



## Original Article

# First Course of Treatment and Prognosis of Exocrine Pancreatic Cancer in Korea from 2006 to 2017

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**Purpose** Hospital-based clinical studies have limitations in holistic assessment of cancer treatment and prognosis, as they omit out-of-hospital patients including elderly individuals. This study aimed to investigate trends in initial treatment and corresponding prognosis of patients with exocrine pancreatic cancer (EPC) in Korea.

**Materials and Methods** The Korea Central Cancer Registry data of patients with EPC from 2006 to 2017 were retrospectively reviewed. We defined the first course of treatment (FT) as the cancer-directed treatment administered within four months after cancer diagnosis according to the Surveillance, Epidemiology, and End Results (SEER) program.

**Results** Among 62,209 patients with EPC, localized and regional (LR) SEER stage; patients over 70 years old; and ductal adenocarcinoma excluding cystic or mucinous (DAC) accounted for 40.6%, 50.1%, and 95.9%, respectively. "No active treatment" (NT, 46.5%) was the most frequent, followed by non-surgical FT (28.7%) and surgical FT (22.0%). Among 25,198 patients with LR EPC, surgical FT increased (35.9% to 46.3%) and NT decreased (45.0% to 29.5%) from 2006 to 2017. The rate of surgical FT was inversely related to age (55.1% [ $< 70$  years], 37.3% [70-79 years], 10.9% [ $\geq 80$  years]). Five-year relative survival rates of LR DAC were higher after surgical FT than after NT in localized (46.1% vs. 12.9%) and regional stage (23.6% vs. 4.9%) from 2012 to 2017.

**Conclusion** Less than half of overall patients with LR EPC underwent surgical FT, and this proportion decreased significantly in elderly individuals. Clinicians should focus attention on elderly patients with EPC to provide appropriate medical advice.

**Key words** Pancreatic neoplasms, Therapeutics, Survival rate, Registries

## Introduction

Despite recent advances in diagnostic modalities, surgical care, medical oncology, and radiation oncology, pancreatic cancer remains the seventh leading cause of global cancer deaths with limited improvements in survival outcomes [1]. However, clinical studies have limitations in holistic assessment of patients who do not present to hospitals for cancer-directed treatments. Little is known, nationally, about the treatment pattern including temporal trends and age-related disparities in many countries.

During the past decades, authoritative guidelines including those from the National Comprehensive Cancer Network (NCCN) [2], American Society of Clinical Oncology (ASCO) [3], European Society for Medical Oncology (ESMO) [4], and other academic societies were globally adopted for pancreatic cancer treatment. Nevertheless, only 48.4% of patients with pancreatic cancer received the nationally expected treat-

ment, while 36.9% did not receive any treatment in the United States from 2004 to 2013 [5]. A recent population-based study in Europe and the United States also revealed wide variations in the proportion of patients receiving chemotherapy (12.5%-61.7%) or radiation therapy (22.6%-32.6%) after resection of pancreatic cancer [6].

However, the life expectancy at birth in countries with an age-standardized incidence rate of pancreatic cancer higher than 7.0 per 100,000 is 81.0 years [1,7], when the median age at diagnosis of pancreatic cancer is 70 years [8]. However, few studies have focused on the disparities in treatment pattern according to the patients' age. In the United States, from 2004 to 2011, patients with stages I and II pancreatic adenocarcinoma in the age groups 56-64, 65-75, and 76 years or older were 17%, 40%, and 83% less likely to undergo surgery and receive chemotherapy in combination, either as adjuvant or neoadjuvant treatment, compared to those aged 18-55 years [9]. From 2011 to 2016, 52% of patients in their 80s with local-

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ized pancreatic head ductal adenocarcinoma did not receive any cancer-directed treatment in the United States [10].

Therefore, identifying the treatment pattern for an entire nation may provide a better insight into cancer management in the population, especially taking into consideration those that are under-represented in hospital-based clinical studies. In this study, trends in initial treatment pattern and corresponding prognosis of exocrine pancreatic cancer (EPC) were investigated using a nationally representative population-based cancer registry data in Korea from 2006 to 2017.

## Materials and Methods

### 1. Data source

Epidemiologic data were obtained from the Korea Central Cancer Registry (KCCR), which has annually collected incidence data from the entire Korean population in all regions since 1999 [11]. In KCCR, the Surveillance, Epidemiology, and End Results (SEER) stage has been formally recorded since 2006 as localized (a malignancy limited to the organ of origin), regional (tumor extension beyond the limits of organ of origin), distant (a tumor that has spread to areas of the body distant from the primary tumor), and unknown (sufficient evidence is not available to adequately assign stage) tumors [12]. Therefore, this study analyzed data from 2006 to 2017 to stratify treatment pattern and prognosis in relation to the SEER stage.

