

Pancreatic Cancer Patients Who Cannot Undergo Curative Surgery Live As Much As Patients Over 70 Years Old

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Research

Keywords: pancreatic cancer, geriatric, 70 years

Posted Date: January 21st, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-150867/v1>

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Abstract

INTRODUCTION

Patients over the age of 65 (≥ 65) constitute approximately 54% of newly diagnosed cancers and approximately 70% of cancer-related deaths. These patients aged ≥ 65 years, who form the majority of clinical practice, are represented less in clinical studies than in real life. We designed this retrospective study to examine the treatment and response of patients to pancreatic cancer in patients over 70 years of age.

MATERIAL-METHOD

Our study is a retrospective study that included patients from 5 centers in Turkey. Inclusion criteria were being over the age of 18 years, diagnosed with pancreatic cancer, and with ECOG performance score between 0-2. These patients were divided into two groups according to their age. The classification was made as patients over 70 years of age in the first group (geriatric group) and patients under 70 years of age (<70 age group) in the second group.

RESULTS

Overall survival of the <70 age group was found to be statistically significantly longer (median 10 months vs 9.1 months $p = 0.027$). When the patients who only underwent curative surgery were examined, the survival was statistically significant in favor of the <70 age group (median 20.96 months vs 14.5 months $p = 0.011$). No statistically significant difference was found between the two groups in terms of the overall survival of patients with metastatic diagnosis (median 8.1 months vs 8.4 months $p = 0.182$).

CONCLUSION

The survival of patients with a diagnosis of pancreatic cancer aged 70 and over was shorter than other age groups. While this difference was significant in patients who could undergo surgery at an early stage, it was not found in the metastatic patient group. Prospective larger-scale studies are needed to evaluate the treatment of geriatric patients better.

Introduction

Pancreatic cancer is a fatal disease due to its aggressive nature and the advanced stages of patients when diagnosed. Annually, approximately 60,000 people are diagnosed with pancreatic cancer in the USA (1). The majority of these patients die due to pancreatic cancer. 5-year survival is approximately 7–8% (2–3). The only curative treatment chance is surgery. Survival is poor even in patients who can undergo surgery for curative-intent (4–5). In metastatic disease, there are not many treatment options other than chemotherapy. Survival in locally advanced and metastatic disease does not exceed 12 months even with modern treatments. Although FOLFIRINOX is the chemotherapy regimen that creates the highest survival,

it reached a mean value of 11.3 months (6). This regimen provides the best survival results, but it is very toxic. Not all patients can receive this treatment due to the side effects.

Patients over the age of 65 (≥ 65) constitute approximately 54% of newly diagnosed cancers and approximately 70% of cancer-related deaths (7–8). These patients aged ≥ 65 years, who form the majority of clinical practice, are represented less in clinical studies than in real life (9–13). Therefore, there are fewer studies and data in this patient group. Also, elderly individuals are less likely to receive standard treatment than younger patients (14–18). Toxicity, high amounts of comorbid diseases, clinicians' and patients' preferences affect the treatment of the elderly.

It is difficult to treat pancreatic cancer both in the early period in which surgery can be performed and in the metastatic period. This difficulty increases a little more with age. What changes in treatment and response to treatment with advanced age is an important research area. However, although there are many studies in elderly patients in diseases such as breast cancer and colon cancer, the number of studies on pancreatic cancer is very low. Therefore, we designed this retrospective study to examine the treatment and response of patients to pancreatic cancer in patients over 70 years of age.

Material And Method

Our study is a retrospective study that included patients from 5 centers in Turkey. Patients admitted to these centers between 2012 and 2017 and diagnosed with pancreatic cancer were included in the study. The files of the patients were reviewed retrospectively. Inclusion criteria were being over the age of 18 years, diagnosed with pancreatic cancer, and with ECOG performance score between 0–2. These patients were divided into two groups according to their age. The classification was made as patients over 70 years of age in the first group (geriatric group) and patients under 70 years of age (< 70 age group) in the second group.

