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ARTICLE



Assessing the utilization of the decision to implement a palliative goal for the treatment of cancer patients during the last year of life at Helsinki University Hospital: a historic cohort study

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ABSTRACT

Background: To avoid aggressive treatments at the end-of-life and to provide palliative care (PC), physicians need to terminate futile anti-cancer treatments and define the palliative goal of the treatment in time. This single center study assesses the practices used to make the decision that leads to treatment with a palliative goal, i.e., the PC decision and its effect on anti-cancer treatments at the end of life.

Material and methods: Patients with a cancer diagnosis treated in tertiary hospital during 1st January 2013 – 31st December 2014 and deceased by the end of 2014 were identified in the hospital database ($N = 2737$). Of these patients, 992 were randomly selected for this study. The PC decision was screened from patient records, i.e., termination of cancer-specific treatments and a focus on symptom-centered PC.

Results: The PC decision was defined in 82% of the patients during the last year of life (49% >30 days and 33% ≤30 days before death, 18% with no decision). The median time from the decision to death was 46 days. Systemic cancer therapy was given during the last month of life in 1%, 36% and 38% ($p < .001$) and radiotherapy 22%, 40% and 31% ($p = .03$) cases, respectively; referral to a PC unit was made in 62%, 22% and 11%, respectively ($p < .001$). In logistic regression analyses younger age, shorter duration of the disease trajectory and type of cancer (e.g., breast cancer) were associated with a lack or late timing of the PC decision.

Conclusion: The decision to initiate a palliative goal for the treatment was frequently made for cancer patients but occurred late for every third patient. Younger age and certain cancer types were associated with late PC decisions, thus leading to anti-cancer treatments continuing until close to the death with low access to a PC unit.

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Background

Anti-cancer treatments may have a detrimental effect on the quality of life of fragile cancer patients. Aggressive treatments during end-of-life (EOL) also impose considerable costs on health care systems [1]. Even though treatment practices may differ between countries, studies from the US and Canada suggest that the trend for aggressive EOL cancer care is increasing [2,3]. Proposed standard benchmarks for 'not overly aggressive cancer care' include less than 10% of patients receiving chemotherapy 14 days prior to death and less than 2% of patients starting a new chemotherapy regimen 30 days prior to death [4]. The response to preceding with anti-cancer treatments in advanced stages of cancer is often uncertain whereas the toxicity increases the decline in performance status. In order to avoid futile treatments at the

EOL, the treatment focus should be on symptom-centered PC rather than on life-prolongation.

There is no clear agreement on the indicators of the over-use of radiotherapy during the final weeks of life because of its palliative nature in some cases. However, it has been suggested that radiotherapy administered during the last 14 or 30 days of life might be a useful quality indicator [5] as there is often insufficient time to reach a response.

The utilization of EOL chemotherapy and radiotherapy has previously been investigated [6–22], but there are no studies on the impact of PC decision-making and timing on anti-cancer treatments at the EOL.

In the present study, we determined the prevalence and timing of PC decision in relation to the use of anti-cancer treatments during the last year of life. The secondary aim

was to investigate which factors affected the decision-making.

Material and methods

Cohort selection

Patients with a cancer diagnosis (ICD-10 C00-C96) treated in the Department of Oncology during 1 January 2013–31 December 2013 and deceased by 31 December 2014 were identified ($N=2737$) from the Helsinki University Central Hospital (HUCH) database. Of these patients, 992 were randomly selected for the study cohort. The final study sample consisted of 949 patients, after 43 patients were excluded because their primary cause of death was other than cancer or they were pediatric (<18-year old) cancer patients.

This historic registry-based study was done with the permission of the authorities of HUCH. According to the Finnish registration for research, no ethics committee approval was needed.

