Association between self-assessed preoperative level of physical activity and postoperative complications – An observational cohort analysis within a randomized controlled trial (PHYSSURG-C)

Aron Onerup a,b,*, Eva Angenete a,c, David Bock a, Eva Haglind a,c

a Scandinavian Surgical Outcomes Research Group (SSORG), Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
b Region Västra Götaland, Sahlgrenska University Hospital, Department of Pediatric Oncology, Gothenburg, Sweden
c Region Västra Götaland, Sahlgrenska University Hospital, Department of Surgery, Gothenburg, Sweden

Abstract

Introduction: Physical activity has been suggested as a modifiable risk factor for postoperative recovery after major surgery. We aimed to further define the association between self-reported leisure time physical activity and postoperative complications and recovery on a group level. Materials and methods: An observational cohort analysis was performed within a randomized controlled trial. Patients ≥20 years with colorectal cancer were eligible. Between January 2015 and May 2020, 761 participants were recruited. Leisure time physical activity was self-assessed on a four-grade scale. The primary outcome in this analysis was postoperative complications within 90 days, measured with the comprehensive complication index (CCI). Secondary outcomes were CCI for the index hospital stay, CCI 30 days postoperatively, specific types of complications, length of hospital stay, and self-assessed physical recovery. Analyses were adjusted for gender, age, study center, alcohol consumption, tumor stage, colon/rectal cancer, neoadjuvant therapy, and open or laparoscopic surgery. Results: Data on preoperative physical activity was available for 614 participants. Participants who reported some physical activity had on average a lower CCI 90 days postoperatively than sedentary participants (odds ratio 0.63, 95% CI 0.43–0.92). Similar patterns were shown for complications during hospital stay and within 30 days. There were trends towards lower risk for several types of complications, reoperations and length of hospital stay but the only difference shown was for respiratory insufficiency. Conclusion: Physically active participants experienced fewer postoperative complications, which suggests the information has a potential prognostic value. The work for increasing physical activity in the general population should continue.

© 2021 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

1. Introduction

Physical activity has several positive health effects, including reduced risk for cardiovascular disease, diabetes mellitus, mental health issues, and several types of cancer, including colorectal cancer [1]. Curative treatment for colorectal cancer includes surgery, with high risk for postoperative complications and morbidity [2], which has led to the development of programs where perioperative measures aimed at enhancing recovery are collected [3]. Preoperative physical activity has been identified as a possible modifiable risk factor for postoperative complications and recovery after colorectal cancer surgery. This has led to several studies where preoperative exercise interventions before colorectal cancer surgery have been tested [4–6], and to recommendations on such interventions [3]. However, results in interventional studies have varied from halved risk for postoperative complications [4] to no effect [5,6]. A non-modifiable risk factor is habitual physical activity. Underlying studies exploring the association between habitual physical activity and postoperative recovery would be of value to create evidence to support advice to the public. There are some
reports in the literature indicating a positive effect of habitual physical activity before colorectal cancer surgery [7–12], but the effect size and effects on specific types of complications remain uncertain.

We have recently reported the main results from PHYSSURG-C, a randomized controlled trial where the effect of short-term preoperative exercise intervention on postoperative recovery after colorectal cancer surgery was studied [6]. We did not find any differences in postoperative recovery depending on preoperative intervention or not. In order to further define the possibilities of preoperative physical activity, we aimed to examine the average effect of preoperative level of leisure time physical activity on postoperative complications and recovery after colorectal cancer surgery in an observational analysis within this randomized controlled trial.

2. Materials and methods

This manuscript reports results from an observational cohort analysis on data from the randomized controlled trial PHYSSURG-C. Methods for PHYSSURG-C have been described in detail previously [13], and results have been reported on both primary outcome [6] and a subgroup analysis [14]. The analyses performed for the current manuscript were not part of the original design of the study and are explorative. Ethical permission was obtained from the Regional Ethics Board in Gothenburg (2014-10-30, DNR:597–14). The study protocol has been published and is also available at www.sssorg.net. The study was registered at ClinicalTrials.gov with trial registration number NCT02299596, date of first registry was November 17, 2014.

