evidence suggests that octreotide administration in the perioperative phase can reduce the rate of POPF following pancreatic surgery[63-66]. Despite this, research has demonstrated that using octreotide prophylactically does not decrease the frequency of POPF after pancreaticoduodenectomy[15,60,67]. In response to the above controversy, Tilak *et al*[68] pointed out in their study evaluating the role of octreotide in preventing POPF that there is considerable heterogeneity in the research results due to different definitions of POPF used by early researchers, different surgical techniques such as distal pancreatectomy and pancreaticoduodenectomy, the use of somatostatin and its analogues, different levels of surgical experience, and single-center/multicenter studies, *etc*., and the results are still inconclusive. Data shows that the new generation somatostatin analogues have good efficacy, but further research is needed. As for whether prophylactic use of octreotide after pancreaticoduodenectomy can reduce the occurrence of POPF, the author concluded that further research is needed to confirm.

Table 4 Clavien-Dindo classification[56]

Grades	Definition
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: Drugs as antiemetics, antipyretics, analgesics, diuretics and electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
II	Requiring pharmacological treatment with drugs other than such allowed for Grade I complications. Blood transfusions and total parenteral nutrition are also included
III	Requiring surgical, endoscopic, or radiological intervention
IIIa	Intervention not under general anesthesia
IIIb	Intervention under general anesthesia
IV	Life-threatening complication (including CNS complications: Brain hemorrhage, ischemic stroke, subarachnoid bleeding, but excluding transient ischemic attacks) requiring IC/ICU management
IVa	Single organ dysfunction (including dialysis)
IVb	Multi-organ dysfunction
V	Death of the patient
Suffix "d"	If the patient suffers from a complication at the time of discharge, the suffix 'd' (for 'disability') is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication

CNS: Central nervous system; IC: Intermediate care; ICU: Intensive care unit.

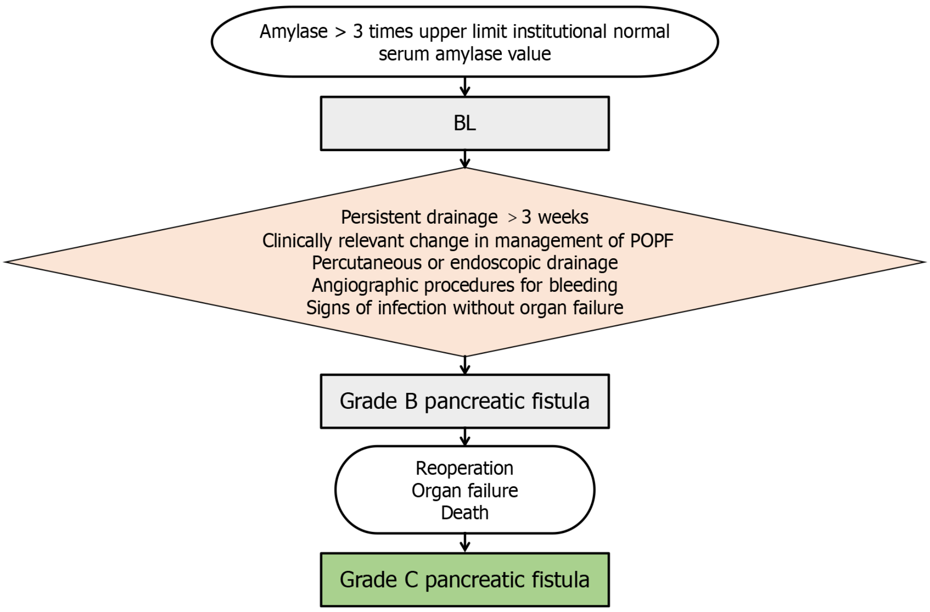

Figure 2 Flowchart of the definition of biochemical leak and postoperative pancreatic fistula grades. BL: Biochemical leak; POPF: Postoperative pancreatic fistula.

Scholars in 2004 found that somatostatin and octreotide were equally effective in closing PFs, with no significant difference between the two (84% *vs* 65%, P = 0.255)[69]. No substantial difference in closure rates was noted by Gans *et al*[70] when comparing the use of somatostatin and its analogues to the control group in treating PFs. No conclusive evidence exists to indicate that new somatostatin analogues can increase the closure rates of PF.

The use of antibiotics is common in clinical practice. Researchers[71] found that the use of antibiotics in abdominal lavage fluid after pancreaticoduodenectomy did not lower the rate of PF development. However, a recent study[72] found that implementing extended antibiotic therapy (10 days of broad-spectrum antibiotics) in patients who are highly susceptible to POPF resulted in a lower incidence of POPF (11.8% *vs* 37.7%) compared to patients receiving standard perioperative antibiotics. Additional trials with randomized control are needed to analyze how effective antibiotic prophylaxis is for preventing POPF.

