

Hybrid Laparoscopic-Angioembolization Two-Stage Gastric Ischemic Conditioning Prior to Esophagectomy: A Single-Center Retrospective Cohort Study

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ABSTRACT

Background: Gastric conduit necrosis following esophagectomy remains a devastating complication associated with anastomotic failure and mortality. Ischemic conditioning (IC) promotes neovascularization and may reduce this risk. We describe a hybrid two-stage protocol integrating laparoscopic vascular ligation with percutaneous angioembolization, timed within the neoadjuvant treatment pathway.

Methods: We performed a single-center retrospective cohort study (January 2015–December 2025) comparing 7 patients who received a hybrid two-stage IC protocol (laparoscopic short gastric vessel ligation followed by percutaneous angioembolization of the left gastric artery) with 15 non-conditioned patients who received tubular gastric conduit reconstruction. The primary outcome was the Comprehensive Complication Index (CCI®). Secondary outcomes included conduit necrosis, anastomotic leak, and 30-day mortality.

Results: Twenty-two patients with gastric conduit reconstruction were analyzed (IC, n = 7; non-IC, n = 15); five patients with non-gastric reconstruction (colon interposition n = 2, Roux-en-Y esophagojejunostomy n = 3) were excluded from conduit-specific outcome analysis. Median CCI® was 8.7 versus 39.7 (p = 0.192). Conduit necrosis occurred in 0/7 (0%) versus 4/15 (26.7%), anastomotic leak in 0/7 versus 2/15 (13.3%), and 30-day mortality in 0/7 versus 2/15 (13.3%). The conditioned group demonstrated higher pCR rates (42.9% [3/7] vs 14.3% [1/7] in neoadjuvant-treated non-IC patients) and shorter ICU and hospital stays.

Conclusions: In this hypothesis-generating cohort, a hybrid two-stage laparoscopic-angioembolization IC protocol was associated with numerically lower conduit necrosis, morbidity, and mortality, without adding treatment delay. Among the five protocol-adherent cases, no conduit complications or mortality were observed. These findings support prospective multicenter evaluation.

Keywords

Esophagectomy, Gastric conduit, Ischemic conditioning, Angioembolization, Anastomotic leak.

Abbreviations

ASA: American Society of Anesthesiologists physical status classification, BMI: body mass index, CAAE: Certificado de Apresentação de Apreciação Ética (Brazilian IRB certificate), CCI®: Comprehensive Complication Index, CI: confidence

interval, CROSS: Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study, ECCG: Esophagectomy Complications Consensus Group, ECOG: Eastern Cooperative Oncology Group, FLOT: fluorouracil, leucovorin, oxaliplatin, and docetaxel, HMAPA: Hospital Militar de Área de Porto Alegre, IC: ischemic conditioning, ICU: intensive care unit, IQR: interquartile range, SD: standard deviation, SPSS: Statistical Package for the Social Sciences, STROBE: Strengthening the Reporting of Observational Studies in Epidemiology.

Introduction

Esophagectomy with gastric pull-up remains the cornerstone of curative treatment for locally advanced esophageal cancer. Despite advances in perioperative care, the operation carries morbidity of 40–80% and in-hospital mortality of 2–10% in high-volume centers [1,2]. Among the most feared complications is ischemic injury to the gastric conduit, affecting 10–20% of patients and substantially increasing the risk of anastomotic leak, sepsis, reoperation, and death [3,4]. Once the left gastric and short gastric arteries are divided, conduit perfusion depends almost entirely on the right gastroepiploic arcade; the distal anastomotic zone constitutes a tenuous watershed region further compromised by diabetes, prior radiation, vascular disease, and smoking [3,4].

Gastric ischemic conditioning (IC), first described by Akiyama and colleagues using preoperative angiographic embolization [5] and subsequently adapted to laparoscopic ligation by Pham and colleagues and others [6,7], involves staged preoperative devascularization of the gastric fundus to trigger compensatory angiogenesis through the gastroepiploic arcade. A pooled analysis of over 3,800 patients from 24 studies demonstrated significantly lower anastomotic leak (OR 0.54, 95% CI 0.39–0.75) and conduit necrosis (OR 0.38, 95% CI 0.20–0.71) with IC [8–10]. This benefit has also been demonstrated in large database analyses of specific operative approaches [11]. Nonetheless, prospective data remain limited, all published series originate from high-volume Western or Asian centers, and every existing protocol employs single-modality devascularization.

We report our experience with a novel hybrid two-stage IC protocol combining laparoscopic short gastric vessel ligation with percutaneous angioembolization of the left gastric artery, integrated within the existing neoadjuvant oncologic timeline, at a military teaching hospital in southern Brazil, and compare outcomes between conditioned and non-conditioned patients over an 11-year period.

Methods

Study Design and Setting

This was a single-center retrospective cohort study conducted at Hospital Militar de Área de Porto Alegre (HMAPA), Brazil, in accordance with the Declaration of Helsinki. The protocol was approved by the Institutional Review Board (CAAE: 86990325.3.0000.5349; Protocol No. 7.524.942, April 2025). Individual informed consent was waived given the retrospective

design. The study is reported in accordance with the STROBE Statement [12]; a STROBE-compliant participant flow diagram is provided as Supplementary Figure 1.

