

Gastrointestinal leakage after gastrectomy for gastric cancer high-volume center 10-year experience

Ahmed Motamiez^a, Gamal Amira^b, Doaa Maximous^a, Ahmed A.S. Salem^a, Badawy M. Ahmed^a, Yo-Seok Cho^c, Seong-Ho Kong^c, Do-Joong Park^c, Hyuk-Joon Lee^c, Han-Kwang Yang^c

^aDepartment of Surgical Oncology, South Egypt Cancer Institute, Assiut University, Assiut, ^bDepartment of Surgical Oncology, National Cancer Institute, Cairo University, Cairo, Egypt, ^cDepartment of Surgery, Seoul National University Hospital, Seoul, South Korea

Correspondence to Ahmed Motamiez, MD, Department of Surgical Oncology, South Egypt Cancer Institute, Assiut University, Assiut 71111, Egypt. Tel: +20 101 546 3133; fax: +20 882 348 609; e-mail: dr_ahmedmotamiez@aun.edu.eg

Received: 21 October 2023

Revised: 30 October 2023

Accepted: 7 November 2023

Published: 31 January 2024

The Egyptian Journal of Surgery 2024, 43:245–257

Purpose

Gastrointestinal leakage is one of the most detrimental and life-threatening complications that may occur after gastrectomy for gastric cancer. We evaluated the incidence, predictive factors, management strategies, and outcomes of gastrointestinal leakage following gastrectomy for gastric cancer in a high-volume center over a 10-year period and the impact of prospective continuous monitoring of management outcomes.

Patients and methods

A total of 7098 patients who underwent curative radical gastrectomy for gastric adenocarcinoma from January 2012 to December 2021 in Gastrointestinal Surgery Department, Seoul National University Hospital were reviewed.

Results

The overall incidence of gastrointestinal leakage was 2.8% (198/7098). Old age (>60), male sex, high BMI (≥ 25), prolonged operative time (>240 min), open approach, and increased lymph node ratio (>5%) were important risk factors for anastomotic leakage following gastrectomy on multivariate analysis. Leakage increased postoperative hospital stay by fivefolds and was responsible for 20.5% of major complications after gastrectomy. Interventional management was performed in 76.8% of leakage cases while surgery was required in 9.6% of cases with success of initial treatment in 83.8% of patients. Mortality rate was 1.5% (3/198).

Conclusion

Prospective, transparent, and accurate data collection is an essential component of self-improvement cycle. Surgeon experience is an important factor especially in esophagojejunal anastomosis with tension free well vascularized pedicle is the key. Multidisciplinary team management of leakage with efficient interventional strategies can greatly improve the leakage outcome.

Keywords:

anastomotic leakage, gastrectomy, gastric cancer, management, risk factors

Egyptian J Surgery 43:245–257

© 2024 The Egyptian Journal of Surgery

1110-1121

Introduction

Gastric cancer is one of the most common cancers in Korea and the world which ranks fifth in incidence (5.6%) and fourth leading cause of death (7.7%) among all solid cancers, globally in 2020 [1,2].

Currently the only potential curative treatment for gastric cancer is radical surgery, however radical gastrectomy is technically challenging operation and involves a variety of surgical approaches and reconstructive methods which carry a significant risk of complications [3].

Despite improvement in surgical outcomes after gastrectomy for gastric cancer over the past two decades due to advancement in surgical techniques, introduction of minimally invasive approaches and improvement of perioperative care through enhanced

recovery after surgery protocols, still serious complications could occur [4–7].

As one of the most detrimental and potentially life-threatening complications that may arise after gastrectomy is leakage which can prolong hospitalization, increase the reoperation and mortality rates and ultimately amplify the burden on healthcare costs, in addition it adversely affects the oncologic outcomes and overall survival [8–10].

In this study, we evaluated the incidence, predictive factors, management strategies, and outcomes of

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

gastrointestinal leakage following gastrectomy for gastric cancer in a high-volume center over a 10-year period in a large cohort. In addition we evaluated the impact of prospective continuous transparent monitoring of management outcomes.

Patients and methods

Study design

This is a retrospective study of prospectively collected data for gastric cancer patients who underwent curative radical gastrectomy for primary gastric adenocarcinoma at Seoul National University Hospital between January 2012 and December 2021. The data of patients was prospectively recorded in the department weekly meeting and agreed by all faculty staff members of the department [11]. Metastatic, recurrent, palliative, and emergency cases, as well other histologies (gastrointestinal stromal tumor, lymphoma, benign) rather than adenocarcinoma were excluded. A written informed consent was taken from all patients before operation, The study was approved by the institutional review board of Seoul National University Hospital (IRB approval No: H-2301-139-1400).

Data collection

The study collected patient information such as age, sex, BMI, American Society of Anesthesiologists score, preoperative albumin level to assess nutritional status, and preoperative hemoglobin level. In addition, intraoperative parameters were recorded including the surgical approach, extent of resection, lymphadenectomy, method of reconstruction, combined resection, operative time, and primary surgeon. Tumor characteristics were also observed, such as number, site, size, histology, margin status, T-stage, N-stage, lymph node ratio, and pathologic stage (TNM staging system 8th edition). Lymph node ratio refers to the proportion of metastatic lymph nodes to the total resected lymph nodes [12].

Leakage features as diagnosis, timing (early/late), site, severity, and management (conservative/interventional/surgical) were collected. Severity of leakage was determined on the basis of Clavien-Dindo classification. Failure of treatment was in the form of failure of initial management to control the leakage or the need for another modality to control the leakage. Treatment outcome parameters were chosen as hospital stay, reoperation, major complication (Clavien-Dindo grade ≥ 3), and mortality.

Operative method

Approach

- (1) Minimally invasive surgery including laparoscopic assisted, totally laparoscopic and robotic

gastrectomy have been applied according to surgeon preference after patient consultation.

- (2) Open approach was used for more advanced and complicated cases.

Extent of resection

- (1) Distal gastrectomy for distally located tumors in the lower and middle thirds.
- (2) Total gastrectomy for proximally located tumors in the upper third or diffuse types.
- (3) Proximal gastrectomy for early stage proximally located tumors in the upper third.
- (4) Pylorus preserving gastrectomy for early-stage tumors located 5 cm away from pylorus.

