Self-reported quality of life and functional outcome in patients with rectal cancer – QoLiRECT

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ABSTRACT

INTRODUCTION: The treatment of rectal cancer has improved, and survival rates today exceed those of colon cancer, but functional impairments and other adverse effects of treatment are common among patients. The impact of treatment on patients’ quality of life (QoL) remains unclear. Many of the common QoL instruments are brief and not sufficiently detailed to provide a deeper understanding of the factors that determine QoL. The aim of this study was to explore patients’ experiences and long-term QoL in an unselected cohort of patients with rectal cancer.

METHODS: This is a prospective international multicentre study based on a comprehensive, validated questionnaire on functional impairments and QoL administered to an unselected population of 1,500 patients with rectal cancer at diagnosis and after one, two and five years. The clinical characteristics are retrieved from the national quality registers. A total of 14 hospitals in Sweden and Denmark are currently involved in the study. Inclusion is ongoing, and new including hospitals are welcome to join. Full accrual is expected within two years.

CONCLUSION: This study will provide detailed knowledge about the challenges that patients face following diagnosis and treatment of rectal cancer. It will investigate the nature, severity and perceived significance of constraints and symptoms, as well as the impact of a variety of clinical and patient-related factors on QoL. The study will probably identify areas where changes in care routines may improve patients’ QoL.

FUNDING: This study was supported by the Swedish Research Council, grant number 2012-1768; the Swedish Cancer Society CAN 2010/593 and CAN 2013/500; the Swedish Society of Medicine; the Gothenburg Medical Society; the Health & Medical Care Committee of the Regional Executive Board, Region Västra Götaland; ALF grant 138751 and 136151, “Agreement concerning research and education of doctors”; Anna-Lisa and Bror Björnsson Foundation; Assar Gabrielsson Foundation; Mary von Sydow Foundation; Ruth and Richard Julin’s Foundation and Lion’s Cancer Research Foundation of Western Sweden.

TRIAL REGISTRATION: ClinicalTrials.gov (NCT01477229).

The treatment of rectal cancer has improved in past decades, which has resulted in increased survival and lower rates of local recurrence [1, 2]. However, functional dis-

PROTOCOL ARTICLE

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Dan Med J 2014;61(5):A4841
within 15 cm from the anal verge, regardless of tumour stage or intended treatment. Patients aged below 18 years or who are unable to read or understand Swedish or Danish are excluded. A questionnaire is administered to patients at four time-points: at inclusion and after one, two and five years. Clinical data regarding staging, treatment and clinical course are retrieved from the national quality registers for rectal cancer [2, 10].

Inclusion
Patients are invited to participate when clinical staging is completed, the multidisciplinary conference has reviewed the case and the patient has been presented with a treatment plan. The patient is registered at the Regional Cancer Centre in Gothenburg, and patient data are then delivered by encrypted mail to the study secretariat and entered into a logistics database that allows for timely submission of questionnaires during the course of the study.

External validity
Participating hospitals include university as well as county hospitals and will provide a representative sample of rectal cancer cases in Sweden and Denmark. The quality registers for rectal cancer in Sweden and Denmark cover about 99% and 95% of rectal cancer cases, respectively [2, 10]. Each participating hospital registers non-participants with tumour stage, planned treatment and reason for non-participation.

Administration of questionnaires
Patients are contacted by the study secretariat by phone within a few days after inclusion to ascertain that contact information is accurate and that the patient is willing and able to answer and return the questionnaire that will be sent to him/her. The questionnaire is then sent immediately after to enable completion before start of treatment (this also applies to cases involving neoadjuvant radiation and chemotherapy as well as surgery and palliative chemotherapy). In hospitals with short lead times to start of treatment, the initial questionnaire is given to the patient at inclusion and is then returned to the study secretariat by prepaid envelope.

At follow-up (one, two and five years after inclusion) the patient receives a letter, followed a few days later by a telephone call to solicit the patient’s permission to send the questionnaire (Figure 1). Two weeks after the questionnaire has been sent, patients receive a postcard that serves both as a thank you note and as a reminder in case the questionnaire has not been returned. If a patient still does not return the questionnaire, one last contact by phone is attempted. This routine has been used in previous studies where overall response rates of approx. 90% were achieved [11, 12].