In a 2013 study, Hiura *et al*[73] prospectively evaluated the application of fibrin glue sealant and polyglycolic acid sheets to avert the development of PFs post-gastrectomy. The findings unveiled that patients with fibrin glue sealant and polyglycolic acid sheets covering the pancreatic surface after pancreaticoduodenectomy with lymph node dissection had no POPF compared to the control group (P = 0.049). A decade later, Iwasaki *et al*[74] and Ri *et al*[75] arrived at the same conclusion: Covering the lymph node dissection area with a polyglycolic acid sheet post-LG surgery significantly reduces pancreas-related complications and can lower the incidence of POPF. Presently, there are limited studies on this topic, necessitating further investigation in the future.

Finally, the enhanced recovery after surgery program has garnered more backing from surgeons as it strives to diminish surgical trauma, expedite recovery, shorten hospital stays, and reduce the psychological and financial impacts on patients through uniform management practices before, during, and after surgery. The author concluded that adopting this program may also help reduce the incidence of POPF, but there was currently no research on this aspect.

Both nationally and internationally, research on how to prevent PF after laparoscopic GC surgery is limited, but it is an area worth exploring. Therefore, the author held the view that further research can be conducted to explore the prevention of PF after LG.

CONCLUSION

Factors such as patient-related issues, surgeon expertise, surgical approach, and perioperative care are all linked to the incidence of PF following LG for GC. It is important to perform a preoperative evaluation of GC patients, especially the anatomical relationship between the tumor and the pancreas as well as the morphological characteristics of the pancreas. Proper and standardized usage of energy devices by surgeons is essential to prevent thermal injury to the pancreas, thereby reducing the likelihood of PFs. Developing a reasonable surgical plan can minimize the trauma caused to patients by the surgery itself. In addition, early diagnosis and detection of PF, and the implementation of proactive and effective treatment measures, are important for reducing the risks associated with PF. To better understand the mechanisms behind PFs and to develop effective diagnostic and treatment strategies, it is essential to conduct well-designed basic and clinical research. Such advancements could significantly impact the frequency of post-gastrectomy complications and have profound implications for the prognosis and survival outcomes of GC patients. Research on POPF following LG in China is relatively scarce. Thus, conducting this research domestically is essential to understand the risk factors for POPF following laparoscopic GC surgery, formulate tailored prevention strategies for our population, and offer clinical recommendations for optimizing surgical techniques and patient outcomes.

ACKNOWLEDGEMENTS

We acknowledge and appreciate our colleagues for their valuable suggestions for this minireview.

FOOTNOTES

Author contributions: Yan S proposed the title of the article and reviewed the manuscript; Liu SS wrote the manuscript; Xie HY and Chang HD reviewed the literature; Wang L revised the manuscript for important intellectual content; All authors read and approved the final manuscript.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest.

Country of origin: China

ORCID number: Liang Wang 0000-0002-4206-5043; Su Yan 0000-0003-1351-3393.

S-Editor: Fan M
L-Editor: Filipodia
P-Editor: Wang WB

REFERENCES

1 **Nobuoka D**, Gotohda N, Konishi M, Nakagohri T, Takahashi S, Kinoshita T. Prevention of postoperative pancreatic fistula after total gastrectomy. *World J Surg* 2008; **32**: 2261-2266 [PMID: 18670802 DOI: 10.1007/s00268-008-9683-9]

2 **Bassi C**, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J, Sarr M, Traverso W, Buchler M; International Study Group on Pancreatic Fistula Definition. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 2005; **138**: 8-13 [PMID: 16003309 DOI: 10.1016/j.surg.2005.05.001]

3 **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]

4 **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]

5 **Bittar V**, Boneli MF, Reis PCA, Felix N, Braga MAP, Rocha KM, Fogaroli LO, Costa GB, Comini AC, Amaral G, Marini DC, Camandaroba MPG. Laparoscopic Versus Open Gastrectomy for Advanced Gastric Cancer: A Meta-Analysis of Randomized Controlled Trials. *J Gastrointest Cancer* 2024; **55**: 652-661 [PMID: 38564116 DOI: 10.1007/s12029-024-01048-0]

6 **Tsujiura M**, Hiki N, Ohashi M, Nunobe S, Kumagai K, Ida S, Okumura Y, Sano T, Yamaguchi T. "Pancreas-Compressionless Gastrectomy": A Novel Laparoscopic Approach for Suprapancreatic Lymph Node Dissection. *Ann Surg Oncol* 2017; **24**: 3331-3337 [PMID: 28699131 DOI: 10.1245/s10434-017-5974-4]