Reconstruction

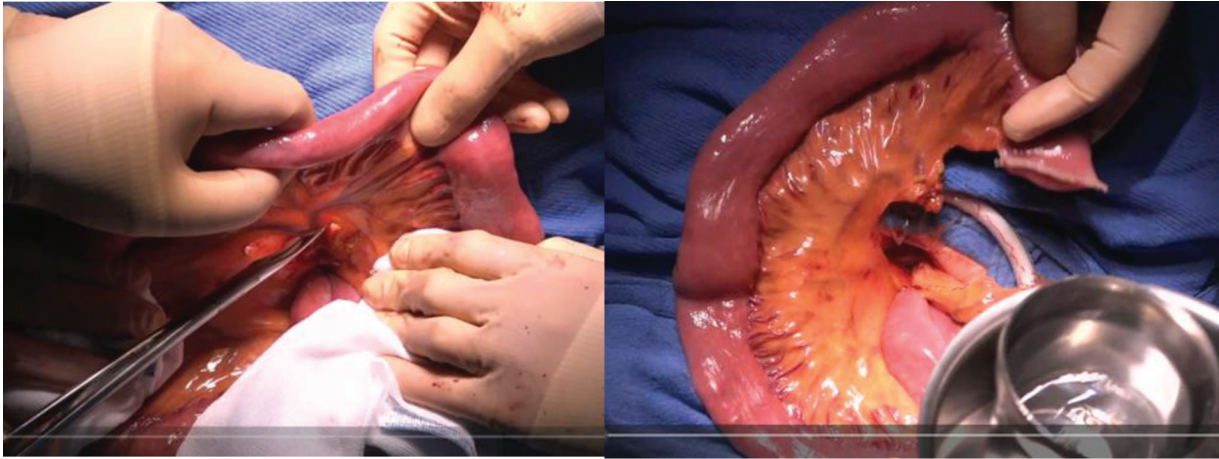
- (1) After distal gastrectomy; Billroth I (gastroduodenostomy), Billroth II (gastrojejunostomy), and Roux en-Y gastrojejunostomy were used according to the tumor location and surgeon preference.
- (2) After total gastrectomy; Roux en-Y esophagojejunostomy (EJ) was applied including the following steps as recommended by surgeon A (Fig. 1).
 - (a) Supra umbilical mini-laparotomy (about 5 cm) for jejunal extraction.
 - (b) Vascular pedicle preparation includes ligation of one jejunal pedicle to allow for tension free EJ.
 - (c) Extracorporeal jejunojunctionostomy by linear stapler.
 - (d) Intracorporeal EJ by circular stapler.
 - (e) Jejunal stump closure by endo GIA linear stapler.
- (3) After proximal gastrectomy; double tract reconstruction method including EJ, DJ, and JJ replaced the old esophagogastronomy method.
- (4) After pylorus preserving gastrectomy; gastrogastrostomy was applied.

Diagnosis of leakage

Diagnosis of leakage was done by clinical signs (change of drain color, abdominal pain, fever, abnormal wound discharge), laboratory results (increased C-reactive protein, leukocytosis, raised amylase level in the drainage fluid), radiological findings on (computed tomography with oral and intravenous contrast, upper gastrointestinal series, tubogram), or endoscopic visualization of the anastomotic defect on EGD.

Treatment of leakage included conservative, interventional, and surgical management

Figure 1



Vascular pedicle preparation by surgeon A.

Conservative management

It included gastrointestinal rest by nothing per oral, nutritional support either through enteral or parenteral routes and intravenous antibiotic coverage. It was applied for low output well drained leakage cases with no signs of toxicity.

Interventional management

Radiologic intervention

It was in the form of PCD insertion for collection drainage, percutaneous transhepatic biliary drainage for duodenal stump leakage or Glue embolization for residual tract.

Endoscopic treatment

It included stent insertion or endo-clipping.

Surgical management

It was reserved for septic patients with signs of peritonitis and the type of surgical intervention was dependent on the patient general condition and the degree of anastomotic dehiscence.

- (1) Anastomotic revision and primary repair.
- (2) More aggressive surgery in the form of completion total gastrectomy or diversion to another type of reconstruction.
- (3) Drainage or diversion (exteriorization) if the patient was in bad general condition.

Statistical analysis

All variables were tested for normality distribution using Kolmogorov–Smirnov and Shapiro–Wilk tests. For normally distributed continuous variables, Student *t* test was chosen for analysis and the data were presented as mean and SD while nonparametric tests

as Mann–Whitney *U* test were used for non-normally distributed continuous and ordinal variables and the results were shown as median and interquartile range. The χ^2 test was used to test the distribution between nominal variables which were demonstrated as numbers and percentages. Binary logistic regression model was used for multivariate analysis and all variables which show *P* value less than 0.05 in univariate analysis were included in the multivariate model. *P* value was considered statistically significant below 0.05. All analysis was made using IBM SPSS Statistics for Windows, version 27 (IBM Corp., Armonk, New York, USA).

Results

Incidence

A total of 7098 patients who underwent curative radical gastrectomy for gastric adenocarcinoma from January 2012 to December 2021 at GI Surgery Department, Seoul National University Hospital were identified. Among them 198 (2.8%) patients experienced gastrointestinal leakage after gastrectomy.

Patient characteristics

Clinical variables are listed in Table 1.

Median age of patients who experienced leakage was older than those with no leakage especially for old patients more than 60 years. Leakage incidence was greater among male and obese patients with BMI more than or equal to 25 as well as patients with severe systemic disease (ASA score >2). Anemic (Hb <11 g/dl) and hypoalbuminemic (albumin <3.5 g/dl) patients were more prone to leakage than normal correspondents.

Table 1 Patient characteristics

	Leakage [198 (2.8%)] [n (%)]	No leakage=6900	Total=7098	P value
Age [median (IQR)]	65 (58–71)	62 (54–70)		0.002
≤60	65 (2)	3202	3267	<0.001
>60	133 (3.5)	3698	3831	
Sex				<0.001
Male	159 (3.5)	4337	4496	
Female	39 (1.5)	2563	2602	
BMI [median (IQR)]	24.9 (23–26.8)	23.8 (21.8–26)		<0.001
<25	101 (2.2)	4455	4556	<0.001
≥25	97 (3.8)	2445	2542	
ASA score				0.005
1	48 (2.2)	2114	2162	
2	130 (2.9)	4417	4547	
3	19 (5)	363	382	
4	1 (14.3)	6	7	
≤2	178 (2.7)	6531	6709	0.004
>2	20 (5.1)	369	389	
Hb [median (IQR)]	13.7 (11.7–14.7)	13.5 (12.2–14.6)		0.882
<11 g/dl	32 (3.9)	781	813	0.035
≥11 g/dl	166 (2.6)	6119	6285	
Albumin [median (IQR)]	4.2 (3.8–4.4)	4.2 (4–4.5)		<0.001
<3.5 g/dl	22 (6.1)	339	361	<0.001
≥3.5 g/dl	176 (2.6)	6561	6737	

ASA, American Society of Anesthesiologists; Hb, hemoglobin; IQR, interquartile range.

Operative characteristics

Operative variables are listed in Table 2.

