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Effectiveness of conversion surgery in stage IV gastric cancer

Tran Quang Dat [a], Dang Quang Thong [a], Doan Thuy Nguyen [a], Nguyen Viet Hai [a], Nguyen Nam Thang [c], Nguyen Hoang Bac [a,b], Vo Duy Long [a,b,*]

[a] Gastro-intestinal Surgery Department, University Medical Center, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Viet Nam
[b] Department of General Surgery, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Viet Nam
[c] Department of General Surgery, Tay Nguyen Regional General Hospital, Daklak Province, Viet Nam

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ABSTRACT

Background: For patients with stage IV gastric cancer (GC), systemic therapy is often the standard treatment, but the prognosis remains poor. Conversion surgery (CS) has emerged as a potential therapeutic option for selected patients who had certain response to chemotherapy. This study aims to compare the survival outcomes of CS versus continued chemotherapy (CT) in stage IV GC.

Methods: We conducted a retrospective cohort study of 52 patients with stage IV gastric adenocarcinoma, from January-2018 to June-2023. Patients were divided into two groups: those who underwent CS (CS group) after a response to chemotherapy and those who continued with systemic chemotherapy (CT group). Baseline characteristics, chemotherapy toxicity, surgical outcomes, and survival data were analyzed and compared.

Results: Among 52 patients, 26 patients underwent CS, while other 26 continued with CT. The CS group showed a significantly higher 3-year overall survival (OS) rate and median survival time (MST) compared to the CT group (36 % vs. 15 %, HR = 0.39, 95%CI: 0.19–0.79, $p = 0.009$; 23.4 months vs. 14.7 months, $p < 0.001$, respectively). Subgroup analysis by Yoshida classification revealed superior survival outcomes for CS in category 3 (MST: 26.1 months vs. 12.6 months, $p < 0.001$). Multivariate analysis indicated that CS were associated with a longer survival. No major postoperative complications were observed in the CS group.

Conclusions: Conversion surgery improved survival outcomes in selected stage IV GC patients compared to systemic chemotherapy alone. CS should be considered as a treatment option for patients who responds to initial chemotherapy, particularly those in Yoshida category 3.

1. Introduction

Gastrectomy combined with D2 lymphadenectomy remains the primary curative treatment for resectable locally advanced GC [1]. However, a significant challenge lies in managing patients with stage IV gastric cancer (GC), in which systemic therapy is still considered the standard approach [1]. The prognosis among these patients remains extremely poor, with 5-year overall survival (OS) rates ranging from 6 % to 14.9 % [2]. Additionally, upfront surgery is not the fisrt option for these patients, except for those who experienced bleeding, obstruction, or perforation caused by the tumor, required palliative gastrectomy. The phase III REGETTA trial revealed that upfront reductive gastrectomy followed by adjuvant chemotherapy for stage IV GC with a single incurable factor did not improve the OS compared to chemotherapy alone [3].

Recently, conversion therapy has emerged as a novel therapeutic strategy for stage IV GC. This approach involves administering systemic therapy followed by a conversion gastrectomy. It targets unresectable or marginally resectable metastatic lesions and aims to convert non-curative cases into potentially curative ones. Yoshida classificated stage IV GC into 4 categories based on its heterogeneous characteristics, and suggested different theurapeutic approaches for each category [4]. Several prior studies have shown promising survival outcomes for certain subgroups of patients who underwent conversion surgery (CS) [5–11]. The international cohort study (CONVO-GC-1) reported a satisfactory median survival time of 36.7 months in the CS patients [10]. Moreover, the AIO-FLOT3 trial and META-GASTRO study demonstrated the potential benefit of surgery after chemotherapy for patients with limited metastasis [12,13]. However, there are few studies comparing the long-term survival outcomes between the CS approach and systemic therapy alone. Thus, the optimal treatment for each category is still unclear because of insufficient scientific evidences. In patients with

* Corresponding author. University Medical Center at Ho Chi Minh City, 215 Hong Bang, Ward 11, District 5, Ho Chi Minh City, Viet Nam.
E-mail address: long.vd@umc.edu.vn (V.D. Long).

