

The Analysis of Failure Pattern in Locally Advanced Stomach Cancer Treated with Surgery and Post-Op Chemotherapy; To Explore The Role of Post-Op Irradiation

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A Retrospective study to analyze the failure pattern in locally advanced stomach cancer, treated with radical surgery and post-op chemotherapy was performed. Among 107 patients who underwent radical gastrectomy in Asan Medical Center between June 1989 and August 1990, there were 20 stage II (T₂N₀, T₂N₁) and 87 stage III (T₃N₁, T₃N₂) and 91 patients were eligible for study. 57 patients treated with 6 cycles of postop adjuvant chemotherapy. Among 57 patients treated with postop adjuvant chemotherapy, local failure occurred in 21% and distant failure in 12%. Among 34 patients who were not treated with postop chemotherapy, local failure occurred in 24% and distant failure in 26%. Among 29 failures including 13 locoregional, 9 distant metastasis and 7 locoregional and distant metastasis, 11 cases recurred in the anastomotic site, 3 in the gastric bed, 7 in the regional lymph nodes and peritoneal seeding occurred in 6 cases.

The true incidences of gastric bed, nodal and peritoneal failures may be higher in the longer follow-up or reoperative or autopsy series. Our data suggest that postop chemotherapy is beneficial by reducing distant failure rate. Our data suggest that postop chemotherapy is beneficial by reducing distant failure rate. Postop adjuvant locoregional radiotherapy in addition to the systemic adjuvant therapy may reduce the local failure rate and potentially benefit in at least 20% of patients who developed the local failure only.

Key Words: Stomach cancer, Chemotherapy, Failure pattern

INTRODUCTION

Gastric cancer is the most common cause of cancer death Korea and the most common cancer in Korean man¹⁾. Radical surgery has been the treatment of choice, but complete surgical resection is possible in only 30% of patients. Disseminated disease can be found in 75% of patients at autopsy and the magnitude of locoregional failure has been demonstrated in clinical²⁾, autopsy³⁻⁵⁾ and reoperation series⁶⁾. In view of the patterns of failure in resectable gastric cancer, it appears that postop adjuvant combination therapy with chemotherapy and radiation therapy may alter the natural history of disease and prolong the survival of the patients. To investigate the possible benefit of the postoperative radiotherapy, we performed a retrospective study to analyze the failure pattern in locally advanced stomach cancer who were treated with radical gastrectomy and followed for minimum period of 1 year. Two thirds of these patients

received postop adjuvant chemotherapy and one third of them did not.

MATERIALS AND METHODS

The study population consisted of 107 patients who were treated from June 1989 to August 1990. There were 67 males and 40 females. The age ranged from 31 to 81 with a median age of 60 years. 20 cases were stage II (T₃N₀, T₂N₁) and 87 stage III (T₃N₁, T₃N₂) (Table 1).

Because 16 cases were lost to follow-up after surgery and during postop adjuvant chemotherapy, 91 patients were analysed. The follow up period ranged from 12 to 25 months with a median of 15 months. All patients underwent radical gastrectomy. 70 patients were treated with radical subtotal gastrectomy and 21 patients with total gastrectomy (Table 2). 57 patients received 6 cycles of postop adjuvant chemotherapy (Table 3). There were no significant difference in performance, staging and patient characteristics

Table 1. Patient Characteristics (1989.6 – 1990.8)

Characteristics	No. of Patients (%)
Sex	
Male	67 (63)
Female	40 (37)
Age (years)	
Range	31 – 81
Median	60
Stage	
II	20 (23)
III	87 (77)

Table 2. Type of Operation

	No. of patients (%)
Radical Subtotal gastrectomy	70 (77)
Radical total gastrectomy	21 (23)
Total	91 (100)

Table 3. Postoperative Therapy

	Chemotherapy	Observation
Stage II	8	9
Stage III	49	25
Total	57	34

Table 4. Postop Chemotherapy

	No. of Patients (%)
FP*	34 (60)
EAP**	23 (40)
Total	57 (100)

* 5 FU, Cis-DDP

** VP-16, Adriamycin, Cis-DDP

between chemotherapy group and observation group. Mainly surgeon's preference decided to give or not to give chemotherapy following radical surgery. 34 cases received FP chemotherapy (5 FU 1 g/m², Cisplatin 60 mg/m²) and 23 EAP chemotherapy (VP-16 90 mg/m², Adriamycin 30 mg/m²,

Table 5. Failure Patterns

	No. of Patients (%)
LR* only	13/91 (14)
LR + DM**	7/91 (8)
DM only	9/91 (10)
Total	29/91 (32)

* Locoregional

** Distant metastasis

Table 6. Failure Patterns

	Chemotherapy (%)	Observation (%)
Local Failure	12/57 (21)	8/34 (24)
Distant Metastasis	7/57 (12)	9/34 (26)
Total	19/57 (33)	17/34 (52)

Table 7. Locoregional Failure Site

	No. of Patients (%)
Anastomosis site	11 (52)
Gastric bed	3 (14)
Lymph node	7 (34)
Total	21 (100)

Cisplatin 60 mg/m²) (Table 4). The patterns of failure were defined as locoregional when recurrence was confined to the upper abdomen, as distant when there were metastasis outside the upper abdomen, and as combined if both of these two component occurred together in one patient.

