JAMA Surgery | Original Investigation

Prophylactic Drain Placement and Postoperative Invasive Procedures After Gastrectomy

The Abdominal Drain After Gastrectomy (ADIGE) Randomized Clinical Trial

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IMPORTANCE Evidence suggests that prophylactic abdominal drainage after gastrectomy for cancer may reduce postoperative morbidity and hospital stay but this evidence comes from small studies with a high risk of bias. Further research is needed to determine whether drains safely meet their primary purpose of identifying and managing postoperative intraperitoneal collections without the need for reoperation or additional percutaneous drainage.

OBJECTIVE To determine whether avoiding routine abdominal drainage increased postoperative invasive procedures.

DESIGN, SETTING, AND PARTICIPANTS The Abdominal Drain in Gastrectomy (ADIGE) Trial was a multicenter prospective randomized noninferiority trial. Enrollment spanned from December 2019 to January 2023. Follow-up evaluations were completed at 30 and 90 days. Eleven centers within the Italian Research Group for Gastric Cancer, encompassing both academic medical centers and community hospitals, were included. Patients with gastric cancer undergoing subtotal or total gastrectomy with curative intent were eligible, excluding those younger than 18 years, with serious comorbidities, or undergoing procedure types outside the scope of the study. Of 803 patients assessed for eligibility, 404 were randomized and 390 were included in final analyses.

INTERVENTIONS Patients were randomized 1:1 into prophylactic drain or no drain arms.

MAIN OUTCOMES AND MEASURES The primary end point was a modified intention-to-treat (mITT) analysis measuring reoperation or percutaneous drainage within 30 postoperative days. The null hypothesis was rejected when the 90% CI upper limit of the proportion difference did not exceed 3.56%. The calculated sample size to achieve 80% power with a 10% dropout rate was 404 patients (202 in each group). Surgeons and patients were blinded until gastrointestinal reconstruction.

RESULTS Of the 404 patients randomized 226 (57.8%) were male; the median (IQR) age was 71 (62-78) years. Intraoperative identification of nonresectable disease occurred in 14 patients, leading to their exclusion from the study, leaving 390 patients. In the mITT analysis, 15 patients (7.7%) in the drain group needed reoperation or percutaneous drainage by postoperative day 30 vs 29 (15%) in the no drain group, favoring the drain group (difference, 7.2%; 90% CI, 2.1-12.4; $P = .02$). Of note, the difference in the primary composite end point was entirely due to a similar difference in reoperation (5.1% in the drain group vs 12.4% in the no drain group; $P = .01$). Drain-related complications occurred in 4 patients.

CONCLUSIONS AND RELEVANCE The findings of this study indicate that refraining from prophylactic drain use after gastrectomy heightened the risk of postoperative invasive procedures, discouraging its avoidance. Future studies identifying high-risk groups could optimize prophylactic drainage decisions.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT04227951

JAMA Surg. doi:10.1001/jamasurg.2024.5227
Published online November 27, 2024.

Visual Abstract

Invited Commentary

Supplemental content

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Group Information: A full list of the Italian Research Group for Gastric Cancer (GIRCG) members appears in Supplement 3.

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Despite technical advancements, gastric cancer surgery still has a high morbidity rate, even in high-volume centers.[1] According to recent data, the most frequent postoperative complications include anastomotic leak (9.8%) and fluid collections requiring drainage (9.3%). Many patients also experienced duodenal leaks (3.5%) and pancreatic fistula (4%).[1] Prophylactic drainage aims to identify and treat intraperitoneal fluid collections from surgical complications. However, its routine use has been questioned following evidence from colorectal surgery studies and Enhanced Recovery After Surgery (ERAS) protocols.[2-5] In the past decade, numerous studies—mainly from Korea, China, and Japan—with retrospective designs and limited sample sizes, have sought to determine the utility of anastomotic drainage after gastrectomy.[6-9] Our meta-analysis of randomized clinical trials (RCTs) and cohort studies found that drainage seemed to reduce postoperative morbidity and hospital stay.[10] These findings were corroborated by a recent meta-analysis.[11] Despite this, both meta-analyses highlighted a high risk of bias due to study designs. Examining only English-published RCTs, there are 3 with sample sizes ranging from 60 to 170 patients focusing on morbidity and mortality.[12-14] Notably, these outcomes are unsuitable for understanding the actual utility of prophylactic drainage, which aims to identify and treat postoperative intraperitoneal collections without needing reoperation or additional drainage. Despite these limitations, ERAS Society guidelines strongly recommend against prophylactic drainage after gastrectomy.[15]

Currently, prophylactic drainage is widespread internationally.[16,17] Our recent survey in Italy showed that prophylactic drainage exceeds 90% of procedures.[16] The Abdominal Drain in Gastrectomy (ADIGE) Trial was designed to determine whether drainage can yield comparable results to nondrainage in terms of reoperation risk or the need for additional drainage.

