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Evaluation of long-term outcomes after gastric cancer surgery combined with adjuvant chemotherapy

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Abstract

Objective: *To investigate selected clinical and paraclinical characteristics of patients with gastric cancer and to evaluate long-term outcomes following gastric cancer surgery combined with adjuvant chemotherapy.* ***Subjects and method:*** *A cross-sectional descriptive study with prospective interventional and longitudinal follow-up was conducted on 63 patients diagnosed with distal one-third gastric cancer who underwent subtotal gastrectomy combined with chemotherapy between January 2018 and December 2024.* ***Result:*** *The mean age of patients was 58.2 ± 10.8 years, with a predominance of males (73.0%). Most patients underwent open surgery (79.4%), primarily involving 3/4 and 4/5 gastric resections. TNM stage III accounted for the highest proportion (36.5%), with adenocarcinoma being the most common histological type (87.3%). Non-hematologic adverse effects related to the ECX regimen were mostly mild to moderate, with grade 2 nausea/vomiting (77.8%) and grade 3 alopecia (74.6%) being the most frequent. Metastases occurred mainly between 12 and 18 months post-treatment, commonly involving the liver (42.9%) and peritoneum (35.7%). The 1-year and 5-year overall survival rates were 95.8% and 64.5%, respectively; disease-free survival rates were 93.2% and 61.3%, respectively. Quality of life declined over time, with the proportion of patients achieving high scores (9–10) decreasing, while those with poor scores (5–6) increased to 20.9% at 24 months.* ***Conclusion:*** *Surgery combined with adjuvant chemotherapy using the ECX regimen provides relatively favorable survival outcomes in patients with gastric cancer. However, the risk of early metastasis and the trend of declining quality of life underscore the need for long-term monitoring and supportive interventions.*

Keywords: *Gastric cancer, long-term outcomes, adjuvant chemotherapy.*

I. Background

Gastric cancer is one of the leading causes of cancer-related mortality worldwide, with approximately 1.1 million new cases and 770,000 deaths in 2020. The incidence is particularly high in Asian countries such as Japan and South Korea [1]. Curative surgery remains the mainstay treatment for early-stage gastric cancer; however, the 5-year survival rate remains low due to a high risk of recurrence [2]. Numerous studies have demonstrated that adjuvant chemotherapy following surgery can improve survival rates and reduce recurrence risk. A meta-analysis of 17 randomized clinical trials showed that adjuvant chemotherapy increased the 5-year survival rate from 49.6% to 55.3% and reduced the risk of death with a hazard ratio (HR) of 0.82 [2]. The ECF regimen (epirubicin, cisplatin, and 5-fluorouracil), as studied in the MAGIC trial,

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demonstrated that perioperative chemotherapy significantly improved 5-year survival (36% compared to 23% in the surgery-only group) [3]. However, despite its short-term benefits, ECF has limited long-term survival outcomes, and data on long-term outcomes such as late recurrence, long-term complications, and quality of life after treatment remain limited. Therefore, we conducted the study entitled "Evaluation of Long-Term Outcomes After Gastric Cancer Surgery Combined with Adjuvant Chemotherapy" with the objectives: (1) To investigate some clinical and paraclinical characteristics of patients with gastric cancer and (2) To evaluate long-term outcomes after curative gastric cancer surgery combined with adjuvant chemotherapy.

2. Subject and method

Study Population

The study included 63 patients who were diagnosed with distal third gastric cancer and underwent subtotal gastrectomy combined with chemotherapy between January 2018 and December 2024.

Inclusion Criteria

Underwent distal subtotal gastrectomy with D2 lymph node dissection.

Histologically confirmed diagnosis of distal third gastric cancer, with clinical staging according to TNM from IB to III.

Karnofsky performance score ≥ 70%.

Completed 6 cycles of postoperative adjuvant chemotherapy using the ECX regimen.

Provided informed consent to participate in the study.

Exclusion Criteria

Patients with comorbid systemic diseases such as diabetes, hypertension, ASA score ≥ 3.

Patients who received additional adjuvant therapies postoperatively.

Patients who declined to participate in the study.

Study Design

This is a cross-sectional descriptive study with a prospective interventional component and longitudinal follow-up.

Sample Size and Sampling Method

A convenient sampling method was applied. All patients meeting the inclusion criteria from January 2018 to December 2024 were enrolled, resulting in a sample of 63 patients.

Data Collection and Analysis

Research Indicators

Characteristics of the study group: age, sex, surgical approach, type of resection (3/4 or 4/5 of the stomach), type of lymphadenectomy (standard D2 or extended D2), cancer stage, histopathological features, and non-hematologic chemotherapy-related adverse events.

Long-term outcomes after curative gastric cancer surgery combined with adjuvant chemotherapy: assessed by time to metastasis, overall survival (OS), disease-free survival (DFS), and quality of life at the last follow-up before death, recurrence, or end of study.

