Preoperative predictors of physical functioning in patients after gastrointestinal- or lung cancer surgery.

Masterthesis

Physiotherapy Science

Program in Clinical Health Sciences

Utrecht University

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"ONDERGETEKENDE

Jacoba Herremijntje van Dijk,

bevestigt hierbij dat de onderhavige verhandeling mag worden geraadpleegd en vrij mag worden gefotokopieerd. Bij het citeren moet steeds de titel en de auteur van de verhandeling worden vermeld."

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Masterthesis, Physical Therapy Sciences, Program in Clinical Health Sciences, Utrecht University, Utrecht, 2021

ABSTRACT

Background: Undergoing gastrointestinal- or lung cancer surgery is a major life event, and recovery after surgery significantly impacts physical, psychological, and social functioning. However, the course of recovery varies between patients. Knowledge of preoperative predictors of functional recovery can be used to inform patients about the likely course of their recovery and can contribute to developing therapeutic and preventive interventions. Physical functioning after hospital discharge is not often used as an outcome in prediction models, although it is relevant for patients and rehabilitation professionals. Furthermore, modifiable preoperative nutritional and physical factors, often omitted in current prediction models, predict physical functioning after discharge.

Aim: To identify preoperative predictors, including physical and nutritional factors, for change in physical functioning at four weeks after hospital discharge in patients who underwent gastrointestinal- or lung cancer surgery.

Methods: A multicenter longitudinal observational study was conducted in patients undergoing gastrointestinal- or lung cancer surgery. The primary outcome was physical functioning at four weeks after hospital discharge using the Dutch-Flemish Patient Reported Outcome Measure Information System for Physical Functioning. Potential preoperative predictors included demographic factors (i.e., age), clinical factors (i.e., physical health status, tumor location, and operation technique), physical factors (i.e., physical activity and measures of physical performance), and nutritional factors (i.e., fat-free mass index and protein intake). Univariable and multivariable linear regression analyses were conducted. *Results:* Data from 88 patients were available for analysis. The average physical functioning decreased from 46.99 (SD = 6.7) before surgery to 40.84 (SD = 6.0) at four weeks after hospital discharge. Univariable regression analysis showed that physical activity and physical health were associated with changes in physical functioning at four weeks after hospital discharge (p<0.2). Multivariable linear regression analysis did not identify any significant predictors for change in physical functioning at four weeks after hospital discharge. *Conclusion and key findings:* No significant preoperative predictors for change in physical

functioning were identified in patients who underwent gastrointestinal- or lung cancer surgery. Further research is necessary to gain more insight into predictors of physical functioning after cancer surgery.

Keywords: functional recovery, physical functioning, cancer surgery, preoperative predictors

INTRODUCTION

Gastrointestinal (GI) and lung cancers are among the most common types of cancer, and in 2020, they were accountable for approximately 7,24 million new cases and 4,7 million deaths (1). Cancer is a complicated disease that is often not easy to cure. However, the five-year survival rates for colon cancer have increased from 40% to 70% and for lung cancer from 15% to 23% over the past 70 years (2). Surgical treatment is a necessary part of treatment for patients who have a chance to be cured and is followed by a period of recovery in the hospital, which continues after discharge (3,4). It is an intensive process that significantly impacts physical, psychological, and social functioning (3).

Physical Functioning (PF) is an important outcome after surgery, determining quality of life (5). PF includes the ability to perform daily activities required to participate in society and is a patient-reported outcome (6). Surgery greatly impacts PF, and the course of recovery varies between patients. Studies show that more than 50 percent of older patients undergoing major abdominal surgery do not return to baseline levels of functional status six months after surgery (7), and 76 percent of patients undergoing lung cancer surgery do not recover from preoperative PF at three months after surgery (8).

Despite the importance of PF from the patient's perspective, many studies often prioritize factors such as length of stay and morbidity risk after cancer surgery (10,12,13, 14), sidelining PF recovery predictors. A recent study concluded that a longer surgery duration, prolonged stay, and postoperative treatments diminish the likelihood of good functional recovery one month after colorectal surgery (12). Additionally, comorbidities, a higher number of symptoms, reduced mental health, and lower income resulted in a reduced PF six months after cancer surgery (13).

Even if survival were ensured, more than 70 percent of older adults would not choose a treatment that caused severe functional impairment (14). The importance of PF is underrecognized in hospitals during the shared decision-making process. While surgeons use risk calculators to predict the risk of postoperative complications and readmissions, PF is not often used as an outcome in prediction models. However, it is essential for informed patient decision-making (15).