Key Points

Question Is avoiding routine abdominal drainage after gastrectomy for cancer safe?

Findings This randomized clinical trial found a statistically significant difference in the rate of reoperation or percutaneous drainage within 30 days after surgery.

Meaning The findings suggest that drain avoidance after gastrectomy for cancer may lead to an increased risk of postoperative invasive procedures.

Methods

Study Design

The ADIGE trial was a multicenter noninferiority RCT with a parallel design. Enrollment took place from December 2019 to January 2023, and patients were followed up at 30 and 90 days. The study was conducted in 11 academic medical centers and community hospitals belonging to the Italian Research Group for Gastric Cancer to investigate whether avoiding prophylactic drain placement in gastrectomy increased the need for postoperative invasive procedures. The study received approval from the research ethics board of all the participating centers and adhered to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) and Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines. All patients provided written informed consent. Data were collected, secured, and anonymized using a dedicated internet-based case report form accessible at http://www.gastrodata.org. The complete study protocol was previously published and is available in Supplement 1.[18]

Participants

All patients who underwent total or subtotal gastrectomy with curative intent for histologically proven gastric cancer or esophagogastric junction cancer (Siewert type II or III) and met the following inclusion and exclusion criteria were considered eligible for the study. Inclusion criteria were esophageal involvement ≤2 cm, upfront surgery or neoadjuvant/perioperative treatment, any surgical approach, and any type of anastomosis. Exclusion criteria were refusal to sign informed consent, younger than 18 years, severe heart disease (New York Heart Association class IV), severe liver disease (Child Pugh classification ≥B7), pregnancy, metastatic disease, emergency or palliative surgery, operation other than total or subtotal oncological gastrectomy with reconstruction methods other than Roux-en-Y or Billroth II, less than D1 lymph nodal dissection, multiple organ resection (except for cholecystectomy), gastric cancer with duodenal involvement, and intraoperative hyperthermic intraperitoneal chemotherapy.

Randomization and Masking

A medically authorized staff member randomized the participants using the secure online module of the ADIGE trial (https://www.gastrodata.org/node/10) before the start of the operation. Participants were randomized in a 1:1 ratio, stratified by the type of gastrectomy (subtotal or total gastrectomy), with competitive enrollment. The 2 arms were defined as follows: patients with a prophylactic drain placed at the end of the operation (control group) and those without any abdominal drain at the end of the operation (experimental group).

The leading surgeon and the patient remained blinded to the assigned arm until the completion of gastrointestinal reconstruction. Before discovering the assigned arm, the surgeon assessed whether the patient should be excluded (intraoperative dropout) based on the following criteria: intraoperative identification of non-radically resectable disease (R2 resection), unplanned multiple organ resection (except for cholecystectomy), a high-risk anastomosis defined as either an intraoperative positive test results for leak or evidence of a positive resection margin, or any other intraoperative complication specified on the case report form. If a patient was deemed ineligible, the operating surgeon had the discretion to place any drain independently from the randomization. There was no blinding of the patient, health care professionals, or coordinating researcher after the operation.

