Gastric transcatheter chemoembolization combined with systemic chemotherapy vs. systemic chemotherapy alone for patients with advanced gastric cardiac cancer presenting with dysphagia: A case control study

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Abstract. The present study aimed to assess the effectiveness of gastric transcatheter chemoembolization (GTC) combined with systemic chemotherapy (SYS) compared with SYS alone in managing dysphagia, and improving the quality of life (QoL) and nutritional status of patients with advanced gastric cardiac cancer (AGCC). A retrospective review was performed using data from consecutive patients with AGCC who experienced dysphagia and underwent either SYS alone or SYS combined with GTC from January 2018 to December 2022. Propensity score matching (PSM) analysis was performed to address potential confounding factors. Ogilvie dysphagia scores were used to assess dysphagia, the Functional Assessment of Cancer Therapy-General 7 (FACT-G7) was used to assess QoL, and the Patient-Generated Subjective Global Assessment (PG-SGA) was used to evaluate nutritional status. After PSM, a total of 228 patients were included in the analysis, with 114 in each group. At 4 and 8 weeks after the initial treatment, the GTC + SYS group demonstrated significantly lower median Ogilvie scores compared with the SYS alone group (P<0.001). Similarly, the median PG-SGA score at 4 weeks after the initial treatment was 2.0 in the GTC + SYS group and 6.0 in the SYS alone group. The median FACT-G7 scores in the GTC + SYS group was 13.0, compared with 10.5 in the SYS alone group. These differences remained significant at 8 weeks (P<0.001). In conclusion, the addition of GTC to SYS may more effectively and promptly relieve dysphagia, improve nutritional status and enhance QoL compared with SYS alone in patients with AGCC presenting with dysphagia.

Introduction

Advanced gastric cardiac cancer (AGCC) is a challenging malignancy that typically presents with dysphagia and primarily affects the proximal stomach, often extending to the gastroesophageal junction. Previous studies showed that 23.3% of early gastric cancer was gastric cardiac carcinoma in China (1), which is a higher rate compared with the 7.0% recorded in Japan (2) and the 11.9% recorded in a Western cohort (3). Patients with AGCC face the risk of malnutrition and decreased quality of life (QoL) (4-8). In one study, the 5-year survival rate was <10% at the advanced stage (9). Dysphagia further complicates treatment, as it hampers the delivery of oral medications, reducing the effectiveness of systemic chemotherapy (SYS). As a result, malignant dysphagia is a common and difficult clinical manifestation in cases of AGCC, necessitating effective symptom management for enhanced patient comfort (4-6,10). According to literature reports, 60-90% of patients with cancer at the gastroesophageal junction experience significant swallowing difficulties (11-14). SYS is the mainstay treatment for AGCC, aiming to improve symptom remission rates and prolong patient survival; however, the efficacy of SYS alone is limited, highlighting the need for alternative approaches (15).

Endoscopic stent implantation is a conventional treatment option for alleviating dysphagia caused by AGCC; however, stent placement carries the risk of complications such as stent obstruction, migration and perforation (7,16-19). Other interventions, such as percutaneous gastrostomy and naso-jejunal feeding, have demonstrated a certain amount of symptomatic

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Abbreviations: GTC, gastric transcatheter chemoembolization; SYS, systemic chemotherapy; AGCC, advanced gastric cardiac cancer; QoL, quality of life; PSM, propensity score matching; FACT-G7, Functional Assessment of Cancer Therapy-General 7; PG-SGA, Patient-Generated Subjective Global Assessment; OS, overall survival; PFS, progression-free survival; AE, adverse effect

Key words: AGCC, dysphagia, GTC, QoL

relief, but are associated with higher risks of complications, including infections, bleeding and dislodgement (20,21). Therefore, gastric transcatheter chemoembolization (GTC), a minimally invasive technique, has emerged as a promising therapeutic option for AGCC with dysphagia. This technique involves the intra-arterial infusion of chemotherapeutic drugs directly into the tumor-feeding artery, followed by the injection of embolic agents to induce ischemic necrosis of the tumor. GTC allows for high local drug concentrations, effectively reducing tumor vascularity and size, thereby improving dysphagia control in patients with AGCC (4-6,10,22-24).

Despite its potential benefits, the use of GTC in combination with SYS for AGCC with dysphagia remains controversial, and comparative studies with SYS alone are lacking. Therefore, the objective of the present retrospective study is to evaluate the efficacy of combining GTC with SYS compared with SYS alone in patients with AGCC and dysphagia.

Materials and methods

Study design and participants. A retrospective review was performed of consecutive patients with AGCC who presented with dysphagia and underwent either SYS alone or a combination of GTC and SYS between January 2018 and December 2022. The patients and their families made the decision to undergo GTC after consultation with the multidisciplinary team of experts from the gastric cancer group of the Affiliated Cancer Hospital of Shandong First Medical University of China (Jinan, China). This decision was influenced by the presence of dysphagia symptoms, irrespective of tumor size. AGCC diagnosis was confirmed through endoscopy and biopsy, and staging was performed using the 8th edition of the American Joint Committee on Cancer (AJCC) criteria (25). To be included in the present study, patients had to meet the following criteria: i) Histologically-confirmed AGCC; ii) advanced stage of the disease (AJCC stage III or IV); iii) dysphagia as a presenting symptom [at least Ogilvie Dysphagia Scale (26) grade 1]; iv) age ≥18 years; v) Eastern Cooperative Oncology Group (ECOG) performance status of 0-2; vi) treatment with either GTC combined with SYS or SYS alone; and vii) sufficient medical records available for review. The exclusion criteria included the following: i) Previous treatment for AGCC; ii) co-existing malignancies; and iii) other significant comorbidities.

Procedures

Systemic chemotherapy. The SYS group received a combination of two first-line chemotherapy regimens: tegafur-gimeracil-oteracil (S-1) plus oxaliplatin (SOX) (27) r capecitabine and oxaliplatin (XELOX) (28). In the SOX regimen, patients took oral S-1 at a dosage of 40-60 mg twice a day on days 1-14, every 3 weeks, and received intravenous oxaliplatin at a dosage of 130 mg/m^2 on day 1, every 3 weeks. For the XELOX regimen, patients took oral capecitabine at a dosage of 1,000 mg/m^2 twice a day on days 1-14, every 3 weeks, and received intravenous oxaliplatin at a dosage of 130 mg/m^2 over 2 h on day 1, every 3 weeks.

Second-line chemotherapy regimens included irinotecan (29) and paclitaxel monotherapy (30). In the irinotecan monotherapy regimen, patients received intravenous irinotecan at a dosage of 150 mg/m^2 on days 1 and 15, every 4 weeks. For the paclitaxel monotherapy regimen, patients received intravenous paclitaxel at a dosage of 60 mg/m^2 on days 1 and 8, every 3 weeks.

