

# Effect of Palliative Care Decision on Use of Hospital Services in Pancreatic Cancer Patients: A Retrospective Study

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**Abstract.** *Background/Aim:* Continuing chemotherapy or using hospital services near the end of life (EOL) and delaying the approach to palliative care (PC) services are factors impairing quality of life near the EOL. *Patients and Methods:* Records of patients with pancreatic cancer treated at Helsinki University Hospital in 2013 and deceased by the end of 2014 were reviewed (N=221). The PC decision establishes the point when anticancer treatment is interrupted and the focus shifts to symptom-centered PC. The timing of the PC decision, referrals to specialized PC, use of hospital services at the EOL, and place of death were examined. *Results:* The median overall survival was 13 months from diagnosis. The PC decision was made <30 days prior to death or not at all for 44% of patients. In addition, 68% of these patients used hospital service in the last month of life compared to 32% of patients with an earlier PC decision ( $p<0.001$ ). A later or lacking PC decision correlated with a larger proportion of deaths in a secondary or tertiary hospital (64% vs. 36%), but the difference was not statistically significant ( $p=0.25$ ). *Conclusion:* A late or lacking PC decision for patients with pancreatic cancer was found in almost half of the patients. There was a significant difference in the use of hospital services depending on the timing of the decision. An earlier PC decision might improve

EOL care, since a late or lacking PC decision relates to a more abundant use of hospital services and an increased risk of hospital deaths.

In 2020, around 1,200 new pancreatic cancer diagnoses were made in Finland (1). Only approximately 20% of the patients are suitable for operative care and will undergo potentially curative surgical resection. The prognosis is poor even after resection (2). Pancreatic cancer is a fatal disease with an overall 5-year survival rate of only 5-12% (3, 4) that has remained stagnant for decades in the Nordic countries and worldwide (5). Therefore, most patients with pancreatic cancer are beyond curative care and the goal of care is life-prolonging or palliative.

In advanced pancreatic cancer, anticancer treatment can improve overall survival, but the prognosis is generally poor (3). There is no evidence of efficacy of subsequent lines of chemotherapy for patients with advanced pancreatic cancer. Nonetheless, studies have shown a trend toward more aggressive end-of-life (EOL) cancer care (6, 7). Early integrated palliative care (PC) and advance care planning may reduce aggressive treatments and hospitalizations at the EOL and enable earlier referral to specialized PC services (8, 9). Patients with pancreatic cancer are often dealing with a wide spectrum of severe symptoms such as early cachexia, anorexia, and fatigue. Therefore, the need for early integrated PC and psychosocial support early in the disease trajectory is critical. Systematically integrated early PC has been shown to correlate with a higher use of hospice services and less anticancer therapy during the last month of life (10). Early integrated PC occurs concurrent with the disease-modifying therapy and even though it is recommended (10, 11), it was not yet the praxis during the time of this study, nor is it the reality everywhere nowadays.

The PC decision is defined as the decision to interrupt anticancer treatment with a life-prolonging goal and shift the focus to symptom-centered care. The decision is made by the

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oncologist overseeing the patient's care. The period following this decision is defined as the palliative phase.

We used the term 'early' PC, when the PC decision was done at  $\geq 1$  month prior to death and 'late' when it occurred after this or not at all. We decided on the 1-month breakpoint since previous studies have used 30-90 days as the cut point concerning 'early' referrals to PC (12-14). In addition, indicators of an aggressive care close to death have been suggested to include starting a new anticancer treatment during the 30 days of life or continuing the ongoing treatment until the last 14 days of life, as well as several emergency room visits, inpatient hospital admissions or intensive care unit days during the last 14-30 days of life (15).

In a recent Finnish study, late or lacking PC decision-making was found to be associated with more aggressive care close to death (16). PC intervention and an early PC decision have been shown to be associated with a drop in hospitalizations and visits to the emergency department (ED) during the last month of life, also creating cost benefits (17, 18). Starting a new anticancer treatment or continuing ongoing treatment very close to death, repeated ED visits, inpatient hospital admissions, or intensive care unit stays near the EOL have been considered indicators of a poor quality of life (19).

