

Change in quality of life and psychological distress in patients with resected non-metastatic vs unresectable advanced cancer undergoing systemic treatment

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Abstract

Purpose: Cancer and its treatments changes patients' quality of life. The aim was to analyze quality of life, psychological distress, and life satisfaction in patients with resected versus unresectable cancer.

Methods: Two prospective, multicenter (15 medical oncology departments), studies with consecutive patient recruitment were conducted, NEOetic, in individuals with unresectable advanced disease (2020-2021) and NEOcoping, in subjects with resected non-metastatic cancer (2016-2018). Participants completed quality of life (EORTC QLQ-C30), emotional distress (Brief Symptom Inventory, BSI), and life satisfaction (Satisfaction with Life Scale, SWLS) questionnaires before systemic antineoplastic treatment and after treatment. A descriptive, bivariate chi-square analysis and t-tests were performed to ascertain the differences between localized and advanced cancer.

Results: A total of 1450 patients were recruited, 941 (65%) with a resected cancer and 509 with unresectable advanced cancer with a mean age of 59.0 and 64.9 years, respectively. The most common cancers were colorectal (42%) and breast (34%) in resected group and bronchopulmonary (29%), colorectal (17%), and pancreatic (11%) in unresectable advanced cancer group. Subjects with advanced disease exhibited worse scores on functional scales (physical, cognitive, emotional, and social), and had more symptoms than those with resected disease prior to initiating systemic treatment. Individuals with advanced cancer displayed better functional status and fewer symptoms, but more fatigue and nausea and those with resected cancer presented worse physical and cognitive function, more psychological distress, and more symptoms post-treatment.

Conclusion: This sample reveals how antineoplastic treatment can enhance quality of life for people with unresectable advanced disease and negatively affect individuals with resected, non-metastatic cancer.

Structured Abstract: Our study shows the potential quality of life benefit of systemic antineoplastic treatment in patients with unresectable advanced cancer. In addition, it shows the deterioration of quality of life in patients with resected non-metastatic cancer after completion of adjuvant treatment.

Introduction

The prevalence of cancer is ever on the rise in our society, representing a health problem that affects patients physically, emotionally, socially, and economically [1]. The headway made in cancer detection and treatment in recent times has led to greater survival, contributing to increasing prevalence by up to 30% in the last decade. Additionally, populational aging has also played its part in augmenting the incidence of oncological disease, which was 19.3 million worldwide in 2020 and estimated to rise to 28.9 million in 2040 [2,3].

The literature has reported that people with cancers experience worse quality of life compared to the general population [4,5]. Quality of life in the context of cancer is a dynamic, multidimensional concept, concerning all aspects of the individual's life and needs, describing the balancing between the actual

situation and the ideal one at a given point in time [6]. This decline in the quality of life is due to the disease process itself, the treatment, and its duration, which in unresectable advanced disease usually lasts for life. The various somatic, emotional, and socioeconomic issues influence such impairment. Physical symptoms occur at all stages of the disease and are associated with greater disability and diminished quality of life, with a higher prevalence of these symptoms in patients with more advanced cancer and in those undergoing more prolonged treatment [7,8].

Numerous studies have proven that oncology patients exhibit functional deterioration that limits their daily physical activity and is associated with the onset of multiple somatic symptoms [7]. Pain is present in up to 72% of all cases [9]; dyspnea, weight loss, and lack of appetite are present in up to 71% [10]; constipation, nausea, and vomiting in up to 60% [11]; sleep disturbances in up to 38%, and high indices of fatigue in as many as 90% of the patients and is particularly common in advanced stages of cancer [7,9,12–14].

From a psychological and psychosocial perspective, some studies have documented depression in 54% of the oncological population undergoing chemotherapy (CT) [9], as well as high rates of adaptive disorders, anxiety, fear/ uncertainty regarding the disease and its prognosis, and dissatisfaction with life [15–18]. Likewise, one study conducted with 768 individuals with cancer revealed that 98.3% felt uncomfortable having a social life; proof that this area of life is also often affected [9].