7 **Wu J**, Tang Z, Zhao G, Zang L, Li Z, Zang W, Li Z, Qu J, Yan S, Zheng C, Ji G, Zhu L, Zhao Y, Zhang J, Huang H, Hao Y, Fan L, Xu H, Li Y, Yang L, Song W, Zhu J, Zhang W, Li M, Qin X, Liu F. Incidence and risk factors for postoperative pancreatic fistula in 2089 patients treated by radical gastrectomy: A prospective multicenter cohort study in China. *Int J Surg* 2022; **98**: 106219 [PMID: 34990829 DOI: 10.1016/j.ijsu.2021.106219]

8 **Pratt WB**, Maithel SK, Vanounou T, Huang ZS, Callery MP, Vollmer CM Jr. Clinical and economic validation of the International Study Group of Pancreatic Fistula (ISGPF) classification scheme. *Ann Surg* 2007; **245**: 443-451 [PMID: 17435552 DOI: 10.1097/01.sla.0000251708.70219.d2]

9 **Kumagai K**, Hiki N, Nunobe S, Kamiya S, Tsujiura M, Ida S, Ohashi M, Yamaguchi T, Sano T. Impact of anatomical position of the pancreas on postoperative complications and drain amylase concentrations after laparoscopic distal gastrectomy for gastric cancer. *Surg Endosc* 2018; **32**: 3846-3854 [PMID: 29435751 DOI: 10.1007/s00464-018-6114-3]

10 **Migita K**, Matsumoto S, Wakatsuki K, Ito M, Kunishige T, Nakade H, Nakatani M, Kitano M, Nakajima Y. The anatomical location of the pancreas is associated with the incidence of pancreatic fistula after laparoscopic gastrectomy. *Surg Endosc* 2016; **30**: 5481-5489 [PMID: 27126620 DOI: 10.1007/s00464-016-4909-7]

11 **Kinoshita J**, Yamaguchi T, Saito H, Moriyama H, Shimada M, Terai S, Okamoto K, Nakanuma S, Makino I, Nakamura K, Tajima H, Ninomiya I, Fushida S. Comparison of prognostic impact of anatomic location of the pancreas on postoperative pancreatic fistula in laparoscopic and open gastrectomy. *BMC Gastroenterol* 2020; **20**: 325 [PMID: 33023478 DOI: 10.1186/s12876-020-01476-9]

12 **Kumagai K**, Nunobe S, Hiki N, Hayami M, Ishizuka N, Ida S, Makuuchi R, Jiang X, Ohashi M, Sano T. Anatomical Position of the Pancreas as a Risk Factor for Pancreatic Fistula after Laparoscopic Gastrectomy for Gastric Cancer. *World J Surg* 2023; **47**: 1744-1751 [PMID: 36964789 DOI: 10.1007/s00268-023-06972-z]

13 **Kobayashi N**, Shinohara H, Haruta S, Ohkura Y, Mizuno A, Ueno M, Udagawa H, Sakai Y. Process of Pancreas Head as a Risk Factor for Postoperative Pancreatic Fistula in Laparoscopic Gastric Cancer Surgery. *World J Surg* 2016; **40**: 2194-2201 [PMID: 27142626 DOI: 10.1007/s00268-016-3536-8]

14 **Hayashi K**, Inaki N, Sakimura Y, Yamaguchi T, Obatake Y, Terai S, Kitamura H, Kadoya S, Bando H. Pancreatic thickness as a predictor of postoperative pancreatic fistula after laparoscopic or robotic gastrectomy. *Surg Endosc* 2023; **37**: 5358-5367 [PMID: 36997651 DOI: 10.1007/s00464-023-10021-0]

15 **Yeo CJ**, Cameron JL, Lillemoe KD, Sauter PK, Coleman J, Sohn TA, Campbell KA, Choti MA. Does prophylactic octreotide decrease the rates of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo-controlled trial. *Ann Surg* 2000; **232**: 419-429 [PMID: 10973392 DOI: 10.1097/00000658-200009000-00014]

16 **Miedema BW**, Sarr MG, van Heerden JA, Nagorney DM, McIlrath DC, Ilstrup D. Complications following pancreaticoduodenectomy. Current management. *Arch Surg* 1992; **127**: 945-9; discussion 949 [PMID: 1353671 DOI: 10.1001/archsurg.1992.01420080079012]

17 **Yang YM**, Tian XD, Zhuang Y, Wang WM, Wan YL, Huang YT. Risk factors of pancreatic leakage after pancreaticoduodenectomy. *World J Gastroenterol* 2005; **11**: 2456-2461 [PMID: 15832417 DOI: 10.3748/wjg.v11.i16.2456]

18 **Gaujoux S**, Cortes A, Couvelard A, Noullet S, Clavel L, Rebours V, Lévy P, Sauvanet A, Ruszniewski P, Belghiti J. Fatty pancreas and increased body mass index are risk factors of pancreatic fistula after pancreaticoduodenectomy. *Surgery* 2010; **148**: 15-23 [PMID: 20138325 DOI: 10.1016/j.surg.2009.12.005]

