The effect of trimodal prehabilitation on the physical and psychological health of patients undergoing colorectal surgery: a randomised clinical trial

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Summary
Prehabilitation aims to increase the endurance capacity of patients who are awaiting major surgery. However, there are no studies investigating the implementation of this demanding and expensive intervention in low-income countries. This study aimed to assess the impact of a 4-week trimodal prehabilitation program on the physical and psychological health of patients waiting for colorectal surgery compared with a control group managed according to enhanced recovery after surgery principles supplemented by nutritional care. This study was a single-centre, randomised controlled trial. The primary outcome measures for the physical aspects were 6-minute walking distance (6MWD) and incentive spirometry, whereas the psychological elements were measured using the 36-item short form survey questionnaire and the hospital anxiety and depression score. In total, data from 149 patients were analysed (77 in the prehabilitation group and 72 in the control group). At the time of surgery, patients in the prehabilitation group had improved 6MWD and incentive spirometry compared with the control group (median (IQR [range]) percentage improvement 131% (112–173 [68–376]) vs. 107% (99–120 [63–163]); p < 0.001 and 113% (100–125 [75–200]) vs. 100% (100–112 [86–167]); p < 0.001 respectively). Patients in the prehabilitation group also had reduced anxiety scores compared with the control group (mean (SD) anxiety score (4 (3) vs. 5 (3) respectively; p = 0.032). However, these effects did not translate into improvements in postoperative mortality and morbidity, or a reduction in duration of hospital stay. Trimodal (physical, emotional and nutritional) prehabilitation is able to improve functional status as well as some parameters of emotional and physical well-being of patients waiting for colorectal surgery.

Introduction
The incidence of colorectal cancer is rising rapidly in many middle-income countries [1] and surgical resection remains the primary treatment [2]. However, surgery is a major stressor especially to frail patients: 75% of patients with colorectal cancer are diagnosed at age > 65 years, and about one-third of patients have an impaired baseline functional capacity [3]. These vulnerable patients have limited physiological reserves and are highly sensitive to surgical stress.

Theoretically, there are a number of ways to limit surgical stress and increase the endurance capacity of patients during the peri-operative course. In the 1990s, Henrik Kehlet developed the concept of enhanced recovery after surgery (ERAS); this is an evidence-based, multimodal treatment concept, which can reduce peri-operative stress,
resulting in fewer complications and shorter duration of hospital stay [4]. Nowadays, the concept of ERAS is widely accepted [5].

Dietetic items in ERAS protocols focus mainly on avoiding pre- and postoperative fasting (e.g. carbohydrate loading 2 h before surgery, early oral refeeding, etc.) but they do not concentrate on the patients’ nutritional status. However, malnutrition is common in patients with colorectal cancer due to the metabolic effect of the tumour, as well as bowel obstruction and malabsorption [6]. Therefore, nutritional assessment and therapy, including dietary counselling and fortification of the diet, are recommended early after the diagnosis of colorectal cancer in order to prevent malnutrition-related deterioration pre- and postoperatively [7]. Pre-operative nutritional protocols may enhance the efficacy and cost effectiveness of colorectal ERAS programs [8]. However, nutritional support alone is not able to improve the functional reserves of patients and no studies have shown that pre-operative nutrition can reduce morbidity after colorectal surgery.

Pre-operative optimisation of a patient’s endurance capacity by physical prehabilitation could further increase their resilience. A new concept of trimodal prehabilitation is defined as “a process in the continuum of care that occurs between the time of diagnosis and the beginning of treatment and includes physical, nutritional and psychological assessments that establish a baseline functional level, identify impairments, and provide interventions that promote physical and psychological health to reduce the incidence and/or severity of future impairments” [9].