Patient Selection

Of the 27 consecutive patients who underwent esophagectomy or esophageal resection between January 2015 and December 2025, 22 who received tubular gastric conduit reconstruction constitute the primary analytic cohort (IC, $n = 7$; non-IC, $n = 15$); 5 patients who received non-gastric reconstruction were excluded from conduit-specific outcome analyses. Patients were classified as IC or non-IC based on whether preoperative conditioning was performed. IC was introduced as a pilot in 2019 following an internal audit identifying unacceptable conduit necrosis rates, and adopted systematically from 2021 onward for all eligible patients without contraindications to interventional angioembolization. Patients who declined or required emergency esophagectomy proceeded without conditioning.

Ischemic Conditioning Technique

The IC protocol consisted of two sequential conditioning procedures performed prior to definitive esophagectomy, integrated into the existing oncologic treatment timeline to minimize additional delay.

Stage 1 was performed laparoscopically at the time of staging laparoscopy during the initial oncologic workup. Under general anesthesia, the short gastric vessels were ligated and divided, and the entire greater curvature of the stomach was mobilized, preserving the right gastroepiploic arcade as the sole remaining vascular pedicle. No separate hospital admission was required, as this procedure was performed concurrently with oncologic staging. A post-pyloric nasoenteral feeding tube was placed at this time for perioperative nutritional support, if patient needs.

Stage 2 consisted of percutaneous angioembolization of the left gastric artery, performed by an experienced interventional radiology group 7–10 days following completion of neoadjuvant chemotherapy or chemoradiotherapy. Deferral until after neoadjuvant completion was deliberate: intact left gastric artery perfusion during systemic treatment was hypothesized to maximize chemotherapy bioavailability at the primary tumor site. All procedures were performed on an outpatient basis via radial or femoral access. Celiac axis angiography was performed to delineate left gastric artery anatomy; selective catheterization was achieved using a microcatheter. Embolization was performed using standard metallic microcoils (pushable or detachable, 0.018- or 0.035-inch platform, selected according to target vessel diameter), deliberately preserving the proximal left gastric segment to facilitate subsequent surgical ligation. A completion arteriogram confirmed target vessel occlusion (Supplementary Figure 2). Definitive esophagectomy was scheduled 4–5 weeks after Stage 2, allowing time for compensatory neovascularization through the gastroepiploic arcade.

Esophagectomy Procedure

Esophagectomy was performed using minimally invasive (thoracoscopic/laparoscopic or robotic-assisted) or open techniques according to surgeon preference and patient factors, with gastric conduit reconstruction in all cases. Reconstruction was via Ivor Lewis (posterior mediastinum, intrathoracic anastomosis) or McKeown three-field (cervical anastomosis) approach, depending on tumor location. Cervical or intrathoracic anastomosis was performed as a side-to-side (functional end-to-end) anastomosis using three firings of a 45-mm linear endoscopic stapler, with the common enterotomy closed with a running 3-0 polydioxanone or 3-0 absorbable barbed suture. Perioperative enteral nutritional support was maintained through the nasogastric feeding tube.

Data Collection and Variables

Demographic, clinical, operative, pathologic, and outcome data were abstracted from electronic medical records. No missing data were identified for any variable of interest among the 27 included patients; two BMI values contained data-entry errors that were corrected prior to analysis.

Outcomes

The primary outcome was overall postoperative morbidity quantified by the Comprehensive Complication Index (CCI®), a validated metric weighting all complications on a continuous scale from 0 (no complications) to 100 (death) [13]. Secondary outcomes included gastric conduit necrosis (endoscopically or intraoperatively confirmed ischemic injury requiring intervention), anastomotic leak (classified per Esophagectomy Complications Consensus Group [ECCG] definitions) [14], mid-conduit fistula, anastomotic stricture, Clavien-Dindo classification [15], ICU and hospital length of stay, in-hospital mortality, 30-day mortality, and pathologic response to neoadjuvant therapy. Pathologic response was graded using the modified Ryan/CAP tumor regression grading system: grade 0 (complete response, no residual viable tumor); grade 1 (near-complete response, single cells or rare small groups); grade 2 (partial response, residual tumor with predominant fibrosis); grade 3 (poor or no response).

Statistical Analysis

Continuous variables are reported as median [IQR] or mean \pm SD; categorical variables as frequencies and percentages. Between-group comparisons used the Mann-Whitney U test for continuous and Fisher exact or chi-square for categorical variables (two-tailed, $\alpha = 0.05$). No multivariable adjustments were performed given the small sample size. Exact 95% CIs for proportions with zero events used the Clopper-Pearson method. Analyses were performed in SPSS v29.0 (IBM Corp.) and R v4.3.

