Medical Oncology (2019) 36:85
https://doi.org/10.1007/s12032-019-1310-0

ORIGINAL PAPER

Outcomes in patients ≥ 80 years with a diagnosis of a hepatopancreaticobiliary (HPB) malignancy

A. R. Lewis[1] · C. Cipriano[2] · X. Wang[1] · R. Ward[1] · A. Fitzpatrick[1] · A. R. M. Scott[1] · A. Rashed[1] · H. Raja[1] · A. Lamarca[1] · R. A. Hubner[1] · J. W. Valle[1,3] · M. G. McNamara[1,3,4]

Received: 7 May 2019 / Accepted: 27 August 2019

Abstract

Older patients are underrepresented in oncological clinical trials. The incidence of hepatopancreaticobiliary (HPB) malignancies is higher in older patients, but data on outcomes are lacking. This study assessed patient outcomes in those < 80 and ≥ 80 years with a HPB malignancy seen at a tertiary referral centre, The Christie NHS Foundation Trust. Data on patients with a HPB malignancy were collected retrospectively between 2012 and 2017 via on-line case-note review. Survival was calculated using the Kaplan–Meier method and prognostic factors using log-rank analysis. Of 1421 patients, 10% were ≥ 80 years. Of patients < 80 and ≥ 80 years, 56% and 57% had pancreas cancer, 39% and 36% biliary tract cancer, and 5% and 7% had hepatocellular carcinoma, respectively. Amongst patients ≥ 80 years, 75% had an Eastern Cooperative Oncology Group performance status (ECOG PS) 0–2. Patients ≥ 80 years had higher rates of comorbidity; 28% received systemic anti-cancer therapy (SACT), compared with 62% of patients < 80 years. Best supportive care (BSC) was instituted in 44% of older patients, compared with 13% in those < 80 years. Of patients ≥ 80 years who received SACT, 82% received monotherapy. Median overall survival (OS) for patients receiving palliative SACT was 10.07 months (95% CI 8.89–11.08) and 10.10 months (95% CI 6.30–12.30) in patients < 80 and ≥ 80 years, respectively, p 0.41; ECOG PS ($p < 0.001$) was prognostic for OS in older patients but Adult Comorbidity Evaluation-27 comorbidity score ($p = 0.07$, when comparing groups of ACE score ≤ 1 and > 1) was not. Baseline factors were similar in both age cohorts, but more comorbidities were present in older patients. Older patients were less likely to receive SACT, but when they did, they had an equivalent benefit in OS to younger patients.

Keywords Elderly oncology · Geriatric · Hepatobiliary · Cancer

Introduction

It is well recognised that despite people aged over 75 years representing 31% of all patients with cancer, older patients are underrepresented in clinical trials [1]. In fact, those aged over 75 years represent only 9% of oncological clinical trial participants, and data suggest that only 25.7% of people aged over 80 years are treated with systemic anti-cancer therapy (SACT), which is the lowest of all age groups [1, 2]. It has been reported that older adults with good performance status have a better overall survival (OS) when treated with anti-cancer surgery and treatment regimens than their lower performing younger counterparts [3, 4], although the definition of an older patient varies amongst studies. Historically, 65 years has been considered the cut-off for defining "elderly", and is still the accepted definition according to guidelines [5], without reference to patient fitness. Clearly

These data were presented in part at the International Society of Geriatric Oncology Conference in 2017 in Warsaw, Poland.

A. R. Lewis and C. Cipriano contributed equally to this manuscript.

✉ M. G. McNamara
Mairead.McNamara@christie.nhs.uk

1 The Christie NHS Foundation Trust, Manchester, UK

2 University of Manchester Medical School, Manchester, UK

3 Division of Cancer Sciences, University of Manchester, Manchester, UK

4 Department of Medical Oncology/Division of Cancer Sciences, The Christie NHS Foundation Trust/University of Manchester, Manchester M20 4BX, UK

Published online: 06 September 2019

this has significant limitations given wide variations between biological and chronological age across many populations. Indeed, many studies now use 70 or 75 years as a cut-off in view of increasing life expectancy and improving fitness [3, 4, 6, 8]. Older adults can also have a comparable survival and tolerance of treatment when compared to younger patients with the same malignancy [6–15]. However, data on treatment of the older patients with a diagnosis of a Hepatopancreaticobiliary (HPB) malignancy are limited [16]. Due to the paucity of data available in the ≥ 80-year-old age group particularly, this study focused on this age category.

Hepatopancreaticobiliary malignancies include hepatocellular carcinoma (HCC), pancreatic ductal adenocarcinoma (PDAC) and biliary tract cancers (BTCs) (including intra- and extra-hepatic cholangiocarcinoma, gallbladder and ampulla of Vater tumours), and overall these are a rare group of malignancies.

