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Self-assessed preoperative level of habitual physical activity predicted postoperative complications after colorectal cancer surgery: A prospective observational cohort study

Aron Onerup [a, b, *], Eva Angenete [a, c], Pierre Bonfre [a], Mats Börjesson [d, e, f], Eva Haglind [a, c], Catrin Wessman [a, g], Hanna Nilsson [a, c]

[a] Scandinavian Surgical Outcomes Research Group (SSORG), Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, 416 85, Gothenburg, Sweden
[b] Region Västra Götaland, Sahlgrenska University Hospital, Department of Pediatric Oncology, 416 85, Gothenburg, Sweden
[c] Region Västra Götaland, Sahlgrenska University Hospital, Department of Surgery, 416 85, Gothenburg, Sweden
[d] Department of Physiology, Institute of Neuroscience and Physiology, Sahlgrenska Academy, Gothenburg University, 405 30, Gothenburg, Sweden
[e] Center for Health and Performance, Institute of Food, Nutrition, and Sports Science, University of Gothenburg, 405 30, Gothenburg, Sweden
[f] Region Västra Götaland, Sahlgrenska University Hospital, Department of Medicine, Geriatrics, and Emergency Medicine, 416 85, Gothenburg, Sweden
[g] Health Metrics Unit, The Sahlgrenska Academy, University of Gothenburg, Sweden

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ABSTRACT

Introduction: There is a growing interest in physical activity in relation to recovery after surgery. One important aspect of measuring recovery after surgical procedures is postoperative complications. The aim of this study was to determine if there is an association between the preoperative level of habitual physical activity and postoperative complications in patients undergoing elective surgery for colorectal cancer.

Materials and methods: 115 patients scheduled for elective surgery due to colorectal cancer between February 2014 and September 2015 answered a questionnaire regarding physical activity and other baseline variables. Physical activity was assessed using the Saltin-Grimby physical activity level scale. Complications within 30 days after surgery were classified according to Clavien-Dindo, and the Comprehensive Complications Index (CCI) was calculated. Primary outcome was difference in CCI and key secondary outcome was risk for CCI $\geq$20.

Results: Physically inactive individuals had a CCI that was 12 points higher than individuals with light activity ($p = 0.002$) and 17 points higher than regularly active individuals ($p = 0.0004$). Inactive individuals had a relative risk for a CCI $\geq$20 that was 65% higher than for individuals reporting light activity (95% confidence interval (CI) for relative risk (RR) = 1.1–2.5) and 338% higher than for regularly active individuals (95% CI for RR = 2.1–9.4).

Conclusion: Self-assessed level of habitual physical activity before colorectal cancer surgery was associated with fewer postoperative complications measured with CCI, in a dose-response relationship.

Introduction

In order to enhance recovery and minimise complications after major surgery, several interventions for the benefit of both patient and society have been suggested and implemented to various extents. Enhanced Recovery After Surgery (ERAS) offers a standardised, evidence-based protocol including the implementation of more than 20 items before, during and after surgery [1,2]. Adherence to this protocol has been reported to reduce both the

Abbreviations: ASA, American Society of Anesthesiologists; AUDIT, Alcohol use disorders identification test; BMI, Body mass index; CCI, Comprehensive complications index; CI, Confidence interval; ERAS, Enhanced recovery after surgery; RR, Relative risk; TNM, Tumour, node, metastasis.

* Corresponding author. Scandinavian Surgical Outcomes Research Group (SSORG), Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, 416 85, Gothenburg, Sweden.
E-mail address: aron.onerup@gu.se (A. Onerup).

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length of hospital stay and postoperative morbidity [3–5]. According to current ERAS recommendations there is not enough evidence for recommending physical activity before colon or rectal surgery [1,2].

