

Changes in fatigue, health-related quality of life and physical activity after a one-week educational program for cancer survivors

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Abstract

Background: Rehabilitation programs aim to improve function, but the effects of different programs are not clear. The aims of the present study were to: 1) compare the level of fatigue and health-related quality of life (HRQOL) of cancer survivors admitted to a one-week inpatient educational program (IEP) to the general population (NORMS), 2) examine changes in fatigue, HRQOL and level of physical activity after the IEP, and 3) examine the proportions of survivors for female and male separately with clinically relevant improvement (>10% of maximum scale).

Methods: Cancer survivors ≥ 18 years, diagnosed with breast-, prostate- or gastrointestinal cancer within the last 10 years, about to attend a one-week IEP were invited. The IEP included lectures, group discussions and physical activity. The participants completed a questionnaire on the arrival day (T0) and three months after the stay (T1). Physical- (PF), mental- (MF) and total fatigue (TF) was assessed by the Fatigue Questionnaire and HRQOL by Short Form (SF)-36.

Results: Compared to the NORMS, both female and male cancer survivors had significantly higher mean levels of fatigue and poorer HRQOL at T0 and T1. From T0 to T1, among all participants mean score in PF was significantly reduced from 12.6 (SD 3.9) to 11.8 (SD 3.8) ($p < 0.001$), MF from 6.3 (SD 2.2) to 6.0 (SD 2.2) ($p = 0.044$) and TF from 19.0 (SD 5.3) to 17.8 (SD 5.4) ($p = 0.001$). Among female participants, 30% experienced clinically relevant improvement in PF, 28% in TF and 36% in general health. Thirty-one percent of male participants displayed a clinically relevant improvement in role limitations due to physical problems.

Conclusion: Participants in the IEP reduced their levels of fatigue and improved aspects of HRQOL, more often among female participants than among males. This might point to a need for a gender-related adjustment of the content of the program.

Introduction

The number of cancer survivors rapidly increases due to advances in diagnostics and cancer treatment [1]. However, cancer survivors often experience physical and psychosocial adverse effects from the disease and its treatment affecting their health-related quality of life (HRQOL) [2-4]. These adverse health effects can become clinically apparent during treatment or emerge months or even years after end of treatment [5]. The severity and frequency of the adverse effects will vary across cancer types and negatively affect upon HRQOL differently, in part due to individual variability such of personality traits, coping strategies and health literacy [6,7]. Many cancer survivors are able to return to a normal everyday life without support, but about 20-60% report need for health professional assistance [8,9].

Existing rehabilitation programs for cancer patients and survivors differ in terms of aims, content and structure. Knowledge of the effects of such programs and of information about the optimal delivery in terms of intensity, volume and components is still lacking. Further, characteristics of those who attend the programs and those who gain a potential clinically relevant improvement are also of importance. Scott and colleague [10] concluded that multidisciplinary interventions, consisting of a physical component and a psychosocial component, had positive effects on physical aspects of HRQOL function among cancer survivors. Programs focusing on a specific outcome such as diet, physical activity or stress management appeared to be more effective than those with multiple aims. Further, interventions with longer duration (range six to 12 months) showed no additional improvement than interventions conducted over a period of up to 12 weeks (range four to 12 weeks) [10] The effects of rehabilitation programs for cancer survivors have mainly been studied within an outpatient setting and most of the inpatient settings have lasted for three to

four weeks. To our knowledge, only a few studies have investigated the effects of a short one-week inpatients educational program (IEP) on HRQOL and fatigue [11,12].

The aims of the present study were therefore to: 1) compare the level of fatigue and HRQOL at admission to a one-week IEP for cancer survivors to the general population (NORMS), 2) examine changes in fatigue, HRQOL and physical activity following the IEP for all participants combined and for female and male separately, and 3) examine the proportions of survivors for female and male separately with clinically relevant improvement (>10% of maximum scale) for the outcomes that statistical significantly improve after the IEP and factors associated with clinically relevant improvement.