The aim of this retrospective single-center study was to evaluate the timing of PC decision on the use of hospital services, referral to specialist palliative services (PC ward, at home care or hospice), and place of death. The patients were divided into two groups for comparison, defined as patients with an 'early' ( $\geq 30$  days prior to death) or 'late' ( $< 30$  days prior to death) PC decision.

## Patients and Methods

*Cohort selection.* Patients with pancreatic cancer were identified from the hospital charts using the ICD-10 code C25. Included patients were those treated in the Department of Oncology at Helsinki University Hospital (HUS) in 2013 and who were deceased by the end of 2014. The number of patients fulfilling the criteria was 221. This study is continuum to a recently published Finnish study (17). However, in the previous study, the larger cancer entities dominated and only a part of the pancreatic cancer patients were included. Consequently, the same conclusions are not necessarily applicable for pancreatic cancer patients and only a part of these findings has been reported earlier. This retrospective study was done with the permission of the authorities of HUS. No ethics committee approval was needed, according to Finnish legislation for research.

The vast majority of cancer patients in Finland are initially evaluated and treated at public university and central hospitals. HUS is the largest one of the five university hospitals in Finland, providing cancer care for approximately 1.7 million residents in Southern Finland. HUS provides all secondary and tertiary care for the municipalities in the area. Although there are a PC Unit and Psychosocial Support Unit at the Department of Oncology, at the time covered by this study, early integrated PC was not yet systematically provided at HUS. The PC Unit is an outpatient unit

within the Cancer Center, with no consult team nor inpatient ward. It coordinates the PC, but the municipalities organize primary care and are responsible for EOL care. In 2013-2014, a specialized hospice, two specialized community wards, and several specialized home care teams were providing EOL care in Southern Finland.

*Data sources and collection.* In Finland, patient records are electronic and are systematically collected and documented. Data on patient demographics, ICD-10 codes, given chemotherapy and radiation therapy, hospitalization, and visits to ED and outpatient units were extracted automatically from hospital records. Referrals to home care, home hospital care, a primary care hospital ward, and hospice care were obtained from patient medical records. Additional data were manually retrieved from patient medical records, including PC decision, do-not-resuscitate (DNR) order, and reason for treatment termination. Information on cause, time, and place of death was obtained from death certificates.

*Statistical analysis.* Patient characteristics were reported using descriptive statistics. Comparisons were based on the timing of the PC decision. For continuous variables, one-way ANOVA was used for comparisons, e.g., the time from PC decision to death. Correlations between age and timing of the PC decision and the association between PC decision and use of healthcare services at the EOL were tested using cross-tabulations. The statistical significance of differences for categorical variables (e.g., ED visits, place of death) was tested with Pearson's chi-squared test. The impact of timing of radiation therapy was considered minor and therefore, excluded from further analyses. Radiation therapy is used for pancreatic cancer patients with a curative intention and a symptom-relieving goal, both early and late during the disease trajectory. The timing of radiation therapy does not therefore correlate well to the onset of PC. In addition, the radiation therapies were given only rarely in this cohort and its impact was not considered relevant to analyze.

## Results

The patient characteristics are presented in Table I. The study cohort consisted of 221 patients with a median age of 69 years (range=62-76 years) and was equally balanced between the sexes. Only 12% of the tumors were primarily operable and the treatment intention was curative in 9%. Approximately every second patient had distant metastases (52%).

Anticancer treatment was given to 65% of the patients. Median duration of life-prolonging treatments was 5.4 months. Nine percent of the patients had chemotherapy during the last month of life and 4% during the last 2 weeks. No systemic therapy was started in 35% of the patients (n=78), thus the primary treatment intention was palliative. The reason for interruption of the latest anticancer treatment was progression of disease in 48.5% (N=73) of cases, deterioration of the patient's condition in 26.5% (N=40), adverse effects of treatment in 8%, patient's request in 7%, and death of the patient in 5% (eight patients).

For most patients (88%) a PC decision was made at some point of the disease trajectory, median 2 months before death. However, it was either missing or made late ( $< 30$  days

Table I. Patient characteristics.

