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Frailty indicators and functional status in older patients after colorectal cancer surgery

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ABSTRACT

Objectives: The number of older survivors from colorectal cancer is increasing, but little is known regarding long-term consequences of cancer treatment in this patient group. Physical function is an important outcome for older patients, affecting both autonomy and quality of life. We aimed to investigate physical function in older patients with colorectal cancer before and after surgery, and to examine the role of individual frailty indicators as predictors of functional decline.

Material and Methods: We present 16–28 months follow-up data of older patients after elective surgery for colorectal cancer. During a home-visit, physical function was evaluated by activities of daily living (ADL), instrumental activities of daily living (IADL), the timed up-and-go (TUG) test, and grip strength. Measurements were compared with those obtained preoperatively using the Wilcoxon signed rank test. Frailty indicators were dichotomized and implemented in logistic regression models to explore their associations to a decline in the physical function scores.

Results: Eighty-four patients were included and the median age was 82 years. There was a significant decrease in ADL ($p = 0.04$) and IADL scores ($p \leq 0.001$) at follow-up. We found no associations between frailty indicators and the risk of decline in physical functioning.

Conclusion: In our population of older patients with surgically treated colorectal cancer, there was a significant decline in ADL- and IADL-scores at follow-up. No change was found in TUG or grip strength, and frailty indicators did not predict decline in physical function.

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1. Introduction

Colorectal cancer is one of the most common cancer types. In Norway, approximately 85% of patients are older than 60 years at diagnosis. Thus, colorectal cancer is a disease that

mainly affects older individuals.¹ Surgery is the main treatment modality, supplemented with adjuvant or palliative chemotherapy or radiation in selected cases. Survival from colorectal cancer is improving in all patient groups, and the number of older survivors is increasing. However, little

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is known of long-term effects of cancer surgery in this population.

In geriatric oncology, the use of a Geriatric Assessment (GA) is suggested to aid clinicians when caring for older patients with cancer.² A GA generally includes evaluation of comorbid conditions, medications, physical function, nutrition, depression, cognitive function and social support, and may detect unknown – and possibly reversible – health problems.^{3,4} A systematic review from 2012 concluded that conducting a GA is feasible in the heterogeneous population of older patients with malignant disease, though studies investigating targeted interventions based on a GA are scarce.⁵ Furthermore, little is known about the possible predictive role of a GA with regards to long-term outcomes after cancer treatment.

The GA may serve as an approach to identifying frailty in an older individual.⁶ Frailty is defined as a state of increased vulnerability towards stressors, and several ways to measure frailty in clinical practice have been proposed. Among the definitions of frailty, the “frailty phenotype”, and the “accumulation of deficits”, developed by Fried et al. and Rockwood et al., respectively, are widely used.^{7,8} It is hypothesized that activation of inflammatory pathways and of the coagulation system contributes to the pathogenesis of frailty, and markers of inflammation such as C-reactive protein (CRP) and interleukin-6 (IL-6) have been linked to different frailty measures.^{9–11} Identifying frailty in older patients with cancer may be relevant in order to optimize treatment and predict treatment outcomes. We have previously shown that frailty as determined by a GA can predict postoperative complications in older patients undergoing elective surgical resections of colorectal cancer, and that IL-6 is an independent predictor of postoperative complications in the same patient population.^{12,13}

While several authors have dealt with postoperative mortality and morbidity after colorectal cancer surgery in older patients, only a few studies have investigated consequences for immediate and long-term functional status in this patient population. We therefore conducted a longitudinal study of older patients with colorectal cancer in order to describe and compare their physical function before and after elective surgery. Further, we explored the impact of the following variables on functional outcomes: individual frailty indicators, inflammatory biomarkers, and the occurrence of postoperative complications.

2. Material and Method

The study was approved by the Regional Committee for Medical and Health Research Ethics in Eastern Norway. All patients provided a written informed consent.

The patients were recruited from an observational prospective cohort study evaluating predictors of postoperative complications in older patients with colorectal cancer.¹² All participants were aged ≥ 70 years, and had undergone elective resection of colorectal cancer in one of three Norwegian public hospitals; Oslo University Hospital–Ullevål or Aker divisions, or Akershus University Hospital. TNM-stage and scoring of

American Society of Anesthesiologists Physical Status Classification System (ASA) were retrieved from patients’ medical records. A preoperative GA was performed by a physician trained in geriatrics (SRK), and formed the basis for classification of patients into frail or non-frail. The GA included measurements of ADL- and IADL-function by the Barthel index and the Nottingham Extended Activities of Daily Living Scale (NEADL), respectively; cognitive function by the Mini Mental State Examination (MMSE); nutritional status by the Mini Nutritional Assessment (MNA); depressive symptoms by the Geriatric Depression Scale (GDS); and comorbidity by the Cumulative Illness Rating Scale (CIRS).^{14–18} Physical performance measures included the timed “up-and-go” (TUG) test and grip strength.¹⁹ In addition, The European Organisation of Research and Treatment of Cancer Quality of Life Questionnaire C-30 (EORTC-QLQ C30) and the European Cooperative Oncology Group Performance Status (ECOG PS) were used.^{20,21} These scales evaluate self-rated physical, psychological and social function, and physical performance status, respectively. Postoperative complications were retrospectively registered from patients’ medical records, and classified as minor (grade 1), potentially life-threatening without (grade 2) or with (grade 3) permanent sequelae, or fatal (grade 4), based on the classification system developed by Clavien et al.²²

Preoperative blood samples were collected and serum was obtained by centrifugation at 3400–3700 rpm for 10–12 min, and stored at -70 °C until analyzed. CRP levels were determined by an enzyme linked immunosorbent assay (DRG Instruments GmbH, Germany), with a detection limit of 0.1 mg/L and a coefficient of variation (CV) of <5%. Levels of IL-6 were determined using another commercially available enzyme linked immunosorbent assay (R&D Systems Europe, Abingdon, Oxon, UK, CV 10.5%).

Patients from the original study were consecutively contacted by post and telephone in order to inform them about the follow-up study. Patients who consented to participation received a home visit from the head researcher (BR) between 16 and 28 months after surgery. During this visit, functional dependency was assessed by the Barthel index and the NEADL-scale, while physical performance was measured with TUG and grip strength. TUG was measured as the number of seconds spent on standing up from a chair, walking a distance of 3 m, turning, walking back, and sitting down again.¹⁹ Grip strength was measured in kilograms with a Jamar® handheld dynamometer. The highest value of three attempts on either hand was noted.

3. Statistical Approach and Definition of Cut-off Values

Non-parametric statistical methods were applied due to skewed distribution of most variables. To determine significant changes in functional measure scores before surgery and at follow-up, the Wilcoxon signed rank test was used. Exploratory analyses indicated that there was no homogeneous relationship between preoperative frailty indicators and the odds of certain postoperative functional outcomes. Accordingly, the requirements for

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