

Physical and mental factors associated with recovery of physical functioning after oncological surgery

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"ONDERGETEKENDE

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ABSTRACT

Background Oncological surgery is the most effective treatment for several cancers and is often curative. Undergoing oncological surgery negatively affects physical functioning. Little is known about the combination of physical and mental factors predicting recovery of physical functioning after oncological surgery. Physical and mental health are fundamentally linked. Identifying factors that predict the recovery of physical functioning benefits therapist and/or patients, through a better understanding of the expected recovery of physical functioning and patients with a poor prognosis of recovery can be monitored more extensively.

Aim The aim of the study is to identify which preoperative physical and mental factors are associated with recovery of physical functioning one month after hospitalization in patients undergoing oncological surgery

Methods A longitudinal observational cohort study was conducted in patients undergoing oncological surgery. Several physical and mental factors (anxiety and depression, physical activity, fatigue, illness acceptance, self-efficacy and mobility) were measured by questionnaires prior to surgery and one month after hospitalization. To determine their association with recovery of physical functioning, univariable linear regression analysis was performed. Multivariable linear regression analysis was performed with backward stepwise selection for predicting recovery of physical functioning.

Results Data from 56 participants were available for analysis. Univariable linear regression analysis showed that preoperative physical activity was associated with recovery of physical functioning. The other measured factors were not associated with recovery of physical functioning. In the final predicting model, based on multivariable linear regression, physical activity (p .023) was identified as a predictor of recovery of physical functioning. The lower the degree of physical activity, the worse the predicted recovery of physical functioning. The model explained 9.2% of the total variance.

Conclusion and key findings Physical activity was a predictor of recovery of physical functioning after oncological surgery. Patients with a low level of physical activity prior to surgery may have a worse prognosis of recovery of physical functioning and can be monitored more extensively. Further research is needed to examine the causal relationship for developing and deploying preventive interventions which may contribute to optimal recovery of physical functioning.

Keywords: Oncological surgery, physical functioning, recovery, physical and mental factors

INTRODUCTION

Oncological surgery is the most effective treatment for several cancers and is often curative (1–3). With recent technical advances and improved perioperative care, the number of individuals eligible for oncological surgery has increased substantially (4,5). At the same time, undergoing oncological surgery is a major stress factor and an impactful life event that negatively affects physical functioning (6).

Physical functioning is defined as: ‘a patient-oriented health outcome that contains aspects of individual daily functioning, including physical-, psychological-, and social factors’ (7,8). A low level of physical functioning is associated with shorter survival, reduced quality of life, depression, economic burden, disability and loss of independence (9,10). Gianotti et al. shows that a decline in physical functioning was seen in 23% of the patients after oncological surgery (3). If the decline continues for up to three months, the chances of a full recovery of physical functioning decrease (11). After six months, the chance of a full recovery is rare (11,12).

In earlier studies, multiple cross-sectional associations between physical and mental factors and recovery of physical functioning following oncological surgery have been described. For instance, presence of comorbidities, a high number of symptoms, unfortunate cancer categorization and a long duration of surgery have been associated with a poor recovery of physical functioning (13–15). On the contrary, good mental health, psychological well-being and greater self-efficacy were associated with a better recovery of physical functioning (13–16). Pain, fatigue, psychological distress and a higher pre-operative BMI should also be regarded as factors inducing a risk for a poor recovery of physical functioning (14,17).

Evidence shows that health outcomes reported by patients themselves differ from healthcare professionals and that proxy judgments about physical, social or emotional status are often inaccurate (18). Patient-reported outcome measures (PROMs) are a valuable tool to assess patients’ experience regarding their disease and treatment and to ensure these experiences are represented in the measurement of health. PROMs can contribute to patient centeredness by improving patient-provider communication and shared decision making (19,20). Therefore, this study will only focus on PROMs.

Little is known about the combination of physical and mental factors predicting recovery of physical functioning after oncological surgery. Physical and mental health are fundamentally linked, physical health can impact mental health and vice-versa. Aside from the distinction between physical and mental factors, some factors are modifiable, whereas others are inevitably connected to the surgical procedures. This study will focus on modifiable factors. Identifying the factors that predict the recovery of physical functioning benefits therapist and/or patients, through 1) a better understanding of the expected recovery of physical functioning, which can be shared with the patient, and 2) the opportunity to monitor patients more extensively in case the prognosis of recovery of physical functioning is poor.

