Impact of Early Palliative Care on End of Life in Advanced Biliary Tract Cancer Patients

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Abstract

Background: Majority of biliary tract cancer (BTC) patients have not access to surgery. They receive chemotherapy and/or palliative care (PC). We studied if early palliative care referral could influence overall survival (OS) and the aggressiveness of end-of-life care.

Participants and Design: We conducted a retrospective cohort study in patients with non-curative BTC, diagnosed between 2013 and 2019 in 6 hospitals of Eastern France. PC was defined a specialist-delivered palliative care encounter.

Results: 200 patients with BTC were included in our study, with 188 deaths. 87 (44%) had no PC, 30 (15%) had a very early PC (<3 months after diagnosis), 20 (10%) had an early PC (3-6 months), and 63 (32%) a late PC (>6 months). The median time between referral and death was 0.9 to 1.3 months (depending on groups). OS were 12.4 months (no PC), 3.0 months (PC<3 m), 6.4 months (PC 3-6 m), 16 months (PC>6 m). We had no evidence for survival improvement with early PC. PC seemed to reduce chemotherapy near death (37% without PC, 30% with PC<3m, 11% with PC 3-6m, 10% with PC>6m), visits in emergency department (ED) during final month (respectively: 36%, 20 %, 15%, and 7%), intensive care unit hospitalizations (ICU) near death (13%, 0%, 0%, 2%). Place of death seemed to be positively impacted by PC (conventional acute unit, respectively: 73%, 21%, 21%, 25% and ICU or ED: 8%, 0%, 5%, 2%).

Conclusion: Referral to PC seems too late for changing disease course. Our practice should evolve, with the objective that each advanced BTC patient has early-PCR after diagnosis, for improving management of end-of-life, symptoms, and family needs.

Trial registration number: 2019PI274 , 05/28/2020.

Introduction

Biliary tract cancer (BTC) are rare diseases but incidence is increasing (1). Prognosis remains poor with overall survival (OS) between 6 to 11 months (1, 2). BTC are frequently diagnosed at advanced stage of the disease due to delayed symptoms. Uncomfortable symptoms are frequent at advanced stage such as jaundice (3), anorexia, asthenia, abdominal pain, weight loss, psychological suffering...

Only 20 to 30% of the patients have access to surgery, which is the only curative-intent treatment (4). Most of patients receive palliative systemic therapy (chemotherapy, targeted therapy, immunotherapy) or exclusive supportive care. Palliative care teams (PCT) are composed of several actors making possible a multidisciplinary and global comprehensive care : physical, emotional, social (family caregivers...), spiritual (meaning, dignity, faith...), informational (prognosis, illness understanding...) (5). PC and active treatment are not opposed but they are rather complementary approaches, that should be associated early for more benefits. In general, in daily practice, patients' referral to PCT is late, when no more active treatment is possible.

Some recent studies have shown the positive impact of PC on aggressiveness of end-of-life care, that includes chemotherapy, intensive care unit admission, emergency department (ED) visit and acute unit hospitalization, during last month of life (6). In pancreatic cancer, Jang *et al.* shown in a retrospective study the positive impact of a PC consultation on these end-of-life indicators (7). These results were confirmed in a randomized Italian study of 206 metastatic pancreatic cancer patients (8).

Recently, the concept of PC has evolved with the issue of the timing of palliative care referral (PCR), and the benefits of an early palliative care. An Australian retrospective study published in 2019 highlighted the use of early PC to improve aggressiveness of end-of-life care, compared to late PC (> 90 days before death) in pancreatic cancer patients (9).

Considering this, some studies has recently studied if early PC could have also an impact of OS. A retrospective study among patients in advanced lung cancer has found that early PC (30 to 365 after diagnosis) was associated with increase of OS (10). In 2021, a randomized study of advanced esophagogastric cancer found an OS improvement in case of early interdisciplinary supportive care (11).