Understanding the influence of preoperative factors on PF can help improve therapeutic interventions, such as prehabilitation. Prehabilitation is expected to enhance patient's functional capacity by offering exercise training and improving nutritional status, which results

in fewer postoperative complications, increased survival, and improved quality of life (16,17). Recent studies identify preoperative factors associated with postoperative complications and conclude that poor physical performance and impaired nutritional status increase the risk of complications after major cancer surgery (18,19). However, despite the established influence of nutritional and physical factors on PF (20–22), these factors are often missing in current prediction models. Notably, while factors such as age and physical health are often included in current models, their non-modifiable nature sets them apart from the modifiable potential of nutritional and physical factors.

Knowledge of physical and nutritional predictors can be used to inform patients about the likely course of their recovery, which supports a better shared decision-making process and contributes to developing therapeutic and preventive interventions. Therefore, this study aims to identify preoperative predictors, including physical and nutritional factors, for change in PF at four weeks after hospital discharge in patients who underwent GI- or lung cancer surgery.

METHODS

Study design and Population

The study design was a multicenter longitudinal observational study, performing a secondary analysis of data gathered from a randomized controlled trial (RCT) called 'Optimal Physical Recovery After Hospitalization' (OPRAH) (23). This RCT explores the efficacy of a blended intervention, focusing on personal feedback and coaching regarding physical activity (PA) and protein intake after hospital discharge in patients who have undergone elective GI- or lung cancer surgery at Amsterdam UMC, location VUmc or St. Antonius Hospital Nieuwegein, on the outcome of recovery of PF compared to usual care. Our study population consists of patients enrolled in the OPRAH study between June 2022 and August 2023.

Eligible patients for the OPRAH study were individuals aged 18 or above, scheduled for curative intent GI- or lung cancer surgery, and with a planned hospital stay of \geq 2 nights. Besides, they needed to be able to fill in online questionnaires in Dutch and give informed consent. Exclusion criteria encompassed patients undergoing pulmonary wedge resection, those who had surgery with an open/close procedure, or those with less than five days between inclusion and surgery. Additionally, patients were excluded if they were wheelchair dependent, already participating in a conflicting study, possessed a Mini-Mental State Examination (MMSE) \leq 24, or lacked access to a mobile device compatible with applications.

Data collection

Primary outcome

The primary outcome of this study is the pre- to postoperative change in PF. PF was assessed using the Dutch-Flemish Patient Reported Outcome Measure Information System for Physical Functioning (PROMIS–PF). This questionnaire comprises inquiries about a broad spectrum of activities, demonstrating reliability and sensitivity to changes in surgical patients (24,25). A recent systematic review found high-quality evidence for measurement precision and structural validity for PROMIS-PF (26). In cancer patients, the minimal important difference (MID) range for the PROMIS PF varies from 4.0 to 6.0 (27). Utilizing a 5-point Likert scale; a higher score on the scale indicates reflects better functioning. Assessment of PF was conducted both before surgery and four weeks after hospital discharge in this study.

Potential predictors

Demographic factors

Age in years was selected for inclusion in the prediction model based on existing literature, which indicates a negative impact of age on PF in older cancer patients(28).

Clinical factors

Physical health was assessed using The American Society of Anaesthesiologists Classification of physical health (ASA score). This is a subjective assessment of a patient which is an important tool for predicting short- and long-term outcomes in patients undergoing hepatic resections (29). In surgical techniques, a distinction is made between open and laparoscopic techniques. Laparoscopic surgery has demonstrably better quality-oflife outcomes than open surgery for oncological surgery (30). Finally, tumor location was included based on clinical knowledge, distinction was made between lung and GI cancer. Regarding GI cancer, esophagus, stomach, pancreas, and hepar cancer types were included. Physical health, tumor location, and operation technique were extracted from the Electronic Patient Record System (EPRS).

Physical factors

PA was objectively measured using the ActivPAL. The ActivPAL is an accelerometer that measures PA and totals the time spent lying, sitting, standing, and walking every second of the day. The ActivPAL is one of the most commonly, used activity trackers in clinical research and is a valid measure of posture and steps (31–33). Prior to surgery, patients were asked to wear the ActivPALI™ on the thigh for five days. The total number of minutes of stepping and standing per day was recorded to provide insight into PA Physical performance was assessed in the patient's home one to four weeks prior to surgery using the 30-second chair stand test (30CST), handgrip strength, and 2-minute step test (TMST). The 30CST measures functional lower extremity muscle function. The 30CST has good reliability and criterion validity (34). Grip strength can determine generalized muscle strength and was measured using the Jamar grip strength dynamometer. The grip strength in kilograms was divided into percentiles according to Dodds et al. (35), which are further divided into low (percentile 0 - 10), average (percentile 25-75), and high (percentile 90 -100) categories. The Jamar grip strength shows good reliability and can measure changes in strength over time (36,37). The TMST measures exercise capacity and has good reliability in older adults (38). Exercise capacity was defined as the number of steps completed in two minutes.