The concept of prehabilitation is relatively novel and thus evidence of clinical benefit is limited. Results from studies suggest that multimodal prehabilitation has a positive impact on pre-operative physiologic reserve and on postoperative recovery; however, these beneficial effects have not been translated into improvements in postoperative mortality and morbidity, or duration of hospital stay [10–12]. Other barriers to the implementation of prehabilitation services are the lack of qualified staff and limited financial resources [13]. As a consequence, the establishment of a complex prehabilitation programme in developing countries remains challenging. While the concept of ERAS has been successfully implemented in some middle- and low-income countries (e.g. Poland and Hungary), there are no studies assessing the feasibility of a prehabilitation programme in Central European countries whose expenditure on healthcare is limited [14, 15].

The aim of our study was to assess the impact of trimodal prehabilitation on the physical and psychological health of patients waiting for colorectal surgery compared with a control group managed according to ERAS principles supplemented by nutritional care. This study represents the first attempt to introduce a complex prehabilitation programme in the central European healthcare environment.

Methods
The study was approved by a local ethics committee and the Hungarian Medical Research Council. Written informed consent was obtained from all patients prospectively. Adult patients (aged > 18 years) who required colorectal resection surgery were evaluated by a chief surgeon for eligibility. We did not study patients meeting the following criteria: emergency surgical procedures; palliative resection; ostomy or internal bypass due to peritoneal carcinomatosis; and/or extensive metastatic or unresectable disease.

Patients were randomly allocated using computerised random numbers to treatment groups by a study coordinator who was not involved in the clinical management of the patients. During the first outpatient appointment, detailed medical history data were recorded for all patients including: body weight; height; BMI; body composition – fat ratio; and malnutrition universal screening tool (MUST) score. Surgical risk was evaluated using the colorectal physiological and operative severity score for the enumeration of mortality and morbidity (CR-POSSUM score) [16].

Patients allocated to the prehabilitation group underwent a 3–6 week prehabilitation programme before surgery, in addition to standard ERAS peri-operative care. Patients allocated to the control group received a standard ERAS protocol supplemented by nutritional assessment and support if needed. Patients allocated to the prehabilitation group were provided with an information booklet containing instructions, figures depicting the elements of the program and a work diary in which patients had to record all activities related to the programme. Using the data recorded in the work diary, patient compliance was calculated as follows: completed exercises/prescribed exercises x 100. Following an initial assessment, a multimodal home-based exercise programme was prescribed. The patients were required to attend weekly in-hospital exercise sessions that were supervised by a physiotherapist. The program comprised both aerobic and breathing exercises (walk/breathing prehabilitation). Thirty minutes of daily moderate intensity aerobic activity (walking
or jogging according to patient abilities) was recommended. In addition, deep breathing/coughing exercises (10–15 min daily) and incentive spirometer exercises were suggested (four or five times a day). Participants were required to return once a week to the hospital, where they underwent physical assessment and work diary checking; feedback was provided and training intensity was increased according to the patient’s abilities. Patients were also evaluated by a nutritionist during the first outpatient visit and individualised dietary goals were agreed. Patients were provided with oral nutritional supplementation when necessary based on the European Society of Parenteral and Enteral Nutrition (ESPEN) guidelines [17]. Patients were asked to record the consumption of prescribed oral nutritional supplementation units. In addition, each patient received a 60-min session under the supervision of a trained psychologist, who provided personalised techniques for reducing anxiety as well as lifestyle advice such as smoking cessation and alcohol abstinence. Patients allocated to the control group were managed according to current ERAS guidelines for colorectal surgery. The ERAS protocol was supplemented with nutritional therapy. The fortification of the diet by oral nutritional supplementation was performed as necessary according to ESPEN guidelines [5, 15].

Both groups proceeded to the scheduled surgical procedures. In both groups, outcomes were assessed at the time of the first surgical outpatient clinic as a baseline, the day before the operation and at 4 and 8 weeks postoperatively. Surgeons and each clinician performing the operation and postoperative follow-up were blinded and were not involved in the final study evaluation.

