Treatment Patterns, Toxicity, and Outcomes of Older Adults With Advanced Pancreatic Cancer Receiving First-line Palliative Chemotherapy

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Objectives: Advanced pancreatic cancer (APC) disproportionately impacts older adults. Randomized trials demonstrate improved overall survival (OS) with combination chemotherapy including 5-fluorouracil, irinotecan, leucovorin, and oxaliplatin (FOLFIRINOX) or *nab*-paclitaxel and gemcitabine compared with gemcitabine alone, but with increased toxicity. Older adults are at increased risk of side effects from chemotherapy. The aim of this study was to assess the efficacy and toxicity of chemotherapy in older adults with APC.

Methods: Patients diagnosed with APC from 2011 to 2016 were identified using the Manitoba Cancer Registry. Patient and treatment characteristics, toxicity, and outcomes of patients 65 years of age and above treated with palliative chemotherapy were compared by treatment regimen. OS was assessed using the Kaplan-Meier method. A Cox regression was used to identify independent predictors of OS.

Results: A total of 87 patients aged 65 years and above received palliative chemotherapy: 52 (59.7%) FOLFIRINOX, 21 (24.1%) *nab*-paclitaxel and gemcitabine, and 14 (16.1%) gemcitabine, with a median age of 69 (65 to 84), 75 (65 to 88), and 73 (67 to 82), Eastern Cooperative Oncology Group (ECOG) performance status difference in hematologic toxicity between regimens ($P = 0.807$). An increase in nonhematologic toxicity was seen with FOLFIRINOX ($P < 0.001$), specifically neuropathy ($P = 0.008$), fatigue ($P < 0.001$), and nausea/vomiting ($P = 0.008$). FOLFIRINOX was associated with improved radiologic response ($P = 0.05$) and OS ($P = 0.035$). PS, baseline carbohydrate antigen 19-9 level, and chemotherapy regimen were independent predictors of survival.

Conclusions: FOLFIRINOX is associated with improved response and OS in older adults with APC. FOLFIRINOX has a manageable safety profile in this population and should be considered in fit older adults with APC.

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Pancreatic cancer is the fourth leading cause of cancer-related death in America,[1] with only 10.8% of patients alive 5 years after diagnosis.[2,3] Pancreatic cancer is often diagnosed at an advanced and incurable stage.[2] First-line treatment for advanced pancreatic cancer (APC) consists of combination chemotherapy with fluorouracil, leucovorin, irinotecan, and oxaliplatin (FOLFIRINOX) or *nab*-paclitaxel with gemcitabine (NG). These 2 regimens have shown improved progression-free survival, and overall survival (OS) compared with single-agent gemcitabine (GEM) in phase III clinical trials.[4,5] However, the median age of patients enrolled in these trials was less than 65, even though APC disproportionally impacts older adults, with a median age at diagnosis of 70 years.[3] As such, the benefit and tolerability of combination chemotherapy in older adults with APC is unclear.

Within the medical literature, the definition of older adults (also referred to as elderly) ranges from 50 to 80 years old.[6] Most commonly, older adults are defined as people 65 years and above.[6,7] As chronological age increases, comorbidities occur more commonly, and there is heterogeneity in functional status among older adults.[8] With advancing age, there is also an increased risk of frailty and subsequent risk of side effects from chemotherapy.[8–10] Due to this individualized process of aging, it is important to consider biological age in addition to chronological age when advising the optimal treatment for patients.[11] Studies have shown that oncogeriatric assessments can provide information on the risk of chemotherapy toxicity and aid in the appropriate selection of older patients who are candidates for aggressive surgical and chemotherapeutic intervention.[12,13] However, accessing comprehensive geriatric assessments in the clinic can be difficult, and there remains limited data regarding the efficacy and toxicity of combination chemotherapy for older adults with APC.

There may be a subset of older adults who benefit from aggressive combination chemotherapy.[14] The objective of this study was to describe the treatment patterns, toxicity, and outcomes of patients 65 years of age and above treated with first-line palliative intent chemotherapy for APC.