Leakage rate was higher for open approach in comparison with other minimally invasive approaches and total gastrectomy was more prone to leakage than partial gastrectomy types. As regards reconstruction, leakage occurred more frequently in Roux in Y esophagojejunostomy and esophagogastric types than other methods. Combined resection especially for organs other than gallbladder and positive microscopic margin raised the leakage rate significantly. Leakage occurrence was associated with longer operative time and this effect was more pronounced if operation time exceeded 240 min.

Pathological characteristics

Tumor variables are listed in Table 3.

Leakage incidence was significantly increased with more advanced gastric cancer than early stage and this effect was more observed with advanced T stage than N stage ($P \leq 0.001$, $P = 0.251$ respectively). On analysis of N stage, we found no difference in the mean of resected lymph nodes between both groups (around 40), but lymph node ratio was greater in the leakage group especially if greater than 5% ($P = 0.002$). Large tumor size was associated with rise in leakage rate and this effect was significant if tumor diameter exceeded 4 cm furthermore multiplicity was associated

with increase in leakage incidence. There was no significant difference in leakage occurrence as regard tumor histology or Lauren classification. Upper third tumor location was accompanied by increase in leakage occurrence but still clinically insignificant ($P = 0.074$).

Multivariate analysis

Summarized in Table 4.

On multivariate analysis, out of 18 variables which showed significant difference ($P < 0.05$) on univariate analysis only six variables (patients over 60 years old, male sex, BMI ≥ 25 , open approach, prolonged operative times over 4 h, and increased lymph node ratio above 5%) added a significant risk for leakage occurrence on multivariate analysis.

Timing

Early leakage (within 4 days of surgery) occurred in 35 (17.7%) while late leakage (≥ 5 days of surgery) in 163 (82.3%) of patients and the mean time for leakage detection was 10 days.

Leakage rate over time

Presented in Figs 2 and 3.

Over all leakage rate doubled during 2017 and 2018 then returned back to baseline while leakage after total gastrectomy had the highest rate over time.

Table 2 Operative characteristics

	Leakage 198 (2.8%) [n (%)]	No leakage=6900	Total=7098	P value
Approach				<0.001
Open	70 (4.3)	1569	1639	
Laparoscopic assisted	46 (1.9)	2369	2415	
Totally laparoscopic	72 (3)	2367	2439	
Robotic	10 (1.7)	595	605	
Open	70 (4.3)	1569	1639	<0.001
MIS	128 (2.3)	5331	5459	
Extent of resection				0.001
DG	119 (2.8)	4074	4193	
TG	52 (4.1)	1224	1276	
PG	7 (2.4)	284	291	
PPG	20 (1.5)	1318	1338	
Reconstruction				0.001
BI	55 (2.4)	2249	2304	
BII	53 (3.2)	1578	1631	
RY GJ	11 (4.3)	247	258	
RY EJ	52 (4.1)	1224	1276	
GG	20 (1.5)	1318	1338	
DTR	4 (1.8)	219	223	
EG	3 (4.4)	65	68	
Comb resection				0.016
No CR	155 (2.6)	5861	6016	
GB	24 (3.5)	664	688	
Other than GB	19 (4.8)	375	394	
LND				0.070
<D2	41 (2.2)	1826	1867	
≥D2	157 (3)	5074	5231	
Radicality				0.014
R0	198 (2.8)	6887	7085	
R1	2 (13.3)	13	15	
Op time (min) [median (IQR)]	230 (195–283)	210 (175–250)		<0.001
<240	104 (2.1)	4743	4847	<0.001
≥240	94 (4.2)	2157	2251	
Operator				0.092
A	67 (2.5)	2612	2679	
B	81 (3.6)	2187	2268	
C	32 (2.7)	1139	1171	
D	8 (1.7)	476	484	
E	10 (2)	479	489	

BI, Billroth 1; BII, Billroth 2; DG, distal gastrectomy; EG, esophagogastrostomy; GB, gallbladder; GG, gastrogastrostomy; LND, lymph node dissection; MIS, minimally invasive surgery; PG, proximal gastrectomy; PPG, pylorus preserving gastrectomy; RY EJ, Roux en-Y esophagojejunostomy; RY GJ, Roux en-Y gastrojejunostomy; TG, total gastrectomy.

Severity of leakage

Presented in Table 5.

The majority of leakage cases were grade IIIa on Clavien-Dindo classification (71.2%). While 5.5% of patients transferred to ICU for serious conditions.

Site of leakage

Listed in Table 6.

The most frequent sites of leakage were esophagojejunostomy and esophagogastrostomy (2.9, 4.4%, respectively) but esophagogastrostomy had not

been used in the last 4 years and replaced totally by double tract reconstruction after proximal gastrectomy.

Treatment of leakage

Presented in Figs 4 and 5.

The most frequent management option was interventional type representing more than 76% of cases while reoperation was required in less than 10% of cases with increase the role of minimally invasive interventions over time.

The most frequent intervention was radiologic PCD insertion 128 (64.6%) followed by endoscopic option

Table 3 Pathological characteristics

	Leakage [198 (2.8%)] [n (%)]	No leakage=6900	Total=7098	P value
Stage (TNM 8th ed)				0.003
Stage I	119 (2.4)	4927	5046	
Stage II	43 (4.2)	980	1023	
Stage III	36 (3.6)	969	1005	
Others	0	24	24	
T stage				<0.001
T1	108 (2.3)	4630	4738	
T2	28 (3.5)	774	802	
T3	42 (4.7)	857	899	
T4	20 (3.1)	615	635	
Others	0	24	24	
N Stage				0.251
N0	135 (2.6)	5020	5155	
N1	20 (2.6)	740	760	
N2	19 (3.3)	550	569	
N3	24 (3.9)	590	614	
Involved LNs [mean (SD)]	2.3 (5.3)	1.9 (5.7)		0.079
Resected LNs [mean (SD)]	39.3 (16.1)	40.5 (16.1)		0.249
LNR Involved/resected LN	5.6%	4%		0.065
LNR				0.002
<5%	142 (2.5)	5573	5715	
≥5%	56 (4)	1327	1383	
Diameter (cm) median (IQR)	3.6 (2.1–5.1)	3 (2–4.5)		0.002
Diameter (cm)				<0.001
<4	108 (2.3)	4553	4661	
≥4	90 (3.7)	2347	2437	
Cancer number				0.039
Single	182 (2.7)	6565	6747	
Multiple	16 (4.6)	335	351	
Gross type				<0.001
EGC	119 (2.5)	4685	4804	
BI	5 (3.4)	143	148	
BII	21 (5.6)	352	373	
BIII	45 (3.3)	1307	1352	
BIV	8 (4)	190	198	
Unknown	0	223	223	
Tumor histology				0.220
Differentiated	82 (2.9)	2735	2817	
Undifferentiated	95 (2.5)	3633	3728	
Mixed	21 (3.8)	532	553	
Lauren classification				0.835
Intestinal	98 (3)	3216	3314	
Diffuse	83 (2.6)	3065	3148	
Mixed	17 (2.7)	611	628	
Unknown	0	8	8	
Location				0.074
Upper third	50 (3.9)	1245	1295	
Middle third	56 (2.5)	2144	2200	
Lower third	91 (2.6)	3449	3540	
Entire	1 (1.6)	62	63	

IQR, interquartile range; LNR, lymph node ratio.

either stent or clipping five (2.5%) and the least choice was glue embolization one (0.5%) while multimodality combinations was required in 25 (12.6%) of patients. Endoscopic treatment was performed in 18 (9.1%)

patients, five of them as a single modality and 13 as part of multimodality treatment. While nine cases were managed with stent insertion, the other nine were handled by endoclipping.

