

Quality Of Life Of Early Stage Colon Cancer Patients At Least One Year After Surgery: Experience In A Small Community In Southern Catalonia.

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Quality Of Life Of Early Stage Colon Cancer Patients At Least One Year After Surgery: Experience In A Small Community In Southern Catalonia.

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Abstract

Aim Colorectal cancer (CRC) is one of the most common cancers and causes of cancer death worldwide. In the long term (5 or more years), the quality of life (QoL) of CRC survivors have been observed comparable to that of the normal population. However, very few studies have reported data on the QoL of early stage CRC patients (Stage I and II). The objective of this study was to evaluate the QoL in patients with early stage colon cancer who have undergone a surgery at least one year ago. The results have been compared with the QoL in the general population of a small community in southern Catalonia.

Methods A descriptive cross-sectional study was performed on the QoL of 72 early stage (Stage I and II) colon cancer patients (cases group) who were operated on between January 1, 2000 and April 31, 2010 at the Hospital de Tortosa Verge de la Cinta (HTVC). The QoL of the patients group was compared with 144 controls without prior history of cancer (controls group) selected from the general population covered by the HTVC area. QoL parameters were measured using the EORTC QLQ-C30 questionnaire (version 3.0) which had been adapted and validated into Spanish.

Results No significant difference in Global Health Status QoL was found between the cases and controls groups. However, CRC patients present significant better emotional and cognitive functioning but also more diarrhoea and less pain that controls group. No differences have been observed according to the age or the stage of colon cancer patients. Regarding the gender, women of the study present worse scores for functional and symptoms items that men. However, it is the women of controls group that appear to suffer more from emotional and cognitive functioning that colon cancer patients (both gender). Patients with colostomies showed more diarrhoea. Patients with left-sided colon cancer have better physical function that those with right-sided colon cancer. Patients with a follow up longer than 5 years suffer more from nausea/vomiting and insomnia.

Conclusion Survivors of colon cancer seemed to be relatively satisfied after treatment. Our data showed that QoL reached quite high levels in this group when compared to general population.

However, further studies are needed to develop a more comprehensive understanding of QoL and its determinants in colon cancer survivals.

KEYWORDS: Colorectal cancer, Quality of Life

Introduction

It is a common belief that cancer patients have poor quality of life as the disease affects them not only physically but mentally as well. This study gives a comparison of stage 1 and 2 colon cancer patients with general population and concludes that there is not much difference in the quality of colon cancer patients post resection as compared to controls at one-year follow-up. To date there is a scarcity of literature in this regard and most of the available studies describe the QoL among the patients without a control group of normal healthy individuals.

Colorectal cancer (CRC) is currently a worldwide major public health problem. It is the third most common cancer in men (663,000 cases, 10.0% of total cancer cases in men) and the second most common cancer in women (571,000 cases, 9.4% of total cancer cases in women) worldwide [1]. Almost 60% of CRC cases occur in developed regions. The incidence is higher in men than in women (overall sex ratio 1.4:1. About 608,000 deaths from CRC are estimated worldwide, accounting for 8% of all cancer deaths and making it the fourth most common cause of death from cancer [1].

In Spain, where CRC has an annual incidence of 2.6%, about 28,500 new cases of CRC were diagnosed and 14,300 people died from the disease in 2008 [2]. The overall CRC survival is around 50% at 5 years [3] and this mortality is directly correlated with tumour stage [4]. TNM Stage I (T1-2, N0, M0) has an estimated 5-year survival of 80 to 90%, Stage II (T3-4, N0, M0) 60-80%, Stage III (Any T, N1-2, M0) between 30% and 60% depending on the degree of differentiation, the number of affected lymph nodes and serosal invasion and Stage IV (Any T, Any N, M1) 3 to 10% at 8-10 months [5].