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certain responses after systemic treatment, it is controversial whether continuing chemotherapy or converting to surgery is a better option. Therefore, we conducted this study to compare survival outcomes of conversion surgery and systemic chemotherapy alone in stage IV GC patients.

2. Patients and methods

2.1. Study design

This retrospective cohort study reviewed patients with stage IV GC, who received systemic chemotherapy as first-line therapy, followed by conversion surgery (CS group) or continuing chemotherapy (CT group). We collected data from January 2018 to June 2023 at the Department of Gastro-Intestinal Surgery of the University Medical Center Ho Chi Minh City, a tertiary hospital in Ho Chi Minh city, Vietam. The study was approved by the Institutional Review Board of the hospital.

2.2. Patients

Inclusion criteria comprised of: (i) histologically confirmed gastric adenocarcinoma, (ii) clinical or surgical stage IV GC with limited metastasis*; received first-line systemic chemotherapy; (iii) adequate hematological, liver, and renal functions, including white blood cell count between 4000 and 12,000/mm3; neutrophil count $\geq$2000/mm3; hemoglobin >10 g/dL; platelet count $\geq$100,000/mm3; aspartate aminotransferase (AST) and alanine aminotransferase (ALT) $\leq$100 IU/L; total bilirubin $\leq$1.5 mg/dL; creatinine $\leq$1.2 mg/dL and creatinine clearance $\geq$60 mL/min, and (iv) an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1.

Exclusion criteria included (a) progression disease (PD) after 3–4 courses of systemic chemotherapy; (b) concurrent cancer or history of previous other cancers, (c) not complete at least 3 courses of chemotherapy.

(*) We defined limited metastatic tumors including one or more factors as following:

- Limited peritoneal metastasis:
  - o No clinically visible or symptomatic carcinomatosis of peritoneum or pleura, ie. peritoneal metastasis without omental cake images, diffuse peritoneal plaques, non-invasive mesenteric retractions and no peritoneal fluid roughly
  - o PCI <12 on diagnostic laparoscopy.
- Fewer than 5 liver metastases with diameter of each lesion less than 5 cm.
- Para aortic lymph nodes metastasis
- Supraclavicular lymph nodes
- Solitary lung metastases
- Krukenberg tumors and/or adrenal gland metastases.

2.3. Treatment

After systemic chemotherapy, patients with posibility of R0 resection were considered for CS. If patients declined the operation, further chemotherapy would be administered. In cases of acception for surgery, gastrectomy with standard D2 or extended lymph node dissection (with metastasectomy if needed) was performed. Based on the primary tumor's location, we performed subtotal or total gastrectomy with lymphadenectomy by laparoscopy or laparotomy. Combined resection of the invaded organs was conducted to achieve R0 resection. For patients with persistent para-aortic lymph node (PAN) involvement after preoperative chemotherapy, dissection of para aortic lymph nodes was carried out. Intraoperative lavage cytology was routinely performed both before and after the gastrectomy. Peritonectomy was not performed in any of the cases.

Patients underwent CS after 2–5 weeks from the last preoperative chemotherapy course, depending on the recovery from the adverse events and toxicity. We administered postoperative chemotherapy to patients who maintained good performance status and adequate nutritional status. The specific chemotherapy regimen and its duration were determined by the tumor board.

2.4. Follow-up

Patients were followed up with a 3-month interval in the first two years, 6-month interval in the next three years, and then annually. The follow-up visit consisted of physical examination, laboratory blood tests, and abdominal ultrasonography. Computed tomography was performed every six months for the first three years and then every year. Endoscopy was performed every year. If a patient had suspected symptoms or signs of recurrence or metastasis, computed tomography and/or endoscopy were performed regardless of their follow-up schedule. We did not perform positron emission tomography and computed tomography (PET CT) routinely.