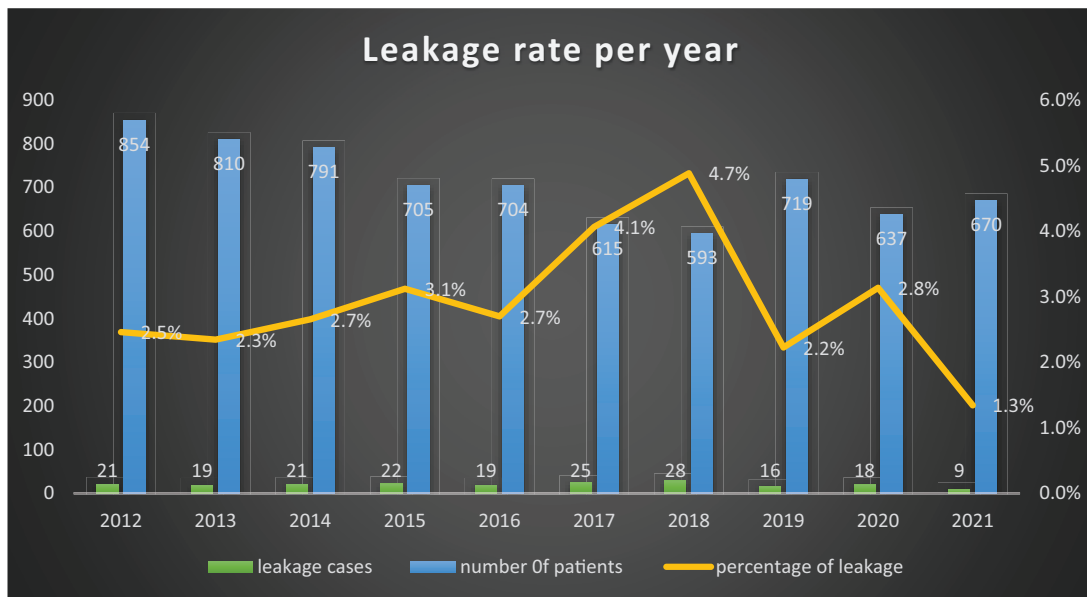
Table 4 Multivariate analysis

Variables	Group	Odds ratio (95% confidence interval)	P value
Age	>60 years	1.4 (1–2)	0.026
Sex	Male	2 (1.4–2.9)	<0.001
BMI	≥25	1.6 (1.2–2.2)	0.001
Approach	Open	1.7 (1.1–2.5)	0.012
Operative time	>240 min	1.8 (1.4–2.5)	<0.001
LNR	>5%	1.9 (1–3.4)	0.036

LNR, lymph node ratio.

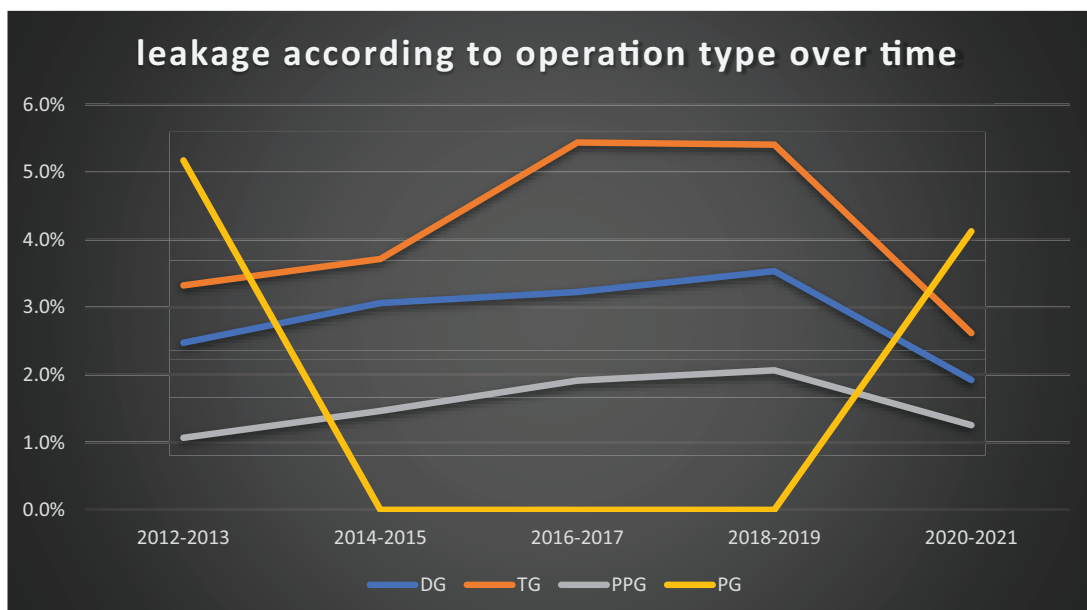
Surgical intervention was applied to 19 (9.6%) patients, 16 of them were upfront surgery (primary decision), and three after failure of interventional procedures. Ten (52.6%) cases underwent anastomotic revision and primary repair while six (31.6%) patients needed more aggressive surgery in the form of completion total gastrectomy or conversion to another type of reconstruction and three (15.8%) patients were in bad general condition so the decision was just diversion (exteriorization) or drainage.

Figure 2



Leakage rate per year.

Figure 3



Leakage according to operation type over time.

Treatment outcomes

Shown in Fig. 6 and Table 7.

The overall success of initial treatment was observed in 166 (83.8%) while failure of treatment occurred in 32 (16.2%) of patients. Management of treatment failure in the three groups was as follows: first, the three (11.1%) cases in conservative arm underwent interventional PCD insertion. Second, the 23 (15.1%) cases in interventional arm were managed as 18 to another intervention, three to surgery and

unfortunately three cases died. Lastly, the six (31.6%) patients in the surgical group were treated as four to PCD and two to another surgery. The overall median of postoperative hospital stay of patients was 8 days but it was 39 days for leakage patients. The overall major complication rate (Clavien-Dindo classification ≥ 3) was 12.3% and reoperation rate was 1.2%.