In recent years, a growing consensus among healthcare providers is that treatment efficacy should be judged not only by its effects on longevity but also on quality of life (QoL). There is general agreement among the medical and scientific community that patients are the source of information regarding their QoL. The use of self-reported QoL assessment has been reported in numerous recent studies, becoming a valuable tool in both clinical practice and research. Normally, the assessment of Health Related QoL (HRQoL) is done through self-administered questionnaires or by personal interview. The questionnaires are composed of a number of items, which in turn are grouped into areas according to their size or content and can be analyzed separately by each dimension. There are numerous general questionnaires for various diseases, including some specific questionnaires to assess QoL in patients with cancer. The European Organization for Research and Treatment of Cancer (EORTC) has designed and validated several questionnaires for the assessment of QoL in cancer patients. Among them, the Quality of Life Core-30 (QLQ-C30) [6] has been translated and validated into 81 languages, including for Spain, and has been used in more than 3,000 studies worldwide. The assessment of QoL can improve our

understanding of how cancer, by itself or by therapies applied to patients, influences their lives [7].

Recent CRC QoL studies have assessed the direct effects of the treatments during the first month after treatment and have shown that the QoL in these patients is reduced immediately after starting treatments but gradually improved after the conclusion of treatments, provided that there is no recurrence or progression of disease [8, 9]. This time period can be influenced by several factors [10], among which are the patient's age [11] and stage [12]. A recently published systematic review showed that the QoL in survivors of CCR, in the long term (5 or more years), seems comparable to that of the normal population. However, these survivors have a slightly lower quality of physical life, suffer from long-term symptoms such as digestive problems, common concerns about cancer and have worse rates of depression [10]. Other studies have shown that not only in long-term QoL, but also early stage CRC patients, present a better assessment of the overall QoL when compared with general population [13]. It has been hypothesized that these patients change their dimensions of QoL or establish a new concept of QoL [13] or find some benefits in the cancer experience, well known as post-traumatic growth found or benefits [14]. Another methodological explanation for the positive psychological aspects of CRC found on HRQoL despite these patients' higher rates of depression and worry about cancer, could be the lack of sensitivity of the versions of the scale or questionnaires used in the studies [10]. Very few studies have been conducted to analyze the QoL of patients with early stage colon cancer using the latest version of a validated questionnaire.

The objective of this study was to evaluate the QoL in patients with early stage colon cancer who have undergone a surgery at least one year ago by means of the QLQ-C30 version 3.0. The results were compared with the QoL in the general population of a small community in southern Catalonia.

Materials and Methods

Study design

A descriptive cross-sectional study design was used. The patients' samples consisted of early stage colon cancer patients (cases group) who were operated on between January 1, 2000 and April 31, 2010 at the Hospital de Tortosa Verge de la Cinta (HTVC), the reference hospital of a small community in southern Catalonia (Terres de l'Ebre). Inclusion criteria of the patients were as follows: men or women between 18 to 85 years old, operated on for Stage I or II colon cancer, with at least one year disease free follow up. The study was conducted in accordance with the "Ethical principles for medical research involving human subjects" of the Helsinki Declaration and was approved by the Ethics

Committee of the University Rovira i Virgili de Tarragona (Spain). One hundred nine patients who met the inclusion criteria were selected consecutively, while 37 were excluded because they refused to participate or they completed the questionnaire incorrectly. A total of 72 patient cases were included in the study.

The QoL of the patients group was compared with the general population. For this purpose, subjects who had no prior history of cancer (controls group) were selected from the general population covered by the HTVC area (a total of 180,000 inhabitants). The controls group subjects should not have been admitted to hospital or had hospital visits in the 3 months before the study. They were randomly selected from the primary care registry area and were matched with cancer patients for gender and age (stratified for +/- 3 years). Two controls were selected per case. A total of 144 control subjects were included in the study.

Eligible patients and controls were contacted by phone were enrolled in a monitoring visit, where they were offered to participate in the study. If they agreed to participate, their data was collected, and they were invited to complete the questionnaires EORTC QLQ-C30 in their primary care centre or in the HTVC.

Instruments

QoL parameters were measured using the EORTC QLQ-C30 questionnaire (version 3.0) which had been transculturally adapted and validated into Spanish [15]. The systemic evaluation of the QLQ-C30 consists of 30 items and incorporates five functioning scales (physical, role, emotional, social and cognitive functioning), three symptom scales (fatigue, pain and nausea/vomiting), a two-item global health status/QoL scale and six individual items which may occur in colon cancer patients (dyspnoea, appetite loss, insomnia, constipation, diarrhoea and financial difficulties).