The majority of Finnish cancer patients are initially evaluated at public university and central hospitals. HUCH is one of the five university hospitals in Finland and provides cancer care for approximately 1.6 million residents in Southern Finland. During the time of this study, the HUCH Department of Oncology was responsible for the radiation therapy treatments of all cancer patients and the systemic cancer treatments of all except pediatric, hematological, gynecological and lung cancer patients; these patients received systemic therapy in other departments. In the Department of Oncology, there is a PC outpatient unit, but municipalities are responsible for EOL care. Early integrated PC was not systematically organized at the time of the study.

Data sources and collection

The cohort of patients and their respective clinical information were identified from electronic medical records. The patient-level data included age, gender, and cancer diagnosis, oncological systemic treatments, radiation therapy, visits to the PC unit, PC decision (date) and date of death.

Patients were divided into 13 diagnosis groups: (i) head and neck cancers, (ii) upper gastro-intestinal (GI) cancers, (iii) colorectal cancers, (iv) lung cancer, (v) melanoma and other skin cancers, (vi) breast cancer, (vii) gynecological cancers, (viii) prostate cancer, (ix) sarcomas, (x) cancers of the urinary tract, (xi) primary CNS malignancies, (xii) lymphomas and (xiii) others. When a deceased patient had more than one malignancy, the cancer diagnosis was recorded in accordance with the primary cause of death. The primary cause of death was collected from the death certificates of the national death certificate registry of Statistics Finland.

Most data used in this study was available in a structured format, but some information was manually derived from the medical records, e.g., the PC decision. The two researchers reviewed all medical records according to the study protocol. The consistency of the derived recordings was randomly cross-checked. One researcher is a PhD and a specialist in

medical oncology and the other is a PhD student and a general practitioner. Due to the nature of the data, there were no missing values: diagnoses, dates and treatments given to the patients are mandatory information to be recorded.

Palliative care decision and period

The PC decision, i.e., the decision to terminate life prolonging anti-cancer treatments and focus on symptom centered PC, is made by the oncologist responsible for the care of the patient. The PC period was initiated by the PC decision and defined as the period of time after termination of cancer-specific chemotherapy or biological treatments. However, endocrine treatment could continue during the palliative period, e.g., LHRH analog for prostate cancer patients. In addition, short courses of palliative radiotherapy, e.g., to relieve pain were allowed. A search for the PC decision was made in the medical records of all patients. The decision was recorded if there was an explicit and clear mention of it in medical records.

Patients were divided into three groups based on the timing of the PC decision: (1) no explicit PC decision, (2) the PC decision made during the last 30 days before death and (3) the PC decision made more than 30 days before death. The variables studied for each segment were: a visit to the palliative care (PC) unit and the last systemic cancer treatment and radiation therapy given before death. The date of the last radiation therapy was defined as the date of the last fraction and for systemic cancer treatment the last date of the treatment administered in hospital. With orally administered systemic cancer treatment, the last day of treatment was defined as the date when the oncologist recorded the termination of the treatment in the medical records.

Statistical analysis

Descriptive statistics such as means and medians were used for patient characteristics. The influence of the PC decision on treatments was studied by testing the difference between the three groups with cross-tabulation. The statistical significance of the differences of the distributions was tested with a chi-squared test. A one-way ANOVA was used to analyze whether the age groups significantly differed depending on the duration of time between the PC decision and death. ANOVA was also used to analyze pairwise whether the three groups of patients (based on timing of the PC decision) differed with respect to receiving radiation therapy before death. The same analysis of differences in systemic cancer treatments before death was done using the Kruskal-Wallis test because the variances in the groups were not equal. A logarithmic transformation was performed to normalize the distribution of time between the PC decision and death. A logarithmic regression model was built to show the factors associated to the PC decision. The dependent variable was defined as whether the PC decision was made earlier than 30 days prior to death or not. The variables tested in the model were age, cancer diagnosis and time from diagnosis to death. Both age and time from diagnosis to death were

standardized (average = 0, stdev =1) to normalize the distributions. Gender was not included due to its perfect correlation with gender specific cancer diagnoses. Two-sided p values less than .05 were accepted as statistically significant. All analyses were conducted with SPSS (version 25).