The primary objective of this study was to assess the effect of prehabilitation on physical function, quality of life and mental state. Primary outcome measures were functional capacity (as measured by the 6-minute walking distance (6MWD)), respiratory reserve, quality of life and hospital acquired anxiety and depression. The 6MWD was measured as described previously [18]: participants were instructed to walk on a treadmill for 6 min at a speed that would make them tired. The total distance covered in 6 min was recorded in metres. Relative change in 6MWD was calculated using the following equation: 6MWD% = measured 6MWD/ baseline 6MWD (at the time of diagnosis) x 100. Respiratory reserve was assessed using standard spirometry (SpiroSonic FLO; Uscom, Sydney, Australia). Forced vital capacity (FVC) was recorded in ml. In addition, to measure deep breathing effort, incentive spirometry was also used (results were recorded in ml). Relative changes in respiratory values were calculated using the following equation: measured parameters/ baseline parameters (at the time of diagnosis) x 100. Health-related quality of life was assessed using the 36-item short form survey (SF-36) questionnaire [19]. Patients’ mental state was assessed using the hospital anxiety and depression score (HADS) [20]. Secondary outcomes included: duration of hospital stay after surgery; postoperative 7- and 30-day morbidity (classified according to Clavien-Dindo criteria [21]); 30-day mortality; and time from hospital discharge to the commencement of the first adjuvant chemotherapy.

A power calculation was performed for all physical (6MWD, FVC, incentive spirometry) and mental (a combined score of HADS and emotional well-being dimension of the SF-36 score) parameters, based on locally collected, unpublished data. In order to determine a clinically important 20% difference between the arms using a two-sided, two-sample equal-variance t-test at a 5% level of significance with 80% power, 65–72 patients per arm were required depending on the different endpoints. Considering that the greatest number of patients was required based on 6MWD, the study was powered on the basis of that parameter. Assuming a dropout rate of 20%, we aimed to enrol 90 patients per group. Continuous variables were compared using Student’s t-test or the Mann–Whitney U-test. Categorical variables were compared using chi-squared tests. The effect of therapy on time to the first occurrence of complications (≥ Clavien-Dindo grade 3) or death from any cause, was investigated using a Cox proportional hazards model. Adjustment factors were selected based on stepwise backward selection, using a likelihood ratio test. All statistical analyses were done using SPSS version 24.0 (SPSS Inc., Chicago, IL, USA).

Results
Between October 2017 and February 2019, 186 consecutive patients listed for elective colorectal resection were screened for inclusion. The flowchart for the study is shown in Figure 1. After completion of the whole study, a sub-group of patients who underwent low-risk trans-anal minimally invasive surgery (TAMIS) were excluded from the statistical analysis (23 cases) as both the primary and secondary outcomes were dramatically different in this group (e.g. much shorter duration of hospital stay (2 days) and very low morbidity). A joined analysis with patients undergoing high-risk, major colorectal surgery would have been misleading. This resulted in the data from 149 patients (77 allocated to the prehabilitation group and 72 allocated to control group) being analysed on an intention to treat basis. Patient and tumour characteristics as well as operation details are summarised in Table 1.
Both groups were well matched at baseline, including baseline 6MWD.

Compared with baseline, patients allocated to the prehabilitation group had a statistically significant improvement in 6MWD at time of surgery (median (IQR) [range] 131% (112–173 [68–376]); p < 0.001). This benefit was not seen in patients allocated to the control group ((median (IQR) [range]) 107% (99–120 [63–163]); p = 0.250) (Table 2). The difference in 6MWD between patients allocated to the prehabilitation and ERAS groups was sustained at 4 and 8 weeks postoperatively; however, the difference only reached statistical significance at 8 weeks postoperatively (Table 2). Similarly, incentive spirometry at the time of surgery significantly improved from baseline in patients allocated to the prehabilitation group but not the control group ((median (IQR) [range]) 113% (100–125 [75–200]); p < 0.001) vs. 100% (100–112 [86–167]); p = 0.891 respectively) (Table 2). Objective measurement of FVC, however, did not change over the whole course of the study in both groups (Table 2).