2.1. Participants and setting

Study participants were recruited at six hospitals in Sweden including both county and university hospitals, from January 22nd 2015 until June 28th 2020. Individuals ≥20 years old scheduled for elective curative surgery due to colorectal cancer were eligible. Exclusion criteria included inability to perform study-specific procedures, inability to understand given information, emergency surgery, local excision (e.g., transanal endoscopic microsurgery), and cytoreductive surgery with subsequent hyperthermic intra-peritoneal chemotherapy. For the main purpose of the study, participants were randomized to intervention with home-based prehabilitation trials. The de

2.2. Variables and data sources

2.2.1. Exposure

At inclusion in the study, approximately two weeks before surgery, participants were asked to complete a baseline questionnaire on important demographic variables. This included the Saltin-Grimby physical activity level scale [15], a single item instrument where participants report their level of leisure time physical activity on a four-grade scale. The instrument has been validated for reproducibility and concurrent validity [15] It has been reported to predict several aspects of morbidity and mortality [15], and has been used previously for colorectal cancer patients [9,10]. In PHYSSURG-C, participants were asked to report their level of leisure time physical activity during the preceding week. This variable was used as exposure in the analyses described in this manuscript. As previously described [9,10,16,17], regular physical activity and regular hard physical training were combined due to low number of participants reporting regular hard physical training. The answering alternatives were:

- Level 1: Sedentary leisure time. Reading, TV watching, movies, using computers or doing other sedentary activities during leisure time.
- Level 2: Some physical activity during at least 4 h/week. Walking, riding bicycle, or other physical activity for at least 4 h per week. This includes riding a bicycle or walking to work, Sunday walks, gardening, fishing, table tennis, bowling, etc.
- Level 3: Regular physical activity and training 2–3 h per week. Running, swimming, calisthenics, tennis, badminton and similar activities. Heavy gardening and similar is included here. Please note that it must reach an average of at least 2–3 h per week.
- Level 4: Regular hard physical training or competition sports. Hard physical training or competition in running, orienteering, skiing, swimming, soccer, European handball, etc. regularly or several times per week.

2.2.2. Outcomes

The primary outcome measure in this manuscript was postoperative complications 90 days postoperatively, measured with the comprehensive complication index (CCI) [18]. This is a scale 0–100 derived from the Clavien-Dindo classification of surgical complications [19]. The scale is used as a continuous variable in all analyses. Information on postoperative complications was collected from medical charts by a single investigator blinded in terms of exposure, as previously described in detail [6]. Postoperative complications were chosen as primary outcome measure in these analyses instead of self-assessed physical recovery due to the general interest in including measures of postoperative complications in prehabilitation trials. The definitions for postoperative complications can be seen in the supplementary material. Secondary outcome measures were:

- Postoperative complications during index hospital stay and 30 days postoperatively, measured with comprehensive complication index.
- Complications up to 90 days postoperatively: cardiovascular events, respiratory insufficiency, pneumonia, infection, surgical leakage, and nausea (including paralytic ileus and small bowel obstruction). Information from medical charts.
- Total length of hospital stay during 90 days postoperatively, information from medical charts. Measured in days.
- Risk for re-operation during 90 days postoperatively, information from medical charts. Definitions described in detail previously [6].
- Self-assessed physical recovery four weeks postoperatively. Participants categorized themselves as not recovered at all, recovered to 25%, 50%, 75%, or completely recovered. Described in detail previously [6].

2.2.3. Confounders

Since these analyses are observational, bias could occur due to confounding. To minimize the risk for confounding all analyses were adjusted for variables deemed to be possible confounders. These were included in a directed acyclic graph (DAG) and were decided upon before any analyses were performed. In the statistical models, we included the following confounders:
leisure time physical activity) as a physical activity (OR 0.60, 95% CI 0.36–0.43) or no physical activity (OR 0.63, 95% confidence interval (CI) 0.43–0.92) (Fig. 2). This was also the case for those with regular physical activity (OR 0.60, 95% CI 0.36–0.99). Similar results were seen for complications during index hospital stay and 30 days postoperatively. There were no apparent differences between participants who were regularly physically active and those who performed some physical activity in terms of postoperative complications in our analyses.

