Postoperative recovery of accelerometer-based physical activity in older cancer patients

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ABSTRACT

Introduction: Recovery of physical activity is an important functional outcome measure after cancer surgery. However, objective data on physical activity for older cancer patients is scarce. The aims of this study were to quantify perioperative physical activity levels, assess recovery of physical activity three months after surgery, and characterise patients who achieved recovery.

Materials and methods: This observational cohort study analysed physical activity data collected from patients aged >65 who were scheduled for cancer surgery between May 2018 and July 2019. Perioperative daily step count was measured using a Fitbit device. The primary outcome measure was the percentage of patients who returned to (≥90%) of their preoperative (baseline) physical activity levels three months after surgery.

Results: Fifty patients (mean age 73) were recruited, and available Fitbit data was analysed. Median daily step counts at baseline (n = 40), before hospital discharge (n = 40), and three months postoperative (n = 37) were 5,971 (IQR 4,250–7,922), 1,619 (IQR 920–2,839), and 4,674 (IQR 3,047–7,592), respectively. The 15/37 (41%) patients who had reached baseline levels three months after surgery seemed to have more preoperative self-reported physical activity, better anaesthesiologists’ physical status classification, and fewer in-hospital complications compared to patients who had not, although the differences were statistically non-significant.

Conclusion: Perioperative physical activity was quantified for older cancer patients, and 41% returned to baseline levels within three months. Accelerometer-based physical activity provided a valuable outcome measure for postoperative physical recovery. Future studies using objective physical activity measures are needed to evaluate effects of interventional studies aimed at improving physical activity.

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Introduction

Worldwide, the number of older adults diagnosed with cancer is expected to increase to 14 million annually by 2035, accounting for 60% of cancer incidence [1]. Over 40% of this population is considered to be frail [2], defined as having decreased physiologic reserves in multiple domains of functioning that result in an increased vulnerability to stressors [3–5]. Frailty is highly predictive for postoperative adverse outcomes following cancer surgery [6–9]. Historically, disease- or progression-free survival rates were the most common outcome measures reported for cancer treatment; however, functional recovery and patient-reported outcomes are considered even more important today, particularly for older cancer patients [10,11]. Physical activity is not only a predictor of physical and functional outcome but also an essential outcome in itself [12,13].

Physical activity has mostly been measured with self-reporting questionnaires [5,12]. Recently, accelerometer-based wearable activity monitors have been introduced to objectively, remotely, and continuously measure recovery of postoperative physical activity [14]. Objective measurement of physical activity contributes to a
complete assessment of functional recovery after cancer surgery, along with physical function tests and questionnaires regarding patients' self-reported functional recovery [15–17]. To date, wearable devices have mostly been used for younger surgical patients [18–20], in patients [21–25], preoperative monitoring [17], or postoperative monitoring for a relatively short period after hospital discharge [19,26].

However, perioperative physical activity data for older cancer patients is scarce. Wearable activity monitors could provide a more accurate, continuous, and comprehensive understanding of physical activity in the pre- and postoperative phase extending into the home setting [14]. Therefore, the main objectives of this study were to i) quantify perioperative physical activity using an accelerometer-based wearable activity monitor, ii) assess recovery of physical activity at three months after surgery, and iii) characterise patients who recovered to their preoperative physical activity. In addition, we compared recovery of objectively measured physical activity with self-reported physical activity.

Materials and methods

Study design

The physical activity data used for analysis in this study was collected in a single-centre prospective observational cohort study with perioperative remote home monitoring of older cancer patients. The study was conducted in the University Medical Centre Groningen, a tertiary academic hospital in the north of the Netherlands and approved by the local medical ethics committee (local registration number: 2017/286, Netherlands trial registration number: NL8253). This study was performed as part of the Conneicare research consortium funded by the European Union’s Horizon 2020 Research & Innovation Program [project grant agreement number 689802] [27].