Therefore, the aim of the study is to identify which preoperative physical and mental modifiable factors are associated with recovery of physical functioning one month after hospitalization in patients undergoing oncological surgery.

METHODS

Study design and population

This was a single-center, prospective, longitudinal, observational cohort study performed at University Medical Centre Utrecht (UMCU). Data collection was performed between November 2020 and May 2021. This study was approved by the Medical Ethical Committee of UMCU, the Netherlands. Participants were approached for participation after surgery by one of the investigators when they appeared to be eligible. Patients were included if they were \geq 18 years old and had oncological surgery of the bladder or gastrointestinal tract. Patients were excluded if they were completely dependent on a wheelchair, had a life expectancy of less than three months and if the patient was unable to sign informed consent due to cognitive problems.

Data collection

Primary outcome

The primary outcome in this study is recovery of physical functioning. Physical functioning was evaluated with the Boston University Activity Measure for Post-Acute Care (AM-PAC) outpatient short-form basic mobility routine questionnaire (21). This 18-item questionnaire assesses basic movement and physical mobility activities. Content includes transfers, walking skills, bending and carrying, housekeeping and strenuous activities. All activities have to be scored on a 4-point difficulty scale. The AM-PAC has a good reliability and validity (α ranges from .90 to .95) (22). Since the AM-PAC outpatient short-form basic mobility is not available in Dutch, this questionnaire was translated to Dutch using a forward-backward protocol following the guideline for the process of cross-cultural adaption of self-reported measures (23). The psychometric properties for the Dutch version are unknown.

To quantify recovery of physical functioning in this study, the preoperative AM-PAC score (T0) was subtracted from the AM-PAC score one month after hospitalization (T1)

Independent variables

Several independent variables were measured to determine which mental and physical factors were associated with recovery of physical functioning. These variables were selected based on literature and clinical perspective.

Anxiety and depression were measured with the Dutch version of the Hospital Anxiety and Depression Scale (HADS) (24). The HADS is widely used in oncology settings (25,26). The HADS consists of two 7-item scales, one for anxiety and one for depression. Answers have to be scored on a 4-point Likert scale, with a maximum score of 21 per subscale. Higher scores indicate higher risk of anxiety and depression. The psychometric properties of the Dutch version for general medical patients are good (α ranges from .84 to .90) (24).

Physical activity was measured by two predefined questions: 1. 'How many days a week did you move continuously for more than 30 minutes at moderate intensity (e.g. walking, cycling)?'

2. 'How many days a week did you do muscle strength exercises?' These questions have been formulated following the '2017 Dutch Physical Activity Guidelines' (DPAG) (27). This guideline states that adults should be physically active with moderate intensity for at least 150 minutes a week, spread over several days. Besides that, muscle- and bone strengthening activities should be performed for at least twice a week (27). The outcome range between 0-14 days, with higher numbers indicating better physical activity. As this is a guideline, no information of validity or reliability is available.

Fatigue was assessed with the 'Abbreviated Fatigue Questionnaire' (Dutch: 'Verkorte Vermoeidheidsvragenlijst' (VVV)). This questionnaire consist of four questions about the patient's bodily fatigue during the last two weeks. The participants rate each item on a 7-point scale. The score ranges from a minimum of 4 to a maximum of 28. The higher the score, the greater the experienced intensity of fatigue. The VVV is a reliable and easily used instrument (28).

Illness acceptance was measured using the 'Disease-Cognition-List' (Dutch: 'Ziekte-Cognitie-Lijst' (ZCL)) (29). Acceptance is one of the three subscales of the ZCL and consists of six items. Participants indicate on a 4-point Likert scale the extent to which they agree with these six items (1= not at all, 2= somewhat, 3= to a large extent, 4= completely). Higher scores indicate higher levels of illness acceptance. The psychometric properties of this questionnaire were tested on patients with Rheumatoid Arthritis and Multiple Sclerosis. The reliability of the acceptance subscale is very good ($\alpha = .90$)(30).

Self-efficacy was assessed with the Dutch Adaptation of the General Self-Efficacy scale (D-GSE). This 10-item survey assesses optimistic self-beliefs in general settings. Explicitly this survey measures someone's self-confidence regarding their own actions in relation to successful outcome measures. In other words, that the patient is in control of challenging situations in their environment. The items are measured on a four-point (1-4) Likert-scale ranging from (1) 'completely incorrect' to (4) 'completely correct'. A higher score indicates a higher degree of Self-Efficacy. The GSE is translated in over thirty languages and the reliability varies between $\alpha = .5$ and $.9$. The validity and reliability for the Dutch version of the GSE is unknown.