2.5. Outcomes

The primary outcome was the 3-year OS. Secondary outcomes included the toxicity and adverse events, R0 resection, short-term surgical outcomes, and median survival time (MST).

R0 resection. the surgery achieved curative intent, with no residual tumor remaining at any site, including surgical margins and metastatic lesions. This is determined based on postoperative histopathological examination and peritoneal cytology.

R1 resection. residual tumor is detected postoperatively based on histopathological examination or peritoneal cytology.

R2 resection. residual tumor is identified intraoperatively, and the surgery is performed with the aim of tumor reduction.

Postoperative complications were classified according to the Clavien–Dindo classification [14].

OS was defined as the length of time from the beginning of the systemic chemotherapy to death for all causes.

2.6. First-line chemotherapy and prior response assessment

After 3–4 courses of first-line systemic chemotherapy, we assessed the response of disease by the Response Evaluation Criteria in Solid Tumor (RECIST) 1.1 using computed tomography (CT) [15].

The Common Toxicity Criteria of the National Cancer Institute (NCI–CTC) 4.0 was used to report toxicities and adverse events.

2.7. Statistical analysis

Descriptive analyses encompassed the calculation of mean $\pm$ standard deviation, or median (25th; 75th percentiles) for continuous variables, and the presentation of patient count along with percentage for categorical variables. Baseline characteristics were summarized for patients by two distinct groups: CS and non-CS. The differences between the two groups were tested using Fisher's exact test for categorical variables, and Kruskal Wallis test for continuous variables.

Survival outcomes of the CS group were assessed using the Kaplan–Meier method to estimate OS with corresponding 95 % confidence intervals (CI), visually depicted through Kaplan–Meier plots.

A subgroup analysis was performed for each group of category 1 + 2 and category 3, using the same approach. The comparison of OS between groups utilized the Cox proportional hazard model, and outcomes were expressed as hazard ratios (HR) with corresponding 95 % confidence intervals (CI). Prognostic factors for survival were analyzed using a multivariate Cox proportion-hazards model.

All statistical analyses were performed using Stata, version 17.

3. Results

Between January 2018 and June 2023, a total of 52 patients diagnosed with limited metastatic gastric adenocarcinoma were included in the study. Of these, there were 26 patients in the CS group and 26 patients in the CT group. All patients had a partial response or stable disease status after 3 or 4 courses of systemic chemotherapy (Fig. 1).

3.1. Patient characteristics

The baseline characteristics of the patients were summarized in Table 1. The mean age of the patients was 56.0 ± 11.5 years, and was similar between the two groups (55.9 ± 11.7 years and 56.0 ± 11.5 years, p = 0.749, respectively). There was no significant difference in age, gender distribution, BMI, or comorbidity disease between the groups. The clinical tumor and lymph node stages were balanced between the two groups. The differentiation status and Yoshida classification were also comparable between the two groups. Most of patients were classified with category 3 (50.0 % vs. 61.5 %, respectively).

The CS group had a lower incidence of anemia (26.9 % vs. 53.9 %, p = 0.048, respectively) and a relatively smaller tumor size before chemotherapy (7.0 ± 2.8 cm vs. 8.7 ± 3.5 cm, p = 0.031, respectively). Moreover, the CS group had a better response after chemotherapy than the CT group (46.2 % of PR vs. 15.4 % of PR, p = 0.016, respectively).

3.2. Toxicity

The incidence of chemotherapy-related toxicities of grade ≥3 was presented in Table S1. Neutropenia, which was the most common major toxicity (15.4 %), was similar between the two groups. Other toxicities, including rash, leukopenia, neutropenia, anemia, thrombocytopenia, elevated SGPT, and hypokalemia, did not show significant differences between the groups.