Results

Study Population

During the 11-year study period, 27 patients underwent esophagectomy or esophageal resection at the institution. Twenty-two patients who received tubular gastric conduit reconstruction constitute the primary analytic cohort (IC, $n = 7$; non-IC,

$n = 15$). Five patients received non-gastric reconstruction (colon interposition, $n = 2$; Roux-en-Y esophagojejunostomy, $n = 3$) and are excluded from conduit-specific outcome analyses, as gastric conduit necrosis and anastomotic leak rates are not applicable to non-gastric reconstructions. Two pilot IC cases were performed in 2019; systematic adoption began in 2021.

Baseline Characteristics

Baseline characteristics are presented in Table 1. Groups were balanced for age (60.0 vs 62.0 years, $p = 0.887$), BMI (23.1 vs 24.9 kg/m², $p = 0.502$), ASA score (median 2.0 in both, $p = 0.441$), and Charlson Comorbidity Index (6.0 vs 5.0, $p = 0.105$). There was a borderline difference in sex distribution (85.7% vs 46.7% male, $p = 0.165$). All IC patients received neoadjuvant therapy (57.1% CROSS; 42.9% FLOT) versus 46.7% of non-IC patients (7/15; $p = 0.022$). Among the 22 gastric conduit patients, tumor histology was squamous cell carcinoma in 12 (54.5%) and adenocarcinoma in 10 (45.5%), distributed similarly between groups ($p = 1.000$). No patients were classified as other histology within the primary analytic cohort.

Pre-Conditioning Details

The median interval from Stage 1 to esophagectomy was 150 days [IQR 129–159]; from Stage 2 to esophagectomy, 29 days [IQR 26–45] among patients who completed the standard protocol ($n = 5$). Two patients deviated from the standard protocol: Case 04 received simultaneous two-stage laparoscopic conditioning (without an inter-stage interval) due to nutritional compromise precluding staged admissions; Case 06 received Stage 1 only due to failed Stage 2 angioembolization secondary to severe atherosclerotic disease of the celiac axis. Both were retained in the IC group for intention-to-treat analysis.

Operative Details

Surgical approach and intraoperative parameters were similar between groups (Table 1). All IC patients (100%) and 93.3% of non-IC patients underwent minimally invasive esophagectomy ($p = 1.000$). Among IC patients, 57.1% had McKeown three-field reconstruction and 42.9% had Ivor Lewis reconstruction. Mean operative time (427.9 ± 89.3 vs 402.0 ± 124.7 min, $p = 0.670$), estimated blood loss (418.6 ± 166.6 vs 447.5 ± 259.3 mL, $p = 0.972$), lymph node yield (30.0 ± 8.8 vs 29.8 ± 9.7 , $p = 0.750$), and R0 resection rates (100% vs 93.3%, $p = 1.000$) were comparable.

Postoperative Morbidity

Postoperative outcomes are presented in Table 2. Median CCI® was 8.7 [IQR 0.0–26.2] in the IC group versus 39.7 [IQR 0.0–81.3] in the non-IC group ($p = 0.192$). No IC patient developed gastric conduit necrosis (0%; 95% CI 0.0–41.0%) versus 4/15 (26.7%; 95% CI 7.8–55.1%) in the non-IC group ($p = 0.263$) (Figure 1). No anastomotic leak occurred in the IC group (0%; 95% CI 0.0–41.0%) versus 2/15 (13.3%; 95% CI 1.7–40.5%) in the non-IC group ($p = 1.000$), including one ECCG Type II and one Type III event. Clavien-Dindo Grade 0 was present in 3/7 IC patients (42.9%) versus 5/15 (33.3%) in the non-IC group; Grade I occurred in 1/7

IC patients (14.3%). Clinically relevant complications (\geq Grade IIIa) occurred in 3/7 IC versus 9/15 non-IC patients (42.9% vs 60.0%, $p = 0.652$) (Figure 2). In a per-protocol analysis restricted to the five patients who completed the standard hybrid two-stage protocol, CCI[®] was 0.0 in all cases, with no conduit necrosis, no anastomotic leak, and no in-hospital mortality.

Both IC complications arose in protocol-deviant cases: a mid-conduit mediastinal fistula (Clavien-Dindo IIIa; managed with 3 sessions of endoscopic vacuum therapy) in Case 04, who received simultaneous two-stage laparoscopic conditioning; and an anastomotic stricture (Clavien-Dindo IIIa; managed with 4 sessions of balloon dilation) in Case 06, who received Stage 1 only due to failed angioembolization. All five patients who completed the standard hybrid protocol had CCI[®] = 0.0.

Recovery and Mortality

Median ICU stay was shorter in the IC group (2.0 [IQR 2.0–3.0] vs 5.0 [IQR 3.0–24.0] days, $p = 0.190$) as was total hospital stay (7.0 [IQR 6.0–11.0] vs 10.0 [IQR 6.0–30.0] days, $p = 0.859$). No IC patient died during the index hospitalization (0%; 95% CI 0.0–41.0%) compared with 4/15 (26.7%; 95% CI 7.8–55.1%) in

the non-IC group ($p = 0.263$). Among the four non-IC gastric-conduit deaths, three were attributable to conduit necrosis and its septic sequelae; one occurred without conduit ischemia and was attributed to pulmonary sepsis. Thirty-day mortality was 0% in the IC group (95% CI 0.0–41.0%) versus 2/15 (13.3%; 95% CI 1.7–40.5%) in the non-IC group ($p = 1.000$).