Nutritional factors

Protein intake was evaluated through a 48-hour dietary recall conducted by trained interviewers, with calculations based on the 'Netherlands Nutrition Center' database. Protein intake was reported as protein intake in grams (g)/kilogram (kg)/fat-free mass (FFM)/day, which is proved to be more reliable than protein intake based on body weight in kg (39). Fat-free mass index was measured one week before surgery using Bioelectrical Impedance Analysis (BIA) with the Bodystat500, a single-frequency bioelectrical impedance meter. According to Schutz et al. (40), fat-free mass index was divided into percentiles, which are further divided into low (percentile 0 - 10), average (percentile 25-75), and high (percentile 90 - 100) categories. The BIA was chosen because this is a non-invasive validated method for assessing body composition and FFM in cancer patients (41).

Additional demographic data, including, gender, marital status, number of comorbidities, stage of cancer, pre- or post-treatment with chemo- or radiotherapy, length of stay, and hospital readmission < 30 days after discharge, were extracted from the EPRS.

Study procedures

For this study, the procedures for the OPRAH study were followed (23). Before surgery, recruitment took place during the preoperative consultation; by interest, the patient received information about the study. The following day, the investigator phoned the patient to check if the patient was eligible and willing to participate. The investigator scheduled an appointment for the measurements at the patient's home one to four weeks before surgery (T0). Before the baseline measurements, the informed consent letter was signed. A link to fill in questionnaires at baseline and after discharge was sent to the patient by e-mail via the online PROMS platform by Interactive Studios. After the baseline measurements, patients were randomized into the intervention or control group.

After surgery, all patients received usual care. Besides, patients in the intervention group received a blended intervention focus on personal feedback and coaching regarding PA and protein by a hospital physiotherapist and dietician after discharge. Patients were required to wear a PAM accelerometer and maintain a dietary record using a self-monitoring smartphone application for three months after hospital discharge. Additionally, the smartphone app served as a platform for patients to receive coaching from a physiotherapist and a dietician. Further details of the intervention are described in the OPRAH protocol (23).

During the trial, there are multiple follow-up measurements; at hospital discharge (T1) and one week (T2), four weeks (T3), eight weeks (T4), twelve weeks (T5), and six months (T6) after hospital discharge. For this study data at baseline and four weeks after hospital

discharge were used. During the current analysis, a distinction between these two groups has not yet been made because blinding could not yet be removed and both groups are included. The trial protocol has been approved by the Medical Ethical Research Committee (METC) of Amsterdam UMC, location VUMC (METC 2021.0627).

Sample size

The sample size was based on the number of variables in the study. Ten patients per variable were the required sample size for linear regression analysis to ensure an accurate prediction (42). It is expected that at most eight predictors will be included in the multivariable regression analysis, which resulted in a required sample size of at least 80 patients.

Statistical Analysis

IBM SPSS Statistics, version 29, was used for statistical analysis. Multiple imputation was used in case of missing data at random. Sensitivity analyses were performed to estimate the effect of missing data on the results. Ten imputed data sets were generated using multiple imputation in SPSS software and the results were pooled according to Rubin's rules (43).

Baseline characteristics were presented using descriptive statistics. Continuous variables were reported in mean and standard deviation (SD) in case of normal distribution. Otherwise, continuous variables were presented with a median and interquartile range (IQR). Categorical data were reported using frequencies and percentages.

Univariable and multivariable linear regression analyses were performed to assess the association between potential predictors and the postoperative change of PF. Each regression analysis was corrected for PF at baseline to model change in PF. First, univariable associations were assessed using linear regression. P-values along with their corresponding 95% confidence intervals were reported. Assumptions for multiple linear regression were checked. A residual plot was generated to assess linearity and homoscedasticity, and the normality of residuals was examined using histograms and QQ plots. Multicollinearity was assessed using Variance Inflation Factor (VIF) values. Second, all candidate variables shown to have a p-value of < 0.2 from the univariable analysis were entered into a multivariable analysis using the backward stepwise method (44). The variables were excluded stepwise until all remaining variables had a p-value of \leq 0.05. To demonstrate the explained variance in the final model, R² was calculated for the independent variables.

RESULTS

For this study, a total of 115 patients were potentially eligible. However, eighteen patients were excluded based on exclusion criteria. Following baseline assessments, nine patients were lost to follow-up, with an additional five patients voluntarily withdrawing from the study. Tragically, two patients passed away, and two were discharged to a rehabilitation center. The detailed reasons for exclusion and loss to follow-up can be found in Figure 1. Consequently, data from 88 patients were available for analysis.



Figure 1 Patient participation flowchart

Missing data occurred randomly and were addressed through Multiple Imputation. Most of the missing data pertained to PF, with rates of 1.1% at baseline and 11.4% at follow-up. Notably, demographic data had no missings. At baseline, two patients did not complete the food diary, and one lacked data for the fat-free mass index. Additionally, PA data was absent from three patients. A sensitivity analysis revealed no significant differences between the imputed and the original datasets.