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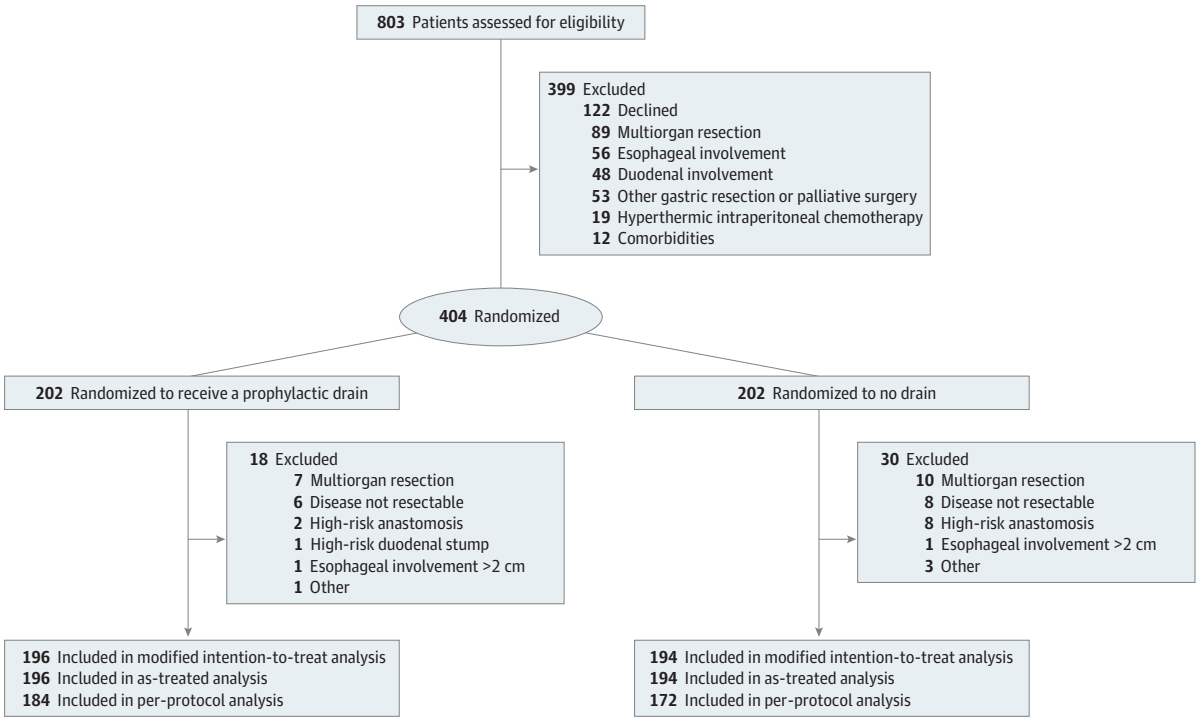
Figure. CONSORT Flow Diagram



Surgical Procedure and Perioperative Management

Randomized patients in the control group received 1 abdominal drain (of any type) positioned below the liver and passed by the duodenal stump, with the apex positioned posterior to the esophagojejunal or gastrojejunal anastomosis. Patients assigned to the no drain group did not have any drainage placed.

All patients followed the standard post-operative pathway of their respective participating centers, except for drain management. A methylene blue test (200 mL of water with 5 mL of methylene blue) was performed on postoperative day 4. If the test result was negative, the drain could be removed. Drain management in patients with a suspicious debt or positive blue test result was left to surgeon discretion.

Primary and Secondary Outcomes

The primary composite end point was the cumulative incidence of reoperation or percutaneous drainage placement by postoperative day 30. Secondary end points included incidence, severity, and time to diagnosis of anastomotic and duodenal leaks; length of hospital stay; overall morbidity within 30 days or during the in-hospital stay if longer than 30 days; overall 90-day mortality; and the 30-day readmission rate. Drain-related complications were also recorded. We also conducted a subanalysis considering the rate of reoperation and percutaneous drainage placement in academic and nonacademic hospitals to understand whether the different infrastructure could impact the decision to reoperate rather than place a percutaneous drain.

Complications were classified according to the International Consensus on Complications After Gastrectomy for Cancer[19] and stratified using the Clavien-Dindo classification.[20] No data monitoring committee was established, and no interim analysis was planned due to the trial's expected short duration and minimal calculated risks. Nonetheless, adverse events related to drain placement or avoidance were recorded, and the principal investigator reported any serious adverse events to the local institutional review board.

Statistical Analysis

The sample size was calculated based on a systematic review published in May 2020[10] and considering a dropout rate of 10%. A total of 404 patients (202 in each group) were needed to achieve 80% power. To have a balanced number of total and subtotal gastrectomy, recruitment was stopped at 202 patients for each planned operation. Complete sample size calculation has been previously described.[18]

The normal distribution of data was assessed using the Shapiro-Wilk test. The descriptive analysis summarized the categorical variables as absolute and percent frequencies and continuous variables as medians and IQRs.

When appropriate, Fisher exact or χ^2 test were used for nominal variables to evaluate the significance of differences between the control and experimental arms. The Wilcoxon-Mann-Whitney test was used for continuous variables.

The primary analysis consisted of a modified intention-to-treat (mITT) analysis, including all randomized patients who had undergone gastrectomy. Patients were analyzed according to the treatment assigned at preoperative randomization.