To our knowledge, no study evaluated this concept of early PCR in advanced BTC patients. In this retrospective multicentric study, we studied the relationship between early PCR and survival (primary outcome). We also explored the impact of early PCR on treatment aggressiveness near the end of life.

Methods

Study Design

We conducted a retrospective study in 200 patients with a diagnosis of advanced BTC (cholangiocarcinoma and gallbladder) between January 1, 2013 and December 31, 2019. We included patients of 6 University hospitals of Eastern France (Nancy University Hospital, Besançon University Hospital, Dijon University Hospital, Reims University Hospital, Strasbourg University Hospital, and Strasbourg ICANS Center for the Treatment of Cancer). Follow-up data were available until January 2021. Ethics approval was obtained from the Ethics Committee of Nancy CHU (September 8, 2020), Licence number 272. Patients received an information letter and had 30 days to ask their withdrawal from the study. After this delay, they were considered as participants.

Cohort Selection

We included adults (> 18 years old) with histologically confirmed, locally advanced or metastatic cholangiocarcinoma or gallbladder adenocarcinoma, diagnosed between January 1, 2013 and December 31, 2019. Hospitals' administrative database was used to identify eligible patients using the International Classification of Diseases codes C22.2 (Intrahepatic bile duct carcinoma), C23 (malignant neoplasm of gallbladder), C24 (malignant neoplasm of other and unspecified parts of biliary tract). Database was closed for analysis in January 2021. We excluded patients who died within a week after diagnosis.

Exposure

PC was defined as a specialist-delivered palliative care encounter received inpatient or outpatient setting after a BTC diagnosis. It could be with a mobile PCT, in hospitalization (palliative care units) or in consultation. Data were collected in electronic medical records (DxCare software).

We defined four groups according to the date of this first meeting: patients who met the PCT less than three months after diagnosis (early PC), 3–6 months after diagnosis, more than 6 months after diagnosis (late PC) or no PC.

Study Objectives

Primary outcome was OS after diagnosis according to PCR. We secondary evaluated the impact of early PCR on the aggressiveness of end-of-life care, which included place of death (at home with home hospitalization, at home without home hospitalization, intensive care unit, conventional acute unit, palliative care unit), last-month chemotherapy, last-month ED visit and last-month intensive care unit hospitalization. Continuous variables were summarized by descriptive statistics (number of cases, mean, median, quartile) and categorical variables were summarized using percentages. We also compared the most frequently reported reasons to referral and proposals made by PCT.

Statistical Analysis

Characteristics of sample were described by percentage for categorical variables and median with inter-quartile range [Q1-Q3] for continued variables. OS was calculated from the date of diagnosis of advanced BTC until the date of death or date of last follow-up and Kaplan-Meier curve was realized for each group. A second analysis was made by calculating the time from the date of first meeting with PC until the date of death or date of last follow-up. To address potential selection bias, we have planned to make a propensity score of receiving palliative care, composed of metastatic stage, age (> 75 years old), performans status OMS (2, 3 and 4), Charlson score (> 3). This approach minimized selection bias by comparing patients with a similar likelihood of receiving PC. Due to heterogeneity between study groups, propensity score has not been achieved. Clinical characteristics among these four groups were too different to produce a reliable comparison. The significant threshold was fixed at 5%. All analyses were performed using SAS® software version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patients' Characteristics

200 patients with advanced BTC were included. Median age was 67.6 years old. 61% of the patients were men (Table 1). Most of the tumors were intrahepatic CCA (51%), then perihilar (24%), gallbladder (18%) and distal CCA (7%). 62.5% of the cases were metastatic, and 62.5% were locally advanced. Concerning

risk factors, 27% were smokers and 18% had a heavy alcohol consumption, 19% were obese, 31% had diabetes, 14% had a cirrhosis. Only 2 patients had a primary sclerosing cholangitis. The most common symptoms were abdominal pain (40%), jaundice (33%), asthenia (31%) and anorexia (28%). A quarter (26%) had a prior curative-intent treatment before their relapse. Chemotherapy was prescribed for 82.5% of the patients, and 17.5% received exclusive supportive care.