Among the patients, 56 (63.6%) were male, while 32 (36.4%) were female, with an average age of 64 (SD 10.7). Most underwent lung (n=28) or esophageal (n=28) surgery, and 59.1% were classified as ASA 2. Approximately 67% underwent laparoscopic surgery, with an average length of stay of 6.5 days. Additional characteristics are detailed in Table 1.

Table 1 Patients' outcomes		
Characteristics	n = 78	n = 88
Gender, male, n (%)	48 (61.5)	56 (63.6)
Age, mean \pm SD, years	64.59 ± 10.7	64.17 ± 10.7
Marital status, n (%)		
Living together	62 (79.5)	71 (80.7)
Living alone	16 (20.5)	17(19.3)
Comorbidities, n (%)		
No comorbidities	37 (48.1)	41 (46.6)
Diabetes mellitus type 2	8 (10.4)	8 (8.8)
COPD	4 (5.2)	8 (8.8)
Cardiovascular disease	16 (20.8)	19 (20.9)
OSAS	3 (3.9)	4 (4.4)
Gout	3 (3.9)	3 (3.3)
Hypertension	19 (24.7)	21 (23.1)
Hypercholesterolemia	3 (3.9)	5 (5.5)
BMI, mean ± SD, kg/m ²	26.10 ± (5.3)	26.36 ± (5.2)
Physical Health, n (%)		
ASAI	3 (3.8)	3 (3.4)
ASA II	46 (59.0)	53 (60.2)
ASA III	28 (35.9)	32 (36.4)
Unknown	1 (1.3)	
lumor location, n (%)	00 (00 0)	
Lung	26 (33.3)	28 (31.8)
Esophagus	24 (30.8)	28 (31.8)
Stomach	5 (0.4) C (7.7)	6 (6.8) 9 (0.1)
Pancreas	0 (7.7) 45 (40.2)	8 (9.1)
Colorectal	15 (19.2)	16 (18.2)
Depai Dilioir	1 (1.3)	1 (1.1)
	1 (1.3)	1 (1.1)
1 unor size, ii (%)	12 (16 7)	14 (15 0)
1	13 (10.7) 21 (26.0)	14(13.9)
2	21 (20.9)	20 (26.4)
Л	20 (33.9) 8 (10.3)	10(114)
	8 (10.3)	9(10.2)
Surgical technique n (%)	0 (10.0)	5 (10.2)
Open	16 (20 5)	21 (23.9)
	62 (78.5)	67 (76.1)
Pre-treatment. n (%)	0_(.0.0)	0. (. 0)
None	34 (43.6)	36 (40.9)
Neoadjuvant chemotherapy	14 (17.9)	18 (20.5)
Neoadjuvant chemoradiation	27 (34.6)	30 (34.1)
Neoadjuvant radiotherapy	3 (3.8)	4 (4.5)
Post-treatment, n (%)		
None	49 (62.8)	56 (63.6)
Adjuvant chemotherapy	23 (29.5)	25 (28.4)
Adjuvant radiotherapy	1 (1.3)	1 (1.1)
Unknown yet	5 (6.4)	6 (6.8)
Length of stay, mean (IQR), days	6.32 (6.0)	6,51 (5.75)
Hospital readmission < 30 days after discharge, n (%)		
Yes	12 (15.4)	14 (15.9)
No	65 (82.3)	72 (81.8)
Unknown yet	1 (1.3)	2 (2.3)

Abbreviations: SD, standard deviation; IQR, Interquartile range, ASA, American Society of Anesthesiologists; GI, Gastrointestinal; HPB, Hepato-Pancreatic-Biliary; BMI, Body Mass Index; COPD: Chronic Obstructive Pulmonary Disease.

The average PF decreased from 46.99 (SD = 6.7) before surgery to 40.84 (SD= 6.0) at four weeks after hospital discharge. At baseline, the mean daily PA was 96.22 minutes, and the mean protein intake was 1.96 per g/kg/FFM. All outcomes are presented in Table 2, distinguishing between observed data with complete cases, and imputed data.