Twenty-eight of these items have four scoring possibilities, ranging from 1 (not at all) to 4 (very often) and 2 items present 7 alternatives (visual analogue scale where 1 is "bad" and 7 "excellent"). The time frame should refer to the previous week. The appropriate statistical procedures for assessment of responses to the questionnaire have been described in an EORTC manual [16]. All scores are linearly transformed into a 0–100 scale. Higher functioning scores represent better functioning/QoL, whereas higher symptom scores represent more severe symptoms. In case of missing items, the values were replaced with the rounded mean of the remaining items of the corresponding subscale when at least 50% of the items of the scale were answered. Finally, the total score is simply defined as the mean of these 30 (partly transformed) items. This procedure assures that

the items with the 0–3 answer format and those with the 1–7 formats contribute equally to the total score.

Statistical analysis

QoL parameters using EORTC QLQ C30 questionnaires and medical secondary endpoints were analyzed using SPSS 15.00 statistics software (SPSS® Inc, Chicago, IL, USA). The medical records of the patients and controls were analyzed for age, sex, place of residence, marital status, education, work activity, source of first consultation, tumour location, type of operation, histological type, tumour stage, adjuvant treatment, complications (comorbidity, cardiovascular risk factors and toxic habits) and hospital stay.

A descriptive study was made of each variable using central tendency (mean, median) and standard deviations for continuous variables and frequencies or percentages for categorical variables. Pearson's Chi-square test or Fisher's exact test was used to compare discrete variables. The continuous variables were compared between groups using the Student's t test when Kolmogorov–Smirnov normality test and Levene's variance homogeneity test allowed it. When the data showed a distorted distribution, the non-parametric Mann-Whitney U test was applied. When Levene's variance homogeneity test allowed, an ANOVA was used to investigate the main interactions of gender and age and their effects on the different items of QoL assessed with the QLQ-C30. When the data showed no variance in homogeneity, the non-parametric Kruskal-Wallis test was applied. Post-hoc tests were performed to examine multiple comparisons when significant differences were detected. A p value <0.05 was considered statistically significant (two-tailed test).

Results

The socio-demographic characteristics of the 72 cases and 108 controls are presented in Table 1. Sex, age at the time of questionnaire completion, educational level, living conditions and comorbidity did not appear to differ significantly between the two groups. Only a tendency to higher percentage of subjects from the controls group who are working at time of survey was observed as compared to the cases group ($p = 0.071$).

Table 2 shows the mean patients group scores for the EORTC QLQ-C30 items in comparison to the controls groups. There was no significant difference in the Global health status between the two groups ($p = 0.622$). Early stage colon cancer patients present significantly higher functional scores for emotional and cognitive functions in comparison to the controls group ($p = 0.003$ for both). Regarding symptoms, patients present a significantly lower score for pain ($p =$

0.005) and a higher score with respect to the single item diarrhoea ($p = 0.011$). Physical functioning and financial difficulties items present a tendency to be scored lower by patients but without reaching significance ($p = 0.060$ and $p = 0.068$ respectively).

Variations of the different items according to the gender for the cases and controls are reported in Figure 1. From the patients' perspective, the mean score of pain symptoms for women was higher as compared to men (15.28 ± 20.85 vs. 5.10 ± 9.61 , $p = 0.024$). From the controls perspective, the scores for the pain symptoms and the single item dyspnoea are also significantly higher in women as compared to men (25.69 ± 26.23 vs. 15.51 ± 24.44 , $p = 0.017$ and 10.65 ± 19.24 vs. 5.56 ± 15.82 , $p = 0.043$). In the same way, the mean scores of emotional and cognitive functioning items appear also significantly lower in women as compared to men of the controls group (76.62 ± 23.84 vs. 86.57 ± 22.7 , $p = 0.004$ and 81.71 ± 19.00 vs. 89.35 ± 14.88 , $p = 0.008$). When applying the ANOVA test in order to compare the results from the EORTC QLQ-C30 items with the gender of the cases and controls groups together, the significant interactions between gender and these two groups remained the emotional and cognitive functioning items ($p < 0.0001$ and $p = 0.001$, respectively), the pain symptom ($p < 0.0001$) and also the dyspnoea item ($p = 0.037$). The post-hoc analysis indicates that women of the controls group suffer more from emotional and cognitive functioning than colon cancer patients in general ($p < 0.01$ for men and $p < 0.05$ for women) and that men of the controls group ($p < 0.05$ only for emotional functioning). Women of the controls group suffer also more from pain than men of the cases group ($p < 0.01$).