There is a growing body of evidence that preoperative lifestyle interventions may improve postoperative recovery. Smoking cessation and advice regarding reduction of alcohol consumption before surgery are part of standard preoperative routines, with the intention of decreasing the risk for complications [1,2,6,7]. Several studies have been performed to assess the effect of preoperative physical activity interventions (prehabilitation) before colorectal cancer surgery [8–10], with two recently published studies showing promising results on postoperative complications in risk patients [9,10]. Given the fact that cancer treatment must be performed in a timely manner, and many countries have introduced standardised waiting targets for cancer surgery, there is a potential conflict between these and preoperative optimisation [11]. In a recent systematic review, Hangaard Hansen et al. found no evidence for an association between delayed treatment and overall survival after colon cancer [12]. Due to the conflict between the ambition to shorten lead times to surgery, and the time it takes to achieve a meaningful optimisation of the patient by prehabilitation, it would be of interest to know the association between habitual physical activity and postoperative complications after colorectal cancer surgery. We have previously performed four observational cohort studies with the aim to assess the association between habitual physical activity and the recovery after four different types of surgery, including colorectal cancer surgery [13–16].

With the aim to examine the relationship between self-assessed habitual physical activity and postoperative complications, we have performed additional data collection for the previously published cohort of colorectal cancer patients [15].

Methods

Patients undergoing elective colorectal cancer surgery at one university hospital and one regional hospital, situated in Region Västra Götaland, Sweden, were asked to participate in the study. The time of inclusion was February 2014 to September 2015. Exclusion criteria were lack of informed consent, difficulties to communicate due to language barriers and postponed or cancelled surgery. The methods have been described in detail before [15].

Baseline demographic variables

Participating patients answered a preoperative questionnaire containing questions on demographics, including age, body mass index (BMI), alcohol consumption, smoking habits, and comorbidities (diabetes mellitus, hypertension and/or hyperlipidaemia). The timing of inclusion in the study was at the preoperative visit, which usually took place around 1 week preoperatively during the inclusion period. Smoking habits were measured with one single question, and the answers were dichotomised into non-smoker or current smoker. Alcohol consumption was evaluated with a modified AUDIT-C scale adopted from Steineck et al. [14,15,17]. The answer to each question resulted in a score, and the combined score from all three questions was used to define risk drinking, with a value of at least 3 or 4 points for women and men, respectively. Depression was assessed by one question with the possible answers “yes”, “no” and “I don't know” [18]. Information on physical status and tumour stage were retrieved from the patients' medical charts. The physical status of each patient was classified according to the American Society of Anesthesiologists (ASA) Physical status classifications [19], and this was dichotomised into ASA 1–2 or 3–4 in our analyses. Tumour stage was classified in accordance with the American Joint Committee on Cancer TNM system [20]. In our analyses, stage was categorised into three groups: adenoma/stage 0–2, stage 3, or stage 4.

Assessment of habitual physical activity

The patients' level of habitual physical activity was assessed using the self-reported four-level Saltin-Grimby Physical Activity Level Scale [21]: This scale has been used in more than 500 000 patients in clinical studies [22] and it has been shown to correlate to objective measures of activity, cardiovascular risk factors, morbidity and mortality [23–25]. The patient assessed his/her level of habitual physical activity by answering the following question: “How much do you move and exert yourself physically during leisure time on average?” The answering categories were in four levels, as follows:

1. Physically inactive: Being almost completely inactive, reading, watching television, watching movies, using computers or doing other sedentary activities during leisure-time.
2. Some light physical activity: Being physically active for at least 4 h per week i.e. riding a bicycle or walking to work, walking with the family, gardening, fishing, table tennis, bowling etc.
3. Regular physical activity and training: Spending time on heavy gardening, running, swimming, playing tennis, badminton, calisthenics and similar activities, for at least 2–3 h per week.
4. Regular hard physical training for competition sports: Spending time in running, orienteering, skiing, swimming, soccer, European handball etc. several times per week.

The patients who assessed themselves as performing regular hard physical training in group 4 were merged with patients who assessed themselves as belonging to group 3 in the analyses.