(in)dependent variables	Observed data	Imputed data
	n = 78	n = 88
Dependent variables		
Preoperative PF, mean ± SD	46.99 ± 6.7	47.1 ± 6.7
4 weeks post-discharge PF, mean \pm SD	$40.84\ \pm 6.0$	41.0 ± 6.1
Potential preoperative predictors		
Age, mean \pm SD, years	64.59 ± 10.7	64.17 ± 10.7
Physical Health, n (%)		
ASAI	3 (3.8)	3 (3.4)
ASA II	46 (59.0)	53 (60.2)
ASA III	28 (35.9)	32 (36.4)
Unknown	1 (1.3)	
Tumor location, n (%)		
GI	52 (66.7)	60 (68.2)
Lung	26 (33.3)	28 (31.8)
Surgical technique, n (%)		
Open	16 (20.5)	21 (23.9)
Laparoscopic	62 (78.5)	67 (76.1)
Physical activity, min, mean ± SD	96.2 ± 43.3	96.4 ± 43.6
Physical performance		
30 CST, reps ± SD	12.2 ± 3.3	12.2 ± 3.4
TMST. reps ± SD	73.6 ± 23.1	74.2 ± 22.5
Handgrip strength, n (%)		
Low	7 (8)	7 (8)
Average	59 (67)	59 (67)
High	22 (25)	22 (25)
Relative protein intake, g/kg FFM/day, mean ± SD	1.97 ± 0.8	2.0 ± 0.8
Fat-free mass index. n (%)		
Low	27 (30.7)	27.3 (31.0)
Average	40 (45.5)	40.3 (45.8)
High	20 (22.7)	20.4 (23.2)
HIgn bbreviations: SD, standard deviation: 30 CST, 30-second chair	20 (22.7) stand test: TMST_2-minute :	20.4 (23.2) step test_FFM_Fat-Free Mas

Abbreviations: SD, standard deviation; 30 CST, 30-second chair stand test; TMST, 2-minute step test, FFM, Fat-Free Mass; PF, Physical Functioning.

Univariable associations between change in PF four weeks after hospital discharge and potential preoperative predictors are outlined in Table 3. Based on p-values, physical health (B = 4.045, p = 0.163) and PA (B = -0.023, p = 0.175) are associated with change in PF four weeks after hospital discharge and are selected for multiple regression analysis.

Table 3	Univariable	regression	analysis ^a
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n= 88	В	SE B	Р	95% CI	
Physical health					
ASAI	REF				
ASA II	4.045	3.562	0.163*	-2.935	11.026
ASA III	5.129	3.673	0.256	-2.070	12.328
Operation technique (open)	-1.170	1.821	0.522	-4.789	2.449
Age	-0.010	0.067	0.887	-0.142	0.123
Tumor location (Lung)	0.908	1.504	0.546	-2.050	3.866
Physical activity	-0.023	0.017	0.175*	-0.055	0.010
Physical performance					
30 CST	-0.034	0.214	0.874	- 0.455	0.387
Hand Grip Strength					
Low	REF				
Average	1.767	2.705	0.514	-3.564	7.097
High	2.503	3.060	0.415	-3.543	8.549
TMST	-0.016	0.031	0.598	-0.077	0.045
Relative protein intake	-0.678	0.898	0.451	-2.439	1.084
Fat-Free mass index					
Low	REF				
Average	1.111	1.576	0.481	-1.981	4.204
High	0.932	1.825	0.610	-2.647	4.511

Abbreviations: B, unstandardized regression coefficient; SE, Standard Error of the estimate; CI, Confidence Interval; 30 CST, 30-second chair stand test; TMST, 2-minute step test, ASA, American Society of Anesthesiologist; * p <0.2. ^aAnalyses are adjusted for baseline physical functioning.

A multivariable linear regression was conducted with PA and physical health. The results of the multiple regression analyses are presented in Table 4. No significant predictors of pre- to postoperative change in PF were identified.

Table 4 Multivariable regression analysis^a

n = 88	B	SF B	Р	95% CI	
1 - 00	2	02.0	•		
Model: Physical activity and Physical health					
Physical health					
ASAI	REF				
ASA II	3.011	3.690	0.415	-4.222	10.244
ASA III	3.895	3.902	0.318	-3.754	11.545
Physical activity	-0.017	0.018	0.334	-0.052	0.018
R ² (%)	9.2				

Abbreviations: B, unstandardized regression coefficient; SE, Standard Error of the estimate; CI, Confidence Interval; 30 CST, 30-second chair stand test; TMST, 2-minute step test, ASA, American Society of Anesthesiologist.

^aAnalyses are adjusted for baseline physical functioning.

DISCUSSION

This study aimed to identify preoperative predictors, including physical and nutritional factors, for change in PF at four weeks after hospital discharge in patients who underwent GI- or lung cancer surgery. Knowledge of physical and nutritional predictors, in addition to unmodifiable predictors, can be used to inform patients about the likely course of their recovery, which supports a better shared decision-making process and contributes to developing therapeutic and preventive interventions. In this study, the average PF decreased from 46.99 (SD = 6.7) before surgery to 40.84 (SD = 6.0) at four weeks after hospital discharge, aligning with the MID range of 4.0 to 6.0. Despite exploring various preoperative factors, no significant preoperative predictors for change in PF were identified.