3.3. Operative characteristics

The operative characteristics of the CS group were outlined in Table 2. The majority of patients underwent open surgery (61.5 %). Distal gastrectomy was performed in 15 patients (57.7 %) and total gastrectomy in 11 patients (42.3 %). The median surgical tumor size was 4.8 ± 2.4 cm, with a mean operating time of 192.9 ± 59.8 min and mean blood loss of 121.6 ± 102.3 ml. Combined resections were performed in 15.4 % of patients, and the extent of lymph node dissection was predominantly D2 (80.7 %). The mean number of harvested lymph nodes was 23.4 ± 13.1. R0 resection was achieved in 84.6 % (22/26 patients). There were 3 patients (13.0 %) with R1 resection, of which 2 cases had positive proximal margins, and 1 case had positive peritoneal lavage cytology. One patient (4.4 %) had R2 resection. The overall postoperative complications rate was 23.1 % (6 patients). However, no patient experienced severe complications (Clavien Dindo≥3).

3.4. Survival outcomes

The Kaplan-Meier survival estimates and results from Cox models for OS were summarized in Table 3 and Fig. 2. The 1-, 2-, and 3-year OS rates for the CS group were than those for the CT group. The 3-year OS rate in the CS group was significantly higher than that of the CT group (36 % vs. 15 %, HR = 0.39, 95 % CI: 0.19–0.79, p = 0.009). The MST for all patients was 18.3 months. Patients in the CS group had a significantly longer MST compared to that in the CT group (23.4 months vs. 14.7 months, p < 0.001).

3.5. Subgroup analysis by Yoshida classification

Subgroup analysis by Yoshida classification was showed in Table 4 and Table S2. In categories 2, MST was 24.5 months in the CS group versus 16.1 months in the CT group, p = 0.086. Additionally, in category 3, MST and 3-year OS rate were significantly higher in the CS group than those in the CT group (26.1 months and 53 % vs. 12.6 months and 10 %,

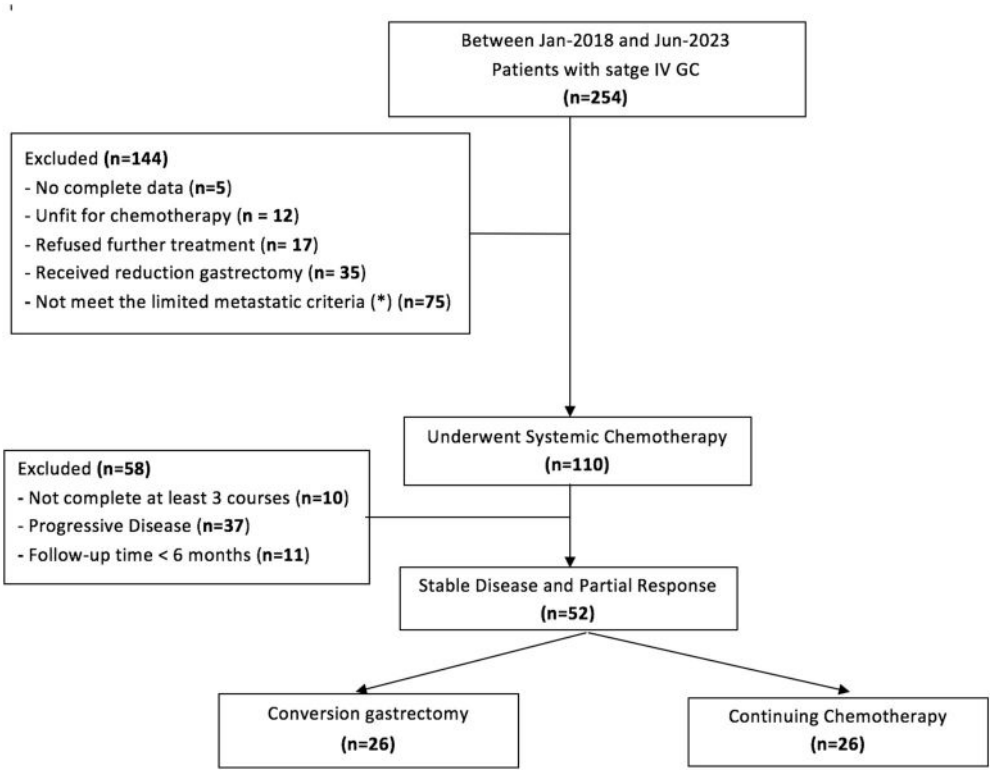

Fig. 1. Flowchart of patient selection.