Material and methods

Participants

The study was an observational study with a pre-post design. Participants about to attend a one-week diagnosis specific IEP at The Norwegian Resource Center for Coping with Cancer (Montebello-Center, MBC), between September 2011 and February 2013, were invited to participate. All participants were referred to MBC by a medical doctor confirming the 'need for participation in the program' and that the participant managed daily routines without assistance.

Inclusion criteria for the current study were age ≥ 18 years and a diagnosis of breast-, prostate- or gastrointestinal cancer within the last 10 years. Participants who between the assessment at admittance to the IEP and follow-up: 1) had experienced progression of their cancer, and/or 2) had undergone surgery, radiotherapy and/or chemotherapy, and/or 3) had experienced a severe health condition such as myocardial infarction were not eligible for the present study and were excluded (n=39).

The general population (NORMS)

Normative data from Norwegian general population (NORMS) on fatigue [n=2323, age range 19-80 years, mean age 44.9 (SD 16.5)] [13] and HRQOL [(n=2118, mean age 55.7 (SD 14.1)] [14] were used for comparison to our sample.

Inpatient educational program (IEP)

Since 1990 the MBC has offered IEP for cancer patients and survivors and their partners/relatives. The overall goal of the program is to improve participants' coping with cancer-specific health problems, as well motivate the participants to adopt a healthy lifestyle by information and activities. During a 6-days program the participants attend standardized lectures on cancer-related topics, such as cancer and its treatment, risk of adverse effects, work, social resources and support, sexuality and lifestyle. Further, the participants attend group discussions related to the lectures and physical activities such as outdoor walking, water gymnastics or physical exercises in the gym. Parts of the IEP are specific for each cancer diagnosis while most of the content is common across the courses. A practical session on nutrition and cooking is also offered. An oncologist, a nurse, a social worker, a psychologist, a nutritionist and a physiotherapist/sports instructor lead the different parts of the program. Approximately 20-30 participants attend each course and their partners/relatives are invited to take part

Procedures

On the day of arrival at MBS, written information about the study, a written consent form and a questionnaire were delivered to the eligible participants. Consenting participants signed the consent form and completed the questionnaire before the program started the next day (T0).

Those who completed the questionnaire at T0 received a follow-up questionnaire by mail with a pre-paid return envelope enclosed three months after the IEP (T1). A reminder was sent to those who did not return the questionnaire delivered at T1 within approximately three weeks.

Measurements

All data were based on the participants' responses to a questionnaire including instruments on fatigue, HRQOL, physical activity, and questions on demographic and medical variables.

Fatigue

Fatigue was measured by The Fatigue Questionnaire (FQ) [15]. FQ consists of seven questions covering physical fatigue (PF) and four questions covering mental fatigue (MF). Each question has four response alternatives scored from 0-3 (Likert scores), with higher scores indicating higher levels of fatigue. Summarized scores for PF range from 0 to 21 and from 0 to 12 for MF. Total fatigue (TF) is the sum of PF and MF and range from 0 to 33 [15]. The FQ has good to very good psychometric properties [16]. According to Osoba et al, a clinically relevant change was defined as a change corresponding to 10% or more of the maximum score in each scale (≥ 3.3 point-change in TF, ≥ 2.1 point-change in PF and ≥ 1.2 point-change in MF) [17,18].

Health-related quality of life (HRQOL)

HRQOL was assessed by The Medical Outcomes Study Short Form 36 (SF-36) version 1 [19]. SF-36 consists of eight scales; physical function, role limitations due to physical problems, bodily pain, general health, vitality, social function, role limitations due to emotional problems and mental health. The responses on each item within each scale were summed and transformed to 0-100 scales (0 = worst health state and 100 = best health state)

[19]. SF-36 has shown to be a valid and reliable measure of self-reported health [20]. A change corresponding to 10% or more of the maximum score (≥ 10 point-change) in each scale of SF-36 was defined as a clinically relevant change [17,18].