Among the 165 patients who received chemotherapy, the most frequent (67%) first-line treatment was gemcitabine-oxaliplatin (GEMOX). Other protocols were less frequent (gemcitabine-cisplatin in 14%, gemcitabine in 10%...). More than half of the patients received a second-line chemotherapy (56%) with a majority (45%) of 5FU-irinotecan (FOLFIRI).

Table 1
Patients' characteristics

Variable	Total (n = 200)
Age, years (median, IQR)	67.6 (60.7–74.4)
Gender, n (%)	
Male	123 (61.5%)
Female	77 (38.5%)
Performance status, n (%)	
0–1	152 (77.2%)
2	29 (14.7%)
3–4	16 (8.1%)
<i>missing</i>	3
Denutrition (IMC < 18.5 or < 21 for patients older than 70 years)	7 (3.7%)
<i>RISK FACTORS of biliary tract cancer</i>	
Obesity (IMC > 30), n (%)	36 (18.8%)
Diabetes, n (%)	62 (31.0%)
Smoker, n (%)	53 (26.5%)
Chronic alcoholism, n (%)	36 (18.0%)
Cirrhosis, n (%)	28 (14.0 %)
Primary sclerosing cholangitis, n (%)	2 (1.0%)
<i>DIAGNOSIS</i>	
Primary tumor site, n (%)	
Intrahepatic	101 (50.8%)
Perihilar (= Klatskin)	48 (24.1%)
Gallblader	35 (17.6%)
Distal	14 (7.0%)
Hepatobiliary carcinoma	1 (0.5%)
Missing	1
Disease status, n (%)	
Locally advanced	75 (37.5%)

Variable	Total (n = 200)
Metastatic	125 (62.5%)
Symptoms at diagnosis (4 most common symptoms for 197 patients with available data)	
Abdominal pain	79 (40.1%)
Jaundice	65 (33.0%)
Asthenia	61 (31.0%)
Anorexia	56 (28.4%)
Absence of symptoms	47 (23.9%)
Albumine median (g/L) (N = 175, IQR)	34 (29–39)
CA 19 – 9 median (N = 153, IQR) (kU/L)	263 (27–1954)
<i>TREATMENT</i>	
Prior curative-intent treatment, n (%)	52 (26.0%)
Chemotherapy received, n (%)	
Yes	165 (82.5%)
No	35 (17.5%)
Type of L1 chemotherapy regimen, n (%)	N = 165 (82.5%)
Among 165 patients who received L1 chemotherapy (N = 165)	
GEMOX	110 (66.7%)
GEMCIS	23 (13.9%)
GEMCITABINE	16 (9.7%)
Others or unknow	16 (9.7%)
Patients treated with L2 chemotherapy, n (%)	N = 93/165 (56.4%)
FOLFIRI	42/93 (45.2%)
LV5FU2 Cisplatin	22/93 (23.7%)
FOLFOX	8/93 (8.6%)
Others or unknow	21 (22.6%)
Patients treated with L3 chemotherapy, n (%)	N = 40/165 (24.2%)

Variable	Total (n = 200)
Patients treated with L4 chemotherapy, n (%)	13/165 (7.9%)
<i>PALLIATIVE CARE</i>	
No encounter with palliative care	87 (43.5%)
Palliative care	113 (56.5%)
<i>HOME HOSPITALIZATION</i>	
Yes	39 (19.6%)
No	160 (80.4%)
Unknow	1

Description of Palliative Care

Most of the cohort (56%) met the PCT at least once (Table 1). The mean time to PCR was more than 6 months after diagnosis (9.7 months) (Table 2). This first PC encounter was in majority through mobile PCT (65%) and less often during a hospitalization (26%) or a consultation (9%). The most frequent reasons for referral were asthenia (58%), decision for place of care (41%) and pain (40%). PCR interventions were “decision for becoming and place of care” (54%), opioids treatment (49%), anxiolytics (36%), mouth care (36%) (not mutually exclusive).