Variations for the different items between the cases and controls groups according to age are reported in Figure 2. No statistical differences were observed between the cases and controls respectively to the different age groups. No significant interactions have been observed either between age groups and the cases/controls groups together.

The analysis of the mean patients group scores for the EORTC QLQ-C30 items in comparison to the tumour stage (1 or 2), the tumour location (left or right side), the type of operation (colostomy or not) and the follow up (more or less than 5 years) has been performed. The results indicate no significant differences related to the stage of colon cancer patients. The mean score of diarrhoea symptoms for patients with colostomies was higher as compared to those without colostomies (15.38 ± 17.30 vs. 5.85 ± 12.79 , $p = 0.028$). Patients with left-sided colon cancer present a higher mean score of physical functioning than those with colon cancer on the right side (88.59 ± 13.93 vs. 74.86 ± 25.11 , $p = 0.015$). Patients with a follow up longer than 5 years suffer more from nausea/vomiting and insomnia than patients with a follow up less than 5 years (1.19 ± 4.45 vs. 0.0 ± 0.0 , $p = 0.050$ and 28.57 ± 31.64 vs. 11.11 ± 19.42 , $p =$

0.041, respectively). The ANOVA analysis of the possible interactions between gender with the tumour stage, the tumour location, the type of operation and the follow up was also carried out (Figure 3). No significant interactions between gender with the stage (Figure 3A), the type of operation (Figure 3B) and the localization of the tumour (Figure 3C) of colon cancer patients were observed. However, significant interactions between the follow up of the patients and the gender were the nausea/vomiting and the pain symptoms (Figure 3D, $p = 0.006$ and $p = 0.021$, respectively). However, the post-op analysis did not allow detection of significance between the different groups, probably due to the low number of cases. Similarly, no significant interactions between age groups with the stage, the type of operation, the localization of the tumour and the follow up of the patients were observed.

Discussion

To date there has been little research among long-term colon cancer survivors. Effectively, research has focused on rectal cancer survivors or on colorectal cancer survivors in general. Furthermore, there are no studies on early stage colon cancer. Some of these recent studies found no difference in the QoL comparisons between colon and rectal cancer survivors. The purpose to this study was to provide an overview of the QoL in early stage colon cancer survivors at least one year after treatment in a small community in southern Catalonia (Terres de l'Ebre) and to compare it with controls from general population.

Although our retrospective study included a relatively small number of patients and lack of control measurements before treatment, the global results are consistent with most previous research on QoL among survivors of colorectal and other cancers [17]. The study of Yabroff and collaborators that demonstrated a poor health status perceived by cancer survivors, even > 11 years after diagnosis, included patients with already known worse prognosis cancers, such as rectal cancer, cancer with recurrence or with metastasis [18]. These differences in the studied cohorts (stages, treatments protocols, etc.) as well as the lack of homogeneity in the techniques utilized in all published studies could be responsible of the discrepancies observed. Other shortcoming of these kinds of studies is that the situation of those patients who have died during a long follow-up period (10 years) was not reflected as well as those who already changed their initial staging by developing metastasis or recurrence. It has to be kept in mind that the EORTC QOL-C30 was developed for oncological patients and its use in a "normal population" may contain some methodological difficulties [19]. However, it is widely recognised that the use of population-based reference values is relevant and provides an important aid to the interpretation of QOL scales [20, 21].

Going into detail about our results, no difference was observed in the global health status/QoL between colon cancer patients and the general population. Concerning the functioning scales and symptoms items, our results suggest that the QoL of colon cancer patients was good, with scores that were comparable to or even higher than those of the population-based controls group. Effectively colon cancer patients tend to present better emotive and cognitive functioning but also lower pain and higher diarrhoea symptoms than the controls group. One explanation may be that patients undergoing treatment for a malignancy expect a different concept of subjective well-being compared with healthy subjects and, as a result, may report a more optimistic assessment of their post-treatment QoL. This phenomenon has been referred to as 'reframing', and is thought to be part of the patient's adaptation to their disease and its treatment [22]. On the other hand, pain is recognised as critical symptom that impacts QoL for patients with colon cancer. Barriers to optimum pain relief include patient-related beliefs and attitudes about the treatment of cancer-related symptoms [23]. Finally, the statistically and clinically significant score difference observed in the diarrhoea symptom between the cases and controls groups may be due to the fact that diarrhoea is a common specific symptom in colorectal cancer and is has been reported in several studies [12, 24].

