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ORIGINAL ARTICLE

Follow-up after rectal cancer: developing and testing a novel patient-led follow-up program. Study protocol

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ABSTRACT

Background: The main treatment for non-metastatic rectal cancer (RC) is surgical resection. Late adverse effects that are highly prevalent and negatively impact patients' symptom burden and quality of life are: bowel-, urological and sexual dysfunctions; psychological distress; fear of recurrence. Patients and clinicians have requested a more patient-centred follow-up, balancing the focus on detection of recurrence, and physiological and psychological late adverse effects. The current follow-up program primarily focuses on detection of recurrence, with less attention on late adverse effects. As a consequence, the randomized controlled trial Follow-up after Rectal Cancer (FURCA) has been launched, testing the effect of a new patient-led, follow-up program. The aim of this paper is to describe the methodology used in the FURCA study and to report results from the development of the patient-led, follow-up program. Adult patients, treated with curative intent for primary adenocarcinoma in the rectum are included from four Danish centers.

Material and methods: Patients are randomized into an intervention group, receiving standardized education and access to self-referral to an assigned project nurse, or a control group following the current follow-up program with routine medicals. The primary outcomes are symptom burden and quality of life, measured by the Functional Assessment of Cancer Therapy – Colorectal (FACT-C) questionnaire. Other outcome and demographic data are collected as patient-reported measures and register-based data.

Results from developing the intervention: The education program is based on data from two focus group interviews and the feedback from experts. An algorithm is developed in order to qualify the research nurses' responses to patients' self-referral.

Discussion and perspectives: The results of the FURCA study will strengthen the evidence base for RC follow-up, and qualify the ongoing transformation in cancer follow-up programs.

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Rectal cancer (RC) is one of the most common cancer types worldwide [1]. In Denmark, a total of 1674 new RC patients were diagnosed in 2014 [2]. Historically, RC has been associated with high risk of local recurrences, and poor long-term survival prognosis. The last decades' improvements in treatment have led to a marked decrease in the risk of local recurrence and mortality from RC [3,4]. The risk of local recurrence is 7–9%, and the overall five-year survival rate is now 62% [2,3]. About 65–70% of RC patients receive treatment with a curative intent. The treatment is mainly surgical resection of the rectum, often combined with oncological treatment (35–40%) [2,3].

In Denmark, current follow-up programs of RC patients comprise one- and three-year postoperative computed tomography (CT) scans to detect distant metastases. The carcinoembryonic antigen (CEA) is measured on the same occasions. Furthermore, patients are invited to frequent outpatient visits including rectal examination to detect local recurrence. This is supplemented by a colonoscopy every five years until the age of 75 years [5].

The majority of local recurrences initially present clinical symptoms, leading to further investigation [6,7]. The evidence for routine examinations in detecting local recurrences is inconclusive [5,8]. Whereas follow-up programs primarily focus on detection of recurrence, there is less attention to late adverse effects. The exception being stoma patients, who systematically receive supportive follow-up care, as described in national guidelines [9].

With an increasing number of RC survivors, we see a rising attention to the late effects of treatment for RC. Recent studies have shown that almost half of the RC patients treated with the sphincter-sparing low anterior resection procedure suffer from severe bowel dysfunction one year after their operation [10,11]. Other common physical adverse effects

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from the treatment are urinary dysfunction, sexual dysfunction, pain and fatigue [12–14]. Psychological distress and fear of recurrence are known psychological adverse effects following treatment for RC [15,16]. All of these effects could influence negatively on the patients' symptom burden, everyday functioning and quality of life [17].

Patients and clinicians have requested a more patient-centred follow-up, with an increased focus on physiological and psychological late adverse effects [5,18]. Also, the Danish Health Authorities recommend a more individualized follow-up, in order to treat the adverse effects of RC treatment and detect recurring cancers [5]. In general, patient involvement aims at empowering patients to make qualified and informed decisions, often reported with positive patient-reported outcomes [19].

As a consequence, the study Follow-up after Rectal Cancer (FURCA) has been launched, testing the effect of a new patient-led, follow-up program. In this program, patients are empowered to actively take a role on the path to their own care, and prescheduled outpatient visits are abandoned.