It is not clear that starting off with better quality of life implies better prognosis in subjects with non-metastatic cancer, albeit it does appear to correlate in cases of advanced cancer [19–22]. Regardless of its impact on survival, improving these people's quality of life throughout the entire process is one of the main objectives of oncology teams. As previously proven, the decline in quality of life is connected to the cancer diagnosis, but also occurs during treatment, with studies reporting a deterioration after CT [23]. Medical oncologists treating cancer patients aim to optimize the approach to prevent and control the somatic and psychosocial symptoms caused by the disease and antineoplastic treatment, sometimes with the treatment goal being to improve quality of life and reduce symptoms, particularly in certain cases of advanced stage tumors.

With this premise, the aim of this study was to analyze the change in patients' quality of life and emotional distress after systemic antineoplastic treatment, comparing those with resected, non-metastatic disease with those with unresectable advanced disease. We also evaluated the influence of biopsychosocial and clinical characteristics on quality of life, psychological distress, and life satisfaction.

Materials And Methods

Study design and population

This study has been conducted through two prospective and consecutive registries. NEOetic study (patients with unresectable advanced disease) conducted in 15 medical oncology departments in Spain from February 2020 to November 2021 and NEOcoping study (patients with resected, non-metastatic

disease) conducted in the same hospitals from January 2016 to December 2018. This research program was funded by the Bioethics Group of the Spanish Society of Medical Oncology (SEOM).

This investigation was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki. and received prior approval from the Medical Research Ethics Committees of each institution and the Spanish Agency for Medicines and Health Products (AEMPS). All patients who agreed to participate signed an informed consent form during the first visit with the oncologist in which they were informed about the systemic antineoplastic treatment and before any other study procedure was performed. Participation was voluntary, anonymous and did not affect patient care and data collection was done through medical records and patient interviews and was similar in all hospitals.

Patients in the NEOetic study cohort were those with a histologically confirmed unresectable, advanced cancer who were candidates, in the discretion of the oncologist, to start systemic antineoplastic treatment. Exclusion criteria comprised patients under 18 years of age, candidates for surgery or other therapies with curative intent, those whose physical conditions, and/or comorbidities presented a contraindication, in the opinion of the responsible medical oncologist, to receive systemic antineoplastic treatment, anyone who had received oncological treatment in the previous two years for this or another advanced cancer, or with an underlying personal, family, sociological, geographic and/or medical condition that could hinder the patient's ability to participate in this study. The study involved the completion of several hardcopy questionnaires by the patient at home after the first clinical interview with the oncologist and prior to the administration of systemic antineoplastic treatment and subsequently, after the first imaging study to assess response to treatment, about 2-3 months after the start of treatment.

Patients in the NEOcoping cohort were those with a resected non-metastatic cancer treated with surgery and who were eligible for adjuvant therapy. Patients under 18 years of age, those who had been treated with preoperative radiotherapy and/or CT, or candidates for adjuvant hormonal therapy or radiotherapy without CT, and those with severe mental illness that prevented them from understanding the study were excluded. The study involved the completion of several hardcopy questionnaires by the patient at home in the month following surgery and after the first visit to the oncologist in which the patient was informed about the possibility of receiving adjuvant antineoplastic treatment and in which a shared decision making on the appropriateness of such treatment was carried out. Some questionnaires were completed again after the end of adjuvant cancer treatment, approximately 6 months after the start of treatment. In both studies, the completed questionnaires were given to the support staff at the next visit.

Variables and questionnaires

The information was collected and updated by medical oncologists especially trained to meet the study's requirements, through a web platform www.neocoping.es and www.neoetic.es. The study and data collection were conducted in accordance with Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines [24].

Demographic and clinical data (age, sex, marital status, educational level, employment status, location, stage, and treatment of cancer) were obtained directly from patients and records.

The questionnaires completed are described below. All the questionnaires applied in the study have been validated in Spanish [25–27].

