Original Research

The effect of early and systematic integration of palliative care in oncology on quality of life and health care use near the end of life: A randomised controlled trial

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KEYWORDS
Early palliative care; Quality of life; Neoplasm; Advanced cancer; End of life; Patient-centred care

Abstract Purpose: This study evaluated the effect of early integrated palliative care (PC) in oncology on quality of life (QOL) near the end of life and use of health care resources near the end of life.
Method: Patients with advanced cancer and a life expectancy of approximately 1 year were randomly assigned to either early and systematic integration of PC into oncological care (intervention) or standard oncological care alone (control). QOL was assessed with the EORTC QLQ-C30 global health status/QOL scale and McGill Quality of Life (MQOL) Single Item Scale and Summary Scale at baseline, 12 weeks and 6 weekly thereafter until death. Use of health care resources was collected from chart review in patient’s electronic medical file for patients who died while participating in the study.
Results: Of the 186 randomised patients, 185 participants had a baseline measurement and were analysed. By November 2017, 128 patients had died while participating in the study. When applying the terminal decline model, patients in the intervention group scored
significantly higher on global health status/QOL of the EORTC QLQ C30, at 6 months (difference: 5.9 [0.06; 11.1], p = 0.03), 3 (difference: 6.8 [1.0; 12.6], p = 0.02), and 1 month (difference: 7.6 [0.7; 14.5], p = 0.03) prior to the patient’s death compared to the control group. Similar results were found for the Single Item Scale and Summary Score of the MQOL. We did not observe differences in use of health care resources between groups.

Discussion: Early integrated palliative care in oncology is a valuable approach since it also increases QOL near the end of life and not only soon after initiation of PC.

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1. Background

Early integration of palliative care (PC) in oncology has been developed to provide guidance about symptom management and discussions on goals of care that engage patients and families to consider their values and care preference of end-of-life care and to improve quality of life (QOL) of patients with advanced disease. This new care approach, as opposed to PC which is traditionally only applied in later stages of the disease trajectory in usual care, has been examined in several studies and consistently showed beneficial effects on patient-reported outcomes such as QOL and mood at 3 or 4 months after diagnosis for patients with advanced cancer [1–5]. The quality of care at the end of life (EOL), however, represents another important outcome of palliative care. Most studies of early integration of palliative care in oncology examined the effect on use of health care resources and aggressiveness of care at the EOL [1,3,4,6,7]. Three [3,4,6] studies found differences in use of health care resources indicating better EOL care, other studies did not find any difference in health care utilisation at the EOL [1,7]. Despite the link in research between quality of EOL care and QOL at the EOL, evidence of early integration of PC on QOL at the EOL is less extensive and only originates from the United States [1,2,7].

We conducted a randomised controlled trial of early and systematic integration of palliative care in oncology care in the Belgian health care setting. In a previous paper, we focused on the primary outcome and revealed benefits in QOL soon after diagnosis or prognosis in favour of early and systematic PC [8]. In a present secondary analysis, the aim is to examine whether early integrated PC in oncology influenced QOL at the EOL and the use of health care resources near the EOL of patients with advanced cancer.

2. Methods

2.1. Study patients

Patients treated at the Medical Oncology department, Thoracic Oncology department, and Digestive Oncology department of the Ghent University Hospital (Flanders, Belgium) were eligible to be enrolled if they were 18 years or older, had an advanced cancer diagnosis (histologically or cytologically confirmed) due to a solid tumour, a European Cooperative Oncology Group performance status of 0–2, an estimated life expectancy of 12 months (assessed by the treating oncologist), were within the first 12 weeks of a diagnosis of a new primary tumour or had a recent diagnosis of progression, and were able to read and respond to questions in Dutch. Patients recruited from a hospital other than Ghent University Hospital had to be within the first 12 weeks of disease progression or still on first-line treatment. Out- as well as inpatients were considered for inclusion [8].

2.2. Study procedures

From 29th April 2013 to 29th February 2016, we randomly assigned participants with advanced cancer (with stratification for department) to receive either early and systematic PC integrated in usual care or usual care alone. Participants assigned to the intervention arm consulted with nurses from the PC team within 3 weeks of enrolment and monthly thereafter. Additional PC consultations could be scheduled at the discretion of the patients. The nurses focused on illness understanding, symptom burden, and provided support in decision-making, and support for emotional, social, and/or spiritual needs. A detailed description of the intervention is reported elsewhere [9]. Patients assigned to usual care only met with the PC team on demand of the patient or treating physician, these patients did not cross over to the early and systematic PC arm. The Ethical Committee of the Ghent University Hospital approved the study protocol before initiation; oncologists introduced the study to patients and all participants provided written informed consent.