The decision to switch from first-line to second-line chemotherapy was based on several factors, including disease progression, treatment response and tolerance. The specific timing and criteria for switching were determined by the treating oncologist.

GTC. GTC was performed by an experienced interventional radiologist under local anesthesia and conscious sedation. The patient was positioned supine, and access to the right femoral artery was obtained using the Seldinger technique. A 5-French (5-F) sheath was inserted, and a 5-F diagnostic catheter was advanced into the abdominal aorta under fluoroscopic guidance. Arteriography of the abdominal trunk was then performed to identify the supply arteries of the tumor. If necessary, additional arterial angiography, including the right gastric artery, short gastric arteries, posterior gastric artery, gastro-epiploic artery and left inferior phrenic artery, was performed to gain a comprehensive understanding of the blood supply arteries of the tumor. If the tumor received blood supply from sources other than the left gastric artery, 300-500-μm Embosphere microspheres (Merit Medical Systems, Inc.) were used to embolize certain non-primary blood supply arteries. Subsequently, a 0.022-inch microcatheter (PROGREAT®; Terumo Medical Corporation) was inserted into the left gastric artery, and fluorouracil (5-FU) (at a dose of 1,000 mg/m^2) was slowly injected via the microcatheter over a period of >10 min. Following the chemotherapy infusion, Embosphere microspheres (300-500 μm) were injected to embolize the left gastric artery. The procedure was determined to be successful when angiography demonstrated that there was no residual arterial flow to the tumor. The imaging data for a 55-year-old patient diagnosed with AGCC who underwent GTC are presented in Fig. S1A-M.

After the intervention, pressure was applied to the femoral artery for 15 min, and patients were closely monitored for 24 h post-procedure to detect any signs of abdominal pain, fever or other complications. Routine blood tests, including liver and kidney function tests, were performed before and after the procedure to identify any changes.

Each cycle was scheduled at intervals of 4 weeks, and patients received GTC treatment once within each cycle. The number of cycles administered to each patient varied based on their response to treatment and the discretion of the treating physician.

Assessment of dysphagia severity, nutritional status, QoL and adverse events (AEs). The primary outcome measure of the present study was symptom remission, which included improvement in dysphagia severity, QoL and nutritional status. These measures were evaluated at baseline, 4 weeks, and 8 weeks after the first cycle of SYS, and were regularly assessed via telephone or at an outpatient clinic visit.

Dysphagia was evaluated using the Ogilvie Dysphagia Scale, which grades dysphagia into 5 levels: 0, no dysphagia; 1, normal diet with certain food restrictions (such as raw apple and steak); 2, semi-solid diet; 3, fluids only; and 4, complete dysphagia, even for liquids.

Nutritional status was assessed by experienced dietitians using the scored Patient-Generated-Subjective Global Assessment (PG-SGA) scale (31). The PG-SGA scale consists of two parts: Patient self-assessment and assessment by medical staff. It evaluates weight, intake, symptoms affecting intake, functional capacity, metabolic demands and physical assessment. Patients assessed the first four aspects themselves, whilst medical staff assessed the last two. Each item was given a score of 0-4 based on its impact on nutritional status, and the total scores were then summed. Nutritional status was categorized as well-nourished (0-1 points), suspected malnutrition (2-3 points), moderate malnutrition (4-8 points), or severe malnutrition (≥9 points) based on the total score.

QoL was assessed using the Functional Assessment of Cancer Therapy-General (FACT-G)7 scale (32), which is a condensed version of the FACT-G scale (33). It includes three items from the physical wellbeing subscale (fatigue, pain and nausea), one item from the emotional wellbeing subscale (concern about the condition worsening), and three items from the functional wellbeing subscale (enjoyment of life, contentment with QoL and sleep). Each item is graded on a 5-point scale, ranging from 'not at all' (0) to 'very much' (4). The functional wellbeing subscale is directly scored from 0-4 points, whilst the physical wellbeing subscale and emotional wellbeing are scored in reverse. The scores from FACT-G7 are summed on a scale of 0-28, with higher scores indicating a better QoL.

AEs were recorded and graded according to the Common Terminology Criteria for Adverse Events version 5.0 (34). Specific AEs related to GTC such as fever, abdominal pain and gastrointestinal ulcers were also assessed.

Treatment response. All patients were regularly followed up after receiving treatment. The response to treatment was assessed using computed tomography (CT) or magnetic resonance imaging at 1, 2 and 6 months after the first cycle of GTC. Evaluation of treatment response was performed in accordance with the Response Evaluation Criteria in Solid Tumors version 1.1 (35). Overall survival (OS) was defined as the duration from the initiation of treatment to either death from any cause or the last follow-up. Progression-free survival (PFS) was defined as the period from the start of treatment to disease progression or death from any cause. Objective response rate (ORR) was defined as the % of patients who achieved either a complete response (CR) or partial response (PR) to the treatment. CR was defined as the disappearance of all target lesions, whilst PR was defined as a ≥30% decrease in the sum of the diameters of target lesions. Disease control rate (DCR) was defined as the % of patients who achieved CR, PR or stable disease (SD). SD was defined as neither PR nor PD.

Statistical analysis. All statistical analyses were performed using MatchIt package version 4.5.5 (36) and the R software version 4.2.2 (R Core Team; https://www.R-project.org/). Baseline characteristics are presented as the median (interquartile range) for continuous variables and the n (%) for categorical variables. The maximum diameter of the tumor at the cardia, Ogilvie score, PG-SGA score and FACT-G7 score were compared between the two groups at 4 and 8 weeks after the first cycle of SYS. For comparison between groups of categorical data, Fisher's exact test or the χ^2 test was used. The Wilcoxon rank sum test was used for the analysis of continuous variables. Univariate and multivariate logistic regression analysis was performed to determine the independent factors associated with presence of dysphagia after 8 weeks of the first cycle of SYS. Kaplan-Meier curves and the log-rank test were used to compare the OS and PFS between the groups. Subgroup analyses were performed to evaluate the impact of baseline characteristics on OS, and the interaction between the treatment groups and subgroups was tested using Cox proportional hazards regression analysis. $P<0.05$ was considered to indicate a statistically significant difference.