The proportion of patients, undergoing reintervention or percutaneous drain placement (primary end point), was com-

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Table 1. Baseline Characteristics of the Modified Intention-To-Treat Population

Characteristic	No. (%)			*P* value
	Drain (n = 196)	No drain (n = 194)	Total (N = 390)	
Sex				
Male	112 (57.1)	114 (58.8)	226 (57.9)	.75
Female	84 (42.9)	80 (41.2)	164 (42.1)	
Age, median (IQR), y	70 (62-78)	71 (63-79)	71 (62-78)	.83
BMI				
<18.5	4 (2.0)	5 (2.6)	9 (2.3)	.50
18.5-24.99	99 (50.5)	100 (51.8)	199 (51.2)	
25-29.99	77 (39.3)	65 (33.7)	142 (36.5)	
≥30	16 (8.2)	23 (11.9)	39 (10.0)	
ASA score				
1	9 (4.6)	5 (2.6)	14 (3.6)	.20
2	96 (49.0)	107 (55.2)	203 (52.1)	
3	84 (42.9)	80 (41.2)	164 (42.1)	
4	7 (3.6)	2 (1.0)	9 (2.3)	
Charlson comorbidity index, median (IQR)	4 (3-6)	5 (4-6)	5 (4-6)	.18
0-2	19 (9.7)	20 (10.3)	39 (10.0)	.44
3-4	83 (42.3)	70 (36.1)	153 (39.2)	
≥5	94 (48.0)	104 (53.6)	198 (50.8)	
Performance status				
0	138 (70.4)	129 (66.5)	267 (68.5)	.67
1	46 (23.5)	50 (25.8)	96 (24.6)	
>1	12 (6.1)	15 (7.7)	27 (6.9)	

(continued)

puted for each group. The difference between the primary end point proportion in the treated and control groups was analyzed with the corresponding confidence interval. The null hypothesis of inferiority was rejected when the upper limit of the 90% CI of the proportion difference did not exceed the noninferiority margin difference of 3.56%.

A secondary analysis was performed in the as-treated population, which included the same patients considered in the mITT, classified according to whether they underwent the prophylactic drain placement or not.

Another secondary analysis was carried out on the per-protocol population, including only patients who underwent surgery according to the arm assigned at randomization and followed up for at least 30 days. Patients who died before 30 days were also included in the per-protocol analysis.

Statistical analyses were performed using Stata/IC version 18.0 (StataCorp). Statistical significance for secondary analyses was set at $P < .05$ with 2-sided statistical tests.

Results

The study commenced in December 2019, and despite the challenges posed by the COVID-19 pandemic, we decided to continue the trial, informing the patients and the participating centers and acknowledging the potential reduction in recruitment. Between December 19, 2019, and December 29, 2022, a total of 803 patients underwent eligibility screening. We successfully enrolled and randomized 404 patients for the ADIGE trial (226 [57.9%] male and 164 [42.1%] female; median [IQR] age, 71 [62-78] years). Intraoperative identification of nonresectable disease (patients who did not undergo gastrectomy) occurred in 14 patients, leading to their exclusion from the study under the mITT planned analysis. The final analysis involved 390 participants, 196 patents in the drain group and 194 in the no drain group (**Figure**). All patients completed 90-day follow-up except for 25 who died before postoperative day 90. No missing data were reported.

Both groups exhibited comparable baseline demographic characteristics, oncological features, and comorbidities (**Table 1**). Nearly half of the patients (181 of 390) had a body mass index of 25 or greater (calculated as weight in kilograms divided by height in meters squared). Most patients were categorized as American Society of Anesthesiologists II (203 [52%]) and III (164 [42%]), with a median Charlson Comorbidity Index of 5. Most of the tumors were adenocarcinomas (363 [93%]), and 157 patients (40%) received neoadjuvant treatment.

Both groups exhibited a marginal predominance of subtotal gastrectomy (111 [57%] in the drain group and 116 [60%] in group the no drain group) compared with total gastrectomy, indicating an approximate 8% deviation from the planned operation. A laparoscopic or robotic approach was used in 242 patients (62%). Reconstruction was predominantly achieved via a Roux-en-Y technique, using

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Table 1. Baseline Characteristics of the Modified Intention-To-Treat Population (continued)

