

Clinicopathological aspects and  
prognostic values with respect to age:  
an analysis of 3362 consecutive  
gastric cancer patients

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prognostic values with respect to age:  
an analysis of 3362 consecutive  
gastric cancer patients

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<ABSTRACT>

Clinicopathological aspects and prognostic value with respect to age:

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**Background & Aims:** Several studies have reported controversial results about clinicopathological features and prognosis in gastric cancer patients with respect to age, partly due to variable definitions of age definition and inhomogeneity of the study population. The aim of study was to analyze clinicopathological features and prognostic value of all stages of gastric cancer patients in a large consecutive series with special reference to age.

**Methods:** Between 2000 and 2005, a total 3362 patients with gastric cancer were enrolled in this retrospective study. Patients were divided into three groups by age standard deviation; group 1 ( $\leq 45$  years old), group 2 (46 to 70 years old), and group 3 ( $\geq 71$  years old).

**Results:** : Upper location, and linitis plastica were more frequent in younger age groups. Younger patients had a significantly higher proportion of poorly differentiated and signet ring cell carcinoma



histopathology with elevated CA19-9 level. Endoscopically, depressed type was more frequent in EGC while Bormann type IV and Lauren's diffuse type were more common in AGC patients in group 1. Peritoneal metastasis was the most common cause for inoperability. In curatively resected patients, 5 year survival rate was significantly higher in group 1 than older groups. In univariate analysis, sex was one of the significant prognostic factor in young age group (group 1). Multivariate analysis showed that tumor stage, vein invasion, curative resection, and initial CA19-9 level were the significant prognostic factors in all gastric cancer patients.

**Conclusions:** Clinicopathological features associated with young gastric cancer ( $\leq 45$  years old) include female, upper location, linitis plastica type, histopathologically diffuse type, and unresectability for operation.

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Key words : young age gastric cancer, prognosis, CA19-9

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## **I. Introduction**

The incidence and mortality of gastric cancer has decreased worldwide in the last several decades but is still one of the most common causes of malignancy in many countries. Gastric cancer is the leading cause of death in Korea and Japan.<sup>1</sup> Gastric cancer is considered a disease of the elderly, with the peak incidence in patients over 60 years of age.<sup>2</sup> The definitions of young age gastric cancer were arbitrarily determined in most studies, thus the incidence or features of young gastric cancer were variable among studies. Gastric cancer patients less than 40-years-old comprised approximately 2% to 8% of all patients with gastric cancer.<sup>3</sup> A recent study showed that the proportion of young gastric cancer patients less than 45-years-old was 8.5% of the total gastric cancer patients.<sup>4</sup> The prognosis for young patients, a significant proportion of the gastric cancer population, also shows considerable variability among studies. Some studies have shown a poor prognosis as a result of delayed diagnosis, a high rate of histologically undifferentiated type lesions, and rapid progression of diseases in young age patients.<sup>5, 6</sup> In contrast, other studies have found no direct relationship

between these factors and young age, indicating that outcome may be related to the cancer stages at the diagnosis irrespective of age.<sup>2,7</sup> This discrepancy may result from inhomogeneity of patient populations among studies. Most studies analyzed only gastric cancer patients who had undergone surgical resection and not all stages of gastric cancer including surgically unresectable patients were evaluated.

This study was designed to analyze the clinicopathologic characteristics and prognostic factors in gastric cancer patients with all stages, including endoscopically treated patients as well as unresectable, advanced gastric cancer patients. We also propose an age criterion for classification as a 'young gastric cancer patient' based on our statistical analysis of a large group of consecutive gastric cancer patients in a single institution.

## II. Materials and Methods

### 1. Patients

Between 2000 and 2005, a total of 3362 consecutive patients (2247 males and 1115 females) were diagnosed and admitted with gastric cancer at Severance Hospital, Yonsei University College of Medicine, Seoul, Korea. The patients were divided into three groups according to age standard deviation (i.e. age  $\leq$  mean-1SD years, mean-1SD < age  $\leq$  mean+1SD, age > mean+1SD). The mean age was 57.1 years and reference age points were made by one age standard deviation (mean  $\pm$  1SD; reference age points were 45 and 70) (Fig. 1). With these age reference points, patients younger than 45 years of age was grouped as group 1, patients 46 to 70 years as group 2, and patients older than 70 years of age group 3 respectively.

The patients included were an early gastric cancer (EGC) group (1393 operated patients and 152 endoscopic mucosal resected patients) and an advanced gastric cancer (AGC) group (1638 patients who underwent operation and 179 inoperable patients).

