Clinical characteristics and prognostic factors in elderly patients with metastatic pancreatic cancer: a population-based study

**CURRENT STATUS:** POSTED

Tao Lianyuan  
Henan Provincial People's Hospital

Yu Haibo  
Henan Provincial People's Hospital

Dong Yadong  
Henan Provincial People's Hospital

Tian Guanjing  
Henan Provincial People's Hospital

Ren Zhiyuan  
Henan Provincial People's Hospital

Deyu Li  
lideyu19@hotmail.com

Corresponding Author  
Henan provincial people's hospital

**ORCID:** 0000-0002-6615-8316

**DOI:** 10.21203/rs.2.11907/v1

**SUBJECT AREAS**  
Oncology

**KEYWORDS**  
*Elderly patients, Pancreatic cancer, Metastasis, Prognostic factors, Survival*
Abstract

Background: The aim of this study was to evaluate the prognostic factors of elderly patients with metastatic pancreatic cancer (mPC). Methods: Patients diagnosed with mPC between 2004 and 2014 were identified from the Surveillance Epidemiology and End Results (SEER) database. Clinical characteristics and prognostic factors in elderly patients with mPC were examined. Results: A total of 10784 mPC patients between 65 and 80 years old were included and divided into three age groups. Elderly mPC patients differed from younger patients in many aspects, including marital status, race, gender, T stage, N stage, treatment regimen, prognosis, cause of death, and metastatic characteristics (p<0.001). An analysis of the prognostic factors showed that chemotherapy, as the main treatment for the elderly, can significantly improve their prognosis, while surgery can improve the prognosis of patients between 65 and 80 years old. Other factors, including gender, marital status, T stage, and site of metastasis, had different effects on patients in different age groups. Conclusion: Elderly patients with mPC are a special group of individuals whose clinical characteristics and prognostic factors are different from those of younger patients and require special treatment and attention.

Background

As the population ages, the incidence of cancer is growing. It is reported that more than half of cancer patients are diagnosed at an age over 60 years, and more than one-third are over the age of 70 [1]. It is expected that in the year 2030, seventy percent of malignancies and 85 percent of tumor-related deaths will occur in the elderly (over 65 years of age)[2]. Although the overall incidence of pancreatic cancer among all age groups is only 11.7 percent, it is 66.4 percent in patients over 65 years old and 91.1 percent in patients over 80 years old[3]. As a highly malignant tumor, pancreatic cancer is
the fourth leading cause of tumor-related death and is expected to become the second leading cause by 2030 in the US [4, 5]. Its poor prognosis is due to difficulties in early diagnosis; therefore, most patients are diagnosed at an advanced stage accompanied by metastasis (stage IV)[3].

The association between aging and cancer has been widely recognized, as the elderly’s internal environment (chronic inflammation and immune system dysfunction) is more likely to induce cancer under the stimulation of carcinogens[6, 7]. Moreover, the immune system plays a key role in the development of pancreatic cancer[8]. Therefore, elderly patients represent a distinct subgroup, and more targeted clinical management plans are needed for these patients. At present, surgery is not recommended for pancreatic cancer patients with distant metastases, especially the elderly, which are more likely to receive chemotherapy, radiotherapy and other nonsurgical treatments[3, 9].

Due to the aging population, it is not difficult to predict that the number of elderly patients with metastatic pancreatic cancer (mPC) will increase further. However, the clinical management of this group of patients is still lacks effective attention; therefore, the aim of this study was to explore the clinical characteristics and prognostic factors in elderly patients with mPC.

Methods

Patient cohort

The data examined in the present study were retrieved from the SEER-18 registry of the National Cancer Institute through SEER*Stat Software Version 8.3.4. As a publicly available database, the SEER database contains deidentified data; therefore, this study did not need approval from the institutional review board. Data from patients with a primary site of ‘pancreas’ between January 1, 2004 and December 31, 2014, with
American Joint Committee on Cancer (AJCC) stage (6th edition) IV and with International Classification of Diseases for Oncology, Third Edition (ICD-O-3) codes 8010, 8020, 8140, 8141 and 8144 were collected, and those who lacked survival data were excluded.