The anxiety, but not the depression, elements of the HADS showed a significant reduction in patients allocated to the prehabilitation arm compared with the control group (Table 2). Quality of life scores were assessed in nine different fields; scores in two areas (emotional well-being and general health function) were significantly better in patients allocated to the prehabilitation group compared with control at the time of surgery (Table 2 and Fig. 2.).

Duration of postoperative hospital stay was similar in both groups. The 7-day discharge plan (generally used measure of a successful ERAS programme) was met in 32/77 (42%) and 31/72 (43%) patients allocated to the prehabilitation and control groups, respectively.

Seven- and 30-day overall morbidity and severe morbidity (≥ Clavien-Dindo grade 3), as well as 30-day mortality were similar in both groups (Table 3). However, a separate assessment showed that 7-day morbidity decreased in male patients allocated to prehabilitation compared with control (5.4% vs. 23.0%, respectively; p = 0.029). The effect of treatment assignment along with baseline parameters was investigated using the composite measure of time to the first occurrence of Clavien-Dindo complication (≥ grade 3) or death from any cause. Using a backward selection, we found that the effect of therapy differed between men and women (test for interaction p = 0.033). While the effect of prehabilitation in male

![Figure 1](https://example.com/image1.png)  
**Figure 1** Study flow diagram. TAMIS, trans-anal minimally invasive surgery. *Non-attendance led to lost of data on functional and quality of life metrics, but all other data were available for analysis.
patients was protective (hazard ratio (95%CI) 0.29 (0.10–0.82)), this was not seen in female patients (hazard ratio (95%CI) 1.77 (0.51–6.17)). Other baseline factors influencing the time to the first occurrence of the composite endpoint were: age (hazard ratio (95%CI) 0.96 (0.93–0.99)); BMI (hazard ratio (95%CI) 1.09 (1.02–1.17)); and time from diagnosis to operation (hazard ratio (95%CI) 1.04 (1.00–1.07)).

Within the entire patient cohort, 55 patients allocated to the prehabilitation group (71%) and 50 patients allocated to the control group (69%) underwent surgery for underlying malignancy, with 39 (71%) and 36 (72%) of patients in each group needing adjuvant chemotherapy. There was no difference in the number of patients deemed not fit enough for chemotherapy between groups (prehabilitation 4 (10%) vs. control 8 (22%); p = 0.15). For those patients treated with adjuvant chemotherapy, the time to the commencement of adjuvant treatment from hospital discharge was not different between the prehabilitation and control groups (median (IQR [range]) time 43 (35–53 [20–96]) days vs. 44 (38–50 [21–74]) days, respectively; p = 0.996).

### Discussion

The primary aim of the study was to assess the effect of prehabilitation on the physical and emotional well-being of patients undergoing elective colorectal surgery. Pre-operative physical capacity is one of the most important patient factors associated with postoperative complication rate. Patients with limited functional reserve have a four times greater risk of having postoperative complications [22]; therefore, improvement of physical status during the waiting period before surgery is essential. As there is no standardised prehabilitation protocol in the literature, we used a simple ‘walk/breathing’ programme as physical prehabilitation. This intervention is easy, cheap, has no special device requirements and its effectiveness has been shown to be greater than that of more strenuous and demanding exercises, such as supervised gym courses [23].

We used 6MWD as the primary indicator of physical/functional capacity. Our study population had a mean (SD) 6MWD of 254 (124) m at the time of diagnosis, which is about 50% of the normal value seen in healthy volunteers [24]. This limited basic functional capacity of our patients could be an indicator of poor prognosis. However, physical prehabilitation was able to improve 6MWD by more than 30% on average by the time of operation. Our results provide proof that pre-operative physical capacity is a potentially influenceable factor. A similar effect of prehabilitation on 6MWD was observed by

### Table 1: Baseline characteristics for patients allocated to received prehabilitation (prehabilitation group) or standard care (control group) before major colorectal surgery. Values are number, median (IQR [range]) or mean (SD).