European Organization for Research, and Treatment of Cancer Quality of Life C30 Questionnaire (EORTC QLQ-C30) [28] contains 30 items grouped into five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), a global health status/quality of life scale, and a number of single items assessing additional symptoms commonly reported by cancer patients (dyspnea, loss of appetite, insomnia, constipation, and diarrhea), and perceived financial impact of the disease. All scale scores are linearly transformed to a 0–100 scale. Higher scores on the functioning scales represent a higher level of functioning. For the symptom scales, the higher the score, the greater the symptom burden. In this sample $\alpha=0.85$.

Satisfaction with Life Scale (SWLS) is a 5-item scale that assesses an individual's global judgment regarding their life satisfaction [29]. Individuals were asked to indicate their level of agreement with the statements on a seven-point Likert-type scale. Raw scores ranged from 5 to 35, with higher scores indicating greater life satisfaction. The reliability (internal consistency) estimates was $\alpha=0.91$ [30].

Brief Symptom Inventory (BSI-18) consists of 18 items assessing the respondent's general emotional adjustment or psychological distress over the previous 7 days [31]. Each item is rated on a 5-point Likert scale, from 0 (not at all) to 4 (extremely). Cronbach's alpha is between 0.81 and 0.90 [31].

All three questionnaires were filled out prior to starting systemic antineoplastic treatment and the EORTC QLQ-C30 and BSI-18 were also completed at the end of adjuvant treatment by patients with resected cancer (6 months after initiating treatment) and after the first radiological response evaluation study in subjects with unresectable advanced cancer (2-3 months after beginning antineoplastic treatment), a date closer to baseline, since this population has a worse prognosis and greater risk of early death.

Statistical analyses

Descriptive statistics were used for demographic data and questionnaires responses. Absolute frequencies were used for categorical data and mean and standard deviation (SD) for quantitative data. Additional descriptive analyses were performed grouping patients by cancer type. Bivariate chi-square and t-tests were performed to assess differences between patients with resected and unresectable advanced cancer in terms of sociodemographic, clinical, and psychological characteristics (EORTC QLQ-C30, SWLS and BSI-18). Paired samples t-test assessed changes in quality of life and psychological distress between pre- and post-treatment. Cohen's effect size (d) was used to estimate the extent to which differences in continuous variables were associated with group status (resected or unresectable advanced cancer). Cohen's d was reported as an indicator of the effect size of differences, with $d > 0.2$ representing a small effect size, $d > 0.5$ a medium effect size and $d > 0.8$ a large effect size [32]. Data

were analyzed using the Statistical Package for Social Sciences (SPSS) for Windows 23.0 (SPSS Inc., Chicago, IL).

Results

Sociodemographic and clinical characteristics

A total of 1,535 patients were recruited; 1,450 were eligible for this analysis and 85 were excluded (20 did not meet the inclusion criteria, 21 met some exclusion criteria and 44 had almost all data incomplete at the time of analysis).

Nine hundred and forty-one (65%) patients had resected non-metastatic cancer [75% stage III and 25% stage I-II] and 509 had unresectable advanced cancer [21% locally advanced and 79% metastatic]. Baseline sociodemographic and clinical characteristics are presented in table 1. The median age of patients with resected and advanced disease was 59.0 and 64.9 years, respectively. Men presented more frequently than women with advanced cancer, older age, and lower educational level. The proportion of patients not working was higher in the advanced disease group, most of whom were retired, while among the cohort of patients with non-metastatic disease most of those not working were unemployed. The most common cancers were colorectal (42%) and breast (34%) in patients with resected cancer and bronchopulmonary (29%), colorectal (17%) and pancreatic (11%) in patients with advanced cancer. In patients with non-metastatic disease, treatment consisted of surgery and adjuvant CT, 67% CT alone and 33% CT associated with radiotherapy. Patients with advanced disease received a greater variety of systemic treatments: CT alone (67%), immunotherapy +- CT (10%) and targeted drug +- CT (11%). Some 17.8% of patients with advanced disease died during the 3-month follow-up of the study (17.8%) compared to 3.3% of deaths during the 6-month follow-up in those with resected cancer (3.3%).