Data collection

Information collected from each patient included the following: year of diagnosis, age, race, gender, marital status, primary site of the tumor, T stage, N stage, M stage, surgical resection of the primary site, chemotherapy recode, cause-specific death classification, survival time, and vital status. Cancer-specific survival (CSS) and OS (overall survival) were defined as the time between diagnosis and death from mPC and between diagnosis and death from any cause, respectively. Detailed information on systematic treatment is not provided in the SEER database.

Statistical analysis

The differences in clinical and demographic features between different patient groups were compared with the chi-square test. The Kaplan-Meier method with the log-rank test was used to examine CSS and OS. A Cox proportional hazards model was applied for multivariable survival analyses of CSS and OS. P<0.05 was considered statistically significant. IBM SPSS Statistics 22.0 (IBM, Armonk, NY, USA) was applied in all statistical analyses.

Results

Patient characteristics

The clinical characteristics of the mPC patients stratified by age are presented in Table 1. A total of 10,784 patients were enrolled in this study, including 3681(34.1%) under 65 years old, 4415(40.9%) between 65 and 80 years old, and 2688(24.9%) over 80 years old. Most patients were White (N = 8560, 79.4%), and male patients accounted for 51.7% (N =
There were 551 patients (5.1%) treated surgically, and 3883 (36%) received chemotherapy. Approximately half of the patients were married (N = 5329, 49.4%). The collection of metastatic location data for the SEER database began in 2010; thus, information about the detailed metastatic sites was derived from 2010 to 2014, and 5463 patients were included.

On the one hand, compared with mPC patients under 65 years old, a larger proportion of mPC patients between 65 and 80 years old were married, White, female, with T1 and T2 stage, and with N0 stage disease (all P < 0.001) and were less likely to be treated with surgery, radiation and chemotherapy. Although the liver is the most common organ that develops metastasis, the elderly have a greater chance of developing lung metastasis compared to younger patients and are less likely to develop metastasis in the liver, brain and bone (all P < 0.001). Detailed information is shown in Table 1.

On the other hand, there was a large proportion of mPC patients older than 80 years who were unmarried (which is adverse to mPC patients between the ages of 65 and 80 years), White, female, with T1 and T2 stage, and with N0 stage disease (all P < 0.001) and were less likely to be treated with surgery, radiation and chemotherapy. Moreover, the elderly may face more difficulties when identifying metastatic sites, which include the liver, lung, brain and bone (all of these sites have a lower diagnosis rate in elderly patients than in younger patients; all P < 0.001, Table 1).

The analysis also indicated that elderly mPC patients had a higher mortality rate at the follow-up deadline but a lower tumor-specific mortality rate than younger patients (all P < 0.001). Of 10784 patients, mortality occurred in 10189 (94.5% of 10784) patients at the end of follow-up. In addition, 8680 (80.5% of 10784) patients died due to pancreatic cancer. Regarding CSS, cancer-specific mortality was 82.8% in the under 65-year-old group, 80.8% in the 65- to 80-year-old group, and 76.8% in the over 80-year-old group.
Concerning OS, mortality accounted for 91.7%, 95.2% and 97.1% in the three age groups, respectively (Table 1).

Prognostic factors of mPC patients between 65 and 80 years old.

Multivariate Cox regression analysis revealed that surgical resection was associated with improved (HR = 0.70, 95% CI = 0.57–0.85) and CSS (HR = 0.72, 95% CI = 0.58–0.90), and chemotherapy was also related to improved (HR = 0.45, 95% CI = 0.41–0.49) and CSS (HR = 0.43, 95% CI = 0.39–0.48) (Table 2). The correlation of chemotherapy to OS and CCS with the log-rank test was also revealed in the survival curve (Figure 1). Moreover, the results demonstrated that factors associated with poor OS included being unmarried, T0 stage and lung metastasis. In addition, poor CSS was inclined to occur in patients with the following characteristics: T0 stage and lung metastasis. The detailed patient characteristics are shown in Table 2.

Prognostic factors of mPC patients over 80 years old.