### 2. Patient cohort

This study focused on EPC, as distinct from that of pancreatic neuroendocrine tumors, which have relatively higher survival rates compared to EPC [13]. Of the 64,308 individuals with pancreatic cancer coded as C25 according to the International Classification of Diseases, 10th revision (ICD-10) [14], 2,099 individuals with the following morphology codes for neuroendocrine tumors were excluded: 8150-8157, 8240-8246, 8249, 8002, 8040-8045, and 8013 [15]. The morphology codes for EPC were used to categorize individuals into three mutually exclusive groups: ductal adenocarcinoma excluding cystic or mucinous (DAC; 8000-8004, 8010-8011, 8020-8039, 8230-8231, 8140-8149, 8490, 8500-8503, 8560-8570), ductal specified as mucinous or cystic adenocarcinoma (ADC<sub>m&c</sub>; 8050-8260, 8440-8479, 8480-8481), and acinar cell carcinoma (ACC; 8550) [16].

Consequently, 62,209 patients with EPC were included in this study, and their demographic characteristics, overall yearly treatment pattern, and survival outcomes were examined. Then, 10,045 patients with missing SEER stage or treatment information were excluded at subgroup analysis regarding treatment pattern related to the SEER stage.

### 3. First course of treatment

In the registry, the “first course of treatment” (FT) was recorded based on the documented cancer-directed treatment methods used to administer treatment to the patients before disease progression or recurrence, within the first four months of the date of initial diagnosis [12,17]. Nine categories of treatment information were included in the registry: surgery alone, surgery with chemotherapy, surgery with radiotherapy, surgery with chemotherapy and radiotherapy, chemotherapy alone, chemotherapy with radiotherapy, radiotherapy alone, no active treatment, and unknown treatment information. In this study, the treatment pattern was aggregated into four groups: surgical FT (surgery alone, surgery with chemotherapy, surgery with radiotherapy, surgery with chemotherapy and radiotherapy); non-surgical FT (chemotherapy alone, chemotherapy with radiotherapy, radiotherapy alone); no active treatment (NT); and unknown.

### 4. Statistical analysis

The study period was divided into periods I (2006-2011) and II (2012-2017). Age was stratified into < 40, 40-49, 50-59, 60-69, 70-79, and ≥ 80 years, then aggregated into four groups (< 60, 60-69, 70-79, and ≥ 80 years) for the statistical tests. Owing to the inability to differentiate the American Joint Committee on Cancer (AJCC) stage or resectability based on the SEER stage, as recorded in the registry, localized and regional stages were considered as a whole to analyze the treatment pattern, which may have included resectable, borderline resectable, and locally advanced unresectable tumors. The categorical variables were compared using the chi-square test. Adjusted risk ratios were analyzed using *binreg* command in STATA ver. 16.1 (StataCorp LLC, College Station, TX). Relative survival rates were estimated using the Ederer II method with some minor modifications, based on an algorithm written in SAS provided by Paul Dickman [18]. Analyses of survival were performed using SAS ver. 9.4 (SAS Institute Inc., Cary, NC). All statistical tests were two-tailed, and results were considered statistically significant at p-values < 0.05.

## Results

### 1. Overall epidemiology, treatment pattern, and prognosis of patients with EPC

Among the 62,209 patients with EPC, 50.1% were aged 70 years or older (Table 1). The proportion of patients aged 70 years or older increased from 47.0% (period I) to 52.3% (period II). Comparing periods I and II, the proportion of regional and distant SEER stage increased while localized and unknown stage decreased.