Mortality

The overall mortality after radical gastrectomy in our series was very low 0.1% (7/7098) but for leakage patients increased to represent 1.5% (3/198) especially for leakage after total gastrectomy to account for 3.8% (2/52).

Table 5 Severity of leakage

Clavien-Dindo classification	Frequency (total 198)	%
II	31	15.7
III-a	141	71.2
III-b	12	6.1
IV-a	9	4.5
IV-b	2	1
V	3	1.5

Discussion

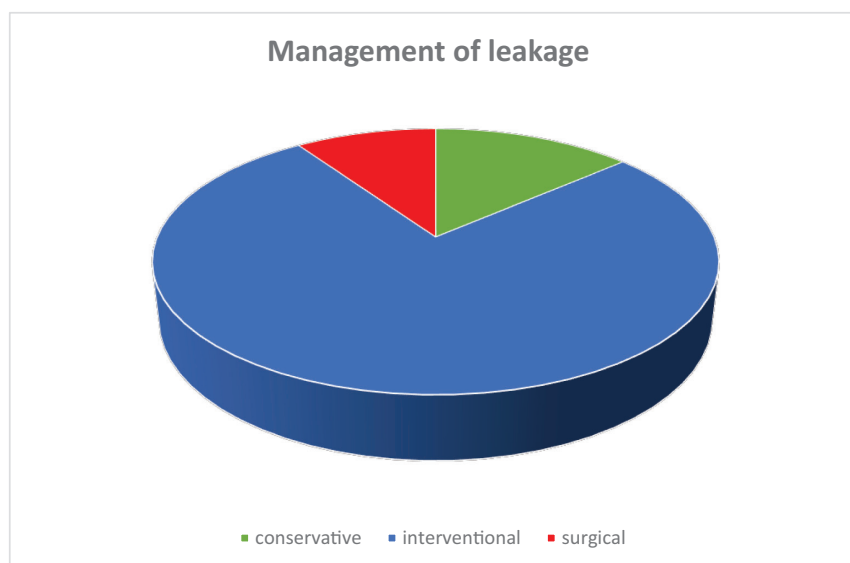
In this large cohort we found 2.8% of patients who developed gastro intestinal leakage after curative radical gastrectomy for gastric cancer which is considered low when compared with leakage rates reported in western

Table 6 Site of leakage

		EJ	GJ	GD	GG	DS	JJ	EG	[n/N (%)]
TG	RY-EJ	39				12	1		52/1276 (4.0)
DG	BI			55					55/2304 (2.4)
	BII		24			27	2		53/1631 (3.2)
	RY-GJ		9			2	0		11/258 (4.6)
PG	DTR	4	0				0		4/223 (1.8)
	EG							3	3/68 (4.4)
PPG	GG				20				20/1338 (1.5)

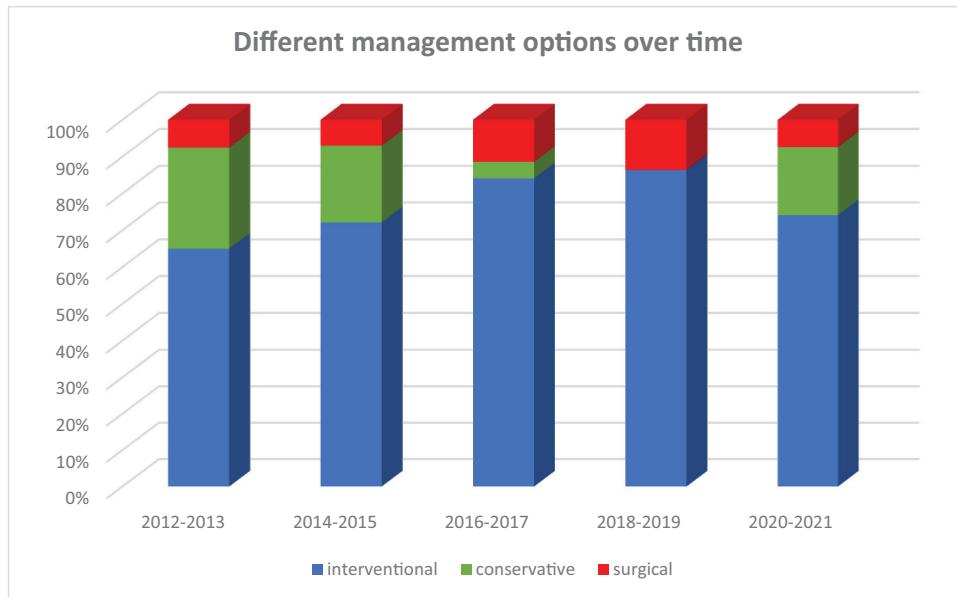
DG, distal gastrectomy; DS, duodenal stump; DTR, double tract reconstruction; EG, esophagogastrostomy; EJ, esophagojejunostomy; GD, gastroduodenostomy; GG, gastrogastrostomy; GJ, gastrojejunostomy; JJ, jejunojejunostomy; OP, operation; PG, proximal gastrectomy; PPG, pylorus preserving gastrectomy; REC, reconstruction; RY, Roux en-Y; TG, total gastrectomy.

Figure 4



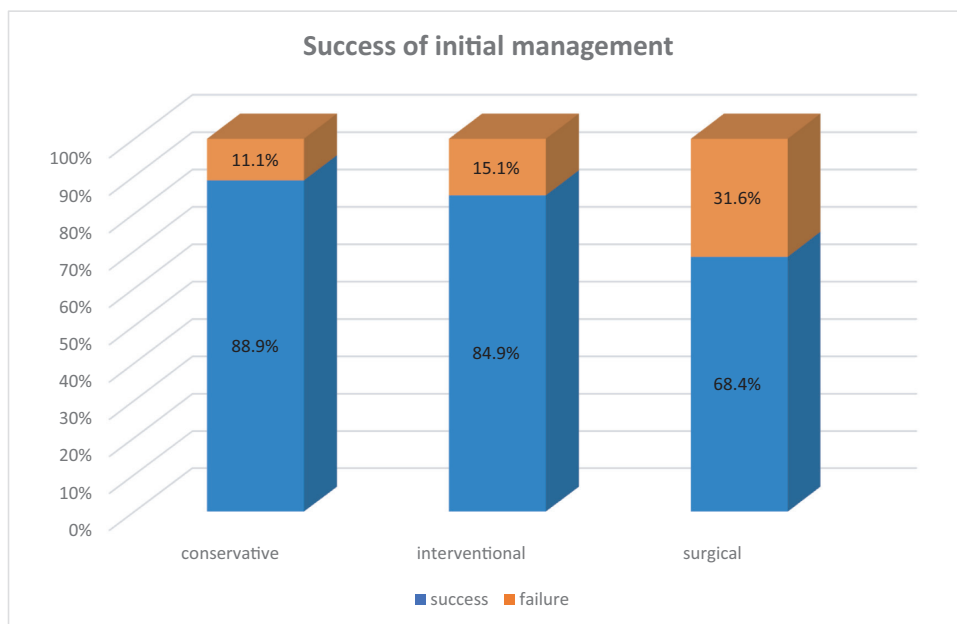
Management of leakage.