Multivariate Cox regression analysis indicated that chemotherapy was associated with improved (HR = 0.45, 95% CI = 0.41–0.49) and CSS (HR = 0.43, 95% CI = 0.39–0.48), and radiation showed a positive effect on OS (HR = 0.64, 95% CI = 0.45–0.92) but not CCS (Table 3). The relation of chemotherapy and surgical resection to OS and CCS with the log-rank test was also revealed in the survival curve (Figure 2). Moreover, the analysis indicated that factors associated with poor OS included male gender and liver metastasis (Table 3).

Discussion

According to the characteristics of the age group reported previously[3], the elderly patients in this study were divided into the 65- to 80-year-old group and the over 80-year-old group. The statistical results showed that the elderly accounted for the majority of all
mPC patients (65.9%), especially those between 65 and 80 years old (40.9%). A comparison of the clinical characteristics of patients of different ages revealed that old age and White race, which may be related to a longer life span, as most Whites hold a higher level of living standards and have more access to medical services) were favorable prognostic factors.

The results also showed that old age and female sex were favorable prognostic factors for mPC patients over 80 years old. Both of these factors can be explained: females pay more attention to their health and have a better lifestyle than males and therefore live longer than males regardless of the development of mPC. In addition, the marriage rate of patients between 65 and 80 years old was the highest (54.3%), while the marriage rate of patients between 65 and 80 years old declined sharply (37.1%), which may be related to the higher death rate of their marriage partner at their age. Further prognostic analysis also indicated that marriage is a favorable prognostic factor for mPC patients between 65 and 80 years old, which agrees with many previous studies[10-13]. Therefore, elderly patients who do not have family members should be given more attention.

Interestingly, although the stage of many patients is unknown, there was an increase in the proportion of patients with T1 and T2 stage disease and a decrease in the proportion of patients with lymph node negative stage (N0) disease in elderly patients ranging in age between 65 and 80 years and above compared to younger patients. As the TNM stages of many patients are unknown, we cannot provide a reasonable explanation, which needs further research to confirm. Surprisingly, prognostic factor analysis suggested that patients with T0 stage disease between 65 and 80 years old had a better prognosis than those with Tn stage disease. This may be because pancreatic cancer has metastasized at an earlier T stage, indicating that the tumor has a stronger ability to invade and metastasize; therefore, the tumor is more malignant, and the prognosis is correspondingly
worse. This result is consistent with those from a previous study[12].

Generally, the older the patient is, the worse his/her health tends to be, and the more serious the basic diseases, the more likely he/she is to die from the basic disease[3, 9], which was confirmed by our results. The present study showed that the overall mortality rate was higher in older patients; however, the tumor-specific mortality rate decreased gradually with increasing age. Such a result suggests that attention should be paid not only to the treatment of tumors in aging patients, especially those over 80 years old, but also to their systemic conditions and basic diseases.

Moreover, the analysis of the metastatic sites (collected from 2010 to 2014) suggested that the sites most likely to metastasize, in order, are the liver, lung, bone and brain. The comparison among the three age groups suggested that with the increase in age, except for the increase in lung metastasis between 65 and 80 years old, the metastasis of all sites showed a decreasing trend. This may be because tumors in the elderly are often less aggressive than those in the young. The liver and lungs are vital organs in the human body. Once metastasis occurs in these sites, patients may experience a terrible prognosis. Similarly, the present analysis also indicated that lung metastasis, which is related to both OS and CCS, is a poor prognostic factor for patients between 65 and 80 years old, while liver metastasis is related to OS in those over 80 years old.

