

Recommending early integration of palliative care — does it work?

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Received: 10 December 2010 / Accepted: 2 February 2011 / Published online: 19 February 2011
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Abstract

Background In 2006, our comprehensive cancer center decided to implement *early integration* (EI) of palliative care (PC) by (a) literally adopting the WHO definition of PC into cancer care guidelines and (b) providing a PC consulting team (PCST) to provide EI on in- and outpatient wards. The experience with this approach was assessed to identify shortcomings.

Methods A retrospective systematic chart analysis of a 2-year period was performed.

Results A total of 862 patients were treated (May 2006–April 2008). Many patients consulted by the PCST for the first time were already in a reduced performance status (ECOG 3 & 4: 40%) or experiencing burdening symptoms (i.e., dyspnoea 27%). After the first year (period A; “getting started”), the overall prevalence of symptoms identified on first PC contact decreased from seven to three, ($p < 0.001$) as well as surrogate measures for advanced disease (i.e., frailty: from 63% to 33%; CI: [−36%; −23%], $p < 0.001$).

Conclusion Surrogate measures (symptom burden, performance status) indicate that PC was integrated earlier in the course of the disease after a 1-year phase of “getting started” with EI. Yet, the WHO recommendation alone was too vague to successfully trigger EI of PC. Therefore, the authors advocate the provision of disease specific guidelines to institutionalize EI of PC. Such guidelines have been developed for 19 different malignancies and are presented separately.

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Keywords Palliative care · Early integration · Cancer · Patient

Introduction

Background

Early integration (EI) of palliative care (PC) is being increasingly recommended [1]. In our comprehensive cancer center [Center for Integrated Oncology (CIO) Cologne Bonn], we decided to follow this approach by (a) advocating the WHO recommendation for EI of PC (“applicable early in the disease”) in the cancer care directives and (b) establishing a multidisciplinary PC hospital support team (PCST) consisting of specialized PC nurse, a senior PC consultant in close cooperation with

social worker, case manager, chaplain, and psycho-oncologist based on the recommendations of the European Commission's recommendations for such teams [2]. The main assignment of the PCST was to provide PC early in the course of the disease on (oncology) in- and outpatient wards in addition to routine (anti-) cancer therapy.

Objective

To identify shortcomings or characteristics of this approach, a retrospective systematic chart analysis of a 2-year period of the first PC consultation provided for each cancer patient was performed. Specifically we assessed (a) at what point in the disease trajectory integration of PC could be achieved (surrogate measures: i.e., performance status and symptom burden) and (b) which interventions were delivered by the PCST.

Previous assessments

A preceding assessment aimed at the PC provision for lung and breast cancer [3, 4]. While these two assessments aimed at paradigmatically evaluating a rapidly progressive (lung cancer) and a more chronically progressing malignancy (breast cancer), the study presented here was initiated to gather information about the entire range of (hemato-) oncologic malignancies including the previously published data on lung and breast cancer [3, 4].

Methods

Lectures and workshops were initiated to communicate the consented approach and this was conveyed in the interdisciplinary tumor boards. Moreover, the PCST regularly attended staff meetings of different departments. Consultations could be requested by any team member (physician, nurse, social worker, etc.) of the primarily treating department. The PCST concept fulfills the recommendations of the European Commission for the formation of PC teams [1]. The team consists of an experienced specialized PC physician, PC nurse in close cooperation with social worker, chaplain, and psycho-oncologist.

Indicators for “early” integration of PC

When a patient received the first consultation of the PCST, this was considered the point in his specific disease trajectory when PC was integrated into routine (anti-) cancer therapy. Routine data documented at these consultations (PCST documentation) and routine data from the primarily treating department (electronic patient charts) were analyzed. As surrogate measures to estimate how early

in the disease trajectory the patients were consulted, (a) physical performance status and (b) symptom burden (i.e., number of symptoms and prevalence of dyspnoea) were assessed. It was decided to analyze these parameters rather than TNM data to focus on the *patient reported situation* rather than the *anatomic-pathologic* status [5].