Studies have reported that there are similar toxicity events experienced by older patients receiving SACT for PDAC compared to those aged < 65 years [17]. One study looking at those aged ≥ 75 years receiving gemcitabine for PDAC in the advanced setting reported a median OS in those aged ≥ 75 years of 9.1 months, which was comparable to the survival reported in younger patient groups [18].

Biliary tract cancers have poor prognoses and the incidence of BTC in older patients is two times higher than in younger patients [14]. The 5 years OS of patients with BTC (across all stages) has been reported as 40% for those < 50 years compared to a survival of approximately 10% in those aged 70–89 years [19].

As data are limited on the treatment practices in patients aged ≥ 80 years with a HPB malignancy, this study assessed what treatment was offered to older patients and examined the outcomes of patients presenting with these diagnoses to a tertiary referral centre.

Materials and methods

Patients with any HPB malignancy (all stages) seen at The Christie NHS Foundation Trust over a 5-year period from January 2012 to January 2017 were included.

Those patients whose malignancy could not be defined specifically as PDAC, BTC or HCC were not included (patients with neuroendocrine tumours of these sites were also excluded). Patients aged ≥ 80 years whose disease was considered benign were also excluded. Patient selection is summarised in Fig. 1.

Demographic data were initially extracted retrospectively from case notes. Chemotherapy regimens for each patient were identified via the institutional chemotherapy prescription system. The number of cycles administered and reasons for non-completion were extracted from prescribing systems and patient notes.

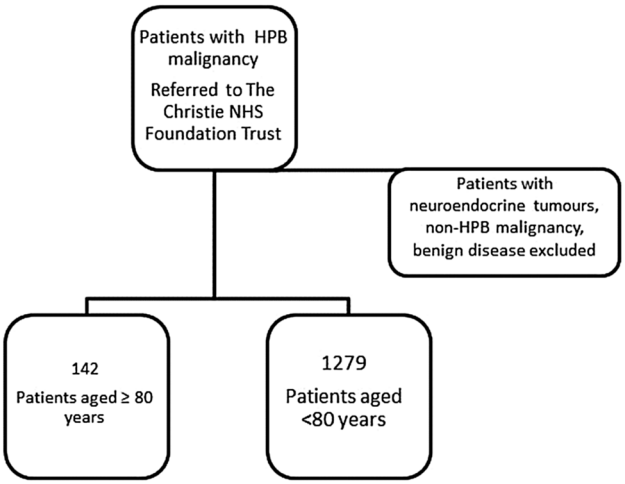

Fig. 1 Flow diagram of patient selection

For comparisons in relation to SACT records, data were recorded on patients receiving treatment for PDAC and BTCs. Because there were no patients aged ≥ 80 years with HCC who received sorafenib in this cohort study, patients with HCC were not included in the analyses of palliative SACT.

Eastern Cooperative Oncology Group Performance status (ECOG PS) was assessed by the physician at initial patient review. A comorbidity score was also recorded during the initial consultation with the patient, using the Adult Comorbidity Evaluation-27 (ACE-27) score [20]. This score is calculated based on both number and severity of comorbidities; hence, an increasing score correlates with either increasing frequency of minor comorbidities or a potentially smaller number of more serious conditions.

Median follow-up time was calculated from the date that the patient was first seen at The Christie up to the date of their last outpatient appointment or death from any cause.

Overall survival was calculated using the date of diagnosis, up to the point of last contact: either date of death or date of their last contact for patients still alive at time of analysis. Survival was calculated using the Kaplan–Meier method and the Cox Proportional Hazards model was applied to assess the association between prognostic factors and survival outcome. Log-rank tests for equality of survivor functions were performed. A p value of < 0.05 was considered statistically significant. Univariate and multivariable analyses were applied. In the multivariable analysis of the < 80-year-old dataset, time-dependent covariate was implemented in order to keep the validity of the Cox PH model. Log–log plot of survival and the scaled Schoenfeld residuals test were applied to assess the appropriateness of proportional hazard assumption. This study was approved by the internal review

board of The Christie NHS Foundation Trust, the Clinical Audit Committee (reference 17/1923). The data analysed were a retrospective, anonymised dataset.

Results

Patient demographics

Of 1421 patients with a HPB malignancy seen between January 2012 and January 2017, 142 (10%) were aged ≥ 80 years. In both age groups (< 80 and ≥ 80 years), there were similar numbers of female and male patients. Primary disease site in both age groups were similar; in patients aged ≥ 80 years, 57% had pancreatic cancer, 36% had BTC, 7% had HCC, and these rates were comparable with younger patients (Table 1).