**Table 1.** Characteristics of patients with exocrine pancreatic cancer in Korea from 2006 to 2017

Variable	Total (2006-2017) (n=62,209)	Period I (2006-2011) (n=26,212)	Period II (2012-2017) (n=35,997)
<b>Age at diagnosis (yr)</b>			
0-39	859 (1.4)	381 (1.5)	478 (1.3)
40-49	3,396 (5.5)	1,631 (6.2)	1,765 (4.9)
50-59	10,159 (16.3)	4,351 (16.6)	5,808 (16.1)
60-69	16,654 (26.8)	7,523 (28.7)	9,131 (25.4)
70-79	20,485 (32.9)	8,436 (32.2)	12,049 (33.5)
≥ 80	10,656 (17.1)	3,890 (14.8)	6,766 (18.8)
<b>Sex</b>			
Male	33,554 (53.9)	14,442 (55.1)	19,112 (53.1)
Female	28,655 (46.1)	11,770 (44.9)	16,885 (46.9)
<b>Location</b>			
Head of pancreas (C25.0)	24,773 (39.8)	10,358 (39.5)	14,415 (40.1)
Body and tail of pancreas (C25.1-2)	20,225 (32.5)	7,510 (28.7)	12,715 (35.3)
Others (C25.3-8)	4,339 (7.0)	1,808 (6.9)	2,531 (7.0)
Pancreas, NOS (C25.9)	12,872 (20.7)	6,536 (24.9)	6,336 (17.6)
<b>SEER stage</b>			
Localized	6,120 (9.8)	2,657 (10.1)	3,463 (9.6)
Regional	19,108 (30.7)	7,635 (29.1)	11,473 (31.9)
Distant	26,977 (43.4)	10,963 (41.8)	16,014 (44.5)
Unknown	10,004 (16.1)	4,957 (18.9)	5,047 (14.0)
<b>First course of treatment (FT)</b>			
Surgical FT	13,694 (22.0)	5,388 (20.6)	8,306 (23.1)
Non-surgical FT	17,861 (28.7)	6,801 (25.9)	11,060 (30.7)
No active treatment	28,912 (46.5)	13,098 (50.0)	15,814 (43.9)
Unknown	1,742 (2.8)	925 (3.5)	817 (2.3)
<b>Histology</b>			
Ductal adenocarcinoma excluding cystic or mucinous (DAC)	59,685 (95.9)	25,244 (96.3)	34,441 (95.7)
Ductal specified as mucinous or cystic adenocarcinoma (ADC <sub>m&amp;c</sub> )	2,338 (3.8)	878 (3.4)	1,460 (4.1)
Acinar cell carcinoma (ACC)	186 (0.3)	90 (0.3)	96 (0.3)

Values are presented as number (%). Non-surgical FT, chemotherapy with/without/or radiation therapy; NOS, not otherwise specified; SEER, Surveillance, Epidemiology, and End Results.

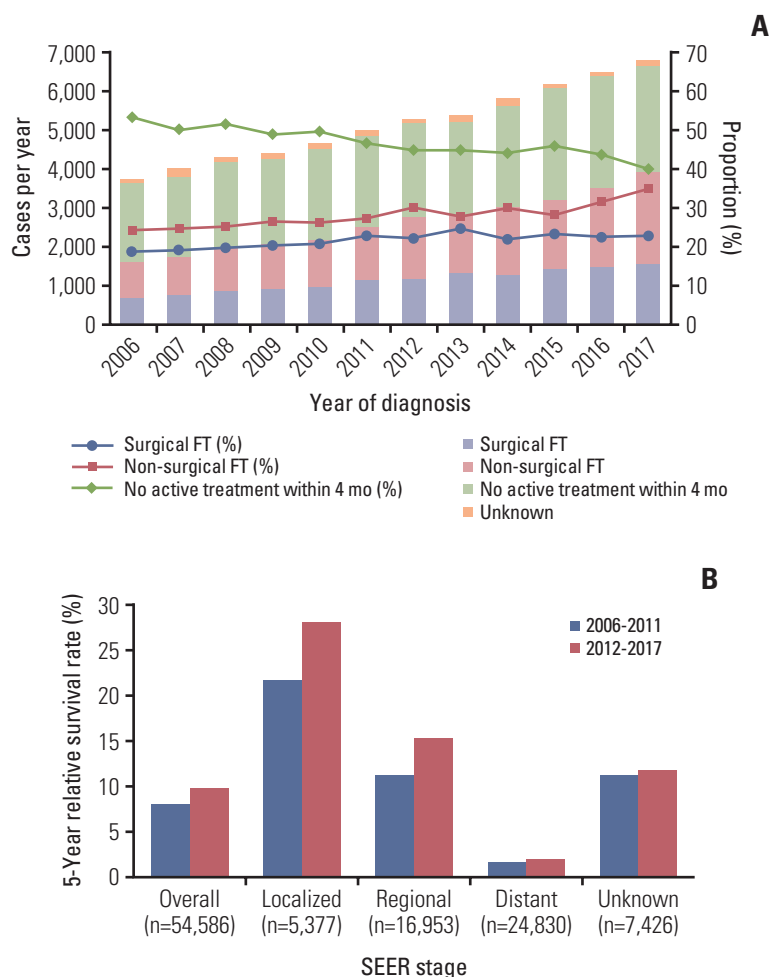
The proportion of unknown SEER stage was higher in elderly patients (11.5% [ $< 60$  years,  $n=1,656$ ] vs. 11.9% [60-69 years,  $n=1,988$ ] vs. 16.2% [70-79 years,  $n=3,309$ ] vs. 28.6% [ $\geq 80$  years,  $n=3,051$ ],  $p < 0.001$ ). Among patients with available information on SEER stage, the proportion of localized and regional stage was comparable across age groups (48.1% [ $< 60$  years,  $n=6,142$ ] vs. 48.5% [60-69 years,  $n=7,120$ ] vs. 48.2% [70-79 years,  $n=8,281$ ] vs. 48.5% [ $\geq 80$  years,  $n=3,685$ ],  $p=0.896$ ).