Physical activity

Physical activity was assessed by the Nord-Trøndelag Health Study Physical Activity Questionnaire (HUNT 1 PA-Q) [21]. HUNT 1 PA-Q consists of three questions regarding frequency, duration, and intensity in specific activities, e.g., outdoor walking, skiing, swimming or training. An index score was calculated based on the product of frequency, duration and intensity, giving a score from 0 (lowest physical activity) to 15 (highest physical activity). The HUNT 1 PA-Q has shown acceptable test-retest reliability in a Norwegian adult male population [21].

Demographic and medical variables

Demographic variables included gender, age, marital status (living alone/living with a partner [married or cohabitant]), education (≤ 12 years/ > 12 years) and work status (full-time/part-time/retired/disability or social support).

Medical variables included type of cancer (prostate-, breast- or gastrointestinal cancer), time since diagnosis (months), type of treatment (non-systemic [surgery and/or radiotherapy]/systemic [chemotherapy and/or hormone therapy +/- surgery and/or radiotherapy]), relapse or progression of cancer before T0 (no/yes), comorbidity (no/yes) (defined as any long-lasting [>12 months] physical and/or psychiatric condition which had led to reduced daily functioning).

Statistical analysis

One-sample *t*-tests were used to analyze for differences in levels of fatigue and HRQOL between participants at the IEP and the NORMS [13,14]. Mean changes in fatigue, HRQOL and level of physical activity from T0 to T1 were analyzed with paired sample *t* test. For the outcomes that statistical significantly improved from T0 to T1, the proportions of participants with clinically relevant improvements were calculated. Univariate logistic regression analyses were used to evaluate demographic and medical variables significantly associated with the clinically relevant improvements (versus no clinically relevant improvement). A *p*-value less than 0.05 was considered statistical significant. Variables statistically associated with the outcome variables in the univariate analysis were included as explanatory variables in the multivariate logistic regression analyses. Adjusted odds ratios (aOR) were presented with 95% confidence intervals (95% CI). The analyses were performed using SPSS version 21.0 for Windows (SPSS, Chicago, IL, USA). Due to content wise overlap between the fatigue questionnaire and the vitality scale of the SF-36, only results from the fatigue questionnaire were used as outcome related to aim 3.

Ethics

The study was approved by the South-East Regional Committee for Medical and Health Research Ethics (2010/1132a/REK South-East A) and the Institutional Review Board of Oslo University Hospital. Written consent forms were provided from all participants.

Results

Participants flow and characteristics at T0

Three hundred and thirty two of 482 participants agreed to participate at T0, giving a response rate of 69%. A final sample of 235 evaluable participants completed the questionnaire at both T0 and T1, giving a response rate of 49% at T1 (235/482). For all participants, median age at

survey was 59.4 years (range 30-83), 75% were living with a partner, 57% had been diagnosed with breast-, 32% with prostate- and 11% with gastrointestinal cancer. Median time since diagnosis was 12.4 months (range 2-119) and 11% had experienced a relapse or progression of cancer before T0 (table 1). Compared to the female participants, the males were older (65.4 years versus 54.3 years, $p<0.001$), a higher proportion had retired and had experienced a relapse or progression of cancer before T0 (48% versus 13%, $p<0.001$ and 17% versus 7%, $p=0.01$, respectively). Female participants had more often received systemic treatment compared to male participants (88% versus 48%, $p<0.001$) (Table 1).

(table 1 approximately here)

Fatigue and health-related quality of life compared to NORMS

Compared to the NORMS, both the female and male participants reported significantly higher mean levels of PF, MF and TF (figure 1a and 1b) and lower levels on all SF-36 scales (figure 1c and 1d) at T0 and T1, $p<0.05$ for all.