Mobility was measured with the Life-Space-Assessment (LSA). The LSA measures mobility of five space-levels of the past four weeks (bedroom, in- and around the house, the neighborhood, inside the city and outside the city). Frequency of mobility and the use of assistance from devices or persons were assessed. The total score was calculated based on life-space level, the frequency of attaining each level and the degree of assistance. Total score range from 0 to 120, with higher scores representing greater community mobility. Although the psychometric properties of the Dutch version of the questionnaire are unknown, other translations have shown to be valid and reliable (31–33).

Demographic and clinical data were extracted from the electronic patient record system, including age, gender, social environment, comorbidities, tumor location, operation technique, ASA-classification, complications during hospitalization, pre- and/or posttreatment and length of hospital stay.

Study procedures

Potential participants were approached by one of the involved researchers, after having been provided with permission of the nurse (daily coordinator) of the department surgical gastrointestinal oncology. Immediately after obtaining informed consent, participants that met the inclusion criteria were asked to complete the questionnaires at baseline (AMP-PAC, HADS, DPAG, VVV, ZCL, D-GSE and LSA) within 7 days after surgery (T0). In addition, the participants were asked to complete the questionnaires retrospectively for the last month before surgery. Completing these questionnaires took approximately 30 minutes. The follow-up assessment (T1) was done one month after hospitalization. The participants received an e-mail from one of the involved investigators with a link to the AM-PAC outpatient questionnaire. Completing this questionnaire took approximately 5 minutes.

Sample size

Sample size was calculated with a widely adopted rule of thumb, which states that 10 participants per variable is the required sample size for linear regression analysis to ensure an accurate prediction in subsequent participants (34). This study aimed to include six independent variables which results in a required sample size of at least 60 participants.

Statistical analysis

IBM SPSS statistics (version 27, IBM corp. Armonk, NY, USA) was used for statistical analysis. Missing data were imputed with Multiple Imputation. Analyses were performed with the pooled imputed data. Normality of residuals was checked with histograms and QQ-plots. A residual plot was made to check linearity and homoscedasticity. Multicollinearity was assessed by examining the Variance of Inflation Factor (VIF).

To assess the association of the independent variables with recovery of physical functioning both univariable and multivariable linear regression analyses were performed.

The association between the independent variables and dependent variable was assessed using univariable linear regression. As suggested by prediction modeling guidelines, an alpha of $<.2$ was chosen for pre-selection of variables to prevent premature deletion of variables from the model (35).

Multivariable regression analysis with backward stepwise elimination was used to determine the strongest independent predictors for the recovery of physical functioning. R^2 was calculated for the independent variables in the final predicting model and showed the explained variance in the final model.

RESULTS

A total of 60 participants were included in the study of which 4 (6.7%) participants were lost to follow-up; one participant died, one participant did not have time to complete the questionnaires before discharge and two participants decided to discontinue with the study. As a result, data from 56 participants was available for analysis. The mean age was 62.8 ± 12.2 years and 31 (55.4%) were male and 25 (44.6%) were female. Most participants underwent esophagus surgery (n=16) or bladder surgery (n=15). Open surgery was performed in 19 participants and laparoscopy was performed in 37. Mean duration of hospital stay was 9.6 ± 5.3 days. Sample characteristics are presented in Table 1.

Table 1: Sample characteristics

Characteristics	N=56
Age , mean \pm SD	62.8 \pm 12.2
Sex , male (%)	31 (55.4)
BMI , mean \pm SD	25.8 \pm 3.9
Tumor location , n (%)	
Bladder	15 (26.8)
Intestine	9 (16.1)
Liver	9 (16.1)
Esophagus	16 (28.6)
Stomach	1 (1.8)
Other	6 (10.7)
Surgery technique , n (%)	
Laparoscopic	37 (66.1)
Open	19 (33.9)
Complications , no (%)	22 (39.3)
Comorbidities , n (%)	
Pulmonary	11 (19.6)
Cardiovascular	17 (30.4)
Diabetes Mellitus	5 (8.9)
Other	4 (7.1)
None	33 (58.9)
ASA-classification , n (%)	
I	1 (1.8)
II	28 (50)
III	21 (37.5)
Unknown	6 (10.7)
Length of stay in hospital , mean \pm SD	9.6 \pm 5.3
Pre-treatment , n (%)	
No	29 (51.8)
Chemotherapy	8 (14.3)
Radiotherapy	1 (1.8)
Chemoradiation	16 (28.6)
Immunotherapy	2 (3.6)