Propensity score matching (PSM) was used to minimize the influence of confounding factors and improve the validity of the findings, making the results more applicable to real-world clinical practice. PSM were calculated using logistic regression, accounting for the aforementioned demographic and clinical characteristics. Furthermore, 1:1 greedy nearest neighbor matching was performed with a caliper of 0.3. The method functionally relied on the MatchIt R package. The distance between the unit of one group and another was calculated, and each unit was assigned a control unit as a match. The matching was 'greedy' as no action was taken to optimize an overall criterion; each match was selected without accounting for the other matches that may have subsequently occurred. Fig. S2 presents the balance of baseline covariates before and after PSM for both the GTC + SYS and SYS alone groups.

Results

Study population. Initially, 954 patients were screened, and a total of 295 patients with AGCC presenting with dysphagia, who matched the inclusion criteria, were included in the present retrospective study. Of these, 138 patients received GTC combined with SYS, whilst 157 patients received SYS alone. PSM yielded 114 well-balanced pairs in terms of baseline demographics and clinical characteristics. A notable reduction in SMDs after matching can be observed, indicating that the PSM effectively improved the balance of covariates between the two treatment groups. This improvement in balance allowed for a more reliable comparison of treatment effectiveness, as the potential influence of confounding factors was minimized. The screening process is presented in Fig. 1.

Table I presents the baseline characteristics of the study population before and after PSM. Prior to PSM, there were significant differences in ECOG, WBC, Ogilvie score, PG-SGA score, and the first-line chemotherapy regimen between the two groups. Following PSM, the baseline characteristics were well balanced between the two groups and there were no significant differences. The majority of participants were male, accounting for 73% in the GTC + SYS group and 70% in the SYS group. The age distribution showed a median of 62 years in both groups. Biomarker analysis revealed no significant differences between the two groups. The main tumor characteristics also did not significantly differ. The median follow-up time for the GTC + SYS group was 12 months (range, 6-24 months), whilst it was 10 months (range, 5-22 months) for the SYS alone group. There was no statistically significant difference in the follow-up time between the two groups (P=0.234). In the GTC + SYS group, the median number of GTC procedures performed was 2, with a range of 1-4 procedures.

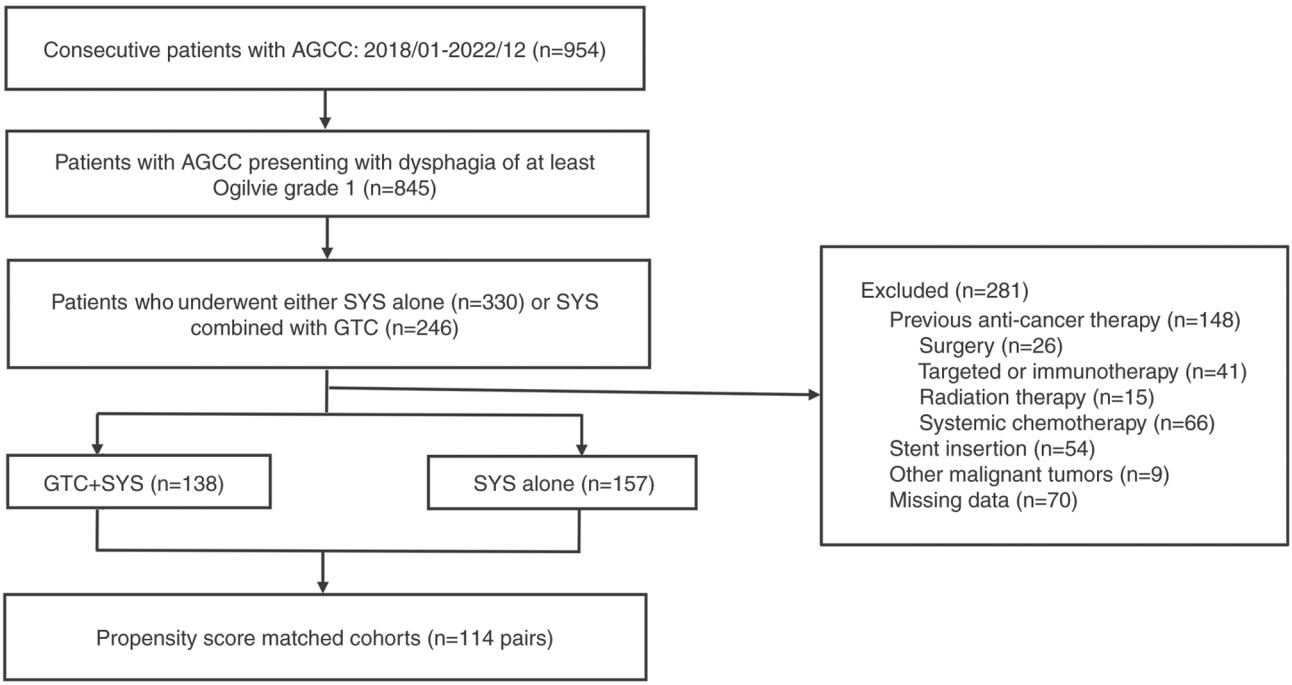

Figure 1. Flowchart of the patient selection process. AGCC, advsanced gastric cardiac cancer; GTC, gastric transcatheter chemoembolization; SYS, systemic chemotherapy.

Comparison of the clinical symptoms and clinical symptom relief between the two groups

Comparison of the severity of dysphagia between the groups. At baseline, there were no significant differences in the severity of dysphagia between the two treatment groups (P>0.05). After 4 weeks of the initial cycle of SYS, the severity of dysphagia in the SYS group was significantly higher compared with the GTC + SYS group (P<0.001). Following the initial treatment period, it was observed that ~25% of patients in the GTC + SYS group no longer experienced symptoms of dysphagia, whilst all patients in the SYS group continued to report difficulties with swallowing. This trend persisted at 8 weeks after the first cycle of SYS, with the SYS group also experiencing significantly more severe dysphagia than the GTC + SYS group (P<0.001; Table SI). Specifically, at both 4 and 8 weeks, the GTC + SYS group demonstrated significantly lower median Ogilvie scores than the SYS only group (Table II). Additionally, at 8 weeks after the initial treatment, the percentage of patients with dysphagia in the SYS group was significantly higher compared with that in the GTC + SYS group (84 vs. 28%; P<0.001). Regarding clinical symptom relief, the GTC + SYS group had a significantly higher rate of improvement in dysphagia compared with the SYS group (P<0.05). Specifically, 110/114 patients in the GTC + SYS group reported improvement in dysphagia symptoms, whilst only 86/114 patients in the SYS group reported similar improvements at 8 weeks after the first cycle of SYS (96 vs. 75%; P<0.001) (data not shown).