The primary endpoint of the study was determined as overall survival. Overall survival was defined as the period from the time of diagnosis to death or the last examination. Also, some factors affecting survival between the two groups were investigated. These were gender, ECOG performance score, primary tumor location, rates of pancreatic surgery performed for curative-intent, and first-line treatment regimens in metastatic patients. While examining these factors, ECOG performance score and primary tumor locations were divided into two groups (ECOG 0–1 vs 2, and head vs tail-body). Our study was conducted as per the Declaration of Helsinki and performed with the approval of the Local Ethics Committee.

All analyses were performed using the SPSS statistical software program package (SPSS version 20.0 for windows). The chi-square test analyzed the differences in the clinical characteristics between the two groups. OS was calculated with the log-rank test. The Kaplan–Meier method was used to draw survival curves. The Cox proportional hazards regression model was used to determine statistically significant variables related to OS. Differences were assumed to be significant when the p-value of less than 0.05.

Results

A total of 363 patients were included in the study. Of these patients, 78 were over 70 years old (geriatric group), and the remaining 285 were under 70 years old (< 70 age group). There were 48 female and 30 male patients in the geriatric group. In the < 70 age group, there were 171 female patients vs 114 male patients. When the gender distributions were compared between the two groups, no significant difference was found ($p = 0.45$).

When the distribution of the ECOG performance score in the two groups was examined, the number of patients with ECOG score of 0–1 in the geriatric group was 56, and the number of patients with ECOG score of 2 was 22. In the < 70 age group, the number of patients with an ECOG score of 0–1 was 245, ECOG score of 2 was 40. When the two groups were compared, the ratio of patients with an ECOG performance score of 2 was statistically significantly higher in the geriatric group ($p = 0.004$).

When the distribution of the primary tumor location in the two groups was examined, the number of patients with pancreatic tumor originating from the head was 54 in the geriatric group, and the body-tail part was 24. In the < 70 age group, the number of patients with pancreatic tumor originating from the head was 174, and the body-tail part was 111. No statistically significant difference was found between the two groups in terms of primary tumor location ($p = 0.116$).

When the rate of performing pancreatic surgery for curative-intent in the two patient groups was considered, the number of patients who underwent curative surgery in the geriatric group was 15 and who did not undergo was 63 patients. In the < 70 age group, the number of patients who underwent curative surgery was 45, and those who did not undergo was 229. No statistical difference was observed between the two groups in terms of the rate of performing pancreatic surgery for curative-intent ($p = 0.539$).

There were 292 patients diagnosed as metastatic. The number of patients who received first-line chemotherapy was 260. Forty-eight patients had received metastatic first-line therapy in the geriatric group. Thirty of these patients received single-agent gemcitabine treatment, while 18 patients were able to receive other regimens. Other regimens were cisplatin-gemcitabine for 16 patients and FOLFIRINOX for two patients. While 71 of 212 patients who received first-line chemotherapy in the < 70 years age group received gemcitabine as a single agent, 141 patients received other regimens. Other regimens were cisplatin-gemcitabine for 99 patients, FOLFIRINOX for 32 patients, FOLFOX for four patients, Xelox for three patients, and Capecitabine for three patients. When the two groups were compared, the rate of patients receiving gemcitabine alone was statistically significantly higher in the geriatric group ($p < 0.000$). The characteristics of the patients are presented in Table-1.

When the overall survival, which was the primary endpoint of our study, was examined, the overall survival of the < 70 age group was found to be statistically significantly longer (median 10 months vs 9.1 months $p = 0.027$) (Figure-1). When the patients who only underwent curative surgery were examined, the survival was statistically significant in favor of the < 70 age group (median 20.96 months vs 14.5 months $p = 0.011$) (Figure-2). No statistically significant difference was found between the two groups in terms of

the overall survival of patients with metastatic diagnosis (median 8.1 months vs 8.4 months $p = 0.182$) (Figure-3).