Data on treatment showed that the older the patient is, the less likely he or she is to receive treatment, including surgery, radiation and chemotherapy. By contrast, chemotherapy is the most common form of treatment, followed by surgery, and radiation is minimal. Further analysis suggested that the greatest therapeutic benefit for patients between 65 and 80 years old and older is chemotherapy. Chemotherapy has been proven to be the primary treatment for mPC[14][15-17]. Gemcitabine alone or in combination with other chemotherapeutic drugs and the FOLFIRINOX regimen (leucovorin, fluorouracil,
irinotecan, and oxaliplatin) are recommended according to the performance status as well as the comorbidity profile of the patient\textsuperscript{[18]}. Surgical treatment is not suggested for mPC, especially for elderly patients, according to clinical guidelines. However, it was demonstrated to improve the prognosis of mPC patients [12]. The present analysis also indicated that patients between 65 and 80 years old may still benefit from surgery but not those over 80 years old, which may be because they are too old and in poor health to tolerate surgery. Metastatic cancers originating from renal cells\textsuperscript{[19]}, the colorectum\textsuperscript{[20]}, and prostate\textsuperscript{[21, 22]} have been proven to benefit from local treatment of the primary tumor. Two recent large-scale population-based studies demonstrated that survival can be prolonged through local treatment for metastatic prostate cancer\textsuperscript{[22, 23]}. All the above information suggests the clinical value of surgical treatment in the management of mPC. Although radiotherapy has a positive effect on OS among those between 65 and 80 years old, it fails to show a correlation with CCS, which also shows no association with death in patients over 80 years old. Possible reasons for this finding may be that pancreatic cancer is less sensitive to radiotherapy or the intolerance to radiotherapy in the elderly\textsuperscript{[15, 24]}. The present study utilized a population-based cohort, which has the advantage of minimizing selection bias in the comparison. However, there are still some limitations to our analysis, such as the relatively uncomplete clinical information of many patients. For example, data about the sites of metastasis were collected only from 2010 to 2014, and previous patients lacked relevant data. A large proportion of data regarding T stage, N stage, or metastasis sites were recorded as not otherwise specified or unknown in the SEER database. Because of these limitations, particularly because the specific chemotherapy regimen used was not available, further evaluation of treatment in elderly patients is hindered, and we cannot rule out an alternative explanation for some of our
findings. The remaining questions could be answered in future studies with more detailed information regarding clinical characteristics and treatment protocols.

Conclusion

Our results show that elderly patients with mPC are a special group of patients whose clinical characteristics and prognostic factors are different from those of young patients and require special treatment and attention. Chemotherapy can improve the prognosis of elderly patients and is the most reasonable treatment.

Abbreviations

CI: Confidence interval
CSS: Cancer-specific survival
HR: Hazard ratio
OS: Overall survival
mPC: Metastatic pancreatic cancer
SEER: Surveillance, Epidemiology, and End Results
AJCC: American Joint Committee on Cancer

Declarations

Acknowledgements

The authors would like to thank SEER for open access to the database.

Funding

This study was supported by a grant from the Doctoral Venture Capital fund of Henan Provincial People’s Hospital (No. ZC20180077) and the Special Project of Henan Provincial Key Research, Development and Promotion (Science and Technology) (No.192102310119). These funds provided support for personnel and data collection.
Availability of data and materials

Not applicable.

Authors’ contributions

LD and TL conceived and designed the study; TL, LD, and YH performed the analysis and interpretation of data; TL and LD wrote the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The current study was approved by the Clinical Ethics Committee of Henan Provincial People’s Hospital. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from individual participants included in the study. All authors signed authorization forms and received permission from the SEER database to access and use the dataset.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Siegel RL, Miller KD, Jemal A: Cancer statistics, 2019. CA Cancer J Clin 2019, 69(1):7–34.

2. Yancik R, Ries LA: Cancer in older persons: an international issue in an aging world. Semin Oncol 2004, 31(2):128–136.

3. Higuera O, Ghanem I, Nasimi R, Prieto I, Koren L, Feliu J: Management of pancreatic cancer in the elderly. World J Gastroenterol 2016, 22(2):764–775.
4. Siegel RL, Miller KD, Jemal A: *Cancer Statistics, 2017. CA: a cancer journal for clinicians* 2017.

5. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM: *Projecting Cancer Incidence and Deaths to 2030: The Unexpected Burden of Thyroid, Liver, and Pancreas Cancers in the United States. Cancer research* 2014, 74(11):2913–2921.

6. Grimes A, Chandra SB: *Significance of cellular senescence in aging and cancer. Cancer Res Treat* 2009, 41(4):187–195.

7. Lasry A, Ben-Neriah Y: *Senescence-associated inflammatory responses: aging and cancer perspectives. Trends Immunol* 2015, 36(4):217–228.