Results

There were 949 patients in the final sample, out of which 53% were male (Table 1). The key characteristics of the patient population are presented in Table 1.

Decision for PC was made >30 d and ≤30 d before death in 49% and 33% of the patients, respectively. No PC decision was made for 18% of the patients.

The distribution of patients in the three groups varied depending on the cancer diagnosis (Table 2). Most often the

PC decisions were made earlier than 30 days prior to death for patients with colorectal cancer, sarcomas and prostate cancer, while the decisions were typically made within the last month before death for breast and skin cancer patients. For 61% of head and neck cancer patients, a PC decision was made at any point in time. The differences in the distributions between cancers were statistically significant ($p = .02$).

The distribution of patients into the three groups depending on the patient's age at death is presented in Table 3. There were statistically significant differences between the age groups (F -value 5,186, p value < .001), but only the group of patients >80-year old were statistically different from other age groups ($p < .01$ for all pairwise comparisons).

Characteristics associated with a PC decision made >30 days before death in a logarithmic regression model are shown in Table 4. As the proportion of patients receiving a PC decision >30 d before death was lowest in breast cancer

Table 1. Characteristics of the patient population.

Characteristic	Male 499 (52.6%) Female 450 (47.4%)	773 (81%)	
		Median	IQR
Age at death (years)		68 y	61–75 y
Time from diagnosis to death		539 d (19 mos)	243–1133 d (8–38 mos)
Time from diagnosis to palliative care decision		443 d (15 mos)	153–1057 d (5–35 mos)
Time from the palliative care decision to death		46 d (1.5 mos)	16–131 d (0.5–4.5 mos)
Time from the last systemic cancer treatment to death		78 d (2.6 mos)	37–155 d (1.2–5.1 mos)
Time from the last dose of radiotherapy to death		74 d (2.5 mos)	27–174 d (0.9–5.8 mos)

M: male; F: female; IQR: interquartile range; y: years; d: days; mos: months

Table 2. Time from palliative care decision to death in different cancer groups.

Cancer diagnosis	Time from the palliative care decision to death			N (% from total)
	>30 d	≤30 d	No decision	
Head and neck	36%	36%	29%	28 (3%)
Upper gastrointestinal	55%	32%	14%	218 (23%)
Colorectal	61%	25%	14%	123 (13%)
Lung ^a	47%	31%	23%	118 (12%)
Melanoma and other skin cancers	38%	44%	19%	32 (3%)
Breast	31%	46%	23%	106 (11%)
Gynecological ^a	36%	32%	32%	28 (3%)
Prostate	57%	24%	19%	67 (7%)
Sarcomas	60%	23%	17%	30 (3%)
Urinary tract	52%	38%	10%	61 (6%)
Primary CNS malignancies	45%	28%	27%	60 (6%)
Lymphomas	41%	43%	16%	37 (4%)
Others	41%	34%	24%	41 (4%)
TOTAL	416	312	176	949

^aOnly patients receiving radiotherapy are included.

Table 3. Time from PC decision to death in different age groups.

Age group	>30 days, % (n)	≤30 days, % (n)	No decision, % (n)	Mean, days (SD)
20–40 years	36% (12)	39% (13)	24% (8)	78 d (120.3)
41–60 years	42% (85)	35% (72)	23% (46)	100 d (182.7)
61–70 years	46% (152)	32% (109)	22% (72)	95 d (150.4)
71–80 years	51% (136)	33% (88)	16% (42)	110 d (168.5)
>80 years ^a	67% (76)	26% (30)	7% (8)	165 d (259.6)
TOTAL	49% (461)	33% (312)	19% (176)	109 d (180.9)

^aStatistically significant ($p < .05$) difference with other age groups.

patients, we selected the breast cancer as the reference category for cancer groups. A statistically significant positive association was found for age (OR 1.3) and number of days from diagnosis to death (OR 1.2). Thus, the PC decision was more probable >30 days before death the older the patient and the longer the disease trajectory. From the diagnoses, the odds were highest for colorectal cancers and sarcomas (OR 5.2 and OR 4.3, respectively), hence these diagnoses were associated most often with the PC decision >30 days before death.