Comparison of nutritional status and QoL between groups. There were significant differences for nutritional status and QoL between the groups at 4 and 8 weeks following the initial cycle of SYS. Specifically, both at 4 and 8 weeks post the first cycle of SYS, the GTC + SYS group demonstrated significantly lower median PG-SGA scores and significantly higher median FACT-G7 scores compared with the SYS group (P<0.001; Table II). At 4 weeks post the initial SYS cycle, there was a significantly higher proportion of well-nourished individuals in the GTC + SYS group than in the SYS group, whilst the SYS group had a significantly higher proportion of severe and moderate malnutrition cases than the GTC + SYS group (P<0.001; Table SI). By the end of 4 weeks of treatment, ~41% of patients in the GTC + SYS group no longer displayed signs of malnutrition, whereas all patients in the SYS group still exhibited varying degrees of malnutrition (Table SI). This pattern persisted at 8 weeks post the first SYS cycle, with a significantly higher proportion of well-nourished individuals in the GTC + SYS group than the SYS group, and the SYS group displaying significantly more cases of suspected, moderate and severe malnutrition than the GTC + SYS group (P<0.001). After 8 weeks following the initial SYS cycle, the improvement in malnutrition status was compared between the two groups. In the GTC + SYS group, 99 patients (87%) showed notable improvements in their malnutrition status, whilst in the SYS alone group, only 8 patients (7%) showed a marked improvement. The difference in improvement rates between the two groups was found to be statistically significant (P<0.001; Table SI).

Comparison of the maximum diameter of the tumor at the cardia between groups. A similar trend was observed for the maximum diameter of the tumor at the cardia. Significant reductions in tumor size were seen in the GTC + SYS group compared with the SYS group at 4 and 8 weeks after the first cycle of SYS. Specifically, after 4 weeks of the first cycle of SYS, the median reduction in the maximum tumor diameter in the GTC + SYS group was 1.7 cm, compared with 0.8 cm in the SYS alone group (P<0.001). Similarly, after 8 weeks of the first cycle of SYS, the median reduction in the maximum tumor diameter in the GTC + SYS group

Table I. Baseline characteristics of patients before and after propensity score matching.

	Unmatched			Matched		
Characteristic	SYS (n=157)	GTC + SYS (n=138)	P-value	SYS (n=114)	GTC + SYS (n=114)	P-value
Sex			0.320			0.660
Male	103 (66)	98 (71)		80 (70)	83 (73)	
Female	54 (34)	40 (29)		34 (30)	31 (27)	
Age, years	62 (57-65)	63 (55-68)	0.193	62 (59-66)	62 (55-68)	0.638
ECOG			0.014[a]			0.618
0	15 (10)	12 (9)		12 (11)	11 (10)	
2	36 (23)	53 (38)		35 (31)	42 (37)	
1	106 (68)	73 (53)		67 (59)	61 (54)	
WBCs, n ($x10^9$/l)	5.69 (4.31-7.16)	6.23 (4.65-8.19)	0.026[a]	5.70 (4.22-7.14)	6.07 (4.58-8.19)	0.099
HGB, g/l	129 (114-141)	129 (112-138)	0.687	129 (114-141)	130 (112-139)	0.926
PLTs, n ($x10^9$/l)	229 (164-290)	216 (162-278)	0.432	211 (155-289)	216 (165-278)	0.674
AST, U/l	23 (16-31)	25 (17-39)	0.405	25 (17-32)	24 (17-37)	0.759
Albumin, g/l	40.6 (38.3-43.7)	39.7 (36.0-42.6)	0.263	40.6 (37.7-43.7)	40.1 (36.0-43.8)	0.586
Cr, μmol/l	59 (37-78)	61 (52-72)	0.069	60 (37-78)	61 (52-72)	0.195
CEA, ng/ml	4 (2-9)	4 (2-16)	0.283	4 (2-11)	4 (2-16)	0.658
CA 19-9, U/ml	30 (12-166)	36 (12-288)	0.398	28 (12-152)	36 (12-216)	0.528
Maximum diameter of the tumor at the cardia, cm	3.40 (2.70-4.10)	3.50 (2.90-4.30)	0.268	3.40 (2.80-4.10)	3.50 (2.90-4.18)	0.930
Grade of differentiation			0.634			>0.999
Poor	111 (71)	101 (73)		80 (70)	80 (70)	
Well	10 (6)	11 (8)		9 (8)	9 (8)	
Moderate	36 (23)	26 (19)		25 (22)	25 (22)	
TNM stage			0.811			0.791
III	82 (52)	74 (54)		62 (54)	60 (53)	
IV	75 (48)	64 (46)		52 (46)	54 (47)	
Ogilvie score			0.024[a]			0.684
1	6 (4)	11 (8)		6 (5)	8 (7)	
2	39 (25)	49 (36)		35 (31)	39 (34)	
3	112 (71)	78 (57)		73 (64)	67 (59)	
PG-SGA Score	9 (7-10)	9 (8-11)	0.024[a]	9 (8-11)	9 (8-10)	0.570
FACT-G7 Score	9 (7-11)	9 (7-10)	0.537	9 (7-11)	9 (7-10)	0.548

Table I. Continued.

Characteristic	Unmatched			Matched		
	SYS (n=157)	GTC + SYS (n=138)	P-value	SYS (n=114)	GTC + SYS (n=114)	P-value
Trastuzumab			0.052			0.467
Yes	60 (38)	38 (28)		31 (27)	36 (32)	
No	97 (62)	100 (72)		83 (73)	78 (68)	
Immunotherapy			0.094			0.546
No	60 (38)	38 (28)		31 (27)	36 (32)	
Tislelizumab	60 (38)	55 (40)		49 (43)	41 (36)	
Sintilimab	37 (24)	45 (33)		34 (30)	37 (32)	
First line chemotherapy regimen			0.033[a]			0.891
SOX	82 (52)	89 (64)		72 (63)	73 (64)	
XELOX	75 (48)	49 (36)		42 (37)	41 (36)	
Second line chemotherapy regimen			0.872			0.891
Irinotecan	97 (62)	84 (61)		71 (62)	72 (63)	
Paclitaxel	60 (38)	54 (39)		43 (38)	42 (37)	
Number of first line therapy cycles	5 (4-6)	5 (4-6)	0.859	5 (4-6)	5 (4-6)	0.585
Number of second line therapy cycles	6 (4-7)	6 (4-7)	0.732	6 (4-7)	6 (4-7)	0.881

Data are presented as n (%) or median (interquartile range), and analyzed using the χ^2 test or Wilcoxon rank sum test. [a]P<0.05. GTC, gastric transcatheter chemoembolization; SYS, Systemic chemotherapy, ECOG, Eastern Cooperative Oncology Group; WBC, white blood cell; HGB, hemoglobin; PLT, platelet count; AST, aspartate aminotransferase; Cr, creatinine; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9; TNM, tumor-node-metastasis; PG-SGA, Patient-Generated Subjective Global Assessment; FACT-G7, Functional Assessment of Cancer Therapy-General 7; SOX, tegafur-gimeracil-oteracil + oxaliplatin; XELOX, capecitabine + oxaliplatin.