The clinicopathologic features of these patients including age, sex, location, histopathological type, stages, types of surgery, and curative resectability were reviewed retrospectively. TNM stages were assigned in accordance with the International Union Against Cancer.<sup>8</sup> The macroscopic types of AGC were determined by Borrmann's classification. The endoscopic findings of EGC were classified according to criteria of the Japanese Research Society for Gastric Cancer,<sup>9</sup> namely, elevated (types I or IIa), flat (type IIb), depressed (types IIc, IIc+III, or IIa+IIc), or mixed type. Histological evaluation was performed according to the Lauren classification and the Japanese General Rules for Gastric Cancer Study in Surgery and Pathology of the Japanese Research Society for Gastric Cancer.<sup>9</sup> The surgery was considered curative when all resected margins were clear, nodal involvement was N2 or less, and there was no evidence of spread to other distant organs. Assays for the tumor

markers CEA and carbohydrate antigen (CA) 19-9 were performed when patients were initially diagnosed with gastric cancer. Abnormal cut off values were set at 5 ng/mL for CEA and 37 U/mL for CA19-9. The 5-year survival rates of each age group were evaluated and survival after curative resection of group 1 was compared with those of older age groups.

## **2. Statistical analysis**

Correlation between variables was tested with the Pearson  $\chi^2$  test. Overall survival curves were estimated by the Kaplan-Meier product limit method. The log rank test was used to assess differences between subgroups. Significance was defined at *P* value less than 0.050. A Bonferroni adjustment was made when multiple comparisons were made. In all cases, survival was calculated from the date of diagnosis to the date of the most recent follow-up visit or to the date of death. The hazard ratio and confidence intervals were estimated for each variable using the Cox univariate model. A multivariate Cox proportional hazard model was also developed using stepwise regression (forward selection) with predictive variables which were significant in the univariate analysis. SPSS<sup>®</sup> version 12.0 (SPSS, Chicago, Illinois, USA) was used for the statistical analysis

### III. Results

#### 1. Clinicopathologic characteristics of gastric cancer

Of the 3362 patients, 654 (19.5%) patients were younger than 45 years (group 1), 2317 (68.9%) patients between 46 and 70 years (group 2), and 391 (11.6%) patients older than 70 years (group 3) respectively. The age of patients ranged from 16 to 92 years and the median age was 57.1 years (Fig. 1). Mode of treatments included were as follows. EGC group included 1393 operated patients and 152 endoscopic mucosal resected patients. AGC group included 1638 patients who underwent operations and 179 patients who were treated by chemotherapy for palliative aim or best supportive care (Table 1).

The most common symptom in the young age group (group 1) was dyspepsia. Other common symptoms were weight loss, melena, and symptoms related to anemia (Table 2). The results of the sex distribution of gastric carcinoma according to age group are shown (Table 3). Overall, there was a male predominance for all stages of gastric cancer. There was no significant sex differences in EGC among the three age groups. However, the male to female ratio with AGC in the young age group was 1.1:1. Therefore, the proportion of females with AGC was significantly greater in the young age group compared to the other groups ( $P < 0.001$ ). The results of the comparison of clinicopathologic findings in gastric cancer patients according to age groups are presented in Table 4. The lower third of the stomach was the most common site of cancer involvement in all three groups. However, the upper third location of the stomach and diffuse involvement were more frequent in the young age group compared to other groups ( $P < 0.001$ ). The young age group also had a greater proportion of poorly differentiated histology ( $P < 0.001$ ) and signet ring cell carcinoma ( $P < 0.001$ ). Endoscopically, a significantly larger proportion of Borrmann type III and IV gastric cancer were common in group 1 compared to the other groups (groups 2 and 3). The CA19-9 level of group 1 tended to be higher than other age

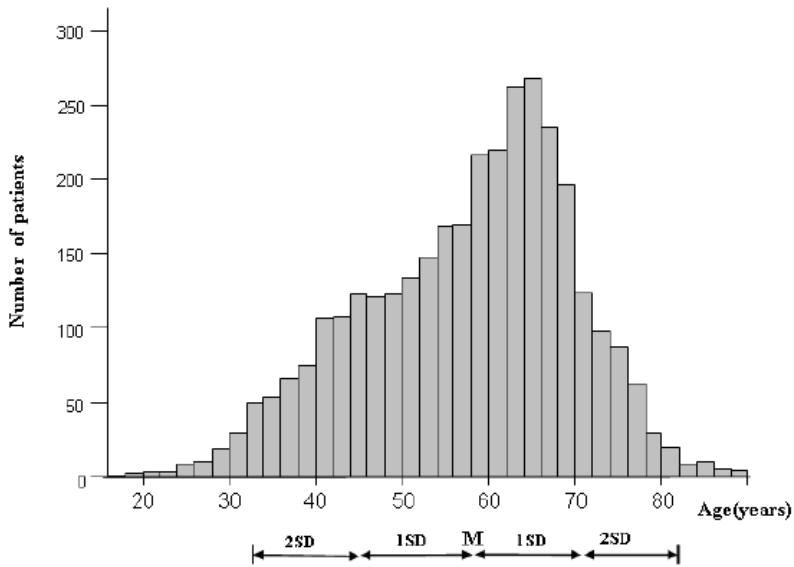
groups, but this was not statistically significant ( $P = 0.080$ ).

