

Preoperative optimization of diagnostic work-up and physical fitness predicts and improves outcome of patients with colorectal cancer

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Chapter 10

Impact paragraph

Impact paragraph

Colorectal cancer is the third most common cancer worldwide. With the further rise of a gradually aging population and without taken the further development and adoption of additional preventive precautions into account, the incidence of cancer is expected to increase.¹ Such an increase may result in an expansion of health care demands, paralleled with increasing costs. Nowadays, the focus of public health interventions, more and more in coalition with interventions from the healthcare system, is not only on primary prevention of diseases like cancer (e.g., elimination of environmental pollution/toxins, antismoking policies, healthy nutrition programs, educational activities that promote the healthy lifestyles), but also on secondary prevention (e.g., comprehensive screening strategies)¹ and tertiary prevention. As such, the focus in perioperative care is on the prevention of (the impact and consequences of) postoperative complications and prevention of a delayed recovery or even permanent loss of (physical) functioning known under the term “hospitalization-associated disability”.² Nowadays, the overall complication rate after colorectal surgery, which remains the cornerstone of curative treatment for colorectal cancer,³ is still significant with percentages up to 30%.³⁻⁵ Patients at risk for postoperative complications (i.e., high-risk patients) might benefit from prehabilitation.^{6,7} Prehabilitation aims to increase a patient’s health and fitness between diagnosis and surgery in order to reduce postoperative complications and their impact, and enhance recovery of (physical) functioning postoperatively.⁸ Adequate screening, assessing, diagnosing, and prognosing of patients that are potentially at risk for an impaired postoperative outcome are essential for successful personalized healthcare-related prevention. Therefore, the main objective of this thesis was to find tools that can be used in the preoperative period to screen, assess, and diagnose patients with colorectal cancer who are at risk for postoperative complications (with the focus on physical fitness in the preoperative phase) and to investigate whether postoperative outcomes of these patients can be improved with a community-based prehabilitation program, here focused on the effectiveness of physical exercise training.

The research described in this thesis highlights the role of body composition, as assessed by using the computed tomography (CT) scan, as a tool to preoperatively diagnose and/or identify patients scheduled for colorectal surgery who are at risk for postoperative complications. Reduced muscle quality and the combination of obesity and low skeletal muscle mass were found to be associated with postoperative complications. Body composition was found to be moderately associated with objectively assessed aerobic fitness of these patients during a cardiopulmonary exercise test (CPET). Moreover, we found that a relatively new aerobic fitness variable (the oxygen uptake efficiency slope, OUES) might be a valid diagnostic measure of aerobic fitness of elderly patients scheduled for colorectal surgery that can be objectively determined in all patients without requiring

a maximal effort during a CPET. This OUES variable might also help to more appropriately identify those patients at higher risk of postoperative morbidity. Finally, we showed that a three-week community-based exercise prehabilitation program ('prehabilitation study') substantially reduced the number of patients with one or more complications in a group of high-risk patients scheduled for colon resection for (pre)malignancy.

Relevance

Scientific impact

The insights gained during these thesis projects led to several adaptations in the perioperative work-up and care in patients with colorectal cancer in the Medisch Spectrum Twente. Previously, a patient's aerobic fitness was not routinely assessed in the perioperative work-up and still the outcomes of such an assessment are not registered in the nationwide quality registry for colorectal cancer patients. Since these thesis projects started, a patient's aerobic fitness became more and more a routinely assessed parameter by using a CPET in our hospital, and also in other hospitals. In this way high-risk patients can be identified, as a low aerobic fitness achieved on the CPET indicates an increased risk for postoperative complications. The results of the CPET are used to inform the patient and his/her relatives/informal caregivers and to consequently make a well-informed shared decision about whether or not to participate in specifically targeted preoperative (physical exercise) prehabilitation interventions. Given our positive results of prehabilitation in reducing postoperative complications in high-risk patients undergoing colorectal surgery, the next step should be to implement prehabilitation (at least consisting of validated physical exercise training presented in this thesis) in the hospital's standard perioperative trajectory by use of a perioperative trajectory continuum of care (CoC) protocol. The presented and/or validated physical factors (CPET values such as the oxygen uptake at the ventilatory anaerobic threshold and the OUES, and body composition variables such as radiation attenuation and sarcopenic obesity) described in this thesis, together with other recent insights and evidence in improving perioperative care, should also be incorporated in this CoC protocol.