Pathologic Response

Among patients who received neoadjuvant therapy (IC $n = 7$; non-IC-neoadjuvant $n = 7$), pathologic complete response (Ryan/CAP grade 0) was observed in 3/7 IC patients (42.9%: 2 after CROSS, 1 after FLOT) and 1/7 non-IC-neoadjuvant patients (14.3%). The pCR denominator of 7 for the IC group includes Case 04, who achieved no pathologic response (Ryan grade 3, pT4bN3aM1); the 42.9% pCR rate therefore reflects the full neoadjuvant-treated IC population without exclusion of unfavorable cases. Major pathologic response (Ryan grade 0–1) was achieved in 5/7 IC patients (71.4%). Due to regimen heterogeneity, between-group comparison was not performed; data are presented descriptively.

Sensitivity Analyses

In an era-stratified analysis restricted to the 15 non-IC gastric

Table 1: Baseline Demographics, Clinical Characteristics, Operative Parameters, and Conditioning Intervals.

Variable	IC Group (n = 7) Median [IQR] or n (%)	Non-IC Group (n = 15) Median [IQR] or n (%)	p-value
Demographics			
Age, years	60.0 [54.0–69.5]	62.0 [57.5–67.5]	0.887
Male sex	6 (85.7)	7 (46.7)	0.165
BMI, kg/m ²	23.1 ± 4.8	24.9 ± 3.1	0.502
Caucasian race	5 (71.4)	12 (80.0)	1.000
ASA score	2.0 [2.0–3.0]	2.0 [2.0–2.0]	0.441
Charlson Comorbidity Index	6.0 [4.5–7.0]	5.0 [4.5–5.0]	0.105
ECOG 0	3 (42.9)	11 (73.3)	0.343
Weight loss >10%	7 (100.0)	10 (66.7)	0.135
Active smoking	4 (57.1)	10 (66.7)	1.000
Alcohol use	3 (42.9)	4 (26.7)	0.630
Tumor Characteristics			
Squamous cell carcinoma	4 (57.1)	8 (53.3)	1.000
Adenocarcinoma	3 (42.9)	7 (46.7)	
Esophageal body location	4 (57.1)	10 (66.7)	1.000
GEJ location	3 (42.9)	5 (33.3)	
Neoadjuvant Therapy			
Any neoadjuvant therapy†	7 (100.0)	7 (46.7)	0.022
CROSS protocol	4 (57.1)	6 (40.0)	
FLOT protocol	3 (42.9)	0 (0.0)	
Upfront surgery	0 (0.0)	8 (53.3)	
Ischemic Conditioning Intervals‡			
Stage 1 → Esophagectomy, days	150 [129–159]	—	—
Stage 2 → Esophagectomy, days‡	29 [26–45]	—	—
Intraoperative Data			
Minimally invasive approach	7 (100.0)	14 (93.3)	1.000
McKeown reconstruction	4 (57.1)	12 (80.0)	0.334
Operative time, min	427.9 ± 89.3	402.0 ± 124.7	0.670
Estimated blood loss, mL	418.6 ± 166.6	447.5 ± 259.3	0.972
Lymph nodes harvested	30.0 ± 8.8	29.8 ± 9.7	0.750
R0 resection	7 (100.0)	14 (93.3)	1.000

conduit patients, those operated before 2021 (n = 11) had conduit necrosis in 3/11 (27.3%), in-hospital mortality in 4/11 (36.4%), and a median CCI® of 39.7, compared with conduit necrosis in 1/4 (25.0%), in-hospital mortality in 1/4 (25.0%), and a median CCI® of 28.1 in non-IC patients operated from 2021 onward (n = 4). The modest improvement in outcomes between eras does not eliminate temporal confounding as a competing explanation for differences observed between IC and non-IC groups, since concurrent perioperative advances may have contributed independently of conditioning. In a neoadjuvant-restricted sensitivity analysis (IC n = 7; non-IC-neoadjuvant n = 7), IC patients had lower conduit necrosis (0% vs 42.9%), lower mortality (0% vs 42.9%), and lower median CCI® (8.7 vs 56.3). Given the very small sample size (n = 7 per group), these figures are presented descriptively without formal between-group comparison; the consistency of direction nonetheless represents the most methodologically comparable available subgroup.

Data presented as median [interquartile range], mean ± SD, or n (%). ASA: American Society of Anesthesiologists; BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; GEJ: gastroesophageal junction; CROSS: carboplatin/paclitaxel plus radiotherapy; FLOT: fluorouracil/leucovorin/oxaliplatin/docetaxel. †Conditioning intervals presented for IC group only; conditioning strategy: Cases 01, 02, 03, 05, 07 = standard

hybrid two-stage; Case 04 = modified simultaneous two-stage laparoscopic; Case 06 = Stage 1 only (Stage 2 not completed due to severe atherosclerotic disease). ‡From Stage 2 to esophagectomy for 5 patients with completed standard protocol (excludes Case 04 and Case 06). p-values: Mann-Whitney U (continuous) or Fisher exact/chi-square (categorical). §One non-IC patient received a modified MAGIC regimen (capecitabine substituted for infusional fluorouracil for tolerability, perioperative 3 + 3 cycles); classified under 'Any neoadjuvant therapy but not under CROSS or FLOT.