Setting and participants

We identified cancer patients aged 65 years and over who were scheduled for surgery on a solid malignant tumour and recruited them at the outpatient clinic or by telephone from May 2018 until July 2019. Inclusion criteria were internet access at home, sufficient understanding of the Dutch language, and signed informed consent. Exclusion criteria were non-elective surgery, being wheelchair- or bed-ridden, and severe limitation in hearing, vision, and/or cognition that were expected to impair the patient’s ability to read the tablet, consult by telephone, or understand how to synchronise wearables with the tablet. Patients were visited for assessments at home or in the hospital at three moments in time: at preoperative assessment, at hospital discharge, and at three months postoperative. Waiting time for surgery ranged from a few days to three months due to differences in surgery indication, urgency, and operational capacity. Patients’ preoperative functioning and postoperative recovery until three months were monitored with a tablet-based health application (Conneicare) connected to several monitoring devices. However, for the purposes of this study, we focused on remote monitoring of physical activity. Patients were included in the data analysis if their step count data was available at hospital discharge.

Physical activity measurements

The accelerometer-based wearable activity monitor used was the Fitbit Charge 2 (Fitbit Inc., San Francisco, CA, USA), which uses an accelerometer to capture body motion in 3-dimensional space [28]. The Fitbit was provided at the preoperative assessment and worn on the patient’s non-dominant wrist all days of study participation except during surgery, intensive care unit admission, bathing/showering, and battery charging. We instructed patients to synchronise Fitbit data daily via Bluetooth to the Fitbit application installed on a study tablet (ASUS ZenPad™ 10, ASUSTek Computer Inc., Taipei, Taiwan or Samsung Galaxy Tab A, Samsung, Seoul, South Korea). Step count was visible to the patient, though no step goal was provided. Data from the Fitbit application was automatically imported via the Conneicare-application to a professional interface (the study website), which enabled day-to-day-monitoring by a case manager. If data was missing or if physical activity was very low (<1000 steps/day if 1000-steps/day had been achieved in the previous days), patients were contacted to provide assistance in performing synchronisation or to detect clinically relevant reasons for low physical activity levels. The treating physician was available to discuss further actions if deemed necessary. Fitbit data values used for analysis were daily step count and time engaged in moderate-vigorous physical activity (MVPA). These were measured in 24-h periods from 12:00 a.m.–11:59 p.m. from the day after the baseline assessment until the day before follow-up assessment. The Fitbit measured MVPA as the minutes per day spent on activities with an intensity of ≥3 metabolic equivalents of tasks [29].

Self-reported MVPA was assessed with the SQUASH [30] (Short Questionnaire to Assess Health-enhancing physical activity) at baseline and at three months follow-up. The SQUASH is demonstrated to be fairly reproducible (Spearman’s correlation of 0.58) and reasonable valid (Spearman’s correlation of 0.45) compared with other physical activity questionnaires [30]. Also, a high internal consistency was found in other studies that have used the SQUASH (Cronbach’s alpha of 0.85–0.88) [31,32].

Physical function was measured by the Timed Up & Go (TUG [33]).

Data collection and handling

Demographics and surgical and clinical data were collected from medical records and face-to-face assessments with validated questionnaires. Collected baseline patient characteristics included preoperative physical status as classified by the American Society of Anaesthesiologists (ASA) Physical Status Classification System [34], comorbidity (measured using the Charlson Comorbidity Index [35]), body mass index (BMI), frailty (Groningen Frailty Indicator [36]), instrumental activities of daily living (IADL) [37,38], nutritional status (Mini Nutritional Assessment – Short Form [39]), and mental status (Hospital Anxiety and Depression Scale [40]). Complications (classified using Clavien–Dindo [41]) were prospectively collected from medical records and were completed with medical information from external locations if the patient mentioned at the three-month assessment that complications had been treated by a general practitioner or another hospital. Data collected by the Fitbit was securely stored in a server from Eurecat S.A. (Barcelona – Spain), was handled confidentially and anonymously, and complied with the Dutch Personal Data Protection Act.