Figure 5



Different management options over time.

Figure 6



Success of initial management.

studies which range between 6 and 17% [13–15]. This low rate of leakage may be due to many factors. First, screening programs and early detection of gastric cancer, in our series stage I represent more than 70% of cases. Second, patient factors as 64% of patients are slim with BMI less than 25 and only 4% with BMI more than 30 in addition to good nutritional status with mean albumin and hemoglobin levels are 4.2 and 13.3 g/dl, respectively.

Thirdly, surgeons experience only five main surgeons performing more than 7000 cases over 10 years in a well-equipped high-volume center with a highly qualified team (nursing, anesthesia, ICU, radiology, nutrition, endoscopy, pathology) [16].

Leakage after gastrectomy had serious consequences on hospital stay, health care costs, morbidity, reoperation and mortality of patients. Gastrointestinal leakage

Table 7 Cost of leakage

	Leakage [198 (2.8%)]	No leakage [6900 (97.2%)]	Total=7098	P value
Postoperative hospital-stay [median (IQR)]	39 (29–49)	8 (7–10)		<0.001
Major complications (Clavien-Dindo grade ≥ 3)	179 (20.5)	696	875	<0.001
Reoperation	19 (22.9)	64	83	<0.001
Mortality	3 (42.9)	4	7	<0.001

increased the hospital stay by fivefolds and represented 20.5% of all major complications (Clavien-Dindo grade 3 or more) that had occurred after gastrectomy. Leakage was responsible for 23% of reoperation cases and the mortality rate among patients with leakage was 1.5%. These effects represent a great burden on the patient and healthcare system [8].

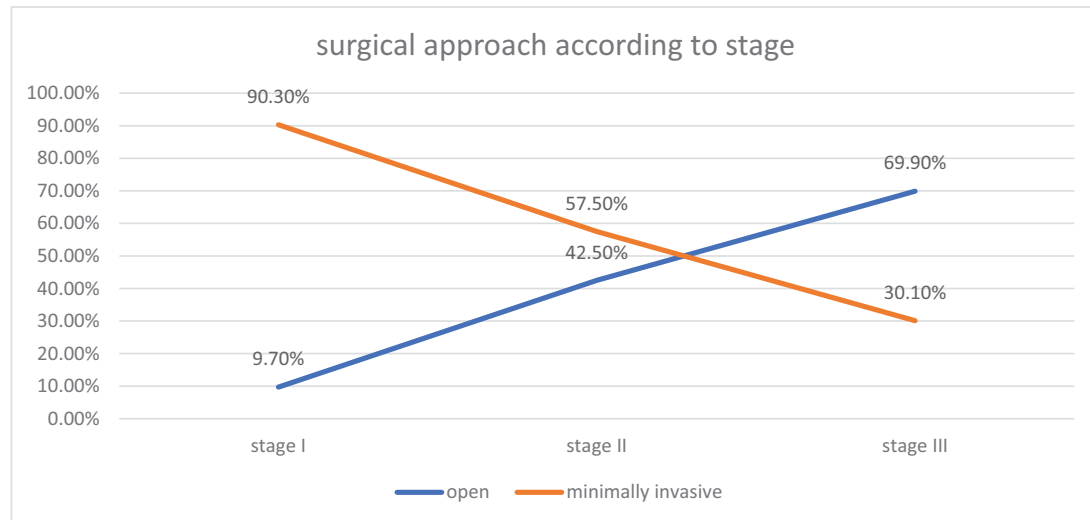
In our study, patient risk factors for leakage after gastrectomy include elderly (>60 years), obese ($\text{BMI} \geq 25$), comorbid ($\text{ASA} > 2$) male patients with anemic and hypoalbuminemic state. Age is a significant risk factor for postoperative complications including leakage because of associated comorbidities and altered physiology which adversely affect the healing capacity and respiratory reserve [17]. Obesity is associated with poor surgical outcomes as it is correlated to increased surgical difficulty, prolonged operative time and increased blood loss which increase the postoperative morbidity and anastomotic leakage [18,19]. Patients with severe systemic disease were associated with a significant increase in leakage rate which may reflect the negative influence on the healing process and body response to stress. Kim *et al.* [20] reported that comorbidity is a significant predictive factor for both local and systemic complications after gastrectomy which deserve to pay more attention to the perioperative care offered to this group of patients. Male sex was found to increase the leakage rate but the explanation of this finding is still unclear and may be related to increased abdominal visceral fat area in men [21]. Malnutrition has approved adverse effect on postoperative morbidity and prognostic nutritional index was found to be an independent risk factor for anastomotic leakage after gastrectomy for gastric cancer so perioperative nutritional support may improve the surgical outcomes and decrease the incidence of leakage [22,23].

Regarding operative predictive factors, prolonged operative time (>240 min) and open approach were associated with increase in leakage rate. Many authors reported an increase in postoperative morbidity with prolonged operative times and this effect may be multifactorial as dealing with advanced tumor stage

or the need for combined organ resection in addition prolonged operative time associated with increased blood loss and more exposure of the patient to anesthetic drugs [24]. In fact open approach association with increased leakage occurrence was an extraordinary finding and contrary to many previous studies that correlate the leakage occurrence with minimally invasive approaches and the explanation for this finding that laparoscopic gastrectomy was established as gold standard technique for early gastric cancer after KLASS-1 trial and open approach was reserved for difficult and advanced cases (Fig. 7) additionally the accumulated experience over years in performing and improving laparoscopic techniques has led to improved surgical outcomes and decreased complication rates including leakage [25]. Advanced tumor stage with increased lymph node ratio contributed to leakage vulnerability as advanced cancer constitutes a burden on body physiology and nutritional status furthermore it increases the surgical challenge, extent of lymphadenectomy, combined organ resection, operative time, and blood loss [26].

Leakage after total gastrectomy was higher than other types of gastrectomy 4.1% and associated was more mortality rate 3.8% (2/52) therefore great attention should be paid during esophagojejunostomy reconstruction especially in the early phase of laparoscopic total gastrectomy [27]. Surgeon factor is an important factor which affect the treatment outcome especially in total gastrectomy and esophagojejunal anastomosis which was reflected in our study by heterogenous leakage rates among different surgeons after total gastrectomy (Fig. 8) with decreasing leakage trend of surgeon A reaching to 0% in last 2 years and he recommended meticulous surgical techniques with tension free well vascularized jejunal pedicle during reconstruction of esophagojejunal anastomosis (Fig. 1) [28]. Leakage rate was observed to duplicate during 2017 and 2018 may be due to introduction of intracorporeal method for accomplishing the anastomosis but returned to base level subsequently due to prospective transparent monitoring of complications and continuous sharing of experience [29].