Eastern Cooperative Oncology Group Performance status (ECOG PS) was ≤ 2 in 86% of patients ($N = 1108$) < 80 years and in 76% ($N = 108$) of patients ≥ 80 years. The proportion of patients with an ECOG PS of 2 compared to 0–1 was higher in the group aged ≥ 80 years ($p = 0.001$).

Of patients aged < 80 years, 77% had an ACE-27 score encompassing no or mild comorbidities, compared with 69% of patients aged ≥ 80 years ($p = 0.041$).

More patients aged < 80 years presented with stage 4 disease; 39% of patients aged < 80 years presented with stage 1–3 disease and 60% with stage 4 disease (data unavailable in < 1%). In comparison, 52% of patients aged ≥ 80 years presented with stage 1–3 disease, and 37% with stage 4 disease (data unavailable in 11%). Patient characteristics and primary disease sites included are detailed further in Table 1.

Patient management

The most prescribed management pathway in both age groups was either palliative SACT or Best Supportive Care (BSC). Numerically, more patients < 80 years received curative treatment than in the ≥ 80-year-old group. In the group aged ≥ 80 years, one patient was offered neo-adjuvant SACT and 10 patients were referred for consideration of adjuvant treatment; 3 were offered adjuvant SACT, with < 3% of the total group of patients aged ≥ 80 years proceeding to commence SACT, as part of a potentially curative treatment pathway (adjuvant/neo-adjuvant SACT plus surgery). In comparison, 9% of patients aged < 80 years commenced treatment as part of a curative intent treatment pathway and of these, 7% received adjuvant SACT and 2% received neo-adjuvant SACT.

Fewer older patients received palliative SACT (26%) compared to the younger group (53%) ($p < 0.001$). More patients in the ≥ 80-year-old group received BSC as initial management, compared to patients < 80 years, 44% versus 13%, respectively (Fig. 2). Treatment was declined by 3 (2%) patients aged ≥ 80 years and 6 patients < 80 years (< 1%).

Of the patients aged ≥ 80 years who did receive SACT, 82% received single-agent and 18% double-agent regimens. Single-agent gemcitabine was the most common regimen received amongst older patients and cisplatin and gemcitabine the most common combination. The majority of patients aged ≥ 80 years, who received chemotherapy, did not complete all planned doses (72%). This is comparable to patients aged < 80 years, where 70% of patients did not complete all planned doses. The most frequent reasons for non-completion in both groups were toxicity, disease progression and deteriorating PS. Twenty-three percent of younger patients and 21% of the older patient group stopped SACT due to toxicities. Of patients aged ≥ 80 years, who stopped treatment due to toxicities, 50% of these stopped receiving SACT after one cycle of therapy (11% of the group who did not complete SACT). The median number of cycles of SACT administered was 3 for patients aged ≥ 80 years old with PDAC and BTCs and in the < 80 year age group, the median number of cycles received was 4. The reasons for non-completion of planned SACT are detailed in Table 2.

Patient survival

When assessed by disease site across all stages, survival was worse in patients aged ≥ 80 years, as detailed in Table 3. However, when survival was assessed according to treatment type prescribed (comparing BSC and palliative SACT), there was no significant difference in survival between the two cohorts (< 80 and ≥ 80 years). Median OS for all patients (all disease sites) in patients aged < 80 years receiving palliative SACT was 10.07 months (95% Confidence interval [CI] 10.89–11.08) and 6.36 months with BSC (95% CI 4.26–7.77), $p = 0.003$. For all patients aged ≥ 80 years who received palliative SACT, the median OS was 10.10 months (95% CI 6.30–12.30), and with BSC was 6.36 months (95% CI 3.77–7.67), $p = 0.0098$. When comparing the median OS for patients aged < 80 and ≥ 80 years receiving palliative SACT, there was no significant difference, $p = 0.41$. These data are detailed in Table 3.

Multivariable analysis revealed that an ECOG PS > 2 correlated with worse OS in both age cohorts (for patients ≥ 80 years: hazard ratio [HR] 5.92, 95% CI 4.45–7.88, $p < 0.001$, and for patients < 80 years: HR 3.57, CI 2.99–4.25, $p < 0.001$). An ACE-27 score of > 1 was prognostic for worse survival for both older and younger patients (for patients ≥ 80 years HR 1.15, 95% CI 0.98–1.34, $p = 0.07$), but did not reach statistical significance. Male gender was prognostic for better survival in both groups (for patients ≥ 80 years: HR 0.88, 95% CI 0.77–0.99, $p = 0.048$) and a diagnosis of PDAC was prognostic for worse survival compared to a diagnosis of HCC

Table 1 Patient characteristics and primary disease sites for patients aged < 80 years and ≥ 80 years with a hepatopancreaticobiliary malignancy