The main hypothesis is that the patient-led, follow-up program will lead to early identification and treatment of late adverse effects after RC treatment. First, this is expected to reduce the symptom burden from physical and psychological symptoms and improve the quality of life of each individual patient. Second, the new program might lead to earlier detection of local recurrence. Finally, the assumption is that the new program will optimize the use of economic resources. Thus, the objectives of the FURCA study are:

1. Developing and implementing a new patient-led, follow-up, RC program, based on thorough patient education and involvement, and self-referral by direct access to a project nurse.
2. Examining the effect of the new follow-up program on symptom burden and health-related quality of life.
3. Examining the effect of the new follow-up program on specific physiological and psychological symptoms and late adverse effects from treatment, event-free survival, time to recurrence, patient experienced satisfaction, information and involvement.
4. Evaluating the cost-effectiveness of the new follow-up program.

Aim

The aim of this paper is to describe the methodology used in the FURCA study and to report results from the development of the intervention – a patient-led, follow-up program after RC.

Material and methods

Design

The study is designed as a multicentre, randomized controlled trial (RCT) with follow-up in three years (see Figure 1).

Participants

Patients treated for RC in four Danish colorectal surgical departments in Aarhus, Randers, Herning and Aalborg are invited to participate. These centers cover one third of all Danish RC patients [2].

Inclusion criteria

1. >18 years of age;
2. Surgical resection for primary adenocarcinoma in the rectum (0–15 cm from the anal verge, determined by endoscopy);
3. Pathologically verified R0/R1 resection;
4. Reads, speaks and understands the Danish language;
5. Written informed consent.

Exclusion criteria

1. Dementia or other mental disorders affecting cognitive functions;

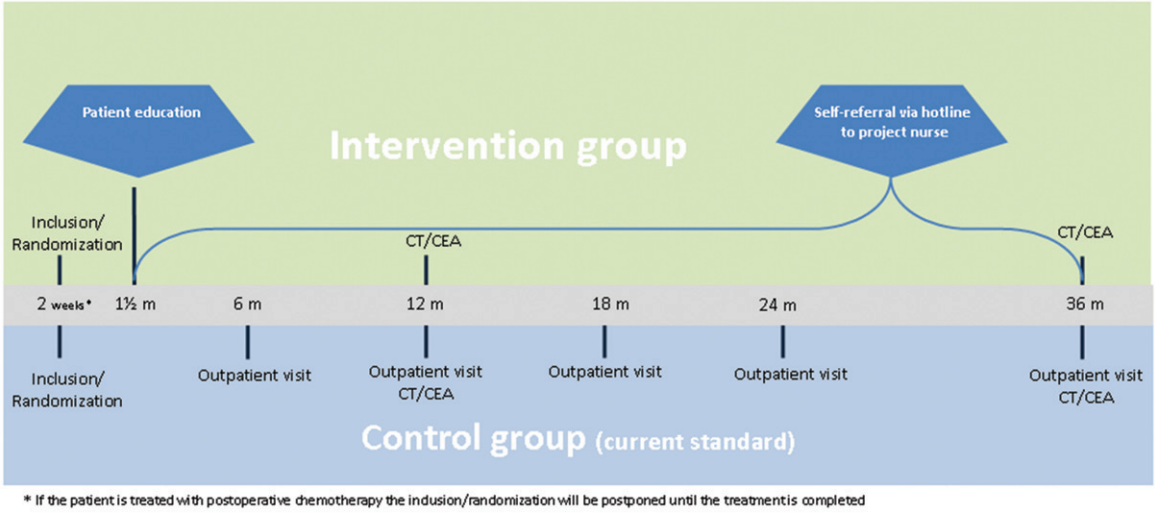

Figure 1. The trajectory of the FURCA study: randomization, intervention and control group.

2. Patients treated with local excision of the tumor (without resection of the rectum);
3. Non-radical resection (R2);
4. Known metastases;
5. Residual life expectancy less than two years;
6. Synchronous cancer;
7. Concurrent participation in other scientific studies which affect frequency and content of the follow-up program.

Verified recurrence, death, emigration from the participating regions or if a patient requests to interrupt participation is registered as loss to follow-up.

Recruitment

Patients are approached at the first postoperative visit in the outpatient clinic, approximately two weeks after the operation, where they are presented with the pathology results from the surgery. The surgeon provides a short verbal presentation about the FURCA study and hands out written information. The information is followed by a telephone call from a research nurse a few days later. Participants are asked to submit informed written consent and baseline information prior to randomization.