Despite these findings, our results deviate from prior research, which consistently demonstrates the association between preoperative PA and postoperative functional recovery in patients who underwent cancer surgery (20–22,45). Mylius et al. (22) found that objectively measured preoperative PA is linked to the time to functional recovery after HPB cancer surgery. Heldens et al. (20) confirmed that patients undergoing colorectal surgery with higher levels of perceived fatigue and lower levels of preoperative PA tended to have a longer time to recover from PF. The exploration of nutritional factors remains limited within the scope of this study. Nevertheless, Yanagisawa et al. found no association between the prognostic nutrition index and postoperative PF (21).

Several factors may contribute to the deviation of our results from the existing literature. The relatively small sample size and short follow-up time might have limited the robustness of our findings. Many studies that assert PA as a predictor of PF after oncological surgery have a follow-up time of three to six months after surgery. Current literature estimates that most patients do not fully recover in the first three to six months after surgery (7,8). This suggests that patients have not recovered sufficiently in PF four weeks after discharge, which may confound results. A more prolonged follow-up, such as three to six months, is essential to determine the predictive value of physical and nutritional predictors accurately. Furthermore, due to our limited sample size, we pre-selected variables based on clinical experience and literature and focused primarily on physical and nutritional factors. Unfortunately, our analysis did not include essential variables such as comorbidities or prior chemo- or radiotherapy, which could significantly contribute to explaining variations in PF. Recognizing and addressing this limitation is essential for a better understanding of the factors influencing PF in patients who underwent GI- or lung cancer surgery.

The present study has several strengths. First, nutrition and exercise interventions are increasingly combined in the prehabilitation phase. Most studies focused on PA or nutritional status separately (19,20,22). In this study, the factors were researched together. Second, including various tumor locations in this study allows for greater generalizability. This study had some limitations. First, the data is derived from a larger ongoing trial investigating the effectiveness of the OPRAH intervention. The lack of distinction between patients who received the OPRAH intervention and those who did not could have influenced the results, as postoperative interventions in nutrition and exercise have the potential to affect PF outcomes following discharge. Secondly, the results must be interpreted cautiously due to the small sample size. With a small sample size, there is a greater likelihood that the estimated regression coefficients are not reliable. Estimates can vary widely from sample to sample, limiting the generalizability of the results. Finally, adjusting for preoperative PF in regression analyses showed a strong correlation between preoperative PF and PF four weeks after discharge. This suggests that introducing additional predictors may have a limited impact, as much of the variation is already explained by preoperative PF. Whether predicting PF might be more effective at discharge than preoperatively is a consideration that arises from this study. This observation raises the question of whether predicting changes in PF might be more accurate at the time of discharge, with factors such as complications and length of hospital stay providing a more comprehensive insight into PF after discharge.

Further research is necessary to identify the predictive value of preoperative physical and nutritional factors on PF after hospital discharge in patients who underwent GI- or lung cancer surgery. In addition, extending the follow-up period to at least three months, increasing the sample size, and considering the prediction of PF at discharge may provide deeper insights into potential predictors. This approach may improve the generalizability of the findings.

CONCLUSION

This study did not identify significant preoperative predictors for change in PF four weeks after hospital discharge in patients who underwent GI- or lung cancer surgery. These results deviate from findings in other studies, indicating a need for further research to gain more insight into potential modifiable preoperative predictors of PF after cancer surgery.