Of all SEER stages, the proportion of patients receiving surgical FT and non-surgical FT increased while those with NT decreased (Fig. 1A). Among patients with localized and regional stage EPC with available information on treatment ( $n=25,198$ ), the proportion of patients receiving surgical

FT (39.3% to 45.2%) and non-surgical FT (19.9% to 20.7%) increased while those with NT decreased (40.8% to 34.1%). In distant-stage EPC with available information on treatment ( $n=26,966$ ), the proportion of non-surgical FT increased (36.4% to 43.2%), and those with NT (54.9% to 48.5%) and surgical FT (8.7% to 8.3%) decreased.

From period I to II, the overall 5-year relative survival rate (5YRS) significantly increased in all stages (8.0% [period I] to 9.8% [period II],  $p < 0.001$ ), localized stage (21.6% to 28.1%,  $p=0.035$ ), and regional stage (11.2% to 15.3%,  $p < 0.001$ ) (Fig. 1B).

Comparing among the three histology groups, patients with DAC had higher proportion of patients aged 70 years or older (50.9% [ $n=30,383$ ] vs. 30.7% [ $n=718$ ],  $p < 0.001$ ), with a



**Fig. 1.** Yearly cases, treatment pattern, and prognosis of exocrine pancreatic cancer from 2006 to 2017. (A) All Surveillance, Epidemiology, and End Results (SEER) stages (n=62,209). (B) Overall 5-year relative survival rates according to SEER stage. FT, first course of treatment.

lower percentage of surgical FT (20.1% [n=11,981] vs. 69.0% [n=1,613],  $p < 0.001$ ) and localized and regional SEER stage (39.4% [n=23,508] vs. 69.3% [n=1,621],  $p < 0.001$ ) compared to those with ADC<sub>m&c</sub>. The proportion of patients receiving surgical FT was higher in younger patients, males, and patients with ADC<sub>m&c</sub> and ACC histology (Table 2). After adjusting for period, sex, and histology groups, patients in their 70s and 80s or older had a 29.7% and 79.3% reduced incidence of surgical FT compared to those under the age of 60 years (Table 3).

## 2. Changes in the treatment pattern and prognosis of patients with ductal adenocarcinoma

Among 59,685 patients with DAC, 39.4% had localized and regional stage and 44.2% had distant SEER stage. Among 23,481 patients with localized and regional stage DAC with available information on treatment, the proportion of

patients undergoing surgical FT increased from period I to II (Fig. 2A), for both localized (21.6% [n=513] to 23.0% [n=674]) and regional (41.3% [n=3,003] to 46.8% [n=5,106]) stages.

Patients' age was inversely related to the proportion of surgical FT. The proportion of patients receiving surgical FT in patients aged < 60 years, 60-69 years, 70-79 years, and  $\geq 80$  years were 52.4%, 44.2%, 29.1%, and 5.6%, respectively, in period I and 55.5%, 53.6%, 38.8%, and 12.1%, respectively, in period II. On the contrary, the proportion of patients with NT was the highest in patients aged  $\geq 80$  years (87.1% [period I] to 79.7% [period II]) (Fig. 2B).

Among 26,359 patients with distant stage DAC and information available on treatment, the proportion of patients undergoing non-surgical FT increased from period I to II (36.3% to 55.3%) while the proportion of patients with NT decreased (55.3% to 48.9%) (Fig. 2C).

The overall 5YRS of DAC increased from 6.8% to 7.9%

**Table 2.** Characteristics of patients according to first course of treatment in localized and regional stage exocrine pancreatic cancer

Variable	No.	Surgical FT (n=10,781)	Non-surgical FT (n=5,134)	NT (n=9,283)	p-value <sup>a)</sup>
<b>Age at diagnosis (yr)</b>					
0-59	13,241	3,588 (58.5)	1,592 (26.0)	953 (15.5)	< 0.001
60-69	7,108	3,707 (52.2)	1,760 (24.8)	1,641 (23.1)	
70-79	8,272	3,084 (37.3)	1,491 (18.0)	3,697 (44.7)	
≥ 80	3,685	402 (10.9)	291 (7.9)	2,992 (81.2)	
<b>Sex</b>					
Male	13,324	6,098 (45.8)	2,869 (21.5)	4,357 (32.7)	< 0.001
Female	11,874	4,683 (39.4)	2,265 (19.1)	4,926 (41.5)	
<b>Histology</b>					
Ductal adenocarcinoma excluding cystic or mucinous (DAC)	23,481	9,296 (39.6)	5,035 (21.4)	9,150 (39.0)	< 0.001
Ductal specified as mucinous or cystic adenocarcinoma (ADC <sub>m&amp;c</sub> )	1,618	1,403 (86.7)	91 (5.6)	124 (7.7)	
Acinar cell carcinoma (ACC)	99	82 (82.8)	8 (8.1)	9 (9.1)	

Values are presented as number (%). FT, first course of treatment; NT, no active treatment. <sup>a)</sup>Chi-square test across three types of treatment pattern.