Table 1
Patient characteristics.

	All patients (N = 52)	Surgery (N = 26)	Chemo alone (N = 26)	p-value
Age (years)	56.0 ± 11.5	55.9 ± 11.7	56 ± 11.5	0.749
Sex				0.163
Male	29 (61.8)	17 (65.4)	12(46.2)	
Female	23 (38.2)	9 (34.6)	14 (53.8)	
BMI (kg/m2)	20.5 ± 2.6	20.8 ± 2.3	20.2 ± 2.9	0.319
Hypertension	10 (19.2)	4 (15.4)	6 (23.1)	0.726
Diabetes	5 (9.6)	3 (11.5)	2 (7.7)	1.000
Cardiovascular disease	2 (3.9)	1 (3.9)	1 (3.9)	1.000
Chronic hepatic disease	7 (13.5)	4 (15.4)	3 (11.5)	1.000
Chronic lung disease	2 (3.9)	1 (3.9)	1 (3.9)	1.000
Chronic renal disease	1 (1.9)	1 (3.9)	0 (0.0)	1.000
CEA (U/L)	81.7 ± 368.1	54.9 ± 131.3	108.5 ± 507.5	0.241
Preoperative WBC (g/L)	7.7 ± 1.8	8.0 ± 1.4	7.3 ± 2.2	0.164
Hemoglobin (g/dL)	12.1 ± 2.6	12.7 ± 2.4	11.6 ± 2.8	0.098
Anemia	21 (40.4)	7 (26.9)	14 (53.9)	**0.048**
Gastric outlet obstruction	8 (15.4)	5 (19.2)	3 (11.5)	0.703
Pre-chemotherapy tumor size (cm)	7.9 ± 3.3	7.0 ± 2.8	8.7 ± 3.5	**0.031**
Differentiation status				0.200
Well differentiated	2 (3.9)	1 (3.9)	1 (3.9)	
Moderately differentiated	18 (34.6)	12 (46.2)	6 (23.1)	
Poorly differentiated	26 (40.4)	10 (38.5)	11 (42.3)	
Signet ring cell	11 (21.1)	3 (11.5)	8 (30.7)	
Yoshida Classification				0.223
Category 1	4 (7.7)	4 (15.4)	0	
Category 2	9 (17.3)	5 (19.2)	4 (15.4)	
Category 3	29 (55.8)	13 (50.0)	16 (61.5)	
Category 4	10 (19.2)	4 (15.4)	6 (23.1)	
Clinical T stage				0.249
T3	1 (1.9)	0 (0.0)	1 (3.8)	
T4a	32 (61.5)	14 (53.9)	18 (69.2)	
T4b	19 (36.6)	12 (46.1)	7 (26.9)	
Clinical N stage				0.107
N1	8 (15.4)	4 (15.4)	4 (15.4)	
N2	24 (46.1)	14 (53.9)	10 (38.5)	
N3	11 (18.2)	2 (7.7)	9 (34.6)	
Bulky	9 (16.4)	6 (23.1)	3 (11.5)	
Response after 4 cycles				0.016
PR	16 (30.8)	12 (46.2)	4 (15.4)	
SD	36 (69.2)	14(53.8)	22 (84.6)	
Regimen				0.337
TS_1 base	39 (75)	21 (80.8)	18 (69.2)	
Xelox	13 (25)	5 (19.2)	8 (30.8)	

Statistical summary is mean ± standard deviation or n (%).
Abbreviations: BMI, body mass index; CEA, carcinoembryonic antigen; PR: partial response; SD: stable disease.

$p < 0.001$, respectively). There was no difference in survival outcomes in category 4.

