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Research Paper

Prognostic impact of Geriatric 8 and comprehensive geriatric assessment in older patients with advanced pancreatic ductal adenocarcinoma

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ABSTRACT

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is an aggressive malignancy with poor prognosis, particularly in older patients (≥70 years), who represent an increasing proportion of cases. However, this population is underrepresented in clinical trials. This study aimed to evaluate the prognostic impact of the Geriatric 8 (G8) screening tool and the comprehensive geriatric assessment (CGA) in older patients with advanced PDAC.

Materials and Methods: We conducted a retrospective observational study of patients aged ≥70 years with locally advanced or metastatic PDAC treated at Fondazione Policlinico Gemelli IRCCS between January 2018 and August 2023. Clinical, demographic, and treatment data were extracted through structured and unstructured data mining. All patients underwent G8 screening at the start of first-line therapy; if G8 was ≤14, patients could have received CGA. Primary endpoints were progression-free survival (PFS) and overall survival (OS), analyzed through Kaplan-Meier estimates and Cox regression models.

Results: Of 268 eligible older patients, 210 (78.4 %) received first-line chemotherapy. Most received gemcitabine plus nab-paclitaxel (58.1 %). Median PFS and OS were 6.5 (95 % CI: 5.7–7.3) and 9.9 months (95 % CI: 9.1–11.7), respectively. Baseline Geriatric 8 score was ≤14 in 149 out of 210 (70.9 %) patients and ≥ 15 in 61 out of 210 (29.1 %). A baseline G8 score ≥ 15 was significantly associated with higher PFS (7.9 vs. 5.3 months, HR 0.57, $p = 0.001$) and OS (16.6 vs. 7.8 months, HR 0.39, $p < 0.001$), both at univariate and multivariate analyses. Among the 149 patients with a baseline G8 ≤ 14, 97 (65.1 %) were referred for CGA, and 60 (40.3 % of the overall G8 ≤ 14 population) completed the assessment. No difference in mPFS ($p = 0.28$) nor in mOS ($p = 0.25$) emerged according to CGA assessment. However, the 12-month survival rate was higher in patients who underwent CGA (31.8 %) compared with those who did not (14.2 %).

Discussion: First-line chemotherapy provides particular clinical benefit to older adults with PDAC with higher G8 scores, though benefit was observed across the broader cohort. The G8 score was a strong independent prognostic tool for treatment response and survival.

1. Introduction

Pancreatic ductal adenocarcinoma (PDAC) is the 13th most common cancer globally but ranks among the most lethal malignancies, accounting for approximately 460,000 deaths annually [1]. Its incidence is steadily increasing and PDAC is projected to become the second leading cause of cancer-related mortality by 2030 [2–6].

The majority of PDAC cases occur in individuals aged ≥70 years, referred to here as older adults with pancreatic cancer (OAPC) [7], likely due to the aging population in Western countries. Globally, the population aged ≥60 years is expected to double by 2050, while those aged ≥80 years will reach approximately 400 million [8]. Consequently, by 2030, it is estimated that nearly 70 % of PDAC diagnoses will occur in older adults [9].

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In recent years, several randomized clinical trials and meta-analyses have demonstrated improved survival in patients with advanced PDAC treated with combination chemotherapy regimens. In the PRODIGE 4 trial, modified FOLFIRINOX (5-fluorouracil, leucovorin, irinotecan, and oxaliplatin) demonstrated superior overall survival compared to gemcitabine monotherapy [10]. Similarly, the MPACT trial showed that gemcitabine combined with nab-paclitaxel outperformed gemcitabine alone [11]. A recent systematic review and Bayesian network meta-analysis comparing the efficacy and toxicity of first-line treatment options for locally advanced and metastatic PDAC identified triplet regimens such as FOLFIRINOX and NALIRIFOX (which includes nanoliposomal irinotecan) as the preferred options for patients eligible for intensive therapy [12,13].

However, older patients with PDAC have been consistently underrepresented in these randomized clinical trials. This underrepresentation was notably highlighted by the U.S. Food and Drug Administration, which compared the proportion of older adults with PDAC enrolled in registration trials from 1995 to 2002 with the rising number of older patients' cases in the general population during the same period [14]. Moreover, older patients with pancreatic cancer enrolled in clinical trials usually present with better overall clinical conditions compared to patients of the same age encountered in routine clinical practice; therefore, the results of these trials are difficult to generalize to the entire population of OAPC [15].

Several tools have been developed to assess frailty in older patients with cancer. However, geriatric screening tools are increasingly recognized as valuable tools not only in older adults, but also in vulnerable populations irrespective of chronological age. In PDAC, vulnerability frequently arises from disease related factors such as rapid weight loss, sarcopenia, and functional decline. These conditions are not restricted to older patients; younger individuals with PDAC may also present with significant frailty or impaired functional reserve due to the aggressive biology of the disease and the catabolic burden it imposes. Therefore, systematic geriatric screening and assessment may provide critical information on patients' functional status, and supportive care needs, ultimately guiding more personalized treatment decisions and improving clinical outcomes across age groups [16].