Data presented as median [IQR] or n (%). CCI®, Comprehensive Complication Index. ¶Major pathologic response (Ryan/CAP grade 0–1) for IC group; pCR (grade 0) for non-IC; assessed only among neoadjuvant-treated patients (IC n = 7; non-IC-neoadjuvant n = 7). Between-group comparison not reported due to regimen heterogeneity. §Mid-conduit mediastinal fistula in Case 04 (simultaneous two-stage laparoscopic conditioning); managed with 3 sessions of endoscopic vacuum therapy. ‡Anastomotic stricture in Case 06 (Stage 1 only; failed Stage 2 angioembolization); managed with 4 sessions of balloon dilation. †One non-IC patient sustained two independent Grade IIIa events; counted once at patient level. p-values: Mann-Whitney U (continuous) or Fisher exact/chi-square (categorical). Exact Clopper-Pearson 95% CIs reported for binary outcomes with zero events in one group.

Table 2: Postoperative Outcomes.

Outcome	IC Group (n = 7) Median [IQR] or n (%)	Non-IC Group (n = 15) Median [IQR] or n (%)	p-value
Primary Outcome			
CCI® score — median [IQR]	8.7 [0.0–26.2]	39.7 [0.0–81.3]	0.192
Conduit Complications			
Gastric conduit necrosis	0 (0.0)	4 (26.7)	0.263
Anastomotic leak	0 (0.0)	2 (13.3)	1.000
Anastomotic leak Type II (ECCG)	0 (0.0)	1 (6.7)	
Anastomotic leak Type III (ECCG)	0 (0.0)	1 (6.7)	
Mid-conduit fistula§	1 (14.3)	0 (0.0)	0.259
Grade IIIa	1 (14.3)	0 (0.0)	
Anastomotic stricture‡	1 (14.3)	0 (0.0)	0.259
Grade IIIa	1 (14.3)	0 (0.0)	
Clavien-Dindo Classification			
No complications (Grade 0)	3 (42.9)	5 (33.3)	
Grade I	1 (14.3)	0 (0.0)	
Grade II	0 (0.0)	1 (6.7)	
Grade IIIa	2 (28.6)	1 (6.7)†	
Grade IIIb	0 (0.0)	2 (13.3)	
Grade IVa	0 (0.0)	1 (6.7)	
Grade IVb	1 (14.3)	1 (6.7)	
Grade V (in-hospital death)	0 (0.0)	4 (26.7)	
Clinically relevant (≥ Grade IIIa)	3 (42.9)	9 (60.0)	0.652
Recovery and Mortality			
ICU stay, days — median [IQR]	2.0 [2.0–3.0]	5.0 [3.0–24.0]	0.190
Total hospital stay, days — median [IQR]	7.0 [6.0–11.0]	10.0 [6.0–30.0]	0.859
30-day mortality	0 (0.0)	2 (13.3)	1.000
In-hospital mortality	0 (0.0)	4 (26.7)	—
Pathologic response¶	5/7 (71.4)	1/7 (14.3) [pCR]	—

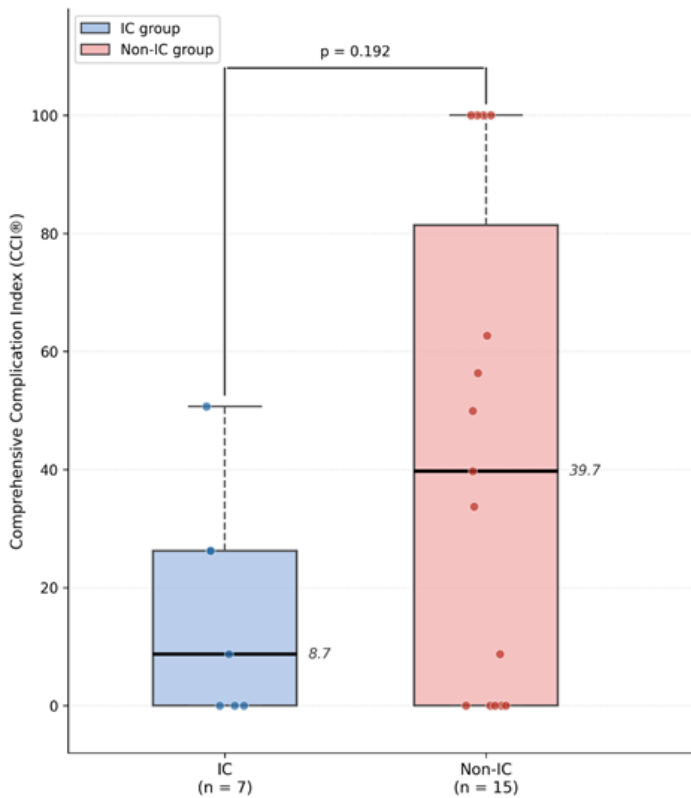


Figure 1: CCI® distribution by group. Box-and-whisker plots (Tukey method) for IC (n = 7) and non-IC gastric conduit cohort (n = 15) groups. Median CCI®: 8.7 [IQR 0.0–26.2] vs 39.7 [IQR 0.0–81.3] (p = 0.192, Mann-Whitney U test). Boxes span the IQR; center line = median; whiskers extend to 1.5 × IQR; individual data points beyond the whiskers displayed as outliers.

