Gastrointestinal complications after concurrent chemoradiotherapy in locally advanced pancreatic cancer

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Gastrointestinal complications after concurrent chemoradiotherapy in locally advanced pancreatic cancer

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ABSTRACT

Gastrointestinal complications after concurrent chemoradiotherapy in locally advanced pancreatic cancer

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Objectives

Locally advanced pancreatic cancer has a short survival of six to ten months. Chemoradiotherapy (CRT) is considered a treatment of choice. There is little information about the gastrointestinal toxicities of CRT in pancreatic cancer. Clinical features of gastrointestinal toxicities in patients with locally advanced pancreatic cancer underwent CRT and the effect of gastrointestinal toxicities on survival were investigated.

Methods

Patients enrolled in this study had received concurrent CRT for pathologically proven locally advanced pancreatic cancer. Their medical records were retrospectively analyzed.

Results

One hundred fifty-six cases with locally advanced pancreatic cancer between August 2005 and March 2009 were enrolled (Table 1). The median age was 65 years and male patients 61.5%. The chemotherapy included 5-FU-based regimen (30.8%), gemcitabine-based regimen (59.6%), and 5-FU/gemcitabine-based regimen (9.6%). The delivered radiotherapy modalities included 3D conformal radiotherapy (76.3%) and intensity-modulated radiotherapy (23.7%). The median follow-up period from the start of CRT was 13.2 months (2-52.2 months). Gastrointestinal

toxicities are summarized in Table 2; Abdominal pain or dyspepsia developed in 30 patients and nausea/vomiting in 4 patients with grade 1-2 toxicity. There were two patients with anorexia with greater than grade 3 toxicity. Fifty-three patients had significant complications such as gastric ulcer (n=26), duodenal ulcer (n=17), radiation gastritis (n=17), and radiation duodenitis (n=5). Forty patients had upper gastrointestinal bleeding, such as hematemesis and melena. Eight patients were dead due to uncontrolled bleeding. The median onset time of gastrointestinal complication was 5.2 months (0.8-50.8 months). Acute gastrointestinal complications (less than 90 days) occurred in 13 patients (24.5%) and late complications (more than 90 days) in 40 patients (75.5%). The location of the tumor (body, P=0.033) and chemotherapy regimen (5-FU+gemcitabine, P=0.015) were related with the risk factors of gastrointestinal complications. The median overall survival was 13.1 months in the non-gastrointestinal complication group and 14.0 months in the gastrointestinal complication group.

Conclusions

Gastrointestinal bleeding after CRT does not reduce survival of patients with LAPC. However, gastrointestinal complications are common, and bleeding is highly prevalent and may be fatal. Further investigation is needed to reduce serious radiation-induced gastrointestinal complications.

Key words : Gastrointestinal complications, chemoradiotherapy, locally advanced pancreatic cancer, Gastrointestinal bleeding

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I. INTRODUCTION

Pancreatic cancer is the fourth leading cause of cancer-related death in the United States[1]. Surgical resection is the only curative treatment for the disease. However, only 5-25% of the patients are candidates for pancreatectomy[2-4]. Locally advanced pancreatic cancer is a disease with surgically unresectable but non-metastatic condition. The tumor is unresectable in the cases of extensive peripancreatic involvement, lymph node involvement, or major vasculatures involvement[5]. Locally advanced pancreatic cancer has a short median survival of six to ten months. Although there is a controversy, the treatment to increase survival is known as concurrent chemoradiotherapy (CRT) as compared to radiotherapy alone and chemotherapy alone[6-14]. However, overall toxic effects of CRT is higher than those of chemotherapy alone[15-19]. These toxicities of CRT can limit the maximum dose of radiotherapy and chemotherapy and may lead to unfavorable treatment results.

Generally, gastrointestinal toxicities of CRT include non-specific gastrointestinal symptoms, such as nausea, vomiting, and abdominal pain, as well as life-threatening gastrointestinal hemorrhages. Gastrointestinal toxicities of CRT on locally advanced pancreatic cancer are unique because the stomach and duodenum are included in the radiation field. The stomach and duodenum are readily approached by conventional endoscopy, and therapeutic endoscopy can manage gastrointestinal toxicities of CRT. However, to our knowledge, there are few data about gastrointestinal toxicities of CRT on locally advanced pancreatic cancer. In addition, its effect on survival has not been evaluated. The

information about clinical characteristics of gastrointestinal toxicities of CRT on locally advanced pancreatic cancer is necessary to help prevent adverse events and to develop methods to reduce the occurrence. In addition, a gastrointestinal endoscopist's role will become important in patients receiving CRT on locally advanced pancreatic cancer.