Outcome measures

The primary outcome was the percentage of patients who returned to their preoperative (baseline) physical activity levels three months after surgery. This was defined as ≥ 90% of baseline daily step count, based on comparable research [18,20]. An overview of outcome measures is provided in Table 1.
Statistical analysis

Baseline and surgery characteristics of patients who were included and excluded from analysis were presented using means with standard deviations (SD) for parametric continuous data, median with interquartile range [IQR] for nonparametric continuous data, and percentages for categorical data. Continuous parametric data, non-parametric data, and categorical data from these two groups were compared using the independent Student’s t-test, the Mann-Whitney U test, and Fisher’s exact test, respectively. A p-value < 0.05 was considered statistically significant. The mean daily step count and MVPA for each individual patient were computed i) preoperative, at home (1–7 days before surgery), ii) postoperative, at hospital discharge (day before and day of hospital discharge), and iii) at three months postoperative (81–90 days after surgery). We presented daily step count, MVPA, and TUG at these three moments in time in box-whisker plots in absolute numbers and in percentages of baseline to demonstrate perioperative changes in physical activity on a group level. Differences in TUG score over time were tested with the Wilcoxon signed-ranks test. We dichotomised recovery of physical activity at a cut-off point of 90% of patients’ preoperative baseline step count to assess recovery of each patient individually. Baseline characteristics and the occurrence of in-hospital complications (Clavien-Dindo grade ≥ 2) of patients who recovered were presented using descriptive statistics and odds ratios with a 95% confidence interval. To investigate the association between objective physical activity and self-reported physical activity, we used Spearman’s correlation to test the correlation between step count and MVPA reported by the Fitbit and MVPA self-reported with the SQUASH. Data was analysed with IBM SPSS Statistics version 23 (IBM Corporation, Armonk, NY).

Results

Participants

Fifty patients with a mean age of 73 ± 5.4 years (68% male) were recruited for participation in the study. Patients who were excluded from participation (n = 52) were more often female (56% versus 32%, p = 0.018) and older (mean age 76 ± 5.8 versus 73 ± 5.4, p = 0.009) compared to the patients willing to participate (n = 50). Step count data was available for 40 patients at the time of hospital discharge and 37 patients at three months after surgery, as illustrated in Fig. 1.

The ten patients excluded from analysis had a significantly lower mean BMI (24.6, SD 5.2 versus 28.0, SD 4.0, p = 0.039) and longer median anaesthesia time (551, IQR 338–578 versus 250, IQR 165–418, p = 0.039) than the 40 patients who were included in the analysis. Additional baseline characteristics of analysed and excluded patients are presented in Supplementary Table A. Because of the variation in types and indications for surgery, types of surgery are classified roughly in intracavitary and superficial, similar to previous research [42]. Intracavitary surgery in analysed patients included colorectal surgery (n = 20), esophago-gastric surgery (n = 4), small bowel surgery (n = 2), and liver surgery (n = 1), while superficial surgery included local resection of vulva carcinoma (n = 3), axillary (n = 2) or pelvic (n = 2) lymph node dissection, thyroidectomy (n = 1), and excision of sarcoma on the gluteus (n = 1). A detailed list of surgeries is provided in supplementary Table A.

Perioperative objective physical activity and physical function

The box-and-whisker plots in Fig. 2 demonstrate the variety in absolute daily step count and time spent on MVPA between patients (Fig. 2a + 2c) as well as the variance in recovery to their preoperative level of physical activity (Fig. 2b + 2d). Median step count at three months was 4,674 [3,047–7,592], which was approximately 80% of the baseline median step count of 5,974 [4,250–7,922]. Median step counts preoperative and three months after surgery were significantly higher in patients with ASA scores of I or II compared with III, superficial surgery compared with intracavitary surgery, and uncomplicated compared with complicated postoperative hospital stays (Supplementary Figure B). The median TUG measured at three months postoperative (8.7 s, IQR 7.3–9.4) was slightly increased compared with preoperative TUG values (7.8 s, IQR 6.3–8.2, p = 0.001) (Fig. 2e).

Recovery of physical activity

At hospital discharge, 5.0% (2/40) of the patients had returned to their preoperative levels of physical activity (≥90% of baseline), as measured by absolute step count. At three months after surgery, this had been achieved by 40.5% (15/37) of patients (Fig. 3). Nine patients who recovered to ≥90% baseline MVPA, of which five (55.6%) also recovered physical activity as measured by absolute step count. Of the sixteen patients who recovered to baseline TUG, nine (56.3%) also returned to ≥ 90% step count.