**Table 3.** Risk ratio of receiving surgical treatment within 4 months after diagnosis of localized and regional exocrine pancreatic cancer, adjusted for time period, age at diagnosis, sex, and histology

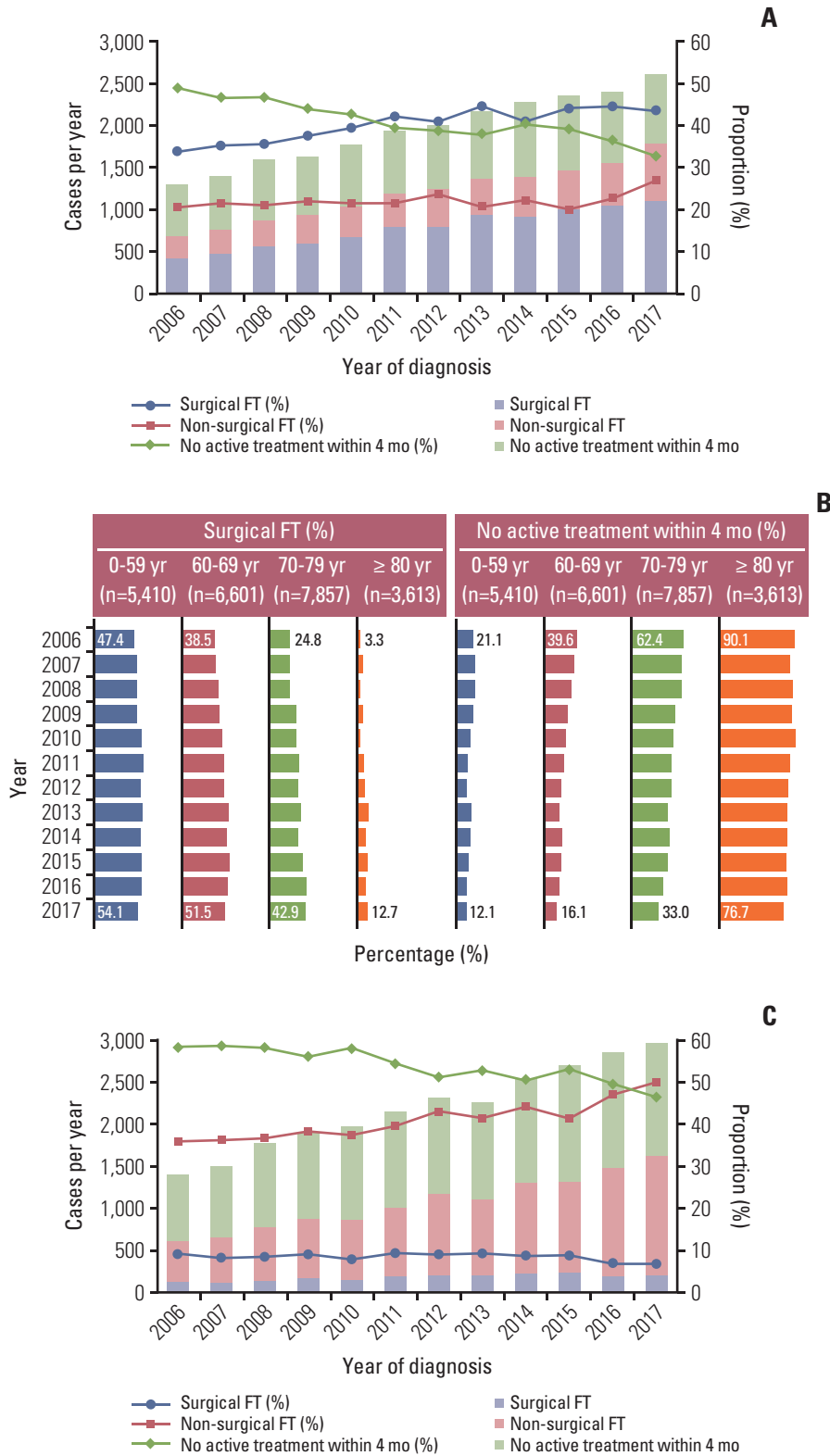
	Risk ratio	95% CI	p-value
<b>Year</b>			
2006-2011	1		
2012-2017	1.141	1.112-1.170	< 0.001
<b>Age (yr)</b>			
< 60	1		
60-69	0.956	0.932-0.980	< 0.001
70-79	0.703	0.680-0.727	< 0.001
≥ 80	0.207	0.189-0.228	< 0.001
<b>Sex</b>			
Male	1		
Female	0.990	0.969-1.012	0.371
<b>Histology</b>			
Ductal adenocarcinoma excluding cystic or mucinous (DAC)	1		
Ductal specified as mucinous or cystic adenocarcinoma (ADC <sub>m&amp;c</sub> )	1.749	1.707-1.792	< 0.001
Acinar cell carcinoma (ACC)	1.662	1.516-1.823	< 0.001

CI, confidence interval.