Discussion

FOLFIRINOX and gemcitabine/nab-paclitaxel took their place in metastatic pancreatic cancer after using the only agent gemcitabine for many years. Two large randomized controlled studies have been conducted in which the contribution of these regimens to survival has been demonstrated. In the first study, the FOLFIRINOX regimen was compared with single-agent gemcitabine. In this study, subgroup analysis was performed by dividing the patients into two groups (< 65 years vs > 65 years) by their age (6). As per this analysis, overall survival was prolonged with FOLFIRINOX treatment in both age groups, but patients under 65 years of age benefited more (hazard ratio 0.61 vs 0.41). In the second study, the gemcitabine/nab-paclitaxel combination was compared with gemcitabine. Patients were also divided into two groups by their age (< 65 years vs > 65 years) in this study. Overall survival of all age groups was prolonged with combination therapy. However, the group under 65 years of age benefited more (hazard ratio 0.65 vs 0.81) (19).

In both large randomized studies, efficacy was less in patients over 65 years of age. Although 70-year of age was determined as the limit in our study, although there was a difference in overall survival when all patients were considered, this difference disappeared when only metastatic patients were evaluated. Even numerically, the overall survival was higher in patients over 70 years old (median 8.1 months vs 8.4 months $p = 0.182$). These results were despite the disadvantage of patient selection between groups. The proportion of patients with an ECOG performance score of 2 was higher in patients over 70 years of age. A second data supporting this is that patients who had gemcitabine alone were also more likely to be in the group over 70 years of age because single-agent gemcitabine was mostly given to patients with low clinical performance scores. As a result, patients with low performance and therefore, overall survival based on these two data were more in the group with patients over 70 years old. Despite this disadvantage, the reason that the overall survival was not statistically different between the two groups may be that patients had less access to effective treatments. Because in our study, metastatic patients did not receive gemcitabine/nab-paclitaxel treatment in the first-line treatment. Also, the number of patients who had FOLFIRINOX was low. When first-line treatments were evaluated, patients mostly took the combination of cisplatin-gemcitabine, whose survival benefit could not be demonstrated in prospective studies (20).

As a result, it was observed in our study that the survival of patients over 70 years old was lower than other patients. However, this difference was due to the patients who had surgery for curative-intent ($p = 0.027$). No survival difference was found among metastatic patients. Therefore, it can be stated that the main difference between these two age groups was surgery. Earlier diagnosis and more widespread use of curative treatments are what needs to be done to bring patients to longer survival rates. As can be seen in our study, as long as the patients are in the metastatic stage, age and the treatments given cannot make a significant difference.

Conclusion

The survival of patients with a diagnosis of pancreatic cancer aged 70 and over was shorter than other age groups. While this difference was significant in patients who could undergo surgery at an early stage, it was not found in the metastatic patient group. Prospective larger-scale studies are needed to evaluate the treatment of geriatric patients better.

Declarations

Funding This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors

Conflicts of interest/Competing interests The authors are in agreement with the content of this manuscript. They also declare that they have no conflict of interest **Availability of data and material** I understand that my manuscript and associated personal data will be shared with Research Square for the delivery of the author dashboard.

Code availability My manuscript has data included as electronic supplementary material

Authors' contributions Atike Pınar Erdoğan, participated in the design of the study, Cengiz Yılmaz and Ahmet Özveren performed statistical analysis, Ferhat Ekinci and Gülcan Bulut helped to draft manuscript. All authors read and approved the final manuscript.