Questionnaire
The questionnaire has been constructed according to a well-established method in collaboration with Steineck et al [13, 14], and it includes questions previously used in studies on urological and gynaecological cancer [14-16]. In the development of the questionnaires used in this study, patients with rectal cancer at different stages of disease were interviewed in depth. A semi-structured form was used and the contents analysed using a qualitative methodology. The interviews were sorted and the hypotheses were refined accordingly. Based on this analysis, a first draft of the questionnaire was constructed. An expert panel consisting of oncologists, surgeons, gynaecologists, anaesthetists and specialist nurses then performed item selection and contents validation. The questionnaire draft was then subject to face-to-face validation with patients with different tumour levels and stages of rectal cancer. In this process, patients answered the questionnaire in the presence of a study
The two national registers do not contain exactly the same information. To make sure that data are complete for all included patients, clinical record forms (CRF) different for Denmark and Sweden are used.

**Study organisation**

The study is run within the framework of the Scandinavian Surgical Outcomes Research Group (SSORG), a research network of surgeons in Sweden and Denmark. So far, fourteen university and county hospitals participate, and the study is open to participation for other hospitals. The study secretariat is located at the SSORG headquarter at Department of Surgery, Sahlgrenska University Hospital/Östra in Gothenburg. At each participating hospital, a local investigator is responsible for inclusion and control of internal validity.

**Data analysis**

Most analyses will be descriptive in nature. As soon as full accrual to each questionnaire has been reached, data will be processed, analysed and published in order to avoid unnecessary delay in the translation of new

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**Figure 2**

Development of a study-specific questionnaire. In the pilot study, applicable questions from the questionnaire were administered to a retrospective cohort of 82 consecutive patients operated with APE at our institution.

APE = abdominoperineal excision; AR = anterior resection.
knowledge into improvements of patient care. In the questionnaires, ordered response options in a Likert-type response format are provided for most questions. Responses will be dichotomised using cut-offs according to the nature of the question as described previously [14]. The answers in the questionnaires will be compared between different patient groups, taking into account tumour stage, disease characteristics, treatment and type of surgery. Differences between groups will be estimated using parametric or non-parametric methods after appropriate evaluation of the data.

Sample size
Assuming that the smallest sub-groups to be compared will consist of 100 patients each, the study will have a power of 80% for detecting a difference to a dichotomised response between these groups assuming a true difference of approximately 20% (absolute difference). This is based on a proportion of 0.5 (50%) in one group and a significance level of 0.05. We have estimated that a sample size of 1,500 patients with rectal cancer will ensure that all relevant subgroups will each include > 100 patients. Thus, we intend to include 1,500 patients in the study.

Ethical aspects
The Regional Ethical Review Board in Gothenburg approved the study (Dnr. 595-11). The study was registered with ClinicalTrials.gov (NCT01477229) and with the local Data Protection Officer (register id 29724). Permission to use the EQ-5D and the Sense of Coherence Scale was obtained. In Denmark, the study was approved by the Danish Data Protection Agency (2007-58-0015/HEH.750.89.21).

DISCUSSION
Patient-perceived QoL and functional results are important outcome measures in the evaluation of cancer treatment. Regarding rectal cancer, adverse effects of the treatment may be considerable. Previous studies have provided some important insights about the QoL of patients with rectal cancer in relation to different surgical procedures as well as to radiation treatment [3, 7, 19, 20]. However, most of them have utilised established generic and cancer-specific or symptom-specific instruments, and there is a need for a deeper and more detailed knowledge of the patients’ experiences. This study uses a comprehensive questionnaire developed in close co-operation with patients with rectal cancer. Unlike most other instruments, it includes considerations about the degree of bother associated with each specific symptom. This will provide novel and useful data and probably increase our knowledge and understanding as data indicate that the physician’s perception of what bothers patients is not fully in concordance with what patients perceive.

The specific strengths of this study include the cohort size, the inclusion of baseline data, the inclusion of an unselected cohort and the length of the follow-up period. Control of external validity through the use of the quality registers increases the intrinsic value of the study. Furthermore, the construction of the study-specific questionnaire in a multidisciplinary setting and in cooperation with patients with rectal cancer at all stages of disease decreases the risk of measurement errors and ensures a good content validity.

The QoLiRECT study will contribute important and novel insights on the experiences of patients with rectal cancer and thereby provide results that have implications for treatment and care.

None of the funding sources have had any impact on design, acquisition of data, analysis of data, interpretation of results or the drafting of the manuscript.

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ACCEPTED: 5 March 2014

CONFLICT OF INTERESTS: none. Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk.

ACKNOWLEDGEMENTS: We would like to extend our gratitude to the research nurses at Scandinavian Surgical Outcomes Research Group in Sweden: Carina Rosander, and in Denmark: Rikke Søby Andersen and Katja Halladin Rauh.

LITERATURE