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Early, integrated palliative rehabilitation improves quality of life of patients with newly diagnosed advanced cancer: The Pal-Rehab randomized controlled trial

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Abstract

Background: Early integration of palliative care into oncology treatment is widely recommended. Palliative rehabilitation has been suggested as a paradigm which integrates enablement, self-management, and self-care into the holistic model of palliative care.
Aim: We hypothesized that early integration of palliative rehabilitation could improve quality of life.
Design: The Pal-Rehab study (ClinicalTrials.gov NCT02332317) was a randomized controlled trial. The 12-week intervention offered by a specialized palliative care team was two mandatory consultations and the opportunity of participating in an interdisciplinary group program. Supplementary individual consultations were offered, if needed.
Setting/participants: At Vejle University Hospital, Denmark, adults diagnosed with advanced cancer within the last 8 weeks were randomized 1:1 to standard oncology care or standard care plus intervention. Assessments at baseline and after six and 12 weeks were based on the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30). At baseline participants were asked to choose a "primary problem" from a list of QLQ-C30 domains. The primary endpoint was the change in that "primary problem" measured as area under the curve across 12 weeks (*T*-scores, European mean value = 50, SD = 10).
Results: In all, 288 were randomized of whom 279 were included in the modified intention-to-treat analysis (146 in the standard care group and 133 in the intervention group). The between-group difference for the primary outcome was 3.0 (95% CI [0.0–6.0]; $p = 0.047$) favoring the intervention.
Conclusion: Early integration of palliative rehabilitation into standard oncology treatment improved quality of life for newly diagnosed advanced cancer patients.
Trial registration: Clinicaltrials.gov Identifier: NCT02332317, registered on December 30, 2014.

Keywords

Palliative care, rehabilitation, quality of life, neoplasms, randomized controlled trial

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What is already known about the topic?

- Systematic reviews have found that early palliative care interventions may have more beneficial effects on quality of life and symptom intensity than usual cancer care alone among patients living with advanced cancer. However, the optimal model of delivery has not yet been established.
- Incorporating elements of rehabilitation into the palliative care of patients living with advanced cancer has been theorized to be beneficial, but evidence is still sparse.

What this paper adds?

- In this study an early integration of palliative rehabilitation into standard oncology care significantly improved quality of life over a 12-week period.
- Significantly more patients in the group receiving palliative rehabilitation reported they had been helped with their prioritized problem after 12 weeks compared to the standard care group.

Implications for practice, theory or policy

- The study adds to the evidence on the effect of early integrated palliative care and offers additional and new knowledge of a highly flexible and interdisciplinary model of delivery.
- Further trials are needed to establish and isolate the effective components and the optimal timing of palliative rehabilitation.

Introduction

Palliative care is defined as an approach aiming to improve the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual.[1] Early palliative care is recommended by international cancer and health organizations[1–3] but is not widely implemented. The optimal model of delivery and time for referral remains uncertain.[4]

Several clinical trials have investigated the effect of "earlier than usual" referral to specialised palliative care for outpatients with advanced cancer. At least 16 randomized controlled trials have been published on the subject—the majority within the last 6 years.[5–20] In seven of the studies the intervention could be classified as specialised palliative care integrated in the standard disease-modifying treatment from the onset of an advanced cancer diagnosis (up to 100 days after diagnosis).[6,8,9,13,16,17,20] In other trials the study population was primarily selected by a perceived prognosis, for example, an expected survival time of less than 1 year or between six and 12 months at the time of enrolment.[5,11,12,14,18,19]

Although all seven studies representing early, integrated care for newly diagnosed patients with advanced cancer used patient reported outcomes, they differed in choice of outcome measures and findings. Four of the studies reported a single pre-specified primary outcome measure of change in quality of life over 12 weeks.[8,9,13,20] Three met their primary endpoint,[9,13,20] while the fourth study found a greater improvement in quality of life for intervention patients after 24 weeks.[8] However, despite the focus on early intervention none of the studies mentioned supporting the patient's independence or functioning as a mean of improving quality of life. Nor did they include other healthcare professionals besides nurses and physicians in the intervention models.

Rehabilitation is defined by WHO as a set of measures that assist individuals who experience, or are likely to experience, disability to achieve, and maintain optimal functioning.[21] Rehabilitation for patients with advanced cancer may be useful in improving quality of life through a focus on function, mobility, activities of daily living, endurance, and the psyche while helping to maintain as much independence as possible.[22]

Tiberini and Richardson[23] from the United Kingdom suggested a definition of Palliative rehabilitation as "a paradigm which integrates rehabilitation, enablement, self-management, and self-care into the holistic model of palliative care" and "an approach that empowers people to adapt to their new state of being with dignity [. . .] and cope constructively with losses resulting from deteriorating health."