**Table 1. Treatment modality of gastric cancer**

	<b>Treatment</b>	<b>No. of patients (%)</b>
Early gastric cancer	Operation	1,393 (41.4)
	EMR	152 (4.5)
Advanced gastric cancer	Curative op.	1,469 (43.7)
	Palliative op.	169 (5)
	Inoperable AGC	179 (5.4)

EMR, Endoscopic mucosal resection; AGC, advanced gastric cancer; op, operation

**Fig. 1. Age distribution of the patients**



(SD, standard deviation; M, mean age)

**Table 2. Presentation symptoms of gastric cancer patients according to different age groups**

Symptoms	Age≤45, No (%)	45<Age≤70, No (%)	Age>70, No (%)
None	111 (16.97)	507 (21.88)	67 (17.13)
Dyspepsia	498 (76.14)	1602 (69.27)	278 (71.09)
Weight loss	34 (5.19)	112 (4.83)	28 (7.16)
Melena	28 (4.28)	46 (1.98)	23 (5.88)
Anemia	10 (1.52)	39 (1.68)	16 (4.09)

**Table 3. Sex distribution (Male:Female) of gastric carcinoma according to age groups**

Types	Group 1 (age≤45 yr)	Group 2 (45<Age≤70 yr)	Group 3 (age>70 yr)	<i>P</i>
EGC	1.8:1	2.2:1	2.5:1	NS
AGC	1.1:1	2.3:1	2.1:1	< 0.001
Total	1.3:1	2.2:1	2.3:1	< 0.001

NS : not significant; EGC, early gastric cancer; AGC, advanced gastric cancer



**Table 4. Clinicopathologic features of gastric carcinoma according to age groups**

<b>Variables</b>	<b>Group 1 n=654 (%)</b>	<b>Group 2 n =2317 ( %)</b>	<b>Group3 n =391 ( %)</b>	<b>P</b>
Location				< 0.001
Upper	127 (20.1) <sup>*,†</sup>	318 (14.1)	51 (13.6)	
Middle	121 (19.2) <sup>*,†</sup>	291 (12.9)	45 (12)	
Lower	357 (56.6)	1609 (71.1)	267 (71)	
Diffuse	26 (4.1) <sup>*,†</sup>	45 (2)	13 (3.5)	
Histological type				< 0.001
WD	31 (5.0)	387 (17.8)	72 (20.4)	
MD	93 (15.1)	670 (30.8)	108 (30.5)	
PD	282 (45.7) <sup>*,†</sup>	751 (34.5)	128 (36.2)	
Mucinous	15 (2.4)	46 (2.1)	10 (2.8)	
Signet ring cell	196 (31.8) <sup>*,†</sup>	321 (14.8)	36 (10.2)	
Gross type of EGC				< 0.001
Elevated	13 (4.9)	176 (17.4)	34 (25.2)	
Flat	43 (16.3)	171 (16.9)	22 (16.3)	
Depressed	207 (78.7) <sup>*,†</sup>	664 (65.7)	79 (58.5)	
AGC(Bormann type)				0.001
I	15 (4.2)	81 (7)	13 (6)	
II	97 (27.3)	422 (36.4)	87 (40.3)	
III	167 (47) <sup>*,†</sup>	481 (41.5)	83 (38.4)	
IV	76 (21.4) <sup>*,†</sup>	174 (15)	33 (15.3)	
Venous invasion	85 (50.9)	303 (54.8)	52 (61.2)	0.299
Lymphatic invasion	125 (69.7)	425 (71.7)	65 (75.9)	0.575
Depth of invasion				0.048
T1	257 (43.9)	1013 (47.3)	140 (42.6)	
T2	77 (13.2)	301 (14.1)	47 (14.3)	
T3	223 (38.1)	769 (35.9)	125 (38)	
T4	28 (4.8) <sup>*</sup>	58 (2.7)	17 (5.2)	
LN metastasis				0.253
N0	339 (58.0)	1228 (59.4)	161 (52.8)	
N1	136 (23.3)	481 (23.3)	79 (25.9)	
N2	58 (9.9)	205 (9.9)	42 (13.8)	
N3	51 (8.7)	153 (7.4)	23 (7.5)	
TNM stage				0.001
IA	238 (37.7)	932 (42.25)	128 (36.7)	
IB	60 (9.5)	252 (11.5)	36 (10.3)	
II	86 (13.6)	272 (12.4)	39 (11.2)	
IIIA	85 (13.5)	296 (13.5)	49 (14.0)	
IIIB	37 (5.9)	153 (7.0)	27 (7.7)	
IV	125 (19.8) <sup>*</sup>	290 (13.2)	70 (20.1)	

Curative resection rate	281/333 (84.4) <sup>*,†</sup>	1041/1121 (92.9)	169/190 (88.9)	< 0.001
Distant metastasis				
Hepatic metastasis	15 (4.0)	49 (4.1)	16 (7.2)	0.110
Peritoneal metastasis	53 (14.3) <sup>*,†</sup>	77 (6.4)	16 (7.2)	< 0.001
Other distant metastasis <sup>‡</sup>	15 (4.0) <sup>*,†</sup>	13 (1.1)	3 (1.3)	0.001
CA19-9 (U/ml) <sup>§</sup>	116.47 ± 754	97.03 ± 815	101.25 ± 771	0.080
CEA (ng/ml) <sup>§</sup>	6.48 ± 50.9	25.46 ± 417	9.13 ± 40.4	0.659