Table 2
Description of Palliative care

Variable	N = 113 (palliative care)
Mean time of first PC encounter after diagnosis (months)	9.7
Timing of the encounter after diagnosis	
< 3 months after diagnosis	30 (26.5%)
3–6 months after diagnosis	20 (17.7%)
>6 months after diagnosis	63 (55.7%)
Type of first encounter	
Mobile palliative care teams	74 (65.5%)
Palliative care units/beds	29 (25.7%)
Consultation	10 (8.8%)
Encounter during the last hospitalization (before death)	13 (11.5%)
Most frequently reasons for referral Among 111 patients with available date	
Asthenia	64 (57.7%)
Decision for becoming and place of care	46 (41.4%)
Pain	45 (40.5%)
Psychological symptoms	13 (11.7%)
Following the cessation of active therapeutics	19/92 (10.9%)
Most frequently treatment/take of care by the PC team Among 106 patients with available data	
Decision for becoming and place of care	57 (53.9%)
Opioids (start or dose increase)	52 (48.6%)
Anxiolytics	38 (35.8%)
Mouth care	38 (35.8%)

Impact of Palliative care on Overall Survival

Among the 200 included patients, 188 died. 87 (43.5%) did not received PC, 30 (15%) early PC (< 3months after diagnosis), 20 (10%) PC 3 to 6 months after diagnosis, and 63 (31.5%) late PC (> 6months) (Table 3). Median OS were respectively in the four groups 12.4 months (no PC), 3.0 months (PC < 3months), 6.4 months (PC 3–6 months) and 16.0 months (PC > 6 months).

Figure 1 represents OS with or without PC ($p = 0.34$). OS was not significantly different between PC and no PC group ($p = 0.34$). Figure 2 represents survival according to the first PCR ($p = 0.79$). Time between PC contact and death were 0.9 months (PC < 3m), 1 month (PC 3-6m) and 1.3 months (PC > 6m).

Impact of Palliative Care on Aggressiveness in End-Of-Life Care

Place of Death

Place of death seemed to be influenced by PC, especially when PCR was early (< 3 months after diagnosis). PC seemed to be associated with less death in conventional acute unit, intensive care unit and ED (respectively 72% no PC vs 21% early PC and 8% no PC vs 0% early PC) and more death in palliative care unit (Table 3).

Last-month Chemotherapy

PC seemed to be associated with less chemotherapy during last month of life: 36% (no PC), 30% (PC < 3m), 10% (PC 3-6m), 10% (PC > 6m). In early PC group (< 3m), this result is hard to explain, because only 12 patients received chemotherapy in this group (including 3 in the last month).

Last-Month Emergency Department Visit

Results were similar for ED visits near death. PC was associated with less visits (20% PC < 3m, 15% PC 3-6m, 7% PC > 6m ; vs 35% no PC), but the impact of early PCR did not appear.

Last-Month Intensive Care Unit Hospitalization

Hospitalizations in intensive care unit seemed to be impacted by PC: 10 patients for the no PC group vs 1 patient in the PC group.