Characterisation of patients who recovered to their preoperative physical activity

Patients who achieved recovery of physical activity at three months after surgery (n = 15) did not significantly differ in age and gender from the patients who did not (n = 22) (Table 2). If patients met the Dutch physical activity guidelines [43] at baseline (self-reported MVPA > 150 min/week), they seemed more likely to achieve recovery of physical activity in step count compared with patients who did not meet the guidelines (58.3% versus 41.7%, p = 0.148, OR 3.36 [CI 0.71–15.85]). Patients who achieved ≥90% recovery at three months after surgery (n = 15) had lower ASA scores (48.4% ASA I/II versus 0% ASA III/IV, p = 0.069) and experienced fewer in-hospital complications (46.7% versus 14.3%, p = 0.204). Differences were statistically non-significant, and samples were too small to perform multivariable logistic regression. Baseline characteristics such as frailty, (Q)ADL, nutritional status, and mental status did not differ between patients who did or did not recover to preoperative physical activity level. Odds ratios for all baseline characteristics are depicted in Table 2.

Table 1

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>Assessment tool</th>
<th>Definition recovery at 3 months follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome measure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Objective physical activity</td>
<td>Daily step count</td>
<td>Fitbit (absolute number of steps)</td>
</tr>
<tr>
<td><strong>Secondary outcome measures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Objective physical activity</td>
<td>MVPA</td>
<td>Fitbit (minutes/day)</td>
</tr>
<tr>
<td>Objective physical function</td>
<td>Physical function test</td>
<td>TUG (seconds)</td>
</tr>
<tr>
<td>Self-reported physical activity</td>
<td>Self-reported MVPA</td>
<td>SQUASH (minutes/week)</td>
</tr>
</tbody>
</table>

Legend: Table 1. MVPA: Moderate-Vigorous Physical Activity; TUG: Timed Up & Go [33]; SQUASH: Short Questionnaire to ASses Health enhancing physical activity [30].
Self-reported physical activity

The SQUASH questionnaire was completed by 29 patients at baseline and by 32 patients at three months follow-up. Twenty-seven patients completed the SQUASH questionnaires at both baseline and at three months follow-up. Compared with their baseline SQUASH, 17/27 (63.0%) returned to their baseline score of self-reported MVPA. Preoperative self-reported MVPA had a moderate positive correlation with preoperative step count (Spearman's rho: 0.42, \( p = 0.016 \)) and a weak non-significant positive correlation with preoperative objectively measured MVPA (Spearman's rho: 0.33, \( p = 0.076 \)). At three months after surgery, self-reported MVPA had a weak non-significant positive correlation with steps (Spearman's rho: 0.216) and objectively measured MVPA (Spearman's rho: 0.287).

Discussion

In this study, we have quantified perioperative physical activity of older cancer patients and assessed recovery of physical activity using an accelerometer-based wearable activity monitor. On a group level, the median step count decreased directly after surgery and increased over three months' time but did not reach median baseline physical activity values. At three months after surgery, 41\% of the patients had returned to \( \geq 90\% \) of their individual preoperative physical activity level. Patients who returned to their baseline physical activity level seemed to have more self-reported MVPA before surgery, a lower ASA score, and fewer in-hospital complications compared to patients who did not return to baseline, although the numbers were small and the results were not statistically significant. There was a discrepancy between accelerometer-measured and self-reported physical activity.

In most physical activity studies, postoperative recovery is quantified at a group level, which does not adequately illustrate physical activity for the individual patient because of the large variance observed between patients' physical activity measures [15,16,19]. Van der Meij et al. assessed recovery of physical activity after minor to intermediate surgery at an individual level and found that 44\% of patients (mean age 45 years old) had reached their individual preoperative step count by 5 weeks after surgery [18]. It seems reasonable that the 41\% of our high-risk and older population who reached their individual baseline physical activity level needed more time (three months) to achieve recovery. Previous studies using wearables in comparable age categories showed similar physical activity patterns for older patients before and after cancer surgery, although different postoperative follow-up periods and measurements of recovery were used [15,16]. Guinan et al. [15] demonstrated that 6 months after esophagectomy, sedentary time increased significantly and MVPA was significantly reduced compared to preoperative levels. Compared to Guinan's more frail population with oesophageal carcinoma who underwent extensive resection, our population spent more time in MVPA before and after surgery. Ferrioli et al. [16] demonstrated a return to approximately 50\% of preoperative median step counts at 5–6 weeks after colorectal surgery. Our population took a median of 4,674 (IQR 3,047–7,592) steps at three months, which was 78\% of their baseline median step count.