II. MATERIALS AND METHODS

Patients

Patients who had locally advanced pancreatic cancer and received concurrent chemoradiotherapy at Severance Hospital (Seoul, Korea) were selected. The inclusion criteria were pathologically-proven pancreatic adenocarcinoma, the ages of over 20 years, and Eastern Cooperative Oncology Group (ECOG) performance status of 0-2. The exclusion criteria included patients who received chemotherapy or surgery before CRT, and the dose of scheduled radiotherapy less than 4000 cGy. We also excluded patients who had not finished their scheduled radiation therapy.

Treatment

Chemotherapy regimens were classified as follows: (1) gemcitabine group: gemcitabine (gemcitabine of 1000 mg/m^2 was given on days 1, 8, and 15 of a four-week regimen) or gemcitabine (same as above) plus cisplatin (cisplatin of 70 mg/m2 was given on day 1 of a four-week regimen) , (2) 5-fluorouracil (5-FU) group: 5-FU (5-FU of 1000 mg/m^2 was given on days 1-3 of a four-week regimen) or TS-1 (TS-1 of 60-80 mg for two weeks of a four-week regimen) or 5-FU plus etoposide plus cisplatin (5-FU of 1000 mg/m2 was given on days 1-3, etoposide of 100 mg/m2 was given on days 1-3, cisplatin of 70 mg/m2 was given on day 1 of a four-week regimen) , and (3) 5-FU plus gemcitabine group (5-FU of 1000 mg/m2 was given on days 1-3, and gemcitabine of 1000 mg/m2 was given on days 1, 8, and 15 of a four-week regimen).

The radiation therapy was classified into two groups either three-dimensional conformal radiotherapy (total dose: 4000-5400 cGy, one dose: 180-250 cGy, fraction: 28) or intensity modulated radiotherapy (total dose: 4200-6000 cGy, one dose: 200-293 cGy, fraction: 25).

Gastrointestinal toxicities

Gastrointestinal toxicities were classified according to the common-terminology criteria for the adverse events version 3.0.

Endoscopically, radiation-induced injuries were defined as telangiectasia, diffuse erythema of mucosa, shallow or deep ulcers, and scar formation[20,21].

Statistical analysis

x^2 was used to find the risk factors of gastrointestinal toxicities, and a logistic regression was used for multivariate analysis. Cox-regression test was used to evaluate the risk of gastrointestinal bleeding for survival. The Kaplan-Meyer method and the log-rank test were used to compare survival.

All analyses were performed using statistical software SPSS version 11 (SPSS, Chicago, IL, USA). P values less than 0.05 indicated statistical significance.

III. RESULTS

Patient Characteristics

Between August 2005 and March 2009, 156 patients with locally advanced pancreatic cancer were eligible for analysis (Table 1). The median age at the time of the diagnosis of pancreatic cancer was 65 years, ranging from 35 to 90 years. The male patients were 61.5%. 43 patients had hypertension and 48 patients had diabetes mellitus with medications. The tumors were mostly located at the head (63.5%). The median size of the tumor was 3.0 cm with a range from 1.1 to 7.0 cm. The median level of CA19-9 was 384 U/mL with a range from 0.1 to 20000 U/mL. Three-dimensional conformal radiotherapy was delivered to 119 patients (76.3%) and intensity modulated radiotherapy was delivered to 37 patients (23.7%). The median delivered dose was 5040 cGy (4000-5400 cGy) for three-dimensional conformal radiotherapy and 5842 cGy (4200-6000 cGy) for intensity-modulated radiotherapy. The median follow-up period was 13.2 months with a range from 2 to 52.2 months.