|                        | Pre-habilitation group n = 77 | Control group n = 72 |
|------------------------|-------------------------------|----------------------|
| Sex; female            | 40                            | 33                   |
| Age; years             | 70 (60–75 [25–87])            | 70 (64–75 [27–88])   |
| Comorbidities          |                               |                      |
| Previous laparotomy    | 40                            | 42                   |
| Diabetes mellitus      | 7                             | -                    |
| Cerebrovascular disease| 7                             | 8                    |
| Pulmonary              | 6                             | -                    |
| Peripheral vascular disease| -                         | 2                    |
| Heart disease          | 12                            | 10                   |
| Smoking                | 39                            | 34                   |
| Alcohol abuse          | 40                            | 38                   |
| CR-POSSUM score        | 2.5 (2.0–3.5 [0.3–21.5])      | 2.4 (1.2–3.5 [0.7–21.5]) |
| Regular medication     |                               |                      |
| Anticoagulant drugs    | 9                             | 7                    |
| Anti-thrombotic drugs  | 12                            | 20                   |
| Steroids              | 3                             | 2                    |
| BMI; kg.m⁻²            | 27.9 (5.6)                    | 27.9 (5.3)           |
| Body fat percentage    | 34.3 (11.7)                   | 33.7 (10.9)          |
| MUST score             | 1                             | 4                    |
|                        | 2                             | 24                   |
|                        | 3                             | 45                   |
|                        | 45                            | 46                   |
| Tumour characteristics |                               |                      |
| Location (colon/rectum)| 38/39                         | 27/45                |
| Benign                 | 22                            | 22                   |
| T1                     | 4                             | 2                    |
| T2                     | 9                             | 12                   |
| T3                     | 33                            | 30                   |
| T4                     | 9                             | 6                    |
| N0                     | 33                            | 29                   |
| N1                     | 18                            | 11                   |
| N2                     | 4                             | 10                   |
| M0                     | 43                            | 43                   |
| M1                     | 12                            | 7                    |
| Operation details      |                               |                      |
| Open/laparoscopic surgery| 7/70                        | 7/65                 |
| Conversion to open surgery| 5                           | 3                    |
| Operation duration; min| 170 (120–260 [30–390])        | 170 (138–224 [55–445]) |
| Stoma formation        | 29                            | 18                   |

MUST, malnutrition universal screening tool; 6MWD, 6-minute walk distance; FVC, forced vital capacity.
Table 2 Functional outcomes and hospital anxiety and depression scores for patients allocated to received prehabilitation (prehabilitation group) or standard care (control group) before major colorectal surgery. Values are median (IQR [range]) or mean (SD).