Ethics approval Our study was conducted as per the Declaration of Helsinki and performed with the approval of the Local Ethics Committee

Consent to participate I approve that my manuscript can be published in Journal of Supportive Care in Cancer

Consent for publication I approve that my manuscript can be published in Journal of Supportive Care in Cancer

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Tables

Table-1

	≥70 age group (n:78)	<70 age group (n:285)	Overall (n:363)
Sex	48	171	219
Female	30	114	144
Male			
<i>p</i> =0,45			
ECOG			
0-1	56	245	301
2	22	40	62
<i>p</i> =0,004			
Primary tumor side			
Head	54	174	228
Body-Tail	24	111	135
<i>p</i> =0.116	15	45	60
Curative-intent surgery	48	212	260
<i>p</i> =0.539	30	71	
Metastatic first line therapy	16	99	
Gemcitabine	2	32	
Gemcitabine-Cisplatin			
FOLFIRINOX			
<i>p</i> <0.000			

Figures

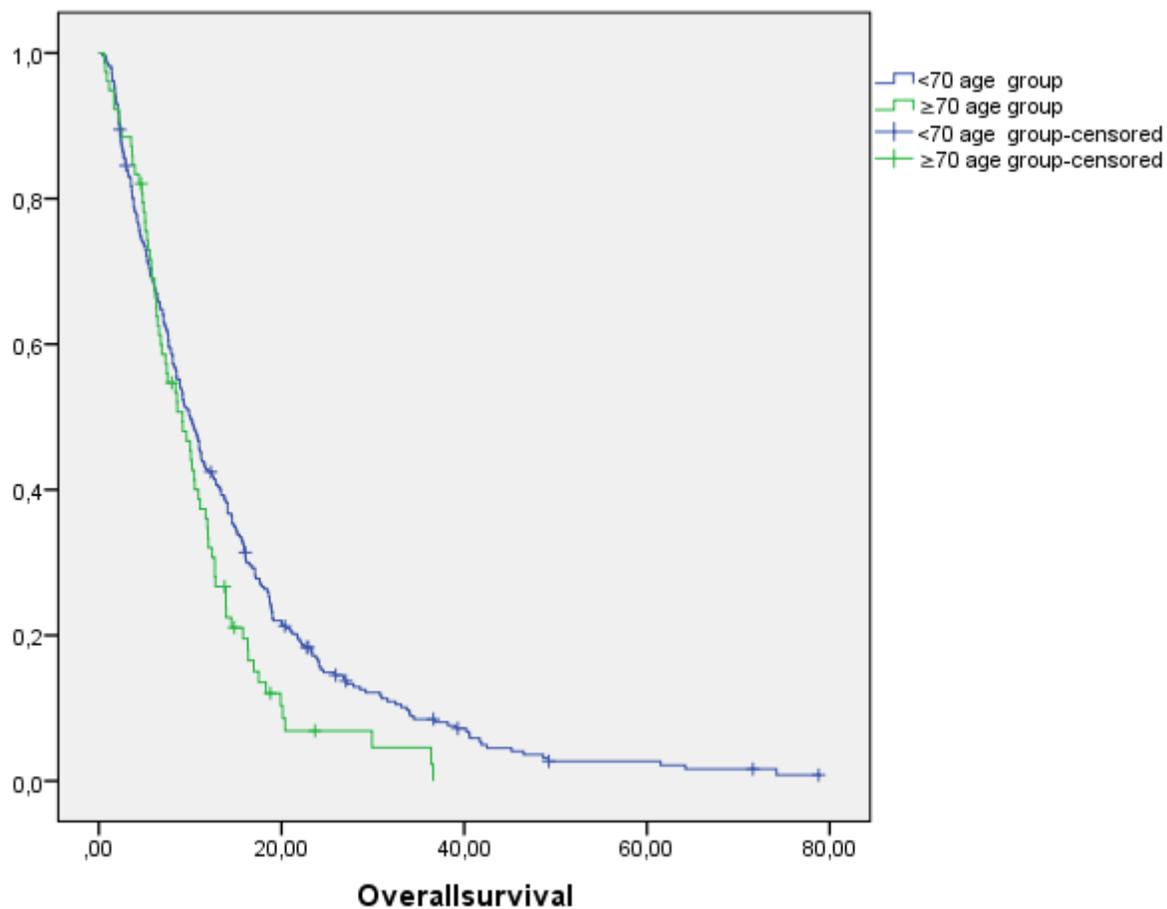


Figure 1

When the overall survival, which was the primary endpoint of our study, was examined, the overall survival of the <70 age group was found to be statistically significantly longer (median 10 months vs 9.1 months $p = 0.027$)