	Patients < 80 years *N* (%)	Patients ≥ 80 years *N* (%)	*p* value
Total	1279 (89)	142 (11)	
Gender			
Male (ref)	666 (52)	78 (54)	0.518*
Female	613 (48)	64 (45)	
ECOG performance status [*N* (%)]			
0 (ref)	187 (15)	4 (3)	< 0.001
1	646 (50)	60 (42)	
2	275 (21)	44 (31)	
3	161 (13)	28 (20)	
4	7 (0.5)	5 (3.5)	
N/A	3 (< 0.5)	1 (0.5)	
Adult comorbidity evaluation 27			
None (ref)	476 (37)	31 (22)	0.003
Mild	502 (39)	66 (47)	
Moderate	222 (17)	33 (23)	
Severe	76 (6)	12 (8)	
N/A	3 (< 0.5)		
Primary disease site			
BTC (ref)	489 (38)	50 (35.5)	0.251
HCC	78 (6)	10 (7)	
PDAC	711 (56)	81 (57)	
Other	1 (< 0.5)	1 (0.5)	
Stage of disease at initial presentation			
1 (ref)	38 (3)	16 (11)	< 0.001
2	224 (17.5)	26 (18)	
3	239 (19)	33 (23)	
4	771 (60)	52 (37)	
N/A	7 (0.5)	15 (11)	
Initial proposed treatment type			
Neo-adjuvant SACT	21 (1.5)	1 (0.7)	< 0.001
Adjuvant SACT	91 (7)	3 (2)	
Palliative SACT	679 (53)	37 (26)	
Surveillance	58 (5)	14 (10)	
BSC	168 (13)	63 (44.3)	
Other	262 (20.5)	24 (17)	

ECOG Eastern Cooperative Oncology Group, *NA* not available, *BTC* biliary tract cancer, *HCC* hepatocellular carcinoma, *PDAC* pancreatic ductal adenocarcinoma, *ref* reference

*Chi-squared tests were applied to assess the association between two age groups and the baseline characteristics. (N/A data were not included in the tests)

and BTC in both age groups (HR 1.66, 95% CI 1.45–1.91, $p < 0.001$ for patients < 80 years and HR 2.02, 95% CI 1.75–2.33, $p < 0.001$ for patients aged ≥ 80 years). Stage 4 disease at presentation was prognostic for worse survival in both age groups (patients aged ≥ 80 years: HR 2.80, 95% CI 1.44–5.43, $p = 0.002$ and for patients aged < 80 years: HR 1.99, 95% CI 1.32–2.93, $p = 0.001$) compared to earlier stage disease. Further details of multivariable analysis are provided in Table 4. Survival is shown in Kaplan–Meier curves in Fig. 3.

Discussion

Approximately 10% of patients referred to The Christie NHS Foundation Trust included in this study were identified as being ≥ 80 years at the time of their presentation. It has been reported in another study that patients > 75 years encompassed 31% [1] of all patients with cancer, and it is known that 47% of diagnoses of PDAC are in people aged ≥ 75 years, with the highest incidence in those aged > 85 years [11]. Therefore, it is likely that not all

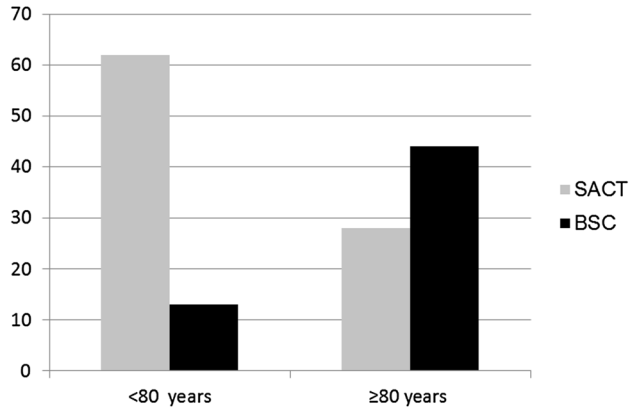

Fig. 2 Percentage of patients with hepatopancreaticobiliary malignancies offered the most popular treatment choices (SACT and BSC) aged < 80 years and ≥ 80 years. *SACT* systemic anti-cancer therapy, *BSC* best supportive care

Table 2 Reasons for non-completion of systemic anti-cancer therapy

Reason for non-completion	Aged < 80 years (%)	Aged ≥ 80 years (%)
Toxicity	23	21
Deteriorating ECOG PS	26	21
Disease progression	22	19
Patient decision	10	21
Death	14	18
Unknown	5	0

ECOG PS Eastern Cooperative oncology group performance status

patients aged ≥ 80 years diagnosed with a HPB malignancy were referred to Oncology services for review, due to patient comorbidities, wishes or poor performance status.