The analyses of specific types of postoperative complications showed a lower risk for experiencing a postoperative respiratory insufficiency for regularly active than for sedentary participants (OR 0.40, 95% CI 0.18–0.87). Our analyses did not reveal any statistically significant differences between the groups for other outcomes. There were however trends for dose-response relationships for cardio-logic complications with 8.4%, 5.6%, and 2.1% of participants in the three groups experiencing a cardio-logic complication. A similar trend was seen regarding need for intensive care (grade IVa & IVb) with 11.8%, 6.2%, and 4.5% in the three groups (data not shown). There seemed to be no dose-response trends for nausea & vomiting, surgical leakage, or infections. There were no statistically significant differences between the groups for length of hospital stay, reoperations, or self-assessed physical recovery, although the point estimates for all these outcomes showed trends towards positive associations. For unadjusted results, see supplementary table.

4. Discussion

This study found that patients who had regular physical activity on average had a lower risk for postoperative complications after colorectal cancer surgery than sedentary patients.

There are few previous studies on the association between baseline physical activity and postoperative complications and recovery after colorectal cancer surgery, as shown by a systematic review [7]. Dronkers et al. reported that physical activity was associated with lower levels of in-hospital mortality, discharge destination and length of hospital stay in 169 patients with colorectal cancer [8]. They did not examine the association with postoperative complications. You et al. performed a propensity score observational study with 4632 individuals with colorectal cancer in Taiwan [11]. Participants were categorized as performing <12 metabolic equivalents (MET) or ≥12 MET. Unfortunately, they did not include information on how physical activity was measured, and did not assess postoperative morbidity using any validated instrument, which reduces validity and hinders interpretation of the results. They reported that participants with MET ≥12 had lower risk for overall complications, but that this could not be explained by differences in any specific type of complications. Whelan et al. recently reported results from a study on 125 patients with colorectal cancer in South Africa [12]. They reported an association between baseline physical activity and length of hospital stay, but not postoperative complications. In summary, the only previous report of the association between habitual physical activity and postoperative complications where a validated instrument for measuring complications is our previous report from a similar but considerably smaller cohort.

We have previously found in a study with 115 patients that participants with regular physical activity were more than 3 times as old as the other two groups.

Participants who were not included due to missing information on baseline level of leisure time physical activity were similar to those reporting level of physical activity in terms of age, sex, BMI, and had similar tumor and surgical characteristics.
more likely to feel highly physically recovered three weeks postoperatively than sedentary participants, and that sedentary participants had a CCI 12 points higher than participants with some physical activity and 17 points higher than participants with regular physical activity [9,10]. The effect sizes seen in our previous study could not be confirmed by the present study, where the differences between the groups were smaller. The overall level of postoperative complications was also higher in the present study, which is probably explained by a more rigorous collection of information of postoperative complications. Interestingly, the difference between the groups in terms of absolute burden of postoperative complications is the same between the two studies. Since CCI is the result of a squared root function, a decrease from CCI 32 to CCI 24 corresponds to a decrease by a single grade II complication. The difference between the groups of exposure in the present study could perhaps be explained somewhat by the randomized intervention as 50% did exercise more than usual, but we found no average efficacy and it had no influence on the results as reported by the supplementary analysis (data not shown). This should reduce the risk for the intervention masking actual associations between baseline physical activity and postoperative complications and recovery.

There are several intervention studies on the effect of preoperative exercise interventions before colorectal cancer surgery. These have reported mixed results, with two recent trials reporting no effects on postoperative complications or other clinically relevant outcomes [5,6]. However, a previous trial including six weeks of high intensity training in before major abdominal surgery reported impressive results with a 50% decrease in postoperative complications [4]. Interestingly, they also reported effect mainly on medical complications such as cardiovascular complications and respiratory complications, while there was no effect on surgical complications except for paralytic ileus. This is in line with the results from our present study where physical activity was associated with a lower risk for cardiologic complications and respiratory insufficiency, but not surgical complications. We also saw a trend towards more ICU care in sedentary patients, possible driven by more medical than surgical complications. This information could be used when planning future interventional studies. It would be more rational to aim these at improving rate of cardiovascular and respiratory complications, and possibly the need for ICU than the combined burden of postoperative complications, as there are many other factors influencing surgical complications. Also, these results can be used to calculate risk for medical complications, which may influence the shared decision-making prior surgery.