(n = 7) and non-IC gastric conduit cohort (n = 15). Note the absence of Grade V events in the IC group versus 26.7% (4/15) in non-IC patients, and the higher proportion with Grade 0 in the IC group (42.9% vs 33.3%).

Discussion

This single-center retrospective cohort study examined a novel hybrid two-stage laparoscopic-angioembolization gastric IC protocol at a military teaching hospital in southern Brazil. Although none of the observed differences reached statistical significance—a predictable consequence of the small sample size—the consistent direction and magnitude of effects across all measured outcomes provide hypothesis-generating data supporting the biological rationale and clinical feasibility of this approach.

The most notable finding was the complete absence of conduit necrosis in the IC group (0/7) versus 26.7% (4/15) in the non-IC gastric conduit cohort. This result aligns with the proposed mechanism—staged devascularization triggering compensatory angiogenesis through the gastroepiploic arcade—and is consistent with the pooled odds ratio of 0.38 (95% CI 0.20–0.71) for conduit necrosis favoring IC reported by Aiolfi and colleagues [8].

The present protocol differs from all previously published series in its hybrid two-stage design, combining laparoscopic short gastric vessel ligation at staging laparoscopy with subsequent percutaneous angioembolization of the left gastric artery post-neoadjuvant therapy. A relevant consideration is that deliberate preoperative gastric mobilization has been reported to complicate subsequent esophagectomy [16]. Our approach capitalizes on the staging laparoscopy already required as part of standard oncologic workup, avoiding any additional admission. Progressive devascularization in two steps is hypothesized to provide a more graduated angiogenic stimulus, and using angioembolization for Stage 2 avoids repeat laparoscopy in patients who may have peritoneal adhesions from prior staging.

The 31-point absolute difference in median CCI® (8.7 vs 39.7) substantially exceeds the minimum clinically important difference of 12 points established for major abdominal surgery [17]. Although non-significant, this magnitude is consistent across all secondary endpoints and supports the clinical relevance of the signal.

Critically, both IC complications occurred exclusively in the two protocol-deviant cases (Cases 04 and 06). All five patients who completed the standard hybrid protocol had CCI® = 0.0, suggesting that protocol adherence may be a determinant of outcome. This pattern warrants prospective evaluation with standardized protocols.

No IC patient died during the index hospitalization versus 26.7% (4/15) in the non-IC gastric conduit cohort. Among these four deaths, three were directly attributable to conduit necrosis and septic sequelae, and one to pulmonary sepsis—representing precisely the spectrum of complications IC is designed to prevent. As detailed in the sensitivity analyses, substantial temporal confounding precludes causal inference; nonetheless, even in the

Figure 2. Clavien-Dindo Grade Distribution by Group

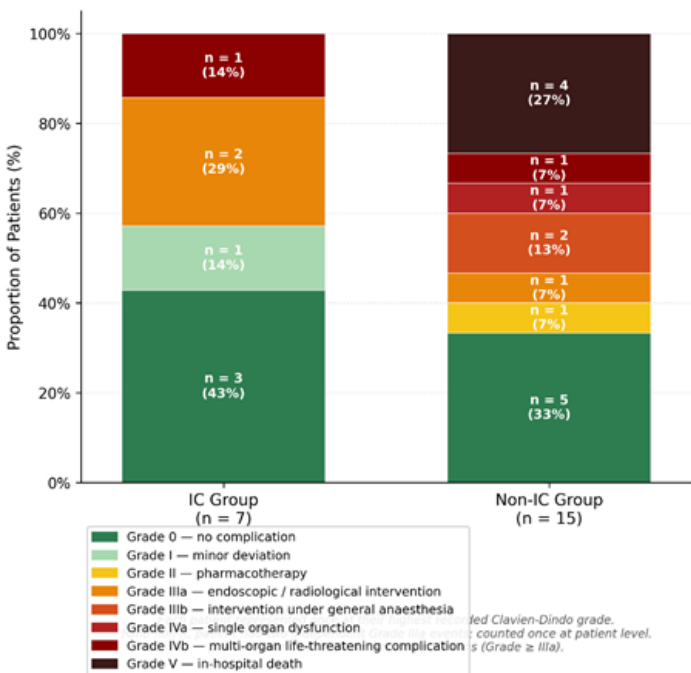


Figure 2: Clavien-Dindo classification by group. Stacked bar chart for IC

neoadjuvant-restricted analysis, mortality remained 0% vs 42.9%, and the signal warrants prospective investigation.