2.3. Data collection and study outcomes

Questionnaires measuring socio-demographic information and QOL were administered at baseline, QOL was further assessed at 12 weeks and 6-weekly thereafter
until death of the patient. QOL was measured with the global health status/QOL scale of the EORTC QLQ-C30, a two-item scale that is converted to a 0–100 scale [10]. It was also measured with Single Item Scale and Summary Score of the McGill Quality of Life Questionnaire (MQOL) that weighs the domains (physical, psychological, existential/spiritual, and social) of QOL equally [11]. The MQOL was added because of its high construct and content validity and because it addresses existential aspects of QOL. For this analysis, we looked at the QOL measures at 6, 3, and 1 month prior to death since quality of life is the central focus of palliative care.

For participants who had died by 8th November 2017 while participating in the trial, the electronic medical records were reviewed to obtain data such as type of treatment at baseline, dates of hospitalisation, dates of discharge, location of hospitalisation, date of last treatment, time of death, and place of death at the Ghent University Hospital. The indicators of use of health care resources at the EOL are based on the literature [3,12–14]. These include (1) systemic treatment in the last 14 days of life and (2) any emergency room (ER) visit, any intensive care unit (ICU) admission, any hospital admission, more than two hospital admissions, hospitalisations longer than 14 days, or systemic treatment in the last 30 days of life (3) admission in the PC unit, and (4) hospital death. We also used a composite aggressive EOL care score [15] in which 1 point is given for each of the 6 indicators that occurred in the last 30 days of life: death in the hospital, 2 ER visits, 2 hospital admissions, >14 days of hospitalisation, an ICU admission, or receipt of chemotherapy. A higher score is indicative of more aggressive care.

2.4. Statistical analysis

The patient’s QOL at 12 weeks was the primary outcome on which this study was powered, resulting in a sample size of 186 patients with advanced cancer. We performed statistical analysis using SPSS software (version 25), SAS (version 9.4), and R (version 3.4.1). Data obtained from 29th April 2013 to 8th November 2017 were included. All patients were analysed according to their original randomisation. A terminal decline joint model [16] was applied to model patient’s QOL backward from the time of death rather than prospectively from the time of enrolment [16] for all patients with a baseline measure. This approach controls for the known relationship between the deterioration in QOL as the patient’s death is nearing. It combines two sub-models to analyse both the terminal trend of the outcome scores of QOL (EORTC QLQ C30 global health/QOL scale; the Single Item Scale and the Summary Score of the MQOL) and survival. This is a recent technique that has the advantage of considering the dependence between QOL and survival while accounting for missing data and is often used in early PC trials [2,7].

The first sub-model is a semi-parametric mixed effects model to compare the longitudinal trend of the outcome scores between groups, including variables ‘department’ (the stratification factor) and ‘baseline scores’ as covariates. The second sub-model is a Cox model comparing the survival outcomes between groups correcting for department. The knots were selected based on Akaike information criterion (AIC). All analyses were applied using R code made available by the authors Li et al. [16]. For each time point of interest (6, 3, and 1 month prior to death), a model-based 95% confidence interval for the mean outcome score is presented. For the indicators of use of health care services, logistic regression was applied, adjusting for the stratification factor. In case of complete separation, exact logistic was applied in SAS version 9.4 with group and department as predictors. The observed proportions are reported in combination with Wilson score 95% confidence intervals. This trial is registered with ClinicalTrials.gov, number NCT01865396

3. Results

3.1. Patient characteristics

Of the 358 eligible patients presenting to the Medical Oncology, Thoracic Oncology, and Digestive Oncology department from 29th April 2013, through 29th Feb 2016, 186 were enrolled into the study (Fig. 1). Baseline characteristics are shown in Table 1. Sixty-nine percent of the patients were male, 48% was between 55 and 64 years old, the most frequent cancer diagnosis was advanced gastrointestinal (38%) or digestive cancer (28%). By 8th November 2017, 147 participants of the original sample had died and 128 had died while participating in the study. Baseline characteristics of patients that died while participating in the trial are shown in Supplementary Table 1.