This study has several limitations. The most important being that it is an ad hoc observational analysis within an RCT. This must be kept in mind when interpreting the results. However, the method of performing observational studies on associations between physical activity or functional capacity and postoperative outcomes within an RCT has been done before. Gillis et al. performed an observational analysis of frail participants with colorectal cancer who had low functional capacity at the time of surgery [23]. They reported that participants with low functional capacity at the time of surgery were more likely to suffer postoperative complications. Meyerhardt et al. performed a similar observational study within a randomized controlled adjuvant chemotherapy trial [24]. They reported that physical activity six months after completion of therapy was associated with approximately a 50% reduction in cancer recurrence or death from any cause. Performing observational analyses within randomized trials has both pros and cons. Participants are generally followed up in detail. However, the intervention introduces a possible confounding. Since we have reported previously that groups were balanced for the intervention, and that the intervention had no significant effect on the outcomes reported in the present manuscript we believe that randomization should cause no serious bias in the present study. Another limitation in this study is that it is observational, which makes it harder to claim causality. This is even more true in the case of habitual physical activity usually a long habit where it is hard to conclude the effect

| 1870 patients assessed for eligibility | 1109 ineligible |
|--------------------------------------|------------------|
| 93 excluded from study               | • 405 declined participation |
| 45 withdrew consent                   | • 329 too short waiting time |
| 6 surgery cancelled                   | • 36 cannot perform intervention |
| 2 emergency surgery                   | • 83 no physiotherapist |
| 6 no colorectal cancer                | • 34 no nurse |
| 9 logistical issues                   | • 55 not informed about study |
| 8 can’t perform intervention          | • 77 language/cognitive barriers |
| 17 other                              | • 90 other |
| 761 enrolled                          | 668 included in primary analysis |
| 614 included in this observational cohort | 54 no information on baseline leisure time physical activity |
| 107 sedentary                         | 410 some physical activity |
| 97 Regular physical activity          | |
| Characteristic | Overall, N = 614 | Sedentary, N = 107 | Some physical activity, N = 410 | Regular physical activity, N = 97 |
|---------------|-----------------|-------------------|-------------------------------|---------------------------------|
| Age, Mean (SD)| 68 (11)         | 68 (13)           | 69 (11)                       | 65 (11)                         |
| BMI, Mean (SD)| 25.8 (4.5)      | 27.2 (5.4)        | 25.7 (4.0)                    | 24.4 (4.6)                      |
| Unknown       | 11              | 4                 | 7                             | 0                               |
| Sex, n/N (%)  |                 |                   |                               |                                 |
| Female        | 250/614 (41%)   | 44/107 (41%)      | 176/410 (43%)                 | 30/97 (31%)                     |
| Sense of coherence, n/N (%) |              |                   |                               |                                 |
| <120          | 17/536 (3.2%)   | 8/94 (8.5%)       | 6/360 (1.7%)                  | 3/82 (3.7%)                     |
| 120–140       | 81/536 (15%)    | 22/94 (23%)       | 54/360 (15%)                  | 5/82 (6.1%)                     |
| >140          | 438/536 (82%)   | 64/94 (68%)       | 300/360 (83%)                 | 74/82 (90%)                     |
| Unknown       | 78              | 13                | 50                            | 15                              |
| Marital status, n/N (%) |             |                   |                               |                                 |
| Married or cohabiting | 457/607 (75%) | 72/106 (68%)     | 307/404 (76%)                 | 78/97 (80%)                     |
| Single household | 150/607 (25%) | 34/106 (32%)     | 97/404 (24%)                  | 19/97 (20%)                     |
| Unknown       | 7               | 1                 | 6                             | 0                               |
| Ethnicity, n/N (%) |             |                   |                               |                                 |
| Born abroad   | 85/607 (14%)    | 20/106 (19%)      | 46/404 (11%)                  | 19/97 (20%)                     |
| Education, n/N (%) |             |                   |                               |                                 |
| Compulsory school | 122/603 (20%) | 26/105 (25%)     | 84/403 (21%)                  | 12/95 (13%)                     |
| Gymnasium     | 266/603 (44%)   | 41/105 (39%)      | 181/403 (45%)                 | 44/95 (46%)                     |
| University    | 215/603 (36%)   | 38/105 (36%)      | 138/403 (34%)                 | 39/95 (41%)                     |
| Unknown       | 11              | 2                 | 7                             | 2                               |