Postoperative complications

Information regarding complications within 30 days of surgery was retrieved from the medical charts. The postoperative complications were classified according to the Clavien-Dindo system [26,27], and a Comprehensive Complication Index (CCI) was calculated [28,29]. The CCI is an expansion of the Clavien-Dindo classification and considers not only the severity of a single complication, but incorporates all postoperative complications, including their relative severity [29]. The index is a linear scale ranging from 0 (no complication) to 100 (death). CCI above 20 has been used as a cut-off between no or minor complications, and clinically relevant complications [30], hence we used this cut-off point in one of our analyses to dichotomise the outcome into two groups. The definitions of types of complications (see below) were determined beforehand. Regarding nausea, this was defined as postoperative vomiting. Pain was defined as receiving pain-relieving drugs on more than 4 occasions during 24 h, in addition to the basic pain relief planned before surgery.

Our outcome measures were (all within 30 days postoperatively):

- The primary outcome measure was defined as difference in CCI, measured as a continuous variable. Interaction effect with age was analysed.
- The key secondary outcome measure was a postoperative period with clinically significant complications, defined as CCI $\geq$20.
- Other secondary outcome measures were:

- Occurrence of the following types of complications: Infections, fistula/leakage, bleeding, nausea, cardiopulmonary complications, pain, allergic reactions, other complications.
- Total number of complications.
- Complications with a Clavien-Dindo grade ≥ IIIa.

Statistics

The sample size was estimated for the previously reported primary outcome, recovery after surgery [15]. All analyses performed for this additional data collection were prespecified in a statistical analysis plan. The analysis for the primary outcome measure consisted of a multiple regression model comparing the preoperative level of physical activity, measured with Saltin-Grimby Physical Activity Levels Scale, and the burden of postoperative complications, measured with CCI. In addition to habitual level of physical activity, variables that could potentially influence the risk for postoperative complications were prespecified. These were alcohol consumption, smoking, age, sex, marital status, depression, surgical technique (open or laparoscopic), tumour site (colon/rectum), use of preoperative radiotherapy, ASA classification, and tumour stage. The recommendation of Bursac [31] was used. The first step was bivariate analysis removing covariates with a p-value above 0.25. The second test was a multiple model with the remaining covariates. In this step we removed the co-variates which had a p-value above 0.10, but not those defined as confounders, i.e. changing the estimates more than 15%. In the third and final step we refitted the multiple model, adding the previously abolished covariates stepwise, keeping those with a p-value <0.15. We also analysed the interaction effect between level of physical activity and age in the final model.

The model-building procedure was reproduced using the dichotomised variable of CCI, where CCI was dichotomised into ≥20 or <20.

We performed Poisson-Regression for associations between level of physical activity and total number of complications, complications ≥ grade IIIa (yes/no), and for each category of complication (infection, cardiopulmonary, etc., defined as yes/no).

Ethical permission

Permission to conduct the study was obtained from the Regional Ethics Board in Gothenburg, Dnr 180-12. An additional permission was obtained for data collection of postoperative complications, Dnr T815-16. The protocol was registered at Clinicaltrials.gov NCT01707121.

Results

The flow chart for participants in this study is shown in Fig. 1. Baseline characteristics of the patients are seen in Table 1. Two thirds of the patients assessed themselves as lightly physically active during leisure time (level 2/4). A higher proportion of patients who were inactive were found to have pre-existing cardiovascular comorbidity (61%) compared to their peers with light activity (49%) and regular activity (35%). Eight percent of the patients were found to have no cancer in the pathological examination after surgery, only various types of adenoma. Since they had undergone colorectal surgery due to suspected cancer, and the final diagnosis given around 30 days postoperatively, i.e. after the time frame for postoperative complications in this study, they were included in the final analyses.

Seventy percent of all patients were found to have at least one postoperative complication, with 60% registered for grade I-II complications and ten percent registered for grade III-V complications (Table 2). Forty-six percent of all patients had a CCI≥20.