19 **Lee SH**, Hong TH. Pancreatic parenchymal injection of ethanol and octreotide to induce focal pancreatic fibrosis in rats: Strategies to eliminate postoperative pancreatic fistula. *Hepatobiliary Pancreat Dis Int* 2018; **17**: 81-85 [PMID: 29428110 DOI: 10.1016/j.hbpd.2018.01.009]

20 **Mathur A**, Pitt HA, Marine M, Saxena R, Schmidt CM, Howard TJ, Nakeeb A, Zyromski NJ, Lillemoe KD. Fatty pancreas: a factor in postoperative pancreatic fistula. *Ann Surg* 2007; **246**: 1058-1064 [PMID: 18043111 DOI: 10.1097/SLA.0b013e31814a6906]

21 **Sato Y**, Inokuchi M, Otsuki S, Fujimori Y, Kojima K. Risk Factor of Pancreatic Fistula after Radical Gastrectomy from the Viewpoint of Fatty Pancreas. *Dig Surg* 2017; **34**: 455-461 [PMID: 28196352 DOI: 10.1159/000455332]

22 **Tanaka K**, Yamada S, Sonohara F, Takami H, Hayashi M, Kanda M, Kobayashi D, Tanaka C, Nakayama G, Koike M, Fujiwara M, Kodera Y. Pancreatic Fat and Body Composition Measurements by Computed Tomography are Associated with Pancreatic Fistula After Pancreatectomy. *Ann Surg Oncol* 2021; **28**: 530-538 [PMID: 32436185 DOI: 10.1245/s10434-020-08581-9]

23 **Zhou L**, Xiao WM, Li CP, Gao YW, Gong WJ, Lu GT. Impact of Fatty Pancreas on Postoperative Pancreatic Fistulae: A Meta-Analysis. *Front Oncol* 2021; **11**: 622282 [PMID: 34926236 DOI: 10.3389/fonc.2021.622282]

24 **Kobayashi N**, Shinohara H, Haruta S, Udagawa H, Ueno M. Reducing the risk of postoperative pancreatic fistula in radical gastrectomy: pre-assessment with computed tomography for the diagnosis of pancreatic steatosis. *Langenbecks Arch Surg* 2022; **407**: 587-596 [PMID: 34559268 DOI: 10.1007/s00423-021-02337-z]

25 **Jiang X**, Hiki N, Nunobe S, Kumagai K, Nohara K, Sano T, Yamaguchi T. Postoperative pancreatic fistula and the risk factors of laparoscopy-assisted distal gastrectomy for early gastric cancer. *Ann Surg Oncol* 2012; **19**: 115-121 [PMID: 21739317 DOI: 10.1245/s10434-011-1893-y]

26 **Milligan WA**. Outbreaks of 'tetanus'. *Vet Rec* 1991; **129**: 104 [PMID: 1926723 DOI: 10.1136/vr.129.5.104]

27 **Martiniuc A**, Dumitrascu T, Ionescu M, Tudor S, Lacatus M, Herlea V, Vasilescu C. Pancreatic Fistula after D1+/D2 Radical Gastrectomy according to the Updated International Study Group of Pancreatic Surgery Criteria: Risk Factors and Clinical Consequences. Experience of Surgeons with High Caseloads in a Single Surgical Center in Eastern Europe. *J Gastric Cancer* 2021; **21**: 16-29 [PMID: 33854810 DOI: 10.5230/jgc.2021.21.e3]

28 **Tanioka T**, Kojima K, Saito T, Kanemoto E, Okuno K, Gokita K, Kobayashi K, Nakagawa M, Inokuchi M. Intraoperative Body Fluid Amylase as a Novel Indicator of Postgastrectomy Pancreatic Fistula. *World J Surg* 2019; **43**: 2061-2068 [PMID: 30903245 DOI:

10.1007/s00268-019-04961-9]

29 **Katai H**, Mizusawa J, Katayama H, Kunisaki C, Sakuramoto S, Inaki N, Kinoshita T, Iwasaki Y, Misawa K, Takiguchi N, Kaji M, Okitsu H, Yoshikawa T, Terashima M; Stomach Cancer Study Group of Japan Clinical Oncology Group. Single-arm confirmatory trial of laparoscopy-assisted total or proximal gastrectomy with nodal dissection for clinical stage I gastric cancer: Japan Clinical Oncology Group study JCOG1401. *Gastric Cancer* 2019; **22**: 999-1008 [PMID: 30788750 DOI: 10.1007/s10120-019-00929-9]