Regarding the subgroup of colon cancer patients, the colostomy appears to have a significant impact on the diarrhoea symptom. We think that this matter is the result of the selection criteria we adopted for this study, excluding rectal cancers and Stages III and IV colon cancers which may have a high percentage of permanent colostomy that could bias the results. The presence of colon cancer on the left side appears to have a significant impact on the physical functioning scale and a follow up longer than 5 years has a significant impact on the nausea/vomiting and insomnia symptoms.

As mentioned by Giesinger and collaborators, the great majority of studies on gender-associated differences in QoL comparing men and women oncological patients and neglect the issue of the disease-specificity of such differences [25]. The differences due to gender-specific reaction or due to disease and/or its treatment have been scarcely clarified. Our results indicate that globally, women of the controls group present worse emotional and cognitive functioning than colon cancer patients (both genders) and also worse emotional functioning than men of the controls group. On the other hand, women of the controls group present higher pain symptoms than men with cancer colon. These results highlight the fact that healthy women are more likely to experience negative emotional distress than men but also than individuals who suffer an oncological problem [26]. On the other hand, this may also suggest that individuals whom have been treated for a CRC present a more positive attitude, probably due more to psychological and social variables than to biological factors.

In conclusion, our results point to the relatively good QoL of early stage colon cancer patients at least one year after treatment. However, the relatively small sample size and the borderline significance of a great number of items advocate that these results need to be confirmed in a longitudinal survey, focusing on how prior treatment affects QOL in the long term.

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Table 1. Sociodemographic characteristics of study the cases and controls responding to the questionnaire EORTC QLQ-C30 (v.3.0).

	Cases (n=72)	Controls (n=144)	Total (n=216)	p-value
Gender				
Male	36 (50.0)	72 (50.0)	108 (50.0)	1.000*
Female	36 (50.0)	72 (50.0)	108 (50.0)	
Age, years				
Mean \pm SD	72.4 \pm 8.5	71.2 \pm 9.3		0.391**
Current employment				
Working at time of survey	4 (5.6)	20 (13.9)	24 (11.1)	0.071*
Not working	67 (93.1)	124 (86.1)	191 (88.4)	
Educational level				
\leq primary school	67 (94.4)	128 (88.9)	195 (90.7)	0.193*
\geq secondary school	4 (5.6)	16 (11.1)	20 (9.3)	
Living condition				
With spouse	38 (52.8)	75 (52.1)	113 (52.3)	0.923*
Without spouse	34 (47.2)	69 (47.9)	103 (47.7)	
Comorbidity				
Yes	44 (61.1)	92 (63.9)	136 (63.0)	0.690*
No	28 (38.9)	52 (36.1)	80 (37.0)	

Data are numbers or mean numbers with percentages in parentheses. SD, standard deviation. Comorbidity was defined as treatment received for cardiovascular diseases, diabetes mellitus, chronic obstructive pulmonary disease, asthma or arthritis at least during the last three months. Comparison of the cases and controls groups by means of Student's t test* or Chi-squared test**. Accepted level of significance: $p < 0.05$.

Table 2. Results for the EORTC QLQ-C30 scales and items of the 72 controls and 108 cases from the Catalonian region.