We designed this study to investigate whether quality of life is improved by systematic use of early palliative care in the form of palliative rehabilitation. The study tested the effect of a 12-week individually tailored, interdisciplinary program initiated shortly after an advanced cancer diagnosis and integrated into standard oncology care.

Material and methods

Study design and participants

In this randomized parallel-group controlled trial, patients newly diagnosed with cancer were recruited from a single

center, Department of Oncology, Vejle University Hospital, Denmark. Eligible patients were 18 years or older and were receiving systemic medical treatment for a metastatic or otherwise unresectable solid tumor diagnosed within the last 8 weeks. Patients were excluded if they had received specialized palliative care within a year prior to enrolment.

Study participants were enrolled following written and verbally informed consent. The study was approved by The Regional Committees on Health Research Ethics for Southern Denmark on April 2nd, 2014 (ID S-20140038).

The study design and set-up were discussed thoroughly with and approved by the hospital's Patient and Relatives Council.

Details of the study protocol appear in a previous publication.[24]

Recruitment strategy

Given that recruitment is a known barrier for successful completion of palliative care trials[25] a recruitment strategy was formed. All staff involved in recruitment were given pocket cards with bullet points about the trial and suggested phrases for information of potential study participants. The recruitment rate was presented graphically at brief monthly staff meetings, thus creating an ongoing focus and a milieu where the personnel felt safe to engage with the research group about their experiences when recruiting. Milestones during recruitment were communicated and celebrated.

Randomization and masking

Patients were randomly assigned (1:1) to standard oncology care or standard care plus palliative rehabilitation. The randomization list was made at randomizer.org without stratification[26] and concealed from all personnel involved in recruitment. A research nurse assigned unique identification numbers to all study documents and managed the allocation sequence.

Study documents for outcome measures were double-entered manually by blinded personnel using the Research Electronic Data Capture-software (REDCap).[27] The statistician carrying out the analyses was blinded to intervention allocation.

Procedures

Standard care. Standard care was provided at the discretion of the medical oncologist. Upon indication, referral could be made to specialized palliative care, dieticians, physiotherapists, and psychosocial support from chaplains, psychologists, and social workers. Thus, patients in the standard arm were not refused help with palliative or rehabilitation needs emerging during their treatment.

The intervention. The intervention was systematic referral to a palliative rehabilitation outpatient clinic developed as a new function under the hospital's specialized palliative care team.[28] The usual members of the team counting physicians, nurses, physiotherapists, and psychologists were supplemented by part time engagement of an occupational therapist, a dietician, a social worker, and a chaplain to form the palliative rehabilitation team.

The mandatory elements of the palliative rehabilitation intervention were (1) a 1-h consultation with a physician and a nurse specialized in palliative care as soon as possible after randomization, (2) a 40-min consultation with a specialized palliative care nurse 6 to 7 weeks after enrolment, and (3) the possibility of contacting the palliative rehabilitation outpatient clinic during the study period. Depending on individual needs identified during the mandatory assessment and follow up patients were encouraged to participate in a 12-week patient/caregiver school combined with individually tailored physical exercise in groups (Figure 1) and/or offered individual consultations with members of the palliative rehabilitation team.

All patients were discussed at least once at the interdisciplinary, palliative rehabilitation team conferences which were held weekly.

A template was used for the initial consultation drawing on the ambulatory guideline used during a previous trial of early palliative care by Temel et al.[13] but with the addition of questions about barriers to activities of daily living and physical activity. More details on the palliative rehabilitation intervention are provided in a previous publication.[28]

Data collection. Participants were asked before randomization to choose a "primary problem" that they needed help with the most. The choice could be made from a list of 12 domains from the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)[29] and a 13th option of "none of the above" (Table 1).

Before randomization, at six, and 12 weeks participants completed a questionnaire consisting of short forms measuring the 15 domains of the QLQ-C30. The domains of the QLQ-C30 were supplemented with items from the EORTC computerized adaptive testing (CAT) item banks[30] for more precise measurements within each domain (Supplemental Table S1).

All contacts with the palliative rehabilitation team and adverse events were registered prospectively.