Chemotherapy Regimen

Systemic chemotherapy followed the ECX protocol (Epirubicin, Cisplatin, Capecitabine/ Xeloda), including 6 cycles starting 4 weeks after surgery, with each cycle administered every 21 days.

Quality of Life Assessment

The Spitzer Quality of Life Index was used, which evaluates five criteria: patient activity, daily living, health, support, and self-assessment. The score ranges from 0 to 10, with higher scores indicating better quality of life.

Data Analysis

Data were analyzed using SPSS version 22.0. Quantitative variables were presented as mean ± standard deviation, while qualitative variables were expressed as percentages. The T-test was used to compare two means, and a p-value < 0.05 was considered statistically significant.

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3. Result

Table 1. Clinical and Histopathological Characteristics of Gastric Cancer Patients

Characteristic		Number (n)	Percentage (%)
Mean age (năm)		58,2 ± 10,8 [30 - 85]	
Gender	Male	46	73,0
	Female	17	27,0
Surgical approach	Open surgery	50	79.4
	Laparoscopic surgery	13	20.6
Type of resection	3/4 gastrectomy	35	55.6
	4/5 gastrectomy	28	44.4
Lymph node dissection	D2	28	44,4
	D2+	35	55,6
TNM stage	0	1	1.6
	I	22	34.9
	II	17	27.0
	III	23	36.5
Histopathological type	Adenocarcinoma	55	87.3
	Squamous cell carcinoma	5	7.9
	Others (GIST, Lymphoma)	3	4.8

Comment: The average age of gastric cancer patients was 58.2 ± 10.8 years. Males accounted for the majority (73.0%). Open surgery was the predominant method (79.4%), with two main resection types being 3/4 gastrectomy (55.6%) and 4/5 gastrectomy (44.4%). D2+ lymph node dissection was performed in 55.6% of cases. TNM staging revealed that Stage III was the most common (36.5%), followed by Stage I (34.9%) and Stage II (27.0%). Histopathologically, adenocarcinoma was the predominant type (87.3%), while squamous cell carcinoma and other types were less frequent (7.9% and 4.8%, respectively).

Table 2. Non-Hematologic Adverse Effects of the ECX Regimen (n = 63)

Adverse Effect	Grade 1	Grade 2	Grade 3
	n (%)	n (%)	n (%)
Anorexia	9 (14.3)	2 (3.2)	0 (0)
Nausea/Vomiting	1 (1.6)	49 (77.8)	1 (1.6)
Stomatitis	2 (3.2)	2 (3.2)	0 (0)
Diarrhea	2 (3.2)	0 (0)	0 (0)
Hand-foot syndrome	2 (3.2)	2 (3.2)	3 (4.8)
Hair loss	3 (4.8)	11 (17.5)	47 (74.6)
Elevated SGOT	18 (28.6)	5 (7.9)	0 (0)
Elevated SGPT	16 (25.4)	3 (4.8)	0 (0)
Elevated Creatinine	7 (11.1)	2 (3.2)	0 (0)

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Comment: Most non-hematologic adverse effects related to the ECX regimen were mild to moderate. The most common side effect was nausea/vomiting, predominantly at grade 2 (77.8%). Grade 3 hair loss occurred in 74.6% of patients. Biochemical disturbances such as elevated SGOT and SGPT were mostly grade 1, occurring in 28.6% and 25.4% of cases, respectively. Elevated creatinine was seen in 11.1% (grade 1). Other side effects such as anorexia, stomatitis, diarrhea, and hand-foot syndrome were infrequent and mostly mild (grades 1-2).

Table 3. Time to Metastasis (n=14)

Time (month)	**n**	**%**
< 6	3	21,4
6 - <12	2	14,3
12 - <18	5	35,7
18 - <24	2	14,3
≥ 24	2	14,3
Total	***14***	***100,0***

Comments: Among the 14 patients who experienced metastasis, the majority developed metastases between 12 and 18 months (35.7%), followed by those within 6 months (21.4%). Other intervals (6 - < 12 months, 18 - < 24 months, and ≥ 24 months) each accounted for 14.3%. This indicates that metastasis can occur both early and as late as 1-2 years after treatment. Common sites of metastasis included: liver (6 cases, 42.9%), peritoneum (5 cases, 35.7%), lung (2 cases, 14.3%), and distant lymph nodes (1 case, 7.1%).

Table 4. Overall and Disease-Free Survival Probabilities (n = 63)

After surgery	**Overall Survival (%)**	**Disease-Free Survival (%)**
1 year	95,8	93,2
2 years	82,3	78,6
3 years	74,1	71,4
4 years	68,9	65,2
5 years	64,5	61,3

Comment: Both overall and disease-free survival rates declined over time. At 1 year post-surgery, the overall survival rate was 95.8%, and disease-free survival was 93.2%. By 5 years, these rates dropped to 64.5% and 61.3%, respectively.