Study design

A retrospective review of prospectively collected patient data from all patients seen by the PCST was performed (May 2006–April 2008). We assumed that after initiating and communicating the EI approach, the concept might become increasingly accepted (more patients, earlier in the course of the disease) during the course of time [6, 7]. Therefore, the first and the second half of the observation period were compared [period A (“getting started”): May 1, 2006 to April 30, 2007 and period B (“getting settled”): May 1, 2007 to April 30, 2008].

Data collection and processing

Consultations are requested and documented via an electronic documentation system (ORBIS®) and paper files. The following data was retrieved from the latter:

Demography, performance status [Eastern-Cooperative-Oncology-Group (ECOG) score], physical symptoms reported by the primarily treating department, and interventions performed by the PCST. Routine PCST documentation for each patient in our institution also includes assessment following the German national Hospice and Palliative care Evaluation (HOPE) [8]. Symptoms (i.e., pain, dyspnoea, and anxiety) and problems (i.e., “home care problematic” or “high care giver or family burden”) as reported by the patients were documented by staff via HOPE with an integrated symptom checklist using a four-point grading scale (0=none, 3=severe). HOPE provides a standardized basic documentation tool for PC patients [9]. It has been developed, evaluated, and amended accordingly by a multi-professional working group since 1996. The self assessment tool [MIDOS(2)] is the German version of the Edmonton Symptom Assessment Scale and has been validated lately [9]. German inpatient PC services participate every year in a 3-month census. Between 2002 and 2005, an average of more than 50% of all existing German PC wards participated. Since 2005, the census has been repeated annually, as the infrastructure was optimized and the instrument can be used as a standard documentation tool. In the yearly census, the institutions are asked to document up to 30 consecutive PC patients at admission to the service and at the time of discharge or death. The anonymized data can be submitted via use of an online database or a two-page paper questionnaire and is processed centrally [10]. This data as

Table 1 Most frequent diagnoses and symptoms

Diagnosis	Patients % (n)	Pain % (n)	Frailty % (n)	Fatigue or tiredness % (n)	Loss of appetite % (n)	Anxiety % (n)
Lung cancer	17.1 (147)	59.9 (88)	53.1 (78)	44.2 (65)	44.2 (65)	41.5 (61)
Hematological malignancy	11.4 (98)	59.2 (58)	43.9 (43)	35.7 (35)	32.7 (32)	19.4 (19)
Breast cancer	9.6 (83)	69.9 (58)	39.8 (33)	30.1 (25)	26.5 (22)	26.5 (22)
Prostate cancer	7.9 (68)	76.5 (52)	52.9 (36)	39.7 (27)	39.7 (27)	30.9 (21)
Melanoma	6.1 (53)	52.8 (28)	49.1 (26)	39.6 (21)	45.3 (24)	30.2 (16)
Non-oncological disease	5.8 (50)	50.0 (25)	22.0 (11)	24.0 (12)	18.0 (9)	24.0 (12)
Head and neck cancer	5.5 (47)	51.1 (24)	42.6 (20)	31.9 (15)	25.5 (12)	12.8 (6)
Brain tumor	5.0 (43)	41.9 (18)	30.2 (13)	27.9 (12)	9.3 (4)	20.9 (9)
Total	100 (862)	61.1 (527)	45.8 (395)	35.6 (307)	34.8 (300)	29.1 (251)

reported by the patient (and documented by the PCST) was compared to the patient assessment according to the electronic files of the primarily treating department. Moreover, the provided PCST intervention (i.e., provision of on-demand opioids, family rounds, etc.) was assessed according to the electronic PCST documentation.

Primarily, data from 131 of the lung cancer patients and all 83 breast cancer patients had been retrieved and analyzed previously [3, 4]. These patients are included in the total group of cancer patients reported in this paper.