Table 3

Impact of palliative care on survival and aggressiveness of end-of-life care: Comparison between the 4 groups (*No palliative care, PC < 3 months after diagnosis, PC 3–6 months after diagnosis, PC > 6 months after diagnosis*)

Variable (N = 200 patients)	No PC N = 87 (43.5%)	PC < 3m N = 30 (15.0%)	PC 3-6m N = 20 (10.0%)	PC > 6m N = 63 (31.5%)	All PC N = 113 (56.7%)
<i>DESCRIPTION OF THE GROUPS</i>					
Age ≥75 years old	22 (25.3%)	7 (24.1%)	6 (30.0%)	12 (19.0%)	25 (27.2%)
Performans status ≥2	19 (21.8%)	18 (62.1%)	3 (15.8%)	5 (8.1%)	26 (23.6%)
Unknow		1	1	1	3
Charlson ≥2	31 (35.6%)	14 (46.7%)	9 (45.0%)	20 (31.7%)	43 (38%)
Metastasis	56 (65.1%)	19 (63.3%)	14 (70.0%)	38 (60.3%)	71 (62%)
Unknow	1				
Chemotherapy received	73 (83.9%)	12 (40.0%)	19 (95.0%)	61 (96.8%)	92 (81.4%)
Death	78 (89.7%)	30 (100%)	20 (100%)	60 (95.2%)	110 (97.3%)
<i>SURVIVAL (N = 188 patients dead)</i>					
Overall survival in months (median)	12.4	3.0	6.4	16.0	
Delay between PC contact and death in months (median)		0.9	1.0	1.3	
<i>COMPARISON OF END-OF-LIFE CARE (N = 188 patients dead)</i>					

Variable (N = 200 patients)		No PC N = 87 (43.5%)	PC < 3m N = 30 (15.0%)	PC 3- 6m N = 20 (10.0%)	PC > 6m N = 63 (31.5%)	All PC N = 113 (56.7%)
Place of death	N = 188	No PC N = 78	PC < 3m N = 30	PC 3- 6m N = 20	PC > 6m N = 60	All PC N = 110
Home	26 (13.8%)	7 (9.6%)	4 (13.8%)	2 (10.5%)	13 (22.0%)	19 (17.3%)
Home hospitalization	12 (6.4%)	7 (9.6%)	1 (3.4%)	0	4 (6.8%)	5 (4.5%)
Conventional acute unit	78 (41.5%)	53 (72.6%)	6 (20.7%)	4 (21.1%)	15 (25.4%)	25 (22.7%)
Palliative care unit	56 (29.8%)	-	18 (62.1%)	12 (63.2%)	26 (44.1%)	56 (50.9%)
Intensive care unit or emergency department	8 (4.3%)	6 (8.2%)	0 (0%)	1 (5.3%)	1 (1.7%)	2 (1.8%)
Unknow	8	5	1	1	1	3
Cause of death (3 most frequents)						
Deterioration of general condition		39 (59.1%)	27 (93.1%)	17 (89.5%)	50 (92.6%)	94 (85.4%)
Sepsis		16 (24.2%)	2 (6.9%)	0 (0%)	1 (1.9%)	3 (2.7%)
Gastro intestinal bleeding		3 (4.5%)	0 (0%)	0 (0%)	0 (0%)	0%
Unknow		12	1	1	6	8
Chemotherapy near death (last month) (among the 157 dead patients who received chemotherapy)		23/63 (36.5%)	3/12 (30.0%)	2/19 (10.5%)	6/58 (10.3%)	11/89 (12.4%)
Unknow		1	2	-	-	2

Variable (N = 200 patients)	No PC N = 87 (43.5%)	PC < 3m N = 30 (15.0%)	PC 3-6m N = 20 (10.0%)	PC > 6m N = 63 (31.5%)	All PC N = 113 (56.7%)
Emergency department visit near death (last month)	27 (35.5%)	6 (20.0%)	3 (15.0%)	4 (6.8%)	13 (11.8%)
Unknow	2	-	-	1	
Intensive care unit hospitalization near death (last month)	10 (12.8%)	0 (0%)	0 (0%)	1 (1.7%)	1 (0.9%)
Unkow	2	-	-	1	1

Discussion

To our knowledge, the present study was the first to provide real-world data about PC settings and the impact of this approach on survival of patients with advanced BTC.