8. Lianyuan T, Dianrong X, Chunhui Y, Zhaolai M, Bin J: *The predictive value and role of stromal tumor-infiltrating lymphocytes in pancreatic ductal adenocarcinoma (PDAC). Cancer Biol Ther* 2018, 19(4):296–305.

9. Gajda M, Kenig J: *Treatment outcomes of pancreatic cancer in the elderly - literature review. Folia Med Cracov* 2018, 58(3):49–66.

10. Baine M, Sahak F, Lin C, Chakraborty S, Lyden E, Batra SK: *Marital status and survival in pancreatic cancer patients: a SEER based analysis. PLoS One* 2011, 6(6):e21052.

11. Tao L, Xiu D, Sadula A, Ye C, Chen Q, Wang H, Zhang Z, Zhang L, Tao M, Yuan C: *Surgical resection of primary tumor improves survival of pancreatic neuroendocrine tumor with liver metastases. Oncotarget* 2017, 8(45):79785–79792.

12. Tao L, Yuan C, Ma Z, Jiang B, Xiu D: *Surgical resection of a primary tumor improves survival of metastatic pancreatic cancer: a population-based study. Cancer Manag Res* 2017, 9:471–479.

13. Wang XD, Qian JJ, Bai DS, Li ZN, Jiang GQ, Yao J: *Marital status independently predicts pancreatic cancer survival in patients treated with surgical resection: an analysis of the SEER database. Oncotarget* 2016, 7(17):24880–24887.
14. Kamisawa T, Wood LD, Itoi T, Takaori K: Pancreatic cancer. Lancet 2016, 388(10039):73-85.

15. Kuroda T, Kumagi T, Yokota T, Azemoto N, Hasebe A, Seike H, Nishiyama M, Inada N, Shibata N, Miyata H et al: Efficacy of chemotherapy in elderly patients with unresectable pancreatic cancer: a multicenter review of 895 patients. BMC Gastroenterol 2017, 17(1):66.

16. Macchini M, Chiaravalli M, Zanon S, Peretti U, Mazza E, Gianni L, Reni M: Chemotherapy in elderly patients with pancreatic cancer: Efficacy, feasibility and future perspectives. Cancer Treat Rev 2019, 72:1-6.

17. Shin SH, Park Y, Hwang DW, Song KB, Lee JH, Kwon J, Yoo C, Alshammary S, Kim SC: Prognostic Value of Adjuvant Chemotherapy Following Pancreat icoduodenectomy in Elderly Patients With Pancreatic Cancer. Anticancer Res 2019, 39(2):1005-1012.

18. Sohal DPS, Mangu PB, Khorana AA, Shah MA, Philip PA, O’Reilly EM, Uronis HE, Ramanathan RK, Crane CH, Engebretson A et al: Metastatic Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2016, 34(23):2784-+.

19. Flanigan RC, Salmon SE, Blumenstein BA, Bearman SI, Roy V, McGrath PC, Caton JR, Munshi N, Crawford ED: Nephrectomy followed by interferon alfa–2b compared with interferon alfa–2b alone for metastatic renal-cell cancer. N Engl J Med 2001, 345(23):1655-1659.

20. Temple LKF, Hsieh L, Wong WD, Saltz L, Schrag D: Use of surgery among elderly patients with stage IV colorectal cancer. J Clin Oncol 2004, 22(17):3475-3484.

21. Fossati N, Trinh QD, Sammon J, Sood A, Larcher A, Sun M, Karakiewicz P, Guazzoni G, Montorsi F, Briganti A et al: Identifying optimal candidates for local treatment of the primary tumor among patients diagnosed with metastatic prostate cancer: a SEER-based study. Eur Urol 2015, 67(1):3-6.
22.Culp SH, Schellhammer PF, Williams MB: *Might Men Diagnosed with Metastatic Prostate Cancer Benefit from Definitive Treatment of the Primary Tumor? A SEER-Based Study.* *Eur Urol* 2014, 65(6):1058-1066.