(figure 1a, 1b, 1c and 1d approximately here)

Mean changes in fatigue, health-related quality of life and physical activity from T0 to T1

Among all participants combined, the mean PF-score was reduced from 12.6 (SD 3.9) to 11.8 (SD 3.8) ($p<0.001$), the mean MF-score reduced from 6.3 (SD 2.2) to 6.0 (SD 2.2) ($p=0.044$) and the TF-score reduced from 19.0 (SD 5.3) to 17.8 (SD 5.4) ($p=0.001$) (table 2). For the females separately statistically significant reductions from T0 to T1 were found for PF (-1.1 SD 3.8) and TF (-1.4 SD 5.2), whereas no statistically significant changes were found in the

levels of fatigue among the males (- 0.4 SD 3.4 and - 0.6 SD 4.4 for PF and TF respectively) (figure 1a and 1b and additional file 1).

No statistically significant changes in mean scores were found from T0 to T1 for any of the eight SF-36 scales or in self-reported physical activity for both genders combined (table 2). For the females separately, significant improvements of mean scores were found of the general health (+ 3.4 SD 18.3) and vitality (+ 3.1 SD 17.7) scales. Among the males, the mean score of the scale on role limitations due to physical problems, improved from T0 to T1 (+ 7.4 SD 33.9) (figure 1c and 1d and additional file 1).

(table 2 approximately here)

(additional file 1 approximately here)

Clinically relevant improvements in females and males separately and associated factors

Clinically relevant improvements were analyzed only for the outcomes which improved statistically significant from T0 to T1 in females and males separately (additional file 1).

Among female participants, 30 % reported a clinically relevant improvement in PF, 28 % in TF and 36 in GH (figure 2). In the univariate analyses among the female participants, high education [aOR 2.56; 95% CI (1.13-5.75), p=0.023] and relapse or progression of cancer before T0 [aOR 4.46; 95% CI (1.19-16.7), p=0.027] were associated with increased odds for clinically relevant improvement in TF (table 3). In multivariate analysis, adjusted for the TF baseline score, none of these variables were associated with a clinically relevant improvement in TF. No sociodemographic- or medical variables were significantly associated with clinically relevant improvements in PF and GH in the univariate analysis.

In male participants, 31% had a clinically relevant improvement in role limitations due to physical problems (figure 2). No sociodemographic- or medical variables were significantly associated with clinically relevant improvement in the univariate analysis.

(figure 2 approximately here)

(table 3 approximately here)

Discussion

In the present study we showed that both female and male cancer survivors admitting the IEP reported significantly higher mean levels of fatigue and poorer HRQOL at T0 and T1 compared to their NORMS [13,14]. For both genders combined PF, MF and TF significantly improved from T0 to T1. Among female participants separately statistically significant improvements were found in PF, TF, and the SF-36 scales general health and vitality. Male participants only improved in the SF-36 scale on role limitations due to physical problems. Overall, more female participants had clinically relevant improvements than male participants after the IEP.

In line with a previous study we observed higher levels of fatigue and lower HRQOL at admission to an IEP compared to NORMS [22]. These results indicate that the MBS has attracted participants who might experience a need for rehabilitation. Three months after end of the IEP the levels of fatigue were still higher and HRQOL poorer compared to the NORMS. These findings are in line with other recent findings in larger samples of cancer patients and cancer survivors, and the most noticeable differences were found for role functioning, social functioning, fatigue and sleep loss [23].

Our results showed improvements in TF including PT and MF among all participants. In line with our results, Bertheussen and colleagues [22] found improvements in fatigue after three to four week of inpatient rehabilitation. Contrary to our findings, Rottman et al [12] and Ross et al [24] found no positive effects on distress or well-being (including fatigue-related dimensions) after a comparable one-week IEP at 1-, 6- and 12-month follow-up compared to a control group. However, Rottman et al [12] did not evaluate whether the changes over time within each group were significant. Their finding might be explained by the baseline scores were almost similar to the general the Danish population limiting the potential for improvement [12]. The baseline scores of our population were significantly poorer than similar scores in the general Norwegian population thus allowing for potential effects of the IEP.