30 **Inaki N**, Etoh T, Ohyama T, Uchiyama K, Katada N, Koeda K, Yoshida K, Takagane A, Kojima K, Sakuramoto S, Shiraishi N, Kitano S. A Multi-institutional, Prospective, Phase II Feasibility Study of Laparoscopy-Assisted Distal Gastrectomy with D2 Lymph Node Dissection for Locally Advanced Gastric Cancer (JLSSG0901). *World J Surg* 2015; **39**: 2734-2741 [PMID: 26170158 DOI: 10.1007/s00268-015-3160-z]

31 **Nakauchi M**, Suda K, Kadoya S, Inaba K, Ishida Y, Uyama I. Technical aspects and short- and long-term outcomes of totally laparoscopic total gastrectomy for advanced gastric cancer: a single-institution retrospective study. *Surg Endosc* 2016; **30**: 4632-4639 [PMID: 26703126 DOI: 10.1007/s00464-015-4726-4]

32 **Yu HW**, Jung DH, Son SY, Lee CM, Lee JH, Ahn SH, Park DJ, Kim HH. Risk factors of postoperative pancreatic fistula in curative gastric cancer surgery. *J Gastric Cancer* 2013; **13**: 179-184 [PMID: 24156038 DOI: 10.5230/jgc.2013.13.3.179]

33 **Lee HJ**, Hyung WJ, Yang HK, Han SU, Park YK, An JY, Kim W, Kim HI, Kim HH, Ryu SW, Hur H, Kong SH, Cho GS, Kim JJ, Park DJ, Ryu KW, Kim YW, Kim JW, Lee JH, Kim MC; Korean Laparo-endoscopic Gastrointestinal Surgery Study (KLASS) Group. Short-term Outcomes of a Multicenter Randomized Controlled Trial Comparing Laparoscopic Distal Gastrectomy With D2 Lymphadenectomy to Open Distal Gastrectomy for Locally Advanced Gastric Cancer (KLASS-02-RCT). *Ann Surg* 2019; **270**: 983-991 [PMID: 30829698 DOI: 10.1097/SLA.0000000000003217]

34 **Yamada S**, Yagi S, Sato K, Shin'e M, Sakamoto A, Utsunomiya D, Okikawa S, Aibara N, Watanabe M, Obatake M, Ono R, Fujii M, Otani H, Kawasaki H. Serum C-reactive protein level on first postoperative day can predict occurrence of postoperative pancreatic fistula after laparoscopic gastrectomy. *J Med Invest* 2019; **66**: 285-288 [PMID: 31656290 DOI: 10.2152/jmi.66.285]

35 **Katai H**, Yoshimura K, Fukagawa T, Sano T, Sasako M. Risk factors for pancreas-related abscess after total gastrectomy. *Gastric Cancer* 2005; **8**: 137-141 [PMID: 16086115 DOI: 10.1007/s10120-005-0317-8]

36 **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]

37 **Kitano S**, Iso Y, Moriyama M, Sugimachi K. Laparoscopy-assisted Billroth I gastrectomy. *Surg Laparosc Endosc* 1994; **4**: 146-148 [PMID: 8180768]

38 **Obama K**, Okabe H, Hosogi H, Tanaka E, Itami A, Sakai Y. Feasibility of laparoscopic gastrectomy with radical lymph node dissection for gastric cancer: from a viewpoint of pancreas-related complications. *Surgery* 2011; **149**: 15-21 [PMID: 20627337 DOI: 10.1016/j.surg.2010.04.014]

39 **Ida S**, Hiki N, Ishizawa T, Kuriki Y, Kamiya M, Urano Y, Nakamura T, Tsuda Y, Kano Y, Kumagai K, Nunobe S, Ohashi M, Sano T. Pancreatic Compression during Lymph Node Dissection in Laparoscopic Gastrectomy: Possible Cause of Pancreatic Leakage. *J Gastric Cancer* 2018; **18**: 134-141 [PMID: 29984063 DOI: 10.5230/jgc.2018.18.e15]

40 **Ushiku H**, Sakuraya M, Washio M, Hosoda K, Niihara M, Harada H, Miura H, Sato T, Nishizawa N, Tajima H, Kaizu T, Kato H, Sengoku N, Tanaka K, Naitoh T, Kumamoto Y, Sangai T, Yamashita K, Hiki N. Pancreas-contactless gastrectomy for gastric cancer prevents postoperative inflammation. *Surg Endosc* 2022; **36**: 5644-5651 [PMID: 34981230 DOI: 10.1007/s00464-021-08961-6]

41 **Ebihara Y**, Kurashima Y, Murakami S, Shichinohe T, Hirano S. Robotic Distal Gastrectomy With a Novel "Preemptive Retropancreatic Approach" During Dissection of Suprapancreatic Lymph Nodes for Gastric Cancer. *Surg Laparosc Endosc Percutan Tech* 2021; **31**: 457-461 [PMID: 33900223 DOI: 10.1097/SLE.0000000000000897]