Figure 1 illustrates the association between the PC decision and its timing to the last radiation therapy visit or last course of systemic cancer treatment before death. The analysis was done only for the patients that received radiation therapy ($n=468$) or systemic cancer treatments ($n=580$) during the last year of life. Of these patients, 29% and 20% received radiation therapy and systemic cancer treatment during the last month of life, respectively. However, for those receiving radiation therapy, the goal of the last treatment was palliative for 87%. The majority of the patients who received radiation therapy or systemic cancer treatment

during the last month did not have a PC decision or the decision was made within the last month. Comparing the distributions in Figure 1, the chi-squared test only indicated a statistically significant difference in the distributions for the systemic cancer treatments ($p<.001$ for systemic cancer treatments and $p=.03$ for radiation therapy). Pairwise comparisons revealed that for radiation therapy the difference between the three patient groups was statistically significant only between those with a PC decision made over 30 days prior to death and those with a PC decision within one month of death ($p=.003$). For systemic cancer treatment, the differences in the distributions were statistically significant between those with a PC decision made over 30 days prior to death and both other groups ($p<.001$). The difference between the two other patient groups, however, was not statistically significant (data not shown).

Sixty-two percent of the patients with a PC decision made >30 days before death visited the PC unit as compared to 22% of the patients with the decision ≤ 30 days and 11% without the decision. The differences between the groups were statistically significant ($p<.001$).

Table 4. Characteristics associated with a PC decision made > 30 days before death in the logistic regression model: odds ratios and confidence intervals.

Characteristics	Odds ratios	95% CI	<i>p</i> Value
Diagnoses			
Breast cancer (ref)	1		
Sarcomas	5.2	2.11–12.59	<.001
Colorectal cancers	4.3	2.37–7.81	<.001
Upper gastrointestinal (GI) cancers	3.5	1.97–6.06	<.001
Prostate cancer	2.9	1.50–5.63	<.001
Cancers of urinary tract	2.9	1.43–5.69	.003
Primary CNS malignancies	2.8	1.38–5.73	.004
Lung cancer	2.5	1.35–4.61	.004
Others	2.0	0.91–4.41	.084
Lymphomas	1.9	0.85–4.42	.115
Gynecological cancers	1.8	0.70–4.46	.230
Head & Neck cancers	1.8	0.70–4.42	.228
Melanoma and other skin cancers	1.6	0.66–3.66	.318
Age (standardized)	1.3	1.16–1.54	<.001
Time from diagnosis to death (standardized)	1.2	1.02–1.39	.03

Breast cancer diagnosis is used as the reference value for the diagnosis variable.

Discussion

In this assessment of EOL care at a Finnish university hospital, a PC decision defining the symptom-centered goal of the care was frequently made, but often occurred late in the disease trajectory. Patients with no or a very late decision received more aggressive cancer treatments at the EOL and made infrequent visits to the PC unit. Age, duration of the disease trajectory and type of cancer were associated with the timing of the decision.

Frequency and timing of PC decision

According to previous studies, only a minority of patients with a prognosis of less than one year, have discussed EOL