3.2. Palliative care visits

Eighty-five patients (92%) in the intervention arm attended at least one PC consultation (median 6; inter-quartile range (IQR) 2–11.5), 41 control patients (44%) received at least one PC consultation (median 0; IQR 0–2) within the trial period.

3.3. Quality of life near the end of life

We applied the terminal decline model to handle missing data correctly: intervention group (n = 94): 73 patients had died, control group (n = 91): 74 patients had died. Patients in the intervention group scored significantly higher on global health status/QOL of the EORTC QLQ C30, at 6 months (difference: 5.9 [0.06; 11.1], p = 0.03), 3 (difference: 6.8 [1.0; 12.6], p = 0.02), and 1 month (difference: 7.6 [0.7; 14.5], p = 0.03) prior to the
patient’s death compared to the control group. Significantly higher scores for patients in the intervention group were also found in the Single Item Scale (difference: 6 months: 1.2 [0.6–1.8], p < 0.0001; 3 months: 1.6 [0.8–2.1], p = < 0.0001; 1 month: 0.6 [0.3–1.4], p = < 0.0001) and Summary Score of the MQOL (difference: 6 months: 0.6 [0.2–1.1], p = 0.002; 3 months: 0.7 [0.3–1.1], p = 0.02; 1 month: 0.7 [0.2–1.2], p = 0.005) (See Fig. 2).

3.4. Use of health care resources

When examining the use of health care resources in the last 30 days of life, we observed no significant different odds between the intervention group and the control group. The odds for aggressive EOL care were also not significantly different between both groups (p = 0.42) (See Table 2).

4. Discussion

This study shows that early and systematic integration of PC concurrent with oncology care results in higher QOL at 6, 3, and 1 month prior to death of patients with advanced cancer. The intervention had no apparent effect on the use of health care resources or aggressiveness of care at the EOL.

To our knowledge, this is the first European study that examined the effect of early integration of PC in oncology on QOL near the EOL of cancer patients. Further strength of this study lies in the prospective randomised controlled design. This study has also some limitations. First, we did not pre-specify the terminal decline joint modelling approach in our protocol as we were unaware of that approach at that time. As a result, we did not plan the sample size to evaluate QOL near death. Secondly, we are not able to exclude a cross-over effect since full blinding of the patients, clinicians, and assessors was not possible. Third, data of use health care services is based on data collection via chart review of the University Hospital, it is possible that we may have missed use of resources of participants who transferred their care. The use of routinely collected comprehensive databases could address this limitation [17]. Fourthly, attainment of one’s goals of care is also an important outcome of EOL care. We did not assess patient’s preferences of EOL care and hence, are not able to evaluate the extent of concordance between preferences and the care received [18].

The research field of early PC in cancer is relatively new and has mostly focused on the effect of QOL earlier, soon
after diagnosis of advanced disease, in the disease trajectory. In this study, we explored the effect of early integration of PC in oncology on QOL near the EOL. We found statistically significant beneficial effects in QOL at the EOL by providing patients with monthly semi-structured consultations with a specialised PC nurse, starting early in the disease trajectory and continuing until death. The plausible mechanism of the long-term benefit of early integrated PC versus on-demand PC could be related to the fact that patients and PC professionals have more time to build a relationship, to focus on coping with the progressive and worsening illness, to address decision-making in relation to cancer treatment and EOL care, and to enhance symptom assessment and management. Research has shown that adequate symptom management, effective communication, and a strong therapeutic bond contribute to quality EOL care [19–21].

Our results are consistent with the literature since we observe lower QOL when death approaches in both groups [1,2]. However, our result also suggests an increasing difference in QOL between the two groups over time, with a growing benefit for patients receiving early integrated PC with the largest discrepancy at 1 month prior to death. In addition, a clinically meaningful difference [22] in QOL at 1 month was found in favour of early and integrated PC. These results in combination with the positive effects on QOL early in the disease trajectory highlight the importance of early integration of PC in oncology [23].