In our study, 17% of the patients did not received active treatment, which is different from other studies (63% of iCCA received only PC in a study published by Neuzillet *et al.* in 2020(12), which included 3650 iCCA patients, not systematically with histological proof).

Histologically-proven CCA conduct to more specific treatment and most of the patients who do not have a biopsy are not accessible to active treatment. In the same way, more than a half (56%) of chemotherapy-treated patients had a second-line chemotherapy, which is more than other studies (less than one third (13)).

Our main objective was to analyse if early PC could improve OS. We found no evidence that OS was better in PC group compared to no PC group. It can be partially explained by the heterogeneity between groups. Indeed, groups were incomparable: patients who were addressed earlier, were suffering worse comorbidities and advanced diseases. It reveals that the group of patients who met PCT early after diagnosis has the worst survival due to several poor prognosis factors: high performans status (≥ 2 for 62% of them), more comorbidities (Charlson Index Score ≥ 2 for 47% of them), and only one third of them receive chemotherapy. Consequently, causes of death seem to be also different between groups. As explained before, patients from early PC groups are more fragile with more comorbidities and more advanced cancer. They died more from deterioration of general conditions (93% for early PC vs 59% no PC), and less of acute disease as sepsis (7% early PC vs 24% no PC) or gastro-intestinal bleeding (0% early PC vs 4% no PC). On the contrary, patients who did not receive PC died more from acute complication as sepsis or bleeding, with more hospitalizations in intensive care unit.

Differences are due to the retrospective character of our study, which shows our daily practice, with patients referred to PCT 0.9 to 1.3 months before death, generally when active treatments are no more

possible. As a result, role of PC givers is limited, because we let them a very short period to act. They cannot build strong relationship with patient on important issues such as interruption of chemotherapy, end-of-life preferences, and meeting family members to have a global action. These results are similar to a French study showing median survival after first PCT intervention of 31 days(14). In the same study, 18% of the patients first met PCT 3 days before death.

In 2017, the American Society of Clinical Oncology (ASCO), published some recommendations about PC, stating that “patients with advanced cancer should receive dedicated PC services early in the disease course and concurrent with active treatment”(15). In our study, 56% of the patients have met at less once the PCT, which is similar that a retrospective study in pancreatic cancer patients (52%) (7). However, time-to-referral seems too late for impacting prognosis. Average time between diagnosis and PCR was 9.7 months, although median OS fluctuates from 3 to 16 months. Among 11% of the patients who met PCT, this meeting happened during the last hospitalization (a few days before death), which is extremely late.

The most frequently reasons for PCR in our study were asthenia (58%), “decision for becoming and place of care” (41%), pain (40%), psychological symptoms (12%) and then following the cessation of active therapeutics (11%) (which means that the oncologist stops taking care of the patient and a relay is made with PCT at the end of the active therapeutics).

To compare, Vinant *et al.* (14) showed in their study that the 3 major reasons for referral (for all cancer types) were pain (57%), early encounter (24%), decision for place of care (18%) and then in 6th position “decision to withhold or withdraw treatments” (9.3%). In our study, we saw that patients were mostly referred to PCT for difficulties for end-of-life management. Late PCR does not allow PCT to be a part of the decision about active treatment.

In our study, meeting PCT seemed to have a great impact on place of death (Table 3), because fewer patients died in conventional, emergency or intensive departments. In a retrospective study published in 2015, conducted in more than 500 000 cancer patients, proportion of death in PC units was 10% (16). Vinant *et al.* showed that this proportion raised to 30% when patients are referred to PCT (14). It reflects the positive impact of PC on the place of death, with less deaths in acute care units. Death in appropriate department is important for a better management of end-of-life. In palliative care units or home hospitalization, teams are familiar with these situations and they are able to anticipate future needs of patients, and to discuss of their preferences in order to head off difficult situations of end-of-life.