|                         | prehabilitation group | Control group | p value |
|-------------------------|-----------------------|---------------|---------|
|                         | n = 77                | n = 72        |         |
| Six-metre walking distance (6MWD) |                       |               |         |
| Baseline; m             | 248 (161–300 [49–648]) | 250 (180–300 [79–708]) | 0.962   |
| Time of surgery; m      | 305 (213–407 [107–729]) | 232 (192–341 [96–700]) | 0.005   |
| Time of surgery; % from baseline | 131 (112–173 [68–376]) | 107 (99–120 [63–163]) | < 0.001 |
| 4 weeks postoperative; m | 256 (195–379 [70–664]) | 271 (192–349 [64–682]) | 0.792   |
| 4 weeks postoperative; % from baseline | 123 (92–144 [49–261]) | 109 (95–123 [51–164]) | 0.133   |
| 8 weeks postoperatively; m | 278 (213–406 [131–690]) | 300 (196–400 [120–705]) | 0.787   |
| 8 weeks postoperatively; % from baseline | 133 (102–162 [65–368]) | 116 (101–130 [63–165]) | 0.031   |
| Incentive spirometry    |                       |               |         |
| Baseline; ml            | 2250 (1500–3000 [500–6490]) | 2500 (1875–3000 [1000–5000]) | 0.293   |
| Time of surgery; ml     | 2500 (2000–3500 [1250–5000]) | 2500 (1938–3063 [750–5000]) | 0.329   |
| Time of surgery; % from baseline | 113 (100–125 [75–200]) | 100 (100–112 [86–167]) | < 0.001 |
| 4 weeks postoperative; ml | 2500 (2000–3500 [1250–5000]) | 2875 (1812–3688 [1000–5660]) | 0.389   |
| 4 weeks postoperative; % from baseline | 113 (100–132 [54–167]) | 112 (100–125 [67–189]) | 0.890   |
| 8 weeks postoperatively; ml | 2500 (2063–3500 [1500–5000]) | 3000 (2000–3750 [750–5000]) | 0.405   |
| 8 weeks postoperatively; % from baseline | 113 (104–125 [46–275]) | 110 (100–125 [75–175]) | 0.384   |
| Functional vital capacity|                       |               |         |
| Baseline; ml            | 3100 (2525–3905 [1470–5870]) | 3345 (2772–4400 [1250–6880]) | 0.187   |
| Time of surgery; ml     | 3328 (2460–4060 [1180–6511]) | 3245 (2758–4235 [1670–7080]) | 0.480   |
| Time of surgery; % from baseline | 100 (93–105 [73–237]) | 101 (96–103 [83–130]) | 0.836   |
| 4 weeks postoperative; ml | 3250 (2610–4100 [1440–6060]) | 3330 (2605–4405 [1850–5820]) | 0.405   |
| 4 weeks postoperative; % from baseline | 100 (95–106 [80–220]) | 101 (96–107 [63–135]) | 0.795   |
| 8 weeks postoperatively; ml | 3280 (2610–3890 [1570–5720]) | 3470 (2750–4500 [1820–6380]) | 0.101   |
| 8 weeks postoperatively; % from baseline | 100 (97–107 [86–161]) | 100 (96–106 [79–120]) | 0.655   |
| Hospital acquired anxiety and depression score |         |               |         |
| Anxiety                 | 4 (3)                 | 5 (3)         | 0.032   |
| Depression              | 4 (4)                 | 5 (4)         | 0.167   |

Minella et al., who showed that 60% of patients undergoing a 4-week prehabilitation course had a significant functional improvement [12]. However, in order to achieve such results, some requirements have to be fulfilled: according to the published literature, prehabilitation is more likely to improve functional outcome if its duration is at least 4 weeks and the rate of the patient’s adherence to the pre-operative exercise training is > 70%. In addition, the effect of prehabilitation on functional capacity is better in patients with worse baseline condition [25]. Therefore, evaluation of physical capacity before colorectal resection is recommended for risk assessment and for identification of the patient population who may benefit most from prehabilitation.

To assess further the functional effect of prehabilitation, FVC was measured and incentive spirometry was performed. According to our data, incentive spirometry exercises did not improve FVC but volume measured by incentive spirometry increased significantly after 4 weeks of prehabilitation. This improvement in incentive spirometry skills may be beneficial in the early postoperative phase to prevent pulmonary complications.

To record the psychological effects of the trimodal prehabilitation programme, we measured patients’ HADS. There are three studies in the literature that assess the effect of prehabilitation on pre-operative emotional distress using this self-reported questionnaire. Li et al. showed that symptoms of both anxiety and depression alleviated significantly during prehabilitation [11], whereas the studies of Carli et al. and Gillis et al. did not show any significant psychological benefits with the intervention [18, 23]. According to our data, the pre-operative anxiety score of
patients undergoing prehabilitation decreased significantly, whereas the rate of depression did not differ. Weekly group training sessions gave patients waiting for major surgery the chance to meet their peers with similar conditions and burdens. Sharing their fears and experiences with each other may have helped to reduce pre-operative anxiety. A psychologist can provide patients with additional tools to help them in managing their worries. Theoretically, the decrease in pre-operative anxiety can increase the rate of patients’ adherence to the exercise training, as well as to nutritional support; thus stress reduction may enhance the efficiency of prehabilitation [26].

In addition, we used the SF-36 questionnaire to assess the effect of prehabilitation on modifiable lifestyle factors. Two of the nine measured quality of life scores improved significantly by the time of operation in the prehabilitation group. However, the other parameters of the questionnaire did not change. The SF-36 questionnaire may be too general to capture changes related to our prehabilitation intervention. Currently, experts agree on the need for further, focused studies on the quality of life changes in relation to prehabilitation programs.