42 **Fujita T**, Ohta M, Ozaki Y, Takahashi Y, Miyazaki S, Harada T, Iino I, Kikuchi H, Hiramatsu Y, Kamiya K, Konno H. Collateral thermal damage to the pancreas by ultrasonic instruments during lymph node dissection in laparoscopic gastrectomy. *Asian J Endosc Surg* 2015; **8**: 281-288 [PMID: 25706186 DOI: 10.1111/ases.12177]

43 **Birkmeyer JD**, Finks JF, O'Reilly A, Oerline M, Carlin AM, Nunn AR, Dimick J, Banerjee M, Birkmeyer NJ; Michigan Bariatric Surgery Collaborative. Surgical skill and complication rates after bariatric surgery. *N Engl J Med* 2013; **369**: 1434-1442 [PMID: 24106936 DOI: 10.1056/NEJMsa1300625]

44 **Casciani F**, Trudeau MT, Asbun HJ, Ball CG, Bassi C, Behrman SW, Berger AC, Bloomston MP, Callery MP, Christein JD, Falconi M, Fernandez-Del Castillo C, Dillhoff ME, Dickson EJ, Dixon E, Fisher WE, House MG, Hughes SJ, Kent TS, Malleo G, Partelli S, Salem RR, Stauffer JA, Wolfgang CL, Zureikat AH, Vollmer CM Jr; Pancreas Fistula Study Group. Surgeon experience contributes to improved outcomes in pancreatoduodenectomies at high risk for fistula development. *Surgery* 2021; **169**: 708-720 [PMID: 33386129 DOI: 10.1016/j.surg.2020.11.022]

45 **Irino T**, Hiki N, Ohashi M, Nunobe S, Sano T, Yamaguchi T. The Hit and Away technique: optimal usage of the ultrasonic scalpel in laparoscopic gastrectomy. *Surg Endosc* 2016; **30**: 245-250 [PMID: 25860953 DOI: 10.1007/s00464-015-4195-9]

46 **Ojima T**, Nakamura M, Nakamori M, Hayata K, Katsuda M, Maruoka S, Yamaue H. Robotic radical lymphadenectomy without touching the pancreas during gastrectomy for gastric cancer. *Medicine (Baltimore)* 2019; **98**: e15091 [PMID: 30921243 DOI: 10.1097/MD.0000000000015091]

47 **Ye SP**, Shi J, Liu DN, Jiang QG, Lei X, Tang B, He PH, Zhu WQ, Tang HC, Li TY. Robotic- versus laparoscopic-assisted distal gastrectomy with D2 lymphadenectomy for advanced gastric cancer based on propensity score matching: short-term outcomes at a high-capacity center. *Sci Rep* 2020; **10**: 6502 [PMID: 32300209 DOI: 10.1038/s41598-020-63616-1]

48 **Lu J**, Zheng CH, Xu BB, Xie JW, Wang JB, Lin JX, Chen QY, Cao LL, Lin M, Tu RH, Huang ZN, Lin JL, Zheng HL, Huang CM, Li P. Assessment of Robotic Versus Laparoscopic Distal Gastrectomy for Gastric Cancer: A Randomized Controlled Trial. *Ann Surg* 2021; **273**: 858-867 [PMID: 32889876 DOI: 10.1097/SLA.0000000000004466]

49 **Gong S**, Li X, Tian H, Song S, Lu T, Jing W, Huang X, Xu Y, Wang X, Zhao K, Yang K, Guo T. Clinical efficacy and safety of robotic distal gastrectomy for gastric cancer: a systematic review and meta-analysis. *Surg Endosc* 2022; **36**: 2734-2748 [PMID: 35020057 DOI: 10.1007/s00464-021-08994-x]

50 **Teranishi R**, Takahashi T, Kurokawa Y, Sugase T, Saito T, Yamamoto K, Yamashita K, Tanaka K, Makino T, Yamasaki M, Motoori M, Omori T, Nakajima K, Eguchi H, Doki Y. Robotic Distal Gastrectomy Reduces Drain Amylase Values in Patients With a Small Pancreas-left Gastric Artery Angle. *Surg Laparosc Endosc Percutan Tech* 2022; **32**: 311-318 [PMID: 35583613 DOI: 10.1097/SLE.0000000000001038]

51 **Matsunaga T**, Miyauchi W, Kono Y, Shishido Y, Miyatani K, Hanaki T, Watanabe J, Kihara K, Yamamoto M, Fukumoto Y, Tokuyasu N, Takano S, Sakamoto T, Honjo S, Saito H, Fujiwara Y. The Advantages of Robotic Gastrectomy over Laparoscopic Surgery for Gastric Cancer. *Yonago Acta Med* 2020; **63**: 99-106 [PMID: 32494215 DOI: 10.33160/yam.2020.05.005]