Table II. Summary of symptom scores and maximum diameter of the tumor at the cardia of patients before and after treatment.

Characteristic	Treatment		P-value
	GTC + SYS (n=114)	SYS (n=114)	
Ogilvie score			
Baseline	3.00 (2.00-3.00)	3.00 (2.00-3.00)	0.393
4 weeks after the first cycle of SYS	1.00 (1.00-1.00)	2.00 (2.00-2.00)	<0.001[a]
8 weeks after the first cycle of SYS	0.00 (0.00-1.00)	2.00 (1.25-2.00)	<0.001[a]
PG-SGA score			
Baseline	9.00 (8.00-10.00)	9.00 (8.00-11.00)	0.570
4 weeks after the first cycle of SYS	2.00 (1.00-2.00)	6.00 (4.25-8.75)	<0.001[a]
8 weeks after the first cycle of SYS	1.00 (0.00-1.00)	3.00 (3.00-6.00)	<0.001[a]
FACT-G7 score			
Baseline	9.0 (7.0-10.0)	9.0 (7.0-11.0)	0.548
4 weeks after the first cycle of SYS	13.0 (11.0-14.0)	10.50 (9.0-12.0)	<0.001[a]
8 weeks after the first cycle of SYS	17.5 (16.0-19.0)	12.0 (11.0-14.0)	<0.001[a]
Maximum diameter of the tumor at the cardia, cm			
Baseline	3.50 (2.90-4.18)	3.40 (2.80-4.10)	0.954
4 weeks after the first cycle of SYS	1.60 (1.10-2.38)	2.70 (1.93-3.30)	<0.001[a]
8 weeks after the first cycle of SYS	0.90 (0.60-1.20)	2.20 (1.40-2.80)	<0.001[a]
Reduction in maximum diameter of the tumor at the cardia, cm			
4 weeks after the first cycle of SYS	1.7 (1.6-2.0)	0.8 (0.6-1.1)	<0.001[a]
8 weeks after the first cycle of SYS	2.7 (1.9-3.2)	1.3 (1.2-1.5)	<0.001[a]

Data are presented as median (interquartile range) and analyzed using the Wilcoxon rank sum test. [a]P<0.05. GTC, gastric transcatheter chemoembolization; SYS, Systemic chemotherapy; PG-SGA, Patient-Generated Subjective Global Assessment; FACT-G7, Functional Assessment of Cancer Therapy-General 7.

was 2.7 cm, compared with 1.3 cm in the SYS alone group (P<0.001). After 4 weeks of the first cycle of SYS, the median maximum tumor diameter at the gastric cardia in the GTC + SYS group was significantly smaller than in the SYS alone group (P<0.001). This difference was even more pronounced at 8 weeks after the first cycle of SYS, with the median maximum tumor diameter being significantly smaller in the GTC + SYS group compared with the SYS alone group (P<0.001; Table II).

Independent predictors of the presence of dysphagia at 8 weeks after the first cycle of SYS. Univariate logistic regression analysis of factors associated with presence of dysphagia at 8 weeks after the first cycle of SYS demonstrated that treatment with GTC + SYS was the only significant independent factor for reducing the occurrence of dysphagia [odds ratio (OR)=0.07; 95% CI, 0.04-0.14; P<0.001). Multivariable logistic regression then confirmed that treatment with GTC + SYS remained the only significant factor for reducing the occurrence of dysphagia at 8 weeks after the first cycle of SYS (OR=0.07; 95% CI, 0.03-0.13; P<0.001; Table III). The model coefficients for dysphagia and the model fit measures are shown in Tables SII and SIII, respectively, and the Omnibus likelihood ratio tests are shown in Table SIV.

Comparison of treatment prognosis between groups

Short-term treatment efficacy. There were no cases of complete remission in either treatment group. The rates of CR and PR, SD and PD were not significantly different between the two groups. Additionally, the ORR (45% vs. 45%) and DCR) (82% vs. 79%) showed no statistically significant difference between the two groups (P>0.05) (data not shown).

Long-term treatment efficacy. The Kaplan-Meier survival curves for OS and PFS before and after PSM are presented in Figs. 2 and 3, respectively. The median OS was significantly higher in the GTC + SYS group than in the SYS group before (Fig. 2A) and after (Fig. 2B) PSM. Before PSM, the median OS was 13.0 months (95% CI, 12.0-14.0) in patients who received GTC + SYS vs. 11.0 months (95% CI, 10.0-12.0) in patients who received SYS alone (log-rank P=0.001). After PSM, the median OS was 13.0 months (95% CI, 12.0-14.0) in patients who received GTC + SYS vs. 11.0 months (95% CI, 10.0-12.0) in patients who received SYS alone (log-rank P=0.002) (data not shown). However, there was no significant difference in PFS between the two groups before (Fig. 3A) and after (Fig. 3B) PSM (Table IV). Before PSM, the median PFS was 6.7 months (95% CI, 6.0-8.0) in patients who received GTC + SYS vs. 7.0 months (95% CI, 6.0-7.0) in patients who received SYS alone (log-rank P=0.330). After PSM, the median PFS was 6.7 months (95% CI, 6.0-8.5) in patients who received GTC +

Table III. Univariate and multivariate analysis of predictive factors for presence of dysphagia symptoms after 8 weeks of the first cycle of SYS.