Characteristic	No. (%)			*P* value
	Drain (n = 196)	No drain (n = 194)	Total (N = 390)	
Preoperative chemotherapy	77 (39.3)	78 (40.2)	155 (39.7)	.85
Preoperative chemoradiotherapy	1 (0.5)	1 (0.5)	2 (0.5)	.99
Surgical approach				
Laparoscopy	105 (53.6)	117 (60.3)	222 (56.9)	.24
Open	78 (39.8)	70 (36.1)	148 (37.9)	
Robotic	13 (6.6)	7 (3.6)	20 (5.1)	
Surgical procedure				
Subtotal gastrectomy	111 (56.6)	116 (59.8)	227 (58.2)	.53
Total gastrectomy	85 (43.4)	78 (40.2)	163 (41.8)	
Type of reconstruction				
Billroth II	15 (7.7)	11 (5.7)	26 (6.7)	.43
Roux-en-Y	181 (92.3)	183 (94.3)	364 (93.3)	
Anastomosis				
Circular stapled	79 (40.3)	74 (38.1)	153 (39.2)	.87
Hand sewn	13 (6.6)	12 (6.2)	25 (6.4)	
Linear stapled	104 (53.1)	108 (55.7)	212 (54.4)	
Duodenal stump suture				
Manual	2 (1.0)	2 (1.0)	4 (1.0)	.99
Mechanical	194 (99.0)	192 (99.0)	386 (99.0)	
Lymphadenectomy				
D0	6 (3.1)	6 (3.1)	12 (3.1)	.11
D1/D1+	14 (7.1)	5 (2.6)	19 (4.9)	
D2/D2+	176 (89.8)	183 (94.3)	359 (92.1)	
Resection margin				
R0	186 (94.9)	186 (95.9)	372 (95.4)	.47
R1	10 (5.1)	7 (3.6)	17 (4.4)	
R2	0	1 (0.5)	1 (0.3)	
Tumor histology (WHO classification)				
Adenocarcinoma	179 (91.3)	184 (94.8)	363 (93.1)	.03
Other[a]	13 (6.6)	3 (1.5)	16 (4.1)	
Undifferentiated carcinoma	4 (2.0)	7 (3.6)	11 (2.8)	
Adenocarcinoma type				
Diffuse	46 (25.7)	61 (33.2)	107 (29.5)	.26
Intestinal	90 (50.3)	81 (44.0)	171 (47.1)	
Mixed	22 (12.3)	16 (8.7)	38 (10.5)	
Unknown	21 (11.7)	26 (14.1)	47 (12.9)	
pT				
T0	14 (7.2)	10 (5.2)	24 (6.2)	.56
T1	48 (24.7)	42 (21.9)	90 (23.3)	
T2	20 (10.3)	21 (10.9)	41 (10.6)	
T3	63 (32.5)	77 (40.1)	140 (36.3)	
T4a	49 (25.3)	42 (21.9)	91 (23.6)	
pN				
N0	87 (44.4)	88 (45.4)	175 (44.9)	.58
N1	30 (15.3)	28 (14.4)	58 (14.9)	
N2	27 (13.8)	35 (18.0)	62 (15.9)	
N3	52 (26.5)	43 (22.2)	95 (24.4)	
pM				
M0	191 (97.4)	188 (96.9)	379 (97.2)	.75
M1	5 (2.6)	6 (3.1)	11 (2.8)	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); WHO, World Health Organization.

[a] Other included adenosquamous carcinoma, neuroendocrine carcinoma, and mixed neoplasms.

staplers for the anastomosis (Table 1). Circular staplers were the preferred choice for total gastrectomy (112 of 163 [69%]), whereas linear staplers were predominantly used for subtotal gastrectomy (170 of 227 [75%]) in both groups (eTable 1 in Supplement 2). Surgical outcomes were deemed satisfactory in both groups, with 359 of 390 patients (92%) undergoing a D2 or D2+ lymphadenectomy and achieving an R0 resection rate of 95%. The pathological stage revealed a 55% rate of pN+ and indicated that 107 of 390 patients (30%) had diffuse gastric adenocarcinoma (Table 1).

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Table 2. Dropout Rate, Drain Placement, and Drain Features in the Modified Intention-To-Treat Population