| Occupation, n/N (%) |             |                   |                               |                                 |
| Retired       | 376/605 (62%)   | 66/103 (64%)      | 262/406 (65%)                 | 48/96 (50%)                     |
| Sick/leave/unemployed | 49/605 (8.1%) | 10/103 (9.7%)    | 30/406 (7.4%)                 | 9/96 (9.4%)                     |
| Working       | 180/605 (30%)   | 27/103 (26%)      | 114/406 (28%)                 | 39/96 (41%)                     |
| Smoking, n/N (%) |             |                   |                               |                                 |
| Active regular smoker | 18/606 (3.0%) | 1/105 (1.0%)     | 13/404 (3.2%)                 | 4/97 (4.1%)                     |
| Unknown       | 8               | 2                 | 6                             | 0                               |
| Alcohol, n/N (%) |             |                   |                               |                                 |
| Risk drinking | 86/513 (17%)    | 18/91 (20%)       | 55/342 (16%)                  | 13/80 (16%)                     |
| Unknown       | 101             | 16                | 68                            | 17                              |
| ASA classification, n/N (%) |       |                   |                               |                                 |
| 1             | 102/558 (18%)   | 16/100 (16%)      | 62/367 (17%)                  | 24/91 (26%)                     |
| 2             | 346/558 (62%)   | 49/100 (49%)      | 241/367 (66%)                 | 56/91 (62%)                     |
| 3             | 107/558 (19%)   | 34/100 (34%)      | 62/367 (17%)                  | 11/91 (12%)                     |
| 4             | 3/558 (0.5%)    | 1/100 (1.0%)      | 2/367 (0.5%)                  | 0/91 (0%)                       |
| Unknown       | 56              | 7                 | 43                            | 6                               |
| Cardiovascular disease, n/N (%) |       |                   |                               |                                 |
| Diabetic Mellitus, n/N (%) |       |                   |                               |                                 |
| Pulmonary disease, n/N (%) |       |                   |                               |                                 |
| Neurologic disease, n/N (%) |       |                   |                               |                                 |
| Unknown       | 8               | 3                 | 5                             | 0                               |
| Psychiatric disease, n/N (%) |       |                   |                               |                                 |
| Other disease, n/N (%) |       |                   |                               |                                 |
| Preoperative Hb, Mean (SD) |       |                   |                               |                                 |
| Preoperative Albumin, Mean (SD) |     |                   |                               |                                 |
| Tumor stage, n/N (%) |       |                   |                               |                                 |
| Type of surgery, n/N (%) |       |                   |                               |                                 |
| Colon resection | 264/539 (40%) | 51/95 (54%)      | 177/352 (50%)                 | 36/92 (39%)                     |
| Lower anterior resection | 161/539 (30%) | 26/95 (27%)      | 100/352 (28%)                 | 35/92 (38%)                     |
| Rectum amputation | 114/539 (21%) | 18/95 (19%)      | 75/352 (21%)                  | 21/92 (23%)                     |
| Tumor site, n/N (%) |       |                   |                               |                                 |
| Colon         | 313/614 (51%)   | 59/107 (55%)      | 218/410 (53%)                 | 36/97 (37%)                     |
| Rectum        | 301/614 (49%)   | 48/107 (45%)      | 192/410 (47%)                 | 61/97 (63%)                     |
| Open/Laparoscopic, n/N (%) |       |                   |                               |                                 |
| Neoadjuvant therapy, n/N (%) |       |                   |                               |                                 |
| No            | 399/602 (66%)   | 75/106 (71%)      | 270/400 (68%)                 | 54/96 (56%)                     |
| Preoperative chemoradiotherapy | 56/602 (9.3%) | 10/106 (9.4%)    | 32/400 (8.0%)                 | 14/96 (15%)                     |
| Preoperative isolated radiotherapy | 147/602 (24%) | 21/106 (20%)     | 98/400 (24%)                  | 28/96 (29%)                     |
of short-term changes without performing interventional studies. Hence, these results should not be used for recommending preoperative exercise for colorectal cancer patients, but to guide policy makers developing recommendations and strategies for achieving a more physically active general population.

This study also has several strengths. One is the large sample size in combination with prospectively collected data, improving statistical power and enabling analysis of different types of complications. Another is the use of validated and well recognized instruments for both physical activity and postoperative complications increasing the possibility to compare results with future studies. Collection of information on outcome measures in a structured way by a researcher blinded regarding exposure further increases validity.