\* Group 1 vs. Group 2 ;  $P < 0.017$  (Bonferroni adjustment)

† Group 1 vs. Group 2 + Group 3 ;  $P < 0.050$

‡ Lung, ovary, adrenal gland, brain, pancreas, colon, kidney

§ Values are expressed as means ± SD

EGC, early gastric cancer; AGC, advanced gastric cancer; LN, lymph node;

WD, well differentiated; MD, moderately differentiated; PD, Poorly differentiated

## 2. Clinicopathologic characteristics of young gastric cancer patients according to stage

In EGC, the depressed endoscopic gross type was more frequent in the young age group ( $P < 0.001$ ) (Table 4). The proportion of cancers in the upper third location of the stomach and lesions with poorly differentiated histology, signet ring cell histology, and Lauren diffuse type carcinoma were significantly higher in the young age group compared to the other groups in EGC ( $P < 0.001$ ) (data not shown).

For patients with AGC, there was a significant higher proportion of patients with stage IV in group 1 compared to the other two groups. N3 lymph node metastasis appeared to be higher in the young age group, although this was not statistically significant. The curative resection rate was significantly lower in group 1 compared to the older age groups (84.4% vs 92.9% [group 2] and 88.9% [group 3];  $P < 0.001$ ) (Table 4).

The pattern of metastasis of AGC was different according to age group. Young patients had peritoneal metastasis significantly more frequently than older patients in groups 2 and 3 (14.3% vs 6.4% and 7.2%, respectively,  $P < 0.001$ ) as well as other distant metastases (lung, ovary, adrenal gland, brain,

pancreas, colon, and kidney) (4.0% vs 1.1% [group 2] and 1.3% [group 3];  $P = 0.001$ ). Peritoneal metastasis was the most common site for distant metastasis in young patients.

### **3. Survival rate and prognostic factors**

Univariate analysis showed no significant difference in 5-year survival according to age and sex in all stage gastric cancer (Table 5). But sex was one of the significant prognostic factor in young age group (group 1) (Table 5). Multivariate analysis showed that only curative resection was the significant prognostic factor in young age gastric cancer group (group1) (data not shown). Tumor stage, vein invasion, curative resection, and initial CA19-9 level were the significant prognostic factors for survival in all gastric cancer patients regardless of age (Table 6).

The overall survival curve of all stage of gastric cancer was shown in Figure 2. The 5-year survival rates of young ( $\leq 45$  years) and older ( $>45$  years) gastric cancer patients did not differ statistically (69.97% vs 69.03%;  $P = 0.534$ ) (Fig.3). Interestingly, in curatively resected patients, the 5-year survival rate was significantly better in the young age group ( $\leq 45$  years) than the older age groups ( $>45$  years) (80.81% vs 75.42%;  $P = 0.002$ ) (Fig. 4). When patient survival were further analyzed into curatively resected EGC and AGC patients, the young patients had significant better survival rates compared to the older patients (data not shown). According to the initial CA 19-9 level, the 5-year survival rate was significantly better in patients with lower CA19-9 levels compared with higher CA 19-9 levels (70.63% vs 56.81%;  $P < 0.001$ ). The significance of the initial CA19-9 level remained the same in the young age group ( $P < 0.001$ ) and the old age group ( $P < 0.001$ ) (data not shown).

**Table 5. Prognostic factors of gastric carcinoma between total and young age gastric cancer**

	<b>Total No. of patients (%)</b>	<b><i>P</i></b>	<b>Young age No. of patients (%)</b>	<b><i>P</i></b>
Age		0.534		
Age ≤ 45	654 (19.5)			
Age > 45	2708 (80.5)			
Sex		0.278		0.004
Male	2247 (66.8)		372 (56.9)	
Female	1115 (33.2)		282 (43.1)	
Location		< 0.001		< 0.001
Other	2690 (82.3)		478 (75.8)	
Proximal	580 (17.7)		153 (24.2)	
Lauren classification		0.006		0.578
Intestinal	582 (60.1)		73 (38.6)	
Diffuse	386 (39.9)		116 (61.4)	
Depth of invasion		< 0.001		< 0.001
T1,T2	1835 (54.6)		334 (57.1)	
T3,T4	1220 (36.3)		251 (42.9)	
Nodal involvement		< 0.001		< 0.001
N-	1728 (58.5)		339 (58)	
N+	1228 (41.5)		245 (42)	
Hepatic metastasis		< 0.001		< 0.001
Negative	3239 (97.5)		629 (97.7)	
Positive	83 (2.5)		15 (2.3)	
Peritoneal metastasis		< 0.001		< 0.001
Negative	3161 (94.0)		589 (91.5)	
Positive	157 (4.7)		55 (8.5)	
Others distant metastasis *		< 0.001		< 0.001
Negative	3235 (96.7)		634 (97.7)	
Positive	112 (3.3)		15 (2.3)	
Curative resection		< 0.001		< 0.001
Yes	2831 (93.7)		543 (90.7)	
No	191 (6.3)		56 (9.3)	
Lymphatic invasion		< 0.001		< 0.001
Negative	680 (49)		136 (49.1)	
Positive	707 (51)		141 (50.9)	
Vein invasion		< 0.001		< 0.001
Negative	828 (62.5)		168 (63.6)	
Positive	496 (37.5)		96 (36.4)	
CA19-9		< 0.001		< 0.001
≤ 37 U/ml	1411 (87.3)		285 (88.5)	