3.6. Univariate and multivariate analysis of factors affecting OS

The results of the univariate analysis demonstrated that high age and CS significantly increased OS. In the multivariate analysis, CS (HR = 0.41, 95 % CI: 0.20–0.82, p = 0.012) was identified as an independent factor for increasing OS (Table 5).

4. Discussion

Our study demonstrated the effectiveness of CS for stage IV GC in terms of survival outcomes. This approach provided a high R0 rate (84.6 %) along with longer MST and higher 3-year OS rate when compared to the CT group. These findings were aligned with other previous studies and enhanced the value of this promising treatment.

Table 2
Operative characteristics.

Operative characteristics	Surgery (N = 26)
Operation type	
Laparoscopic	10 (38.5)
Open	16 (61.5)
Operative method	
Distal gastrectomy	15 (57.7)
Total gastrectomy	11 (42.3)
Surgical tumor size (cm)	4.8 ± 2.4
Operating time (mins)	192.9 ± 59.8
Blood loss (ml)	121.6 ± 102.3
Combined surgery	4 (15.4)
Combined surgery specification	
Hepatic segmentectomy	1 (25.0)
segmental transverse colectomy	1 (25.0)
Spleen and pancreatic tail	2 (50.0)
Extent of lymph node dissection	
D1+	1 (3.9)
D2	21 (80.7)
D2 + PAND	4 (15.4)
Number of resected LNs	23.4 ± 13.1
Pathological T stage	
T1	1 (3.9)
T2	1 (3.9)
T3	3 (11.5)
T4a	21 (80.7)
Pathological N stage	
N0	6 (23.1)
N1	9 (34.6)
N2	4 (15.4)
N3	7 (26.9)
Curability	
R0	22 (84.6)
R1	3 (11.5)
R2	1 (3.9)
Adjuvant chemotherapy	
No	5 (19.2)
Yes	21 (80.8)
Clavien-Dindo classification	
Grade 1-2	6 (23.1)
Grade >/ = 3	0 (0.0)

Statistical summary is n (%), mean ± standard deviation, or median (25th; 75th percentiles).
Abbreviations: PAND: para-aortic nodal dissection.

Table 3
Kaplan-Meier estimates and results from Cox models for overall survival.

	Kaplan-Meier probability (%)			Cox model		
	1 years	2 years	3 years	HR	95 % CI	p-value
Total	81 (67, 89)	42 (27, 56)	26 (13, 41)	–	–	
Conversion Surgery	100	52 (31, 69)	36 (16, 55)	0.39	0.19, 0.79	0.009
Chemo alone	61 (40, 77)	31 (11, 53)	15 (3, 37)	–	–	

According to previous reports, the median survival time of stage IV GC ranged from 5.9 to 16.3 months for cases of chemotherapy alone or reduction surgery followed by adjuvant chemotherapy [16–20]. The 1-, 2-, and 3-year OS rates in our CS group were 100 %, 52 %, and 36 %, respectively and the MST was 23.4 months, which was comparable to other studies on CS [8,9,12,21–23]. Moreover, the OS rate and MST of the CS group in our study were statistically better than those in the CT group. Our findings, combined with several limited results from prior comparative studies, could help improve the benefits of the CS approach over standard systemic chemotherapy for stage IV GC.

In Western countries, published and ongoing studies had been established to investigate the management of metastasis GC, such as AIO-FLOT3, RENAISSANCE, Meta-Gastro, OMEC project [12,13,24,25].

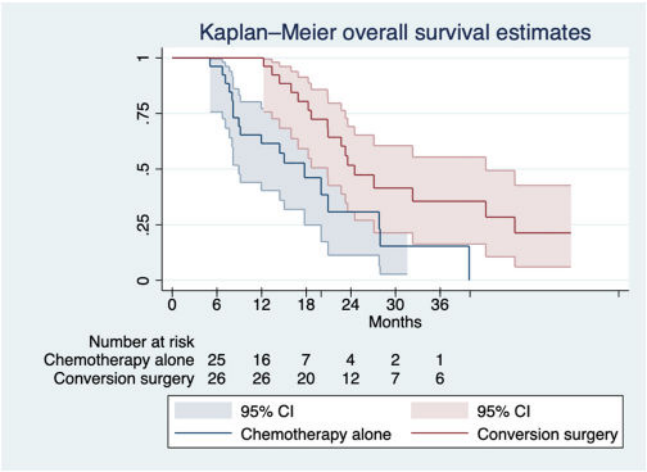

Fig. 2. Kaplan-Meier overall survival estimation.