In the current study, patients in both age groups (< 80 and ≥ 80 years) had similar demographics in terms of primary disease site and gender. Similarly, the proportion of patients with an ECOG PS of 0–2 was also similar. Despite patients theoretically having similar overall fitness levels, patients aged ≥ 80 years were more likely to be offered BSC, and less likely to be offered SACT than younger patients. It may be that this indicates the limitations of the ECOG PS to delineate fitness in older patients and the need for more specific geriatric assessments in this group. It may also be because a higher proportion of patients refused treatment. Despite the poor prognosis for PDAC overall, older patients with PDAC are more likely to present at an earlier stage than younger people, and would therefore potentially be candidates for aggressive local treatment [21]. It does appear that fewer older patients are offered this aggressive treatment, due to the presence of comorbidities or frailty; one study reported that almost half of all older patients with PDAC did not receive any anti-cancer treatment [21], which is similar to the rates of BSC offered in the current study in patients aged ≥ 80 years. However, the current study suggested that higher rates of comorbidities in patients aged ≥ 80 years correlated with better survival. Previous evidence has reported that functional status and not chronological age or comorbidities is a more significant prognosticator of treatment tolerance and survival [5].

Survival for patients with HPB malignancies and advanced disease is poor. Randomised data suggest a median OS for patients with advanced PDAC of approximately 11 months for those who are fit enough to receive first-line combination SACT with 5-fluorouracil/irinotecan/oxaliplatin (FOLFIRINOX) [22]. Patients with PDAC and a poorer PS receiving single-agent gemcitabine have a reported median OS of approximately 6 months [23]. In advanced BTC, a median OS of 11.7 months has been reported for patients receiving cisplatin and gemcitabine, compared with 8 months for those receiving gemcitabine alone [24]. These limited survival gains must be taken in context for older patients, who will have a more limited life expectancy than younger patients and may have influenced older patients' decisions not to proceed with treatment.

In the current study, survival was worse for patients aged ≥ 80 years, compared to younger patients for all primary tumour sites when assessing the disease group overall. This finding is similar to other published data for survival of older patients with PDAC; in one reported study, the median OS in patients aged ≥ 70 years with advanced PDAC was 6.2 months [11]. In the same study, those patients with advanced PDAC who received BSC alone had a survival of 3.4 months [11], which is worse than that reported in the current study. This may be due to the fact that some patients with PDAC in the current study did not have advanced disease, and though not actively treated had a longer survival on this basis. Equally, patients with BTC were also included in this study and these patients can have a longer natural history depending on primary tumour location [25].

Given the similar prognosis for advanced PDAC and BTC with SACT treatment [22, 24], and due to low numbers of older patients, the decision was made to combine these groups when assessing survival of patients receiving SACT, due to small sample size. The survival of patients ≥ 80 years receiving palliative SACT was comparable to patients aged < 80 years old. This result is in agreement with other studies [15, 26], which compared the survival outcomes in patients ≤ 70 or > 70 years with BTC who received palliative chemotherapy, with survival being similar in the older and younger patients receiving palliative SACT [15, 26]. Of the patients ≥ 80 years receiving BSC, their OS was comparable to patients aged < 80 years. The survival of older patients receiving palliative SACT in this study may have been influenced by the higher proportion of patients with earlier stage disease.

Table 3 Overall survival of patients aged < 80 years and ≥ 80 years with a hepatopancreaticobiliary malignancy

	< 80 years					≥ 80 years				
	*N**	Number of deaths	Median survival time (months)	95% confidence interval	Log-rank test *p* value	*N**	Number of deaths	Median survival time (months)	95% confidence interval	Log-rank test *p* value
Primary disease site										
Ampulla of Vater (ref)	78	34	31.87	19.9–48.9	< 0.0001	11	4	20.03	3.8–**	0.0367
BTC	411	325	12.39	11.1–14.4		39	34	8.46	7.3–12.1	
HCC	78	56	17.74	11.0–22.9		10	9	8.79	2.6–21.7	
PDAC	711	560	8.43	7.7–9.4		81	67	6.3	4.8–7.6	
Other	1	1	.	N/A		1	0	.	N/A	
Total	1279	976	10.75	10.0–11.6		142	114	7.67	6.3–8.7	
Treatment										
Palliative SACT*(ref)	679	541	10.07	8.89–11.08	0.0003	35	29	10.1	6.3–12.3	0.0098
BSC	168	135	6.36	4.26–7.77		57	51	6.36	3.77–7.67	

	N	Number of deaths	Median survival time (months)	95% confidence interval	Log-rank test *p* value
Over 80	142	114	7.67	6.30–8.72	< 0.001
Under 80	1279	976	10.75	10.07–11.57	