Patients receiving postoperative chemotherapy are contacted by the research nurse after treatment ended.

Randomization

Randomization is performed using a predefined randomization module in the Research Electronic Data Capture (REDCap) database [20]. A block randomization is set up to stratify by center, sex and treatment type (± postoperative oncological treatment and ± temporary ileal stoma).

Participants are randomized (1:1) into either the intervention group or the control group, and follow-up time is three years (see Figure 1). Non-participants are asked to complete a baseline questionnaire similar to the one filled on by participants.

Participants in the intervention group attend the patient-led, follow-up program, and do not attend regular prescheduled visits in the outpatient clinic. They receive structured education by a nurse, focusing on early signs of recurrence of the cancer and symptoms of adverse effects, and how to respond adequately. The education is performed by the affiliated research nurse, and based on a protocolled manual. Participants are instructed to approach the research nurse in case of symptoms and are informed of the necessity of contacting the research nurse immediately in case of defined alarm symptoms (self-referral). Participants can contact the research nurse by telephone and e-mail all weekdays. The research nurse responds to patient's self-referral according to a predefined, standardized response-algorithm.

The development of the intervention is described in Section 3.

Participants in the control group follow the current standard follow-up program. This comprises prescheduled visits, including rectal examination (digital and/or endoscopic) in the outpatient clinic at 6, 12, 18, 24 and 36 months postoperatively.

Follow-up related to detection of distant metastases is not the objective of this study. Thus, all participants will have a CEA test and a CT scan by 12 and 36 months postoperatively, disregarding randomization group. Patients in the intervention group receive results from the CT scan and CEA by mail, provided that no recurrence is suspected or detected.

Data and measures

The majority of the data for the FURCA study is collected by means of patient-reported outcome measures (PROM's). The PROMs are collected by baseline, and subsequently at one- and three-years follow-up. The remaining data is collected from national registries and databases (Figure 2).

The primary outcomes are symptom burden and health-related quality of life, measured by the 'Functional Assessment of Cancer Treatment – Colorectal' (FACT-C) [21].

Study data is collected and managed using REDCap electronic data capture tools hosted at Aarhus University. REDCap is a secure, web-based application designed to support data capture for research studies [20].

Study procedure

Statistical methods and sample size

Outcomes will be analyzed using methods for repeated measurements, and survival analysis. Any difference between the two groups will be significance tested, and adjusted for covariates, using multiple regression analysis.

Differences in demographics between the two groups will be calculated and significance tested using a χ^2-test (dichotomous and categorical data) and t-test (numerical data). Quality-adjusted life years will be calculated using standard health economic methods and in collaboration with an expert in health economics.

An estimation of sample size shows, that a total of 334 participants are needed in order to obtain statistically significant results in the primary outcome ($p < 0.05$).

Study timeline

Development of the intervention was performed during the second half of 2015. Inclusion of patients in the RCT was initiated in February 2016, and has been ongoing. By the time of writing, the inclusion is progressing as planned and is expected to be completed by the end of 2017. With a three-year follow-up period, the final results from the study will be analyzed and ready for publication by the beginning of 2021.

Ethical principles and description of risk

The risks and ethical concerns related to the project are limited, but there are some potential concerns. Removing routine follow-up could lead to a delay in detecting asymptomatic local recurrences. However, patients having symptoms with the opportunity of self-referral may get an earlier detection of recurrence.

Primary outcome	Data measures
Symptom burden and health-related quality of life	*'The functional assessment of cancer therapy – colorectal' (FACT-C)*
Secondary outcomes	**Data measures**
Bowel function	*'Low Anterior Resection Syndrome Score' (LARS), the 'Bristol Stool Scale' and "The Colostomy bother score"*
Urinary function	*'Male/Female Lower Urinary Tract Symptoms' (ICIQ-MFLUTS/ICIQ-FLUTS)*
Sexual function	*'The sexual function – Vaginal Changes Questionnaire' (SVQ), and the 'International Index for Erectile Function' (IIEF), for men and women respectively*
Pain	*'The Brief Pain Inventory Short Form' (BPI)*
Fatigue	*'The Multidimensional Fatigue Inventory' (MFI)*
Fear of Recurrence	*'The Fear of Cancer Recurrence Inventory' (FCRI)*
Psychological distress,	*'The Hospital Anxiety and Depression Scale' (HADS)*
Self-efficacy	*'Patient Activation Measure' (PAM).*
Patient involvement, information and sense of security	*A combination of two Danish questionnaires.*
Time to recurrence, 3- year survival	*Data from national registries*
Cost-benefit – QALY's	*Health care utilisation data from national registries in combination with data from the project registration and the patient reported data from the 'EuroQol 5-dimensional health state measure' (EQ-5D)*
Background information	**Data measures**
Personality	*'Life orientation test-revised' (LOT-R)*
Socio-economic background	*Data from national registries*
Co-morbidity	*Data from the Danish national colorectal quality database*
Clinical data	*Data from patient records*

Figure 2. Measures for outcomes and background information.