Figure 7



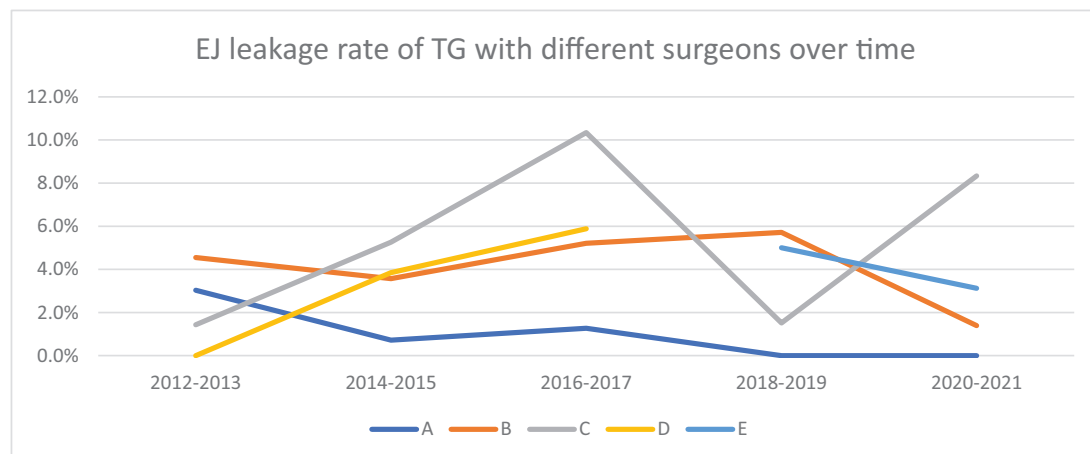
Surgical approach according to stage.

In this study most of the leakage patients were treated interventionally either by radiologic PCD insertion to drain leakage or endoscopically by stent insertion or clipping with success rate of initial management around 84% which is considered high in comparison with other reported studies [30,31]. Surgical intervention for leakage cases was limited to high output or septic patients so the results were not satisfying and the need for more than one modality of treatment was required in third of reoperated patients. This was explained by inflammatory changes occurring at the anastomotic site which led to fragile tissue and the patient's poor general condition caused by sepsis with its sequelae on subsequent healing process. The surgical treatment arm was associated with increased hospital stay compared with other

treatment options (Fig. 9) but no mortality occurred in this arm and still has its essential role in indicated cases [32]. Lastly, team collaboration (experienced surgeon, radiologist, endoscopist, ICU team, nutritionist, and skilled nursing staff) is of paramount importance in dealing with complicated cases to decrease the morbidity and mortality of complications once occurred [33].

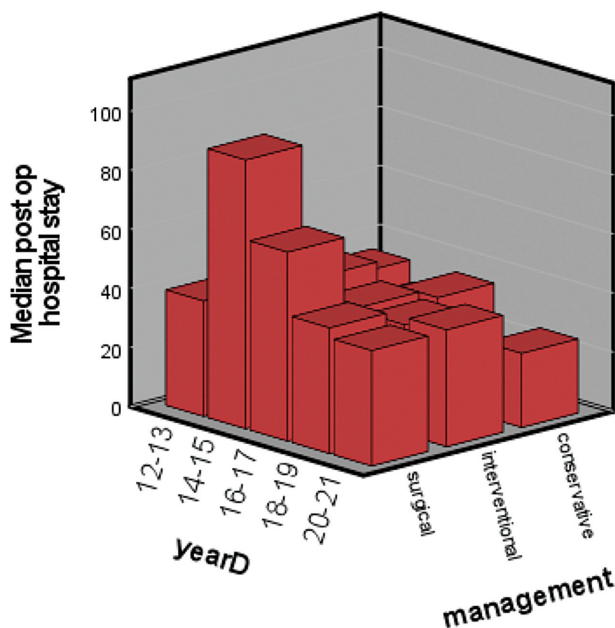
A number of limitations in this study regarding its retrospective nature but the data of patients was prospectively collected and revised by the faculty staff weekly in the tumor clinic department meeting. Although the data belong to a single institution, the large number of patients with such great experience in dealing with complicated cases is considered. Lastly

Figure 8



EJ leakage rate of TG with different surgeons over time. TG, total gastrectomy.

Figure 9



Median hospital stay of different management options over time.

this study was performed in a high-volume center with ideal perioperative circumstances resulting in low incidence of complications and mortality so results should be interpreted with caution when compared with other institutions.

Conclusion

Prospective, transparent, and accurate data collection is an essential component of self-improvement cycle. Surgeon experience is an important factor especially in esophagojejunal anastomosis with tension free well vascularized pedicle is the key. Multidisciplinary team management of leakage patients with efficient interventional strategies can greatly improve the leakage outcome.