Table 1. Baseline characteristics of all patients

Variable	No. of Patients
Total	156
Age (median)	65 years (39-90 years)
Sex (Male : Female)	96 (61.5%): 60 (38.5%)
Hypertension	43 (27.6%)
Diabetes mellitus	48 (30.8%)
Location of tumor	
Head	99 (63.5%)
Body	44 (28.2%)
Tail	13 (8.3%)
Size of tumor (median)	3.0 cm (1.1-7.0 cm)
CA 19-9 at diagnosis (median)	384 U/mL (0.1-20000 U/mL)
Chemotherapy	
Gemcitabine based regimen	93 (59.6%)
5-FU based regimen	48 (30.8%)
5-FU + Gemcitabine regimen	15 (9.6%)
Radiation modality and dose	
3D conformal radiotherapy	119 (76.3%)
Radiation dose (median)	5040 cGy (4000-5400 cGy)
Intensity modulated radiotherapy	37 (23.7%)
Radiation dose (median)	5842 cGy (4200-6000 cGy)
Surgery after CCRT	
No	126 (80.8%)
Yes	30 (19.2%)
Time to GI complication occurred (median)	5.2 months (0.8-50.8 months)
≤90 days (acute)	13 (24.5%)
>90 days (late)	40 (75.5%)
Follow up periods (median)	13.2 months (2-52.2 months)

CCRT: concurrent chemoradiotherapy

Gastrointestinal toxicities

The overall incidence of gastrointestinal toxicities was 57.7% (Table 2). There were 30 patients with grade 1 or 2 abdominal pain or dyspepsia. Two patients had grade 3 anorexia. Nausea and vomiting developed in four patients, and these were well controlled with appropriate medications. Forty patients had bleeding: nine patients with hematemesis (22.5%), 21 patients with melena (52.5%), and 10 patients with hematochezia (25%). There were 18 patients (42.5%) with grade 3 or 4 gastrointestinal bleeding and eight (22.5%) with grade 5 (death) bleeding.

Endoscopy after CRT revealed mucositis (Fig 4A) in 27.2%, ulcer (Fig 4B) in 45%, and gastrointestinal bleeding in 65% greater than a grade 3 toxicity. The median gastrointestinal bleeding occurrence was 5.4 months (Fig 2).

Table 2. Gastrointestinal toxicities after CRT according to the NCI CTC 3.0 version

Variable	No. of patients						
	Total	Portion of G3-G5	G1	G2	G3	G4	G5
Abdominal pain or Dyspepsia	30 (19.2%)	0	16	14	0	0	0
Anorexia	5 (3.2%)	2 (40%)	2	1	2	0	0
Nausea	3 (1.9%)	0	0	3	0	0	0
Vomiting	1 (0.6%)	0	0	1	0	0	0
Mucositis	22 (14.1%)	6 (27.2%)	15	1	6	0	0
Stomach	17 (10.8%)	5 (29.4%)	11	1	5	0	0
Small bowel (duodenum)	5 (3.2%)	1 (20%)	4	0	1	0	0
Ulcer	37 (23.7%)	15 (9.6%)	11	11	14	1	0
Stomach	22 (14.1%)	7 (31.8%)	7	8	7	0	0
Small bowel (duodenum)	15 (9.6%)	8 (5.1%)	4	3	7	1	0
Other							
GI hemorrhage	40 (25.6%)	26 (65%)	0	14	17	1	8
Stomach	20 (12.8%)	9 (45%)	0	11	9	0	0
Duodenum	15 (9.6%)	12 (80%)	0	3	8	1	3
Unknown	5 (3.2%)	5 (100%)	0	0	0	0	5

Figure 1A. Radiation gastritis. Mucosal erythema with telangiectasia and several superficial ulcerations on the antrum.

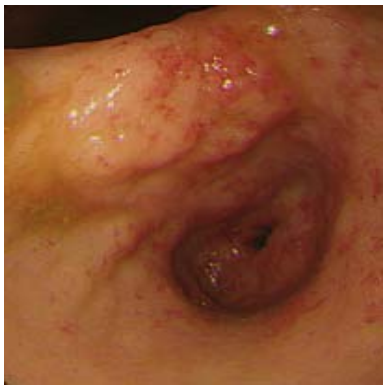


Figure 1B. Gastric ulcer. Oval shaped healing-staged ulceration with some surrounding regenerating epithelium on the antrum.