N number, *BTC* biliary tract cancer, *HCC* hepatocellular carcinoma, *PDAC* pancreatic ductal adenocarcinoma, *SACT* systemic anti-cancer therapy, *BSC* best supportive care, *N/A* not available

*Number of patients

**Not calculable due to the number of events (deaths) was too small for reliable estimate. "Other" group of primary disease site was not included in the Log-rank test due to very small numbers

Table 4 Multivariable analysis of prognostic factors in patients aged < 80 years and ≥ 80 years with a hepatopancreaticobiliary malignancy

	< 80 years			≥ 80 years		
	Multivariable			Multivariable		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Gender						
Female	Reference			Reference		
Male	0.84	0.74–0.96	0.009	0.88	0.77–0.99	0.05
Primary disease site						
BTC	Reference			Reference		
HCC	0.76	0.57–1.01	0.06	0.84	0.62–1.13	0.26
PDAC	1.66	1.45–1.91	< 0.001	2.02	1.75–2.33	< 0.001
ECOG PS						
≤ 2	Reference			Reference		
> 2	3.57	2.99–4.25	< 0.001	5.92	4.45–7.88	< 0.001
ACE 27 comorbidity						
≤ 1	Reference			Reference		
> 1	1.16	0.99–1.35	0.05	1.15	0.98–1.34	0.07

HR hazard ratio, *CI* confidence interval, *BTC* biliary tract cancer, *HCC* hepatocellular carcinoma, *PDAC* pancreatic ductal adenocarcinoma, *ECOG PS* Eastern Cooperative Oncology Group performance status, *ACE* adult comorbidity evaluation