Statistical methods

1. Unpaired binary-valued samples: Chi-square test with Yates' continuity correction, 95% confidence interval (CI) for the difference in proportions according to Newcombe's method [11].
2. Paired binary-valued samples: McNemar's test, 95% CI for the difference in proportions according to Newcombe's method

3. Paired metric samples: Wilcoxon signed-rank test
4. Sample proportion with a fixed value: Exact binomial test
5. Comparing a subgroup of a specific diagnosis to the collective group excluding this subgroup: Chi-square test with Yates' continuity correction

Statistical significance was set at $p < 0.05$ [11]. Data were analyzed using R 2.9.0 software [12] and Excel® 2007.

Results

Eight hundred sixty-two patients were consulted (Table 1). Of these, 499 (62%) were affected by inoperable metastases the others from inoperable locally advanced disease. Median age was 63 (range: 0–96).

Most patients were already in a reduced performance status, but this ratio decreased significantly from period A ("getting started") to B ("getting settled") (Table 2). Symptom

Table 2 Performance status of all consulted patients (ECOG) ($n=862$)

ECOG	All pts. % (n)	A % (n)	B % (n)	Difference	95% CI ^a	<i>p</i> value ^b
0	2.7 (23)	0.8 (3)	4.0 (20)	3.1%	[1.0%; 5.3%]	0.009
1	10.2 (88)	10.1 (36)	10.3 (52)	0.3%	[-4.0%; 4.3%]	0.991
2	17.1 (147)	19.8 (71)	15.1 (76)	-4.8%	[-10.0%; 0.3%]	0.082
3	19.5 (168)	20.7 (74)	18.7 (94)	-2.0%	[-7.5%; 3.3%]	0.515
4	20.3 (175)	24.0 (86)	17.7 (89)	-6.4%	[-12.0%; 0.9%]	0.028
N.D.	30.3 (261)	24.6 (88)	34.3 (173)	9.7%	[3.6%; 15.7%]	0.003
Total	100 (862)	100 (358)	100 (504)			
0 to 2	29.9 (258)	30.7 (110)	29.4 (148)	-1.4	[-7.6%; 4.8%]	0.723
3 and 4	39.8 (343)	44.7 (160)	36.3 (183)	-8.4	[-1.7%; 15.0%]	0.016

The observation period was divided into two equal parts [A ("getting started"): May 1, 2006 to April 30, 2007 and B ("getting settled"): May 1, 2007 to April 31, 2008] to depict differences throughout the process. A: first, and B: second half of the observation period

Pts. patients, *CI* confidence interval, *N.D.* not documented, *ECOG* Eastern-Cooperative-Oncology-Group score

^aNewcombe's method

^bChi-square test with Yates' continuity correction

burden (i.e., pain and dyspnoea) was already high when patients were referred to the PCST for the first time (Table 3). After period A (“getting started”), patients reported less frailty, fatigue, loss of appetite, anxiety, depression, and constipation in period B (“getting settled”) (Table 3) and the overall prevalence of symptoms per patient decreased from 7 to 3, ($p<0.001$). After PC consultation, the number of patients receiving opioid rescue medication for pain increased from 153 (18%) to 443 (51%) (difference: 34%; CI [30%; 37%]; $p<0.001$). Similarly, the number of patients receiving strong opioids increased from 348 (40%) to 507 (59%, difference: 18%; CI [16%; 21%]; $p<0.001$).

The total number of patients with dyspnoea was 229 (27%). This symptom had not been identified prior to consultation in 168 of these 229 patients (73%). The number of the dyspneic patients receiving strong opioids increased from 89 (39%) to 168 (73%) of 229 patients (difference: 35%; CI [28%; 40%]; $p<0.001$) after PC consultation. The number of dyspneic patients receiving a WHO III rescue medication for dyspnoea increased from 29 (13%) to 131 (57%) (difference: 45%; CI [38%; 51%]; $p<0.001$). Moreover, PCST consultation frequently resulted in modification of other medications for symptom management (Table 4).