METHODS

With University of Manitoba Health Research Ethics Board approval, we undertook a retrospective cohort study evaluating patients aged 65 years and above, diagnosed with APC from

TABLE 1. Patient Characteristics by Chemotherapy Regimen

	n (%)			
	FOLFIRINOX (N = 52)	NG (N = 21)	GEM (N = 14)	*P*
Age (median)	69	75	73	0.003
Male sex	31 (59.6)	8 (38.1)	8 (57.1)	0.240
ECOG				
0	13 (25.0)	0 (0.0)	1 (7.1)	< 0.001
1	35 (67.3)	9 (45.0)	11 (78.6)	
2	4 (7.7)	9 (45.0)	1 (7.1)	
3	0 (0.0)	2 (10.0)	1 (7.1)	
Weight loss > 10%	16 (30.8)	11 (55.0)	6 (42.9)	0.108
Nonsmoker (never)	18 (34.6)	11 (52.4)	5 (35.7)	0.200
CA 19-9 (median)	191	171	235	0.847
Lines of chemotherapy				
1	35 (67.3)	17 (81.0)	14 (100.0)	0.033
2	17 (32.7)	4 (19.0)	0 (0.0)	

CA 19-9 indicates carbohydrate antigen 19-9; ECOG, Eastern Cooperative Oncology Group; FOLFIRINOX, 5-fluorouracil, irinotecan, and oxaliplatin; GEM, gemcitabine; NG, nab-paclitaxel and gemcitabine.

2011 to 2016, and treated with palliative chemotherapy in Manitoba, Canada. Patients were identified from the Manitoba Cancer Registry, a population-based central cancer registry that captures all cancer diagnoses in Manitoba.[15,16] Patient and treatment characteristics including demographics, Eastern Cooperative Oncology Group (ECOG) performance status, comorbidities, clinical stage, first-line chemotherapy regimen received (FOLFIRINOX, NG, or GEM), hematologic and nonhematologic toxicities, emergency department (ED), and Urgent Cancer Care (UCC) visits and hospitalizations, radiologic response and survival were recorded. As previously described,[17] chemotherapy toxicities during the first 3 months of treatment were collected by chart review, with toxicities defined as grade ≥ 2 toxicity as per Common Terminology Criteria for Adverse Events (CTCAE), version 4.03,[18] unless stated otherwise. Hematologic toxicities captured included anemia (hemoglobin <100 g/L), neutropenia (absolute neutrophil count $<1.5\times10^9$/L), febrile neutropenia (neutropenia with a measured fever), and thrombocytopenia (platelet count $<100\times10^9$/L).

Transfusion of blood products (including packed red blood cells, platelets, or fresh frozen plasma) were recorded. Nonhematologic toxicities captured included grade ≥ 2 peripheral neuropathy, fatigue, nausea/vomiting, and diarrhea. Nephrotoxicity was defined as an increase in 50 mmol/L.

Visits to the ED, UCC, or hospitalizations were captured via chart review. If an ED or UCC visit occurred within 30 days of chemotherapy administration in the first 3 months of treatment, this was considered to be treatment-related toxicity. Hospitalizations and number of days in the hospital were similarity captured within 30 days of chemotherapy administration during the first 3 months of treatment. Treatment response was assessed based on imaging reports and interpretation by the primary oncologist. Response to therapy was defined as either a radiologic complete response or partial response using the Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST).[19]

Descriptive statistics were used to report baseline characteristics. Patient characteristics, radiologic response, and survival were compared according to the first-line chemotherapy regimen. The Kaplan-Meier method was used to estimate survival over time according to the first-line chemotherapy regimen. Univariable analysis was performed to assess the impact of clinically relevant factors on survival. A Cox proportional hazards multivariable regression model was used to identify independent predictors of survival. Statistical analyses were performed using SPSS (version 24) and R (version 4.1.0).