One of the most used and well-known geriatric screening tools is the Geriatric 8 (G8), which consists of eight items, a selection of seven items from the Mini Nutritional Assessment (MNA) questionnaire as well as an indication of age of the patient [17,18].

The aim of our study is to assess the effectiveness of currently used first-line chemotherapy regimens in older patients diagnosed with PDAC and to evaluate the capability of the G8 to predict the prognosis of the patients and the effectiveness of the treatment.

2. Materials and Methods

2.1. Study design

Our study is a retrospective observational study that included patients with PDAC treated at Fondazione Policlinico Agostino Gemelli IRCCS (FPG) over five years (January 2018 to August 2023). The study population was identified from FPG patients that met at least one of the inclusion criteria. All study data came from clinical practice and were collected using data-mining strategies. No visits, examinations, laboratory tests or ad hoc procedures were required as part of this observational study (Fig. 1). The study protocol was written in compliance with the 1975 Declaration of Helsinki and was approved by the Ethics Committee of Fondazione Policlinico Gemelli (ID: 3334/2020). Privacy issues were analyzed with the Data Protection Officer to design an approach fully compliant with Italian and European GDPR directives and regulations.

2.2. Inclusion and exclusion criteria

The study population was defined as patients with advanced pancreatic adenocarcinoma aged ≥70 years old at the date of diagnosis.

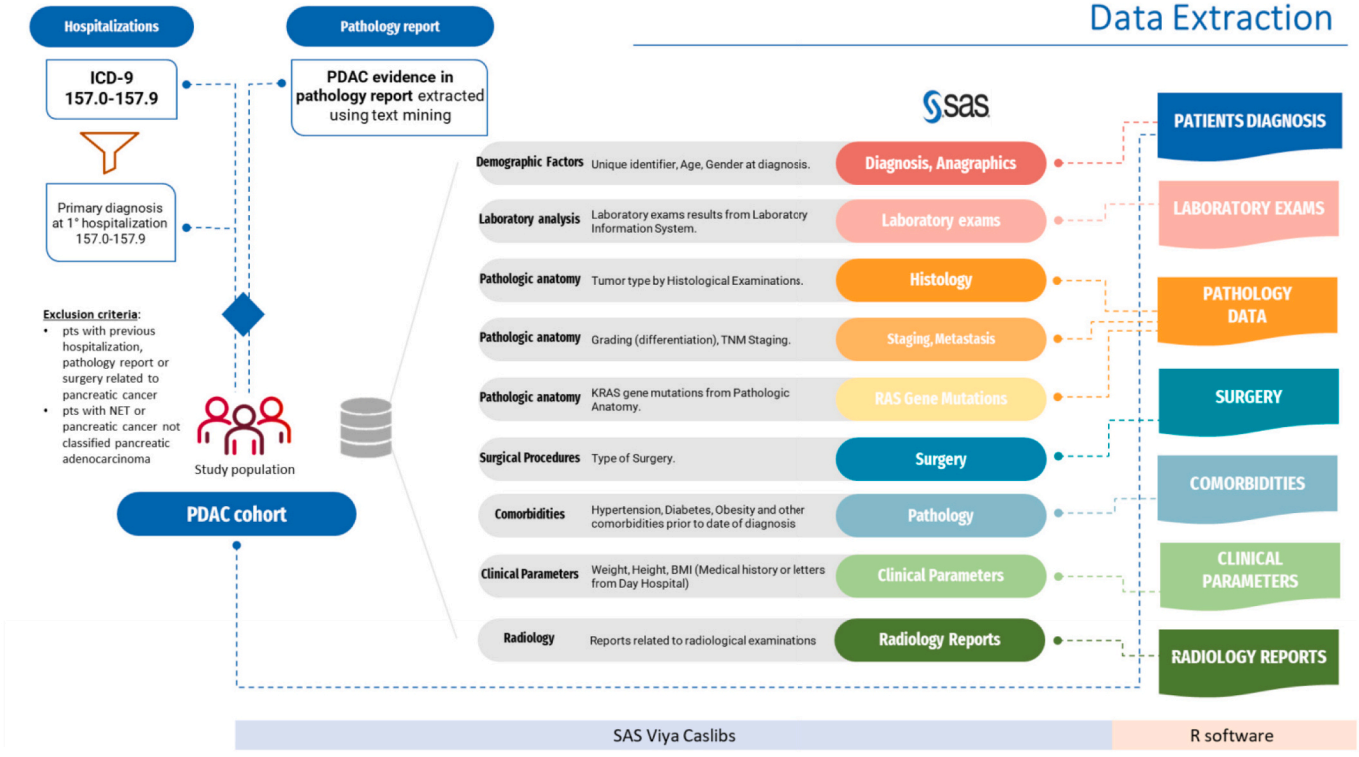

Fig. 1. Summary outline of the Gemelli Generator Project (ICD-9: international classification of disease 9; PDAC: pancreatic ductal adenocarcinoma; NET: neuroendocrine tumors).