52 **Ojima T**, Nakamura M, Hayata K, Kitadani J, Katsuda M, Takeuchi A, Tominaga S, Nakai T, Nakamori M, Ohi M, Kusunoki M, Yamaue H. Short-term Outcomes of Robotic Gastrectomy vs Laparoscopic Gastrectomy for Patients With Gastric Cancer: A Randomized Clinical Trial. *JAMA Surg* 2021; **156**: 954-963 [PMID: 34468701 DOI: 10.1001/jamasurg.2021.3182]

53 **Zhang Z**, Zhang X, Liu Y, Li Y, Zhao Q, Fan L, Zhang Z, Wang D, Zhao X, Tan B. Meta-analysis of the efficacy of Da Vinci robotic or laparoscopic distal subtotal gastrectomy in patients with gastric cancer. *Medicine (Baltimore)* 2021; **100**: e27012 [PMID: 34449473 DOI: 10.1097/MD.0000000000027012]

54 **Itamoto K**, Hikage M, Fujiya K, Kamiya S, Tanizawa Y, Bando E, Terashima M. The impact of pancreas compression time during minimally invasive gastrectomy on the postoperative complications in gastric cancer. *Ann Gastroenterol Surg* 2021; **5**: 785-793 [PMID: 34755010 DOI: 10.1002/ags3.12488]

55 **Bassi C**, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, Allen P, Andersson R, Asbun HJ, Besselink MG, Conlon K, Del Chiaro M, Falconi M, Fernandez-Cruz L, Fernandez-Del Castillo C, Fingerhut A, Friess H, Gouma DJ, Hackert T, Izbicki J, Lillemoe KD, Neoptolemos JP, Olah A, Schulick R, Shrikhande SV, Takada T, Takaori K, Traverso W, Vollmer CM, Wolfgang CL, Yeo CJ, Salvia R, Buchler M; International Study Group on Pancreatic Surgery (ISGPS). The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. *Surgery* 2017; **161**: 584-591 [PMID: 28040257 DOI: 10.1016/j.surg.2016.11.014]

56 **Clavien PA**, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009; **250**: 187-196 [PMID: 19638912 DOI: 10.1097/SLA.0b013e3181b13ca2]

57 **Dindo D**, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205-213 [PMID: 15273542 DOI: 10.1097/01.sla.0000133083.54934.ae]

58 **De Sol A**, Cirocchi R, Di Patrizi MS, Boccolini A, Barillaro I, Cacurri A, Grassi V, Corsi A, Renzi C, Giuliani D, Coccetta M, Avenia N. The measurement of amylase in drain fluid for the detection of pancreatic fistula after gastric cancer surgery: an interim analysis. *World J Surg Oncol* 2015; **13**: 65 [PMID: 25849316 DOI: 10.1186/s12957-014-0428-y]

59 **Katayama H**, Kurokawa Y, Nakamura K, Ito H, Kanemitsu Y, Masuda N, Tsubosa Y, Satoh T, Yokomizo A, Fukuda H, Sasako M. Extended Clavien-Dindo classification of surgical complications: Japan Clinical Oncology Group postoperative complications criteria. *Surg Today* 2016; **46**: 668-685 [PMID: 26289837 DOI: 10.1007/s00595-015-1236-x]

60 **Lowy AM**, Lee JE, Pisters PW, Davidson BS, Fenoglio CJ, Stanford P, Jinnah R, Evans DB. Prospective, randomized trial of octreotide to prevent pancreatic fistula after pancreaticoduodenectomy for malignant disease. *Ann Surg* 1997; **226**: 632-641 [PMID: 9389397 DOI: 10.1097/00000658-199711000-00008]

61 **Fuentes E**, Ahmad R, Hong TS, Clark JW, Kwak EL, Rattner DW, Mullen JT. The impact of neoadjuvant therapy for gastroesophageal adenocarcinoma on postoperative morbidity and mortality. *J Surg Oncol* 2016; **113**: 560-564 [PMID: 26792144 DOI: 10.1002/jso.24179]

62 **Kosaka T**, Akiyama H, Makino H, Kimura J, Takagawa R, Ono HA, Kunisaki C, Endo I. Impact of Neoadjuvant Chemotherapy Among Patients with Pancreatic Fistula After Gastrectomy for Advanced Gastric Cancer. *Anticancer Res* 2016; **36**: 1773-1777 [PMID: 27069158]