The overall median number of identified symptoms per patient increased from 1 to 4 ($p<0.0001$) after PC integration. Psychosocial interventions included, i.e., thorough explanations of PC options, family rounds, and coordination of social work (Table 5). The PCST was increasingly requested for support in social or communicative issues (Table 5) and

the numbers of new patients referred to the PCST increased in period B. Cancer and non-cancer patients and patients with different malignancies differed substantially in terms of symptom burden and performance status (Tables 1).

Discussion

Our institution literally advocated PC integration “early in the course of the disease” and provided an additional PCST to conduct EI on in- and outpatient wards.

Growing acceptance?

Comparing results of the first and second half of this approach (period A; “getting started” vs. period B; “getting settled”), some findings of this study are promising:

1. Over time, PC support was requested more often for psychosocial interventions. One assumption is that this could display a development towards a better understanding of PC competencies by clinicians who were lacking palliative care expertise before the beginning of this project [13].
2. In patients referred to the PCST for the first time, the prevalence of symptoms indicating advanced disease (i.e., frailty) and the average number of burdening symptoms decreased significantly (Table 3). This may be interpreted as seeing patients earlier in the course of the disease or

Table 3 Symptom burden and problems as identified by the support team ($n=862$)

Symptoms:	All pts. % (n)	A % (n)	B % (n)	Diff. %	95% CI ^a	p value ^b
Pain	61.1 (527)	62.3 (223)	60.3 (304)	-2.0	[-8.5%; 4.6%]	0.607
Frailty	45.8 (395)	63.4 (227)	33.3 (168)	-30.1	[-36.3%; -23.4%]	<0.001
Others	37.2 (321)	49.0 (175)	29.0 (146)	-20.1	[-26.5%; -13.5%]	<0.001
Fatigue or tiredness	35.6 (307)	52.8 (189)	23.4 (118)	-29.4	[-35.6%; -22.9%]	<0.001
Loss of appetite	34.8 (300)	52.8 (189)	22.0 (111)	-30.8	[-36.9%; -24.3%]	<0.001
Anxiety	29.1 (251)	48.9 (175)	15.1 (76)	-33.8	[-39.7%; -27.6%]	<0.001
Dyspnoea	26.6 (229)	29.9 (107)	24.2 (122)	-5.7	[-11.8%; 0.3%]	0.075
Constipation	25.1 (216)	37.7 (135)	16.1 (81)	-21.6	[-27.6%; -15.7%]	<0.001
Depression	24.1 (208)	39.4 (141)	13.3 (67)	-26.1	[-31.9%; -20.2%]	<0.001
Nausea	24.6 (212)	30.2 (108)	20.6 (104)	-9.5	[-15.5%; -3.7%]	0.002
Social issues	22.9 (198)	41.9 (150)	9.5 (48)	-32.4	[-38.0%; -26.6%]	<0.001
Neuro-psychiatric	9.8 (86)	14.2 (51)	6.9 (35)	-7.3	[-11.7%; -3.2%]	<0.001

The observation period was divided into two equal parts [A (“getting started”): May 1, 2006 to April 30 2007 and B (“getting settled”): May 1, 2007 to April 31, 2008] to depict differences throughout the process. A: first and B: second half of the observation period; n does not sum up to 83, since patients often suffered from multiple symptoms

Pts patients, *CI* confidence interval, *Diff* difference

^aNewcombe’s method

^bChi-square test with Yates’ continuity correction

Table 4 Pharmaceutical interventions: drugs used before and after the initial PMST consultation ($n=862$)