	Controls	Cases	p-value
Global health status (QoL)	76.91 ± 17.81	78.24 ± 20.29	0.622*
Functional scales			
Physical function	86.53 ± 18.93	81.13 ± 21.31	0.060*
Role function	94.33 ± 16.51	92.82 ± 18.31	0.543*
Emotional function	81.60 ± 23.53	91.55 ± 13.52	0.003**
Cognitive function	85.53 ± 17.44	92.59 ± 11.15	0.003**
Social function	95.92 ± 16.46	93.98 ± 15.90	0.410*
Symptoms			
Fatigue	12.42 ± 17.80	8.41 ± 14.32	0.098*
Nausea / vomiting	1.62 ± 6.92	0.23 ± 1.96	0.107*
Pain	20.60 ± 25.77	10.19 ± 16.91	0.005**
Single items			
Dyspnoea	8.10 ± 17.74	5.09 ± 14.44	0.200**
Insomnia	22.22 ± 32.03	13.89 ± 22.90	0.118**
Appetite loss	4.17 ± 14.68	3.24 ± 9.94	0.630*
Constipation	19.21 ± 33.12	13.43 ± 22.14	0.717**
Diarrhoea	3.94 ± 13.37	7.41 ± 13.96	0.011**
Financial problems	1.88 ± 10.33	4.17 ± 13.63	0.068**

Data are mean ± standard deviation. Comparison of the cases and controls groups by means of student t test* or Mann-Whitney**. Accepted level of significance: $p < 0.005$.

Figure 1. Mean QoL scores for the different subscales of EORTC QLQ-C30 for the cases and controls stratified by sex. * $p < 0.05$ for Student t test or Mann-Whitney as appropriate.

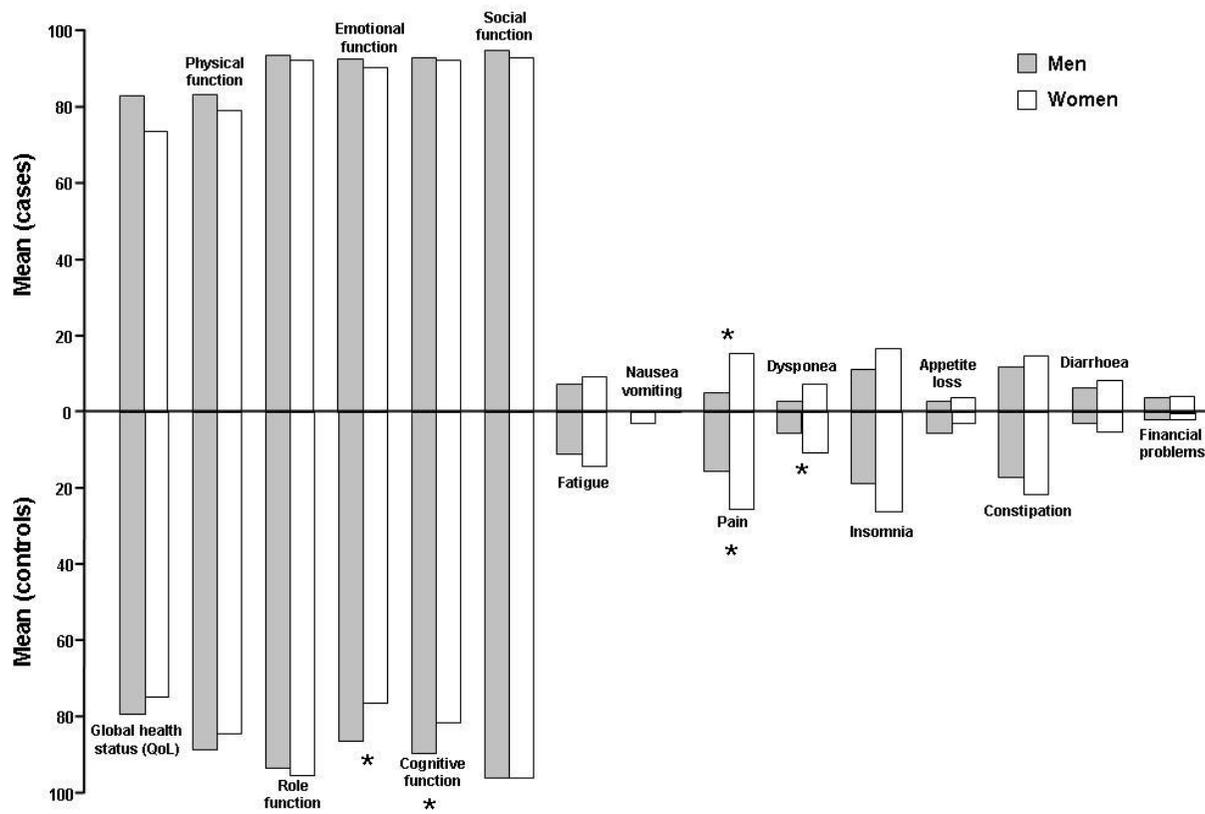


Figure 2. Mean QoL scores for the different subscales of EORTC QLQ-C30 for the cases and controls subjects stratified by age groups.