Outcomes

The primary outcome was quality of life over 12 weeks. This was defined as the change since baseline in the score representing the problem prioritized by the patient. If the

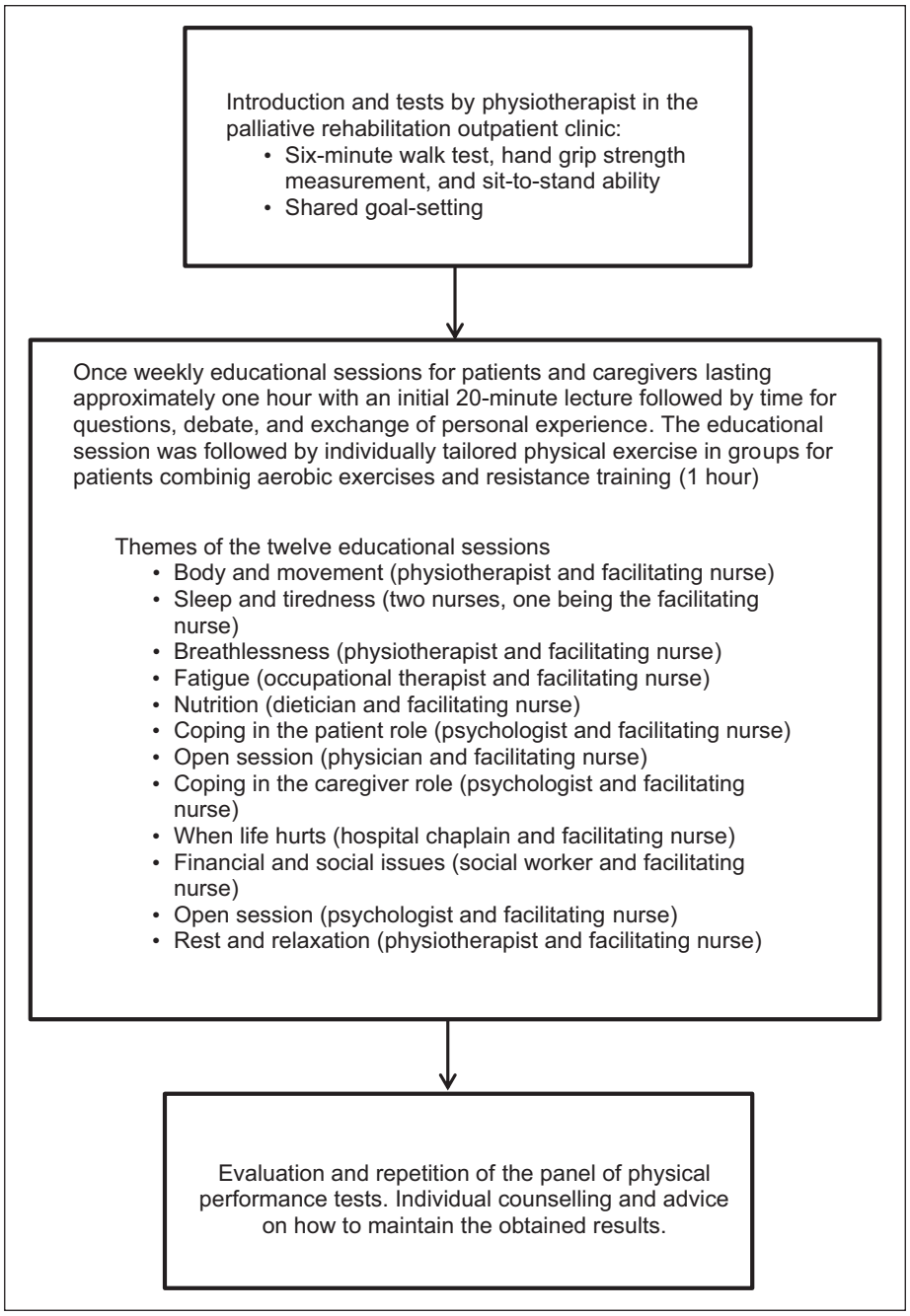

Figure 1. Palliative rehabilitation group offer.

patient chose "none of the above" the global health status/QoL scale was used.

A secondary endpoint was whether the patients felt they had been helped with their "primary problem" (yes/no).

Statistical analysis

Scales based on the EORTC CAT item banks are scored using item response theory (IRT) based *T*-scores without a fixed upper and lower limit but centered so that the European general population has mean = 50 and standard deviation (SD) = 10 for all domains.[31] At the time of trial design no data were available for sample size calculations based on the IRT-based scoring system. Hence, the sample size was estimated based on studies using the original EORTC QLQ-C30.

The probability of avoiding Type II error was set at 90%, Type I error at 5%, and the required sample size was calculated as 266 (133 in each study arm) to detect a clinically meaningful difference of 10 points with the original scoring of QLQ-C30. A sample size of 300 would allow for a 10% drop-out.

Table 1. Baseline characteristics and "primary problems."

