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Health-related quality of life is a prognostic factor for survival in older patients after colorectal cancer diagnosis: A population-based study

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ABSTRACT

Background: Studies carried out in the context of clinical trials have shown a relationship between survival and health-related quality of life in colorectal cancer patients.
Aims: We assessed the prognostic value of health-related quality of life at diagnosis and of its longitudinal evolution on survival in older colorectal cancer patients.
Methods: All patients aged ≥65 years, diagnosed with new colorectal cancer between 2003 and 2005 and registered in the Digestive Cancer Registry of Burgundy were eligible. Patients were asked to complete the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 at inclusion, three, six and twelve months after. Multivariate regression models were used to evaluate the prognostic value of health-related quality of life scores at diagnosis and their deterioration on relative survival.
Results: In multivariate analysis, a role functioning dimension lower than median was predictive of lower survival (hazard ratio = 3.1, $p = 0.015$). After three and six months of follow-up, patients with greater appetite loss were more likely to die, with hazard ratios of 4.7 ($p = 0.013$) and 3.7 ($p = 0.002$), respectively.
Conclusions: Health-related quality of life assessments at diagnosis are independently associated with older colorectal cancer patients' survival. Its preservation should be a major management goal for older cancer patients.

1. Introduction

Colorectal cancer (CRC) is a major cause of cancer morbidity worldwide. A high proportion of colorectal cancers occur in older people, with 75% of colorectal cancers diagnosed in patients aged 65 years and over [1]. The French population is ageing and because of increased life expectancy, a growing number of older subjects will be exposed to the risk of developing CRC. CRC therapies can induce toxicities that alter patients' health-related quality of life (HR-QoL). For older adults, HR-QoL can be preferred to survival, especially if treatments impact their functional capacity, their capacity to perform daily tasks, worsens their social situation or impact their ability to stay at home [2]. In the last decades, HR-QoL has become an important endpoint for clinical research, and is thus of greater importance for elderly patients [2,3].

In addition to quantifying the impact of treatments, there is evidence to suggest that HR-QoL data also have prognostic value. Indeed, several studies have shown a relationship between survival and HR-QoL in patients with colorectal cancer [4,5]. All of these studies were carried out in the context of clinical trials or in selected patients attending specialized hospitals and thus included patients with specific characteristics.

Since survival gain decrease and adverse effects could gradually increase with age, preservation of HR-QoL is a major goal in geriatric oncology [6]. Recently, studies assessing the prognostic value

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of changes in HR-QoL scores on survival have emerged from the literature [7–10]. To the best of our knowledge none investigated the existence of such an association in a cohort of older colorectal cancer patients.

The aims of this study were thus to examine the prognostic value of HR-QoL at diagnosis and to estimate the relationship between early deteriorations in HR-QoL and survival in older patients with colorectal cancer registered in a population-based cancer registry.

2. Materials and methods

2.1. Patients

Patients of at least 65 years of age, living in an administrative area of Burgundy (Saone-et-Loire area, 550,000 inhabitants), diagnosed between March 2003 and September 2005 with primary colon or rectal carcinoma were eligible to participate. All colonoscopies with a positive biopsy of colorectal carcinoma were identified each week by pathology laboratories and notified to the Burgundy Digestive Cancer Registry (for description of methods, see [11]). As soon as the patient was identified, a physician affiliated with the registry contacted the patient's personal physician so that the patient could be informed about the special survey and invited to participate. The questionnaires were given at the time of diagnosis (prior to surgery or any neo-adjuvant treatment), 3, and 6 months after diagnosis, directly to the patient by their general practitioner or sent by post. Registry's physician called back patient's personal physician if a reminder was needed. Completed questionnaires were returned by post to the Cancer Registry. All participants provided written informed consent.

2.2. Data collection

Cancer Registry activities are approved by the National Commission for Data Processing and Civil Liberties (CNIL). The quality of the data collection is evaluated every 4 years by the Institut National de la Santé et de la Recherche Médicale (INSERM), the Institut de Veille Sanitaire (InVS) and the Institut National du Cancer (INCa).