5. Conclusions

Participants who engaged in preoperative leisure time physical activity had on average fewer and less severe postoperative complications after colorectal cancer surgery compared with patients with a sedentary life-style. Information about an individual’s physical activity at baseline could be included into the considerations of possible treatment choices preoperatively. As yet another argument in the ongoing public efforts to achieve a physically active population, BMI was lower with increasing level of physical activity, but smoking and risk drinking behavior was equally distributed between the groups. Cardiovascular disease and diabetes mellitus decreased with increasing level of physical activity.

Role of the funding source

This study was funded by grants from AFA Insurance (150072), the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (ALFGBC-718221, ALFGBC-4307771, ALFGBC-493341, & ALFGBC-784821), the Swedish Cancer Society (CAN 2016/519; 2019/19030), Assar Gabrielsson’s foundation (FB19-07 & FB 16-95), Anna-Lisa and Bror Björnsson’s foundation, Dr. Felix Neubergh’s Foundation (2017-347), Gothenburg Medical Society (GLS-688001, GLS-778731, & GLS-883991), Lions cancer fund west (2019:6), Mary von Sydow’s foundation (1216), the Swedish Society of Medicine (SLS-499811), and the healthcare committee Region Västra Götaland (Hälsos-och sjukvårdsstyrelsen) (VGRFOUREG-309261, VGRFOUREG-659011, VGRFOUREG-837542, VGRFOUREG-739191). The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data statement

Individual participant data that underlie the results reported in this article, after de-identification (text, tables, figures, and appendices), as well as study protocol, statistical analysis plan, and analytic code will be shared with investigators whose proposed use of the data has been approved by an independent review committee (“learned intermediary”) identified for this purpose, and after assuring that this data-sharing complies with ethical
permissions. Data may be used for individual participant data meta-analysis. Data sharing proposals should be sent to the corresponding author.

Declaration of competing interest

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: EA and DB declare no support from any organization for the submitted work: AO reports grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement, grants from Assar Gabrielsson’s foundation, grants from Anna-Lisa and Bror Björnsson’s foundation, grants from Dr Felix Neubergh’s foundation, grants from Gothenburg medical society, grants from Lions cancer fund west during the conduct of the study: EH reports grants from AFA insurance and grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement, and grants from The Swedish Cancer Society during the conduct of the study: AO, EA, and DB declare no financial relationships with any organization that might have an interest in the submitted work in the previous three years: EH reports grants from Mary von Sydow Foundation, grants from the Swedish Research Council, and grants from Göteborg Medical Society outside the submitted work: all authors report no other relationships or activities that could appear to have influenced the submitted work. All authors confirm that they had full access to all the data in the study and accept responsibility to submit for publication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2021.10.033.

Credit author statement

Aron Onerup: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing. Eva Angenete: Conceptualization, Investigation, Methodology, Supervision, Writing – review & editing. David Bock: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – review & editing. Eva Haglind: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