RESULTS

There were 87 patients 65 years of age and above diagnosed with APC who received palliative intent chemotherapy between 2011 and 2016 in Manitoba, Canada. Patient characteristics according to chemotherapy regimen are summarized in Table 1. There were 52 patients (59.7%) who received first-line FOLFIRINOX, 21 patients (24.1%) received NG and 14 patients (16.1%) received GEM. The median age differed by regimen ($P = 0.003$), with a median age of 69, 75, and 73 in those treated with FOLFIRINOX, NG, and GEM, respectively. ECOG performance status also differed according to the regimen ($P < 0.001$), with 48 (92.3%), 9 (42.9%), and 12 (85.7%) having an ECOG of 0 to 1 in those treated with first-line FOLFIRINOX, NG, and GEM,

TABLE 2. Hematologic and Nonhematologic Toxicities by Chemotherapy Regimen

	n (%)			
	FOLFIRINOX (N = 52)	NG (N = 21)	GEM (N = 14)	*P*
Hematologic toxicities*	40 (81.6)	16 (76.2)	11 (84.6)	0.807
Neutropenia	35 (67.3)	11 (52.4)	7 (50.0)	0.225
Febrile neutropenia	5 (9.6)	2 (9.5)	0 (0.0)	0.030
Thrombocytopenia	12 (23.1)	10 (47.6)	1 (7.1)	0.490
Anemia	20 (38.5)	15 (71.4)	6 (42.9)	0.062
Transfusion	6 (11.5)	3 (14.3)	4 (28.6)	0.807
Nonhematologic toxicities	50 (96.2)	21 (100)	7 (50.0)	< 0.001
Neuropathy	19 (36.5)	3 (14.3)	0 (0.0)	0.008
Fatigue	43 (82.7)	21 (100)	5 (35.7)	< 0.001
Nausea/vomiting	26 (50.0)	6 (28.6)	1 (7.1)	0.008
Diarrhea	23 (44.2)	4 (19.0)	3 (21.4)	0.065
AKI	4 (7.7)	2 (9.5)	0 (0.0)	0.270
Hospitalization	25 (48.0)	5 (23.8)	9 (64.3)	0.063
No. ED/UCC visits, mean (SD)	0.88 (1.08)	1.08 (0.96)	0.57 (0.85)	0.270

*Hematologic data available for 49 patients treated with FOLFIRINOX, 21 with NG and 13 with GEM.

AKI indicates acute kidney injury, defined as serum creatinine ≥ 1.5 times the baseline creatinine; ED, emergency department; FOLFIRINOX, 5-florouracil, irinotecan, and oxaliplatin; GEM, gemcitabine; NG, nab-paclitaxel and gemcitabine; UCC, Urgent Cancer Care.

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TABLE 3. Response and Survival Outcomes According to Treatment Received

	FOLFIRINOX	NG	GEM	*P*
Response, n (%)	17 (32.7)	3 (14.3)	0 (0.0)	0.005
Median survival (mo)	9.1	7.7	4.6	0.035

FOLFIRINOX indicates 5-florouracil, irinotecan, and oxaliplatin; GEM, gemcitabine; NG, nab-paclitaxel and gemcitabine; response, complete response and partial response.

respectively. Second-line chemotherapy was received by 17 (32.7%) patients in the FOLFIRINOX group, 4 (19%) in the NG group, and none in the GEM group.

Hematologic and nonhematologic treatment toxicity during the first 3 months of first-line chemotherapy is shown in Table 2. Data on hematologic toxicity was available for 49 patients in the FOLFIRINOX group, 21 in the NG group, and 13 in the GEM group. There was no statistically significant difference in overall hematologic toxicity according to the treatment regimen. Although febrile neutropenia was uncommon, there was a statistically significant increase in the incidence of febrile neutropenia with the use of combination therapy ($P = 0.030$). More patients experienced nonhematologic toxicities with FOLFIRINOX and NG, compared with GEM (96.2% vs. 100% vs. 50.0%, respectively, $P < 0.001$). Furthermore, 19 patients (36.5%) in the FOLFIRINOX group experienced neuropathy, compared with 3 (14.3%) and 0 patients (0%) in the NG and GEM groups, respectively ($P = 0.008$). FOLFIRINOX (82.7%) and NG (100%) were more frequently associated with fatigue compared with GEM (35.7%) ($P < 0.001$). Nausea and vomiting were more common in patients treated with FOLFIRINOX and NG when compared with GEM (50.0% and 28.6% vs. 7.1%, respectively, $P = 0.008$). There were no differences in ED, UCC visits, or days admitted in hospital according to the chemotherapy regimen.