They focused on oligometastases as a limited metastasis which responded to systemic treatment [26]. As results of the Bertinoro consensus, oligometastases should include: para-aortic LNs; technically resectable liver lesions; three unilateral or two bilateral lung metastases; peritoneal metastasis with PCI ≤ 6[26]. In our study, the selection criteria were more extensive than OMEC project (which excluded peritoneal metastasis), or Bertinoro consensus but similar to Meta-Gastro study [13,25,26]. Generally, these patients could be considered as oligometastasis disease, and our study described the similar results that conversion surgery improved survival outcomes compared to the systematic therapy alone.

Regarding the subgroup analysis according to the Yoshida classification, the MST in category 1, 2, 3, and 4 of the CS group were 15.2, 24.5, 26.1, and 23.3 months, respectively. The survival outcomes of patients in category 3 were the most satisfactory among the 4 categories, with a MST of 26.1 months and a 3-year OS rate of 53 %. These results were contrary to those of the CONVO-GC-1 study [10]. It could be interpreted in our study by maintaining the effectiveness of chemotherapy due to the selectiveness of cases with a low total tumor burden, limited peritoneal lesions without abdominal ascites, and no other organ metastases. Additionally, in category 3, patients of the CS group posed better oncological outcomes than the CT group in both 3-year OS rate and MST, consistent with findings from previous studies [27–30]. For patients in categories 1 and 2, although the survival outcomes in the CS group were not statistically different from the CT group, there were still promising results in the MST, which was also supported by data in the CONVO-GC-1 study. Thus, we suggested that patients in category 1, 2, and 3 could be considered for CS approach.

Similar to the results of the previous studies [2,4,9,31,32], the survival of patients in category 4 in our study was the worst (3-year OS 0 % and median survival time of 23.0 months in the CS group) and was not statistically different from the CT group. For these patients who present with a peritoneal metastasis along with other distant organ metastasis, the total tumor burden was remarkably high, hindering the opportunity and effectiveness of CS. However, data from other studies (CONVO-GC-1, Meta-Gastro) suggested that some selected patients in category 4 (with PCI $</=12$) could be benefited from CS if R0 resection was obtained [10,13]. Further researches for this category should be conducted.

In the CS group, although we performed combined resection of invasive organs and para-aortic lymph nodes dissection, there was no major postoperative complications. In respect to short-term surgical outcomes, this study showed similar results compared to previous studies concerning distal and total gastrectomy for GC [28,33,34], which pointed out the safety of CS.

There are several limitations to our study. Firstly, the sample size was relatively small, and the study was conducted at a single institution, which may limit the generalizability of the findings, especially the subgroup analysis. Secondly, there were several heterogeneities in the chemotherapy regimens, the number of preoperative chemotherapy courses. Thirdly, there was an imbalanced in clinical response according to RECIST criteria after chemotherapy between the groups. However, all patients of the two groups had possibility of R0 resection.

In conclusions, conversion surgery provided favorable survival outcomes compared to systemic chemotherapy alone for stage IV gastric cancer patients with certain response after first-line chemotherapy. Further prospective studies are needed to validate our findings and refine patient selection criteria for conversion surgery.

Ethical approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Institutional Review Board, University Medical Center Ho Chi Minh city.

Approval to perform research on human subjects in this study was provided by the Institutional Review Board, University Medical Center Ho Chi Minh city (registration number: 764/HDDD-DHYD)

Data availability statement

The data presented in this study are available on request from the corresponding author.