Number of all patients	N=221	Percent (%)
Age		
Median age, years	69	(range=62-76)
Over 65 years	141	64
65 years or younger	80	36
Sex		
Female	110	50
Male	111	50
Primarily operable	26	12
Primarily inoperable, (M0)	77	35
Distant metastases at diagnosis	114	52
Primary treatment intent		
Curative intent	19	9
Life prolonging intent	135	61
Palliative intent	78	35
Palliative care decision		
≥30 days before death	124	56
<30 days before death	71	32
No PC decision	26	12
DNR order		
DNR issued by oncologist	23	26
DNR issued by other physicians	60	67
Chemotherapy		
Adjuvant or neoadjuvant chemotherapy	36	16
Non curative chemotherapy	143	65
Number of treatment lines		
1 <sup>st</sup> line	87	39
2 <sup>nd</sup> line	43	19
3 <sup>rd</sup> or more lines	13	6
During the last month of life		
During the last 2 weeks of life	8	4
No systemic anticancer treatment	78	35
Palliative Care Unit visit	108	49
Hospitalizations in tertiary or secondary hospital		
During the last month of life	92	42
During the last 2 weeks of life	65	29
ED visits		
During the last month of life	84	38
During the last 2 weeks of life	57	26

DNR: Do-not-resuscitate; ED: emergency department; PC: palliative care

prior to death) for 44% of patients. At a tertiary hospital, DNR orders were generally issued late, during the last 2 weeks of life, and more often (67%) by another physician than an oncologist. Approximately every second patient visited the PC Unit (49%) a median of 2.4 months (SD 5.4 months) prior to death (Table II).

Of the parameters in Table I, age, number of treatment lines, and staging were tested with one-way ANOVA for association with the PC decision. Age was the only parameter that showed a significant association with timing of the PC decision ( $p=0.052$ ), which was made earlier for patients in the older subgroup. The PC decision was made ≥30 days before death for 61% (N=86) of patients in the

Table II. Time intervals.

Time	Median (months)
Time from primary diagnosis of cancer to death	13.2
Duration of life-prolonging anticancer treatment	5.4
Time from latest anticancer treatment to death	2.4
Time from diagnosis to palliative care decision	8.9
Time from Palliative Care Unit visit to death (N=108)	2.4
Time from palliative care decision to death	1.9
Time from do-not-resuscitate (DNR) decision to death	0.6

Table III. Time from palliative care decision to death and use of secondary or tertiary hospital services (emergency department visits and inpatient care) during patient's last 30 days.

Service use in the last 30 days of life	PC decision ≥30 days, % (n)	PC decision <30 days or no decision, % (n)
No	67% (103)	33% (52)
Yes	32% (21)	68% (45)
Total	(124)	(97)
$\chi^2=22,542; df=1; p<0.001$		
ED visits, n	0.32	0.75
Hospital overnight stays, n	2.30	6.10
$p<0.001$		

PC: Palliative care; ED: emergency department.

older age group (≥65 years) but for 48% (N=38) in the younger subgroup ( $p=0.052$ ).

*Service use.* During the last month of life, 42% of the patients were hospitalized in a tertiary care hospital and an additional 38% of the patients visited the ED, without being hospitalized. During the last 14 days, one-third (29%) of the patients were hospitalized and 26% of the patients visited the ED.

Timing of the PC decision was found to be related to the use of hospital services, ED visits, and inpatient care at a tertiary hospital. For patients for whom PC decision was made late or not at all, two-thirds of the patients underwent visits to the ED or hospitalizations, compared to only one-third in the group with a timely PC decision,  $p<0.001$  (Table III). Patients with a late or no PC decision made on average 0.75 ED visits and stayed 6.1 nights in hospital during the last month of life, compared to 0.3 ED visits and 2.3 overnight stays if the PC decision was made early. Both differences are statistically significant ( $p<0.001$ ).