Patients included in the study were selected from a datamart of patients with pancreatic adenocarcinoma identified from inpatient hospitalization and pathology reports to have at least one of the following conditions in the interval of January 2018 to August 2023:

- Hospitalization record at FPG with primary or secondary diagnosis of malignant pancreatic cancer, indicated by codes 157.0–157.9 (according to the 9th International Classification of Diseases, ICD9-CM) reported within the hospital discharge form - SDO method.
- Evidence of pancreatic adenocarcinoma from pathological anatomy reports (biopsies and cytological examinations) obtained through text mining based on searching for diagnosis-related keywords within the reports in free text form - TM method.

For patients included in the study population exclusively by SDO method (ICD9-CM 157), further investigations were carried out in order to include in the study population only patients diagnosed with PDAC and exclude patients with pancreatic neuroendocrine tumors and/or diagnosed with pancreatic neoplasm not specifically classified as pancreatic adenocarcinoma. Specifically, for these patients, text mining analyses were extended to the discharge letters (LD) and to clinical diaries (DCs). All patients without further evidence (derived from LD or DC) of pancreatic adenocarcinoma were then excluded from the study population.

2.3. Data extraction

Real-world data (RWD), obtained from daily clinical practice and collected in the FPG data warehouse (DWH), were extracted as part of the Gemelli Generator Real World Data framework [19]. The methodology used is based on the design and implementation of a patient-centered data repository, which extracts and integrates all relevant data sources for the characterization of patients with pancreatic adenocarcinoma. Specifically, the data repository collects demographic information, hospital contact information (admissions, surgeries, biopsies), clinical and laboratory parameters, comorbidities and risk factors (Fig. 1). For each subset of information, all structured and unstructured data sources collecting the variables of interest were identified within hospital information systems (HIS). In particular, structured data are characterized by a high level of standardization and coding, which invokes specific ontologies and commonly used data formats (e.g., codes for diagnoses according to the ICD9-CM standard). Unstructured data, on the other hand, refers to information contained in medical reports in the form of free text, which requires further processing for subsequent analysis. Specific ETL (Extract, Transform, Load) procedures were implemented with the goal of automatically retrieving data from heterogeneous sources; direct extractions from structured data sources and clinically validated text mining techniques from unstructured data sources.

In the data extraction phase, SAS® v. 9.04 software was used as middleware for ETL tasks from hospital information systems, as a data repository (SAS VIYA Caslibs), and as a text mining tool.

2.4. Geriatric screening and assessment

The patients included in the study received a G8 evaluation as part of routine clinical practice at the beginning of the first-line therapy; the test was administered to patients by the attending oncologists. If the G8 score was $\leq$14, the patients could receive a comprehensive geriatric assessment (CGA). This assessment could include evaluations of comorbidities, neurological status, nutritional function, and patients' social support, through commonly used scales as the Activities of Daily Living (ADL), Functional Independence Measure (FIM), Geriatric Depression Scale (GDS), the Mini-Mental State Examination, Clinical Dementia Rating Scale, and the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) [20–23].

2.5. Statistical analysis

Continuous variables were compared between groups using Student's *t*-test, while categorical variables were analyzed using the Chi-square test. Unless otherwise specified, all statistical tests were two-tailed with a significance level of 5 %.

The co-primary endpoints were progression-free survival (PFS) and overall survival (OS). PFS was defined as the time from the initiation of the first-line treatment to the earliest occurrence of either disease progression or death from any cause. OS was calculated from the date of diagnosis of advanced or metastatic disease to the date of death from any cause, with surviving patients censored at the last follow-up date at which they were known to be alive (data cutoff date: March 31, 2024).

In addition to the predefined co-primary endpoints of PFS and OS, we also performed exploratory analyses regarding the prognostic role of frailty as identified by the G8 screening tool, and to explore the impact of CGA among patients screened as frail, on treatment regimens (doublet: gemcitabine + nab-paclitaxel/FOLFOX vs. triplet: FOLFIRINOX vs. monotherapy: gemcitabine or capecitabine), performance status according to Eastern Cooperative Oncology Group (ECOG PS: 0–1 vs. 2), best response to first-line therapy (according to RECIST criteria version 1.1), and receipt of second-line treatment. These exploratory endpoints were assessed to provide supplementary descriptive information on treatment patterns, functional status, and clinical trajectories in this population.

Kaplan-Meier methodology was used to analyze OS and PFS. To evaluate associations between clinical characteristics and PFS and OS, univariate and multivariate analyses were conducted using Cox proportional hazards regression. Hazard ratios (HRs) with 95 % confidence intervals (CIs) were calculated using a logistic regression model. Data analysis was conducted using R software (version 4.2.1) and Jamovi (version 2.3.28).

3. Results

3.1. Characteristics of older adults withpancreatic cancer

In the period from January 2018 to August 2023, a total of 1576 patients with PDAC were diagnosed: 110 (7 %) patients were younger than 50 years old and 756 (48 %) patients were older than 70 years old; 268 of them (17 %) had advanced disease with available clinical data (Supplementary Fig. 1).