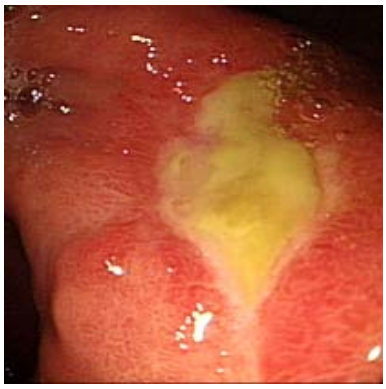
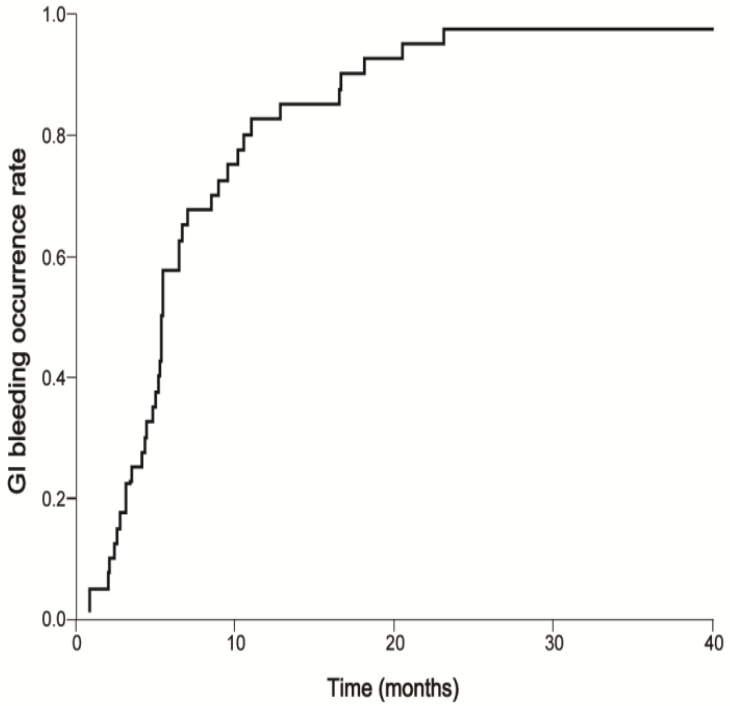


Figure 2. Cumulative incidence of GI bleeding in 40 patients. Median GI bleeding occurrence was 5.4 months.



Gastrointestinal bleeding

Table 3 shows the characteristics of gastrointestinal bleeding. The median onset time was 5.4 months (range: 0.8-50.8 months). Forty patients presented themselves to the hospital for gastrointestinal bleeding. The median initial hemoglobin was 10.1 g/dL (range: 7.1-15.3 g/dL), which decreased to 7.1 g/dL (range: 3.5-10.8 g/dL) at bleeding. Endoscopy showed the cause of bleeding to be a gastric ulcer (Fig 4C) in 15 patients (37.5%), duodenal ulcer (Fig 4D) in 15 (37.5%), and radiation gastritis in five (15%). Endoscopy was not performed in five patients upon their guardians' rejection. As the patients were in terminal status, the guardians did not want them to undergo any examinations. These five patients died without receiving an endoscopic evaluation and treatment. The remaining 35 patients received endoscopic treatment. Bleeding was successfully stopped by endoscopic treatment in 31 patients (77.5%), but not in four patients. Thus, embolization was performed in one of the four patients, and the bleeding was finally stopped, but three others died due to bleeding. The mortality of gastrointestinal bleeding was eight patients in total. The median time to gastrointestinal bleeding from CCRT was 5.4 months (range: 0.8-50.8 months) and the median overall survival was 13.5 months (range: 2.8-50.8 months).

Table 3. Gastrointestinal bleeding after CCRT (n=40)

	No. of patients
Hemoglobin (median)	
Initial	10.1 g/dL (7.1-15.3 g/dL)
At bleeding	7.1 g/dL (3.5-10.8 g/dL)
Origin of GI bleeding	
Gastric ulcer	15 (37.5%)
Duodenal ulcer	15 (37.5%)
Radiation gastritis	5 (15.0%)
Unknown	5 (15.0%)
Extent of bleeding origin	
Focal	27 (77.1%)
Diffuse	8 (22.9%)
Treatment	
Endoscopic treatment	35 (87.5%)
Success	31 (77.5%)
Angiography and embolization	1 (2.5%)
No treatment	5 (12.5%)
Mortality of GI bleeding	8 (20%)
Time to GI bleeding from CCRT(median)	5.4 months (0.8-50.8 months)
Survival (median) with GI bleeding	13.5 months (2.8-50.8 months)

Figure 1C. Gastric ulcer with bleeding. Oval shaped active ulceration with bleeding (stigmata of recent bleeding) on the antrum. Bleeding was stopped by human plasma thrombin injection following hypertonic saline-epinephrine injection successfully.