	Palliative rehabilitation group (*N* = 139)	Standard care group (*N* = 149)
Time from diagnosis to enrolment (days), mean (SD)	35 (16)	36 (16)
Age (years), mean (SD)	66 (9)	66 (10)
Age groups (years), *N* (%)		
⩾60	111 (80)	115 (77)
18–59	28 (20)	34 (23)
Male sex, *N* (%)	80 (58)	89 (60)
Cancer site, *N* (%)		
NSCLC	37 (27)	45 (30)
Colorectal cancer	38 (27)	39 (26)
Prostate cancer	25 (18)	28 (19)
SCLC	17 (12)	16 (11)
Breast cancer	11 (8)	8 (5)
Gynaecological cancer	5 (4)	5 (3)
Other	6 (4)	8 (5)
ECOG performance score[†], *N* (%)		
0	53 (38)	65 (44)
1	69 (50)	66 (44)
2	17 (12)	18 (12)
Education (years), *N* (%)		
⩽10	15 (11)	23 (15)
11–12	32 (23)	35 (23)
⩾13, not university	79 (57)	73 (49)
Academic	10 (7)	15 (10)
Missing	3 (2)	3 (2)
Living status, *N* (%)		
Married or partnered	96 (69)	114 (77)
Living alone	43 (31)	35 (23)
Intention of oncological treatment, *N* (%)		
Non-curative	113 (81)	124 (83)
Potentially curative	26 (19)	25 (17)
Status of disease, *N* (%)		
Distant metastases present	116 (83)	129 (87)
Locally advanced	23 (17)	20 (13)
Brain metastases present, *N* (%)	8 (6)	7 (5)
Bones the only metastatic site, *N* (%)	11 (8)	14 (9)
Primary problem chosen by patients, *N* (%)		
"None of the above"[‡]	35 (25)	40 (27)
Emotional function	15 (11)	19 (13)
Physical function	10 (7)	22 (15)
Fatigue	11 (8)	18 (12)
Pain	16 (12)	9 (6)
Insomnia	12 (9)	11 (7)
Role function	11 (8)	11 (7)
Dyspnoea	11 (8)	3 (2)
Appetite loss	5 (4)	4 (3)
Nausea and vomiting	4 (3)	4 (3)
Cognitive function	4 (3)	4 (3)
Social function	1 (1)	3 (2)
Constipation	1 (1)	1 (1)
Missing	3 (2)	–

SD: standard deviation; NSCLC: non-small cell lung cancer; SCLC: small cell lung cancer; ECOG: Eastern cooperative oncology group; EORTC: European organization for research and treatment of cancer.

Baseline characteristics and "primary problems" of 288 patients with newly diagnosed advanced cancer randomly assigned to receive standard oncology care (*N* = 149) or an additional offer of palliative rehabilitation (*N* = 139). The sum of percentages may not total 100 because of rounding.

[†]ECOG Performance status ranges from 0 to 4, where 0 = able to carry out all normal activity without restriction and 4 = completely disabled; totally confined to bed or chair.

[‡]"none of the above" marked by the patient on a list of 12 possible "primary problems" and a 13th option being "none of the above."