Insert here Table 1

Quality of life and satisfaction with life before treatment

Before starting systemic antineoplastic treatment, patients with advanced disease scored worse on items of the functional scales (physical, role, emotional, cognitive, and social) and symptoms (fatigue, pain, nausea and vomiting, dyspnea, insomnia, appetite loss, constipation, and diarrhea) than patients with resected disease (all $p < 0.001$). There was no difference in the scale of financial hardship between patients with advanced cancer and those with resected cancer. At baseline, more functional limitations, more symptoms, and worse health status (all $p < 0.001$) were reported in patients with advanced cancer.

Patients with resected non-metastatic cancer were more satisfied with their lives and had less psychological distress than those with unresectable advanced cancer ($p < 0.001$) prior to systemic treatment.

Insert here Table 2

Somatic and psychological changes after treatment

Follow-up questionnaires are available for 627 patients with resected non-metastatic cancer and 203 with unresectable advanced cancer in whom we examined change during systemic antineoplastic treatment by completing the EORTC-QLQ-C30 scales before and about 3 months (patients with advanced disease) and 6 months (patients with resected disease) after cancer treatment (see table 3 and table 4). Within the group of patients with resected cancer, 21 deaths were recorded, 86 patients abandoned chemotherapy before the end of adjuvant treatment, probably because of associated toxicity (although this was not evaluated), and in 207 the final questionnaire could not be obtained. In the group of patients with advanced cancer the number of deaths was 36 and 270 patients were lost to follow-up, 215 because of early withdrawal of treatment due to progression or clinical deterioration.

Patients with unresectable advanced cancer had better emotional ($p=0.023$, $d=-0.151$) and cognitive function ($p=0.017$, $d=-0.150$), fewer symptoms of pain ($p=0.001$, $d=1.027$), dyspnea ($p=0.002$, $d=0.205$) and lack of appetite ($p=0.001$, $d=0.286$), but more fatigue ($p=0.044$, $d=-0.143$), more nausea ($p=0.023$, $d=-0.835$), worse health status ($p=0.032$, $d=0.128$) after systemic antineoplastic treatment, see table 3. No differences in psychological distress were identified before and after treatment.

Insert here Table 3

Patients with a resected non-metastatic cancer had worse physical ($p=0.001$, $d=0.155$), and cognitive ($p=0.001$, $d=0.140$) function, more psychological distress ($p=0.001$, $d=-0.142$) and more symptoms ($p=0.001$, $d=-0.139$), such as fatigue ($p=0.001$, $d=-1.182$), pain ($p=0.012$, $d=-0.112$), dyspnea ($p=0.011$, $d=-0.155$), diarrhea ($p=0.012$, $d=-0.122$) and better emotional function ($p=0.001$, $d=-0.150$), and less nausea/vomiting ($p=0.001$, $d=0.801$), on completion of adjuvant treatment, see table 4.

Insert here Table 4

Discussion

In this study we observed that patients with unresectable advanced (incurable) cancer have a poorer quality of life and lower life satisfaction after cancer diagnosis and prior to the initiation of antineoplastic treatment than patients with resected non-metastatic (cured) cancer. At follow-up, patients with advanced cancer improve their quality of life probably because of the benefit of systemic antineoplastic treatment and patients with a resected cancer worsen it probably because of the toxicity of adjuvant treatment, although the overall quality of life at follow-up is still better in patients with cured cancer compared to those with advanced cancer.

Traditionally, antineoplastic treatments were aimed solely at increasing survival. In recent years, this concept has been changing, and numerous tools have been successively incorporated to measure the quality of life of patients undergoing treatment, thus determining a risk-benefit ratio that not only evaluates median survival but also the quality of life that patients have during this time [33,34]. The effort

to find antineoplastic treatments that improve both survival and quality of life should be greater in patients with advanced disease in whom treatments generally provide limited survival benefits [35,36]. In the literature, we have not found other studies comparing the variation in quality of life during antineoplastic treatment in these two populations, cured patients (resected non-metastatic cancer) and patients with incurable cancer (unresectable and advanced).

