QoLiCOL - Quality Of LIfe in COLon cancer

A STUDY WITHIN THE SCANDINAVIAN SURGICAL NETWORK FOR CLINICAL TRIALS

CONTENT

1. INTRODUCTION

1.1 Protocol committe

Eva Angenete, MD, PhD, Department of Surgery, Sahlgrenska University Hospital/Östra and Sahlgrenska Academy.

Eva Haglind, MD, PhD, professor, Department of Surgery, Sahlgrenska University Hospital/Östra and Sahlgrenska Academy.

Stefan Skullman, MD, PhD, Department of Surgery, Skaraborgs Kärnsjukhus, Skövde and Sahlgrenska Academy

Kajsa Holm, research nurse, Department of Surgery, Sahlgrenska University Hospital/Östra and Sahlgrenska Academy.

Elisabeth González, research nurse, Department of Surgery, Sahlgrenska University Hospital/Östra and Sahlgrenska Academy.

1.2 Steering committee

Protocol committee.

1.3 Writing committee

In agreement with internationally accepted guidelines ("the Vancouver criteria") for authorship the members in the protocol group who are active in planning, running, analysis and writing will be part of the writing committee. Doctoral/post.doc students actively working with the trial will also be included in the writing committee. Final decision on participation in the writing committee will be left to the PI and deputy PI. All decisions regarding research questions and extraction of data will be taken by the PI and deputy PI.

Publication of results is planned to be in international "peer review" scientific journal.

1.4 Coordinating centre

SSORG/Göteborg, Department of Surgery, Sahlgrenska Academy at University of Gothenburg, Sahlgrenska University Hospital/Östra

1.4.1 Principal investigator

Eva Angenete, M.D., Ph.D., Department of Surgery, Sahlgrenska Academy at University of Gothenburg, Sahlgrenska University Hospital/Östra

1.4.2 Deputy Principal Investigator

Eva Haglind, MD, PhD, professor, Department of Surgery, Sahlgrenska University Hospital/Östra and Sahlgrenska Academy.

1.4.3 Ph.D.-student

Will be assigned later on in the study.

1.5 Protocol summary

All patients presenting at participating hospitals during the recruitment period with a newly diagnosed colon cancer, regardless of stage and planned treatment, will be eligible for inclusion. They will answer a questionnaire on health related quality of life, physical

symptoms, functional impairments and
socioeconomic status at diagnosis and after 12, 36 months. Clinical data including recurrence, survival, surgical treatment, oncologic result (pathology report) and adjuvant treatment will be collected from the Swedish ColoRectal Cancer Registry (SCRCR)

2. PROTOCOL

2.1 Background

Colon cancer is one of the most common cancers in Sweden as well as in the world [1] and is treated with surgery and postoperatively sometimes with additive treatment such as adjuvant chemotherapy [2]. The overall survival after curative treatment is over 60%. Preoperative information prior surgery for colon cancer may be scarce and need improvement [3], and it is also important to evaluate what information patients retain.

There are indications that pre-treatment QoL and morbidity may affect clinical results and even survival [4-8]. It is often assumed that chemotherapy as an adjuvant (prophylactic) treatment for colon cancer patients may reduce QoL, but there is data indicating otherwise [9], supporting that more studies are needed to fully explore the long-term QoL in this patient group. It has also been shown that tumour stage at presentation has an effect on QoL [10]. Waiting for diagnosis and treatment may cause distress and anxiety, but the studies regarding colon cancer are scarce and evidence is lacking [13]. The effect on the tumour growth and survival in regard to delay of diagnosis and treatment has been studied in a Danish population indicating that it had no effect on stage of the disease at diagnosis [14] for colon cancer patients. However, if it has an effect on the QoL it is still of importance.

Studies indicate that cancer survivors may have different QoL in different age groups, older patients having better QoL than younger [15] and data also indicate that social support may improve QoL in colorectal cancer survivors [15]. There are modifiable factors that impact QoL such as lifestyle changes, financial difficulties, stoma-related problems and thoughts about the future [16-19], and a more thorough study regarding QoL, patient lifestyle and the patient experience of colon cancer may reveal possible interventions to improve QoL. Colon cancer surgery is associated with a substantial morbidity and this may have an effect on the financial situation of the individual patient [20,21]. The morbidity itself, especially if complications occur may negatively affect QoL [22] and this must also be addressed. Also, cultural aspects must be taken into account when addressing QoL [23].