> 37 U/ml	206 (12.7)		37 (11.5)	
CEA		< 0.001		0.001
≤ 5 ng/ml	1857 (83.9)		391 (90.3)	
> 5 ng/ml	358 (16.1)		42 (9.7)	

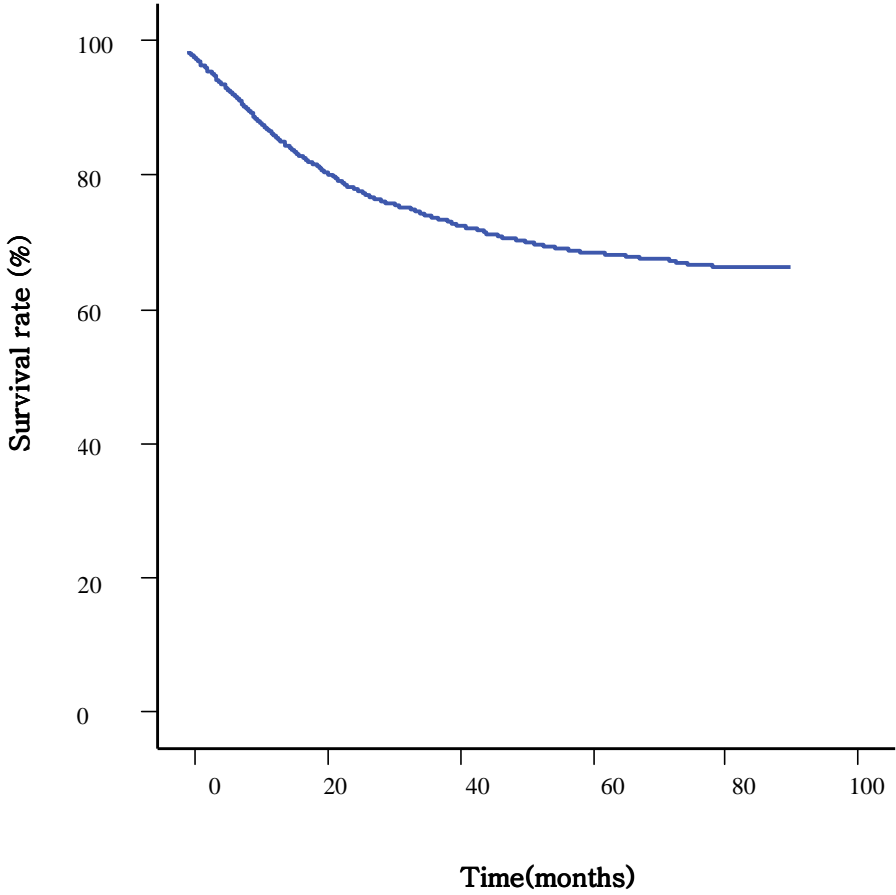
\* Lung, ovary, adrenal gland, brain, pancreas, colon, kidney

**Table 6. Multivariate analysis for overall survival in gastric cancer**

Variables	95% CI	Odds ratio	P <sup>†</sup>
Location (other vs proximal)	0.693-2.303	1.263	NS
Lauren's classification (Intestinal vs diffuse)	0.905-2.276	1.435	NS
Stage (I,II vs III,IV)	1.428-5.895	2.901	0.003
Distant organ* metastasis (no vs yes)	0.527-3.382	1.335	NS
Lymphatic invasion (no vs yes)	0.843-4.279	1.899	NS
Vein invasion (no vs yes)	1.128-3.476	1.980	0.017
Curative resection (yes vs no)	1.484-6.573	3.123	0.003
Type of resection (subtotal vs total)	0.615-1.909	1.084	NS
CEA	0.999-1.022	1.010	NS
CA 19-9	1.000-1.003	1.002	0.020