Age, sex, administration of radiotherapy or chemotherapy and clinical data concerning the cancer were collected for each patient from medical files by the registry's staff. The cancer site was classified according to the International Classification of Diseases for Oncology (ICDO3) [12]. Tumour extension at the time of diagnosis was classified according to the 7th TNM Classification of Malignant Tumours [13]. Non-resected cancers with no evidence of visceral metastasis were classified as 'unclassified' cases and pooled with stage IV metastatic cancer in an 'advanced cancer' group.

An active search for vital status at January 1 2012 was carried out using a standardized administrative procedure. No patient was lost to follow-up within the 5-year follow-up.

2.3. HR-QoL assessment

HR-QoL was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (QLQ-C30) version 3.0 [14,15]. The QLQ-C30 includes five functional dimensions (physical, role, emotional, cognitive, social), three symptom dimensions (fatigue, pain, nausea/vomiting), six single-item symptom scores (dyspnoea, insomnia, appetite loss, constipation, diarrhoea), one single-item estimation of financial difficulties and one global HR-QoL scale. A linear transformation was used to standardize raw scores so that all HR-QoL scores ranged between 0 (worst) and 100 (best) for functional scores and Global Health, and 0 (best) to 100 (worst) for symptom scales.

In accordance with the QLQ-C30 scoring guidelines [15], when at least half of the items from a dimension were answered, all items that were completed were used. As missing data were not linked to the characteristics of any patient or tumour, they were imputed using the simple mean imputation procedure [16]. Scores with less than 50% of items answered were ignored.

To obtain balanced sample size groups, HR-QoL assessments at inclusion were analyzed on dichotomized scores, with the median as the cut-off.

Changes in scores were calculated by subtracting HR-QoL assessments at diagnosis from those at three (T3) and sixth months (T6) for the same cohort of patients. Following recommendations provided by Osoba [17], differences of 10 points or more between T3 and T0 or T6 and T0 were considered clinically relevant. HR-QoL was considered diminished when a decrease of at least 10 points for functioning dimensions or an increase of at least 10 points of symptom dimensions was observed between two time points.

To estimate the survival of non-respondents and compare it with the survival in patients with baseline HR-QoL scores, we studied survival in three groups: patients with at least an HR-QoL assessment at diagnosis, patients who did not reply to the baseline QoL evaluation but replied to at least one QoL questionnaire among the four expected, and patients who did not respond to any questionnaire (non-respondents to the cohort study).

2.4. Statistical methods

Baseline characteristics of patients and tumours according to study participation were compared using the χ^2 test.

HR-QoL dimensions were described as median and interquartile range and mean ± standard deviation.

One and 5-year raw survival of the entire population of patients was computed according to Kaplan–Meier's method [18]. To eliminate the effect of age-related mortality, relative survival (RS) was calculated using the STREL programme [19]. One and 5-year-RS were computed for each group and each level of interest variables. RS at 5-years after diagnosis conditional on being alive at 1-year after diagnosis was also calculated. The calculation of conditional survival provides an accurate evaluation of the patient's changing risk over time. The prognostic value of HR-QoL on 5-year RS was expressed as hazard ratios (HR) with 95% confidence intervals (95% CI) and estimated in univariate and multivariate analysis using Esteve's model [20] with the approach described by Dickman [21]. The proportionality assumption was verified by testing the interaction with time.

The prognostic value of HR-QoL at diagnosis and the exploratory analysis of the relationship between HR-QoL deterioration and older patients' survival were assessed using the same model selection steps. First, in a univariate model, the association of each HR-QoL dimension with survival was independently assessed. Secondly, correlations were tested for eligible variables. When two variables had a strong correlation (Spearman correlation coefficient higher than 0.7), one variable was retained according to the value of the lowest AIC observed in the univariate models. Thirdly, dimensions with a p-value less than 0.20 were introduced simultaneously in a multivariate global model adjusted on sex, age category and tumour stage. In order to take into account the potential effect of treatments on the evolution of quality of life, multivariate analysis of early deterioration of quality of life were moreover adjusted on administration of chemotherapy and radiotherapy.

Statistical analyses were performed using Stata SE 13.1 software (Stata Corporation, College Station, TX, USA). All tests were two-sided with a significance level set at 0.05.