The surgical technique is of importance in the short-term evaluation of QoL [11,12], but there are no indications that it affects long-term function. However, surgical technique affects nerves and may cause sexual dysfunktion. Sexual dysfunction is important to address, most patients want to be assisted in their situation [24]. However, there are many factors to take into account when assessing sexual effects after QoL, such as demographic, medical and psychosocial factors [25].

In the clinical setting, QoL may not always be in focus during long term follow-up [26]thus the surgeon's scientific knowledge about QoL problems may improve patient satisfaction and the patient-doctor relationship.

The aim of the present study is to explore QoL preoperatively, after 1, 2 and 5 years to explore and identify symptoms and problems of QoL in colon cancer patients.

2.2 Study design

QoLiCOL is an explorative, prospective, longitudinal, non-interventional, international, multicenter study of health-related quality of life, physical symptoms, functional impairments and socioeconomic burden in colon cancer patients. All patients presenting at participating hospitals during the recruitment period with a newly diagnosed rectal cancer, regardless of stage and planned treatment, will be eligible for inclusion. Patients will be followed for 3 years. They will be asked to answer questionnaires at three different time points during follow-up: at diagnosis and after 12 and 36 months. Clinical data, including recurrence, surgical treatment, oncologic result (pathology report) and adjuvant treatment will be collected from the national quality registry for rectal cancer in Denmark and Sweden. As these registries differ in some areas between the countries, additional data will be collected through short CRF:s (see below).

2.3 The hypotheses

As this is an exploratory study many hypotheses have been developed:

- A colon cancer diagnosis may affect quality of life
- Quality of life may not necessarily be lower in patients with an advanced colon cancer compared to patients with a localized tumour
- A questionnaire with longitudinal follow-up may detect differences in patient expectations and experiences over time
- Complications associated with colon cancer treatment may affect quality of life as well as the socioeconomic situation for the patient
- Preoperative quality of life may affect coping strategies and quality of life 1, 2 and 5 years after initiated colon cancer treatment
- Patient expectation of cure of the colon cancer influences QoL
- Gender, age and education level may influence QoL during treatment and follow up

2.4 Endpoints

2.4.1. Primary end-point

The primary end-point is to describe QoL, symptoms and functional impairments in an unselected population of colon cancer patients

2.4.2. Secondary end-points

- Generate basic descriptive data of the patient population, such as demography, socioeconomic data, disease stage at diagnosis, type of treatment, recurrence and survival
- Compare differences in QoL between patients with different tumour levels
- Detect differences in QoL in patients over time after colon cancer treatment
- Evaluate the effect of complications after colon cancer surgery on the patients socioeconomic situation
- Evaluate the effect of coping strategies on QoL after initiated treatment
- Describe patient expectations at diagnosis of colon cancer
- Identify differences in QoL between patients in different groups regarding gender, age and education level
- Analyse how clinical factors like oncologic result of operation, morbidity, recurrence and survival influence QoL

- Identify areas of improvement in treatment and patient care
- Enable initiation interventional studies when appropriate
- Analyse health economy aspects of QoL and morbidity in the patient population

2.5 Ethics

The trial must be approved by the appropriate ethics committee for each participating institution prior to entry into the study. In Sweden the coordinating centre (Sahlgrenska University Hospital) will apply for all Swedish participating centres.

In Denmark professor Jacob Rosenberg will apply for all Danish participating centres.

Eligible patients will be informed personally by a surgeon or a research-nurse and given written information about the trial. Informed consent should be obtained from each patient according to the guidelines of the ethical committee. Patients remain free to withdraw their consent to participate in the study at will and at any time without giving their reasons.

2.6 Eligibility

2.6.1 Inclusion criteria

All patients presenting at the participating hospitals with a newly diagnosed colon cancer, regardless of stage at diagnosis and treatment, will be eligible for inclusion.

2.6.2 Exclusion criteria

- Age below18 years at diagnosis.
- No informed consent received or withdrawal of informed consent.

2.6.3 External validity

A screeninglog is held at each participating hospital and will be cross checked with the Swedish ColoRectal Cancer Registry.

All newly diagnosed colon cancer patients are registered in a “screening log”. The “screening log” is kept at each participating hospital and reported quarterly to the study secretariat. The reason for non-inclusion or exclusion should always be noted. Patients who do not wish to participate are registered as “no consent” by initials, clinical stage at presentation, age and gender. Missed patients are registered as ”missed” in the same manner, i.e. by initials etc. The study secretariat will keep a list of all patients with rectal cancer who do not fulfil inclusion criteria or have been excluded or missed. Lists of patients included at each participating hospital will be sent to the respective local investigator. If the patient wants to withdraw her/his earlier consent, all data regarding her/him will be deleted. Patients who do not answer questionnaires are asked if they want to quit the study. If so, no further information will be collected and the patient will be asked if all data collected so far should be deleted or can be kept.