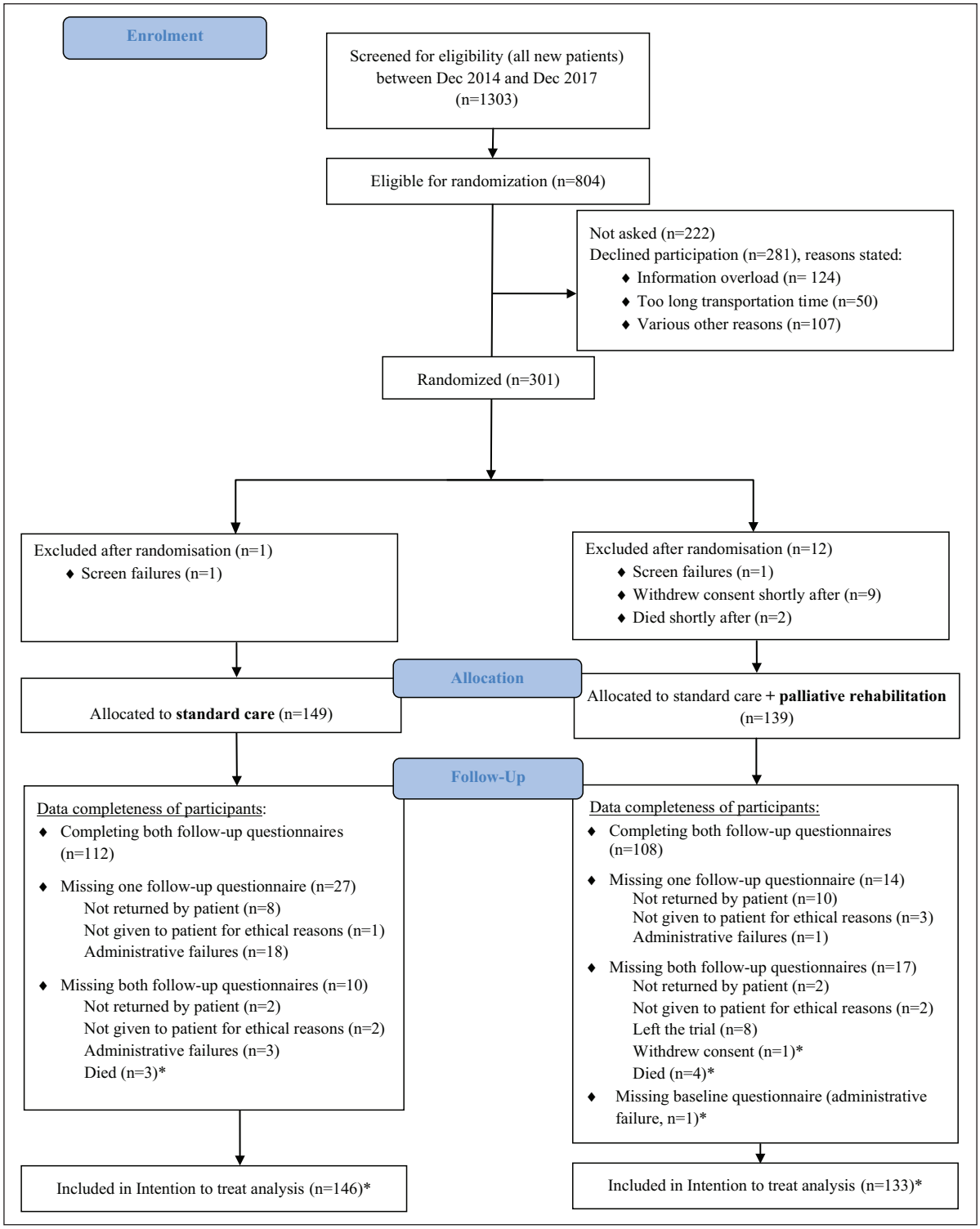

Figure 2. Trial profile.

A modified intention-to-treat (ITT) analysis was conducted meaning that patients who withdrew their consent to participate, died before 12 weeks, or did not have a baseline assessment were excluded from the primary outcome analysis (Figure 2).

Quality of life outcome for the 12-week period was estimated as the area under the curve (AUC) for the relevant EORTC-QLQ scale using the trapezoidal rule.

Analyses were made with SAS® statistical software version 9.4.[32] Multiple imputations were based on the same

Table 2. Baseline characteristics of 288 participants and 290 non-participants.[†]

	Participants (*N* = 288)	Non-participants (*N* = 290)	*p*-Value
Age (years), mean (SD)	66 (10)	70 (8)	<0.001
Male sex, *N* (%)	169 (59)	163 (56)	0.580
Cancer site, *N* (%)			0.001
Lung cancer	115 (40)	158 (55)	
Colorectal cancer	77 (27)	46 (16)	
Prostate cancer	53 (18)	46 (16)	
Breast cancer	19 (7)	8 (3)	
Gynaecological cancer	10 (3)	15 (5)	
Other	14 (5)	16 (6)	
ECOG performance status,[‡] *N* (%)			0.506
0	118 (41)	104 (36)	
1	135 (47)	145 (51)	
2	35 (12)	38 (13)	
Education (years), *N* (%)			<0.001
⩽10	38 (13)	48 (25)	
11–12	67 (24)	77 (40)	
⩾13, not university	152 (54)	61 (31)	
Academic	25 (9)	9 (5)	
Living status, *N* (%)			0.325
Married or partnered	210 (73)	200 (69)	
Living alone	78 (27)	89 (31)	

SD: standard deviation; ECOG: Eastern cooperative oncology group.
The sum of percentages may not total 100 because of rounding. Differences in categorical variables were tested with Chi-squared test. Difference in age was tested with Wilcoxon rank sum test.
[†]Non-participants declined participation (*N* = 281) or regretted giving consent to participate (withdrew consent immediately (*N* = 9)).
[‡]ECOG Performance status ranges from 0 to 4, where 0 = able to carry out all normal activity without restriction and 4 = completely disabled; totally confined to bed or chair.

potentially predictive baseline variables as mentioned below. The fully conditional specification approach for multiple imputations in SAS 9.4 was used[33] and 20 imputed datasets were generated based on regression and predictive mean matching.[33–35]

The analyzes were performed as multiple regressions adjusted for ECOG performance status, sex, age, intention of the oncology treatment (potentially curative or non-curative), primary diagnosis, living status, educational background, and primary problem. This amendment to the statistical analysis plan[24] was based on recommendations from Kahan et al.[36]

As a sensitivity analysis, the primary analysis was repeated for the change from baseline to the six and 12-week follow-up, respectively.

Explorative analyses tested for interactions between the intervention variable and the predictive variables mentioned above using observed data and a linear regression model.

Group comparisons of whether the patients felt that they had been helped with their "primary problem" after 12 weeks were made with Chi-squared tests on observed data.