Tumor response and survival outcomes are shown in Table 3. More patients treated with FOLFIRINOX had a radiologic response compared with NG and GEM (32.7% vs. 14.3% vs. 0%, $P = 0.005$). The median OS was 9.1 months in patients who received FOLFIRINOX, 7.7 months in patients who received NG, and 4.6 months in those who received GEM ($P = 0.035$) (Fig. 1). Characteristics included in the univariable analysis (Table 4) were age, sex, loss of > 10% body weight over the 6 months preceding diagnosis, median baseline carbohydrate antigen 19-9 (CA 19-9), and smoking history. On univariable analysis, receipt of FOLFIRINOX was associated with improved OS with a hazard ratio (HR) of 0.45 (95% confidence interval [CI]: 0.25-0.84, $P = 0.013$), while an ECOG performance status of 2 to 3 was associated with a worse OS with an HR of 2.18 (95% CI: 1.22-3.90, $P = 0.008$), and elevated baseline CA 19-9 was also associated with worse OS with an HR of 1.10 (95% CI: 1.00-1.01, $P = 0.029$). On multivariable analysis, ECOG, baseline CA 19-9, and chemotherapy regimen were independent predictors of survival (Table 5). FOLFIRINOX was associated with improved OS with a HR of 0.46 (95% CI: 0.23-0.93, $P = 0.029$).

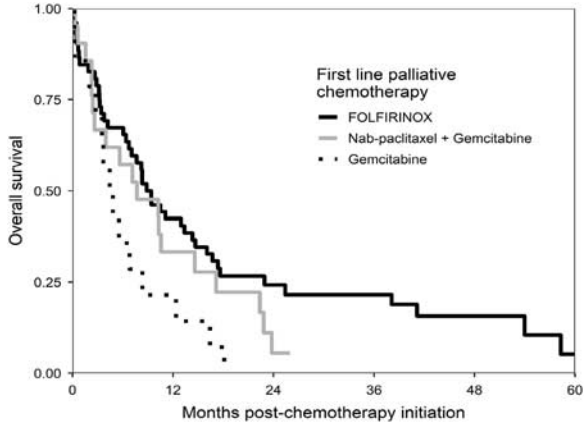

FIGURE 1. Kaplan-Meier curve depicting the cumulative survivorship for FOLFIRINOX (5-fluorouracil, irinotecan, and oxaliplatin) (black), nab-paclitaxel+gemcitabine (gray), and gemcitabine (dashed).

TABLE 4. Cox Regression Hazard Univariable Model Assessing Impact of Multiple Variables on Overall Survival

	HR	95% CI	*P*
Chemotherapy			
FOLFIRINOX	0.45	0.24-0.84	0.013
NG	0.63	0.31-1.26	0.189
GEM	1		
ECOG			
0-1	1		
2-3	2.18	1.22-3.90	0.008
CA 19-9*	1.01	1.00-1.01	0.029
Age	1.02	0.97-1.07	0.475
Sex			
Male	1.17	0.75-1.84	0.491
Female	1		
Weight loss > 10%			
Yes	0.98	0.57-1.69	0.983
Unknown	1.03	0.59-1.81	
No	1		
Never smoker			
Yes	1.10	0.68-1.78	0.914
Unknown	1.10	0.51-2.38	
No	1		

*CA 19-9 was analyzed as a continuous variable and divided by 1000.

CA 19-9 indicates carbohydrate antigen 19-9; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; FOLFIRINOX, 5-florouracil, irinotecan, and oxaliplatin; GEM, gemcitabine; HR, hazard ratio; NG, nab-paclitaxel and gemcitabine.