REFERENCES

- 1. World Health Organization, International Agency for Research on Cancer. Global Cancer Observatory [Internet]. [cited 2022 Sep 19]. Available from: https://gco.iarc.fr/
- 2. Overleving van kanker | Kanker.nl [Internet]. [cited 2022 Sep 19]. Available from: https://www.kanker.nl/algemene-onderwerpen/cijfers-over-kanker/uitleg-cijfers-overkanker/overleving-van-kanker
- 3. Lee L, Tran T, Mayo NE, Carli F, Feldman LS, Montreal C. Surgical Research Review What does it really mean to "recover" from an operation? 2014;
- 4. Miller TE, Mythen M. Successful recovery after major surgery: moving beyond length of stay. Perioperative Medicine 2014 3:1. 2014 Jul 8;3(1):1–3.
- 5. Hofman CS, Makai P, Boter H, Buurman BM, De Craen AJ, Olde Rikkert MGM, et al. The influence of age on health valuations: the older olds prefer functional independence while the younger olds prefer less morbidity. Clin Interv Aging. 2015 Jul 8;10:1131.
- 6. Coster WJ, Haley SM, Jette AM. Measuring patient-reported outcomes after discharge from inpatient rehabilitation settings. J Rehabil Med. 2006 Jul;38(4):237–42.
- Lawrence VA, Hazuda HP, Cornell JE, Pederson T, Bradshaw PT, Mulrow CD, et al. Functional independence after major abdominal surgery in the elderly. J Am Coll Surg. 2004 Nov 1;199(5):762–72.
- 8. van der Leeden M, Balland C, Geleijn E, Huijsmans RJ, Dekker J, Paul MA, et al. In-Hospital Mobilization, Physical Fitness, and Physical Functioning After Lung Cancer Surgery. Annals of Thoracic Surgery. 2019 Jun 1;107(6):1639–46.
- Ahmed J, Lim M, Khan S, McNaught C, MacFie J. Predictors of length of stay in patients having elective colorectal surgery within an enhanced recovery protocol. Int J Surg. 2010;8(8):628–32.
- Hendry PO, Hausel J, Nygren J, Lassen K, Dejong CHC, Ljungqvist O, et al. Determinants of outcome after colorectal resection within an enhanced recovery programme. Br J Surg. 2009 Feb;96(2):197–205.
- Kahokehr AA, Sammour T, Sahakian V, Zargar-Shoshtari K, Hill AG. Influences on length of stay in an enhanced recovery programme after colonic surgery. Colorectal Dis. 2011 May;13(5):594–9.
- 12. Jakobsson J, Idvall E, Kumlien C. Patient characteristics and surgery-related factors associated with patient-reported recovery at 1 and 6 months after colorectal cancer surgery. Eur J Cancer Care (Engl). 2017 Nov 1;26(6):e12715.
- 13. Van Cleave JH, Egleston BL, McCorkle R. Factors Affecting Recovery of Functional Status in Older Adults After Cancer Surgery. J Am Geriatr Soc. 2011 Jan;59(1):34.
- 14. Erri T, Ried RF, Radley LHB, Owle IRT, Hil MP, Eather H, et al. Understanding the Treatment Preferences of Seriously III Patients. 2002 Apr 4;346(14):1061–6.
- 15. Neville A, Lee L, Antonescu I, Mayo NE, Vassiliou MC, Fried GM, et al. Systematic review Systematic review of outcomes used to evaluate enhanced recovery after surgery. 2013;

- de Klerk M, van Dalen DH, Nahar-van Venrooij LMW, Meijerink WJHJ, Verdaasdonk EGG. A multimodal prehabilitation program in high-risk patients undergoing elective resection for colorectal cancer: A retrospective cohort study. European Journal of Surgical Oncology. 2021 Nov 1;47(11):2849–56.
- 17. Van Rooijen S, Carli F, Dalton S, Thomas G, Bojesen R, Le Guen M, et al. Multimodal prehabilitation in colorectal cancer patients to improve functional capacity and reduce postoperative complications: the first international randomized controlled trial for multimodal prehabilitation. BMC Cancer. 2019 Jan 22;19(1).
- Sánchez-Torralvo FJ, González-Poveda I, García-Olivares M, Porras N, Gonzalo-Marín M, Tapia MJ, et al. Poor Physical Performance Is Associated with Postoperative Complications and Mortality in Preoperative Patients with Colorectal Cancer. Nutrients. 2022 Apr 1;14(7).
- van Kooten RT, Bahadoer RR, Peeters KCMJ, Hoeksema JHL, Steyerberg EW, Hartgrink HH, et al. Preoperative risk factors for major postoperative complications after complex gastrointestinal cancer surgery: A systematic review. European Journal of Surgical Oncology. 2021 Dec 1;47(12):3049–58.
- 20. Heldens AFJM, Bongers BC, Lenssen AF, Stassen LPS, Buhre WF, van Meeteren NLU. The association between performance parameters of physical fitness and postoperative outcomes in patients undergoing colorectal surgery: An evaluation of care data. European Journal of Surgical Oncology. 2017 Nov;43(11):2084–92.
- 21. Yanagisawa T, Tatematsu N, Horiuchi M, Migitaka S, Yasuda S, Itatsu K, et al. Preoperative physical activity predicts postoperative functional recovery in gastrointestinal cancer patients. Disabil Rehabil. 2022 Sep 11;44(19):5557–62.
- 22. Mylius CF, Krijnen WP, Takken T, Lips DJ, Eker H, van der Schans CP, et al. Objectively measured preoperative physical activity is associated with time to functional recovery after hepato-pancreato-biliary cancer surgery: a pilot study. Perioperative Medicine 2021 10:1. 2021 Oct 4;10(1):1–12.
- 23. Leeuwerk ME, et al. The efficacy of a blended intervention to improve physical activity and protein intake for optimal physical recovery after oncological gastrointestinal and lung cancer surgery: the Optimal Physical Recovery After Hospitalization (OPRAH) study protocol for a randomized controlled multicenter trial. 2023;
- 24. Van Der Meij E, Anema JR, Huirne JAF, Terwee CB. Using PROMIS for measuring recovery after abdominal surgery: A pilot study. BMC Health Serv Res. 2018 Feb 20;18(1):1–9.
- 25. Patel AA, Dodwad SNM, Boody BS, Bhatt S, Savage JW, Hsu WK, et al. Validation of Patient Reported Outcomes Measurement Information System (PROMIS) Computer Adaptive Tests (CATs) in the Surgical Treatment of Lumbar Spinal Stenosis.
- Abma IL, Butje BJD, ten Klooster PM, van der Wees PJ. Measurement properties of the Dutch–Flemish patient-reported outcomes measurement information system (PROMIS) physical function item bank and instruments: a systematic review. Health Qual Life Outcomes. 2021 Dec 1;19(1):1–22.
- Yost KJ, Eton DT, Garcia SF, Cella D. Minimally important differences were estimated for six PROMIS-Cancer scales in advanced-stage cancer patients. J Clin Epidemiol [Internet]. 2011 May [cited 2023 Oct 24];64(5):507. Available from: /pmc/articles/PMC3076200/