In a retrospective study in pancreatic cancer patients published in 2019, chemotherapy was prescribed during last month in 17% in case of early PCR and 25% in case of late PCR (non-significantly, $p = 0,22$) (9). 18% of our patients received chemotherapy within the last month of life (36% no PC, 10–30% with PC), which is similar to previous studies (18% received last-month chemotherapy in a study published in 2015 (16)). PC seems to reduce end-life chemotherapy. Finally, the use of chemotherapy during the last month is still a common situation. For patients, end-of-life chemotherapy does not seem beneficial, implying all adverse effects of drugs such as asthenia, nausea, infections leading to hospitalizations, without positive impact on prognosis. It could be avoided with early PCT meeting.

In the Australian study on pancreatic cancer patients (9), early PC allows a reduction of last-month visit ED when comparing early (24%) to late PC (42%) ($p = 0,003$). In our study, in the PC group, ED visit proportions varied from 7 to 20%, compared with 35% in the no PC group. Our data suggest that PC reduces ED visits during the last month of life. However, early PCR does not appear as a favourable factor contrary to previous studies. It could be explained by a lack of patients in the present work.

In 2005, Earl *et al.* proposed some objectives to evaluate aggressiveness in end-of-life care (6):

- *Less than 10% of patients should receive chemotherapy in the last 14 days of life.* In our study we collected last-month chemotherapy rate (36% without PC vs 10 to 30% with PC)
- *Less than 4% of emergency room visits.* In our study we had 35% no PC group and 7 to 20% PC group
- *Less than 17% death in an acute care hospital.* We had 8% death in ICU in non-PC group vs 0 to 5% in PC group. In conventional acute unit we had 73% in non PC group vs 21 to 25% in PC group.
- *Less than 4% of admission in ICU.* In our study this objective is achieved for the PC group (0–2%) but no for the no PC group (13%)

Conclusion

This study provides important data about BTC patients, end-of-life management, and partnerships with PCT. We found no evidence for improvement of OS with early PCR. PCR appears too late to change prognosis. However, PC seems to have a positive impact on end-of-life with, with fewer useless chemotherapy, fewer visit in ED, fewer hospitalization in ICU, and fewer death in a conventional acute unit or ICU.

Despite ASCO recommendations of 2017 in favour of early PCR in the disease course (concurrent to active therapy), we mainly address patients to PCR for end-of-life management in daily practise. It may underline limited access to PCR due to reduced workforce. Efforts could be made for a better education about PCR role in a global approach in cancer patients. Early PC should endorse a central role in the BTC cancer journey, with many positive consequences on end-of-life preferences, discontinuation of useless chemotherapy, better management of symptoms, family needs... The question about the definition of “early” PC remains. Thresholds differ among studies, but definition should evolve for each patient according to his disease, prognosis, comorbidities, and symptoms, moving towards a “personalized early PC”.

Abbreviations

BTC: Biliary tract cancer, **CCA:** Cholangiocarcinoma (iCCA : intra hepatic cholangiocarcinoma, eCCA : extra hepatic cholangiocarcinoma, pCCA : peri hilar cholangiocarcinoma), **ED:** Emergency department,

ICU: Intensive care unit, **OS:** Overall survival, **PCU:** Palliative care unit, **PCT:** Palliative care teams, **PCR:** Palliative care referral, **PS:** Performans status

Declarations

Acknowledgment

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Code availability

All analyses were performed using SAS® software version 9.4 (SAS Institute, Cary, NC, USA).

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Conflicts of interest

The authors declare no competing interests.

Ethics approval

Ethics approval was obtained from the Ethics Committee of Nancy CHU (September 8, 2020), Licence number 272

Consent to participate and consent for publication

Permission to publish the case anonymously was obtained from patients.

Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author [MM]. The data are not publicly available due to information that could compromise research participant privacy.

Authors' contributions

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Figures

Figure 1

Association between survival and palliative care: palliative care vs no palliative care

Figure 2

Survival after first meeting with palliative care team