The median age was 76 years (range: 70–88), and 140 patients (52 %) were female. The median body mass index (BMI) was 23.4 kg/m^2 ($\pm$ 4.2); 62 patients (22.8 %) had a BMI index $\leq$20 kg/m^2, 138 (51.7 %) had a BMI 20–25 kg/m^2 and 68 (25.5 %) $\geq$25 kg/m^2. ECOG Performance Status was 0 in 35 patients (13.4 %), 1 in 167 patients (62 %) while 66 patients (24.6 %) had a score $\geq$ 2.

The majority of patients (240; 89.5 %) had at least one comorbidity, the most prevalent being high blood pressure (55.4 %), diabetes (28.4 %), and obesity (12.8 %).

Primary tumor location was in the head of the pancreas in 189 patients (70.5 %) and in the body/tail in 79 patients (29.5 %).

All patients in this study presented with either locally advanced or metastatic disease. Metastatic disease was more prevalent, affecting 166 patients (61.9 %), while 102 patients (38.1 %) had locally advanced disease. Among those with metastatic disease, 90 patients (54.5 %) had a single metastatic site, while 76 (45.5 %) had metastases in multiple organs. The most frequent metastatic sites were liver (70 %), distant lymph nodes (43.8 %), and peritoneum (32.2 %). Baseline characteristics are reported in Table 1.

3.2. First-line treatment outcomes in OAPC with advanced disease

Of the 268 patients with advanced disease included in the study, only 210 (78.4 %) received first-line therapy; the main reasons for

Table 1
Baseline characteristics of patients with pancreatic ductal adenocarcinoma enrolled in our study.

Characteristics	Number of patients: $N = 268$ (total number [%])
Median Age (range)	76 years old (70–88)
Sex	
Female	140 (52)
Male	128 (48)
ECOG PS	
0	35 (13.4)
1	167 (62)
≥2	66 (24.6)
Comorbidities	
Yes	240 (89.5)
No	28 (10.5)
Types of comorbidities	
High blood pressure	148 (55.4)
Diabetes	75 (28.4)
Obesity	33 (12.8)
Heart disease	26 (9.8)
Previous cancer	23 (8.6)
Atrial fibrillation	18 (6.7)
Heart failure	14 (5.2)
Pulmonary Embolism	10 (3.9)
COPD	9 (3.4)
Chronic kidney failure	5 (2.0)
Dementia	3 (1.2)
Liver Cirrhosis	1 (0.5)
BMI	
≤20 kg/m^2	62 (22.8)
20–25 kg/m^2	138 (51.7)
≥25 kg/m^2	68 (25.5)
CA 19.9 at baseline	
<200 U/ml	45 (16.8)
≥200 U/ml	115 (42.9)
Missing	108 (40.3)
Tumor location	
Head	189 (70.5)
Body/Tail	79 (29.5)
Stage	
Metastatic disease	166 (61.9)
Locally advanced	102 (38.1)
Number of metastatic sites	
1	90 (54.5)
≥2	76 (45.5)
Sites of metastasis	
Liver	116 (70.0)
Non locoregional lymph nodes	73 (43.8)
Peritoneum	53 (32.3)
Lung	33 (20.0)
Bones	4 (2.3)
Adrenal gland	1 (0.7)
First-line treatment ($N = 210$)	
Gemcitabine+Nab-paclitaxel	122 (58.1)
Gemcitabine	54 (25.7)
F OLFIRINOX	14 (6.7)
Capecitabine	14 (6.7)
FOLFOX	6 (2.8)
Geriatric 8 score (N = 210)	
≤14	133 (63.3)
≥15	77 (36.7)

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; ECOG PS, Eastern Cooperative Oncology Group performance status.

withholding first-line treatment were poor clinical status (49 patients), patient refusal (six patients), and preference for locoregional rather than systemic therapies (three patients).

The most commonly used first-line regimen was gemcitabine + nab-paclitaxel ($n = 122$; 58.1 %), followed by gemcitabine alone ($n = 54$; 25.7 %), FOLFIRINOX ($n = 14$; 6.7 %), FOLFOX ($n = 6$; 2.8 %), and Capecitabine (n = 14; 6.7 %). Among the patients treated with first-line therapy, 51 (24.3 %) achieved a partial response (PR), 89 (42.2 %) had stable disease, and 70 (33.5 %) experienced disease progression (PD) as their best response. The overall response rate (ORR) was 24.3 %, and the disease control rate (DCR) was 65.5 %. Following progression on first-line therapy, 76 patients (36.2 % of the total) received second-line treatment.

After a median follow-up of 26.9 months (95 % CI: 23.6-NR), the median progression-free survival (mPFS) for first-line therapy was 6.5 months (95 % CI: 5.7–7.3). At univariate analysis, baseline ECOG performance status (0–1 vs. 2; $p < 0.001$) and first-line treatment regimen (doublet: gemcitabine + nab-paclitaxel/FOLFOX vs. triplet: FOLFIRINOX vs. monotherapy: gemcitabine or capecitabine; $p = 0.001$) were significantly associated with PFS (Fig. 2A-B).