Results

Between December 3, 2014 and December 22, 2017, 1,303 patients were screened of which 804 were eligible and 582 were approached (Figure 2). A total of 288 patients with newly diagnosed advanced cancer were randomly assigned to receive standard oncology care (*N* = 149) or the same care supplemented with palliative rehabilitation (*N* = 139). Ultimately, 279 patients were included in the modified intention-to-treat analysis with 146 patients in the standard care group and 133 patients in the palliative rehabilitation group.

Baseline characteristics and "primary problems" chosen at baseline appear from Table 1.

Differences in baseline characteristics between participants and non-participants can be seen in Table 2.

After allocation to the palliative rehabilitation arm of the study 132 patients were seen in the outpatient clinic for an initial consultation followed by an intervention tailored to their needs (Figure 3).

More details on how the palliative rehabilitation offer was utilized and evaluated by the participants appear in a previous publication.[28]

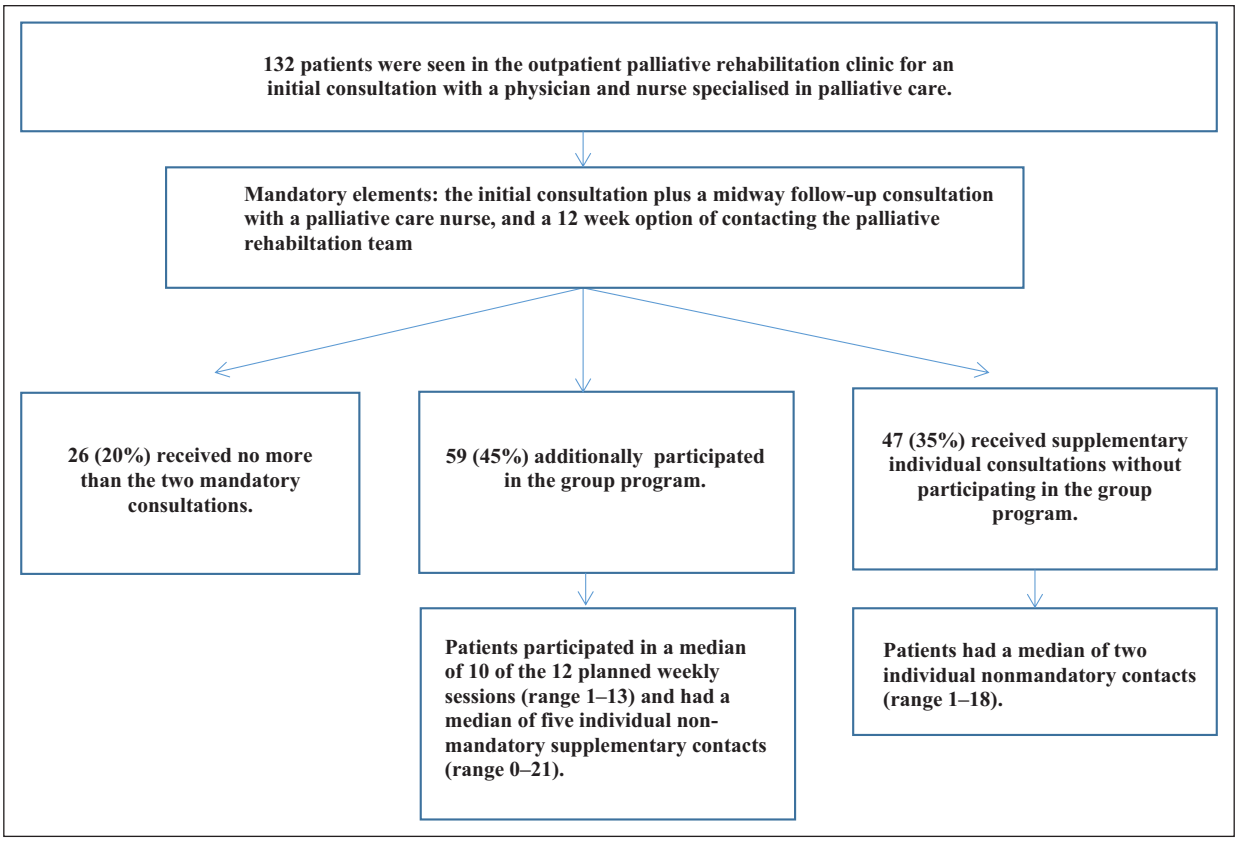

Figure 3. Use of the palliative rehabilitation offer.

Table 3. Effect of the intervention on the "primary problem" chosen by the patient at baseline.