DISCUSSION

While there have been advancements in the treatment of APC over the last decade, the prognosis remains poor.[3]

TABLE 5. Cox Regression Hazard Multivariable Model Assessing Impact of Chemotherapy Regimen and ECOG on Overall Survival

	HR	95% CI	*P*
Chemotherapy			
FOLFIRINOX	0.46	0.23-0.93	0.029
NG	0.48	0.22-1.05	0.068
GEM	1		
ECOG			
0-1	1		
2-3	2.20	1.18-4.10	0.013
CA 19-9*	1.01	1.00-1.02	0.027

*CA 19-9 was analyzed as a continuous variable divided by 1000.

CA 19-9 indicates carbohydrate antigen 19-9; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; FOLFIRINOX, 5-florouracil, irinotecan, and oxaliplatin; GEM, gemcitabine; HR, hazard ratio; NG, nab-paclitaxel and gemcitabine.

Combination chemotherapy regimens such as FOLFIRINOX and NG have demonstrated an improvement in OS in clinical trials.[4,5] However, these trials may not accurately reflect the real-world population of patients with APC, which tends to be older, with a median age of diagnosis of 70.[3] Taking clinical trial data and subsequent age-related subgroup analyses into consideration,[4,5] Higuera et al[11] have recommended that FOLFIRINOX be reserved for patients up to 75 years of age, with an ECOG of 0 to 1. For patients with an ECOG of ≥ 2, or for patients above 75 years with an ECOG of 0 to 1, NG can be considered.[11] However, due to the underrepresentation of older adults in randomized control trials, sample sizes are small, and the level of evidence on which to base clinical decisions for this group of patients is less than ideal.

Underrepresentation of older adults in clinical trials is a well-known issue. A systematic review of 109 phase III and IV randomized control trials found that the mean age of study participants was 61.[20] This review identified 22 trials that excluded individuals over a specific age and 50 trials that had eligibility criteria (functional limitations, decreased life expectancy, cognitive impairment) that would disproportionally exclude older adults.[20] A retrospective study of age-related enrollment in US Food and Drug Administration novel cancer therapy trials between 1999 and 2002 found that only 36% of patients enrolled in registered trials were 65 years and above, while 60% of the US cancer population is 65 years and above.[21] The proportion of patients 70 years and above and 75 years and above was even lower, at 20% and 9%, respectively.[21] Another study showed that only 32% of patients enrolled in phase II and III clinical trials from 3 National Cancer Institute databases were elderly.[22] In trials led by the Canadian Cancer Trials Group (CCTG) from 1990 onwards, only 40.8% of patients were 65 years and above.[23] The deficiency of research in older adults is particularly problematic when a disease such as APC disproportionally affects older adults.[3]

Our study offers insight into the treatment patterns and outcomes of older patients with APC in a real-world setting. A retrospective cohort study of 473 patients with metastatic pancreatic cancer,[24] showed that only 25% of real-world patients with metastatic pancreatic cancer would have been eligible for enrollment in the ACCORD11 trial examining the impact of FOLFIRINOX,[4] whereas 45% of patients would have met the eligibility criteria for enrollment in the MPACT trial investigating the role of NG in APC.[5] The predominant reasons for ineligibility included age and performance status.[24] In a review of 38 phase III trials for APC, the median age of enrollment was only 62.7 years.[25] In our study of older patients receiving chemotherapy for APC, over half of the patients received FOLFIRINOX, with a median age of 69. Patients who received NG and GEM were older. Other studies have confirmed that in real-world practice, combination chemotherapy is being offered to older patients, however, the regimen may differ according to age. In a retrospective population-based analysis of 636 patients with APC across Canada, FOLFIRINOX, NG, and GEM were administered in 27.0%, 32.4%, and 40.5% of patients above 75; 40.6%, 32.7%, and 26.7% patients 65 to 74; and 44.4%, 42.5%, and 13.0% of patients below 65, respectively ($P = 0.007$).[26] The older patients in our study who received FOLFIRINOX had a better ECOG performance status. The observation that FOLIFINOX is often reserved for patients with a maintained performance status has been described in other studies. A retrospective review from the British Columbia Cancer Agency showed that patients treated with FOLFIRINOX were younger and had a better performance status, while patients who received NG were more likely to have an ECOG ≥ 2.[27]