References

[1] Bull FC, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med 2020;54:1451–62. https://doi.org/10.1136/bjsports-2020-102955.
[2] Kennedy RH, et al. Multicenter randomized controlled trial of conventional versus laparoscopic surgery for colorectal cancer within an enhanced recovery programme: EnRCL. J Clin Oncol 2014;32:1804–11. https://doi.org/10.1200/JCO.2013.45.3694.
[3] Gustafsson UO, et al. Guidelines for perioperative care in elective colorectal surgery: enhanced recovery after surgery (ERAS®(R)) society recommendations: 2018. World J Surg 2019;43:659–95. https://doi.org/10.1007/s00268-018-4844-y.
[4] Barberan-Garcia A, et al. Personalised prehabilitation in high-risk patients undergoing elective major abdominal surgery: a randomized blinded controlled trial. Ann Surg 2018;267:50–6. https://doi.org/10.1097/SLA.0000000000002293.
[5] Carl F, et al. Effect of multimodal prehabilitation vs postoperative rehabilitation on 30-day postoperative complications for frail patients undergoing resection of colorectal cancer: a randomized clinical trial. JAMA Surg 2020. https://doi.org/10.1001/jamasurg.2019.5474.
[6] Onerup A, et al. Effect of short-term homebased pre- and postoperative exercise on recovery after colorectal cancer surgery (PHYSSURG-C): a randomized clinical trial. Ann Surg 2021. https://doi.org/10.1097/SLA.0000000000004091.
[7] Steffens D, et al. Is preoperative physical activity level of patients undergoing cancer surgery associated with postoperative outcomes? A systematic review and meta-analysis. Eur J Surg Oncol 2019;45:510–8. https://doi.org/10.1016/j.ejso.2018.10.063.
[8] Dronkers JF, et al. The association of pre-operative physical fitness and physical activity with outcome after scheduled major abdominal surgery. Anesthesiology 2013;66:67–73. https://doi.org/10.1111/ane.12066.
[9] Onerup A, et al. Is preoperative physical activity related to post-surgery recovery?-a cohort study of colorectal cancer patients. Int J Colorectal Dis 2016;31:1311–40. https://doi.org/10.1007/s00384-016-2551-4.
[10] Onerup A, et al. Self-assessed preoperative level of habitual physical activity predicted postoperative complications after colorectal cancer surgery: a prospective observational cohort study. Eur J Surg Oncol 2019;45:2045–51. https://doi.org/10.1016/j.ejso.2019.06.019.
[11] You JF, et al. Association of a preoperative leisure-time physical activity with short- and long-term outcomes of patients undergoing curative resection for stage I to III colorectal cancer: a propensity score matching analysis. Dis Colon Rectum 2020;63:796–806. https://doi.org/10.1097/DCR.0000000000001653.
[12] Whelan M, et al. Preoperative physical activity and functional performance levels are predictors of acute postoperative outcomes in a private South African colorectal cancer cohort. S Afr J Physiother 2021;77. https://doi.org/10.4102/sajp.v77i1.1526.
[13] Onerup A, et al. The effect of pre- and post-operative physical activity on recovery after colorectal cancer surgery (PHYSSURG-C): study protocol for a randomised controlled trial. Trials 2017;18:212. https://doi.org/10.1186/s13063-017-1945-5.
[14] Onerup A, et al. Effects of a home-based exercise program on the insulin-like growth factor axis in patients operated for colorectal cancer in Sweden: results from the randomised controlled trial PHYSSURG-C. Growth Hormone IGF Res 2020;51:27–33. https://doi.org/10.1016/j.yghr.2020.01.005.
[15] Grimby G, et al. "Saltin-Grimby physical activity level scale" and its application to health research. Scand J Med Sci Sports 2015;25(Suppl 4):119–25. https://doi.org/10.1111/sms.12611.
[16] Onerup A, et al. The preoperative level of physical activity is associated to the postoperative recovery after elective cholecystectomy - a cohort study. Int J Surg 2015;19:35–41. https://doi.org/10.1016/j.ijsu.2015.05.023.
[17] Nilsson H, et al. Is preoperative physical activity related to post-surgery recovery? A cohort study of patients with breast cancer. BMJ Open 2016;6:e007997. https://doi.org/10.1136/bmjopen-2015-007997.
[18] Slankamenac K, et al. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. Ann Surg 2013;258:1–7. https://doi.org/10.1097/SLA.0b013e318296c732.
[19] Clavien PA, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187–96. https://doi.org/10.1097/SLA.0b013e3181b13a2.
[20] Bush K, et al. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. Arch Intern Med 1998;158:1799–95.
[21] Harrell JF. Regression modeling strategies : with applications to linear models, logistic and ordinal regression, and survival analysis. Imprint: Springer. In: Springer series in statistics. City: Springer International Publishing; 2015. p. 1. online resource (XXV, 582 pages 157 illustrations, 53 illustrations in color.
[22] Rubin DB. Statistical matching using file concatenation with adjusted weights and multiple imputations. J Bus Econ Stat 1986;4:87–94.
[23] Gilis C, et al. Older frail prehabilitated patients who cannot attain a 400 m 6-min walking distance before colorectal surgery suffer more postoperative complications. Eur J Surg Oncol 2020. https://doi.org/10.1016/j.ejso.2020.09.041.
[24] Meyerhardt JA, et al. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. J Clin Oncol 2006;24:3535–41. https://doi.org/10.1200/JCO.2006.06.0863.