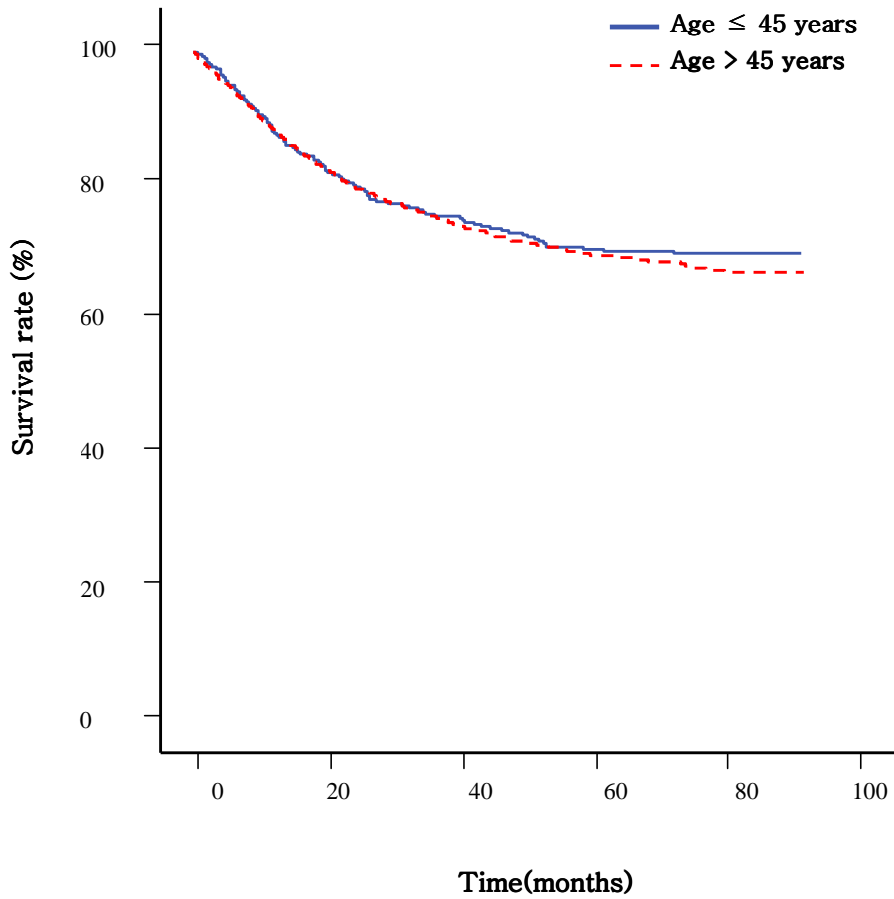
CI : confidence interval; NS : not significant; \* Lung, ovary, adrenal gland, brain, pancreas, colon, kidney, peritoneum, liver; †Cox proportional hazard analysis.

**Fig. 2. Overall survival curve of all stage of gastric cancer**



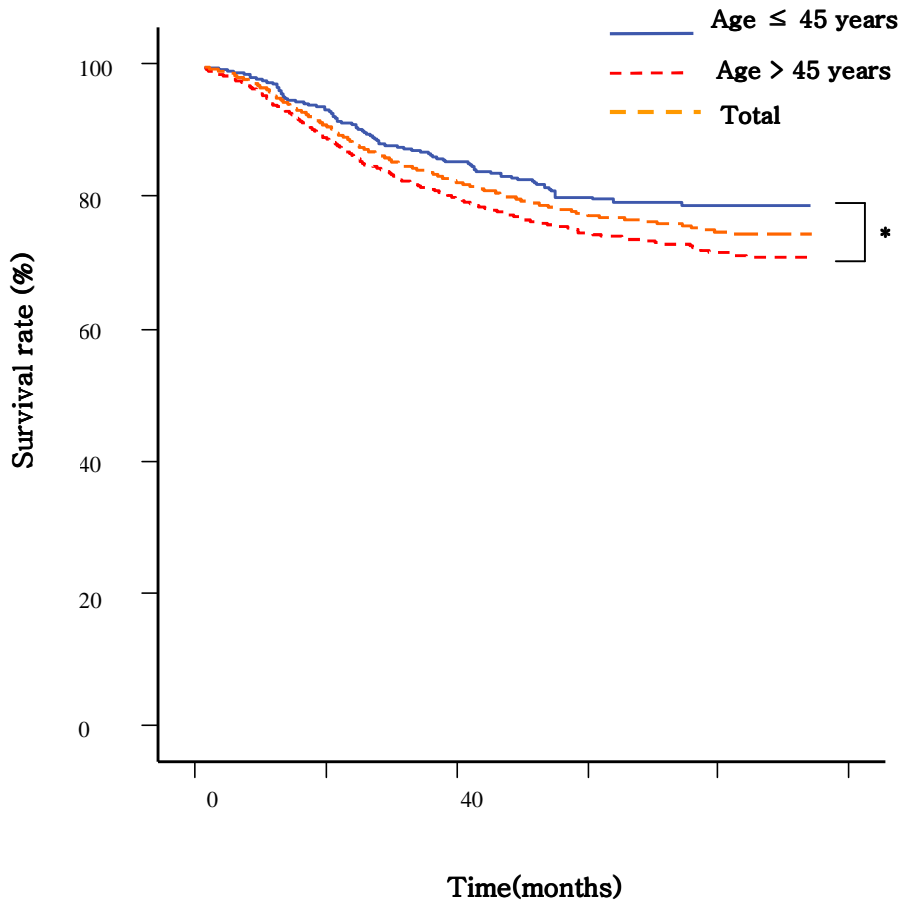
Cumulative survival of all (n=3362) patients with gastric cancer (5 year survival rates = 69.22%).