Abbreviations: SD, standard deviation; ASA, American Society of Anesthesiologist

Missing data were imputed. Most data was missing on the D-GSE questionnaire (32%), due to a change of a self-efficacy questionnaire later on. Furthermore, in several occasions questionnaires at T0 were returned with certain items left blank. In the follow-up assessment (T1), 23% did not complete the AM-PAC questionnaire they received by e-mail, even after sending multiple kindly reminders. Demographic and clinical data had no missing values.

Baseline (T0) and follow-up (T1) data were available for 56 participants. The mean±SD score decreased from 59.0±10.0 before surgery (T0) to 49.9±8.9 at one month after hospitalization (T1), see table 2. The deterioration from baseline to one month after hospitalization was 9.16 (SD 11.24) and significant ($p < .001$).

Table 2: Descriptive statistics of the (in)dependent variables

	<i>Mean ± SD</i>
AM-PAC T0	59.0 ± 10.0
AM-PAC T1	49.9 ± 8.9
Δ AM-PAC (T1-T0)*	-9.16 ± 11.24
Anxiety and Depression (HADS)	20.8 ± 3.0
Physical Activity (DPAG)	7.9 ± 3.4
Fatigue (VVV)	19.3 ± 4.5
Illness acceptance (ZCL)	16.0 ± 4.0
Self-efficacy (D-GSE)	32.1 ± 4.5
Mobility (LSA)	41.2 ± 2.4

* AM-PAC score T0 subtracted from AM-PAC score T1; HADS, Hospital Anxiety and Depression Scale; DPAG, 2017 Dutch Physical Activity Guidelines; VVV, Verkorte Vermoeidheidsvragenlijst; ZCL, Ziekte-Cognitie-Lijst; D-GSE, Dutch General Self-Efficacy scale; LSA, Life Space Assessment

The assumptions for multiple linear regression were met and no multicollinearity was detected. Univariable associations with recovery of physical functioning one month after hospitalization are presented in Table 3.

Table 3: Univariable regression analysis between recovery of physical functioning and physical and mental factors

	<i>B</i>	<i>SE B</i>	<i>p</i>	<i>95% CI</i>	
Anxiety and Depression (HADS)	.029	.513	.954	-.976	1.035
Physical Activity (DPAG)	-2.010	3.710	.033*	-1.779	-.076
Fatigue (VVV)	-.304	.362	.401	-1.015	.407
Illness acceptance (ZCL)	.504	.385	.190**	-.251	1.260
Self-efficacy (D-GSE)	-.229	.360	.525	-.937	.479
Mobility (LSA)	-.602	.671	.371	-1.926	.723

* $p < .05$; ** $p < .2$

B, unstandardized regression coefficient; *SE*, Standard Error of the estimate; *CI*, Confidence Interval; HADS, Hospital Anxiety and Depression Scale; DPAG, 2017 Dutch Physical Activity Guidelines; VVV, Verkorte Vermoeidheidsvragenlijst; ZCL, Ziekte-Cognitie-Lijst; D-GSE, Dutch General Self-Efficacy scale; LSA, Life Space Assessment

Based on the p-values derived from the univariable linear regression, physical activity and illness acceptance were selected for multiple regression analysis. The results of the backward stepwise multiple regression analysis in predicting recovery of physical functioning are presented in Table 4. Illness acceptance was eliminated due to the stepwise backward selection procedure with $p < .10$. Physical activity has been shown as significant ($p .023$) predictor of physical functioning, which explained 9.2% of the total variance.

This final predicting model shows that every day of physical inactivity leads to a decrease of the predicted physical functioning by 1.005. Thus; the lower the degree of physical activity, the worse the predicted recovery of physical functioning.