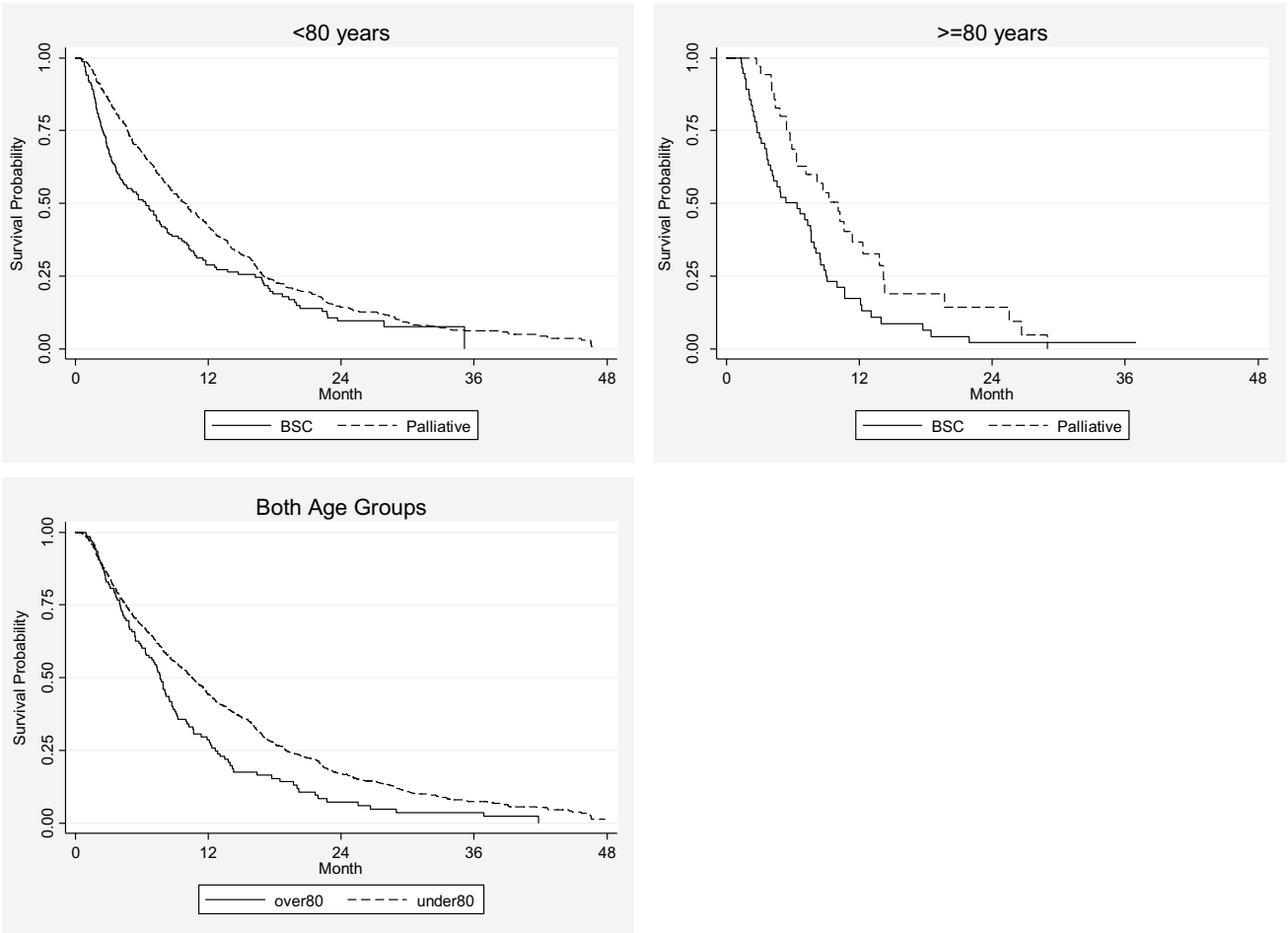

Fig. 3 Kaplan–Meier survival curves for patients aged < 80 years and ≥ 80 years comparing those receiving palliative SACT with those receiving BSC and overall survival for both groups (total groups, unselected by treatment type)

Of the patients aged ≥ 80 years, approximately one quarter completed planned SACT; the median number of cycles of palliative SACT received was 3 for those patients with PDAC and BTC (with most patients receiving single-agent gemcitabine). In comparison, in the randomised trial comparing FOLFIRINOX to gemcitabine in patients with advanced PDAC, the median number of cycles of gemcitabine received was 6 [22]. However, it should be noted that the upper age limit of patients in that study was 76 years. The rate of completion of planned SACT in older patients in the current study was similar to that in younger patients, with nearly three quarters of patients aged < 80 years also not completing planned SACT.

In the ABC-02 study [24], which included patients up to the age of 84 years, 66% of patients received at least 3 cycles of gemcitabine for advanced BTC; results were comparable in the current study with 66% of patients with BTC also receiving at least 3 cycles [24].

The limitations of this study are that it was a retrospective analysis and the population of patients seen who were ≥ 80 years were likely already pre-selected for greater fitness. There are limited data on fitness, as geriatric assessments are not routinely performed at this centre and thus only ECOG PS is available as a marker of fitness. Similarly, limited toxicity data are available, and therefore the impact of SACT on quality of life for older patients cannot be assessed and prospective trials with greater attention to toxicity documentation are necessary. It should be noted though that only 21% of older patients who failed to complete SACT stopped due to side effects. However, this is a large study investigating outcomes in patients ≥ 80 years with a diagnosis of a HPB malignancy, as most studies of older patients reported assess outcomes in patients > 70 years only, without sub-categorisation, and thus provides insight into the management and care of an older patient population in rare disease groups.

In conclusion, this study demonstrated that patients aged ≥ 80 years with HPB malignancies, who are carefully selected, can potentially undergo and gain an equivalent benefit from SACT, when compared to younger patients. The current data do suggest that some patients did not proceed with optimal treatment, despite apparent acceptable fitness levels. The reasons for this cannot be fully elucidated in this study, and may in part represent patient choice. However, it may also be that patients have not been offered treatment due to perceptions regarding their age. It is known that ECOG PS has limited power to assess overall patient fitness [27], or predict toxicity [28] in older patients, though it does have good validation as a prognosticator in many trials. Increased use of frailty screening tools and geriatric assessments [5, 29], which include more detailed assessments of functional status, would improve baseline assessment of patients, and where necessary, this may allow optimisation of their health prior to treatment, and may thus assist with therapeutic decision making.

Author contributions Initial manuscript preparation: LAR and CC. Study concepts and design: McMG, CC and LAR. Data Acquisition: LAR, CC, WR, FA, SA, RA, RH. Quality control of data and algorithms: MMG and LAR. Statistical analysis: WX. Data Analysis and interpretation: WX, LAR, CC, MMG. Manuscript editing: All authors. Manuscript review: LAR, CC, WX, WR, FA, SARM, RA, RH, LA, HRA, VJW, MMG.

Compliance with ethical standards

Conflict of interest Angela Lamarca received funding from ASCO Conquer Cancer Foundation Young Investigator Award and The Christie Charity. All authors declare no conflict of interest.

Ethical approval This retrospective study was carried out 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. This study was approved by the Clinical Audit Committee of The Christie NHS Foundation Trust (reference 17/1923).