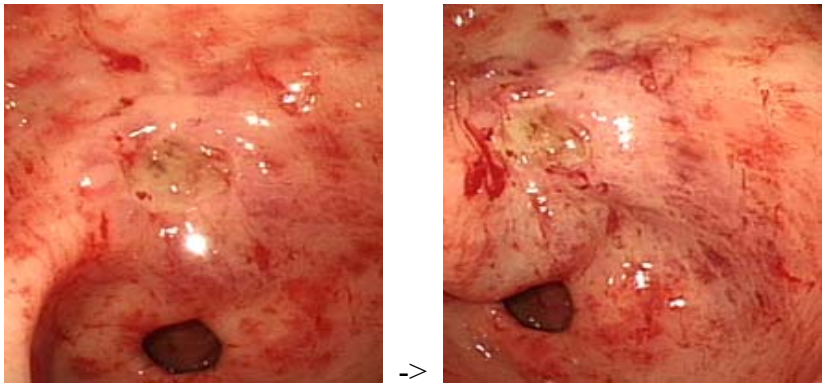
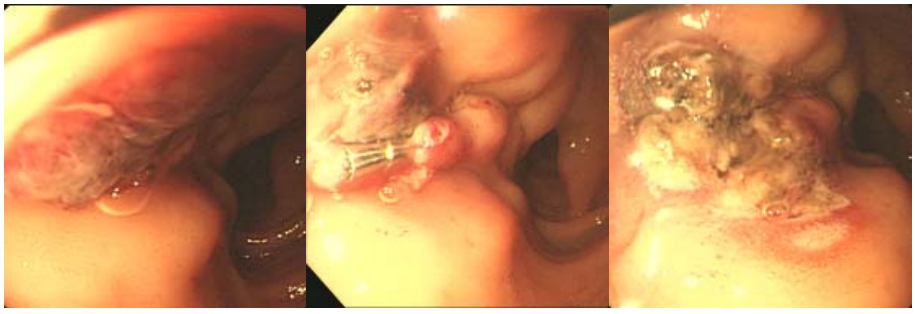


Figure 1D. Duodenal ulcer bleeding. Oval shaped active ulceration surrounded by edematous mucosal crater at duodenal bulb. Bleeding was stopped by argon plasma coagulation following hemoclipping.



Risk factors for gastrointestinal complications

The association between clinical parameters and the risk of gastrointestinal complications are summarized in Table 4. In univariate analysis, the location of the tumor (body, P=0.028) and chemotherapy regimen (5-FU+gemcitabine, P=0.015) were related with the risk factors of gastrointestinal complications. In multivariate analysis, the location of the tumor (body, P=0.033) and chemotherapy regimen were significant for the risk factor of gastrointestinal complications. The hazard ratio was 1.27 for the effect of GI bleeding on survival in Cox regression, but it was not significant (P=0.329, Table 5). Male had higher hazard ratio than female and it was significant (Hazard ratio = 1.621, P=0.020). However, there were no difference in the number of hypertension, diabetes mellitus between male and female.

Table 4. Risk factors of GI toxicities in all patients (n=156)

Variable	GI toxicities		GI toxicities		
	Presence (%)	P value*	Odds ratio	95% CI	P value†
Age		0.082			
≤65 years	33 (40.2)		1		
>65 years	20 (27)		0.60	0.29-1.26	0.181
Sex		0.407			
Female	18 (30.0)		1		
Male	35 (36.5)		1.75	0.79-3.84	0.161
Location of tumor		0.028			
Head	28 (28.3)		1		
Body	22 (50.0)		2.43	1.07-5.52	0.033
Tail	3 (23.1)		0.37	0.08-1.65	0.187
Size of tumor		0.060			
≤3 cm	23 (27.4)		1		
>3 cm	30 (41.7)		1.90	0.90-4.00	0.091
Chemotherapy		0.044			
5-FU group	12 (25.0)		1		
Gemcitabine group	32 (34.4)		1.89	0.81-4.38	0.137
5-FU plus gemcitabine group	9 (60.0)		5.67	1.39-23.10	0.015
Radiation modality		0.570			
3-D conformal radiotherapy	39 (32.8)		1		
Intensity modulated radiotherapy	14 (37.8)		1.33	0.57-3.06	0.502
CA19-9		0.914			
CA19-9≤1200 U/mL	38 (34.2)		1		
CA19-9>1200 U/mL	15 (33.3)		1.01	0.45-2.26	0.983

* Chi-square test was used.
† Logistic regression was used.