Table IV. *Place of death.*

N=215	Home/nursing home	Hospice/specialized palliative ward	General primary care hospital	Tertiary or secondary hospital
PC decision >30 days before death	23 (62%)	39 (58%)	53 (60%)	8 (36%)
PC decision <30 days before death or no PC decision	14 (38%)	28 (42%)	36 (40%)	14 (64%)

PC: Palliative care.

An association between need for hospital services and timing of the PC decision was also found among patients receiving at least one regimen of chemotherapy. If the PC decision was made at least 30 days before death, 24% of patients used hospital services during the last month of life compared to 50% for whom a PC decision was late or non-existent ( $p=0.001$ ).

*Place of death.* Place of death was a general primary care hospital for 41% of patients. One-third (31%) died in hospice or on a specialized palliative ward, 17% at home or in a nursing home, and 10% in a tertiary or secondary hospital.

This tendency was also seen among hospice and specialized PC ward deaths (58% vs. 42%) (Table IV). Moreover, a PC decision made late or not at all correlated with a bigger proportion of deaths in a secondary or tertiary hospital (64% vs. 36%). These differences were nevertheless not statistically significant ( $p=0.25$ ).

## Discussion

In this study, we demonstrated that a late or lacking palliative care (PC) decision seems to be related to a more abundant use of hospital services during the last month of life in patients with pancreatic cancer. In addition, a trend was observed that patients with an early PC decision died more often at specialized PC service and less frequently in a secondary or tertiary hospital.

*Anticancer treatments and PC consultations.* Analysis of our cohort of deceased pancreatic cancer patients confirmed the poor prognosis of the disease; the median overall survival (OS) was 13 months. One-year median OS of pancreatic cancer patients in Finland is 26% for men and 30% for women (1). Treatment with curative intent was rarely an option (<10% of patients). One-third of the patients did not receive any anticancer treatments. Two-thirds of patients were treated with life-prolonging intent and the duration of anticancer treatment was short, median 5.4 months.

In our study, most (N=87) patients received only one treatment line and consecutive treatment lines were only selectively initiated, which is in line with the European Society for Medical Oncology (ESMO) recommendation (3).

In the present study, aggressive anticancer treatments at the EOL were rare and chemotherapy was generally terminated a median 2.4 months before death. Less than 10% of patients received anticancer treatment within the last month of life and 5% during the last 14 days, which is consistent with previous recommendations on avoiding overly aggressive anticancer treatment late in life (15). This observation is in line with previous larger registry-based studies, where 6.4% and 4.1% of pancreatic cancer patients underwent chemotherapy treatment within the last 2 weeks of life (20, 21). However, it is worth noting that our data were retrieved from hospital records and therefore include only patients treated at a university hospital. In other small cohort studies, the percentage of patients who received chemotherapy during the last month of life is significantly higher (17-28%), but these include only patients who were treated with chemotherapy (10, 22), not all deceased pancreatic cancer patients. Our findings are in line with these observations as well. The proportion of patients who did receive chemotherapy during the last month of life is 23%, if one includes only those who started an anticancer regimen during the disease trajectory.

The reason for treatment termination in the present study was progressive disease in approximately half of the patients, and deterioration of the patient's condition, death, adverse effects, or own desire to discontinue treatment in the other half. This indicates that careful patient selection should be implemented when starting or continuing anticancer treatment in patients with this highly aggressive cancer.

The PC decision was on average made 2 months before death. However, it was made earlier for elderly patients. We could not identify other variables related to an early decision, nor if it was associated with different doctor's attitude or interest in PC.

In this study, we found that only every second patient visited the PC Unit. Furthermore, these visits occurred late, upon interruption of the life-prolonging anticancer therapy. This reflects the lack of standardized early integrated PC at the time covered by the study. Even if early integration of PC reduces aggressive treatment at the EOL (8, 10, 23) and improves the quality of life; a vast majority of PC consultations nonetheless occur late (24). Some of the patients with a late or lacking PC decision did not have the time to visit the PC Unit at all.