Variable	No. (%)			*P* value
	Drain (n = 196)	No drain (n = 194)	Total (N = 390)	
Planned operation				
Subtotal gastrectomy	92 (46.9)	95 (49.0)	187 (47.9)	.69
Total gastrectomy	104 (53.1)	99 (51.0)	203 (52.1)	
Dropout				
No	184 (93.9)	172 (88.7)	356 (91.3)	.07
Yes	12 (6.1)	22 (11.3)	34 (8.7)	
Drain placed in the surgical site				
Yes	195 (99.5)	22 (11.3)	217 (55.6)	NA[a]
No	1 (0.5)	172 (88.7)	173 (44.4)	
Drain-related complication[b]				
Pain	3 (1.5)	0	3 (1.5)	.80
Twisting of the anastomosis	1 (0.5)	0	1 (0.5)	
None	191 (98.0)	22 (100)	217 (100)	
Methylene test				
Negative	195 (100.0)	21 (95.5)	216 (99.5)	.004
Positive	0	1 (4.5)	1 (0.5)	
Suspicious debt				
Ascites	1 (0.5)	0	1 (0.5)	.03
Bile	1 (0.5)	2 (9.0)	3 (1.4)	
Blood	4 (2.1)	0	4 (1.8)	
Corpusculated liquid	1 (0.5)	1 (4.6)	2 (0.9)	
Lymphatic	1 (0.5)	0	1 (0.5)	
Pancreatic	4 (2.1)	1 (4.6)	5 (2.3)	
Saliva/food	1 (0.5)	0	1 (0.5)	
None	182 (93.3)	18 (81.8)	200 (92.1)	

Abbreviation: NA, not applicable.

[a] Drain placement a priori differed between the 2 groups by design.

[b] Drain-related complications were computed on the subgroup of individuals (n = 217) who had been treated with drain placement.

Among the 194 patients in the no drain group, 22 were excluded by the operating surgeon according to the established dropout criteria; at least 1 drain was placed at the end of the operation for all patients in this subgroup. In contrast, in the drain group, 12 patients were considered dropouts, but the surgeon decided not to place a prophylactic drain in only 1 case (**Table 2**).

Considering patients with a drain, the methylene test yielded a positive result in only 1 case (0.5%), which was from the no drain group. Conversely, a suspicious debt was observed in 17 of 217 patients with drains (8%), with pancreatic fluid being the primary type of debt (5 patients [2%]).

Drain-related complications were limited to 3 patients reporting pain at the insertion site. An additional patient experienced an anastomosis kinking that was treated with endoscopy.

In the mITT analysis, 15 patients in the drain group (7.7%) required reoperation or percutaneous drainage placement by postoperative day 30, compared to 29 patients in the no drain group (15%). This resulted in a 7.2% difference (90% CI, 2.1-12.4; *P* = .02) in favor of the drain group, thus supporting the null hypothesis of inferiority for the no drain group (**Table 3**). Of note, the difference in the primary composite end point was entirely due to a similar difference in reoperation, which was performed in 10 patients (5.1%) in the drain group and 24 patients (12.4%) in the no drain group. The proportion of percutaneous drainage placement (2.6%) was equal in both groups.

Both the secondary analyses conducted on the as-treated and per-protocol populations confirmed the advantage of placing a prophylactic drain. The difference in the as-treated analysis was 6.6% (90% CI, 1.3-11.9; *P* = .04) and 7.3% (90% CI, 2.0-12.8, *P* = .02) in the per-protocol analysis, favoring the drain group.

Postoperative surgical complications occurred in 89 patients (23%) and were evenly distributed between the 2 groups. The incidence of anastomotic leaks was 4% (n = 16, 6 in the drain group [3%] and 10 in the no drain group [5%]), with a median (IQR) time to diagnosis of 7 (4-10) postoperative days. Duodenal leaks were diagnosed in 2% of the patients (n = 9, 4 in the drain group [2%] and 5 in the no drain group [3%]), with a median (IQR) time to diagnosis of 14 (4-17) postoperative days. Notably, the presence of a drain did not lead to an earlier diagnosis of duodenal leaks (median postoperative day: drain group, 16; no drain group, 4); however, it appeared to slightly anticipate the detection of anastomotic leaks (median postoperative day: drain group, 4; no drain group, 10). All the other surgical complications have been recorded in eTable 2 in Supplement 2. The incidence and severity of medical complications exhibited no significant difference between the 2 groups (eTable 3 in Supplement 2), except for a higher occurrence of acute kidney insufficiency in the no drain group (3% vs 0%; *P* = .02).

Overall, the 90-day mortality rate tended to be higher in the no drain group (n = 17 [8.8%]) than the drain group (n = 8 [4.1%]),

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and the difference was not significant (P = .06) (**Table 4**). However, in-hospital mortality was significantly higher in the no drain group compared to the drain group (n = 9 [4.6%] vs n = 1 [0.5%]; P = .03). Notably, 28 patients (14.4%) in the no drain group needed an escalation in the level of care, while 13 patients in the drain group (6.6%) required such escalation (P = .01).

No difference was observed between the 2 groups in terms of patients' discharge and readmission. Patients were typically discharged home after a median (IQR) of 7 (6-10) postoperative days, with 5 (1.3%) requiring transfer to a secondary hospital or rehabilitation center. The overall readmission rate for the entire cohort was 6.2% (n = 24).