The study empowers the participants in the intervention group to be more involved in their own health care, which is desirable to some, but not to others.

Answering the questionnaire could remind participants about their disease and lead some patients to unpleasant or stressful situations. Patients agreeing to participate should feel secure in whatever group they are randomized to follow. It is the aim to ensure patients of this by thorough and explicit information at the time of inclusion.

All participants are asked to provide written informed consent. Data is handled and stored, according to national law and only anonymised results will be published. The study is reported and approved by the Danish Data Protection Agency. The study follows the ethical principles in the Helsinki Declaration [22], and is reported and approved by The National Committee on Health Research Ethics as required.

Results from developing the intervention

The two central elements of the intervention are the patient education, and the response-algorithm. The process of developing these elements is described below.

Patient education

The first draft of the patient education script was formed on the basis of available research and experience-based knowledge about cancer survivorship, long-term effects after treatment for RC, and patient education [23,24].

Subsequently, two focus group interviews were conducted with six male and seven female RC survivors.

The purpose of the two focus group interviews was first to obtain knowledge about patient experiences with receiving education and information about the course after treatment for RC. Second, to broaden the knowledge about the patients' requests for information regarding potential long-term effects and how to handle them.

Table 1. Participants in the male and female focus groups.

	Male (n = 6)	Female (n = 7)
Median age by time of interview (range)	67 (46–80)	57 (48–64)
Employment status by time of treatment		
• retiree	3	1
• employed	2	6
• self-employed	1	0
Marital status		
• married	6	3
• cohabiting	0	4
Preoperative oncological treatment (yes/no)	1/5	4/3
Postoperative oncological treatment (yes/no)	2/4	4/3
Stoma		
• Permanent	1	1
• Temporary	5	6
• No stoma	0	0

Participants were recruited from patient organizations and from one outpatient clinic. Information of the participants is shown in Table 1. They were selected due to the following criteria:

1. Completion of curative treatment for RC;
2. Co recurrence of the disease;
3. Acceptance of participation in the interview (completion of informed consent).

The interviews were designed and conducted as semi-structured research interviews, following the seven steps described by Kvale: thematization, design, interview, transcription, analysis, verification and reporting [25].

In the analysis of the interviews, a systematic, five-step method of condensation was used, also described by Kvale [25].

Results from the focus group interviews are presented in Table 2.

Table 2. Results from focus group interviews.

Theme	Content
Experiences with information and support	• Nearly all participants reported that they generally experienced a low level of information regarding the late effects from their treatment, especially regarding risk of bowel dysfunctions • All participants were satisfied with information levels and support related to temporary and permanent stoma care • Patients (in both groups) with temporary stomas reported that they lacked support after the closure of the stomas • Nearly all female interviewees agreed that they lacked information about dietary advice, while this was less important for the male participants • Lack of information about the follow-up program and where to get support was mentioned in both focus groups • Three of the female participants described insufficient information regarding chronic pain
Request for information	• The female patients requested more overall information regarding all potential late effects, in particular bowel function, diets and where to address questions and problems • All participants, both men and women, agreed on the need for more information about bowel function after closure of a temporary stoma • The male patients did not agree internally regarding levels of information. Two of them thought it best to know as little as possible, while the rest of the group requested more extensive information
Setting or methods of delivering information to patients	• The interviews revealed several ideas and views on preferred setting and framework for patient information and education. • All agreed on the importance of bringing dialog and attentiveness from a professional into an educational setting • Some preferred the group-based, informal education • Others preferred the more personal, one-to-one method • Some preferred films and written material; others preferred the narrative approach

Content (information)
The follow-up programme – what to expect and when
Signs of local recurrence – and how to react
Physical adverse effects: • *Pain* • *Bowel dysfunction* • *Urinary and sexual dysfunction* • *Fatigue*
Psychological reactions
Support and counselling – options and rights
Setting for the education:
Duration: 1 ½ hours
Participants: groups (max four participants, preferably with same type of treatment) or individual. Mixed gender
Place: outpatient setting
Devices: narratives, film, posters, website

Figure 3. Content and framework for the patient education.