23.Rusthoven CG, Jones BL, Flaig TW, Crawford ED, Koshy M, Sher DJ, Mahmood U, Chen RC, Chapin BF, Kavanagh BD et al: *Improved Survival With Prostate Radiation in Addition to Androgen Deprivation Therapy for Men With Newly Diagnosed Metastatic Prostate Cancer.* *Journal of clinical oncology: official journal of the American Society of Clinical Oncology* 2016, 34(24):2835-2842.

24.Frakes J, Mellon EA, Springett GM, Hodul P, Malafa MP, Fulp WJ, Zhao X, Hoffe SE, Shridhar R, Meredith KL: *Outcomes of adjuvant radiotherapy and lymph node resection in elderly patients with pancreatic cancer treated with surgery and chemotherapy.* *J Gastrointest Oncol* 2017, 8(5):758-765.

Tables

Table 1. Comparison of characteristics of metastatic pancreatic cancer patients in different age groups.

| Age group | All patients | Age65 | Age ≥65 and <80 | Age ≥80 | P value |
|-----------|--------------|-------|-----------------|--------|---------|
| Features of Patients (2004-2014) | 10784 | 3681(100%) | 4415(100%) | 2688(100%) |       |
| Marital status | Others | 5455 | 1748(47.5%) | 2016(45.7%) | 1691(62.9%) | <0.001 |
| | Married | 5329 | 1933(52.5%) | 2399(54.3%) | 997(37.1%) |       |
| Race | Others | 2224 | 902(40.5%) | 885(20%) | 437(16.3%) | <0.001 |
| | White | 8560 | 2779(32.5%) | 3530(40%) | 2251(26.4%) |       |
| Sex | Male | 5573 | 2191(40.8%) | 2288(41.6%) | 1094(40.7%) | <0.001 |
| | Female | 5211 | 1490(40.5%) | 2127(41.8%) | 1594(41.8%) |       |
| T stage | T0 | 515 | 181(4.9%) | 218(4.9%) | 116(4.3%) | <0.001 |
| | T1 | 103 | 32(0.9%) | 47(1.1%) | 24(0.9%) |       |
| | T2 | 766 | 248(6.7%) | 316(7.2%) | 202(7.5%) |       |
| | T3 | 1032 | 390(10.6%) | 422(9.6%) | 220(8.2%) |       |
| | T4 | 1204 | 472(12.8%) | 488(11.1%) | 244(9.1%) |       |
| | Tx | 7164 | 2358(64.1%) | 2924(66.2%) | 1882(70%) |       |
| Variable                  | N0       | N1       | Nx       | P-value |
|---------------------------|----------|----------|----------|---------|
| N stage                   | 3625     | 2125     | 5034     | <0.001  |
| Surgery                   | 10123    | 551      | 110      |         |
| Radiation                 | 10350    | 434      | 110      | <0.001  |
| Chemotherapy              | 6901     | 3883     | 2104     | <0.001  |
| Overall survival          | 595      | 305      | 212      | <0.001  |
| Cancer-specific survival  | 10189    | 3883     | 2104     | <0.001  |
| Metastases of Patients    | 8680     | 6901     | 5463     |         |
| Bone                      | 4318     | 480      | 665      |         |
| Brain                     | 4702     | 67       | 694      |         |
| Liver                     | 1217     | 3892     | 354      |         |
| Lung                      | 3627     | 1165     | 671      |         |