Similar to global cancer statistics [37], in our sample we found a higher frequency of advanced cancer in older men, with a higher frequency of lung, colon and pancreatic cancer, and the most commonly administered treatment being chemotherapy and, to a lesser extent, targeted therapies or immunotherapy. In contrast, in patients with resected non-metastatic cancer, the sample shows a higher proportion of women, mostly young people, with the most frequent cancers being breast and colon cancer and the adjuvant treatment being chemotherapy alone or in combination with radiotherapy. This difference is due to the high incidence of breast and colon cancer in non-metastatic stages, neoplasms that have screening and early detection programs that allow us to diagnose and treat the cancer with curative intent with surgery and adjuvant treatment [38,39].

The poorer quality of life in patients of our series with advanced cancer before starting antineoplastic treatment, compared to patients with resected cancer, is due to the presence of more physical symptoms, with a high prevalence of fatigue and pain, like those reported in other studies [7,9]. A higher prevalence of dyspnea, insomnia, weight loss, constipation and diarrhea were also observed. This higher prevalence of somatic symptoms is expected, considering that patients with advanced cancer present with primary tumor and metastases, affecting multiple organs and functions, while, in contrast, the other cohort does not present neoplastic disease as it has been resected with curative intent. Perhaps the greater presence of nausea and vomiting in this population prior to treatment can be explained by the early sequelae of surgery in digestive cancer, which account for 56% of this sample [40]. On the other hand, we have also found that patients with advanced disease have greater functional limitations at the emotional, cognitive, and social level prior to the start of treatment, which is explained by a worse coping with the disease, most of the time incurable, facing a more complex psychological process [41]. This deterioration in quality of life limits them in their normal social life [9]. Secondary to all this, we have found a lower life satisfaction in patients with advanced disease before starting treatment. We found no differences in patients' financial hardship, probably because our sample was drawn from a Spanish population with a free public health system, allowing universal access to diagnostic procedures and treatment and where, during cancer treatment, patients are able to take time off work.

After the first response assessment imaging study (advanced cancer cohort) and after completion of adjuvant treatment (non-metastatic cancer cohort), there is an improvement in patients with advanced disease probably due to the effect of treatment in decreasing tumor burden and related symptoms. Improvement in quality of life after chemotherapy has already been observed in other studies [42]. However, in patients with curative surgery, adjuvant treatment aims to reduce the risk of recurrence and, since the achievement is higher than in the advanced disease cohort, effective treatments with high toxicity that may cause a transient detriment in quality of life are also accepted [43]. However, it is

important to note that, in multiple studies, some adverse effects have been reported to have long-term repercussions [44,45]. Notably, the only symptoms that worsened at follow-up in patients with advanced disease were fatigue and nausea/vomiting, which are common adverse events in antineoplastic treatments. In contrast, in patients with resected disease, the only symptoms that improved at follow-up were nausea and vomiting, compatible with surgery being the cause. All this results in a worsening of the state of health in patients with non-metastatic cancer at the end of adjuvant treatment, which should be considered in the subsequent follow-up of these cured patients, but with sequelae that could hinder their social and occupational integration. Meanwhile, in patients with unresectable advanced cancer, despite having improved their quality of life and symptoms, health status probably worsens in relation to the primary cancer, and metastases.

This study has several limitations. Firstly, treatment allocation was at the discretion of the oncologist without randomization and therefore potential confounders could not be controlled for. Second, the inclusion of different cancer and treatment types that may have different symptom and quality of life profiles. Third, the study was conducted in the Spanish cancer population and caution is required when transferring our results to other countries, especially non-Western ones, because cancer care depends on the organization of the health system and the country's economy, with public health care in Spain being universally accessible. Fourth, only 56% of patients completed the questionnaires at follow-up and losses are mainly due to clinical deterioration or death (advanced disease cohort) or non-completion of adjuvant treatment (resected disease cohort), which means the loss of the most deteriorated patients. Finally, the questionnaires were completed by the patient at home without supervision.