**Fig. 3. Overall survival curves of gastric cancer according to age**



The 5-year survival rate of young age group ( $\leq 45$  years) and older than 45 years group did not differ statistically ( $P = 0.534$ , log rank test).

**Fig 4. Survival curves of curatively resected gastric cancer according to age**



The 5-year survival rate was significantly higher in young age group ( $\leq 45$  years) than older than 45 years group in curatively resected cases ( $*P = 0.002$ , log rank test).



#### IV. Discussion

Most gastric cancer patients are between the ages of 50 to 70 years and the proportion of young patients with gastric cancer varies according to the definition of young age.<sup>2, 7, 10</sup> In this study, to propose the age criterion statistically, we divided patients into three groups by age standard deviation. In our institution, the proportion of young patients was 19.5%, which is relatively high compared to other reports.<sup>2-4, 6, 7, 10</sup> This high proportion of young patients is probably because of earlier screening and surveillance by endoscopy in Korea, and it highlights the importance of screening in young people in high-risk areas.

It is controversial as to whether gastric carcinoma in young patients differs from that in older patients. There was a significant difference in the male to female ratio between young and old patients. In general, gastric cancer occurs predominantly in males in the older age groups. In the young group, however, gastric cancer was present in females as often or more often than men.<sup>11</sup> This study shows that the proportion of females with AGC but not females with EGC increased in group 1. The reason for the increasing frequency of females with AGC among younger patients is currently unknown, but some studies have proposed that this could be hormonally linked.<sup>12, 13</sup>

A previous study showed histologically that poorly differentiated adenocarcinoma and signet ring cell carcinoma are the most common gastric cancer types in patients 40 years of age or younger patients.<sup>14</sup> Lauren diffuse type gastric cancer also comprises a larger proportion of total gastric cancers in young gastric cancer patients. Our study showed a significantly higher proportion of poorly differentiated and signet ring cell carcinoma in group 1 compared to older age groups ( $P < 0.001$ ). Although the young age group presented more aggressive histologic characteristics than the older age group, there were no differences in survival rates between the two groups. This suggests that these histologic features are not independent prognostic factors

of outcome in young or old gastric cancer patients.

The location of the tumor was significantly different between age groups. The lower third location of the stomach was the most common site in all ages, but the upper third location of the stomach and the linitis plastica type were more frequent in group 1 than groups 2 and 3 ( $P < 0.001$ ). This result explains the higher rate of total gastrectomies in the young group compared to the older groups.

Many previous reports have shown a low curative resection rate in older patients with gastric cancer.<sup>15</sup> On the contrary, Moriguchi and colleagues showed that operative curability is lower in younger patients.<sup>16</sup> In our study, the curative resection rate in group 1 was lower than that in groups 2 and 3 (Table 4). This result might be due to more advanced features such as linitis plastica type and diffuse type histology in young patients than in older patients.

In the AGC group, there was a significantly higher proportion of T4 and stage IV patients in the young age group. However, recent reports based on surgically resected patients from our institution showed that the proportions of T4, N3, and stage IV were similar between young and elderly patients.<sup>17</sup> This discrepancy is due to the inclusion of surgical unresectable patients (i.e. more advanced cases) in our study.

The prognosis of young patients is variable between studies. While some investigators have reported that prognosis is poor for young patients and their survival rates are low, particularly in patients with advanced gastric cancer,<sup>6, 18</sup> others showed that elderly patients have poor prognoses.<sup>19, 20</sup> Furthermore, several studies have shown that the 5-year survival rate does not differ significantly between young and elderly patients.<sup>21, 22</sup> In a few reports, including our surgical study,<sup>17, 23</sup> the prognosis for young patients who undergo curative resection is better than that of older patients. In this study, although curative resection and resectability rate was lower in young patients (Table 4), if curatively resected, the overall survival rate of young patients

was significantly higher than that of older patients. Therefore, it is important to make a prompt, precise diagnosis for gastric carcinoma in young patients and to treat it in the early stages.

The prognostic factors associated with poor 5-year survival were variable. In accordance with most literature reports<sup>23</sup>, curative resection offered the only chance of long term survival. Other studies reported significant survival factors include the stage of the disease, possibility of resection, location of the tumor, and a family history of gastric cancer.<sup>22</sup> In our study, sex was the significant prognostic factor in young age gastric cancer (group 1). There was a significant higher proportion of stage IV, distant organ metastasis, and high level of CA 19-9 in young female group compared to male group (data not shown). These factors might be the reason of poor prognosis in young female gastric cancer patients. In multivariate analysis, stage of disease, vein invasion, curative resection, and initial CA19-9 level were significant prognostic factors regardless of age.