When academic and nonacademic hospitals were analyzed separately for reoperation and percutaneous drain placement (eTable 4 in Supplement 2), the reoperation rate in the no drain group was twice as high in academic hospitals (11.9%), although this increase was not statistically significant (P = .17). In contrast, nonacademic hospitals showed a significantly higher reoperation rate in the no drain group, with a 3-fold increase (13.2%) compared to the drain group (3.7%) (P = .04). Notably, this difference does not reflect an inverse proportion in the use of percutaneous drains, which were rarely used in either type of hospital across both groups.

Table 3. Noninferiority Analysis on the Modified Intention-to-Treat Population and Secondary Analyses on the As-Treated and Per-Protocol Populations[a]

Variable	Difference, % (95% CI)	*P* value
Modified intention-to-treat population	7.2 (2.2-12.4)	.02
As-treated population	6.6 (1.3-11.9)	.04
Per-protocol population	7.3 (2.0-12.8)	.02

[a] In univariable analysis on reoperation and percutaneous drain placement among the study groups, differences were as follows. Reoperation 5.1% in drain group (10/196 patients) and 12.4% in no drain group (24/194 patients) (P = .01); percutaneous drainage 2.6% in drain group (5/196 patients) and 2.6% in no drain group (5/194 patients) (P = .99).

Discussion

The ADIGE RCT yields crucial insights into the role of prophylactic drainage after gastrectomy for cancer. Our findings underscore a significant increase in the risk of postoperative invasive interventions, including reoperation and percutaneous drain insertion, when opting for a no-drain strategy compared to a prophylactic drain.

Over the past 2 decades, the use of drainage following gastrectomy has faced scrutiny. The 2014 ERAS guidelines,[15] supported by a high level of evidence, strongly discourage this practice. While previous trials aimed to assess the impact of drains on patient recovery and complications, it is important to emphasize that drains primarily serve to prevent and treat postoperative abdominal abscesses, regardless of the underlying cause, rather than reducing complications.

Existing RCTs failed to provide conclusive evidence on reoperation and percutaneous drain placement because they lacked the statistical power necessary for definitive conclusions. A meta-analysis by Pang and colleagues[11] highlighted the scarcity of RCTs analyzing percutaneous drain placement or reoperation. This meta-analysis found no significant differences between drain and no drain groups for these outcomes, emphasizing a very low level of evidence due to concerns about bias, inconsistency, and indirectness.

To rigorously evaluate these outcomes, we designed this trial, surpassing the sample sizes of prior studies. According to our meta-analysis,[10] we anticipated a comparable incidence of postoperative invasive procedures between the 2 groups (6.44% in the drain group and 4.16% in the no drain group). Contrary to this expectation, the present RCT unveiled a significant 7.2% increase in postoperative invasive procedures when prophylactic drains were omitted.

Our trial also revealed a comparable percentage of patients requiring an additional drain in both groups (2.6%) but a significant increase in the reoperation rate in the no drain group (12.4% vs 5.1%; P = .01). This result may stem from the preferred treatment approach of participating centers for intra-abdominal abscesses or the severity of patients' conditions associated with these collections.

When academic and nonacademic centers were analyzed separately, we observed an increased reoperation rate in the no drain group for both hospital categories. However, the increase was significantly higher in nonacademic institutions. This difference may be attributed to a more aggressive approach in smaller hospitals when complications arise, compared to larger hospitals with 24/7 services available.

In our secondary analyses, our study demonstrated that a prophylactic drain does not impact the incidence of anastomotic and duodenal leaks or overall morbidity. These findings align with most previously published RCTs,[12-14] although a single-center RCT[13] reported a significant reduction in overall morbidity in the no drain group (9.7% vs 37.9%). Furthermore, the pooled analysis in the meta-analysis by Pang et al[11] suggested a 32% reduction in postoperative complications, albeit with a low quality of evidence due to a high risk of bias.

Previous studies lack the standardization provided in our study through the Gastrectomy Complications Consensus Group.[1] Therefore, the reduced postoperative morbidity suggested by these studies should be approached cautiously, given the highlighted high risk of bias and the absence of standardization in defining and assessing the severity of complications.

Our study revealed a significant 14.4% escalation in the level of care needed for patients in no drain group, compared to 6.6% in drain group. This evidence is likely associated with the increased reoperations in the no drain group, indicating a more intricate management, especially significant for rural hospitals, and potentially entailing higher costs.