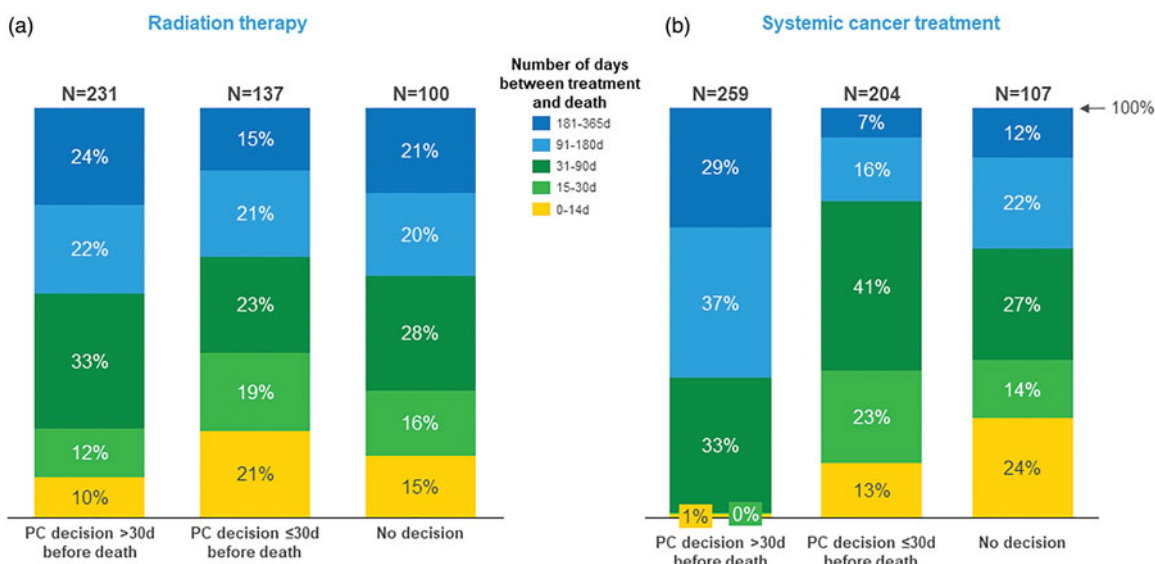


Figure 1. Time between last radiation therapy and death (a) and time between last systemic cancer treatment and death (b) with respect to the timing of the PC decision.

care with their oncologist [23]. In the present study, a PC decision was found in the medical records of 82% of the patients, which is a relatively high figure. However, even though discussions about the termination of anti-cancer treatments were carried out prior to death in a majority of the patients, the decision was only made at least a month before death for half of the patients.

A PC decision was more likely to be made for older patients with the threshold being patients over 80 years of age. In a previous Finnish study [16], patients under the age of 50 were more likely to receive IV chemotherapy during the last months and weeks of life compared to older patients. Likewise, Braga et al. [7] have shown the increased probability of younger patients receiving chemotherapy during the last three months of life. Although our results are in line with these earlier studies, the difference was significant only in the very elderly population (above 80 years) in our study.

As well as the younger age of the patient, the chemosensitivity of the tumor and thus the available alternative treatment options have been found to correlate with the use of chemotherapy during the last months of life [3,7,8,12]. Similarly, in the present study, among the breast cancer patients the decision to terminate cancer-specific treatment, i.e., making a PC decision was done late. On the other hand, the short disease trajectory, like in head and neck cancer, decreases the likelihood of early PC decision [24–26]. Thus, in diseases with a very poor prognosis the integration of PC should take place early, i.e., immediately after the diagnosis of an advanced disease. For diseases with multiple treatment options and a relatively long survival, PC should be introduced at least when the treatment options diminish [27].

Impact of PC decision on cancer treatments in EOL

Chemotherapy late in life does not improve patient's quality of life [28], in fact it is quite the contrary; it has been shown that a patient receiving palliative chemotherapy will most likely require more admissions to hospital, have a lower chance of dying at home, and may also have a shortened survival time [9].