	Univariate				Multivariate			
Characteristic	n	Event n	OR (95% CI)	P-value	n	Event n	OR (95% CI)	P-value
Sex								
Male	163	93	-		163	93	-	
Female	65	35	0.88 (0.49-1.57)	0.659	65	35	0.65 (0.31-1.35)	0.250
Age								
≤60 years	90	46	-		90	46	-	
>60 years	138	82	1.40 (0.82-2.40)	0.217	138	82	1.10 (0.55-2.18)	0.781
ECOG								
0	23	11	-		23	11	-	
1 + 2	205	117	1.45 (0.61-3.49)	0.399	205	117	1.84 (0.59-5.85)	0.291
CEA, ng/ml								
≤5	125	71	-		125	71	-	
>5	103	57	0.94 (0.56-1.60)	0.825	103	57	0.94 (0.47-1.86)	0.851
CA 19-9, U/ml								
>40	106	60	-		106	60	-	
≤40	122	68	0.97 (0.57-1.63)	0.895	122	68	0.84 (0.41-1.72)	0.638
Grade of differentiation								
Poor	160	89	-		160	89	-	
Well	18	9	0.80 (0.30-2.15)	0.650	18	9	0.78 (0.22-2.79)	0.697
Moderate	50	30	1.20 (0.63-2.31)	0.586	50	30	1.36 (0.58-3.31)	0.487
Trastuzumab								
Yes	67	36	-		67	36	-	
No	161	92	1.15 (0.65-2.04)	0.636	161	92	1.20 (0.57-2.53)	0.639
First line chemotherapy regimen								
SOX	145	80	-		145	80	-	
XELOX	83	48	1.11 (0.65-1.93)	0.697	83	48	1.11 (0.52-2.37)	0.784
Number of first line therapy cycles								
≤5	152	89	-		152	89	-	
>5	76	39	0.75 (0.43-1.30)	0.300	76	39	0.86 (0.42-1.75)	0.671
Second line chemotherapy regimen								
Irinotecan	143	75	-		143	75	-	
Paclitaxel	85	53	1.50 (0.87-2.61)	0.146	85	53	1.76 (0.87-3.66)	0.121

Table III. Continued.

Characteristic	Univariate				Multivariate			
	n	Event n	OR (95% CI)	P-value	n	Event n	OR (95% CI)	P-value
Number of second line therapy cycles								
≤5	104	59	-		104	59	-	
>5	124	69	0.96 (0.56-1.62)	0.869	124	69	0.96 (0.49-1.88)	0.911
Treatment								
SYS	114	96	-		114	96	-	
GTC + SYS	114	32	0.07 (0.04-0.14)	<0.001[a]	114	32	0.07 (0.03-0.13)	<0.001[a]

[a]P<0.05. OR, odds ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9; SOX, tegafur-gimeracil-oteracil + oxaliplatin; XELOX, capecitabine + oxaliplatin; SYS, systemic chemotherapy; GTC, gastric transcatheter chemoembolization.

SYS vs. 7.0 months (95% CI, 6.0-7.0) in patients who received SYS alone (log-rank P=0.570). Furthermore, 12-month OS was 53.5% in the GTC + SYS group and 35.1% in the SYS alone group. 12-month OS results were generally consistent across patient subgroups and did not differ significantly (Fig. 4).

The logistic regression analysis revealed that the number of GTC treatment sessions was not significantly associated with the 12-month survival rate of patients (Table SV) or the presence of dysphagia at 8 weeks after initial treatment (Table SVI; P>0.05).

Comparison of AEs between groups. In the GTC + SYS group, the most common severe AEs (grades 3/4) were leukopenia (7.3%), neutropenia (7.3%), and nausea and vomiting (7.3%). In the SYS group, the most common severe AEs were neutropenia (9.8%) and thrombocytopenia (8.2%). No patients in either group discontinued treatment or died due to AEs. The incidence of AEs was similar between the two groups, with no significant difference in the incidence of grade 3/4 events (Table SVII). Out of the 114 patients in the GTC + SYS group, 14 patients experienced superficial mucosal ulceration in the gastric body along the lesser curvature proximate to the fundus. This was confirmed by upper abdominal pain and subsequent gastric endoscopy. These patients were managed with symptomatic supportive treatment and showed improvement without any serious complications such as perforation (data not shown).

Discussion

In the present retrospective study, the effectiveness of GTC combined with SYS compared with SYS alone in the treatment of AGCC presenting with dysphagia was assessed. The findings highlight that GTC may reduce the local tumor burden in the cardia more rapidly and efficiently than SYS alone, leading to improved dysphagia symptom remission, enhanced nutritional status, and an improved QoL for patients. Additionally, GTC + SYS was associated with a longer OS. Overall, the results of the present study suggest that GTC + SYS, as a therapeutic intervention, holds promise in effectively managing dysphagia symptoms and improving outcomes in patients with AGCC. However, it is important to note that data on endoscopic evaluation of esophageal-gastric stenosis and gastric cancer size were not included in the present study. The main reason for excluding endoscopic evaluation data was the retrospective nature of this study. The endoscopic report for patients in the present study described the size of the tumor along the lower end of the esophagus and the longitudinal axis of the cardia but did not specify the thickness of the tumor protruding into the lumen. The thickness of the tumor protruding into the gastric cavity directly influences the degree of stenosis. Therefore, the maximum diameter of the cardiac tumor on the CT image of the patient before initial treatment was considered as a quantitative and accurate index, without including the content of the endoscopic report as a matching factor. Additionally, in certain patients with severe stenosis, the endoscope could not pass through the stenosis segment, limiting the information available about the mass and the stenosis segment. This limitation is one reason why the content of the endoscopic report was not used as a matching factor.

Table IV. Treatment efficacy of response and survival outcomes.

Characteristic	Treatment		P-value
	GTC + SYS (n=114)	SYS (n=114)	
OS, months (95% CI)	13.0 (12.0-14.0)	11.0 (10.0-12.0)	0.002[a]
6 months OS, % (95% CI)	87.7 (81.9-91.4)	67.1 (59.0-76.4)	<0.001
12 months OS, % (95% CI)	53.5 (44.4-63.4)	35.1 (26.4-45.1)	0.010
PFS, months (95% CI)	6.7 (6.0-8.5)	7.0 (6.0-7.0)	0.570
6 months PFS, % (95% CI)	53.49 (44.86-63.78)	51.18 (42.62-61.44)	0.887
12 months PFS, % (95% CI)	15.18 (9.33-24.70)	6.07 (2.63-14.04)	0.063
PR, n (%)	51 (45)	51 (45)	>0.999
SD, n (%)	42 (37)	39 (34)	0.768
PD, n (%)	21 (18)	24 (21)	0.722
ORR, n (%)	51 (45)	51 (45)	>0.999
DCR, n (%)	93 (82)	90 (79)	0.739

Data were analyzed using the Wilcoxon rank sum test, χ^2 test or Kaplan-Meier analysis. [a]P<0.05. GTC, gastric transcatheter chemoembolization; SYS, systemic chemotherapy; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate; DCR, disease control rate; OS, overall survival; PFS, progression-free survival; CI, confidence interval.