The median overall survival (mOS) was 9.9 months (95 % CI: 9.1–11.7). At univariate analysis, baseline ECOG PS (0–1 vs. 2; $p < 0.0001$), first-line treatment regimen (doublet vs. triplet vs. monotherapy; $p = 0.004$) and having received a second line treatment ($p < 0.001$) were significantly associated to OS (Fig. 2C-D, Supplementary Fig. 2 and Table 2).

No statistically significant difference in mPFS or in mOS was observed based on sex (male vs. female), baseline CA 19.9 levels (<200 U/ml vs. ≥200 U/ml), comorbidities (yes vs. no), BMI index (≤20 vs. 20–25 vs. ≥25), primary tumor location (head vs. body/tail), or number of metastatic sites at diagnosis (1 vs. ≥2), (Table 2).

3.3. Geriatric 8 and CGA as prognostic factors for older patients with advanced PDAC

All patients included in the study underwent baseline geriatric screening at the start of first-line treatment using the Geriatric 8: 149 out of 210 patients (70.9 %) had a score ≤ 14, while 61 out of 210 (29.1 %) had a score ≥ 15. Baseline G8 score was significantly associated with baseline ECOG Performance Status ($p < 0.001$), best response to first-line treatment ($p = 0.003$), first-line treatment regimen ($p < 0.001$), and receipt of second-line therapy ($p < 0.001$). No significant association was observed with sex ($p = 0.46$), primary tumor site ($p = 0.13$), baseline CA 19.9 levels ($p = 0.75$), or number of metastatic sites ($p = 0.17$).

Baseline G8 score was also significantly associated with PFS during first-line treatment: mPFS was 5.3 months (95 % CI: 4.4–6.9) in patients with a G8 ≤ 14, compared to 7.99 months (95 % CI: 6.7–11) in those with a score ≥ 15 (HR: 0.57, 95 % CI: 0.4–0.79, $p = 0.001$) (Fig. 3A). In multivariate analysis, baseline G8 score remained significantly associated with PFS, along with baseline ECOG PS, whereas first-line treatment regimen was not: HR for ECOG PS = 1.8 (95 % CI: 1.2–2.6, $p = 0.002$); HR for G8 = 0.67 (95 % CI: 0.50–0.94, $p = 0.02$) (Table 2).

Overall survival was also associated with the baseline G8 score at the start of first-line treatment: mOS was 7.8 months (95 % CI: 6.7–9.5) in patients with a G8 ≤ 14, compared to 16.6 months (95 % CI: 12.4–20.3) in those with a score ≥ 15 (HR: 0.39, 95 % CI: 0.28–0.55, $p < 0.001$) (Fig. 3B). In multivariate analysis, both baseline G8 score and receipt of second-line therapy remained independent prognostic factors for OS, while baseline ECOG PS and treatment regimen were not: HR for G8 = 0.44 (95 % CI: 0.30–0.63, p < 0.001); HR for second-line treatment = 0.48 (95 % CI: 0.34–0.67, p < 0.001) (Table 2).

Among the 149 patients with a baseline G8 score ≤ 14, 97 (65.1 %) were referred for CGA, and 60 (40.3 % of the overall G8 ≤ 14 population) completed the assessment. The most frequent CGA-driven interventions were nutritional support ($n = 65$), physiotherapy/rehabilitation ($n = 28$), medication optimization including deprescribing ($n = 11$), and psychosocial support ($n = 38$). No significant differences were observed in the proportion of patients receiving second-line therapy (29.9 % vs. 23.1 %, $p = 0.37$) or in the overall number of treatment lines ($p = 0.63$) according to CGA completion.

Median PFS was 4.84 months (95 % CI: 3.59–7.47) in patients not undergoing CGA and 5.49 months (95 % CI: 4.34–7.30) in those who did (HR: 1.23; 95 % CI: 0.85–1.77; $p = 0.28$). Median OS was 7.80 months (95 % CI: 5.53–9.70) in patients not evaluated with CGA and 7.60 months (95 % CI: 6.55–9.90) in those evaluated (HR: 1.27; 95 % CI:

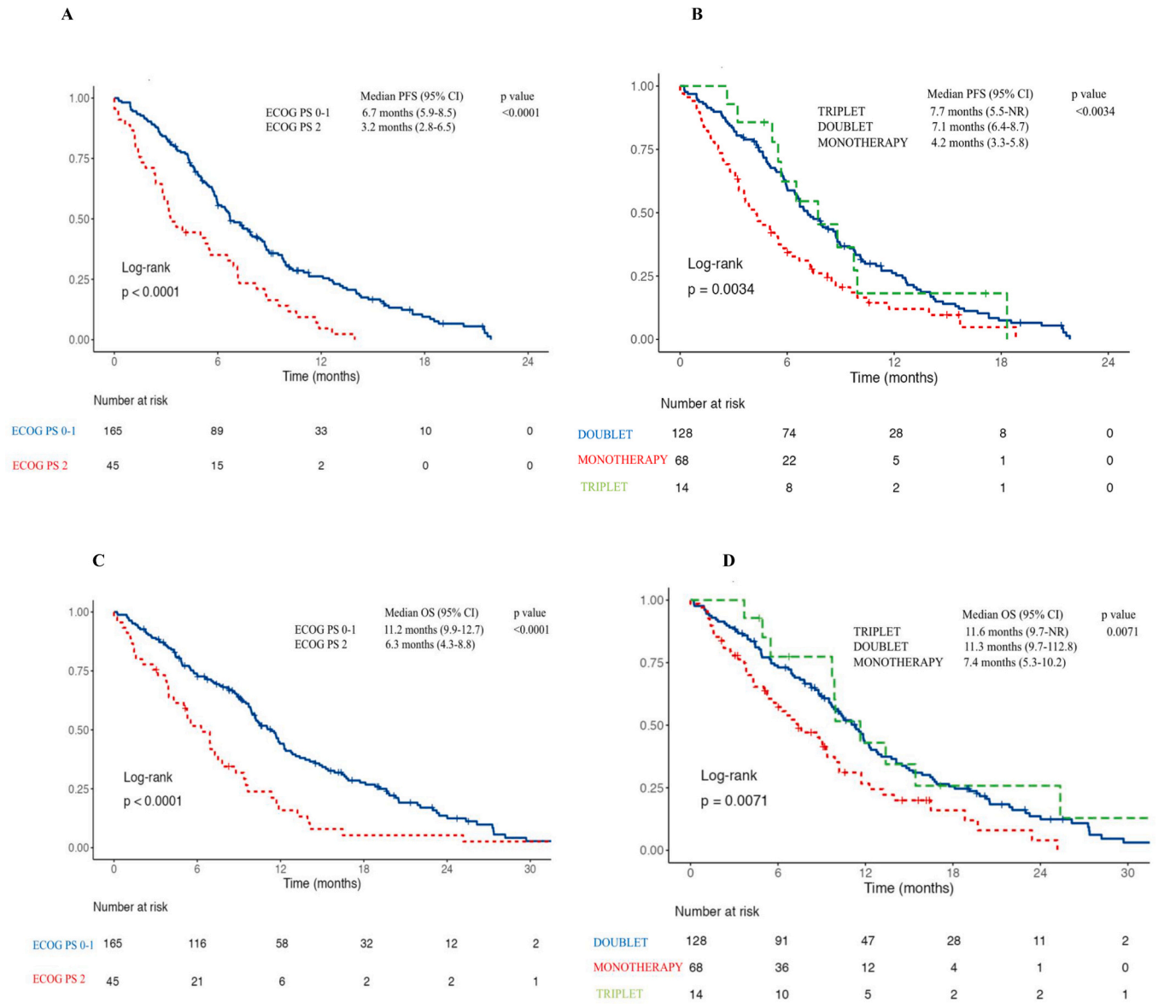

Fig. 2. 2A. First-line treatment progression-free survival (PFS) in older adults with pancreatic cancer according to baseline ECOG PS (0–1 vs ≥2); 2B. PFS in older adults with pancreatic canceraccording to first-line treatment chemotherapy regimen (doublet: two drugs combination; triplet: three drugs combination; monotherapy); 2C. Overall survival (OS) in older adults with pancreatic cancer according to ECOG PS; 2D. OS in older adults with pancreatic cancer patients according to first-line chemotherapy regimen.

0.85–1.88; $p = 0.25$). However, the 12-month survival rate was higher in patients who underwent CGA (31.8 %) compared with those who did not (14.2 %) (Supplementary fig. 3 A-B).

4. Discussion

PDAC remains a highly lethal cancer whose incidence is expected to rise, particularly among older adults, yet this group remains underrepresented in clinical trials. In our retrospective study of 268 patients aged ≥70 years with advanced PDAC, we observed that nearly half of all cases at our center involved older adults, who frequently had comorbidities and reduced functional reserve; most (78.4 %) received first-line chemotherapy, with gemcitabine plus nab-paclitaxel being the most common regimen.

Petrillo et al. [24] evaluated gemcitabine plus nab-paclitaxel in patients aged ≥65 years with metastatic PDAC and reported a median PFS of 8.0 months (95 % CI: 6.3–9.6) and a median OS of 12.0 months (95 % CI: 8.4–15.6), with acceptable toxicity and ECOG performance status as an independent prognostic factor, thereby demonstrating that combination chemotherapy can be effective in older patients when carefully selected.

Vivaldi et al. [25] similarly showed that gemcitabine plus nab-paclitaxel could be safely delivered in older patients, with outcomes comparable to pivotal trials largely including younger individuals, although dose modifications and closer monitoring were more frequently required.

Our findings align with these reports; doublet chemotherapy was the most commonly used regimen, associated with favorable outcomes in patients with good performance status, while monotherapy remained an option for those with limited functional reserve.