In this study, 20% of the patients received systemic cancer treatment during the last month of life. This was in line with another Finnish study [16] where 18% of the patients received IV chemotherapy during the last month. The corresponding figures during the last two weeks of life were 18% in this study and 7% in the study by Rautakorpi et al. [16]. However, in the present study orally given chemotherapy and biological treatments were also included, which could explain the higher rate of patients receiving systemic treatment at the EOL. In previous studies, the prevalence of anti-cancer treatments one month before death have varied from 12% to 43% [2,7,9–15]. Comparison between the studies is, however, challenging, as the health care systems, study designs, and inclusion criteria vary. Nevertheless, according to proposed standard benchmarks for 'not overly aggressive cancer care', no more than 10% of patients should receive chemotherapy 14 days prior to death [4]. Our results showed

that the timing of the PC decision has a distinct correlation with the use of systemic anti-cancer treatments at EOL. If the PC decision was left undone or postponed to the last month of life the risk of aggressive cancer treatments during the EOL was significantly higher compared to patients with an early PC (38%, 36% and 1%, respectively). Interestingly, the risk of aggressive treatment at EOL was as high with a late PC decision as without it.

Thus, not only making the decision to switch to care with a symptom-centered palliative goal is important but its timing is also of vital importance. An early decision enables not only timely advance care planning and access to PC, but also the termination of futile, and potentially quality of life reducing systemic anti-cancer treatments.

In the present study, 29% of the patients received radiotherapy during the last month of life and 14% in the last two weeks, respectively. The prevalence of radiotherapy in the present study is somewhat higher than in the previous studies. In another Finnish study from 2005 to 2013 [22], the corresponding figures were 23% and 12%, respectively. According to previous studies, the proportion of patients receiving radiotherapy one month prior to death varied between 5% and 12% [6,15,17–19]. Interestingly, there was no difference in the number of radiotherapy treatments at the EOL with regards to the timing of the PC decision. One explanation for higher portion of patients getting radiotherapy at the EOL in this study could be the high proportion (87%) of palliative radiotherapy in the present population. However, according to the study by Rautakorpi et al. nearly half of the treatments given in the last two weeks were discontinued, the deterioration of the general condition being the most common reason for the discontinuation [22]. In addition, if radiotherapy is given very late, patients do not obtain any benefit from the treatment [29,30].

Impact of PC decisions on visits in PC unit

Even though we did not study the quality of EOL care, referral to a PC unit could be considered as an indicator of better EOL care [31–33]. In the present study, the earlier the decision of a palliative goal for the treatment was made the more often the patient was referred to a PC unit (62% with early, 22% with late and 11% with no PC decision). In HUCH, the PC decision is made by the oncologist responsible for the cancer treatments instead of a shared decision making with the palliative team as during the study period no systematic early-integrated PC was offered in the center. According to an international consensus, one of the indicators required for decision making is referral to a palliative team [27]. Our findings emphasize the importance of early integration of PC to improve EOL care planning [31–34].

Limitations and strengths of the study

There are some limitations to our study. One limitation is the retrospective nature of our study; the data was based on hospital medical records. Any possible inaccuracies in the records might also be reflected in the results. However, the

information concerning the PC decision and the time it was made was searched for manually and thus reliable. The other limitation is the lack of data on the response to last anti-cancer therapies. Neither did we search for the treatment intention (curative or disease modifying) in systemic cancer therapies at the EOL in relation to PC decision and its timing. Due to the retrospective nature of the study, the data on the quality of life and the need for palliative interventions is missing. Furthermore, we were unable to control any variables outside medical records, such as patient's socioeconomic status or ethnic group. The strength of the study is that it is a population-based real-life study with a relatively large sample size. The study cohort was epidemiologically representative of the prominent oncological diseases found within the population. The information concerning the PC decision made by the oncologists and its timing in relation to death, in addition to the data on the referral to a PC unit provided unique information about the decision making at the end of life.

Conclusions

Our study revealed that for most cancer patients the PC decision as regards a symptom-centered palliative goal for their care was made by the oncologists. However, the decision was made very late. The lack of a PC decision or postponing it to the last month of life reflected a significantly increased risk for aggressive cancer treatments during the EOL and delayed the access to PC services. Early-integrated PC should be offered more systematically to ensure timely advanced care planning and access to palliative and EOL care.

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Disclosure statement

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