As might be expected, patients had an uncomplicated postoperative course, more often recovered to their preoperative baseline activity than patients with in-hospital complications. Van
der Meij et al. demonstrated that patients with minor surgery recovered more often to their baseline than patients with major surgery [18]. Our results suggest that self-reported physical activity and ASA score did not only affect the absolute step count, but also the level of recovery to their preoperative step count. Unfortunately, we were not able to identify independent predictors for recovery of physical activity, due to a relatively small sample size. However, the results of this observational study add to the limited.
knowledge about recovery of objectively measured perioperative physical activity and characterisation of this population.

A strength of our study is the use of accelerometer-based physical activity as an objective functional outcome in older cancer patients. Most studies use self-reported physical activity measures only, which are limited by, for example, recall bias [17,44]. Our results confirm the discrepancy between self-reported and accelerometer-based physical activity, which emphasize the need for a complete assessment of physical activity using objective as well as subjective measuring tools. Moreover, we compared physical activity at three months after surgery with the individual’s baseline measurement. As discussed before, it is important to assess each patient individually, especially in a heterogeneous group of older cancer patients.

A limitation of this study is the probable overestimation of physical activity results of our study population compared with the average older patient undergoing cancer surgery. There might be several explanations for this overestimation. First of all, Fitbit devices tend to overestimate step count in free-living settings [28]. Also, accuracy of Fitbit data could be diminished due to participant compliance with device wearing and data synchronisation. Second, there might have been selection bias in recruiting physically active patients. Patients with walking aids were excluded from study participation, and we only analysed physical activity data of patients who chose to participate in the study and were compliant with data synchronisation. Finally, patients in our study might have achieved a higher step count because they were motivated by the feedback of their Fitbit devices and were contacted if their step count dropped below 1,000. In previous non-surgical studies, participants were likely to increase their physical activity levels by more than 25% after they started to wear an accelerometer-based wearable activity monitor [45]. In addition, patients with feedback from their accelerometer took significantly more steps than patients without feedback on their step count in the first five postoperative days [22]. On the other hand, steps taken at a slow pace or with assistance in the days directly after surgery might not have been adequately measured by the Fitbit [46].

Another limitation was the fact that only 27 patients completed the both SQUASH questionnaires. Because large feasibility issues were encountered by patients and case managers with another validated physical activity questionnaire at the start of the study, we switched to the SQUASH questionnaire from November 2018. However, the 27 patients who completed both SQUASH questionnaires did not differ significantly in baseline characteristics, so bias is limited.

Unfortunately, we were not able to identify independent predictors for recovery of physical activity. This could be due to a relatively small sample size. However, the results of this