Table 5. Cox regression analysis for effect of GI bleeding on survival

Variable	Hazard ratio	95% CI	P value
Age (> 65 years)	1.035	0.70-1.52	0.862
Sex (male)	1.621	1.07-2.43	0.020
Location of tumor			
Body	1.527	0.97-2.39	0.066
Tail	1.118	0.54-2.28	0.759
Size of tumor (> 3 cm)	1.104	0.73-1.65	0.632
Chemotherapy			
Gemcitabine group	0.956	0.62-1.46	0.836
5-FU plus gemcitabine group	1.598	0.78-3.25	0.197
Radiation modality (3-D conformal)	0.915	0.57-1.45	0.708
CA19-9 (> 1200 U/mL)	1.312	0.87-1.97	0.192
GI bleeding (presence)	1.275	0.78-2.07	0.329

Survival

In a total of 156 patients, 117 patients (75%) died at the time of final analysis. Figure 3 shows the Kaplan-Meier curves for overall survival. The median overall survival was 13.1 months (range: 11.3-14.9 months) in LAPC from the start of CRT. The median overall survival was 13.1 months (range: 9.9-16.3 months) in the non-gastrointestinal complication group and 14.0 months (range: 12.3-15.7 months) in the gastrointestinal complication group. Although overall survival was longer in the GI complication group, this difference was not significant (P=0.755, Fig.4)

Figure 3. Overall survival

Median overall survival was 13.1 months in locally advanced pancreatic cancer after CCRT.

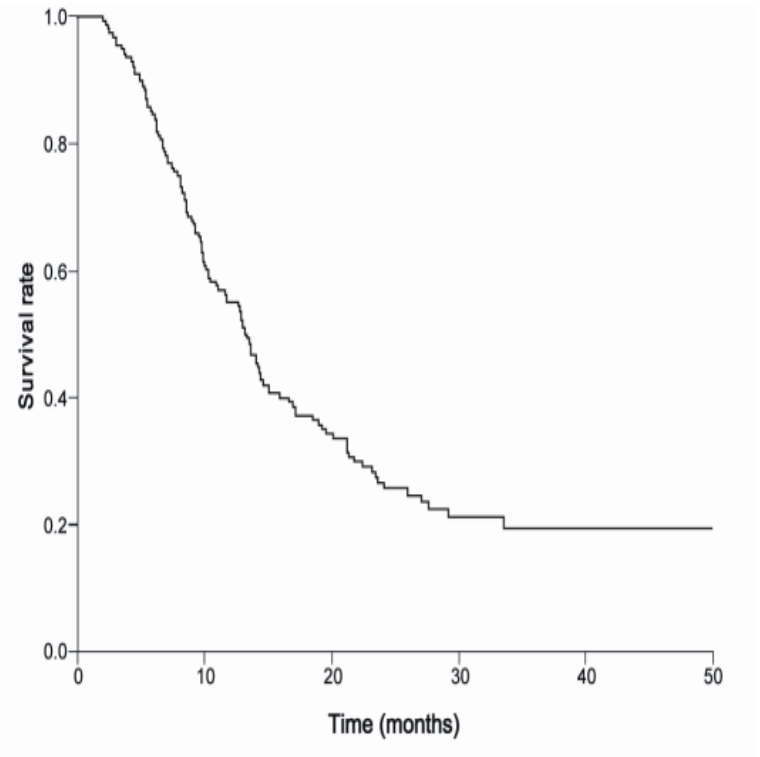
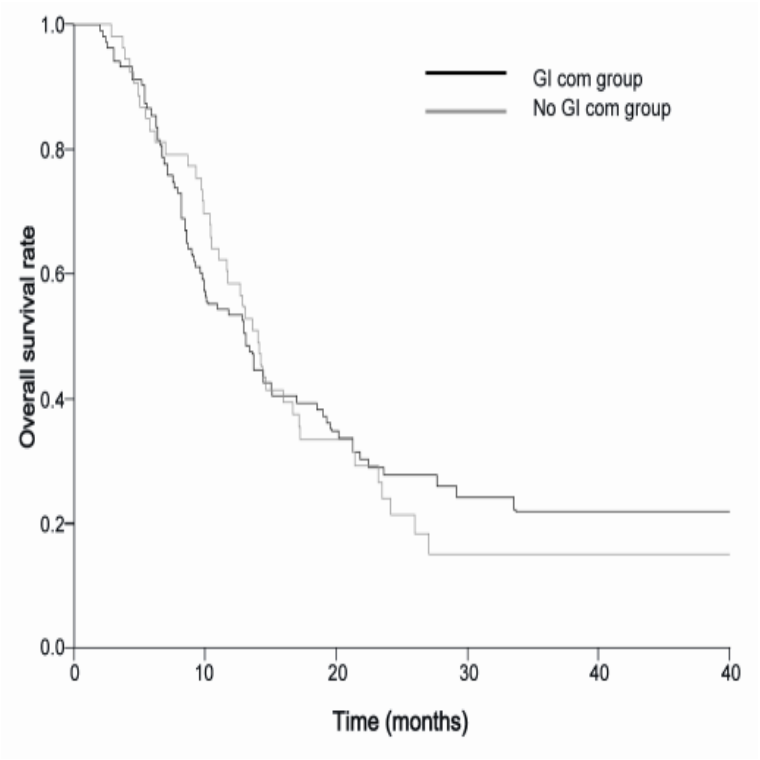