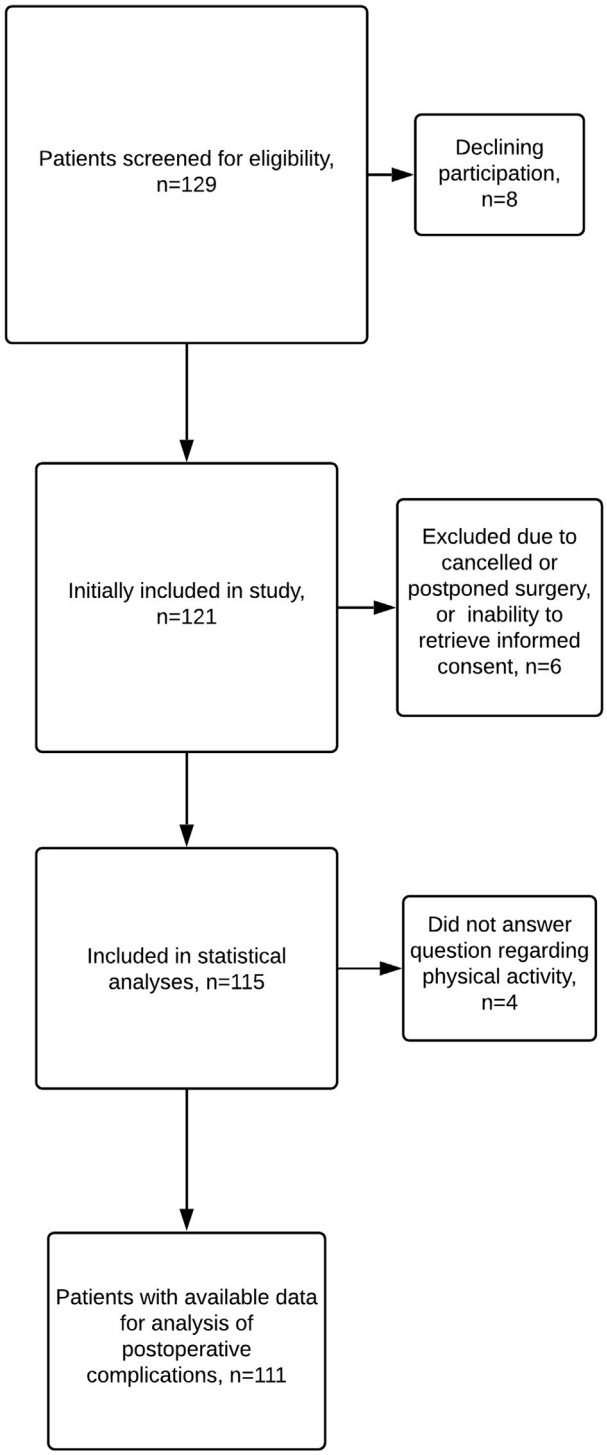

Fig. 1. Flow chart for inclusion of participants.

For our primary outcome measure, CCI as a continuous variable, we found that there was a significantly higher CCI for those who were physically inactive than those who were lightly or regularly active (Table 3). This difference increased with increased level of physical activity, with the largest difference between inactive and lightly active participants. There was no significant interaction between level of physical activity and age in the final model.

Table 1
Descriptive characteristics of patients divided into level of physical activity according to Saltin-Grimby physical activity level scale.