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Characteristics and predictive variables for complete recovery of physical activity in step count at three months after surgery.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovery ≥90% (n = 15)</td>
<td>Not recovered (n = 22)</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>71.7 (4.8)</td>
</tr>
<tr>
<td>Gender, N (%)</td>
<td></td>
</tr>
<tr>
<td>- Female (0)</td>
<td>5 (38.5)</td>
</tr>
<tr>
<td>- Male (1)</td>
<td>10 (41.7)</td>
</tr>
<tr>
<td>ASA, N (%)</td>
<td></td>
</tr>
<tr>
<td>- ASA I (1)</td>
<td>15 (48.4)</td>
</tr>
<tr>
<td>- ASA II (1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index, median [IQR]</td>
<td>3.0 [0.7–7.0]</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>26.9 (2.8)</td>
</tr>
<tr>
<td>Baseline Frailty (GFI), median [IQR]</td>
<td>1.0 [0.0–3.0]</td>
</tr>
<tr>
<td>Baseline ADL, median [IQR]</td>
<td>0 [0.0–0.0]</td>
</tr>
<tr>
<td>Baseline IADL, median [IQR]</td>
<td>8.0 [8.0–8.0]</td>
</tr>
<tr>
<td>Baseline risk of malnutrition (MNA-SF), median [IQR]</td>
<td>14.0 [11.0–14.0]</td>
</tr>
<tr>
<td>Baseline anxiety (HADS-A), median [IQR]</td>
<td>3.0 [1.0–4.0]</td>
</tr>
<tr>
<td>Baseline depression (HADS-D), median [IQR]</td>
<td>4.0 [2.0–5.0]</td>
</tr>
<tr>
<td>Baseline step count, median [IQR]</td>
<td>6241 [5293–7433]</td>
</tr>
<tr>
<td>Baseline measured MVPA, median [IQR]</td>
<td>240 [60–654]</td>
</tr>
<tr>
<td>Self-reported baseline MVPA, N (%)</td>
<td></td>
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<tr>
<td>&lt;150 min/week</td>
<td>5 (29.4)</td>
</tr>
<tr>
<td>&gt;150 min/week</td>
<td>7 (58.3)</td>
</tr>
<tr>
<td>Type of surgery, N (%)</td>
<td></td>
</tr>
<tr>
<td>- Intracavitary (0)</td>
<td>11 (39.3)</td>
</tr>
<tr>
<td>- Other (1)</td>
<td>4 (44.4)</td>
</tr>
<tr>
<td>Type of surgery, N (%)</td>
<td></td>
</tr>
<tr>
<td>- Open (0)</td>
<td>12 (42.9)</td>
</tr>
<tr>
<td>- Laparoscopy/Robot (1)</td>
<td>3 (33.3)</td>
</tr>
<tr>
<td>Length of anaesthesia, minutes, median [IQR]</td>
<td>210.0 [149.0–421.0]</td>
</tr>
<tr>
<td>Length of hospital stay, days, median [IQR]</td>
<td>5.0 [4.0–13.0]</td>
</tr>
<tr>
<td>Complications in-hospital, N (%)</td>
<td></td>
</tr>
<tr>
<td>- No (0)</td>
<td>14 (46.7)</td>
</tr>
<tr>
<td>- Yes (1)</td>
<td>1 (43.2)</td>
</tr>
</tbody>
</table>

Legend: Table 2: SD: Standard Deviation; ASA: American Society of Anaesthesiologists [34]; IQR: Interquartile range; BMI: Body Mass Index; GFI: Groningen Frailty Index [36]; ADL: Activities of Daily Living [37]; IADL: instrumental Activities of Daily Living [38]; MNA-SF: Mini Nutritional Assessment — Short Form [39]; Hospital Anxiety and Depression Scale — Anxiety/Depression [40]; MVPA: Moderate-Vigorous Physical Activity.
observational study add to the limited knowledge about objective perioperative physical activity data for this population. In our study, objectively measured physical activity appeared to be a valuable outcome measure for recovery of physical activity. This is important to better inform patients, manage expectations, and support shared-decision making prior to surgery. Although some characteristics of preoperative functional status are not modifiable, such as ASA score [47] and age, other factors such as physical activity [48] could be targeted and potentially improved. An increasing number of studies are aimed at improving physical activity throughout different phases in the perioperative period: before surgery [49], during hospital admission [25], and after hospital discharge [50]. Accelerometers could be used as an objective measurement tool to evaluate the effect of different interventions aimed at improvement of postoperative outcome in frail elderly patients. These interventions could include prehabilitation, rehabilitation, or early discharge but could also be aimed towards more person-tailored treatment decisions.

Conclusion

In this prospective observational study, we quantified perioperative physical activity of older cancer patients. The 15 out of 37 (41%) patients who returned to baseline activity levels by three months after surgery seemed to have more preoperative self-reported physical activity, lower ASA scores, and fewer in-hospital complications than patients who did not reach baseline levels, although the differences were not statistically significant. The results of our study show that objectively measured physical activity is a valuable outcome measure to assess postoperative recovery of physical activity in older cancer patients, in addition to self-reported measures. Further observational research with accelerometer-based physical activity is needed to improve the understanding of postoperative recovery and to objectively measure and evaluate the effect of future interventional studies aimed at improving physical activity.

CRediT authorship contribution statement

Leonie T. Jonker: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization, Project administration. Sharon Hendriks: Validation, Investigation, Data curation, Writing - original draft. Maarten MH. Lahr: Conceptualization, Methodology, Resources, Writing - review & editing, Project administration, Funding acquisition. Barbara C. van Munster: Methodology, Writing - review & editing. Geertruida H. de Bock: Conceptualization, Methodology, Writing - review & editing. Barbara L. van Leeuwen: Conceptualization, Methodology, Writing - review & editing.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2020.06.012.

References