A key focus of our study was the use of the Geriatric 8 as a geriatric screening tool to stratify patients and predict outcomes. A G8 score ≥ 15 was strongly associated with improved PFS and OS, even after adjusting for ECOG performance status and treatment regimen in multivariate models. Patients with a higher G8 score were also more likely to receive second-line therapy and achieve better treatment responses. These

Table 2
Univariate and multivariable analyses on progression free survival and overall survival in older adults with pancreatic cancer.

	Progression-free survival			Overall survival		
	Median in months (95 % CI)	HR Univariate (95 % CI)	HR Multivariate (95 % CI)	Median in months (95 % CI)	HR Univariate (95 % CI)	HR Multivariate (95 % CI)
ECOG PS						
0–1	6.7 (5.9–8.5)			11.2 (9.9–12.7)		
2	3.2 (2.8–6.5)	2.2 (1.5–3.1, p < 0.001)	1.8 (1.2–2.6, p = 0.002)	6.3 (4.3–8.8)	2.1 (1.5–3, p < 0.0001)	1.27 (0.85–1.9, p = 0.24)
Sex						
Male	6.4 (5.3–7.9)			10.2 (8.7–12.3)		
Female	6.2 (5.5–7.8)	0.9 (0.7–1.2, p = 0.65)	–	9.9 (8.8–11.8)	1.02 (0.7–1.4, p = 0.88)	–
CA 19.9 at baseline						
<200 U/ml	6 (4.9–8.3)			9.9 (6.5–14.1)		
≥200 U/ml	5.8 (4.6–8.7)	1.1 (0.8–1.6, p = 0.60)	–	9.4 (7.3–11.3)	1.18 (0.8–1.7, p = 0.41)	–
Comorbidities						
Yes	6.6 (5.8–7.5)			10.2 (9.1–11.7)		
No	5.3 (4.4–10.1)	0.8 (0.5–1.4, p = 0.50)	–	9.1 (6.9–19.8)	1.16 (0.7–1.9, p = 0.57)	–
BMI						
≤20	3.5 (2.9–7.1)			6.9 (4.4–11.9)		
20–25	6.9 (6–8.3)	p = 0.09	–	9.9 (9.4–11.8)	p = 0.06	–
≥25	6.4 (4.8–9.5)	p = 0.09	–	11.3 (9.3–15)	p = 0.07	–
Tumor location						
Head	5.9 (5.1–7.5)			10.4 (9.1–11.8)		
Body/Tail	6.9 (5.8–8.7)	0.9 (0.6–1.25, p = 0.55)	–	9.6 (7–11.9)	0.98 (0.7–1.37, p = 0.91)	–
Number of metastatic sites						
1	6.2 (4.6–8.5)			9.7 (7.5–11.9)		
≥2	5.5 (4.4–6.9)	0.9 (0.7–1.4, p = 0.50)	–	7.4 (4.8–12.9)	1.06 (0.7–1.5, p = 0.75)	–
First-line treatment						
Doublet	7.1 (6.4–8.7)			11.3 (9.7–12.8)		
Monotherapy	4.2 (3.3–5.8)	1.7 (1.1–2.5, p = 0.001)	1.3 (0.9–1.8, p = 0.12)	7.4 (5.3–10.2)	1.6 (1.2–2.3, p = 0.004)	1.04 (0.7–1.5, p = 0.84)
Triplet	7.7 (5.5-Nr)	0.9 (0.5–1.7, p = 0.82)	0.9 (0.5–1.6, p = 0.71)	11.6 (9.7-Nr)	0.8 (0.4–1.5, p = 0.44)	0.7 (0.36–1-3, p = 0.28)
G8 score						
≤14	5.3 (4.4–6.9)			7.8 (6.7–9.5)		
≥15	7.99 (6.7–11)	0.57 (0.4–0.8, p = 0.001)	0.67 (0.5–0.94, p = 0.02)	16.6 (12.4–20.3)	0.39 (0.28–0.55, p < 0.001)	0.44 (0.30–0.63, p < 0.001)
Second-line						
No	–	–	–	7.8 (5.5–9.5)		
Yes	–	–	–	14.1 (11.9–19.1)	0.4 (0.3–0.57, p < 0.001)	0.48 (0.34–0.67, p < 0.001)

Abbreviations: BMI, body mass index; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio.