	Level of physical activity			
	Inactive (1), n = 18	Light activity (2), n = 76	Regular activity (3–4), n = 17	Total, n = 111
Age, median years (IQR)	74.5 (15)	71 (11)	67 (20)	
Sex, n (%)				
Female	9 (50)	37 (49)	4 (24)	50 (45)
Marital status, n (%)				
Married/cohabiting/live-apart	15 (83)	52 (68)	15 (88)	86 (77)
Not reported		2 (2.6)		2 (1.8)
Body Mass Index, median (IQR)	26.4 (9)	25.3 (4)	24.8 (8)	
Diabetes mellitus[a]**, n (%)**				
Yes	5 (28)	7 (9)	2 (12)	14 (13)
Hypertension[a]**, n (%)**				
Yes	8 (44)	28 (37)	5 (29)	41 (37)
Hyperlipidaemia[a]**, n (%)**				
Yes	3 (17)	9 (12)	4 (24)	16 (14)
ASA level[d]**, n (%)**				
1	0 (0)	18 (24)	6 (35)	24 (22)
2	15 (83)	50 (66)	10 (59)	75 (68)
3	3 (17)	8 (11)	1 (6)	12 (11)
Smoking[b]**, n (%)**				
Smoker	3 (17)	5 (7)		8 (7)
Alcohol intake[c]**, n (%)**				
Risk drinking	6 (33)	8 (11)	4 (24)	18 (16)
Depression, n (%)				
Yes	1 (6)	4 (5)	4 (24)	9 (8)
Not reported		4 (5)	1 (6)	6 (5)
Cancer site, n (%)				
Colon	13 (72)	34 (45)	9 (53)	56 (51)
Rectum	5 (28)	42 (55)	8 (47)	55 (50)
Laparoscopy/Laparotomy, n (%)				
Laparoscopy	8 (44)	29 (38)	11 (65)	48 (43)
Laparotomy	10 (56)	47 (62)	6 (35)	63 (57)
Type of surgery, n (%)				
Right hemicolectomy/Resection of sigmoid colon	10 (56)	23 (30)	7 (41)	40 (36)
Excision of rectum	3 (17)	20 (26)	4 (24)	27 (24)
Left hemicolectomy/Total colectomy/Partial proctectomy	5 (28)	30 (40)	6 (35)	41 (37)
Other		3 (4)		3 (3)
Stage[e]**, n (%)**				
Adenoma (no cancer)	1 (6)	6 (8)	2 (12)	9 (8)
0	0 (0)	2 (3)	0 (0)	2 (2)
I	5 (28)	16 (21)	6 (35)	27 (24)
II	7 (39)	18 (24)	5 (29)	30 (27)
III	4 (22)	26 (34)	1 (6)	31 (28)
IV	1 (6)	8 (11)	3 (18)	12 (11)
Preop radiotherapy, n (%)				
Yes	4 (22)	27 (36)	6 (35)	37 (33)

IQR=Interquartile range.
[a] As reported by patient.
[b] Defined as all forms of current smoking.
[c] For definition, see “methods”.
[d] According to the American Society of Anesthesiologists (ASA) Physical status classifications.
[e] Stage according to the American Joint Committee on Cancer (AJCC) TNM system.

The key secondary outcome measure, risk for CCI≥20, showed a similar pattern (Table 3), with a 60% increased risk for inactive patients compared to their lightly active peers, and a 4.4 times higher relative risk for clinically relevant postoperative complications in the inactive patients, compared to the regularly active patients. The other secondary outcome measures, types of complications, grade of highest complications and total number of complications (Table 2), showed no statistically significant differences (data not shown).

Discussion

In this prospective observational cohort study, we found that the self-assessed preoperative level of habitual physical activity predicted the risk for complications after colorectal cancer surgery.

In a recent systematic review of cancer surgery, there was no significant association between level of physical activity and postoperative complications [32]. In this review, postoperative complications were classified as existing or not, or according to Clavien-Dindo. To our knowledge, we present the first study to assess the association between preoperative level of physical activity and postoperative complications measured with the comprehensive complications index, based on the Clavien-Dindo classification. This is considered a more sensitive measure than using the Clavien-Dindo classification itself [33], and may in part explain why we found a significant association between physical activity and postoperative complications, which was not found in the review.

Regarding the types of complications in our study, there seemed to be no difference regarding the frequency of postoperative nausea or pain. As for infections and other more serious complications, our observation needs to be corroborated in adequately sized studies. Interestingly, the reduction in postoperative complications

Table 2
Frequency of postoperative complications in absolute numbers, divided into level of physical activity according to Saltin-Grimby physical activity level scale.