*Service use and timing of the PC decision.* We found that an early PC decision halved the use of hospital services during the last month of life. In an Australian study, a third of pancreatic cancer patients made ED visits and two-thirds had hospitalizations during the last month of life, those with a late PC referral more often than those referred early (25). In another recently published study, pancreatic cancer patients with an early PC intervention made fewer ED visits than those with late onset PC (12). With a late or lacking PC decision, there is the risk of a more aggressive care approach near the EOL. An increased need for hospital services among patients receiving chemotherapy with life-prolonging intent has previously been shown (20). In this study, the patients that enrolled in hospice received less chemotherapy and were less likely to have acute care hospitalization during the last month of life. Bevins et al. showed that early PC encounters lead to fewer ED visits (12). These findings were reaffirmed in our study. We observed that patients who received chemotherapy at some point of the cancer course and had a late or lacking PC decision, used hospital services during the last month of life twice as much (50%) as patients with an early PC decision (24%).

The reasons for service use were not investigated but has previously been reported to be acute problems such as pain, nausea, infection, obstruction of the biliary duct, and ascites, all of which are complications of pancreatic cancer that patients can encounter (25). With a proactive PC approach, including systemic early-integrated PC, at least some of these acute issues could be somewhat preventable and handled outside an acute hospital setting, decreasing the stress that acute hospitalization implies. This has been reported in a Finnish study in which patients with a contact to the PC Unit underwent fewer hospitalizations and ED visits during the last month of life (18).

*DNR orders.* A late do-not-resuscitate (DNR) order made by another clinician than an oncologist reflects the lack of timely decision-making and of a comprehensive EOL care plan. A DNR order is a part of advance care planning. A previous study reported that patients with a documented DNR order had a better quality of life (26). Likewise, a correlation has been shown between a timely DNR order and less aggressiveness of care near death (27). In the present study, DNR orders were issued late and by other clinicians than the oncologists in charge of the patients' care. Previous studies have revealed the prevalence of DNR orders to be low, around 18-20% (8, 28). Even though it was higher in our study (40%) it is still far from adequate, considering the well-known lethal outcome of pancreatic cancer. PC consultations are important to ensure that conversations about the EOL care take place and that DNR orders are issued. This has been observed in patients in acute settings where PC consultations were associated with more frequent DNR orders (29).

*Place of death.* In our data, only approximately 10% of the patients died in a tertiary hospital, which supports the finding that treatment was not overly aggressive. With a late or lacking PC decision, the patients died twice as often in a tertiary hospital, compared to those with an early PC decision. We also noticed a trend that a PC decision made earlier enhances the probability of specialized PC at the EOL. It has previously been shown that PC increases the number of hospice admissions and duration of hospice stays (10). In our findings, we also noticed that an early PC decision leads to this, even without systemically early integrated PC. Only a few of the patients died at home. Every third died at a specialized PC unit, slightly more often with an early PC decision, but the difference was not statistically significant. This rather high number might be because this cohort consisted of patients treated at a university hospital, to which the most fragile and oldest ones were not referred.

*Strengths and limitations.* There are some limitations to this study, one being the retrospective design, with all data collected from hospital medical records. Another limitation is that the patient cohort was rather small, which could lead to misinterpretations in the statistical analyses. It is also notable that the data are relatively old. Taken into account the fact that systematically integrated early PC is not yet the praxis everywhere, this may, however, still describe the accurate situation in many clinics. Due to the retrospective nature of this study, quality-of-life data are absent. The strength of the study is that it is a population-based real-life study that included all patients with pancreatic cancer over a specified time interval, giving a rather realistic picture of the care of these patients at the time.

## Conclusion

The short life expectancy of patients with pancreatic cancer was confirmed in this study. It is therefore important to not delay the onset of PC and ensure appropriate advance care planning. Delayed timing leads to more aggressive care at the end of life, higher risk of hospital death, and absence of specialized PC.

## Conflicts of Interest

The Authors report no conflicts of interest in relation to this study.

## Authors' Contributions

All Authors participated in the design of the study and interpretation of the data. SM, RL-L, TS and OH read and approved the final manuscript. The data were collected by SM and OH. AR and RL-L performed the statistical analyses. SM drafted the manuscript and tables, which were revised by SM, RL-L, TS, and OH.

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