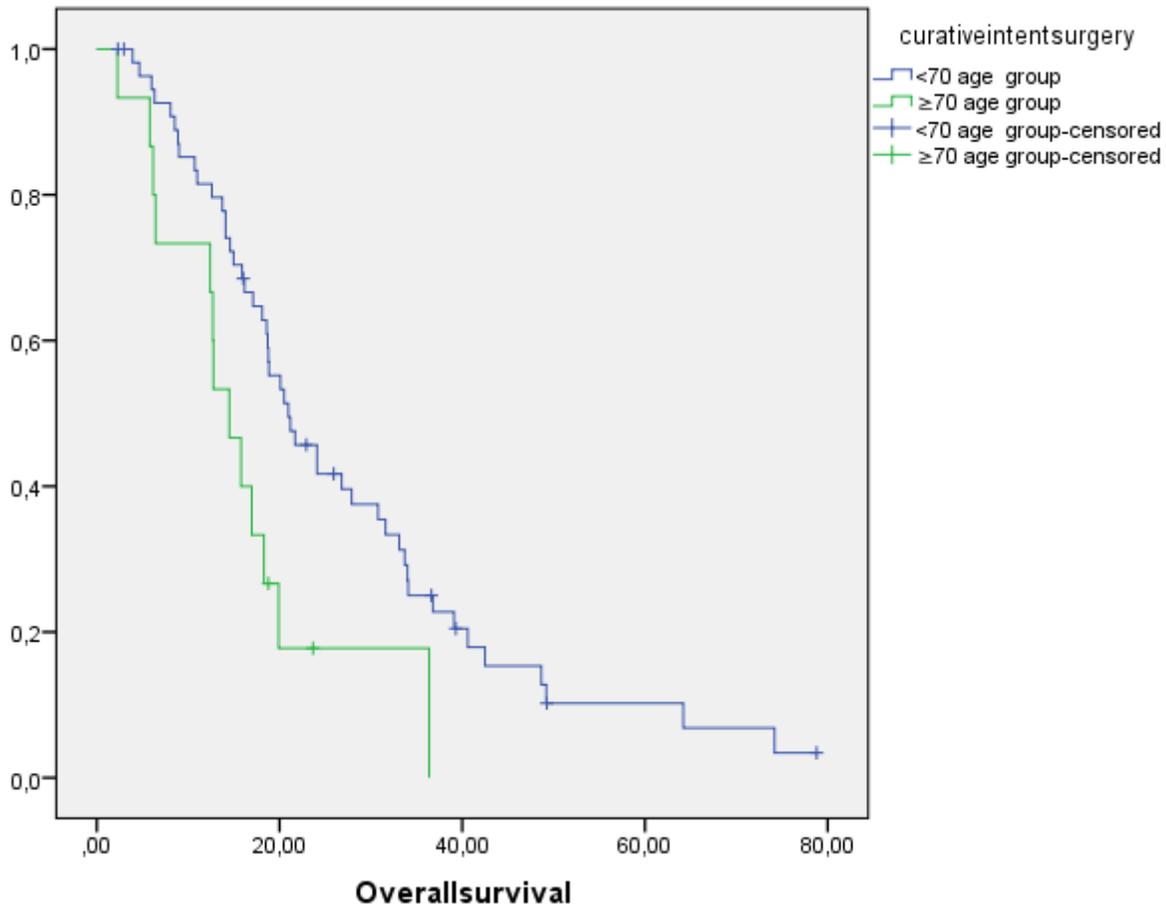


Figure 2

When the patients who only underwent curative surgery were examined, the survival was statistically significant in favor of the <70 age group (median 20.96 months vs 14.5 months p = 0.011)