Figure 4. Survival comparison between the GI complication group and the non GI complication group. Overall survival was 13.1 months in the non GI complication group and 14.0 months in the GI complication group.



IV. DISCUSSION

It was shown in this study that gastrointestinal bleeding after CRT does not reduce survival of patients with locally advanced pancreatic cancer. The median overall survival was similar with other studies[12,15,22,23]. However, the prevalence of CRT-induced gastrointestinal bleeding is considerable and serious.

CRT was first introduced in the GITSG trial[10]. The survival benefit was found to be higher in the group with 5-FU + radiation than in the group with radiotherapy alone. There was no difference in survival benefit between the groups that received different doses of RT (4000 and 6000 cGy). After that, many studies reported the benefit of CRT, and CRT became one of the treatment options for pancreatic cancer[11,16-18]. Based on the results of several studies, the RT dose of 50-60 Gy (182 Gy/day) is generally used[24,25]. A study reported that toxicity was higher in the LAPC group where the radiation dose increased up to 55 Gy than in the LAPC group with the dose up to 50 Gy, but that the compliance was similar between the groups, and the treatment performance in the former was better than that in the latter[26]. In studies comparing CRT and chemotherapy, however, more cases of toxicity were found in the CRT group; thus, care must be taken with regard to the use of CRT[6,27]. Indeed, during clinical practice, we experienced many patients with CRT-induced gastrointestinal bleeding, which led to this study. Due to the low awareness of bleeding, the frequency of endoscopy was quite low. Of the total of 156 patients, 20 received endoscopy before CRT and 78 after CRT. Very few patients who had bleeding received endoscopy before the onset of bleeding. Had endoscopy also been performed in the other patients, the chances of finding complications such as radiation gastritis would have been higher. The locations of the tumor and chemotherapy regimen were related with the risk factors for gastrointestinal complications. As the body of the pancreas is closely located to both the stomach and duodenum, they are affected by radiotherapy. The combination of 5-FU and gemcitabine increased the toxicity of gastrointestinal complications. Also poor prognosis is expected in male with gastrointestinal bleeding. There were no difference in the number of hypertension and diabetes

mellitus between male and female. Other risk factors need to be found in male group.

This study has several limitations. First, the results were obtained by retrospectively reviewing the medical charts. Second, of CRT, the chemotherapy-induced adverse effects could not be excluded. In this study, the number of patients who received gemcitabine was higher than the number of those who received 5-FU. Several studies reported that gemicitabine was shown to be more toxic than 5-FU. In addition, it was difficult to ascertain the cause of bleeding after surgery as well as the change in the chemotherapy regimen after CRT[28,29]. Third, the low number of patients who received endoscopy before CRT made it impossible to determine if the ulcer existed even before CRT. Fourth, the patients who received 3D conformal radiotherapy and intensity modulated radiotherapy were analyzed together, and 37 of them received intensity modulated radiotherapy. To the best of our knowledge, there has been no study that compared 3D conformal radiotherapy and intensity modulated radiotherapy. Thus, a study is required to investigate if there is any difference between the two therapies.