- 28. Bergmann -Instituto Nacional de Câncer José Alencar Gomes da Silva -Rua André Cavalcanti A, Regina Carneiro Ximenes C, Bergmann A, Telles de Oliveira Lima J, Santos Cavalcanti A, Carlos Amorim de Britto M, et al. IMPACT OF AGE IN HEALTH-RELATED QUALITY OF LIFE IN OLDER ADULTS WITH CANCER Impacto da idade na qualidade de vida relacionada à saúde em idosos com câncer. Geriatr Gerontol Aging. 2021;15:210005–6.
- 29. Daabiss M. American Society of Anaesthesiologists physical status classification. Indian J Anaesth. 2011 Mar;55(2):111.
- 30. Velanovich V. Laparoscopic vs open surgery: a preliminary comparison of quality-of-life outcomes. Surg Endosc. 2000 Jan;14(1):16–21.
- Grant PM, Dall PM, Mitchell SL, Granat MH. Activity-Monitor Accuracy in Measuring Step Number and Cadence in Community-Dwelling Older Adults. J Aging Phys Act. 2008 Apr 1;16(2):201–14.
- Bassett DR, John D, Conger SA, Rider BC, Passmore RM, Clark JM. Detection of lying down, sitting, standing, and stepping using two activPAL monitors. Med Sci Sports Exerc. 2014;46(10):2025–9.
- 33. Sellers C, Dall P, Grant M, Stansfield B. Validity and reliability of the activPAL3 for measuring posture and stepping in adults and young people. Gait Posture. 2016 Jan 1;43:42–7.
- 34. Rikli RE, Jones CJ. Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years. Gerontologist. 2013 Apr;53(2):255–67.
- 35. Dodds RM, Syddall HE, Cooper R, Benzeval M, Deary IJ, Dennison EM, et al. Grip Strength across the Life Course: Normative Data from Twelve British Studies. PLoS One [Internet]. 2014 Dec 4 [cited 2023 Nov 28];9(12). Available from: /pmc/articles/PMC4256164/
- 36. Trutschnigg B, Kilgour RD, Reinglas J, Rosenthall L, Hornby L, Morais JA, et al. Precision and reliability of strength (Jamar vs. Biodex handgrip) and body composition (dual-energy X-ray absorptiometry vs. bioimpedance analysis) measurements in advanced cancer patients. 2008 Dec;33(6):1232–9.
- 37. Peolsson A, Hedlund R, Oberg B. Intra- and inter-tester reliability and reference values for hand strength. J Rehabil Med. 2001;33(1):36–41.
- Bohannon RW, Crouch RH. Two-Minute Step Test of Exercise Capacity: Systematic Review of Procedures, Performance, and Clinimetric Properties. J Geriatr Phys Ther. 2019 Apr 1;42(2):105–12.
- Dekker IM, van Rijssen NM, Verreijen A, Weijs PJM, de Boer WB (Elsbeth), Terpstra D, et al. Calculation of protein requirements; a comparison of calculations based on bodyweight and fat free mass. Clin Nutr ESPEN. 2022 Apr;48:378–85.
- Schutz Y, Kyle UUG, Pichard C. Fat-free mass index and fat mass index percentiles in Caucasians aged 18–98 y. International Journal of Obesity 2002 26:7. 2002 Jun 25;26(7):953– 60.
- Ræder H, Kværner AS, Henriksen C, Florholmen G, Henriksen HB, Bøhn SK, et al. Validity of bioelectrical impedance analysis in estimation of fat-free mass in colorectal cancer patients. Clin Nutr. 2018 Feb 1;37(1):292–300.

- 42. Harrell FE. Regression Modeling Strategies With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis Second Edition Springer Series in Statistics.
- 43. Heymans M, Eekhout I. Amsterdam. 2019. Applied Missing Data Analysis with SPSS and (R) Studio.
- 44. Baldi B, Moore DS. The practice of statistics in the life sciences. New York. 2018;
- 45. Kong S, Shin S, Jeon YJ, Lee G, Cho JH, Kim HK, et al. Factors associated with failure of cardiopulmonary function recovery after lung cancer surgery. Respirology. 2023 Nov 1;