While our study was limited to patients with APC who received chemotherapy, other studies have confirmed variable rates of chemotherapy receipt in older adults with pancreatic cancer. In an analysis of patients with APC across Canada, those below 65 were more likely to receive chemotherapy compared with those 65 to 74 and above 75 years old.[26] Using the Surveillance, Epidemiology, and End Results (SEER) database, age was a significant predictor of whether a patient received chemotherapy for APC.[28] A retrospective review from Japan of 895 patients with unresectable pancreatic cancer evaluated the proportion of patients who received the best supportive care instead of chemotherapy.[29] The proportion of patients receiving the best supportive care over chemotherapy was significantly higher in the older adult group compared with, the younger group, at 47.8% versus 25.8% ($P < 0.001$), respectively.[29] Age was identified as a reason for receiving the best supportive care in 51% of patients.[29] Similarly, a multicentre cohort study from The Netherlands found that older adults with APC were less likely to receive chemotherapy, with 81% of patients 65 to 74 years receiving chemotherapy, compared with only 50% patients aged 75 years and above.[30] Our study suggests that combination chemotherapy has a manageable toxicity profile in older patients with APC. There is an increased risk of chemotherapy-related toxicity in older adults.[8,10] In our study, there was no difference in hematologic toxicity according to the treatment regimen. As expected, more nonhematologic toxicities were seen with combination chemotherapy regimens. Despite these differences in toxicities, there were no differences in ED/UCC visits or time admitted to the hospital according to the treatment regimen. This may reflect the highly selected nature of patients in our study, as they were deemed fit for aggressive chemotherapy treatment by their oncologist. Alternatively, because the rates of febrile neutropenia were low, and due to the retrospective nature of our study, the incidence of ED and hospital admissions may be underreported, since the electronic record only captures ED and UCC and hospitalizations if reported by the oncology team in their notes. A single-center retrospective review of 52 patients in France assessed the tolerance and efficacy of FOLFIRINOX for patients 70 years and above with APC or colorectal cancer.[31] The most common toxicities were fatigue (94.2%), diarrhea (67.3%), anemia (52.8%), neutropenia (46.2%), and nausea/vomiting (42.3%).[31] During treatment, 75% of patients required dose reductions.[31] A retrospective study considering 203 patients from China treated with modified FOLFIRINOX or NG followed by modified FOLFIRINOX found that severe adverse events, specifically neutropenia, occurred more commonly in patients above 70.[32] Neutropenia occurred in 50% of patients above 70, compared with 28.3% in those below 70 ($P = 0.001$).[32] While dose modifications may minimize toxicity, it is unclear whether dose reductions result in reduced efficacy of combination chemotherapy for APC.[33,34] The results from the prospective phase II PAMELA-70 trial investigating the efficacy and tolerance of modified FOLFIRINOX in older adults (age 70 y and above) with metastatic pancreatic cancer will help address this question.[35]

Our study demonstrates that in a real-world population of older adults with APC, FOLFIRINOX correlates with improved OS. Another single-center retrospective study of patients above 65 years with metastatic pancreatic cancer found that OS was improved with FOLFIRINOX (13.8 mo), compared with 5-fluorouracil and oxaliplatin (FOLFOX) (7.0 mo) or GEM (6.7 mo) ($P = 0.004$).[36] Among 18 patients with APC above 70 years old treated with FOLFIRINOX, Guion-Dusserre et al[31] reported a median OS of 12.5 months. Another retrospective

analysis of 24 patients with APC aged above 75 years treated with FOLFIRINOX reported a median OS of 11.6 months.[37] The results from our study are further evidence that FOLFIRINOX should be considered in select older patients with APC.