Conclusion

In conclusion, our study shows, in a large and representative sample, that systemic antineoplastic treatment can be useful not only to improve survival in patients with unresectable advanced cancer but also to improve quality of life. Furthermore, we observe that patients with resected disease are subjected to adjuvant treatments with curative intent that may have a negative impact on their quality of life, something that should be considered in the follow-up of this population once treatment is completed.

Statements & Declarations

Disclosures of potential conflicts of interest may be found at the end of this article.

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The sponsor of this research has not participated in data collection, analysis, or interpretation, in writing the report, or in the decision to submit this article for publication.

Competing Interests

The authors have no relevant financial or non-financial interest to disclose.

Author Contributions

A.C.B, C.C. and P.J.F. contributed to the study conception, design and analysis. Material preparation and data collection were performed by A.R.G, A.C.B, R.H, P.C.C, V.V., M.A.B., D.L.E., M.J.C., M.G.M., A.C.T., P.J.F., E.E., and C.C. The first draft of the manuscript was written by A.R.G. and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

NEO coping study was approved by the Research Ethics Committee of the Principality of Asturias (January 19, 2015) and by the AEMPS (April 14, 2015).

NEOetic study was approved by the Research Ethics Committee of the Principality of Asturias (May 17, 2019) and by the AEMPS ((May 8, 2019).

The studies have been performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

These studies are an observational, non-interventionist trials.

Consent to participate

Signed informed consent was obtained from all patients.

Consent for publish

Informed consent and approval by the national competent authorities includes permission for publication and diffusion of the data was obtained.

Availability of data and material

Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) software, 25.0 version (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp). The code is available upon request to the authors.

Code availability

Patients are identified by an encrypted code known only to the local researcher. The code of the analyses is available upon request to the authors.

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A.C.B, C.C. and P.J.F. contributed to the study conception, design and analysis. Material preparation and data collection were performed by A.R.G, A.C.B, R.H, P.C.C, V.V., M.A.B., D.L.E., M.J.C., M.G.M., A.C.T., P.J.F., E.E., and C.C. The first draft of the manuscript was written by A.R.G. and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1 Demographic and clinical characteristics of patients

Demographic and clinical characteristics	TOTAL (n=1450)	Resected cancer (n=941)	Advanced cancer (n= 509)	t/χ ²	p
Sex: n (%)					
Men	808 (56)	235 (46)	573 (61)	29.024	0.001
Women	642 (44)	274 (54)	368 (39)		
Age (years): mean (SD)	61.0 (11.8)	59.0 (12.2)	64.9 (10.1)	9.340	0.001
Marital Status:					
Married/ partnered: n (%)	116 (78)	714 (76)	362 (83)	8.547	0.085
Educational level: n (%)					
Basic	751 (52)	507 (54)	244 (48)	4.671	0.033
Intermediate	699 (48)	434 (46)	265 (52)		
Unemployed: n (%)	887 (61)	390 (41)	497 (98)	439.21	0.001
Cancer: n (%)					
Bronco-pulmonary	190 (13)	42 (5)	148 (29)	475.09	0.001
Colon	484 (33)	398 (42)	86 (17)		
Breast	355 (25)	323 (34)	32 (6)		
Pancreas	56 (4)	16 (2)	56 (11)		
Type of systemic treatment					
Chemotherapy (CT)	912 (63)	629 (67)	283 (55)	530.39	0.001
Chemo- and radiotherapy	327 (23)	312 (33)	15 (3)		
Immunotherapy +- CT	49 (3)	0 (0)	49 (10)		
Targeted drug +- CT	54 (4)	0 (0)	54 (11)		
Others	108 (7)	0 (0)	108 (21)		
Death n (%)	57 (6.9%)	21 (3.3)	36 (17.8)	50.201	0.001

Abbreviations: *n*, number; *SD*, standard deviation.

Bold values indicate significance at the 5% level

Table 2. Differences on quality of life, satisfaction with life, and psychological distress by cancer type

^a Scale from 0 to 100. ^b Scale from 5 to 35 for satisfaction with life.

Abbreviations: *EORTC-QLQ-C30*, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; *SWLS*, Satisfaction with life scale; *BSI-18*, Brief Symptom Inventory 18.