Contribution Author(s)

Study concepts: Tran Quang Dat, Dang Quang Thong, Doan Thuy Nguyen, Nguyen Viet Hai, Nguyen Hoang Bac, Vo Duy Long.

Study design: Tran Quang Dat, Dang Quang Thong, Doan Thuy Nguyen, Nguyen Viet Hai, Nguyen Hoang Bac, Vo Duy Long.

Data acquisition: Tran Quang Dat, Dang Quang Thong, Doan Thuy Nguyen.

Quality control of data and algorithms: Nguyen Viet Hai, Nguyen Hoang Bac, Vo Duy Long.

Data analysis and interpretation: Tran Quang Dat, Dang Quang Thong, Doan Thuy Nguyen.

Statistical analysis: Tran Quang Dat.

Manuscript preparation: Tran Quang Dat, Dang Quang Thong, Doan Thuy Nguyen, Nguyen Viet Hai, Nguyen Hoang Bac, Vo Duy Long.

Manuscript editing: Tran Quang Dat, Dang Quang Thong, Doan Thuy

Table 4
Survival by Yoshida classification.

	Median Survival (IQR 25,75)				3-year OS (%)			
	All patients (N = 52)	Surgery (N = 26)	Chemo alone (N = 26)	p-value	All patients (N = 52)	Surgery (N = 26)	Chemo alone (N = 26)	p-value
All categories	18.3 (13.0, 26.3)	23.4 (18.3, 32.3)	14.7 (8.2, 18.4)	<0.001	26	36	15	0.009
Category 1	15.2 (13.3, 34.8)	15.2 (13.3, 34.8)	N/A	–	25	25	N/A	–
Category 2	23.3 (16.8, 27.8)	24.5 (23.2, 32.3)	16.1 (11.3, 22.3)	0.086	19	27	0	0.387
Category 3	16.9 (12.5, 26.1)	26.1 (18.7, 42.1)	12.6 (8.6, 17.2)	0.0005	32	53	10	0.0009
Category 4	21.8 (17.1, 23.6)	23.0 (21.8, 23.4)	17.7 (8.0, 27.9)	0.394	0	0	0	0.372

Table 5
Uni- and multivariable analysis of risk factors for overall survival.

Characteristic	Univariable model			Multivariable model		
	HR	95 % CI	p-value	HR	95 % CI	p-value
Age (years)	**0.94**	**0.90, 0.99**	**0.013**	**0.97**	**0.94, 1.00**	**0.049**
Sex						
Male		Ref				
Female	0.86	0.30, 2.43	0.776			
CEA (U/L)	0.99	0.90, 1.01	0.116			
Anemia	1.03	0.52, 2.06	0.928			
Gastric outlet obstruction	1.30	0.53, 3.22	0.554			
Pre-chemotherapy tumor size (cm)	1.06	0.97, 1.16	0.172s			
Differentiation status						
Well + Moderately differentiated	1	Ref				
Poorly differentiated + SRC	1.47	0.64, 3.37	0.364			
Yoshida classification						
Categories 1	1	Ref				
Categories 2	0.43	0.08, 2.22	0.315			
Categories 3	0.71	0.35, 1.44	0.348			
Categories 4	0.91	0.54, 1.52	0.715			
Chemotherapy regimen						
TS1_based	0.68	0.23, 1.95	0.470			
Other		Ref				
Response after chemo						
PR		Ref				
SD	1.61	0.76, 3.50	0.207			
Conversion surgery	**0.39**	**0.19, 0.79**	**0.009**	**0.41**	**0.2, 0.82**	**0.012**
Chemotherapy alone		Ref				

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Conflict of interest

Drs. Tran Quang Dat, Dang Quang Thong, Doan Thuy Nguyen, Nguyen Viet Hai, Nguyen Nam Thang, Nguyen Hoang Bac, and Vo Duy Long disclose any potential or actual personal, political or financial conflict of interest in the material, information or techniques described in the paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2024.109485.

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