	Level of physical activity			
	Inactive (1)	Light activity (2)	Regular activity (3–4)	Total
Patients, n (%)	18 (16)	76 (66)	17 (15)	111 (4 missing)
Any complication, n (%)				
Yes	14 (78)	52 (68)	12 (71)	78 (70)
Number of postoperative complications, n (%)				
0	4 (22)	24 (32)	5 (29)	33 (30)
1	5 (28)	17 (22)	8 (47)	30 (27)
2	3 (17)	23 (30)	2 (12)	28 (25)
3	3 (17)	11 (14)	1 (6)	15 (14)
≥4	3 (17)	1 (1)	1 (6)	5 (5)
Grade of highest complication[a], n (%)				
No complication	4 (22)	24 (32)	5 (29)	33 (30)
I	2 (11)	17 (22)	8 (47)	27 (24)
II	8 (44)	30 (39)	2 (12)	40 (36)
IIIa	1 (6)	3 (4)	0 (0)	4 (4)
IIIb	2 (11)	2 (3)	2 (12)	6 (5)
V	1 (6)	0 (0)	0 (0)	1 (1)
Comprehensive Complications Index (CCI), median (IQR)	21.8 (34)	12.2 (23)	8.7 (17)	12.2 (23)
CCI ≥ 20, n (%)				
Yes	12 (67)	35 (46)	4 (24)	51 (46)
Types of complication, n (%)				
Infection	6 (33)	13 (17)	2 (12)	21 (19)
Fistula/leakage	1 (6)	1 (1)	0 (0)	2 (2)
Bleeding	2 (11)	2 (3)	0 (0)	4 (4)
Nausea	9 (50)	35 (46)	7 (41)	51 (46)
Cardiopulmonary	2 (11)	5 (7)	1 (6)	8 (7)
Pain	7 (39)	27 (36)	6 (35)	40 (36)
Allergic reaction	0 (0)	3 (4)	0 (0)	3 (3)
Other	4 (22)	13 (17)	2 (12)	19 (17)

IQR=Interquartile range.
[a] According to Clavien-Dindo Classification.

Table 3
Unadjusted and adjusted analyses for primary and key secondary analyses of postoperative complications, with physical activity according to Saltin-Grimby physical activity level scale.

Modelled	Model	Comparison	Difference	95% confidence interval	p-value
CCI, continuous variable	Unadjusted	Inactive vs light activity	9.9	1.9–17.9	0.015
		Inactive vs regular activity	11.0	0.7–21.3	0.036
		Light vs regular activity	1.1	−7.1–9.3	0.79
	Adjusted[a]	Inactive vs light activity	11.7	4.3–19.1	0.0019
		Inactive vs regular activity	17.3	7.8–26.8	0.0004
		Light vs regular activity	5.5	−2.4–13.5	0.17
			Relative risk		
Risk for CCI ≥ 20	Unadjusted	Inactive vs light activity	1.45	0.96–2.18	0.075
		Inactive vs regular activity	2.83	1.13–7.09	0.026
		Light vs regular activity	1.96	0.80–4.77	0.14
	Adjusted[b]	Inactive vs light activity	1.65	1.09–2.51	0.018
		Inactive vs regular activity	4.38	2.05–9.36	0.0001
		Light vs regular activity	2.65	1.30–5.39	0.0072

A positive difference indicates that the CCI is higher for participants with a lower level of physical activity, compared to participants with a higher level of physical activity. A relative risk >1 indicates that participants with lower level of physical activity has a higher risk for CCI≥20 than participants with higher level of physical activity. CCI = comprehensive complications index.
[a] Covariates included in the final model are sex, depression, tumour site, neoadjuvant radiotherapy, tumour stage, and alcohol consumption.
[b] Covariates included in the final model are depression, tumour site, neoadjuvant radiotherapy, tumour stage, and alcohol consumption.