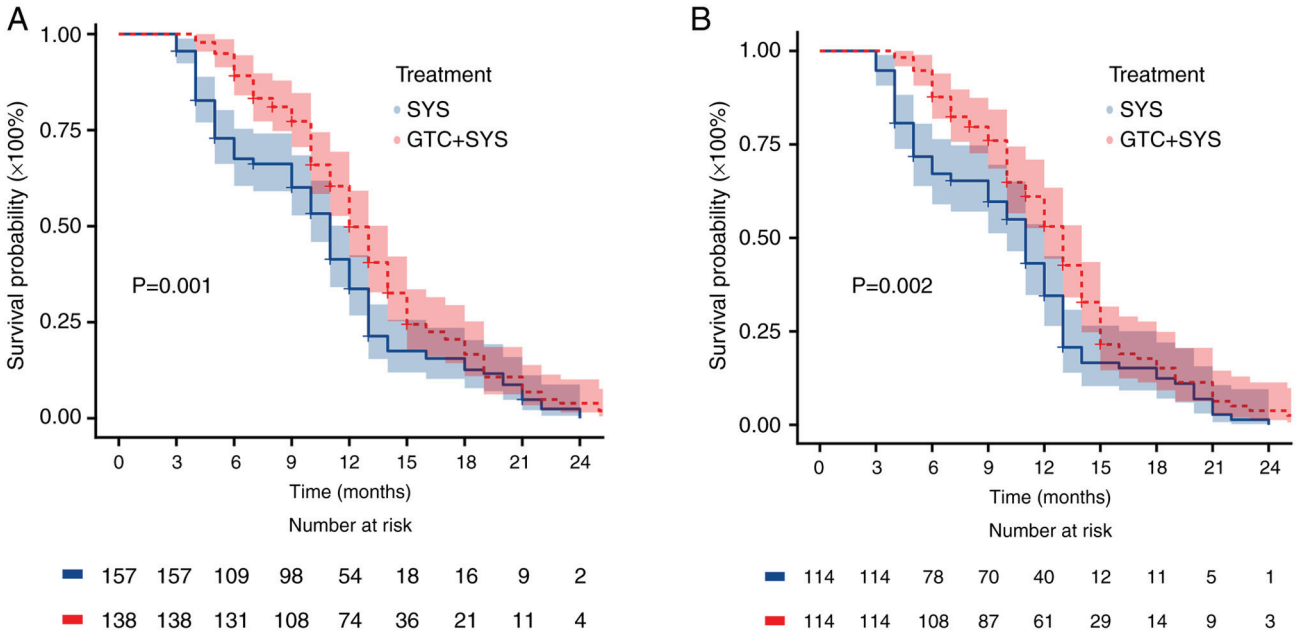

Figure 2. Kaplan-Meier curves of overall survival in patients who took GTC + SYS or SYS alone before and after PSM. (A) Before and (B) after PSM. GTC, gastric transcatheter chemoembolization; SYS, systemic chemotherapy; PSM, propensity score matching.

Several studies have reported the use of GTC in the treatment of gastric cancer, highlighting its potential benefits in terms of symptom remission and survival outcomes (1,3,6,16). Peng *et al* (6) evaluated the safety and efficacy of GTC in 42 patients with advanced gastric cancer with obstruction and reported that GTC could be an alternative treatment for advanced gastric cancer with obstruction. Similarly, Li *et al* (10) reported that GTC could shrink tumors and improve QoL in elderly patients with advanced gastric cancer. Wang *et al* (5) performed a retrospective analysis of patients with advanced gastric cardiac cancer who underwent GTC and reported a marked improvement in dysphagia symptom remission rates, with 100% of patients experiencing complete or partial relief. However, the study design lacked a control group receiving only systematic chemotherapy, which is the unique advantage of the present study.

One of the crucial decisions in the present study was the selection of 5-FU as the primary treatment for GTC. This choice is supported by existing literature, which has demonstrated the effectiveness of 5-FU in treating advanced gastric cancer (27,28). These agents have shown efficacy in both first-line and adjuvant settings, and their use in GTC can complement SYS by directly targeting the tumor. Additionally, 5-FU has shown favorable

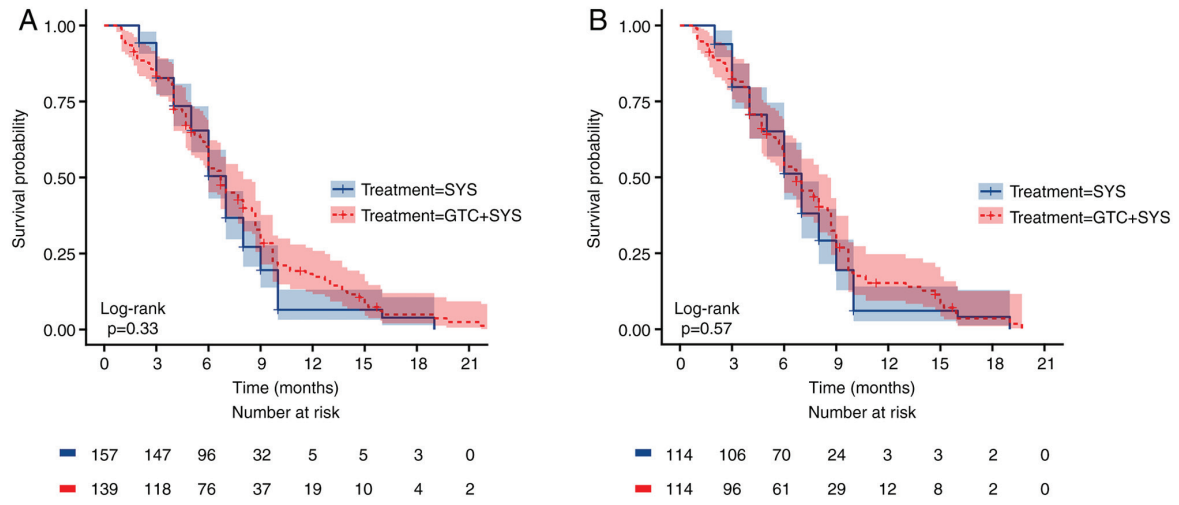

Figure 3. Kaplan-Meier curves of progression-free survival in patents who took GTC plus SYS or SYS alone before and after PSM. (A) Before and (B) after PSM. GTC, gastric transcatheter chemoembolization; SYS, systemic chemotherapy; PSM, propensity score matching.