2.7 Inclusion of patients

All newly diagnosed colon cancer patients presenting at participating hospitals will be asked about participation. Patients will be included when they have received information about their planned treatment.

Full identity, address and telephone numbers are registered by telephone and fax to Regionalt cancercentrum väst (RCCV) in Gothenburg, where the inclusion data base is kept. This data enables SSORG/Gothenburg to contact patients and to send out questionnaires.

2.8 Questionnaires

Patients will answer questionnaires at the following time-points:

- At diagnosis, i.e. at presentation of a plan for the treatment
- At 12 months after start of the treatment
- At 36 months after start of the treatment

The questionnaire has been constructed based on a concept developed by Steineck et al [27,28]. It contains detailed questions about the quality, frequency, intensity and duration of rectal cancer-specific symptoms as well as questions on functional impairments, psychological symptoms, socioeconomic status and demography.

It has been developed using well-validated and previously described methods. The questionnaire was developed using in-depth qualitative interviews as a base together with previously validated questions [29,30], and an expert panel consisting of colorectal surgeons, oncologists, gynaecologists, nurses specialized in surgery then performed a content validation. The questionnaire has been face-to-face validated by colon cancer patients using the validation methods described previously for a questionnaire for prostate cancer patients [30].

The time frame in most of the questions is set to "the last month" to achieve as true answers as possible. When appropriate, patients have been asked about the quality, frequency and intensity of a symptom as well as the corresponding bother [28]. All questions including quality, frequency and intensity of sexual function/activities included the alternative: "Not applicable, I have not had any sexual activity/been sexually aroused within the last month" and some questions also included "I don't know" as an option.

Psychological symptoms, well being, and the subjective quality of life are assessed in an ordinal seven-point Likert-type response format.

To facilitate health economy analyses and comparison with the general population, a commonly used generic instrument, EQ-5D, has been included in the questionnaire. It also includes the Sense of Coherence (SOC) scale (KASAM in Swedish) [31].

2.9 Data collection

The study secretariat at SSORG/Gothenburg, Sahlgrenska University Hospital/Östra handles routines for sending out of all questionnaires: 0, 12 and 36 months after inclusion and reminders. The first questionnaire will be sent out as soon as the patient has been registered in the inclusion database.

Each questionnaire is given a patient specific code. The patient code number and the possibility to identify individual patients is stored at the Sahlgrenska University Hospital, on a server within the hospital IT system, using the inherent security system.

The questionnaires are returned to the study secretariat and collected data is stored within the server of Gothenburg University without any personal identification other than the patient code. Data from the national quality registries for rectal cancer will be retrieved and added. Data may be used for analysis and publication from time "0" as

soon as full accrual has been reached, from time "12 months" when all included patients have passed that time point etc. Data can only be analysed or copied from the database by decision of the principal investigator and the deputy principal investigators together. All such decisions should be discussed by the steering committee.

The database will be registered at "personuppgiftsombudet", Sahlgrenska University Hospital. Monitoring of collected data and compliance to the study protocol is achieved through contacts with the local investigators and annual visits to participating departments.

Clinical and oncologic data is collected from the national quality registries in Sweden and Denmark.

2.10 Study organization

The secretariat will be in the Scandinavian Surgical Outcomes Research Group unit in the Department of Surgery, Område 2, Sahlgrenska University Hospital, Göteborg. In each participating hospital a local investigator will be responsible for the inclusion, the control of the internal validity, the data collection and participate in the steering committee.

The trial will be registered at the website ClinicalTrials.gov for clinical trials.

2.11 Work plan

Ethical permission will be submitted to the Gothenburg Ethical Committee in December 2014. The study will commence in February of 2015.

2.11 Statistical Methods

Depending on tumour stage at presentation, the study population of 1500 patients will fall into the following subgroups: palliative treatment (20-25%), curative surgery (40-45%), curative surgery followed by adjuvant treatment (25-30%). This will allow for prevalence estimation of health related factors with differences between groups down to 15 %, even between the smaller subgroups, with a statistical power of 80 %. This estimate is based on binominal distribution approximation with a prevalence of 50 % and significance of 5 %.

3.0 FINANCING

This study is supported by ALF grant held by Eva Angenete, ALFGBG-526501 and The Swedish Cancer Society CAN 2013/500.

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