Table 2 Multivariate analysis of cancer-specific survival (CSS) and overall survival (OS) in metastatic pancreatic cancer with age above 65 and under 80 years old.
| Variables          | Overall survival | Cancer-specific survival |
|--------------------|------------------|-------------------------|
|                    | HR (95%CI)       | P value                 |
|ewise               | HR (95%CI)       |                         |
| Marital status     |                  |                         |
| Others             | 1 (Referent)     |                         |
| Married            | 0.90 (0.83-0.99) | 0.027                   | 0.95 (0.86-1.06) |
| Race               |                  |                         |
| Others             | 1 (Referent)     |                         |
| White              | 0.96 (0.86-1.07) | 0.467                   | 0.94 (0.83-1.07) |
| Sex                |                  |                         |
| Female             | 0.96 (0.88-1.05) | 0.338                   | 1.05 (0.95-1.17) |
| T stage            |                  |                         |
| T0                 | 1 (Referent)     |                         |
| T1                 | 0.60 (0.40-0.89) | 0.012                   | 0.57 (0.35-0.93) |
| T2                 | 0.74 (0.59-0.95) | 0.015                   | 0.76 (0.57-1.00) |
| T3                 | 0.85 (0.67-1.08) | 0.183                   | 0.85 (0.64-1.12) |
| T4                 | 0.94 (0.75-1.18) | 0.573                   | 0.98 (0.75-1.28) |
| Tx                 | 0.81 (0.66-0.99) | 0.036                   | 0.81 (0.64-1.03) |
| N stage            |                  |                         |
| N0                 | 1 (Referent)     |                         |
| N1                 | 0.96 (0.85-1.08) | 0.496                   | 0.96 (0.83-1.11) |
| Nx                 | 0.99 (0.89-1.10) | 0.817                   | 1.05 (0.93-1.19) |
| Surgery            |                  |                         |
| No                 | 1 (Referent)     |                         |
| Yes                | 0.70 (0.57-0.85) | <0.001                  | 0.72 (0.58-0.90) |
| Unknown            | 1.18 (0.76-1.84) | 0.466                   | 1.34 (0.83-2.17) |
| Radiation          |                  |                         |
| No                 | 1 (Referent)     |                         |
| Yes                | 0.88 (0.69-1.11) | 0.282                   | 0.83 (0.62-1.10) |
| Unknown            | 1.18 (0.76-1.84) | 0.466                   | 1.34 (0.83-2.17) |
| Chemotherapy       |                  |                         |
| No                 | 1 (Referent)     |                         |
| Yes                | 0.45 (0.41-0.49) | <0.001                  | 0.43 (0.39-0.48) |
| Bone metastasis    |                  |                         |
| No                 | 1 (Referent)     |                         |
| Yes                | 1.05 (0.88-1.24) | 0.592                   | 1.02 (0.83-1.25) |
| Unknown            | 1.12 (0.77-1.62) | 0.560                   | 1.03 (0.67-1.58) |
| Brain metastasis   |                  |                         |
| No                 | 1 (Referent)     |                         |
| Yes                | 1.27 (0.85-1.88) | 0.241                   | 1.26 (0.79-2.01) |
| Unknown            | 0.96 (0.66-1.41) | 0.848                   | 0.99 (0.64-1.52) |
| Liver metastasis   |                  |                         |
| No                 | 1 (Referent)     |                         |
| Yes                | 1.09 (0.98-1.22) | 0.130                   | 1.10 (0.96-1.25) |
| Unknown            | 1.05 (0.82-1.36) | 0.692                   | 1.03 (0.76-1.38) |
| Lung metastasis    |                  |                         |
| No                 | 1 (Referent)     |                         |
| Yes                | 1.18 (1.05-1.32) | 0.004                   | 1.21 (1.06-1.38) |
| Unknown            | 0.93 (0.75-1.15) | 0.486                   | 1.02 (0.80-1.30) |
Table 3 Multivariate analysis of cancer-specific survival (CSS) and overall survival (OS) in metastatic pancreatic cancer with age above 80 years old.
| Variables          | Overall survival | Cancer-specific survival |
|-------------------|------------------|--------------------------|
|                   | HR (95%CI)       | P value                  | HR (95%CI)       | P value |
| Marital status    |                  |                          |                  |         |
| Married           | 0.95 (0.84-1.07) | 0.364                    | 1.02 (0.88-1.18) | 0.83    |
| Others            | 1 (Referent)     |                          | 1 (Referent)     |         |