The knowledge extracted from the focus group interviews were used to adjust the first draft of the patient education manuscript. The most important adjustments made were adding dietary information to the script, and extending the didactic approach to include film, narratives and supplementary information on a website. Furthermore, a group-based education style, with room for an individualized approach was chosen.

The adjusted education protocol and manuscript were evaluated by medical experts and an expert in patient didactics. Content and framework for the patient education is displayed in Figure 3. Finally, an evaluation of the education program, including participating patients in the intervention group, was conducted during the first six months of the study.

At present, 17 patients have received the education, 15 of which have completed the semi-structured telephone interview regarding the evaluation of the education program. The results show that all patients were satisfied with the education program. Although all patients gave positive feedback regarding the education, some comments about potential improvements will be taken into consideration:

1. 'It is desirable to receive the education with no other patients present, or at least the other patient(s) taking part should have a similar treatment course'. This feedback will be used to improve planning the group constellations or in some cases lead to the planning of individual education.
2. 'It can be distressing to receive comprehensive information of potential long-term effects'. This will motivate an improved effort to present the information in the least distressing way. Although it will not affect the content, as it is crucial that the patients receive and understand all relevant information (per protocol).

Response-algorithm

The response-algorithm was developed by the participating health professionals in the project group. Initially, symptoms and worries regarding potential signs of recurrence, late effects and psychological wellbeing were identified. Subsequently, the main subjects were elaborated on further and adequate responses were established through a workshop and follow-up correspondence within the project group.

Representatives from the primary sector and other relevant specialities were involved during this process.

The final response-algorithm covers detailed descriptions of potential patient-reported symptoms or problems related to bowel function, urinary and sexual function, pain, fatigue, other somatic symptoms and psychological distress. The symptoms are categorized into four levels of severity and it is clearly described exactly how the project nurses must respond according to type and severity of the symptoms. The response-algorithm can be provided from the authors on request.

Discussion and perspectives

The purpose of the patient-led program is to reduce symptom burden and improve quality of life for all patients attending follow-up after RC treatment, by improving support if needed and by removing unnecessary and potentially stressful routine outpatient visits.

The results from the focus group interviews, in accordance with results from other studies, confirmed that current information and support regarding late effects is insufficient [26]. Furthermore, they supported the assumption that stoma patients receive adequate postoperative support.

The approach to follow-up after cancer treatment is undergoing a transformation, with an increased focus on patients' needs after treatment and how patients value follow-up. Alternative methods to the traditional follow-up programs include shared care models involving primary care practitioners, nurse- or patient-initiated models. Although the evidence for alternative methods is inconclusive, patients consistently report certain conditions for good follow-up: sufficient information, good accessibility of support, and the same affiliated professional during follow-up [18,26].

'Patient involvement' and 'individualized care' are often used as buzz-words. However, this should not lead to unsubstantiated follow-up programs. More evidence is required to develop a safe and supportive follow-up for all cancer patients, disregarding patient background, social resources and place of treatment.

Patient-led follow-up after cancer is built on patient involvement, and the purpose and methods need to be clearly defined to avoid vulnerable patients from being left to their own devices.

The main elements in the FURCA intervention are: empowering the patient, increasing the accessibility to support and lowering the threshold for patients' self-referral. This is in accordance with the common purpose of patient involvement, aimed at empowering patients to make qualified and informed decisions [19].

In the process of developing the FURCA intervention, scientific and experience-based knowledge was utilized in combination with empirical data from focus group interviews. This was crucial to secure a sufficient patient perspective, and to involve relevant stakeholders.

The knowledge derived from the focus group interviews contributed to a more specific approach in the education program used in the FURCA intervention.

Results from the FURCA study will contribute to strengthening the evidence base for RC follow-up, and may impact the future follow-up of RC patients in Denmark and internationally.

If the new follow-up program proves successful, it will be readily implementable in daily clinical practice at a national level. Also, it may attract international attention due to the huge number of affected patients and the high level of costs all over the Western world.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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