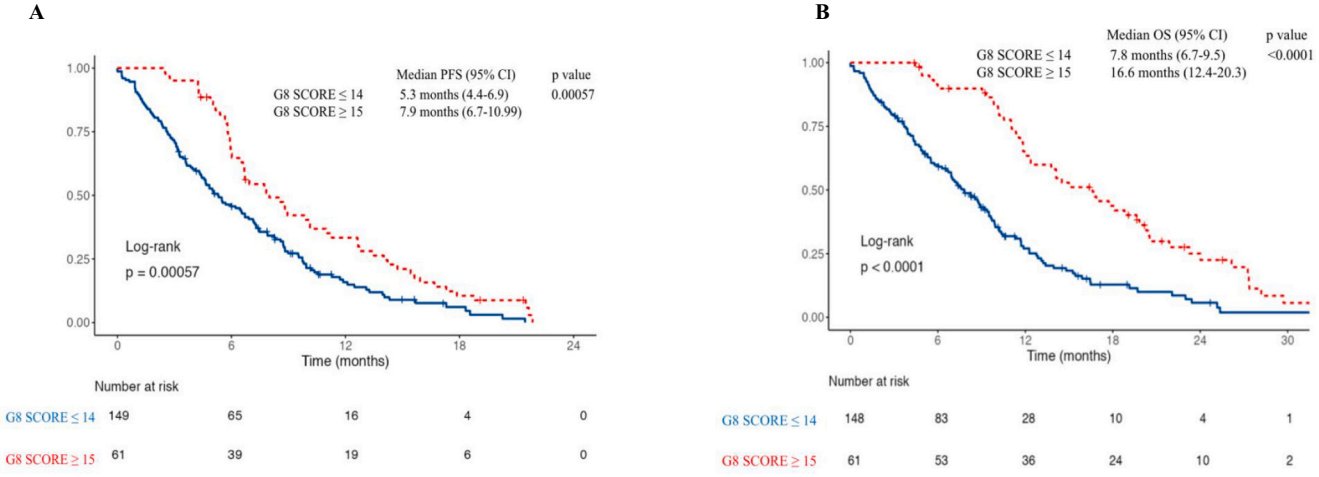

Fig. 3. 3A. First-line treatment progression free-survival in older adults with pancreatic cancer according to baseline G8 (≤14 vs. ≥15); 3B. Overall survival in older adults with pancreatic cancer according to baseline G8 score (≤14 vs. ≥15).

findings support the utility of the G8 as a prognostic tool in older patients with PDAC, aligning with previous studies that advocate for the incorporation of geriatric screening into oncologic decision-making frameworks.

Among patients with G8 score ≤ 14, referral to CGA was feasible and led to targeted interventions such as nutritional support, rehabilitation, medication optimization, and psychosocial support. Although CGA completion was not associated with statistically significant improvements in PFS or OS, we observed a clinically relevant increase in 12-month survival and better treatment continuity among patients

undergoing CGA, findings consistent with geriatric oncology literature where CGA-guided interventions have been shown to improve treatment feasibility and reduce unplanned hospitalizations even in the absence of major gains in conventional survival endpoints [26].

Interestingly, no significant differences in survival outcomes were observed based on sex, BMI, comorbidities, or CA 19.9 levels, suggesting that traditional clinical parameters may have limited predictive value in this subset of patients. Instead, multidimensional assessments, such as those offered by the G8 and CGA tools, may provide a more nuanced evaluation of a patient's functional and physiological reserve.

The retrospective design of our study and reliance on real-world data impose certain limitations, including potential selection bias and incomplete data capture. A substantial proportion of PDAC patients aged ≥70 years (336/756) were excluded from the present analysis due to the unavailability of complete clinical data. This was primarily because many of these patients received systemic treatment following diagnosis in smaller medical centers, in accordance with the Hub-and-Spoke care model. This may have resulted in a non-representative study population and could, at least in part, explain why no significant differences in survival outcomes were observed according to traditional prognostic factors (such as CA 19.9 levels).

An important limitation of the present study is the absence of data regarding patient-centered outcomes, such as quality of life, functional status, and symptom control. While traditional oncological endpoints, including OS and PFS, remain essential measures in clinical research, it is increasingly recognized that they may not fully capture the dimensions of care that matter most to patients with PDAC. Given the typically poor prognosis of PDAC, even among younger and otherwise fit individuals, patient priorities often extend beyond survival to encompass the preservation of daily functioning, alleviation of symptoms, and maintenance of quality of life.

In conclusion, our study highlights the heterogeneity of the older PDAC population and underscores the importance of geriatric screening tools like the G8 in guiding treatment decisions. While combination chemotherapy can be effective in selected older patients, individualized approaches informed by comprehensive geriatric evaluation are crucial to optimizing outcomes in this patient population. Future prospective studies should prioritize the inclusion of older patients and explore how geriatric metrics can be integrated into routine clinical algorithms to personalize care in pancreatic cancer.

Author Contributions

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Manuscript writing: All authors.

Final approval of manuscript: All authors.

Accountable for all aspects of the work: All authors.

Declaration of Competing Interest

CB reports travel and accommodation from Viatris. GTo reports funds from the Ministero della Salute (Ricerca Corrente 2022), the AIRC (Investigator Grant number IG26330), Ministero dell'Università e della Ricerca (PRIN 2022 PNRR Prot P2022LN3KS and PRIN 2022 Prot 2022P79F9N), and Agenzia Italiana del Farmaco, Ministero della Salute (J38D19000690001) FIMP and consulting or advisory role for BMS, AstraZeneca, MSD, Merck, and Servier. LS is supported by the AIRC under My First Grant (MFAG27367) and reports consulting or advisory role for Pierre-Fabre, AstraZeneca, Bayer, SERVIER, Merck, Amgen, GSK, Incyte, Leopharma, MSD, and Takeda. All other authors declare no competing interests.

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Appendix A. Supplementary Data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgo.2025.102782.

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