reported in a recent randomised controlled trial was in part explained by a reduction in infectious complications [9]. When it comes to comparing the effect of habitual physical activity to the effect from prehabilitation trials, this is unfortunately hard to do due to several reasons. One is differences in classification on postoperative complications. Barberan-Garcia et al. reported an impressive 50% reduction in the overall risk for postoperative complications after six weeks of prehabilitation [9]. When comparing the absolute numbers between their results and our observational study, it is obvious that we found significantly higher levels of nausea (46%) and pain (36%) due to strict definitions of these complications, while Barberan-Garcia reported 10% nausea in the control group and do not report any pain complications. This stresses the importance of using defined criteria for what is considered a complication within the same study, whether the absolute level for e.g. nausea is 46% or 10% in the end. Barberan-Garcia also did not use the more sensitive CCI, which makes it hard to compare the results, in addition to the patient cohort in our study reflecting the general population undergoing colorectal cancer surgery in Sweden, while the patients in Barcelona belonged to a selected high-risk population with significantly higher ASA index, higher prevalence of smoking and higher general risk for

serious postoperative complications. These differences will probably also make it hard to perform future direct comparisons between prehabilitation schemes of different durations and intensity, if there is no consensus on how to classify and report postoperative complications between trials. The results from our study may further highlight the need for more prehabilitation trials to corroborate the promising results from Barberan-Garcia et al.

The prospective design of this study is a strength, as is the use of the Saltin-Grimby physical activity level scale, a validated instrument for measuring the baseline level of physical activity [21]. This instrument is also easy to use and implement in routine health care. Postoperative complications were graded in a standardised way, using Clavien-Dindo [27], the only established instrument for classifying complications after surgery. To further improve the sensitivity, the comprehensive complications index (CCI) was used [29].

A limitation of this study is that complications were not one of the original outcomes, thus these results should be regarded as exploratory. There were also few observations for some of the parameters included in the model, e.g. depression, and the results from the adjusted models should therefore be interpreted with caution. On the other hand, the results in the crude and adjusted models indicate similar effects. Another limitation is the observational design, which always makes it hard to claim causality. Ideally, a prospective registration of complications should have been used. Using medical charts for registration of complications might be considered a limitation. However, the classification was performed by an independent reviewer, which possibly resulted in less risk for bias.

Several lifestyle factors are associated, which makes it harder to statistically determine the individual effect of each of them. Similarly, comorbidity, e.g. hypertension and diabetes mellitus, could be a possible mediator for the effect of physical activity on postoperative complications. Hence, we did not adjust for such comorbidity in our multiple regression.

Our study adds to the existing, limited knowledge of long-term habitual physical activity and the risk for postoperative complications after colorectal cancer surgery. The use of the Saltin-Grimby single-item physical activity questionnaire may be clinically used to predict the risk for postoperative complications.

There have been recent reports of positive effects from interventions with physical activity before colorectal cancer surgery [9]. To explore causal mechanisms, and the role for an intervention with physical activity after a colorectal cancer diagnosis, randomised controlled trials are needed.

Conclusion

Self-assessed preoperative level of habitual physical activity was associated with the risk for complications after colorectal cancer surgery. Thus, self-assessment of physical activity is a simple tool that may be used in clinical practice for prediction of postoperative complications.

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Role of the funding source

The funding source had no role in planning or performing of the study, nor in the interpretation or reporting of the results.

Declarations of interest

None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejso.2019.06.019.