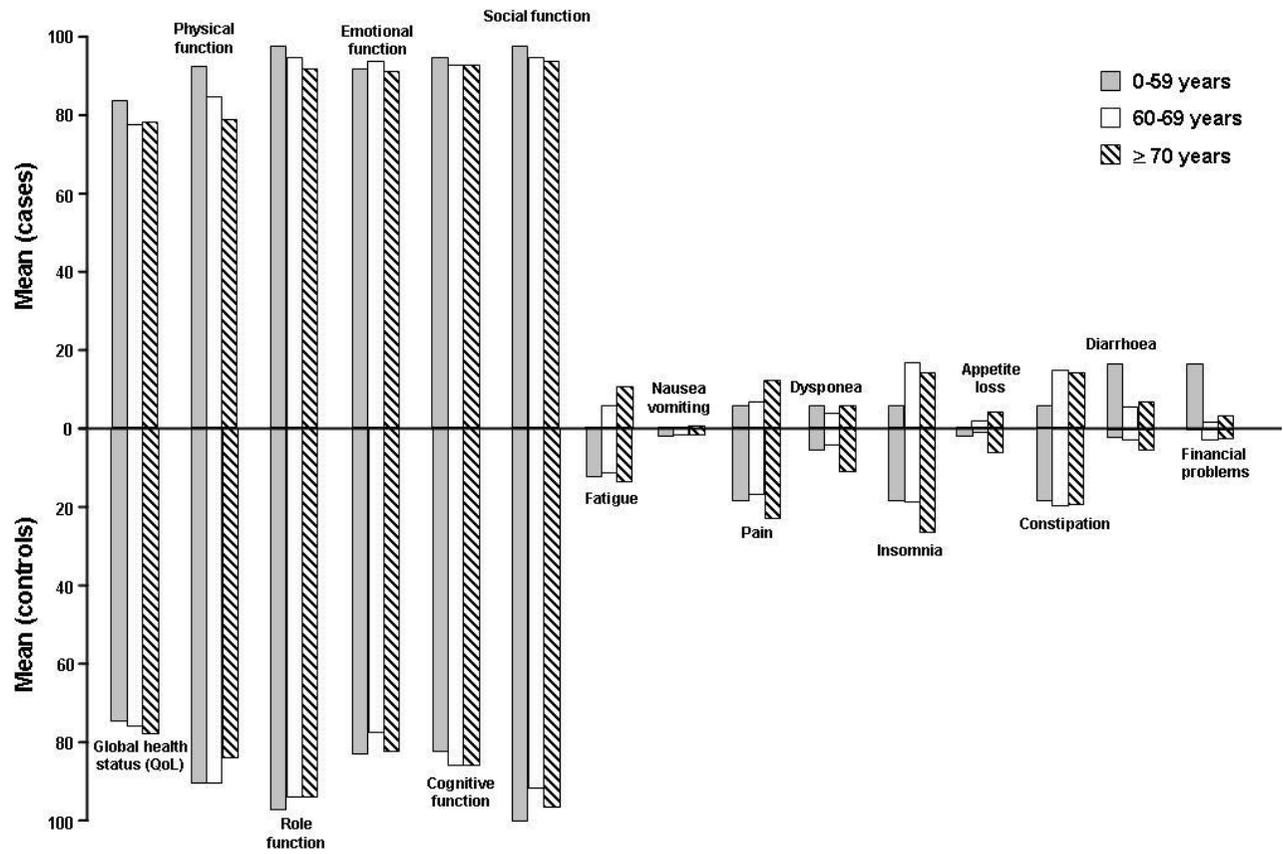


Figure 3. Mean QoL scores for the different subscales of EORTC QLQ-C30 for the cases and controls stratified by stage, ostomy, tumour location and years of follow-up.