Effect of the intervention	Between group difference	95% CI	*p*-Value
Overall effect across the 12 weeks[†]	3.0	0.0 to 6.0	0.047
Change from baseline to 6 weeks	1.3	−0.9 to 3.6	0.234
Change from baseline to 12 weeks	3.3	1.0 to 5.6	0.005

AUC: area under the curve; CI: confidence interval; EORTC QLQ C-30: European organization for research and treatment of cancer quality of life core questionnaire; SD: standard deviation.
A between group difference >0 means the group receiving palliative rehabilitation had a greater improvement over the study period than the group receiving standard care alone. Measurements were made with short forms representing the domains in EORTC QLQ-C30 with extra items added from the EORTC Quality of Life group item banks for computer-adaptive testing to obtain more precise measurements. Scales were scored using T-scores centered so the European general population has a mean value of 50 (SD = 10).
Analyses were performed as multiple regressions adjusted for ECOG performance status, sex, age, intention of the oncological treatment (potentially curative or non-curative), primary diagnosis, living status, educational background, and primary problem. Imputed values were based on the same variables and the 20 imputations resulted in a coefficient of variation of about 1%. To assess the impact of the number of imputations the primary analysis was rerun with 100 imputations. This provided almost identical results, changing the mean difference by 0.03 and the *p*-value by 0.0017. The complete case analysis of the overall effect across the 12 weeks showed a mean difference of 2.96, 95% CI [−0.25−6.16], $p = 0.0705$.
[†]Primary outcome measure. AUC of the six and 12-weeks measurements combined.

Quality of life was significantly improved in the intervention group over the 12 weeks with a group difference of 3.0 (95% CI [0.0–6.0]; $p = 0.047$; Cohen's effect size 0.3) (Table 3). Sensitivity analyses did not show any difference at 6 weeks but a significant difference at 12 weeks (difference = 3.3, $p = 0.005$) (Table 3).

At 12 weeks significantly more patients in the intervention group agreed that they had received help with their chosen "primary problem" (75%) compared to the standard care group (51%), $p = 0.002$.

Explorative analyzes showed no interactions between the intervention and the predictive variables included in

the multiple linear regression model except for a borderline significant effect for sex (better effect for females) and a significant effect for "intention of oncology treatment" (better effect for patients receiving treatment with non-curative intent than those treated with potentially curative intent).

Baseline values and results of the group comparisons across the study period of the EORTC short form scales can be seen in the Supplemental Table S2.

Details of the multiple regression analysis of the primary outcome can be seen in the Supplemental Table S3.

After the data collection at 12 weeks, 26% of group sessions and 18% of individual consultations took place.

Eighteen patients dropped out of the study based on withdrawn consent ($N = 10$) or other types of non-random withdrawal ($N = 8$). All were in the palliative rehabilitation arm. One patient withdrew consent after the initial consultation and similarly, one patient did not want to complete further study procedures after the initial consultation. The remaining 16 patients dropped out before any consultation with the palliative rehabilitation team had taken place. Reasons for dropping out were "feeling no need" ($N = 3$) and "feeling too overwhelmed" ($N = 15$).

Two adverse events were registered during the study, both in the group receiving palliative rehabilitation: one participant felt the physical exercise worsened his nausea, and one participant said the questions asked in the initial consultation added to her emotional distress.

Discussion

Main findings

In this study an early integration of palliative rehabilitation into standard oncology care significantly improved quality of life over a 12-week period.

The primary analysis combined six and 12-week follow-up data. When the analysis was repeated for the change from baseline to 12 weeks, the improvement of integrating palliative rehabilitation was highly significant. Furthermore, significantly more patients in the palliative rehabilitation group reported they had been helped with their "primary problem" after 12 weeks supporting the finding of a positive effect of palliative rehabilitation.

What this study adds

Research in palliative rehabilitation is sparse.[37] A British RCT published in 2013 tested the effect of a complex rehabilitation intervention delivered by a hospice-based multidisciplinary team versus usual care for patients with active progressive breast or hematological cancer and found a psychological benefit of the intervention.[38] The study only included 41 patients and does not represent an example of early or integrated care. We believe this is the first randomized controlled study investigating the effect of systematic integration of palliative rehabilitation in standard care early in the disease trajectory of advanced cancer.

To our knowledge this is the first time a study of early palliative care has been conducted with the aim of improving a domain of quality of life prioritized by the patient. The strength of this approach is that even though the patients may experience multiple symptoms and problems, receiving help with all the symptoms or problems may not be perceived as equally important. Also, some patients with newly diagnosed advanced cancer may not experience a wide range of symptoms and problems but receiving help with the one(s) they do experience is still very relevant. Asking the patients to prioritize meant that the primary outcome measurement ideally was relevant to all participants. Also, it meant avoiding summing up all the different symptoms and problems in the EORTC scales which could potentially dilute the effect measurement.