Initial CA19-9 level was a significant prognostic factor in our multivariate analysis. CA19-9 and CEA are commonly used markers for gastric cancer as they reflect the tumor biology of patients with gastric carcinoma. CA19-9, identified by Koprowski et al.<sup>24</sup>, is a ligand of E-selectin,<sup>25</sup> a molecule that may play a role in the adhesion of cancer cells to endothelial cells in which can result in hematogenic metastasis. Until now, the clinical correlation between CEA and CA19-9 levels has been unclear and controversial.<sup>22, 26</sup> Interestingly, the mean of initial CA19-9 level was much higher in group 1 compared to groups 2 and 3 (Table 4). There are several possibilities for higher levels of serum CA19-9 in young patients than old patients. First, young patients have more frequent peritoneal or distant metastasis compared to old patients, and peritoneal metastasis was the most common cause for unresectability in young gastric cancer patients in this study. Kochi and colleagues reported that patients with elevated serum CA19-9 levels were at

significantly higher risk of having peritoneal metastases and distant metastases than those with normal serum CA19-9 levels.<sup>27</sup> Second, there are some previous reports that show that the intestinal and diffuse types of gastric cancer have several differences in epidemiologic and molecular biologic characteristics;<sup>28</sup> these differences may influence the different patterns of metastasis seen in the two histotypes. Compared to intestinal type cells, the diffuse type shows a greater predisposition to proliferate in the peritoneum.<sup>28</sup> A recent study reported that the intestinal type of gastric cancer has greater proliferative activity in superficial layers than in deeper ones, whereas in the diffuse type proliferation is increased in deeper layers and in tumors infiltrating the serosa, resulting in a greater tendency for endoperitoneal spread.<sup>29</sup>

We also compared cumulative survival in patients with primary gastric cancer who had an elevated serum level of CA19-9 with cumulative survival in those with normal levels of CA19-9. The cumulative survival curves were significantly different for patients with elevated CA19-9 and those with normal serum CA19-9 levels. The survival rate of gastric cancer patients of all ages with serum CA19-9 levels below 37 ng/ml was significantly better than that of patients with levels above that value. These findings indicate that serum CA19-9 levels may provide additional prognostic information in patients with gastric cancer. There are few reports on the prognostic significance of CA19-9 level in gastric cancer,<sup>30</sup> although a previous studies concluded that CA19-9 level by itself is not an independent prognostic factor.<sup>27</sup> However, our study enrolled a relatively higher proportion of young gastric cancer patients compared to other studies and included not only a large number of surgical data but also distant metastatic gastric cancer data. That's why the initial CA 19-9 level was one of prognostic factors in our study.

## **V. Conclusions**

The clinicopathological features associated with young gastric cancer patients include an upper location, linitis plastica type, diffuse histologic type, and unresectability. Although the curative resection rate was lower in young patients, if curatively resected, the survival rate of young patients was significantly better than that of older patients. Therefore, it is important to make a precise, early diagnosis and to perform a curative resection at an earlier stage.

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< ABSTRACT(IN KOREAN)>

3,362명의 위암환자를 대상으로 연령에 따른 위암의  
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**배경:** 위암은 최근 50년 동안 세계적으로 발생률과 사망률이 감소하는 추세이지만 아직 많은 나라에서 가장 흔한 암 중 하나이다. 특히 젊은 연령의 위암에 대한 연구는 나이 기준이 각기 연구들마다 다르며 연구대상 환자군 또한 주로 수술적 절제를 한 환자군에 국한되어 있다. 이로 인해 각 연구들마다 젊은층의 위암 발생률, 특징과 예후에 있어서 다소 차이가 있어 왔다. 그리하여 본 연구는 조기위암부터 4기까지의 병기를 모두 포함하여 젊은 연령층과 노년층의 위암 환자의 임상병리학적 특성의 차이와 예후를 비교하고 생존율에 영향을 주는 인자를 알아 보고자 한다.

**방법:** 2000년도에서 2005년도 사이에 위암으로 내원하여 치료를 받은 모든 병기의 환자를 대상으로 분석하였으며 위암 환자군을 연령별로 그룹1 (45세 이하), 그룹2 (46세부터 70세), 그룹3 (71세 이상)으로 나누어 분석하였다.

**결과:** 상부위암, 경성암, 미분화암이 다른 연령과 비교시 그룹1에서 많았으며 조기위암은 depressive 타입이 진행성 위암은 Borrmann 4형이 그룹1에서 의미 있게 높았다. 전이 특성 또한 복막전이 빈도가 그룹1에서 통계적으로 의미 있게 다른 연령층에 비해 높았다. 5년 생존율에 있어서는 근치적 수술치료를 받은 환자군에서 생존율이 그룹1에서 높았다. 예후인자 중 특징적으로 성별이 그룹1에서 생존율에 영향을 주는 인자 중 하나로 나타났으며 나이와 상관없는 전체 위암 환자의 다변량 분석에서는 TNM병기, 혈관침윤, 근치도, CA 19-9 수치가 통계학적으로 유의하게 생존율에 영향을 미치는 인자로 분석되었다.

**결론:** 젊은 연령(45세이하)의 임상병리학적 특성은 노년층의 위암과 비교하여 다른 임상병리학적 특징을 갖고 있으며 근치적 수술을 받은 환자에서는 젊은 연령층 그룹의 생존율이 다른 연령층에 비해 좋으므로 젊은 연령의 조기진단이 중요하다고 할 수 있겠다.

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핵심되는 말 : 젊은 연령, 위암, 예후