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Original article

Phase I–III development of the EORTC QLQ-ANL27, a health-related quality of life questionnaire for anal cancer

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ABSTRACT

Background and purpose: There is currently no health-related quality of life (HRQoL) measure specific to anal cancer. Our objective was to develop an anal cancer HRQoL module to supplement the EORTC QLQ-C30 questionnaire using EORTC Quality of Life Group Guidelines.

Materials and method: In order to generate a list of HRQoL issues facing anal cancer patients treated with chemoradiotherapy (CRT), we systematically reviewed the literature and conducted semi-structured interviews with patients and health care professionals (HCPs). Our list was then operationalised into questions using the EORTC Item Library. The provisional question list was pilot tested alongside the EORTC QLQ-C30 with patients from 11 centres across 8 countries.

Results: From our literature review and interviews with 43 patients, we generated a list of 197 issues. The list was then refined to 134 issues and reviewed by 34 HCPs and 10 patients. This review resulted in the retention of 65 issues which were used in the draft questionnaire tested by 100 patients. Our analyses led to the modification and removal of questions resulting in a 27 item questionnaire, the EORTC QLQ-ANL27.

Conclusion: We have developed a 27 item questionnaire to supplement the EORTC QLQ-C30, for use with patients treated for anal cancer. This has been pilot tested and is now available upon request for use in clinical trials as well as clinical practice in 8 languages (http://groups.eortc.be/qol/).

Anal carcinoma is rare, accounting for 2% of all gastrointestinal malignancies and 10% of all anorectal malignancies, but with increasing incidence over the past 25 years and higher incidence in women [1,2]. The current standard of care for patients with non-metastatic squamous cell anal cancer is concurrent chemoradiotherapy (CRT) [3–7]. In most cases, this has replaced surgical management and provides definitive treatment with the hope of sphincter preservation. The overall 5 year survival rates reach approximately 75%, colostomy free survival rates are 65–70% and complete clinical response rates around 80–85% [8]. While treatment outcomes are promising, associated toxicities are common, potentially long lasting, and impact on health-related quality of life (HRQoL). Clinician-reported acute grade 3 or 4 toxicities can be as high as 80% [9] with severe late effects (often defined as persisting 5 years or more post-treatment) recorded in about 10% patients [7]. The impact of these toxicities on HRQoL is acknowledged as an important outcome guiding decisions regarding treatment choices [10,11]. Indeed, achieving good HRQoL alongside loco-regional control and the avoidance of a permanent stoma are identified within clinical practice guidelines as the primary aim of anal cancer treatment [3]. However, currently there is no anal cancer specific HRQoL measure.

In the era of precision radiotherapy where clinical trials evaluating dose escalation and de-escalation are pivotal in improving treatment, the importance of accurate measurement of HRQoL and symptomatic toxicity is of uttermost importance [12]. Complications following CRT include radiation enteritis, diarrhoea,

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proctitis, skin desquamation, strictures, stenosis, sexual dysfunction, dyspareunia, pelvic fractures, induced menopause, lymphedema, urgency and frequency of defecation, stool incontinence, and urinary tract dysfunction [13]. Our literature review [13] identified a number of reports of treatment complications and toxicities associated with CRT for the treatment of anal cancer. The majority are from small-scale retrospective case reviews. There is limited information on HRQoL and in particular long-term effects of the disease or treatment. Some of the claims regarding HRQoL issues are speculative and not substantiated by formal assessments. The small number of studies assessing HRQoL of anal cancer patients [10,11,14–22] use questionnaires validated for use with colorectal cancer patients such as the European Organisation for Research and Treatment of Cancer (EORTC) Colorectal Cancer Specific Quality of Life Questionnaire (EORTC QLQ-CR38/CR29) [23,24] and the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) [25]. While anal cancer and colorectal cancer have similar profiles in terms of symptoms and treatment-related side-effects, there are a number of issues, such as skin toxicity, lower limb lymphedema, anal pain and bleeding, which are specific to anal cancer patients treated with CRT [13]. Many of these issues are not covered at all or are inadequately represented in existing questionnaires. It therefore follows that there is a clear need for a validated HRQoL measure specific to the concerns of anal cancer patients treated with CRT.