Table 5. Postoperative Quality of Life Based on Spitzer Index

Spitzer index	**1st time (6 months)**		**2nd (12 months)**		**3rd (24 months)**	
	Number (n)	**Percentage (%)**	**Number (n)**	**Percentage (%)**	**Number (n)**	**Percentage (%)**
5-6 (Poor)	5	7,9	7	12,1	9	20,9
7-8 (Moderate)	38	60,3	32	55,2	20	46,5
9-10 (Good)	20	31,8	19	32,7	14	32,6
Total	***63***	***100,0***	***58***	***100,0***	***43***	***100,0***

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Comment: Postoperative quality of life showed a declining trend over time. The proportion of patients with good quality of life (Spitzer score 9-10) decreased from 31.8% at 6 months to 32.6% at 24 months. Conversely, the proportion of patients with poor quality of life (score 5-6) increased from 7.9% to 20.9% over the same period.

4. Discussion

The study results showed that the average age of patients with gastric cancer was 58.2 ± 10.8 years, with males accounting for 73.0%. This finding is consistent with previous studies indicating that the average age at diagnosis of gastric cancer typically ranges from 60 to 70 years, as reported by Sung et al., along with a growing incidence in adolescents and young adults [1]. The majority of surgeries were performed via open gastrectomy, with 79.4% of patients undergoing this approach, a trend also noted by Zeng et al. in their research on function-preserving surgical methods [4].

Regarding the type of surgery, subtotal gastrectomy involving three-quarters and four-fifths of the stomach were the most common, accounting for 55.6% and 44.4%, respectively. This selection aligns with other studies, including Park et al., which emphasized that function-preserving procedures like proximal gastrectomy are effective choices for early-stage gastric cancer patients to improve postoperative quality of life [5]. The D2+ lymphadenectomy rate of 55.6% indicates adherence to global treatment guidelines. TNM staging showed that stage III was the most frequent (36.5%), which is similar to data reported in Japan, where stage III is also predominant [4]. Histologically, adenocarcinoma was the dominant type in our study population (87.3%), in line with other studies highlighting it as the most common type of gastric malignancy.

Regarding non-hematologic adverse effects of the ECX regimen, most symptoms ranged from mild to moderate in severity. This is consistent with the findings of Lee et al., which identified nausea and hair loss as the most common side effects during chemotherapy [6]. Our study also reported a high incidence of biochemical abnormalities such as Grade 1 elevations in SGOT and SGPT, underscoring the need for close monitoring of chemotherapy-related toxicities [7].

Distant recurrence after surgery in our study was mainly in the form of metastases, particularly peritoneal and hepatic. This pattern is consistent with international data. Riihimäki et al. (2016) analyzed thousands of gastric cancer cases and found the most common metastatic sites to be the liver (48%) and peritoneum (32%) [8]. Mokadem et al. (2019) also reported that in patients receiving neoadjuvant chemotherapy, 88.8% of recurrences were metastatic, with the liver being the most frequent site (46.5%), followed by the lungs (15.5%). The median time to recurrence was 22.5 months overall (10.8 months in the relapsed subgroup), with peritoneal metastasis occurring earlier (median 7.5 months) compared to nodal or other organ metastases (median 14.1 months) [9]. Our findings similarly showed that most recurrences occurred within 1-2 years postoperatively, primarily affecting the liver, peritoneum, or distant lymph nodes. This supports the literature, which emphasizes that gastric cancer tends to recur distantly, particularly in the liver, peritoneum, and lungs, and usually within a few years after initial treatment [9].

Survival and quality of life outcomes after surgery showed a gradual decline over time. The one-year overall survival rate was 95.8%, dropping to 64.5% by the fifth year. This aligns with the analysis by Hsu et al., which found that overall health status and surgical treatment modality significantly impact long-term survival and quality of life in gastric cancer patients [7].

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Long-term quality of life assessment also showed a downward trend over time. Table 5 presents results based on the Spitzer Quality of Life Index, indicating that the proportion of patients with good quality of life (score 9-10) decreased from 31.8% at 6 months to 32.6% at 24 months, while those with poor quality of life (score 5-6) increased from 7.9% to 20.9% over the same period. This reflects a sustained decline in functional status and general health after surgery and chemotherapy. Our findings are consistent with the report by Mondaca et al. (2023), which noted that while adjuvant chemotherapy (e.g., FOLFOX) offers favorable long-term survival, it may "negatively impact quality of life" due to chronic side effects [10].

5. Conclusion

Subtotal gastrectomy combined with adjuvant ECX chemotherapy demonstrated relatively positive survival outcomes in patients with lower third gastric cancer, with encouraging 5-year overall and disease-free survival rates. However, distant metastases remain prevalent, particularly within the first 12-18 months post-treatment, and quality of life tends to decline over time. These findings highlight the importance of long-term follow-up and comprehensive supportive care strategies to improve distant outcomes and enhance the quality of life for gastric cancer patients.

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