Medication	Before n (%)	After n (%)	Relative difference	95% CI ^b	p value ^c
Opioids overall	451 (52.3)	576 (66.8)	+27.7%	[22.7%; 32.6%]	<0.001
WHO-III-opioids	348 (40.4)	507 (58.8)	+45.5%	[38.6%; 52.5%]	<0.001
Rescue medication	153 (17.7)	443 (51.4)	+189.8%	[170.1%; 209.0%]	<0.001
NSAID	322 (37.4)	442 (51.3)	+37.2%	[29.4%; 44.9%]	<0.001
Atypical analgesics ^a	42 (4.9)	82 (9.5)	+93.9%	[59.2%; 132.7%]	<0.001
Lorazepam	21 (2.4)	89 (10.3)	+329.2%	[241.7%; 420.8%]	<0.001
Steroids	85 (9.9)	246 (28.5)	+188.9%	[158.6%; 218.2%]	<0.001
Laxatives	40 (4.6)	235 (27.3)	+491.3%	[428.3%; 556.5%]	<0.001
PPIs	54 (6.3)	193 (22.4)	+255.6%	[212.7%; 301.6%]	<0.001
Antiemetics	47 (5.5)	204 (23.7)	+330.9%	[280.0%; 383.6%]	<0.001
Antidepressants	10 (1.2)	19 (2.2)	+83.3%	[8.3%; 183.3%]	0.052
Neuroleptics	17 (2.0)	43 (5.0)	+150.0%	[85.0%; 230.0%]	<0.001

NSAID non-steroidal inflammatory drugs, PPIs proton pump inhibitors, CI confidence interval

^a Coanalgesics: pregabalin, gabapentin, carbamazepin, clonazepam

^b Newcombe's method

^c McNemar's test with Yates' continuity correction

that PCST consultations during the first year might have enabled the non-SPC teams to more competently care for their PC patients on their own ward (“enabling not deskilling” [14]).

- Patients were in a significantly better performance status when being provided with PCST consultations for the first time (Table 2).
- A non-significant trend for an increase in request for PC was reported over time.

These findings are encouraging as they may reflect growing acceptance of the EI approach as other physician become increasingly acquainted with the concept over time as it has been described previously by Bruera et al. [7].

PC integration—early or late?

Despite of these promising aspects, our approach failed to provide EI of PC for a large number of patients. Specifically, many patients already suffered from a high symptom burden when referred to PC for the first time. This contradicts the concept of EI where PC is integrated before patients experience burdening symptoms for the first time [15]. Together with the fact that many patients were already in a reduced performance status (Table 2), this might reflect the fact that the WHO wording (“PC is applicable early in the course of illness”) adapted to our guidelines was far too vague to reliably trigger PC integration. This supports the findings of two preceding

Table 5 Development of requests and interventions not concerned with symptom control ($n=862$)

	A % (n)	B % (n)	Relative difference	95% CI	p value
Number of patients	41.5 (358)	58.5 (504)	+40.7%	[55.1%; 61.8%] ^a	<0.001 ^a
Social or communicative intervention specifically requested	25.4 (91)	31.3 (158)	+23.2%	[−0.8%; 46.9%] ^b	0.069 ^c
Admission to palliative care ward requested	14.2 (51)	11.1 (56)	−21.8%	[−54.9%; 9.1%] ^b	0.204 ^c
Social or communicative intervention performed	68.4 (245)	69.8 (352)	+2.0%	[−7.0%; 11.3%] ^b	0.715 ^c
Admission to palliative care ward performed	34.1 (122)	22.8 (115)	−33.1%	[−51.0%; −15.2%] ^b	<0.001 ^c

The observation period was divided into two equal parts [A (“getting started”): May 1, 2006 to April 30, 2007 and B (“getting settled”): May 1, 2007 to April 31, 2008] to depict differences throughout the process. A: first and B: second half of the observation period. CI for observational period B

CI confidence interval

^a Exact binomial test

^b Newcombe's method

^c Chi-square test with Yates' continuity correction

evaluations of two subgroups of this population (lung and breast cancer) that have been provided previously [3, 4].