Given our results of the prehabilitation study, the function of the so-called passive "waiting time" between diagnosis and initiation of treatment (treatment interval) in relation to a patient's preoperative aerobic fitness should be transformed into a proactive preparation period. At the first-hand, that might sound rather complicated as "waiting time" is currently used as one of the performance indicators for the quality of hospital care.^{9,10} Recommendations regarding the treatment interval differ widely and can even differ within countries, because fundamental evidence-based guidance is absent.⁹ According to the Dutch so-called Treeknormen,¹¹ it is recommended to treat >80% of patients with colorectal cancer within 5 weeks from pathological confirmation, and 100% within 7 weeks. Another Dutch guideline describes that treatment will ideally start within six weeks



after their first visit at the outpatient clinic.¹² As a result of these guidelines, healthcare professionals are not always motivated to delay surgery in order to preoperatively optimize the health and fitness of their patients. In the literature,¹³ however, it was found that treatment delay (with treatment intervals of even 8-9 weeks) was not associated with impaired long-term outcomes in patients with colon cancer. When hospital logistics are optimized and rescheduled (e.g., a shorter period between time of diagnosis and first visit at the outpatient surgical clinic), and a more optimal collaboration between all disciplines can be realized (as we showed in our prehabilitation study), the currently recommended short “waiting time” can be sufficiently transformed and thereupon regularly used as a “preparation period” in most patients. However, this interval might not be sufficiently long for all patients.⁹ We suggest that if optimization of a high-risk patient’s preoperative condition is preferred (by the healthcare professional and patient), it must be possible to extend the treatment interval. Frequent objective monitoring of training progress is important and sufficient progress in aerobic fitness should be achieved before proceeding with surgery in these patients. By doing so, that what sounded rather complicated, can or even should be tackled in the interest of each individual patient on a personal base, preferably with help of expert logistic- and data-intelligence.

In our prehabilitation study, we experienced that quite a few patients declined to participate in the study because of transportation difficulties. In another study it was found that patients prefer a home-based preoperative physical exercise training program.¹⁴ So, to maximize participation rate, adherence, and effectiveness of a prehabilitation program in high-risk patients, we suggest that the exercise component of the prehabilitation program best can be performed in the patient’s pre-existent living context in which the patient’s informal support system should be involved. An advantage of home-based physical exercise training is that the training program can be combined with functional exercise training of activities of daily living of relevance for the individual patient (e.g., climbing their own stairs, walking the dog in their own environment), which also have been shown to have a beneficial effect on daily function of older people.^{15,16} After gaining this insight, a collaboration with Lode B.V. (Groningen, the Netherlands) was established in which cycle ergometers now can be delivered at a patient’s home and instantaneously customized to their physical requirements. With the help of an experienced and dedicated community physical therapist, the (supervision of) training can be tailored to each patient’s talents to train, to monitor their training progress, and to involve their informal support. With the experiences gained during this collaboration, Lode B.V. was able to further develop and optimize their cycle ergometers. By doing so, we were able to develop quite a doable prehabilitation organization that delivers preventive means for high-risk patients at their home, an organization that is nowadays tested for its feasibility and pre- and postoperative success.¹⁷

The findings and experience gained in this thesis also led to the establishment of an experienced network of community physical therapists in the catchment area of the hospital, which, we think is crucial for an exercise prehabilitation program to be effective. Moreover, at the University Medical Center Groningen (UMCG) a prehabilitation department is being set-up, in which trained and competent healthcare professionals, along with the patient and the patient's informal support system, aim to perform an interdisciplinary preoperative risk assessment and assist the patient to get fit for surgery (executed in primary care). If prehabilitation has become standard care and common sense, risk screening and assessment can also be performed in the primary care. Additionally, the Dutch Society for Surgery established the Workgroup Prehabilitation to give direction to the implementation of prehabilitation in the Netherlands.¹⁸ A nationwide position paper considering prehabilitation in perioperative care is on the way, in which our results (*Chapter 7*) have been used. At the initiative of the Dutch Healthcare Authority (NZA), an innovation arrangement is obtained, whereby financing agreements have been made for prehabilitation in patients undergoing surgery for colon and rectal cancer. Within this arrangement that started on October 1, 2020, a payment title is developed for prehabilitation (Diagnosis Treatment Combination [DBC's] On Their Way to Transparency, DOT) in which also costs for the implementation and organization are covered.¹⁸ These developments will hopefully eventually make the implementation of prehabilitation successful, realistic, and sustainable.