References

[1] Nygren J, et al. Guidelines for perioperative care in elective rectal/pelvic surgery: enhanced Recovery after Surgery (ERAS(R)) Society recommendations. Clin Nutr 2012;31:801–16.
[2] Gustafsson UO, et al. Guidelines for perioperative care in elective colonic surgery: enhanced Recovery after Surgery (ERAS((R))) Society recommendations. World J Surg 2013;37:259–84.
[3] Adamina M, et al. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. Surgery 2011;149:830–40.
[4] Gustafsson UO, et al. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. Arch Surg 2011;146:571–7.
[5] Gustafsson UO, et al. Adherence to the ERAS protocol is associated with 5-year survival after colorectal cancer surgery: a retrospective cohort study. World J Surg 2016;40:1741–7.
[6] Thomsen T, et al. Effect of preoperative smoking cessation interventions on postoperative complications and smoking cessation. Br J Surg 2009;96:451–61.
[7] Eliasen M, et al. Preoperative alcohol consumption and postoperative complications: a systematic review and meta-analysis. Ann Surg 2013;258:930–42.
[8] Boereboom C, et al. Systematic review of pre-operative exercise in colorectal cancer patients. Tech Coloproctol 2016;20:81–9.
[9] 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.
[10] Souwer ETD, Bastiaannet E, de Bruijn S, Breugom AJ, van den Bos F, Portielje JEA, et al. Comprehensive multidisciplinary care program for elderly colorectal cancer patients: "From prehabilitation to independence. Eur. J. Surg. Oncol. 2018;44(12):1894–900.
[11] Leong KJ, Chapman MAS. Current data about the benefit of prehabilitation for colorectal cancer patients undergoing surgery are not sufficient to alter the NHS cancer waiting targets. Colorectal Dis. Offic. J. Assoc. Coloproctol. G. B. Irel. 2017;19(6):522–4.
[12] Hangaard Hansen C, et al. The effect of time from diagnosis to surgery on oncological outcomes in patients undergoing surgery for colon cancer: a systematic review. Eur J Surg Oncol 2018;44:1479–85.
[13] 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.
[14] 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.
[15] 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;31:1131–40.
[16] Angenete E, et al. Physical activity before radical prostatectomy reduces sick leave after surgery - results from a prospective, non-randomized controlled clinical trial (LAPPRO). BMC Urol 2016;16:50.
[17] Steineck G, et al. Quality of life after radical prostatectomy or watchful waiting. N Engl J Med 2002;347:790–6.
[18] Skoogh J, et al. A no means no'–measuring depression using a single-item question versus Hospital Anxiety and Depression Scale (HADS-D). Ann Oncol : Off J Eur Soc Med Oncol 2010;21:1905–9.
[19] Owens WD, et al. ASA physical status classifications: a study of consistency of ratings. Anesthesiology 1978;49:239–43.
[20] Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 2010;17:1471–4.
[21] Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. Circulation 1968;38:1104–15.
[22] Grimby G, et al. The "Saltin-Grimby physical activity level scale" and its application to health research. Scand J Med Sci Sports 2015;25(Suppl 4):119–25.
[23] Rosengren A, Wilhelmsen L. Physical activity protects against coronary death and deaths from all causes in middle-aged men. Evidence from a 20-year follow-up of the primary prevention study in Goteborg. Ann Epidemiol

1997;7:69–75.
[24] Rodjer L, et al. Self-reported leisure time physical activity: a useful assessment tool in everyday health care. BMC Public Health 2012;12:693.
[25] Andersen LB, et al. All-cause mortality associated with physical activity during leisure time, work, sports, and cycling to work. Arch Intern Med 2000;160:1621–8.
[26] Clavien PA, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187–96.
[27] Dindo D, et al. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.
[28] Clavien PA, et al. The comprehensive complication index (CCI(R)): added value and clinical perspectives 3 Years "down the line". Ann Surg 2017;265:1045–50.
[29] Slankamenac K, et al. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. Ann Surg 2013;258:1–7.
[30] van Rooijen S, et al. Preoperative modifiable risk factors in colorectal surgery: an observational cohort study identifying the possible value of prehabilitation. Acta Oncol 2017;56:329–34.
[31] Bursac Z, et al. Purposeful selection of variables in logistic regression. Source Code Biol Med 2008;3:17.
[32] Steffens D, Beckenkamp PR, Young J, Solomon M, da Silva TM, Hancock MJ. 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(4):510–8.
[33] Slankamenac K, et al. The comprehensive complication index: a novel and more sensitive endpoint for assessing outcome and reducing sample size in randomized controlled trials. Ann Surg 2014;260:757–62. discussion 62-3.