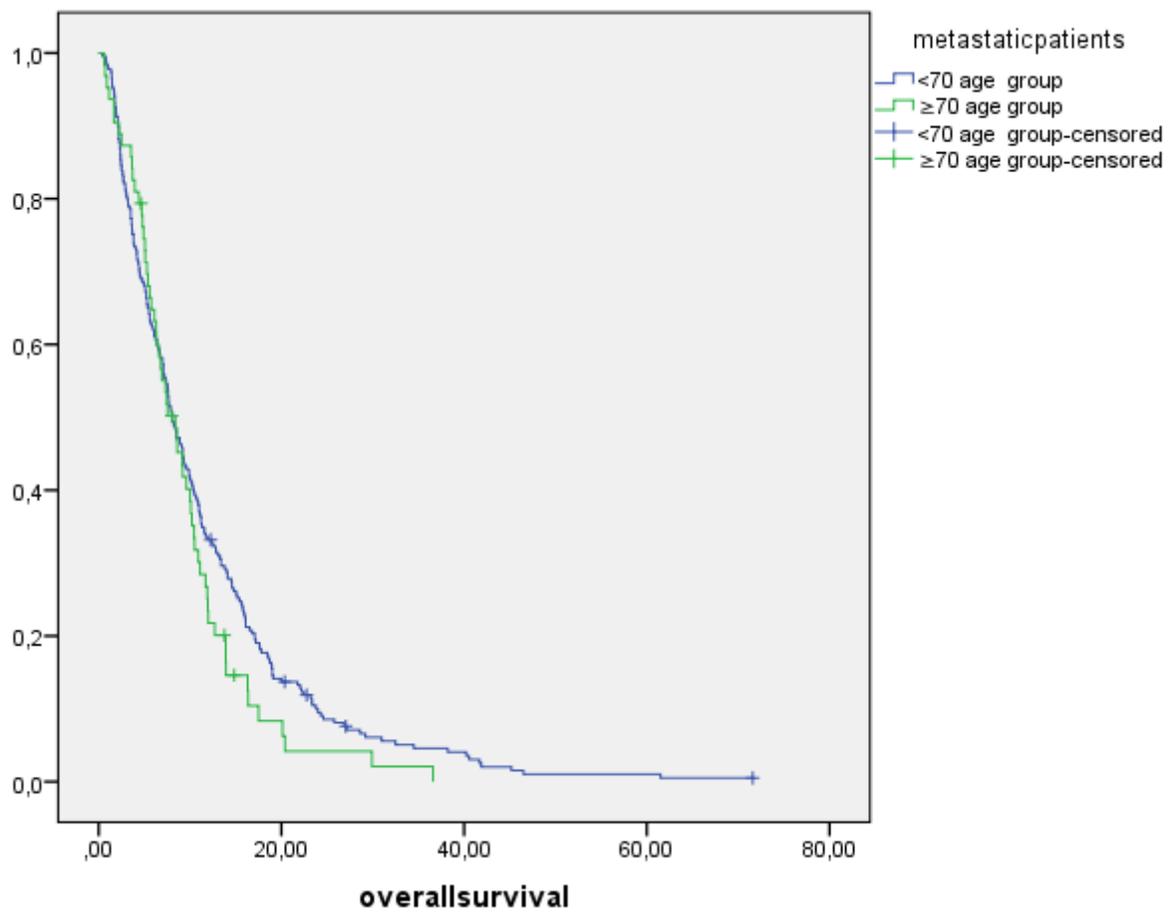


Figure 3

No statistically significant difference was found between the two groups in terms of the overall survival of patients with metastatic diagnosis (median 8.1 months vs 8.4 months $p = 0.182$)