In-hospital mortality in our study was significantly increased in patients without drains with respect to those with drains (0.5% vs 4.6%), but the difference was only borderline significant for 90-day mortality (4.1% vs 8.8%). In the 4 RCTs encompassed in the meta-analysis by Pang et al,[11] involving 416 patients and reporting postoperative mortality, no significant difference was noted between the drain and no drain groups. The odds ratio stood at 1.30 (95% CI, 0.14-11.92; P = .82).

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Table 4. Mortality, Discharge Site, and Readmission Rate in the Modified Intention-To-Treat Population

Variable	No. (%)			*P* value
	Drain (n = 196)	No drain (n = 194)	Total (N = 390)	
Escalation in level of care	13 (6.6)	28 (14.4)	41 (10.5)	.01
Blood product utilization	36 (18.5)	38 (19.6)	74 (19.0)	.78
Discharge location				
Died in hospital prior to discharge	1 (0.5)	9 (4.6)	10 (2.6)	.03
Discharge to any other medical facility	3 (1.5)	2 (1.0)	5 (1.3)	
Discharge to home	191 (97.9)	183 (94.3)	374 (96.1)	
Readmission related to gastrectomy				
No	185 (94.4)	181 (93.3)	366 (93.8)	.66
Yes	11 (5.6)	13 (6.7)	24 (6.2)	
Length of postoperative hospitalization, median (IQR; range), d	7 (6-10; 4-74)	7 (6-10; 4-136)	7 (6-10; 4-136)	.57
90-d Mortality	8 (4.1)	17 (8.8)	25 (6.4)	.06

The reduction in hospitalization stands out as one of the most emphasized advantages highlighted by previous RCTs focusing on avoiding prophylactic drainage after gastrectomy. This observation is corroborated in our and Pang et al's[11] meta-analyses. Nonetheless, the length of hospital stay is influenced by numerous factors related to patients' general and social conditions, the health care system, ERAS protocols, and the complexity of the operation.

Our study revealed comparable hospital stays between the 2 groups, with a median of 7 days for both. It is noteworthy that this median stay is 2 days shorter than that reported in the 2020 GASTRODATA database[1] and lower than that reported in our previous meta-analysis[10] on prophylactic drain. The observed outcome can be attributed to the experience of the participating centers in gastric cancer surgery and ERAS, which may have been lacking in older studies, and the exclusion of multiple resections as well as hyperthermic intraperitoneal chemotherapy.

Complications related to the drain were minimal (2%), affirming the safety of drain placement after gastrectomy. This aligns with existing studies included in our meta-analysis[10] reporting similar outcomes, ranging between 1.5% and 7.1%.

We tried to determine whether an inexpensive test, such as the methylene blue test, was reliable in detecting anastomotic leaks. However, of 16 anastomotic leaks, 1 patient had a positive test result, suggesting that surgeons should not rely on this test.

The strengths of our study are grounded in the selection of a critical outcome for defining the efficacy of prophylactic drains, the multicentric design, the substantial sample size, and the broad inclusion criteria that mirror the intricacies of gastrectomy in the era of neoadjuvant treatment and signet ring cell tumors, particularly in Europe and the Americas.

Limitations

One limitation of our study is the lack of investigation int drainage amylase levels as predictor of anastomotic and duodenal leaks and pancreatic fistula. While this aspect has primarily been explored in studies concentrating on postgastrectomy pancreatic fistula, it could contribute to defining an optimal drainage removal strategy, especially for low-risk patients.[21,22]

Conclusions

While prophylactic drainage in gastrectomy has been questioned in previous studies and is strongly discouraged in ERAS guidelines,[15] our call for a reassessment postgastrectomy is grounded in this extensive multicenter RCT. This recommendation gains importance in Europe and the Americas, considering the high percentage of advanced tumors and the decentralization of gastrectomy procedures across numerous hospitals, each handling a limited number of cases annually and potentially facing resource constraints.

ARTICLE INFORMATION

Accepted for Publication: September 18, 2024.

Published Online: November 27, 2024. doi:10.1001/jamasurg.2024.5227

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Administrative, technical, or material support: Weindelmayer, Mengardo, de Pascale, Gelmini, Reddavid, Solaini.
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Conflict of Interest Disclosures: None reported.

Funding/Support: RicerchiAmo Onlus supported the present study by funding the development of the online CRF.

Role of the Funder/Sponsor: [Name] had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: A full list of the Italian Research Group for Gastric Cancer (GIRCG) members appears in Supplement 3.

Data Sharing Statement: See Supplement 4.

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