Acknowledgements

The first author thanks the Egyptian Ministry of Higher Education (Culture Affairs and Mission Sector) for the educational scholarship under joint supervision program.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021; 71:209–249.
- Association ICotKGC. Korean Gastric Cancer Association-led nationwide survey on surgically treated gastric cancers in 2019. *J Gastric Cancer* 2021; 21:221.
- Papenfuss WA, Kukar M, Oxenberg J, Attwood K, Nurkin S, Malhotra U, Wilkinson NW. Morbidity and mortality associated with gastrectomy for gastric cancer. *Ann Surg Oncol* 2014; 21:3008–3014.
- Yang SY, Roh KH, Kim Y-N., Cho M, Lim SH, Son T, *et al.* Surgical outcomes after open, laparoscopic, and robotic gastrectomy for gastric cancer. *Ann Surg Oncol* 2017; 24:1770–1777.
- Kim W, Kim H-H., Han S-U., Kim M-C., Hyung WJ, Ryu SW, *et al.* Decreased morbidity of laparoscopic distal gastrectomy compared with open distal gastrectomy for stage I gastric cancer. *Ann Surg* 2016; 263:28–35.
- Lee H-J., Hyung WJ, Yang H-K., Han SU, Park Y-K, An JY, *et al.* 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.
- Rosa F, Longo F, Pozzo C, Strippoli A, Quero G, Fiorillo C, *et al.* Enhanced recovery after surgery (ERAS) versus standard recovery for gastric cancer patients: the evidences and the issues. *Surg Oncol* 2022; 101727:101727.
- Gertsen EC, Goense L, Brenkman HJ, van Hillegersberg R, Ruurda JP, group DUGCA. Identification of the clinically most relevant postoperative complications after gastrectomy: a population-based cohort study. *Gastric Cancer* 2020; 23:339–348.
- Nagasako Y, Satoh S, Isogaki J, Inaba K, Taniguchi K, Uyama I. Impact of anastomotic complications on outcome after laparoscopic gastrectomy for early gastric cancer. *J Br Surg* 2012; 99:849–854.
- Aurello P, Cinquepalmi M, Petrucciani N, Moschetta G, Antolino L, Felli F, *et al.* Impact of anastomotic leakage on overall and disease-free survival after surgery for gastric carcinoma: a systematic review. *Anticancer Res* 2020; 40:619–624.
- Kim T-H., Suh Y-S., Huh Y-J., Son Y-G., Park J-H., Yang J-Y., *et al.* The comprehensive complication index (CCI) is a more sensitive complication index than the conventional Clavien-Dindo classification in radical gastric cancer surgery. *Gastric Cancer* 2018; 21:171–181.
- Yamashita K, Hosoda K, Ema A, Watanabe M. Lymph node ratio as a novel and simple prognostic factor in advanced gastric cancer. *Eur J Surg Oncol* 2016; 42:1253–1260.
- Baiocchi GL, Giacomuzzi S, Reim D, Piessen G, Da Costa PM, Reynolds JV, *et al.* Incidence and grading of complications after gastrectomy for cancer using the GASTRODATA registry: a European retrospective observational study. *Ann Surg* 2020; 272:807–813.
- Kamarajah S, Navidi M, Griffin S, Phillips A. Impact of anastomotic leak on long-term survival in patients undergoing gastrectomy for gastric cancer. *J Br Surg* 2020; 107:1648–1658.
- Gertsen E, Brenkman H, Seesing M, Goense L, Ruurda J, Van Hillegersberg R. Introduction of minimally invasive surgery for distal and total gastrectomy: a population-based study. *Eur J Surg Oncol* 2019; 45:403–409.
- Stillman MD, Yoon SS. Open and minimally invasive gastrectomy in Eastern and Western patient populations: a review of the literature and reasons for differences in outcomes. *J Surg Oncol* 2022; 126:279–291.
- Lee K-G., Lee H-J., Yang J-Y., Oh S-Y., Bard S, Suh Y-S., *et al.* Risk factors associated with complication following gastrectomy for gastric cancer: retrospective analysis of prospectively collected data based on the Clavien-Dindo system. *J Gastrointest Surg* 2014; 18:1269–1277.
- Wu X-S., Wu W-G., Li M-L., Yang J-H., Ding Q-C., Zhang L, *et al.* Impact of being overweight on the surgical outcomes of patients with gastric cancer: a meta-analysis. *World J Gastroenterol* 2013; 19:4596.
- Park D, Kim Y-W., Yang H-K., Ryu K, Han S-U, Kim H-H, *et al.* Short-term outcomes of a multicentre randomized clinical trial comparing laparoscopic pylorus-preserving gastrectomy with laparoscopic distal gastrectomy for gastric cancer (the KLASS-04 trial). *Br J Surg* 2021; 108:1043–1049.
- Kim W, Song KY, Lee H-J., Han SU, Hyung WJ, Cho GS. The impact of comorbidity on surgical outcomes in laparoscopy-assisted distal gastrectomy: a retrospective analysis of multicenter results. *Ann Surg* 2008; 248:793–799.
- Kim S-H., Son S-Y., Park Y-S., Ahn S-H., Park DJ, Kim H-H. Risk factors for anastomotic leakage: a retrospective cohort study in a single gastric surgical unit. *J Gastric Cancer* 2015; 15:167–175.

- 22 Oshi M, Kunisaki C, Miyamoto H, Kosaka T, Akiyama H, Endo I. Risk factors for anastomotic leakage of esophagojejunostomy after laparoscopy-assisted total gastrectomy for gastric cancer. *Dig Surg* 2018; 35:28–34.
- 23 Tu R-H., Lin J-X., Zheng C-H., Li P, Xie J-W., Wang J-B., *et al.* Development of a nomogram for predicting the risk of anastomotic leakage after a gastrectomy for gastric cancer. *Eur J Surg Oncol* 2017; 43:485–492.
- 24 Deguchi Y, Fukagawa T, Morita S, Ohashi M, Saka M, Katai H. Identification of risk factors for esophagojejunal anastomotic leakage after gastric surgery. *World J Surg* 2012; 36:1617–1622.
- 25 Kodera Y, Yoshida K, Kumamaru H, Kakeji Y, Hiki N, Etoh T, *et al.* Introducing laparoscopic total gastrectomy for gastric cancer in general practice: a retrospective cohort study based on a nationwide registry database in Japan. *Gastric Cancer* 2019; 22:202–213.
- 26 Bracale U, Peltrini R, De Luca M, Ilardi M, Di Nuzzo MM, Sartori A, *et al.* Predictive factors for anastomotic leakage after laparoscopic and open total gastrectomy: a systematic review. *J Clin Med* 2022; 11:5022.
- 27 Hyung WJ, Yang H-K., Han S-U., Lee Y-J., Park J-M., Kim JJ, *et al.* A feasibility study of laparoscopic total gastrectomy for clinical stage I gastric cancer: a prospective multi-center phase II clinical trial, KLASS 03. *Gastric Cancer* 2019; 22:214–222.
- 28 Fujita T, Yamazaki Y. Influence of surgeon's volume on early outcome after total gastrectomy. *Eur J Surg* 2002; 168:535–538.
- 29 Milone M, Manigrasso M, Burati M, Elmore U, Gennarelli N, Giglio MC, *et al.* Intracorporeal versus extracorporeal anastomosis after laparoscopic gastrectomy for gastric cancer. A systematic review with meta-analysis. *J Vis Surg* 2019; 156:305–318.
- 30 Roh CK, Choi S, Seo WJ, Cho M, Kim H-I, Lee S-K, *et al.* Incidence and treatment outcomes of leakage after gastrectomy for gastric cancer: experience of 14,075 patients from a large volume centre. *Eur J Surg Oncol* 2021; 47:2304–2312.
- 31 Kim Y-I., Lee JY, Khalayleh H, Kim CG, Yoon HM, Kim SJ, *et al.* Efficacy of endoscopic management for anastomotic leakage after gastrectomy in patients with gastric cancer. *Surg Endosc* 2022; 36:1–10.
- 32 Lee S, Ahn JY, Jung H-Y., Lee JH, Choi K-S., Kim DH, *et al.* Clinical outcomes of endoscopic and surgical management for postoperative upper gastrointestinal leakage. *Surg Endosc* 2013; 27:4232–4240.
- 33 Makuuchi R, Irino T, Tanizawa Y, Bando E, Kawamura T, Terashima M. Esophagojejunal anastomotic leakage following gastrectomy for gastric cancer. *Surg Today* 2019; 49:187–196.