RESULTS

Twenty nine failures were identified in Table 5. 13 patients (14% of 91 patients) experienced locoregional failures only, 9 patients (10%) distant failures only and 7 (8%) locoregional plus distant failures. Among 57 cases who were treated with postop adjuvant chemotherapy local failure occurred in 21% and distant failure in 12%. Among 34 cases who were not received postop chemotherapy, local failure occurred in 24% and distant failure in 26% (Table 6). 11 cases recurred in the anastomosis site, 3 cases in the gastric bed, 7 cases in

Table 8. Distant Metastasis Sites

	No. of Patients (%)
Peritoneum	6 (32)
Bone	4 (21)
Liver	5 (26)
Lung	2 (11)
Brain	1 (5)
Bone marrow	1 (5)
Total	19 (100)

the regional lymph nodes and peritoneal seeding occurred in 6 cases (Table 7). The true incidence of gastric bed, nodal and peritoneal failures may be higher in the reoperative or autopsy series. The most frequent site of distant failure was the liver in 5 patients, followed by the bone in 4 (Table 8).

DISCUSSION

Multidisciplinary cancer treatment utilizes three therapeutic modalities: surgery, radiation therapy, and chemotherapy. The choice of an individual treatment and the appropriate combination of treatments depends on the stage of disease. Patients with locally advanced stomach cancer with tumor invading of the gastric serosa, blood vessels, lymphatic or cancer involvement of perigastric lymph nodes have a poor prognosis following radical surgery with a less than 20% survival probability. Adjuvant chemotherapy following curative resection is of great interest because a successful adjuvant treatment has the potential to improve long term survival. The Veterans Administration Surgical Oncology Group (VASOG) showed that single agent chemotherapy with thiotepa or fluoro-deoxyuridine (FUdR) failed to influence disease free survival at 5 year after resection^{7,8}. The report of the Southwest Oncology Group (SWOG) trial showed no significant differences in relapse rate and survival between patients receiving postoperative FAM and those receiving no additional therapy⁹. There have been a large number of prospectively randomized control trials addressing the efficacy of the adjuvant chemotherapy for stomach cancer but most well designed studies that have been reported have failed to show significant benefit from chemotherapy. Our study shows that postoperative chemotherapy reduced distant metastasis rate from 26% to 12%. This difference is

not significant statistically but shows a trends to reduce the distant metastasis. There was no difference in locoregional failure rate between chemotherapy group and observation group. McNeer and colleagues¹⁰ have presented complete information for patterns of failure on 92 patients autopsied after curative surgery. Some component of local failure was found in 74 (80%) patients, as follows: 46 (50%), disease in the stomach wall or site of gastroenterostomy; in 14 (15%), tumor in the duodenum, with 5 cases associated with recurrence in the gastric remnant and 48 (52%), disease in the perigastric lymph nodes and stomach and we assume that the true incidence of locoregional failure may be higher in longer follow-up or reoperation or autopsy. Radiation therapy, usually in conjunction with chemotherapy plays a major role in patients with locally advanced unresectable stomach cancer. The use of adjuvant chemotherapy and irradiation following curative surgery in high-risk patients has been explored in several centers. Their reports suggest that combined-modality therapy with 40~50 Gy plus variable chemotherapy was tolerable and prolonged the survival by reducing the local failure rates^{11~13}. In a randomized trial from the Mayo Clinic¹⁴, 62 patients with involved nodes were randomized to no further treatment or postoperative radiation plus 5FU. The 5-year survival rate in patients assigned to received additional treatment was 23% versus 4% in those treated by surgery alone ($p < .05$).

Our data suggest that systemic therapy is beneficial by reducing the distant failure rate. Even though duration of follow-up is too short to draw any conclusion, we assume that postop locoregional radiotherapy in addition to chemotherapy following curative resection could potentially benefit in at least 20% of patients and may prolong the survival by reducing the local failure rate.

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= 국문초록 =

수술과 항암요법으로 치료한 국소 진행된 위암 환자에서의 치료실패 양상분석 : 수술후 방사선 치료의 역할에 대한 연구

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수술로 항암요법만으로 치료한 국소 진행된 위암환자에서 치료실패의 양상을 분석해봄으로써 수술후 방사선치료의 가능성을 알아보기 위하여 1989년 6월부터 1990년 8월까지 치료받은 107명의 환자를 대상으로 후향적 분석을 시행하였다.

제 2기(T₂N₁, T₃N₀) 환자는 20이었고 제 3기(T₃N₁, T₃N₂(환자는 87명이었다 16명은 수술후 추적에 어려워 91명에 대한 분석을 시행하였다. 모든 환자는 근치적 절제술을 시행받았고 이중 57명은 수술후 항암요법을 시행하고 24명은 계속적 추적 관찰만을 하였다. 국소재발율은 항암요법 시행군에서는 32%, 추적관찰군에서는 24%로 차이가 없었고 원격전이는 항암요법 시행군에서는 12% 추적관찰군에서는 26%로 항암요법 시행군에서 원격 전이가 적어지는 것을 관찰할 수 있었다. 국소 재발환자의 52%는 anastomosis site에서 재발하였고 원격 전이시 가장 많이 침범되는 장기는 간이었다. 아직 추적 관찰 기간이 짧으나 수술후 방사선 치료가 최소한 20% 이상의 환자에서 도움이 될것으로 생각된다.