Social impact

Previous research showed that the occurrence of a complication within the first 30 days after a major surgery, independent of the patient's preoperative risk, reduced median patient survival by 69%.¹⁹ Postoperative morbidity is also associated with functional decline after surgery and decreased health-related quality of life.²⁰ Identifying patients at risk for a complicated postoperative course (e.g., by the use of their preoperative body composition and aerobic fitness) and performing targeted preventive interventions such as prehabilitation may positively influence patient outcomes, the need of health care resources, and, consequently, costs.

Costs associated with the prevention of (the impact of) complications would probably outweigh costs of the care for the postoperative complications, and preventing complications would – most importantly in the context of patient-centered care – considerably reduce the patient's physical, mental, and social burden.⁴ In the Netherlands, it was shown that the average total hospital costs (primary admission and after discharge up to 90 days) for patients undergoing colorectal cancer surgery ranged from €3,403 (least expensive 2.5%) to €79,953 (most expensive 2.5%).⁴ The average costs for one patient without complications is ~€9,000 versus ~€11,500 and ~€27,000 for one patient



with minor and severe complications, respectively. The estimated costs of a *multimodal* prehabilitation program are €969 per patient (containing twelve physical therapy sessions, protein supplements, project management, and data collection).²¹ We therefore expect prehabilitation to be cost-effective. In future studies, these calculated figures should be investigated in a health technology assessment (HTA) approach in order to provide these assumptions with evidence and also with lessons to be learned from that.

Target groups and activities

First, the overall findings of this thesis are of value to patients and their informal caregivers. Adequate risk assessment prior to surgery can help them to gain insight in the patient's risks for an impaired postoperative course. This preoperative period can be used as a 'teachable moment', in which a patient might be more receptive towards lifestyle advices and more motivated to change their lifestyle than he or she would be in ordinary life.²² Moreover, these insights will help the patient, and also healthcare professionals, in shared decision-making for the choice and use of prophylactic (e.g., prehabilitation), surgical, and anesthetic interventions. Second, our findings can help healthcare professionals (e.g., physical therapists, surgeons, anesthesiologists, general practitioners) to diagnose patients at risk for an impaired postoperative course. They can offer these patients a targeted preventive intervention in order to optimize their health/fitness and the provided care. Third, scientists can use our findings in order to further improve prehabilitation programs for adequately selected low- and high-risk patients. Moreover, our findings will be of benefit for the development of a formal prehabilitation guideline.

The aforementioned target groups can be involved in and informed about the research results in a several ways. Firstly, patients can individually be informed about the research findings during their visit at the outpatient clinic. The results can be used to identify a patient's own (modifiable) risk factor(s) and, if necessary, a prehabilitation program can be offered to the patient. Secondly, gained knowledge during the research period of this thesis was, and will in the future be, shared with several hospitals and colleagues in (inter) national communities of practice in order to transfer/share knowledge and experiences. Thirdly, the research findings are and will be presented at (inter)national conferences. Fourthly, the results and experiences gained in this thesis project will be used to educate physical therapists in order to professionally guide and execute a prehabilitation program. Fifthly, scientific publications are posted and underway. Sixthly, the data gathered in this thesis project is available for (larger) studies, for example to perform a meta-analysis. Seventhly, the findings of this thesis project were, and will in the future be, used to contribute to an online course for multidisciplinary teams about frail high-risk patients and the role of prehabilitation.

Conclusion and ambitions

In conclusion, the studies described in this thesis highlight the role of physical fitness (specifically aerobic fitness) as a means to preoperatively diagnose and/or select patients at high risk for postoperative complications after colorectal surgery and the role of exercise prehabilitation in reducing postoperative complications. We hope that our findings will be used to implement adequate risk assessment and prehabilitation in colorectal cancer care, to ultimately achieve the quadruple aim²³: improving patient experience, improving the health of a (population of) patient(s), reducing costs, and improving the well-being of health care professionals.



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