The median Charlson Comorbidity Index of 5–6 in this cohort substantially exceeds the low comorbidity burden characteristic of patients in high-volume esophagectomy series, where a score of ≥ 2 is typically classified as high-risk²² and the majority of patients score 0–1, reflecting the elevated baseline comorbidity of the military patient population and likely contributing to the elevated baseline mortality in the non-IC group.

Confounders and Limitations

Several limitations must be acknowledged. First, the most significant is temporal confounding: all IC cases were performed in 2021–2025 while most non-IC patients were treated earlier; concurrent perioperative improvements are inseparable from the conditioning effect. Second, all IC patients received neoadjuvant therapy versus 46.7% of non-IC patients ($p = 0.022$), introducing statistically significant treatment heterogeneity. This imbalance means IC patients uniformly had a planned interval between chemotherapy or radiotherapy completion and definitive surgery, potentially contributing to improved outcomes independently of vascular conditioning; the neoadjuvant-restricted sensitivity analysis (IC $n = 7$; non-IC-neoadjuvant $n = 7$) maintains the directional benefit of IC across all endpoints. Third, two IC patients deviated from the standard protocol; furthermore, the per-protocol subgroup may represent a selected population, as both protocol-deviant cases (Case 04 with nutritional compromise; Case 06 with severe atherosclerotic disease precluding arterial access) carried adverse biological or anatomical circumstances that could independently predispose to worse outcomes irrespective of conditioning, and the favourable results in protocol-adherent patients should be interpreted with this selection mechanism in mind. Fourth, with only 7 IC patients, statistical power is approximately 11% to detect a 12-point CCI® difference (pooled SD 37.1) [17], consistent with our pre-defined characterization of this study as hypothesis-generating. Fifth, the conditioning interval (median 29 days from Stage 2) somewhat exceeds the 14-day optimum suggested by experimental evidence [18], reflecting neoadjuvant logistic constraints. Sixth, anastomotic leak grading per ECCG definitions was applied retrospectively from clinical records; prospective ECCG data collection was not performed at the time of the study, and the ECCG grades reported should be interpreted with this limitation in mind.

Strengths

Despite these limitations, this study offers several contributions: it is the first description of a hybrid laparoscopic-angioembolization IC protocol; it includes patient-level data on protocol adherence and outcomes; it contributes outcome data from a Latin American military center underrepresented in the literature; and transparent reporting of protocol deviations provides real-world implementation insight.

Implications and Future Directions

These findings suggest that a hybrid two-stage IC protocol is

safe, technically feasible, and integrates efficiently into existing neoadjuvant treatment timelines. For centers that routinely administer neoadjuvant therapy—now standard for most locally advanced esophageal cancers [19–21]—Stage 1 can be performed at staging laparoscopy and Stage 2 post-neoadjuvant, with esophagectomy proceeding on the existing schedule. A well-designed, adequately powered multicenter prospective trial with standardized conditioning protocols and objective perfusion assessment (e.g., intraoperative indocyanine green fluorescence angiography) [4] is needed to confirm these preliminary observations. Experimental evidence from a Wistar rat model suggested that optimal perfusion recovery after left gastric vessel devascularization occurs by day 14 post-ligation [18], providing biological support for the interval employed in our protocol. The applicability of these findings to percutaneous angioembolization in humans requires cautious interpretation given mechanistic differences between the two techniques. Bearing these mechanistic considerations and logistic constraints in mind, the following patient selection framework is proposed based on our institutional experience. IC should be considered for patients who: (1) are scheduled for esophagectomy and will receive neoadjuvant therapy, enabling natural integration of both conditioning stages into the treatment timeline; (2) carry identifiable conduit perfusion risk factors, including smoking history, diabetes, peripheral vascular disease, or significant weight loss exceeding 10%; and (3) are medically fit for two prior procedural stages without compromising the oncologic timeline. Patients requiring emergency esophagectomy or with severe atherosclerotic disease precluding arterial access remain unsuitable for the complete hybrid protocol. These eligibility criteria are derived from expert consensus and institutional experience rather than from comparative outcome analyses within this cohort, and should be treated as a provisional clinical framework pending prospective validation.

Conclusions

In this 27-patient retrospective cohort, a hybrid two-stage gastric IC protocol combining laparoscopic short gastric vessel ligation with percutaneous angioembolization of the left gastric artery was associated with numerically lower conduit necrosis (0% vs 26.7%), overall morbidity (CCI® 8.7 vs 39.7), and mortality (0% vs 26.7%) compared with non-conditioned patients. Statistical significance was not achieved due to the limited sample size, and important temporal and treatment confounders preclude causal inference. Among the five patients who completed the standard two-stage protocol, CCI® was 0.0 in all cases. The protocol integrates seamlessly into existing neoadjuvant treatment timelines. The primary contribution of this study is the description of a technically original and feasible protocol with a favorable safety profile; the observed directional outcome differences cannot be causally attributed to conditioning given the temporal confounding inherent in this design. These hypothesis-generating data support prospective multicenter evaluation of this hybrid approach.