Approximately 25% in each study arm chose "none of the above" when asked at baseline to choose a "primary problem" that they needed help with the most (Table 1). The experience from the initial consultation in the intervention arm was that many patients were unsure of what type of help they could potentially get, and whether other patients were more deserving of taking up the time and resources of the palliative rehabilitation team. Thus, it was often in a combination of patient thoughts and expectations, assessment by the palliative rehabilitation clinician, and knowledge of available and potential beneficial interventions, that a true need was established. The experience supported the concept of systematic, early referral for a consultation with a palliative rehabilitation clinician and high rates of patient satisfaction in this study regardless of the initial perception of "need" have previously been published.[28]

The intervention used in this trial differs from other trials of early palliative care with its integration of elements of rehabilitation, but also in the sense that it was designed to be time-limited, include a group program, and involve healthcare professionals not generally used in early palliative care trials; especially physiotherapists and dieticians. The results show that the intervention was successful in tailoring the offer to individual needs and that compliance in the group program was very high (Figure 3).

The overall result of the study adds to the evidence presented by the Cochrane Group that early palliative care interventions may have more beneficial effects on quality of life and symptom intensity than usual cancer care alone among patients with advanced cancer.[39] The studies included in the review and meta-analyses were performed in North America, Europe, and Australia and included a total of 1614 participants.[6,13,16–20] As with the present study the effect sizes were small but the authors of the review concluded that they may still be clinically

relevant in a population likely to suffer from a decline in quality of life.[39]

Strengths and weaknesses

The study has several methodological strengths. Blinding was used in all possible steps during allocation, data management, and analysis to reduce the risk of bias. The risk of confounding factors was reduced by using a multivariate regression analysis for the primary outcome.

Some limitations of the study must be noted. The study was performed at a single center due to the novelty of the intervention design, which may limit generalizability, and blinding of participants and the treating personnel was not possible. The individual tailoring of the intervention makes it difficult to isolate effective components and make assumptions about dose-response. Likewise, using an individualized primary outcome measure adds complexity to the interpretation which is not yet fully explored. These issues should be investigated in future research perhaps using a mixed methods design where methods such as semi-structured interviews might also be helpful in understanding the change process.

The risk of selection bias is a challenge in palliative care research.[40] We found that participants were significantly younger and better educated than non-participants (Table 2).

It is noteworthy that 18 patients allocated to the intervention either withdrew consent or did not want to stay in the study resulting in skewed attrition. However, the vast majority of this type of attrition happened before any intervention procedures had taken place.

Rehabilitation services tend to be more effective in the early stages of cancer related functional loss, a time when patients and clinicians perhaps focus too narrowly on treating the malignancy and may postpone interventions relating to the maintenance of function or prevention of functional impairments.[41] The desire to stay mobile may contribute to improved and prolonged quality of life and likewise, inactivity may play a critical role in the interaction between symptom burden and functional decline.[22,42]

Theoretically, there are therefore sound arguments for initiating a palliative rehabilitation intervention as early as possible, but the optimal timing, intensity, and goals should be explored in further research.

The present study was designed to measure the effect of the intervention over 12 weeks. Three previous trials on the integration of early palliative care into standard oncology care showed a significant improvement in quality of life at 12 weeks[9,13,20] whereas another three found improvements at later time points.[6,8,19] Our intervention was not finalized within the planned 12 weeks and our findings suggest that the effect of palliative rehabilitation increases with time. We might have been able to show a stronger effect if we had included a later follow-up assessment, for example, after 18 weeks enabling us to assess the effect of the total intervention.

In conclusion, the quality of life of newly diagnosed advanced cancer patients was significantly improved in the group that received palliative rehabilitation integrated in the anticancer treatment as opposed to the group receiving standard oncology care alone. The study adds to the evidence on the effect of early integrated palliative care and offers additional and new knowledge of a highly flexible and interdisciplinary model of delivery.

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Authors' contributions

MG and TBV conceived the study and its design and have revised the manuscript with substantial contributions. MAP did the statistical analysis of the primary outcome and contributed with revision of the manuscript. LN did the literature search, data collection, remaining statistical analyses, and the first draft of this manuscript. LHJ sponsored the trial and revised the manuscript with a substantial contribution. All authors were involved in the data interpretation and read and approved the final manuscript.

Research ethics and patient consent

Study participants were enrolled following written and verbally informed consent. The study was approved by The Regional Committees on Health Research Ethics for Southern Denmark on April 2nd, 2014 (ID S-20140038) and was performed in accordance with the Declaration of Helsinki.

Declaration of conflicting interests

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Data availability

Sharing of the data is prohibited by Danish Law unless approved by The Danish Data Protection Agency (trial reference 2008-58-0035, approval dates December 1, 2014—June 30, 2023 after which the data will be anonymized and transferred to a national archive).

Supplemental material

Supplemental material for this article is available online.

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