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Usual Care (N = 94)</th>
<th>Early Integrated Care (N = 91)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender n (%)</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>69 (73)</td>
<td>58 (64)</td>
</tr>
<tr>
<td></td>
<td>25 (27)</td>
<td>33 (36)</td>
</tr>
<tr>
<td>Age</td>
<td>18–54 year old</td>
<td>19 (21)</td>
</tr>
<tr>
<td></td>
<td>55–64 year old</td>
<td>43 (47)</td>
</tr>
<tr>
<td></td>
<td>65–85 year old</td>
<td>29 (32)</td>
</tr>
<tr>
<td>Education no (%)</td>
<td>Less than high school</td>
<td>2 (2)</td>
</tr>
<tr>
<td></td>
<td>62 (66)</td>
<td>52 (59)</td>
</tr>
<tr>
<td></td>
<td>College or university</td>
<td>30 (32)</td>
</tr>
<tr>
<td></td>
<td>33 (36)</td>
<td>33 (38)</td>
</tr>
<tr>
<td>Tumour Site</td>
<td>Gastrointestinal</td>
<td>36 (38)</td>
</tr>
<tr>
<td></td>
<td>Lung</td>
<td>26 (28)</td>
</tr>
<tr>
<td></td>
<td>Head and Neck</td>
<td>12 (13)</td>
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<tr>
<td></td>
<td>Breast</td>
<td>7 (7)</td>
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<td></td>
<td>Melanoma</td>
<td>7 (7)</td>
</tr>
<tr>
<td></td>
<td>Genitourinary</td>
<td>6 (6)</td>
</tr>
<tr>
<td></td>
<td>35 (39)</td>
<td>46 (51)</td>
</tr>
<tr>
<td></td>
<td>13 (14)</td>
<td>8 (9)</td>
</tr>
<tr>
<td></td>
<td>6 (6)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Tumour Site</td>
<td>Gastrointestinal</td>
<td>35 (39)</td>
</tr>
<tr>
<td></td>
<td>Lung</td>
<td>25 (28)</td>
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<tr>
<td></td>
<td>Head and Neck</td>
<td>7 (8)</td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>8 (9)</td>
</tr>
<tr>
<td></td>
<td>Melanoma</td>
<td>9 (10)</td>
</tr>
<tr>
<td></td>
<td>35 (39)</td>
<td>31 (34)</td>
</tr>
<tr>
<td>Tumour Site</td>
<td>Gastrointestinal</td>
<td>6 (6)</td>
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<tr>
<td></td>
<td>Lung</td>
<td>25 (28)</td>
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<td>Tumour Site</td>
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<td>Lung</td>
<td>25 (28)</td>
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<td></td>
<td>Head and Neck</td>
<td>7 (7)</td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Quality of Life at baseline</td>
<td>EORTC-QLQ C30 Global Health Status/QoL-scale</td>
<td>60.9 ± (18.6) 58.4± (20.1)</td>
</tr>
<tr>
<td>McGill quality of life Single Item Scale</td>
<td>7.1±(1.82) 6.8 ±(2.01)</td>
<td></td>
</tr>
<tr>
<td>ECOG- Eastern Cooperative Oncology group.</td>
<td>a Three values missing for early and systematic palliative care group.</td>
<td></td>
</tr>
</tbody>
</table>
| b At screening, all patients with ECOG performance status of less than 2 were selected, eight patients deteriorated to ECOG performance status of 3 at baseline, these patients were not excluded.

Fig. 2. Quality of life (Global Health Status/QOL scale (QL2), Single Item Scale and Summary Score) near the end of life.
Table 2
Indicators of use of health care resources at the end-of-life.