| Race              |                  |                          |                  |         |
| White             | 1.08 (0.93-1.25) | 0.304                    | 1.01 (0.85-1.21) | 0.90    |
| Others            | 1 (Referent)     |                          | 1 (Referent)     |         |
| Sex               |                  |                          |                  |         |
| Female            | 0.88 (0.79-0.99) | 0.037                    | 1.05 (0.91-1.22) | 0.47    |
| Male              | 1 (Referent)     |                          | 1 (Referent)     |         |
| T stage           |                  |                          |                  |         |
| T0                | 1 (Referent)     |                          | 1 (Referent)     |         |
| T1                | 0.75 (0.40-1.38) | 0.354                    | 0.73 (0.33-1.63) | 0.44    |
| T2                | 1.08 (0.81-1.45) | 0.593                    | 1.18 (0.81-1.72) | 0.38    |
| T3                | 0.93 (0.69-1.25) | 0.638                    | 1.04 (0.71-1.52) | 0.84    |
| T4                | 1.03 (0.76-1.38) | 0.864                    | 1.14 (0.78-1.66) | 0.50    |
| Tx                | 1.06 (0.82-1.36) | 0.674                    | 1.18 (0.85-1.63) | 0.33    |
| N stage           |                  |                          |                  |         |
| N0                | 1 (Referent)     |                          | 1 (Referent)     |         |
| N1                | 1.06 (0.9-1.240) | 0.47                     | 1.2 (0.99-1.46)  | 0.06    |
| Nx                | 0.94 (0.82-1.07) | 0.326                    | 1.01 (0.86-1.19) | 0.91    |
| Surgery           |                  |                          |                  |         |
| No                | 1 (Referent)     |                          | 1 (Referent)     |         |
| Yes               | 0.78 (0.58-1.05) | 0.101                    | 0.85 (0.60-1.21) | 0.37    |
| Unknown           | 0.88 (0.59-1.32) | 0.545                    | 0.96 (0.61-1.5)  | 0.84    |
| Radiation         |                  |                          |                  |         |
| No                | 1 (Referent)     |                          | 1 (Referent)     |         |
| Yes               | 0.64 (0.45-0.92) | 0.014                    | 0.84 (0.56-1.25) | 0.38    |
| Unknown           | 0.88 (0.59-1.32) | 0.545                    | 0.96 (0.61-1.5)  | 0.84    |
| Chemotherapy      |                  |                          |                  |         |
| No                | 1 (Referent)     |                          | 1 (Referent)     |         |
| Yes               | 0.48 (0.41-0.56) | <0.001                   | 0.43 (0.35-0.53) | <0.0    |
| Bone metastasis   |                  |                          |                  |         |
| No                | 1 (Referent)     |                          | 1 (Referent)     |         |
| Yes               | 0.98 (0.77-1.24) | 0.86                     | 0.76 (0.56-1.05) | 0.09    |
| Unknown           | 1.13 (0.77-1.66) | 0.525                    | 1.07 (0.68-1.70) | 0.76    |
| Brain metastasis  |                  |                          |                  |         |
| No                | 1 (Referent)     |                          | 1 (Referent)     |         |
| Yes               | 1.42 (0.79-2.58) | 0.243                    | 1.48 (0.72-3.04) | 0.28    |
| Unknown           | 1.11 (0.76-1.62) | 0.581                    | 1.28 (0.82-2.00) | 0.28    |
| Liver metastasis  |                  |                          |                  |         |
| No                | 1 (Referent)     |                          | 1 (Referent)     |         |
| Yes               | 1.22 (1.07-1.40) | 0.003                    | 1.17 (1.00-1.38) | 0.05    |
| Unknown           | 0.99 (0.77-1.28) | 0.934                    | 1.04 (0.77-1.40) | 0.81    |
| Lung metastasis   |                  |                          |                  |         |
| No                | 1 (Referent)     |                          | 1 (Referent)     |         |
| Yes               | 1.00 (0.87-1.16) | 0.992                    | 1.00 (0.84-1.19) | 0.99    |
| Unknown           | 0.84 (0.64-1.10) | 0.201                    | 0.79 (0.58-1.10) | 0.16    |
Figures

Figure 1

Survival curves of chemotherapy in elderly mPC patients between 65 and 80 years old with the log-rank test: (A) OS (p<0.001) and (B) CCS (p<0.001).
Figure 2

Survival curves of chemotherapy in elderly mPC patients over 80 years old with the log-rank test: (A) OS ($p<0.001$) and (B) CCS ($p<0.001$); surgical resection: (C) OS ($p<0.001$) and (D) CCS ($p<0.001$).