Taking into account that 6MWD and SF-36 are useful indicators for predicting postoperative complications and duration of hospital stay [27], we assumed that improvement in these parameters would result in better

Table 3 Postoperative outcomes (morbidity and mortality rates) for patients allocated to received prehabilitation (prehabilitation group) or standard care (control group) before major colorectal surgery. Values are number and median (IQR [range]).

|                        | prehabilitation group | Control group | p value |
|------------------------|-----------------------|---------------|---------|
| Morbidity              |                       |               |         |
| 7-day overall          | 11 (11)               | 12 (12)       | 0.430   |
| 30-day overall         | 17 (17)               | 16 (16)       | 0.569   |
| Clavien-Dindo ≥ grade-3 (7-days) | 3 (3)     | 2 (2)         | 0.532   |
| Clavien-Dindo ≥ grade-3 (30-days) | 4 (4)     | 2 (2)         | 0.373   |
| Mortality              |                       |               |         |
| 7-day                  | -                     | 1 (1)         | 0.483   |
| 30-day                 | 1 (1)                 | 2 (2)         | 0.475   |
| Duration of hospital stay; days | 8 (7–10 [5–47]) | 8 (7–9 [5–21]) | 0.712   |
postoperative outcomes. However, we were not able to show any improvement in the number of postoperative complications or duration of hospital stay. Several studies assessing prehabilitation have shown similar results; namely, increased pre-operative functional reserve without improvement in postoperative outcomes [10–12, 18]. However, these studies involved small numbers of patients, and therefore their reliability is questionable. Further well-designed, randomised controlled trials are needed to evaluate in detail the effects of prehabilitation. A number of studies have been initiated recently, including the first international randomised controlled trial (PREHAB trial), which involves more than 700 patients undergoing colorectal surgery for cancer [28]. While waiting for the results of this trial, clinicians should focus on the identification of the patient populations who are most likely to benefit from trimodal prehabilitation. According to our results, significant factors influencing the time to the first occurrence of complications were male sex, age, BMI and time from diagnosis to operation. Adequate patient selection is of great significance in middle- and low-income countries, where the healthcare systems are significantly burdened by the high cost of complex prehabilitation programs. Longitudinal cohorts of well-established prehabilitation programs will provide valuable, robust data for future sub-group analyses.

According to our data, prehabilitation improves not only the pre-operative functional status but may also enhance postoperative recovery. More rapid physical recovery may reduce the time to the initiation of adjuvant treatment as well as increase the tolerability of chemotherapy. However, our multidisciplinary team has not been able to demonstrate any reduction in time to the commencement of adjuvant chemotherapy. A recently-published randomised controlled trial demonstrated that prehabilitation was associated with improved disease-free survival for stage-3 colorectal cancer patients [29]. This could be related to better maintenance of nutritional status and physical activity. Future studies examining the oncological effect of prehabilitation, should be conducted to better understand the long-term effect of the intervention.

Our study has a number of limitations worthy of consideration. Our power calculation was based on functional outcomes, therefore firm conclusions can only to be drawn on these measures. Even though detailed sub-group analysis of the study arms should be assessed with statistical caution, they provide valuable data for future clinical experiments. To explore the ideal sub-group of patients waiting for colorectal surgery regarding the effectiveness of trimodal prehabilitation, further high-volume comparative studies targeting these vulnerable patients are needed.

In conclusion, the findings of the present study suggest that trimodal (physical, emotional and nutritional) prehabilitation is able to improve functional status as well as some parameters of emotional and physical well-being of patients waiting for colorectal surgery. However, the protective effect of prehabilitation does not manifest in improvements in postoperative morbidity and mortality, or duration of hospital stay. However, this is the first study to show that a complex, trimodal prehabilitation program is feasible and effective in a central European country that has limited healthcare expenditure.

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