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Estimated percentages [95CI]</th>
<th>Early Integrated Care (vs. Usual Care) OR [95CI]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Within last 30 d of life</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any ER visit*</td>
<td>Usual Care (n = 63)</td>
<td>Early Integrated Care (n = 65)</td>
<td>0.12</td>
</tr>
<tr>
<td>Yes (vs. No)</td>
<td>4 [0–7]</td>
<td>4 [1–14]</td>
<td>3.0 [0.4–+ inf]</td>
</tr>
<tr>
<td>ICU admission</td>
<td>Usual Care (n = 63)</td>
<td>Early Integrated Care (n = 65)</td>
<td>0.06</td>
</tr>
<tr>
<td>Yes (vs. No)</td>
<td>9 [4–19]</td>
<td>18 [10–30]</td>
<td>2.1 [0.6–8.8]</td>
</tr>
<tr>
<td>Palliative Care Unit admission</td>
<td>Usual Care (n = 63)</td>
<td>Early Integrated Care (n = 65)</td>
<td>0.33</td>
</tr>
<tr>
<td>Yes (vs. No)</td>
<td>30 [19–44]</td>
<td>45 [32–59]</td>
<td>1.8 [0.7–4.8]</td>
</tr>
<tr>
<td>Systemic treatment</td>
<td>Usual Care (n = 63)</td>
<td>Early Integrated Care (n = 65)</td>
<td>0.41</td>
</tr>
<tr>
<td>Yes (vs. No)</td>
<td>29 [18–41]</td>
<td>35 [24–48]</td>
<td>1.3 [0.6–2.9]</td>
</tr>
<tr>
<td>Aggressive EOL care score*</td>
<td>Usual Care (n = 63)</td>
<td>Early Integrated Care (n = 65)</td>
<td>0.45</td>
</tr>
<tr>
<td>0 (vs ≥ 3)</td>
<td>14 [8–25]</td>
<td>17 [8–26]</td>
<td>2.0 [0.5–8.1]</td>
</tr>
<tr>
<td>1 (vs ≥ 3)</td>
<td>27 [17–39]</td>
<td>29 [18–40]</td>
<td>1.0 [0.3–3.4]</td>
</tr>
<tr>
<td>2 (vs ≥ 3)</td>
<td>8 [2–25]</td>
<td>16 [8–26]</td>
<td>1.3 [0.5–3.7]</td>
</tr>
<tr>
<td><strong>Within the last 14 d of life</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic treatment</td>
<td>Usual Care (n = 63)</td>
<td>Early Integrated Care (n = 65)</td>
<td>0.64</td>
</tr>
<tr>
<td>Yes</td>
<td>12 [6–23]</td>
<td>14 [8–26]</td>
<td>1.3 [0.5–3.7]</td>
</tr>
</tbody>
</table>

*Exact logistic regression was applied.

It was hypothesised, similar to the other studies, that early integrated PC would enhance decision-making in relation to cancer treatment and would reduce the use of health care resources at the EOL such as hospitalisations or systemic treatment in the last days of life [1–7]. Our results, however, did not demonstrate a difference and are inconsistent with the findings of three previous trials of early PC [3,4,6]. The latter were based upon a physician-led intervention as opposed to this primarily nurse-led intervention. Other trials of early integrated PC with primarily nurse-led interventions also did not find significant differences in reduced use of hospital, ICU, or ED resources compared to usual care [1,7]. This might indicate that nurse-led interventions are less effective in reducing the use of health care resources indicative of poor quality of care for patients with advanced cancer.

On the other hand, we observed that 77% of all deceased participants scored 1 or less on the composite score of aggressive EOL care. Overall, this indicates low levels of aggressiveness of EOL care compared to other studies where 86% of cancer decedents had at least one indicator of aggressive care or more [15]. This could imply that there was little opportunity for the intervention to decrease the aggressiveness of EOL.

Last, the benefits of early PC on EOL QOL in combination with absence of effect on indicators of poor EOL care could also indicate that the level of integration of our intervention was too limited to observe differences in health care resources. An influential article has proposed three levels of integration: linkage, coordination, and full integration [24,25]. At the highest level of integration, multi-disciplinary teams manage all care and provide care and transitions in care in all key settings. In our intervention, we were not able to reach this level of clinical integration, the focus of the intervention was more on providing a patient-centred care approach [25], with mechanisms of referral and follow-up to the oncology team. It is plausible that the lack of full integration of early PC may have limited the impact on health care utilisation on indicators of poor quality of EOL care.

5. Conclusion

Early integrated PC in oncology, as opposed to PC on demand, results in improved QOL at the EOL. Not only was QOL better throughout the disease trajectory, the difference in benefit also increased towards the EOL. No differences in health care utilisation at the EOL or aggressiveness of EOL care were found. More research is needed with regard to the components of early integrated PC that could lead to less use of health care resources that are indicators of poor quality of EOL care.
Authors contributions

All listed authors contributed to the writing of the article and approved the final version of the manuscript. All authors were involved in the design of the study and the figures; all authors contributed to the data interpretation and the manuscript writing. GV and KP were also responsible for the literature search. GV, SVB, EN, MD, KE, VS, and KG contributed to the data collection. Data analysis was done by GV, KP, RC, and LD. All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Conflict of interest statement

We have no conflict of interest to report.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejca.2019.11.009.

References