Limitations of our study include the small size of the cohort and the retrospective nature of the study. Our cohort represents a highly selected group, as only patients well enough to receive palliative intent chemotherapy were included. Data was collected through chart review, which may lead to misclassification and missing data. Specifically, some toxicities are subjective (fatigue, nausea/vomiting, diarrhea) and rely upon patient reporting and clinician documentation. Data on dose reductions was not included, which may also limit interpretation. Because administrative databases were not used to identify ED presentations, UCC visits, or hospitalizations, these may be underrepresented.

CONCLUSIONS

FOLFIRINOX is a frequently used chemotherapy regimen in patients 65 years and above in a real-world setting. FOLFIRINOX is associated with improved radiologic response and OS in older adults with APC. Although there were more nonhematologic toxicities associated with FOLFIRINOX, we did not observe an increase in ED/UCC visits or hospital admission days. As such, FOLFIRINOX can be considered as a first-line chemotherapy option in select, well-functioning older adults.

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REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin*. 2020;70:7–30.
2. Ilic M, Ilic I. Epidemiology of pancreatic cancer. *World J Gastroenterol*. 2016;22:9694–9705.
3. National Cancer Institute. Cancer Stat Facts: Pancreatic Cancer. Surveillance, Epidemiology, and End Results Program 2021.
4. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med*. 2011;365:768–769.
5. von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med*. 2013;369:1691–1703.
6. Sabharwal S, Wilson H, Reilly P, et al. Heterogeneity of the definition of elderly age in current orthopaedic research. *Springerplus*. 2015;4:1–7.
7. Crews DE, Zavotka S. Aging, disability, and frailty: implications for universal design. *J Physiol Anthropol*. 2006;25:113–121.
8. Pérez-Zepeda MU, Cárdenas-Cárdenas E, Cesari M, et al. Cancer and frailty in older adults: a nested case-control study of the Mexican Health and Aging Study. *J Cancer Surviv*. 2016;10:736–742.
9. Conroy T, Desseigne FF, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med*. 2011;364:1817–1825.
10. Carreca I, Balducci L. Cancer chemotherapy in the older cancer patient. *Urol Oncol*. 2009;27:633–642.
11. Higuera O, Ghanem I, Nasimi R, et al. Management of pancreatic cancer in the elderly. *World J Gastroenterol*. 2016;22:764–775.
12. Castel-Kremer E, de Talhouet S, Charlois AL, et al. An oncogeriatric approach to select older patients for optimal treatments of pancreatic adenocarcinoma. *J Geriatr Oncol*. 2018;9:373–381.
13. Ortland I, Mendel Ott M, Kowar M, et al. Comparing the performance of the CARG and the CRASH score for predicting toxicity in older patients with cancer. *J Geriatr Oncol*. 2020;11:997–1005.
14. Giordano G, Vaccaro V, Lucchini E, et al. Nab-paclitaxel (Nab-P) and gemcitabine (G) as first-line chemotherapy (CT) in advanced pancreatic cancer (APDAC) elderly patients (pts): a "real-life" study. *J Clin Oncol*. 2015;33:424.
15. Roos LL, Mustard CA, Nicol JP, et al. Registries and administrative data: organization and accuracy. *Med Care*. 1993;31:201–212.
16. Robinson JR, Young TK, Roos LL, et al. Estimating the burden of disease. Comparing administrative data and self-reports. *Med Care*. 1997;35:932–947.
17. Rittberg R, Zhang H, Lambert P, et al. Utility of the modified frailty index in predicting toxicity and cancer outcomes for older adults with advanced pancreatic cancer receiving first-line palliative chemotherapy. *J Geriatr Oncol*. 2021;12:112–117.
18. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE), Version 4.03. 2021.
19. Schwartz LH, Litière S, de Vries E, et al. RECIST 1.1—update and clarification: from the RECIST committee. *Eur J Cancer*. 2016;62:132–137.
20. Zulman DM, Sussman JB, Chen X, et al. Examining the evidence: a systematic review of the inclusion and analysis of older adults in randomized controlled trials. *J Gen Intern Med*. 2011;26:783–790.
21. Talarico L, Chen G, Pazdur R. Enrollment of elderly patients in clinical trials for cancer drug registration: a 7-year experience by the US Food and Drug Administration. *J Clin Oncol*. 2004;22:4626–4631.
22. Lewis JH, Kilgore ML, Goldman DP, et al. Participation of patients 65 years of age or older in cancer clinical trials. *J Clin Oncol*. 2003;21:1383–1389.
23. Hernandez-Torres C, Cheung WY, Kong S, et al. Accrual of older adults to cancer clinical trials led by the Canadian cancer trials group—is trial design a barrier? *J Geriatr Oncol*. 2020;11:455–462.
24. Peixoto RD, Ho M, Renouf DJ, et al. Eligibility of metastatic pancreatic cancer patients for first-line palliative intent nab-paclitaxel plus gemcitabine versus FOLFIRINOX. *Am J Clin Oncol*. 2017;40:507–511.
25. White MN, Dotan E, Catalano PJ, et al. Advanced pancreatic cancer clinical trials: the continued underrepresentation of older patients. *J Geriatr Oncol*. 2019;10:540–546.
26. Batra A, Ramjeesingh R, Meyers BM, et al. Treatment patterns and survival outcomes of older patients with advanced pancreatic cancer (APC): a Canadian real-world evidence study. *J Clin Oncol*. 2021;39(suppl):385.
27. Wang Y, Camateros P, Cheung WY. A real-world comparison of FOLFIRINOX, gemcitabine plus nab-paclitaxel, and gemcitabine in advanced pancreatic cancers. *J Gastrointest Cancer*. 2019;50:62–68.
28. Nipp R, Tramontano AC, Kong CY, et al. Disparities in cancer outcomes across age, sex, and race/ethnicity among patients with pancreatic cancer. *Cancer Med*. 2018;7:525–535.
29. Kuroda T, Kumagi T, Yokota T, et al. Efficacy of chemotherapy in elderly patients with unresectable pancreatic cancer: a multicenter review of 895 patients. *BMC Gastroenterol*. 2017;17:1–7.
30. Brada LJH, Walma MS, van Dam RM, et al. The treatment and survival of elderly patients with locally advanced pancreatic cancer: a post-hoc analysis of a multicenter registry. *Pancreatology*. 2021;21:163–169.
31. Guion-Dusserre JF, Bertaut A, Ghiringhelli F, et al. Folfirinox in elderly patients with pancreatic or colorectal cancer-tolerance and efficacy. *World J Gastroenterol*. 2016;22:9378–9386.
32. Li X, Huang DB, Zhang Q, et al. The efficacy and toxicity of chemotherapy in the elderly with advanced pancreatic cancer. *Pancreatology*. 2020;20:95–100.
33. Patel L, Hollmann S, Attard C, et al. Real-world experience with FOLFIRINOX: a review of Canadian and international registries. *Oncol Exch*. 2014;13:18–23.

34. Maroun JA, Ko Y, Ghafoor A, et al. Standard clinical practice of FOLFIRINOX (FFX) in advanced/metastatic pancreatic cancer (PC) patients: a Canadian Retrospective Registry. *Ann Oncol*. 2014;25(suppl 4):iv238.
35. Institut Cancerologie de l'Ouest. Efficacy and tolerance evaluation in FOLFIRINOX dose adjusted in elderly patients with a metastatic pancreatic cancer (PAMELA70). 2020.
36. Costa JG, de Jesus VHF, Camandaroba MPD, et al. Characteristics and survival of older patients with metastatic pancreatic cancer: a retrospective analysis of the AC Camargo Cancer Center experience. *Ther Adv Med Oncol*. 2019;11:1–13.
37. Mizrahi J, Rogers J, Hess KR, et al. FOLFIRINOX in pancreatic cancer patients age 75 years or older. *J Clin Oncol*. 2019;37 (suppl):362.