References

1. 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;22:4626–31.
2. Williams GR, Mackenzie A, Magnuson A, et al. Comorbidity in older adults with cancer. J Geriatr Oncol. 2016;7:249–57.
3. Brunot A, Le Sourd S, Pracht M, Edeline J. Hepatocellular carcinoma in elderly patients: challenges and solutions. J Hepatocell Carcinoma. 2016;3:9–18.
4. Borzio M, Dionigi E, Parisi G, Raguzzi I, Sacco R. Management of hepatocellular carcinoma in the elderly. World J Hepatol. 2015;7:1521–9.
5. Wildiers H, Heeren P, Extermann M, et al. International Society of Geriatric Oncology Consensus on geriatric assessment in older patients with cancer. J Clin Oncol. 2014;32(24):2595–603.
6. Miyamoto DT, Mamon HJ, Ryan DP, et al. Outcomes and tolerability of chemoradiation therapy for pancreatic cancer patients aged 75 years or older. Int J Radiat Oncol Biol Phys. 2010;77:1171–7.
7. Nishikawa H, Kimura T, Kita R, Osaki Y. Treatment for hepatocellular carcinoma in elderly patients: a literature review. J Cancer. 2013;4:635–43.
8. Aduen JF, Sujay B, Dickson RC, et al. Outcomes after liver transplant in patients aged 70 years or older compared with those younger than 60 years. Mayo Clin Proc. 2009;84:973–8.
9. Takahashi H, Mizuta T, Kawazoe S, et al. Efficacy and safety of radiofrequency ablation for elderly hepatocellular carcinoma patients. Hepatol Res. 2010;40:997–1005.
10. Edeline J, Crouzet L, Le Sourd S, et al. Sorafenib use in elderly patients with hepatocellular carcinoma: caution about use of platelet aggregation inhibitors. Cancer Chemother Pharmacol. 2015;75:215–9.
11. Wang P, Meng ZQ, Chen Z, et al. Survival rate of pancreatic cancer in elderly patients. Hepatogastroenterology. 2008;55:681–6.

12. van der Geest LG, Besselink MG, van Gestel YR, et al. Pancreatic cancer surgery in elderly patients: balancing between short-term harm and long-term benefit. A population-based study in the Netherlands. Acta Oncol. 2016;55:278–85.
13. Green MR. Gemcitabine safety overview. Semin Oncol. 1996;23:32–5.
14. Vitale A, Spolverato G, Bagante F, et al. A multi-institutional analysis of elderly patients undergoing a liver resection for intrahepatic cholangiocarcinoma. J Surg Oncol. 2016;113:420–6.
15. McNamara MG, Bridgewater J, Lopes A, et al. Systemic therapy in younger and elderly patients with advanced biliary cancer: subanalysis of ABC-02 and twelve other prospective trials. BMC Cancer. 2017;17:262.
16. Hurria A, Levit LA, Dale W, et al. Improving the evidence base for treating older adults with cancer: American Society of Clinical Oncology statement. J Clin Oncol. 2015;33:3826–33.
17. Neoptolemos JP, Palmer DH, Ghaneh P, et al. Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial. Lancet. 2017;389:1011–24.
18. Hentic O, Dreyer C, Rebours V, et al. Gemcitabine in elderly patients with advanced pancreatic cancer. World J Gastroenterol. 2011;17:3497–502.
19. Website; Cancer Research UK. http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/gallbladder-cancer#heading-Two. Accessed June 2017.
20. Kallogjeri D, Gaynor SM, Piccirillo ML, et al. Comparison of comorbidity collection methods. J Am Coll Surg. 2014;219(2):245–55.
21. Parmar AD, Vargas GM, Tamirisa NP, Sheffield KM, Riall TS. Trajectory of care and use of multimodality therapy in older patients with pancreatic adenocarcinoma. Surgery. 2014;156:280–9.
22. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med. 2011;364:1817–25.
23. Burris HA, Moore MJ, Andersen J, et al. Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: a randomized trial. JCO. 1997;15:2403–13.
24. Valle J, Wasan H, Palmer DH, et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med. 2010;362:1273–81.
25. Bridgewater J, Lopes A, Palmer D, et al. Quality of life, long-term survivors and long-term outcome from the ABC-02 study. Br J Cancer. 2016;114:965–71.
26. Horgan A, Knox J, Aneja P, Le L, McKeever E, McNamara M. Patterns of care and treatment outcomes in older patients with biliary tract cancer. Oncotarget. 2015;6:44995–5004.
27. Repetto L, Fratino L, Audisio RA, et al. Comprehensive geriatric assessment adds information to Eastern Cooperative Oncology Group performance status in elderly cancer patients: an Italian Group for Geriatric Oncology Study. J Clin Oncol. 2002;20:494–502.
28. Hurria A, Togawa K, Mohile SG, Owusu C, Klepin HD, Gross CP, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. J Clin Oncol. 2011;29(25):3457–65.
29. Decoster L, Van Puyvelde K, Extermann M, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations. Ann Oncol. 2014;26(2):288–300.