Limitations

Because of the study design, we are unable to provide data about patients who were not receiving PC and unfortunately we are unable to present prospective data.

Bottom line 1: realizing EI- timing

In one of the most widely perceived PC publications in 2010, Temel et al. [15] reported data from a randomized study assessing the effect of EI of PC to NSCLC patients. EI patients were favored in terms of quality of life and life expectancy. This supports the assumptions of other publications that PC should be provided routinely and should not rely on the comprehension of other disciplines [1, 16–20].

Meanwhile, after the initiation of the EI project evaluated in this publication, ASCO recommendations specifically addressing this topic have been published [1]. ASCO also strongly supports the provision of PC early in the course of cancer (“PC integration at diagnosis”) [1]. Though this wording is more specific (“diagnosis” vs. “early”), we doubt the adaption of this wording would have lead to an earlier integration of PC since these recommendations also lack (a) disease specific algorithms or (b) specifications of PC assignments compared to “routine care” [15].

To overcome such barriers, the identification of specific “green flags” may be considered helpful (Table 6). To overcome this predicament, the NCCN published in 2009 guidelines focus on both expected survival time or symptom burden of patients as triggers to initiate PC integration [5]. Besides the very helpful aspects of these guidelines, limitations should be considered. Specifically, judging survival time is problematic and using only symptom burden as a trigger for PC integration may lead to (too) late referrals [21].

Table 6 Green flags

1. WHO and ASCO recommendations
2. Conjoint interdisciplinary treatment (“shared care”)
3. Best possible symptom control
4. Psychosocial and spiritual issues and quality of life
5. Cross-sectoral PC infrastructure to optimize home care
6. Assure patients and families certainty where to obtain support in case of problematic medical or psychosocial situations
7. Soon after completion of staging and starting of (systemic) tumor specific therapy
8. Disease specific timing

Bottom line 2: realizing EI infrastructure

Apart from such triggers, Bruera et al. ([22]) specified the “whys, wherefores, and hows” of EI. The authors acknowledge that PC has emerged as a specialty and call for a joint approach of cancer therapy by oncology accompanied by specialized PC infrastructure [22, 23]. The working group points out that cancer patients are referred too late and in too low numbers to EI programs even though the majority of families referred to PC programs state that they would have preferred an earlier consultation [22, 24]. According to Bruera et al., an “integrated care model” would allow the oncologist to focus on the management of cancer, whereas the PC team addresses the vast majority of physical, spiritual, and psychosocial concerns. Literally, it is reported that “Oncologists can take advantage of (...) PC teams, which allow them to focus on the complex issues associated with management of cancer. (...) PC can be integrated into the collaborative model that exists among surgical, radiation and medical oncologists as the fourth pillar of comprehensive cancer care, supporting patients, and their families alongside oncologists” [22, 25].

Conclusion

To date, most of the decision to provide EI depends primarily on the notion of single professionals initiating PC (i.e., requesting PC consultation). This leads to late and insufficient provision of PC [26–28]. Therefore, our working group promotes the development of specific guidelines for EI. Particularly, we recommend (a) the identification and definition of *disease specific* points in the disease trajectory (“green flags”) when PC should be integrated into the clinical pathway of each advanced, progressive, and life-threatening disease, (b) definition of as schedule of responsibilities and prerequisites (i.e., multi-professionalism) (“green flags”) for PC, and (c) specification of misunderstandings (“red flags”) to catalyze cooperative and synergistic provision of interdisciplinary treatment. Such guidelines have been developed for 19 malignancies and are presented separately.

Acknowledgment The scientific work of the Department of Palliative Medicine, University Clinic of Cologne is supported by the Federal Ministry for Education and Science (BMBF 01KN0706). The clinical and academic activities of the Department of Palliative Medicine, University Clinic of Cologne, are substantially supported by the German Cancer Aid (Deutsche Krebshilfe e.V.).

Disclaimer The work has not yet been presented elsewhere.

Conflict of interest None.

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