There is no consensus on the best time to perform endoscopy after radiotherapy. After CRT, however, gastrointestinal complications are likely to develop at anytime. Therefore, it is recommended that endoscopy be performed as was done in this study. If abnormal findings are found in endoscopy before CRT, preemptive treatment is necessary. Moreover, endoscopy as a baseline study is recommended for the comparison with the endoscopic results. Usually CRT is followed by chemotherapy or surgery about one month later, endoscopy is recommended before such therapies as gastrointestinal ulcer or bleeding can occur even before 90 days after CRT. As ulcerative bleeding is well responsive to PPI, its early detection and treatment may prevent adverse events. Although the best frequency of endoscopy may be debatable, yearly or more frequent endoscopy, particularly in patients with a history of bleeding, is recommended considering the possibility of delayed ulcer and bleeding.

V. CONCLUSION

Gastrointestinal bleeding after CRT is highly prevalent and may be fatal. This study shows that patients with LAPC are likely to develop a gastric ulcer, duodenal ulcer, or radiation gastritis after CRT, and a large number of them developed bleeding. Some patients in this study died or stopped receiving treatment because of bleeding. Extensive studies are required to compare the benefits and risks in terms of survival rate and complications between CRT and chemotherapy. In addition, studies are required to uncover the tests or treatments that can reduce CRT-induced gastrointestinal complications.

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ABSTRACT(In Korean)

진행성 췌장암에서 동시 항암화학 방사선 치료후 발생 가능한 소화기계 합병증

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이 경 주

국소 진행성 췌장암의 생존률은 6개월에서 10개월 사이로 알려져 있다. 최근 항암화학 방사선 치료가 여러 연구를 통해 치료의 선택이 될 수 있다. 하지만 항암화학 방사선 치료의 소화기계 합병증에 대해서는 많은 연구가 되어 있지 않다. 이번 연구에서는 항암화학 방사선 치료가 어떤 소화기계 합병증을 일으키고 생존에는 어떤 영향을 미치는지 알아보았다. 세브란스병원에서 2005년 8월부터 2009년 3월까지 국소 진행성 췌장암에서 항암화학 방사선 요법을 받은 환자 156명을 대상으로 조사하였다. 중간 나이는 65세였고 남자는 61.5%였다. 항암제는 5-FU base (30.8%), Gemcitabine base (59.6%) 그리고 5-FU/Gemcitabine base (9.6%) 였다. 방사선치료는 3D 입체 조형 방사선 치료 (76.3%) 였고 강도 변조 방사선 치료가 (23.7%) 였다. 항암화학 방사선 치료일로부터 13.2 개월간 추적관찰하였다. 소화기합병증으로는 다음과 같이 나타났다. Grade 1 또는 2 독성을 가지는 복통과 속쓰림 환자가 30명에서 나타났고 오심 또는 구토는 4명의 환자에서 나타났다. Grade 3 이상의 독성을 가지는 식욕 부진이 2명의 환자에서 나타났다. 53명의 환자에서 궤양 또는 방사선으로 유도된 위염 또는 십이지장염이 발견 되었다. 위궤양이 26명, 십이지장 궤양이 17명, 방사선위염이 17명그리고 방사선십이지장염이 5명이였다. 이중 40명의 환자에서는 토혈이나 흑색변으로 상부위장관

출혈이 의심되어 내시경치료를 요하였다. 이중 8명에서는 조절되지 않은 출혈로 인해 사망하였다. 항암화학 방사선 치료일로부터 출혈까지는 5.2개월이 걸렸다. 90일 이내 생긴 급성 위장관합병증은 13명 (23.5%) 였고 90일 이후 생긴 지연 위장관합병증은 40명 (75.5%) 에서 보였다. 종양의 위치 (체부, p=0.033) 와 항암제 종류 (5-FU/Gemcitabine, P=0.015) 가 소화기계 합병증과 연관성을 보였다. 위장관합병증이 있는 그룹에서의 전체생존기간은 14.0 개월이였고 위장관합병증이 없는 그룹에서는 13.1 개월이였다. 이 연구를 통해 소화기계 합병증이 생존률을 감소 시키지 않으나 흔하게 나타나고 치명적일 수 있음을 시사한다. 앞으로 방사선으로 인한 위장관합병증을 줄이는 연구가 필요하다.

핵심되는 말 : 국소 진행성 췌장암, 항암화학 방사선 치료, 소화기계 합병증