The EORTC questionnaire, the EORTC QLQ-C30 [26], was designed to capture the generic aspects of HRQoL for cancer patients and while it is appropriate for all cancer types, it is not specific to any tumour site, treatment modality or HRQoL dimension. The EORTC Quality of Life Group (QLG) advocates a modular approach to the development of questionnaires designed to be used alongside the EORTC QLQ-C30. This paper describes the development of an anal cancer specific questionnaire, the EORTC QLQ-ANL27 using EORTC QLG guidelines [27].

Materials and method

The development of EORTC QLG modules follows four phases [27]. In Phase 1, HRQOL issues are generated through interviews with patients and health care professionals (HCPs), and a literature search. These HRQOL issues are reviewed and revised in Phase 2 and questionnaire items are formulated. In Phase 3, the questionnaire items are pilot tested and a provisional version of the module is developed. In Phase 4 the new module undergoes international field testing. The work reported here describes Phases 1–3. The study protocol was approved by the EORTC QLG. Ethical and research governance approvals were obtained at each centre in accordance with local requirements and all patients provided written informed consent. The study was coordinated from Southampton, UK with additional centres in, Canada, Cyprus, Germany, Greece, Italy, Norway, and Poland. Collaborator meetings were held every six months, with regular email discussion and telephone conferences between these times.

Phase Ia HRQoL issue generation

In order to generate an initial list of HRQoL issues, a systematic review of literature published between January 1996 and March 2014 was undertaken. English language papers describing patients treated with CRT for anal cancer were eligible for inclusion and included randomised controlled trials, case reviews/series, trials of quasi-experimental design, meta-analyses and reviews. Papers reporting conference proceedings and abstracts, study protocols and individual case reports were excluded from the review. Further details of the literature review process are described elsewhere [13].

Patient interviews

Patients with a confirmed diagnosis of primary newly diagnosed or recurrent locoregional anal cancer (squamous or cloacogenic cell cancers with histological confirmation) were invited to participate in semi-structured interviews. Purposive sampling was used to include patients in the acute, early and late treatment phases (<6 months, 6–24 months and 2–5 years from the start of treatment respectively) as well as a good distribution of males and females although we anticipated a bias in recruitment of females. Patients with a stoma were included in the sample. Recruitment of patients continued until data saturation was achieved.

Patients were asked to describe their experiences relating to diagnosis and treatment with CRT. Issues captured from the literature review were used as prompts. Patients were shown the EORTC QLQ-C30 to engage them in further discussion. Patients were also asked to consider which of the issues raised were most important to them. Sociodemographic and clinical data including performance status (Karnofsky Performance Status [28]) were recorded.

Phase 1b HRQoL issue review

Issues generated from the interviews and the literature review were used to devise a list which was distributed to the project collaborators for feedback and to check for missing issues. This led to the combination of some issues, modifications, and removal of issues with obvious overlap with the EORTC QLQ-C30. The revised list was then reviewed by a separate group of patients and HCPs with expertise in anal cancer. HCPs and patients were asked to rate each issue in terms of importance on a 4-point Likert scale ranging from 1 "Not at all" to 4 "Very much". They were then asked to nominate 10 of the most important issues which should be included in the questionnaire and to identify issues which should not be included.

Phase 2 construction of the provisional questionnaire

EORTC QLG guidelines were followed to determine which issues should be removed and whether any new issues should be added to the list [27]. Issues were operationalised into items with a response format and time frame compatible with the EORTC QLQ-C30. The EORTC Item Library was the first reference point when devising items to correspond to the issues identified. Attempts were made to harmonise items, where possible, with existing EORTC QLG modules, such as the EORTC QLQ-CR29 [24]. Items were adapted and new questions devised as required. Items were translated into all the languages required for Phase 3, following the EORTC translation guidelines [29].

Phase 3 pilot testing the provisional anal cancer HRQoL questionnaire

Eleven centres across 8 countries were involved in pretesting the preliminary questionnaire: UK (Leeds, London and Southampton); Cyprus (Nicosia); Canada (Ottawa and Toronto); Poland (Krakow); Germany (Halle); Italy (Florence); Greece (Patras) and Norway (Oslo). The same inclusion criteria were used as in Phase 1. Patients involved in Phase 1 were not eligible to test the questionnaire.

Patients were interviewed and asked to complete the draft questionnaire as well as the EORTC QLQ-C30. Patients were then debriefed and asked to rate whether each of the anal cancer questions had been relevant to them at any time since their diagnosis or treatment, i.e., whether an issue is something they recognise as having happened to them. In addition, if the question was relevant, they were asked to rate how important or bothersome it had been to them using a 4-point Likert scale ranging from "not at all

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