Table 4: Multiple regression analysis between recovery of physical functioning and physical and mental factors

	B	SE B	p	95% CI	
Physical Activity (DPAG)	-1.005	.430	.023*	-1.868	-.143
Illness acceptance (ZCL)	e				
R² statistics (%)	9.2				

* $p < .05$

B, unstandardized regression coefficient; *SE*, Standard Error of the estimate; *CI*, Confidence Interval; *e*, variable excluded from the regression model; DPAG, 2017 Dutch Physical Activity Guidelines; ZCL, Ziekte-Cognitie-Lijst

DISCUSSION

In this longitudinal cohort study, the association between recovery of physical functioning and six mental and physical factors was examined in patients after oncological surgery. Physical activity was identified as a predictor ($p .023$) of recovery of physical functioning, which explained 9.2% of the total variance. The other factors were not associated with recovery of physical functioning.

Physical activity has also been shown to be associated with recovery of physical functioning in earlier studies. Junior et al. suggests that the degree to which elderly are physically active can predict their level of physical functioning (36). Another study showed that preoperative cardiorespiratory fitness and muscle strength were independent risk factors for recovery of physical functioning (37).

In the study of Lee et al., the minimally clinically important difference (MCID) of the AM-PAC is estimated between 3.9 and 5 points (38). With the earlier described B of -1.005 for physical activity found in this study, a clinically relevant difference of the recovery of physical functioning is expected when patients are more physically active or less physically active for 3.9 to 5 days, over a span of 14 days. Since 3.9 to 5 days over a span of 14 days is quite plausible, it can be concluded that physical activity can quickly make a difference to a clinically relevant difference on the recovery of physical function. A qualitative study showed that patients are willing to work on this and that the biggest motivation and drive for patients to be physically active preoperatively, was the pursuit of postoperative independence and recovery (39).

In this study, mental factors were not associated with recovery of physical functioning. This is contradictory to previous studies which do show associations (13,40–42). This could be explained in several ways. The low variance in the outcomes of the questionnaires may be the reason why no association was found in this study. Besides that, the small sample size of this study could also have led to not finding any associations. Finally, in this study, recovery of physical functioning was measured one month after hospitalization. This timeframe was perhaps too short to find any associations, since the recovery trajectory had just started.

This study showed that physical activity is a predictor of the recovery of physical functioning. Patients with a low level of physical activity prior to surgery have a worse prognosis of recovery of physical functioning. Therapists could benefit from this knowledge by carefully monitoring these patients. As Dronkers et al. suggested in his study, integrating screening of preoperative physical activity could be beneficial, because this enables patients and therapists to reflect on the postoperative risk of a decline in physical functioning (43). This could in turn be used to optimize patients' preoperative condition.

Further research is needed to examine the causal relationship of these modifiable PROMs. This knowledge could be used to develop and deploy preventive interventions and to provide appropriate care and support which may contribute to optimal recovery of physical

functioning. Furthermore, stratification or distinction should be made between different groups in the sample, such as the presence or absence of complications, number of comorbidities, surgery technique or tumor location to create a better understanding. This would require a larger sample size and a multicenter study approach.

This study had some limitations. Firstly, this study was conducted in times of the COVID-19 pandemic. This may have influenced the results of the questionnaires, for example the LSA (mobility). Some participants made a note on the LSA questionnaire that they were less likely to mobilize outside their own home due to the COVID-19 restrictions. Secondly, the questionnaires on T0 had to be filled in retrospectively which could have led to recall bias. However, the recall period for this study was only one month and literature showed that a short recall period was preferable over a long one. Thirdly, this study had a small sample size and was conducted in a single center. This may have diminished the statistical power of the study and compromised the generalizability of the current findings. Finally, the timing of data collection may have affected the results. The AM-PAC, which assessed the level of physical functioning was administered one month after hospitalization. Patients may not have been able to perform certain daily activities due to restrictions imposed by the surgeon, such as lifting, which is one of the questions in the AM-PAC questionnaire. A strength of this study is the use of a combination of both physical and mental factors for predicting recovery of physical functioning. In previous research only cross-sectional associations were examined in either physical or mental factors. Physical and mental health are fundamentally linked, therefore this study gives an overall picture. Besides that, this study is a good stepping stone to gain more insight into what may contribute to an optimal recovery of physical functioning.

CONCLUSION

Physical activity was a significant predictor of recovery of physical functioning after oncological surgery one month after hospitalization. Patients with a low level of physical activity prior to surgery may have a worse prognosis of recovery of physical functioning and can be monitored more extensively. Further research is needed to examine the causal relationship for developing and deploying preventive interventions which may contribute to optimal recovery of physical functioning.

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