(15.7% to 18.2% [localized], 9.9% to 13.4% [regional], and 1.5% to 1.6% [distant SEER stage]) (Fig. 2D). Prognosis after surgical FT was better than that after non-surgical FT or NT in patients with localized and regional stage DAC. A higher 5YRS in the NT group than in the non-surgical FT group was due to the lower microscopic verification rate (26.7% [761/2,845] vs. 71.8% [610/850]), respectively.

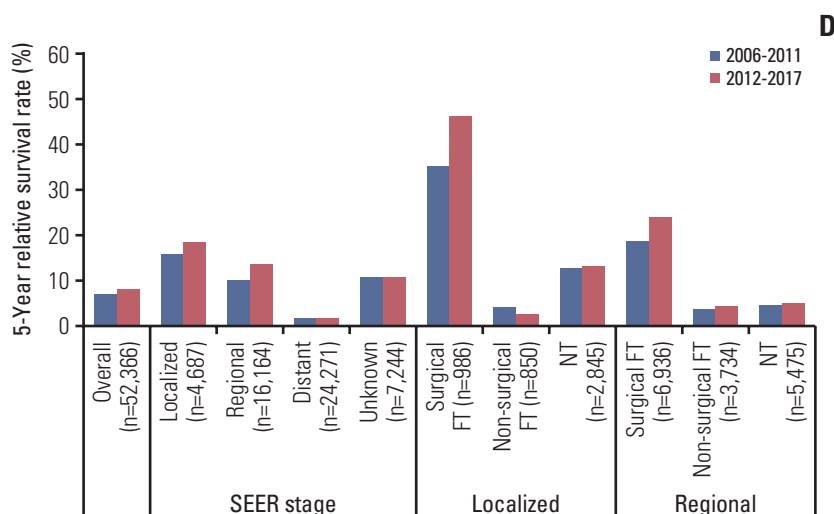
### 3. Epidemiology, treatment pattern, and prognosis of patients with mucinous and cystic adenocarcinomas

Among 2,338 patients with ADC<sub>m&c</sub>, 30.7% were aged over 70 years and the male-to-female ratio was 1.03:1. At the time of diagnosis, 69.3% had localized or regional disease, and 22.8% had distant SEER stage disease. Proportion of patients receiving surgical FT among 1,618 patients with localized and regional stage ADC<sub>m&c</sub> increased from 82.8% (period I,



**Fig. 2.** Treatment pattern and prognosis of patients with ductal adenocarcinoma. (A) Yearly cases and treatment pattern in localized and regional Surveillance, Epidemiology, and End Results (SEER) stage. (B) Proportion of patients receiving surgical first course of treatment and no active treatment according to age group in localized and regional SEER stage. (C) Yearly cases and treatment pattern in distant SEER stage. (Continued to the next page)





**Fig. 2.** (Continued from the previous page) (D) Overall 5-year relative survival rates according to SEER stage and treatment pattern. FT, first course of treatment; NT, no active treatment.

n=468) to 88.9% (period II, n=917) (Fig. 3A). The overall 5YRS of ADC<sub>m&c</sub> increased from 40.3% to 56.5%, with more marked improvement in patients with localized (73.4% to 86.4%,  $p < 0.001$ ) and regional (38.1% to 55.5%,  $p < 0.001$ ) disease (Fig. 3B).

#### 4. Epidemiology, treatment pattern, and prognosis of patients with ACC

Among 186 patients with ACC, 21.5% were aged over 70 years and the male-to-female ratio was 2.32:1. At the time of diagnosis, 53.2% had localized or regional disease, and 40.3% had distant SEER stage disease. The data of ACC were not analyzed according to periods owing to the small sample size in each stratum. Overall, 53.8% had surgical FT, 24.7% had non-surgical FT, and 21.0% had NT. The overall 5YRS of ACC from 2006 to 2017 was 29.7%, which was higher after surgical FT than with NT (44.7% and 12.2%, respectively).