In the analyzes of each gender separately, the female participants experienced reductions in both PF and TF, whereas among the male participants no significant changes were found. HRQOL among the female participants significantly improved in the general health and vitality scales, and the male participants improved in the role limitations due to physical problems scale. This might indicate that female participants are more prone to benefit from this specific IEP than male participants. Other possible explanations might be the skewed gender distribution of our sample (more females) or that the male participants had lower levels of fatigue and better HRQOL at admission to the IEP and therefore less potential to improve. The lack of effect emphasizes the importance of screening for rehabilitation needs prior to admission to IEPs and that participant experiencing impairments such as distress, functional decline(s) or fatigue should be prioritized for enrollment into specialized rehabilitation programs.

Our findings indicate that around one third of the female participants experienced a clinically relevant improvement in PT, TF and in general health. Further around one third of the male participants experienced a clinically relevant improvement in role limitations due to physical problems. Given the potential explanations for these findings stated previously, we still think this finding warrants further investigations. It might be that the content of the program is more in line with rehabilitation needs experienced by females. To our knowledge, differences in perceptions of rehabilitation needs across the genders have not been explored until now. Lamprecht and colleagues [25] point out that at the start of a rehabilitation program prostate cancer patients report the greatest impairments in role physical function while for breast cancer patients the greatest impairment are in emotional functioning.

It is also pertinent to remind about general rule of thumb that rehabilitation should be individualized which is not possible within the present organization of the IEP at the MBC. Also the importance of follow-up should be discussed in terms of conditions that can enhance the effect of the IEP. Scott et al [10] summarize that at least one booster telephone call in addition to the intervention showed a positive significant difference regarding outcomes.

Limitations to this study include lack of a control group and a limited number of males participating. The differences in terms of time since diagnosis and health status is a limitation, but due to the referral patterns of the MBC this could not be changed upon the study. The majority of the participants were women treated for breast cancer and with high education, and the generalization of the results is somewhat restricted to that. And at last, the modest response rate of 49% at T1. Strengths of the study are the use of validated and well-established instruments FQ and SF-36, a robust design and a well described population with a reduced subjective health (fatigue and HRQOL).

In conclusion, the participants in the IEP reduced their levels of fatigue and improved aspects of HRQOL, more often among female participants than among males. The results might point to a need for a gender-related adjustment of the content of the IEP and the content being more oriented towards the participant's specific needs. Practically, the latter could be organized as individual plans following the one-week program focused towards each participant's certain needs.

Acknowledgements: The authors wish to acknowledge all patients who participated and the collaboration of the staff of the Montebello-Center.

Conflicts of interest: The authors report no conflicts of interests.

Funding: The study was supported by a grant from Southern and Eastern Norway Regional Health Authority (Helse Sør-Øst RHF) and The Norwegian Radium Hospital Foundation.

Figure legends:

Figure 1.

- a.** Physical, mental and total fatigue score in female participants at T0 and T1 compared to the general population (NORMS)
- b.** Physical, mental and total fatigue score in male participants at T0 and T1 compared to the general population (NORMS)
- c.** SF-36 scale scores in female participants at T0 and T1 compared to the general population (NORMS)
- d.** SF-36 scale scores in male participants at T0 and T1 compared to the general population (NORMS)

Footnote (for Figure 1a-1d):

† Significant differences between NORMS and female and male participants at T0 and at T1

(one sample t-tests), $p < 0.05$

*Significant differences between T0 and at T1 (paired sample t-tests), $p < 0.001$

PF – Physical fatigue

MF – Mental fatigue

TF – Total fatigue

PF – Physical function

RP – Role limitations, physical

BP – Bodily pain

GH – General health

VT – Vitality

SF – Social function

RE – Role limitations, emotional

MH – Mental health

Figure 2. Proportion of female participants with a clinical improvement from T0 to T1 in physical fatigue, total fatigue and general health and proportion of male participants with a clinical improvement from T0 to T1 in role limitations, physical

Footnote:

*Clinical improvement: ≥ -2.1 point on PF, ≥ -3.3 point on TF, ≥ 10 point on GH, VT and RP

(>10% of maximum scale)

PF – Physical fatigue

TF – Total fatigue

GH – General health

VT – Vitality

RP – Role limitations, physical

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