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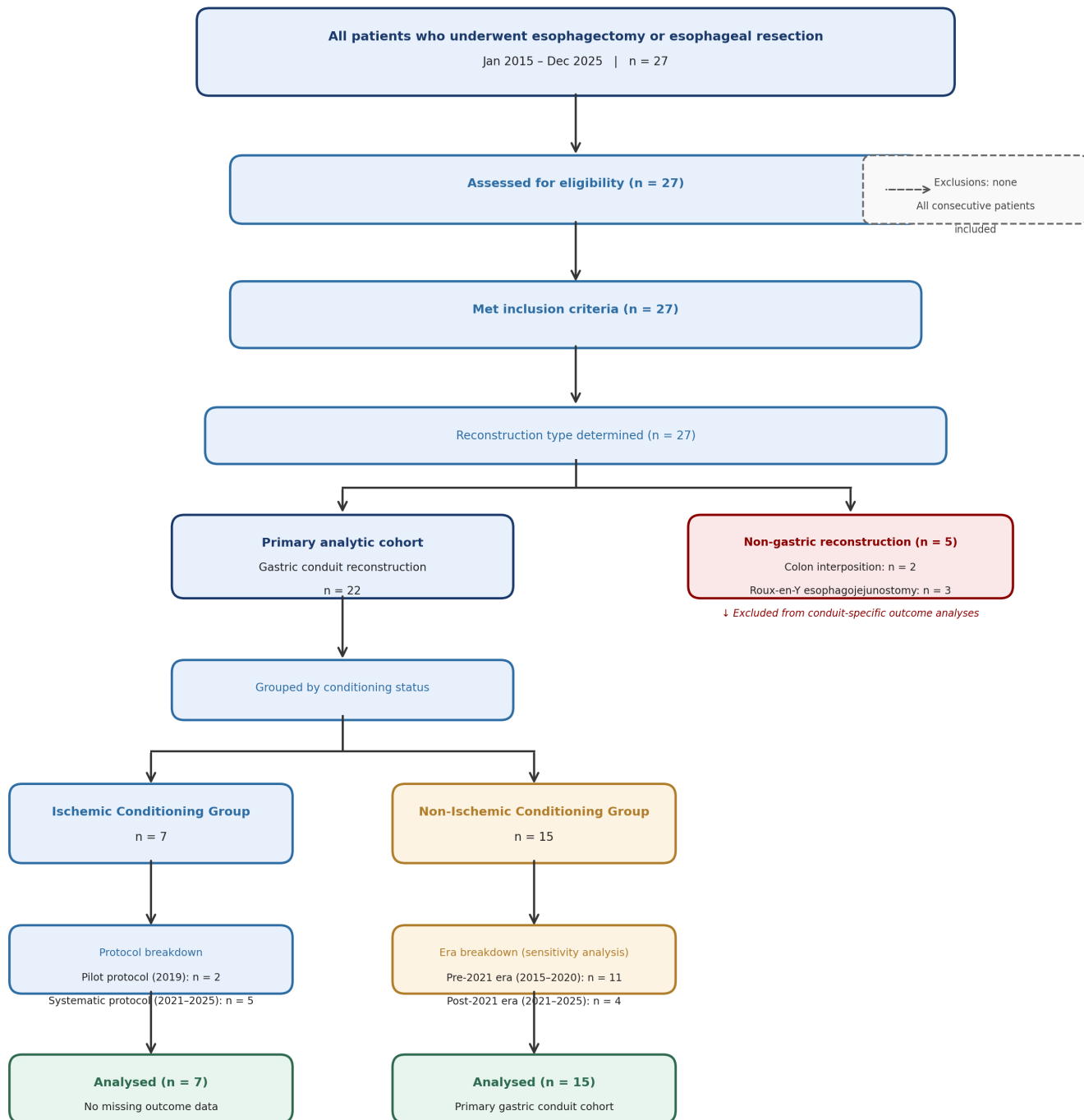
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Supplementary Figure 1: STROBE-compliant participant flow diagram. All 27 consecutive patients who underwent esophagectomy or esophageal resection between January 2015 and December 2025 were screened. Twenty-two patients who received tubular gastric conduit reconstruction constitute the primary analytic cohort; 5 patients who received non-gastric reconstruction are excluded from conduit-specific outcome analyses.

Supplementary Figure 1. STROBE Participant Flow Diagram



IC = Ischemic Conditioning | CCI® = Comprehensive Complication Index | Non-IC = Non-Ischemic Conditioning

STROBE-compliant participant flow diagram. All 27 consecutive patients who underwent esophagectomy or esophageal resection (January 2015 – December 2025) were screened. Five patients with non-gastric reconstruction were excluded from conduit-specific analyses. No patients were lost to follow-up or withdrew after enrolment.

Supplementary Figure 2: Representative completion angiogram confirming left gastric artery occlusion after Stage 2 percutaneous angioembolization.