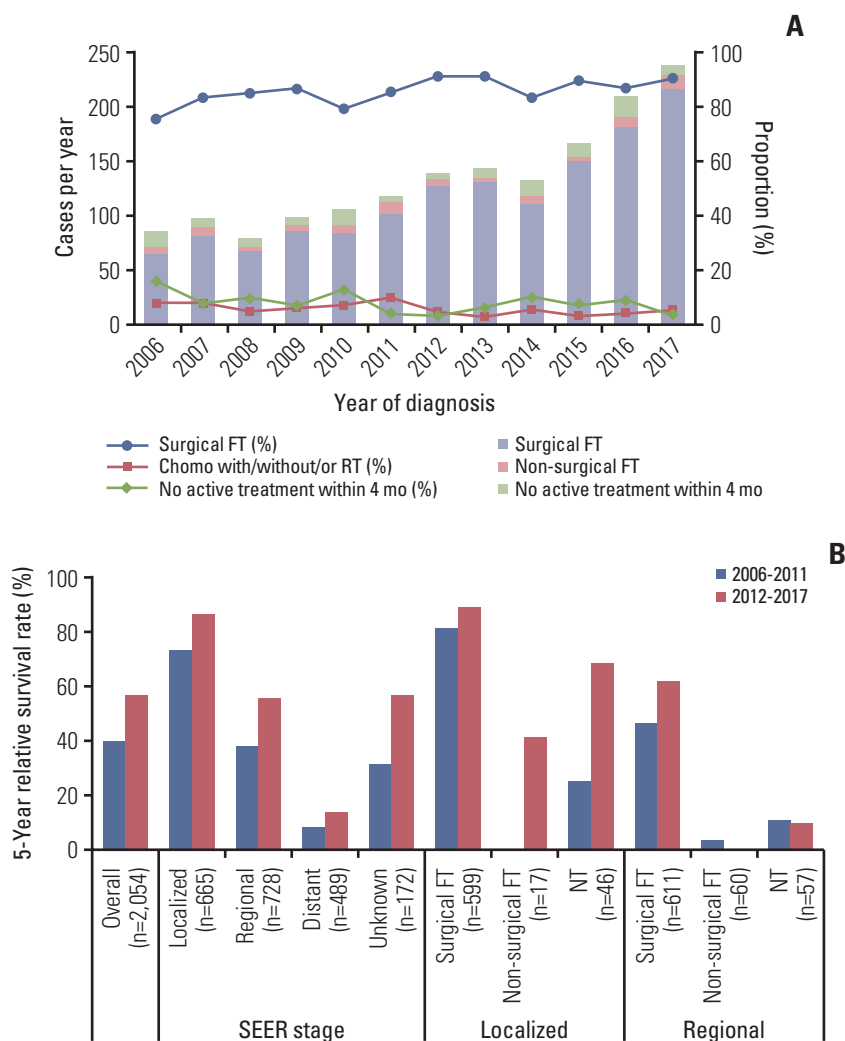
## Discussion

Medical, financial, logistical, psychosocial, and several other barriers can prevent a patient from receiving optimal cancer treatment [19]. Geographical disparities in treatment pattern owing to limited access to specialized consultation have been reported in the United States [20] and Canada [21,22]. However, South Korea is privileged to have the National Health Insurance that has covered the entire nation since 1989 in addition to a well-established one-day life zone across the country [23]. Consequently, patients with cancer in Korea can receive optimal treatment by visiting special-

ized high-volume centers with minimal delay in a nearly homogenous manner [24]. Therefore, the treatment pattern of pancreatic cancer in Korea may serve as a good proxy of population-based data with minimal barriers in geographical distribution and inefficiencies in logistics or health care delivery systems.

Based on the Korean national data, in this study, the proportion of patients with localized and regional stage EPC undergoing surgical FT increased from 39.3% (period I) to 45.2% (period II). The results are comparable to those reported in the United States, where the proportion increased from 29.6% (stage I, 1995-2004) [25] to 41.1% (stage I-II, 2004-2013) [5]. Although the SEER stage used in this study could not differentiate between patients with resectable, borderline resectable, or locally advanced disease, patients who underwent surgical FT for localized or regional stage EPC had better survival outcomes compared to those with non-surgical FT and NT. This was concordant with a previous study that revealed better prognosis in patients with stage III EPC who underwent unexpected surgical FT compared to those who received NT [10]. In this study, treatment modalities administered later than four months after diagnosis were not recorded; therefore, those who received neoadjuvant treatment with surgery could have been classified as non-surgical FT. Moreover, time to treatment in pancreatic cancer was not considered to be related to poor prognosis [26]. However, our data revealed a prognostic benefit in those who began cancer-directed treatment within the first four months after the diagnosis of pancreatic cancer.

Among the elderly individuals with localized and regional stage EPC, 44.2% of those aged between 60 and 79 years in



**Fig. 3.** Treatment pattern and prognosis of patients with mucinous and cystic adenocarcinomas. (A) Yearly cases and treatment pattern in localized and regional Surveillance, Epidemiology, and End Results (SEER) stage. (B) Overall 5-year relative survival rates according to SEER stage and treatment pattern. FT, first course of treatment; NT, no active treatment; RT, radiotherapy.