Subgroup	SYS*	GTC + SYS*	HR (95% CI)	P-value	P for interaction
Overall	97/114 (85.1)	96/114 (84.2)	0.65 (0.49, 0.86)	0.003	
Sex					0.799
Female	29/34 (85.3)	25/31 (80.6)	0.73 (0.42, 1.24)	0.241	
Male	68/80 (85.0)	71/83 (85.5)	0.62 (0.44, 0.87)	0.005	
Age					0.449
> 60 years	65/75 (86.7)	50/63 (79.4)	0.70 (0.48, 1.01)	0.058	
≤60 years	32/39 (82.1)	46/51 (90.2)	0.56 (0.35, 0.89)	0.014	
ECOG					0.896
0	10/12 (83.3)	8/11 (72.7)	0.70 (0.27, 1.84)	0.468	
1 + 2	87/102 (85.3)	88/103 (85.4)	0.65 (0.48, 0.88)	0.005	
CEA					0.766
>5	46/51 (90.2)	45/52 (86.5)	0.67 (0.44, 1.02)	0.06	
≤5	51/63 (81.0)	51/62 (82.3)	0.63 (0.43, 0.94)	0.024	
CA 19-9					0.855
>40	44/52 (84.6)	42/54 (77.8)	0.64 (0.42, 0.99)	0.045	
≤40	53/62 (85.5)	54/60 (90.0)	0.64 (0.44, 0.94)	0.024	
Grade of differentiation					0.315
Moderate	18/25 (72.0)	20/25 (80.0)	0.90 (0.47, 1.71)	0.74	
Poor	71/80 (88.8)	68/80 (85.0)	0.62 (0.44, 0.87)	0.005	
Well	8/9 (88.9)	8/9 (88.9)	0.36 (0.12, 1.12)	0.079	
TNM Stage					0.96
III	54/62 (87.1)	49/60 (81.7)	0.63 (0.43, 0.94)	0.022	
IV	43/52 (82.7)	47/54 (87.0)	0.63 (0.42, 0.97)	0.035	
Trastuzumab					0.536
No	71/83 (85.5)	66/78 (84.6)	0.66 (0.47, 0.94)	0.019	
Yes	26/31 (83.9)	30/36 (83.3)	0.58 (0.34, 0.99)	0.046	
Immunotherapy					0.615
No	26/31 (83.9)	30/36 (83.3)	0.58 (0.34, 0.99)	0.046	
Sintilimab	30/34 (88.2)	34/37 (91.9)	0.40 (0.22, 0.70)	0.001	
Tislelizumab	41/49 (83.7)	32/41 (78.0)	0.71 (0.44, 1.15)	0.162	
First line chemotherapy regimen					0.078
SOX	62/72 (86.1)	58/73 (79.5)	0.55 (0.38, 0.80)	0.002	
XELOX	35/42 (83.3)	38/41 (92.7)	0.90 (0.57, 1.43)	0.65	
Number of first line therapy cycles					0.618
>5	33/36 (91.7)	36/40 (90.0)	0.57 (0.35, 0.92)	0.023	
≤5	64/78 (82.1)	60/74 (81.1)	0.67 (0.47, 0.96)	0.029	
Second line chemotherapy regimen					0.769
Irinotecan	60/71 (84.5)	59/72 (81.9)	0.61 (0.42, 0.88)	0.009	
Paclitaxel	37/43 (86.0)	37/42 (88.1)	0.69 (0.43, 1.10)	0.116	
Number of second line therapy cycles					0.657
>5	50/60 (83.3)	54/64 (84.4)	0.63 (0.43, 0.93)	0.021	
≤5	47/54 (87.0)	42/50 (84.0)	0.67 (0.44, 1.03)	0.065	

* no. of events / total no. (%)

Figure 4. ORs and 95% CIs for OS by subgroup. The forest plot displays the ORs and their corresponding 95% CIs for the comparison of GTC + SYS with SYS alone. Th end-time point of OS calculation was at 12 months. HR, odds ratio; CI, confidence interval; OS, overall survival; GTC, gastric transcatheter chemoembolization; SYS, systemic chemotherapy; ECOG, Eastern Cooperative Oncology; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9; TNM, tumor-node-metastasis; SOX, tegafur-gimeracil-oteracil + oxaliplatin; XELOX, capecitabine + oxaliplatin.

tolerability and safety profiles, making it suitable for combination therapy regimens. Furthermore, the selection of 5-FU for GTC is supported by its ability to exert local cytotoxic effects on the tumor whilst minimizing systemic toxicity (37,38). By delivering the chemotherapy directly to the tumor via the gastric arteries, GTC allows for a higher concentration of the drug at the tumor site, potentially enhancing its antitumor effects. The present study demonstrated that patients in the GTC + SYS group experienced a more rapid and significant reduction in cardia tumor diameter at both the 4- and 8-week follow-up compared with those in the SYS alone group. This suggests that the addition of GTC to SYS resulted in a more effective shrinking of localized tumors in the cardia, leading to a more pronounced alleviation of dysphagia symptoms.

Embospheres are biocompatible and biodegradable, and they have been demonstrated to effectively occlude the blood vessels supplying the tumor without causing significant adverse events. Several studies have investigated the safety of using embospheres for embolization in GTC (39,40). An important factor that has been reported to influence the occurrence of postoperative complications in GTC is the size of the embospheres. Smaller diameter microspheres have been associated with a higher risk of complications such as ischemic necrosis, gastric ulcers and gastric perforation. Conversely, larger microspheres have been reported to have a higher embolization efficacy but may also increase the risk of non-target embolization (41). Consistent with these studies, embolization using 300-500 μm-sized embospheres was well tolerated in patients with AGCC in the present study, without any major complications such as gastric perforation, hepatic infarction or embolic events.

Limitations of the present study need to be acknowledged. Firstly, the study was retrospective and performed at a single center, which may limit the generalizability of the findings. To address this, future studies should consider employing a prospective design with randomization in multiple centers. Secondly, the study lacked long-term follow-up data on the dysphagia, nutritional status and QoL of the patients, which could provide more comprehensive insights into the efficacy and safety of GTC combined with SYS in the treatment of AGCC. Further research with longer-term follow-up is required to validate the efficacy of GTC in improving the nutritional status and QoL of patients. Another limitation of the present study is the lack of data on endoscopic evaluation of esophageal gastric stenosis and gastric cancer size. This information could have provided valuable insights into the severity of dysphagia and the extent of disease in patients. Future studies should consider incorporating these parameters to enhance the robustness of the findings.

In conclusion, the findings of the present study suggest that combining GTC with SYS may be a more effective treatment approach for AGCC presenting with dysphagia than SYS alone. The higher dysphagia symptom remission and improved nutritional status and QoL in the combined treatment group indicate that this approach may help improve OS for these patients. However, further studies are needed to confirm these findings and determine the optimal treatment approach for this challenging condition.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

ZL, PS and RX contributed to the study conception and design, as well as material preparation, data collection and analysis. The first draft of the manuscript was written by ZL and all authors commented on previous versions of the manuscript. All authors have read and approved the final manuscript. ZL and PS confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Shandong Cancer Hospital and Institute (Jinan, China; approval no. SDTHEC 2023004007; approved 4/14/2023). The need for informed consent was waived due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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