63 **Montorsi M**, Zago M, Mosca F, Capussotti L, Zotti E, Ribotta G, Fegiz G, Fissi S, Roviaro G, Peracchia A. Efficacy of octreotide in the prevention of pancreatic fistula after elective pancreatic resections: a prospective, controlled, randomized clinical trial. *Surgery* 1995; **117**: 26-31 [PMID: 7809832 DOI: 10.1016/s0039-6060(05)80225-9]

64 **Roncoroni L**, Violi V, Montanari M, Muri M. Effect of somatostatin on exocrine pancreas evaluated on a total external pancreatic fistula of neoplastic origin. *Am J Gastroenterol* 1983; **78**: 425-428 [PMID: 6191564]

65 **Li-Ling J**, Irving M. Somatostatin and octreotide in the prevention of postoperative pancreatic complications and the treatment of enterocutaneous pancreatic fistulas: a systematic review of randomized controlled trials. *Br J Surg* 2001; **88**: 190-199 [PMID: 11167865 DOI: 10.1046/j.1365-2168.2001.01659.x]

66 **Alghamdi AA**, Jawas AM, Hart RS. Use of octreotide for the prevention of pancreatic fistula after elective pancreatic surgery: a systematic review and meta-analysis. *Can J Surg* 2007; **50**: 459-466 [PMID: 18053374]

67 **You DD**, Paik KY, Park IY, Yoo YK. Randomized controlled study of the effect of octreotide on pancreatic exocrine secretion and pancreatic fistula after pancreatoduodenectomy. *Asian J Surg* 2019; **42**: 458-463 [PMID: 30262436 DOI: 10.1016/j.asjsur.2018.08.006]

68 **Tilak M**, Tewari M, Shukla HS. Octreotide and postoperative pancreatic fistula after pancreaticoduodenectomy: What we know so far? A narrative review. *Indian J Cancer* 2023; **60**: 152-159 [PMID: 37530235 DOI: 10.4103/ijc.IJC_280_21]

69 **Leandros E**, Antonakis PT, Albanopoulos K, Dervenis C, Konstadoulakis MM. Somatostatin versus octreotide in the treatment of patients with gastrointestinal and pancreatic fistulas. *Can J Gastroenterol* 2004; **18**: 303-306 [PMID: 15152279 DOI: 10.1155/2004/901570]

70 **Gans SL**, van Westreenen HL, Kiewiet JJ, Rauws EA, Gouma DJ, Boermeester MA. Systematic review and meta-analysis of somatostatin analogues for the treatment of pancreatic fistula. *Br J Surg* 2012; **99**: 754-760 [PMID: 22430616 DOI: 10.1002/bjs.8709]

71 **Maatman TK**, Weber DJ, Timsina LR, Qureshi B, Ceppa EP, Nakeeb A, Schmidt CM, Zyromski NJ, Koniaris LG, House MG. Antibiotic irrigation during pancreatoduodenectomy to prevent infection and pancreatic fistula: A randomized controlled clinical trial. *Surgery* 2019; **166**: 469-475 [PMID: 31383465 DOI: 10.1016/j.surg.2019.05.053]

72 **Ocuin LM**, Loftus A, Elshami M, Hue JJ, Musonza T, Ammori JB, Winter JM, Hardacre JM. Extended antibiotic therapy is associated with a lower rate of clinically relevant postoperative pancreatic fistula after pancreatoduodenectomy in intermediate- and high-risk patients: A single-institution analysis. *Surgery* 2024; **175**: 477-483 [PMID: 37940433 DOI: 10.1016/j.surg.2023.09.049]

73 **Hiura Y**, Takiguchi S, Yamamoto K, Kurokawa Y, Yamasaki M, Nakajima K, Miyata H, Fujiwara Y, Mori M, Doki Y. Use of fibrin glue sealant with polyglycolic acid sheets to prevent pancreatic fistula formation after laparoscopic-assisted gastrectomy. *Surg Today* 2013; **43**: 527-533 [PMID: 22797962 DOI: 10.1007/s00595-012-0253-2]

74 **Iwasaki K**, Barroga E, Enomoto M, Matsumoto M, Yamada E, Miyoshi K, Shimoda Y, Ota Y, Nakagawa Y. Use of Polyglycolic Acid Sheets for the Prevention of Pancreatic Fistula after Laparoscopic Gastrectomy: A Single-Center Retrospective Study. *Am Surg* 2023; **89**: 5318-5324 [PMID: 36534780 DOI: 10.1177/00031348221146971]

75 **Ri M**, Ohashi M, Makuuchi R, Hayami M, Sano T, Nunobe S. Clinical Impact of Polyglycolic Acid Mesh to Reduce Pancreas-Related Complications After Minimally Invasive Surgery for Gastric Cancer: A Propensity Score Matching Analysis. *J Gastric Cancer* 2024; **24**: 220-230 [PMID: 38575514 DOI: 10.5230/jgc.2024.24.e17]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com