Korea underwent surgical FT, which is comparable to that in the United States (46.7%, 2011-2016) [10]. However, this study revealed that the adjusted risk of undergoing surgical FT in septuagenarians was 28.0% lower than that for patients under the age of 70 years. Moreover, 10.9% of octogenarians or older with localized or regional EPC in Korea underwent surgical FT with an adjusted risk of undergoing surgical FT that was 78.8% lower than that for patients under the age of 70 years. The proportion of Korean octogenarians undergoing surgical FT for localized and regional EPC was higher than that in the Netherlands (5.5%, 2005-2013) [27] or Japan (less than 10%, 2010-2018) [28], but lower than that in the United States (20.9%, 2011-2016) [10]. Although this study did not identify treatment modalities administered more

than four months after the diagnosis of EPC, it has been reported that elderly individuals were less likely to undergo chemotherapy or radiation therapy in combination with surgery [5,6,9]. The fact that elderly individuals undergo fewer cancer-directed treatments emphasizes the importance of taking this group more actively into consideration, especially those in their 70s who are no longer considered as being “too old” to receive surgical or non-surgical anticancer treatment. Owing to non-oncologic comorbidities and declining physical function in elderly individuals, there are still debates on finding a balance between surgical morbidity, mortality, and survival benefit in elderly individuals. Previous studies revealed that elderly individuals tended to “not be offered surgery” [25], even after adjusting for their comorbidities



[29]. Moreover, elderly individuals have been under-represented in clinical trials for cancer treatment. Therefore, objective criteria to screen and select elderly patients for appropriate cancer-directed treatment tailored to this age group should be developed in collaboration with gerontologists [30].

This study has several limitations. First, the cancer registry did not capture information on treatment that was administered later than the first 4 months after the diagnosis of EPC. Therefore, the exact proportion of patients receiving multimodality treatment could not be evaluated in this study. However, the Korea National Health Insurance Claim data that has no limitation of timing or sequence of treatment revealed less than 2% of patients received surgical treatment after the first 4 months (unpublished data). Consequently, we assume that the proportion of surgical FT approaches the real-world data, while NT could have been underestimated in this study. Second, treatment information recorded in the registry was insufficient regarding the name of the operation and the regimen and duration of chemotherapy or radiation therapy. Hence, surgical FT did not mandate a pancreatectomy but could have included palliative surgeries. In addition, reasons for not receiving treatment within the first four months could not be identified in this study. Therefore, future studies utilizing National Health Insurance Claim data in combination with the cancer registry database should be conducted to investigate treatment patterns in detail throughout the entire follow-up period of patients with pancreatic cancer. Third, the SEER stage has limited clinical implications in relation to identifying the AJCC stage or applying the concept of resectability for pancreatic cancer. Therefore, future studies should incorporate information on comprehensive staging and evidence used for the clinical staging in the cancer registries. Lastly, the category of ADC<sub>m&c</sub> could have been underestimated in its number compared to clinical entity because it was classified based only on the morphology codes, without any information on the radiological features. In addition, there was a risk of overestimating the proportion of patients receiving surgical FT and the prognosis of ADC<sub>m&c</sub> and ACC because patients with these morphology codes are more likely to have surgical specimen for a specific

histological diagnosis.

In summary, this study provides broader insights to foster the development of more effective cancer control and management policies for the entire population based on a nationwide assessment of pancreatic cancer treatment patterns. The incidence of surgical FT increased from 20.6% to 23.1% in overall EPC patients in Korea from 2006 to 2017. Less than half of patients with localized and regional stage EPC underwent surgical FT. The proportion of those that receiving surgical FT was inversely related to the patients' age; thus, 37.3% of septuagenarians and 10.9% of octogenarians or older underwent surgical FT. Those who underwent surgical FT had a better prognosis compared to those with non-surgical FT or NT, regardless of histology groups. Pancreatic cancer treatment guidelines need to be tailored to elderly individuals, whose proportions are increasing as life expectancy increases globally. Future clinical studies should be more inclusive of elderly individuals to establish evidence that can support the treatment guidelines for this age group.

#### Ethical Statement

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the human research committee of the National Cancer Center, with an exemption of written informed consent because of the retrospective study design (IRB No. NCC2020-0334).

#### Author Contributions

Conceived and designed the analysis: Kang MJ, Won YJ, Kim SW.

Collected the data: Lim J.

Performed the analysis: Lim J, Kang MJ, Won YJ, Kim SW.

Drafting the article, critical revision, and final approval: Kang MJ, Lim J, Han SS, Park HM, Park SJ, Kim SW, Won YJ.

#### Conflicts of Interest

Conflict of interest relevant to this article was not reported.

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