Bold values indicate significance at the 5% level.

Table 3 Changes in quality of life and psychological distress between pre-treatment and post-treatment in patients with unresectable advanced cancer (n=203)

Scales	Pre Mean (SD)	Post Mean (SD)	t	p	Effect size
Quality of life (EORTC QLQ-C30)					
Physical function	78.7 (22.9)	78.0 (22.1)	0.461	0.645	–
Emotional function	74.8 (32.0)	79.4 (28.7)	-2.299	0.023	-0.151
Cognitive function	70.7 (29.0)	74.9 (26.6)	-2.405	0.017	-0.150
Social function	82.1 (24.0)	81.9 (24.5)	0.111	0.912	–
Fatigue	73.3 (31.9)	77.6 (28.0)	-2.027	0.044	-0.143
Nausea/vomiting	11.0 (23.6)	33.1 (29.0)	-10.965	0.001	-0.835
Pain	38.0 (31.9)	10.0 (21.6)	12.696	0.001	1.027
Dyspnea	26.4 (32.2)	20.1 (28.9)	3.190	0.002	0.205
Insomnia	9.6 (23.4)	8.8 (21.9)	0.420	0.675	–
Appetite loss	39.4 (37.3)	28.8 (36.8)	3.570	0.001	0.286
Constipation	31.0 (37.8)	27.7 (32.8)	1.267	0.207	–
Diarrhea	28.2 (36.0)	31.8 (35.3)	-1.424	0.156	–
Financial difficulties	19.3 (32.8)	22.1 (32.4)	-1.077	0.283	–
FUNCTIONAL scale	11.6 (25.8)	11.3 (25.5)	0.168	0.866	–
SYMPTOM scale	75.9 (21.1)	68.4 (17.1)	5.864	0.001	0.390
HEALTH STATUS Scale	23.9 (19.1)	21.5 (18.2)	2.160	0.032	0.128
Psychological distress (BSI-18)	61.9 (26.8)	63.4 (27.4)	-0.713	0.476	–

Abbreviations: *EORTC-QLQ-C30*, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; *BSI-18*, Brief Symptom Inventory 18; *Pre*, before systemic treatment; *Post*, after treatment; *SD*, Standard Deviation.

Scales	TOTAL (n=1450)	Advanced unresectable cancer (n=509)	Localized Resected cancer (n= 941)	t	p	Effect size
Quality of life (EORTC QLQ-C30)^a						
Physical function	80.8 (21.3)	71.2 (26.9)	86.0 (15.2)	-13.359	0.001	-0.677
Role function	73.5 (29.5)	68.4 (34.3)	76.3 (26.2)	-4.918	0.001	-0.259
Emotional function	68.9 (26.9)	63.1 (29.5)	72.0 (24.9)	-6.020	0.001	-0.326
Cognitive function	83.1 (22.6)	78.6 (25.3)	85.5 (20.6)	-6.638	0.001	-0.299
Social function	73.1 (29.2)	67.4 (34.4)	77.0 (25.4)	-6.029	0.001	-0.317
Fatigue	11.3 (22.3)	15.6 (27.9)	8.9 (18.3)	5.429	0.001	0.283
Nausea and vomiting	35.1 (28.4)	45.7 (32.1)	29.3 (24.4)	10.838	0.001	0.575
Pain	24.0 (29.0)	35.3 (34.7)	17.9 (23.2)	11.315	0.001	0.589
Dyspnea	8.0 (21.4)	13.5 (28.1)	5.0 (15.9)	7.349	0.001	0.503
Insomnia	35.9 (34.9)	44.6 (37.9)	31.3 (32.2)	7.027	0.001	0.378
Appetite loss	25.2 (33.9)	34.5 (38.9)	20.2 (29.6)	7.850	0.001	0.413
Constipation	25.8 (34.0)	34.8 (38.9)	20.9 (30.0)	7.584	0.001	0.400
Diarrhea	15.7 (34.0)	19.3 (32.8)	13.7 (24.3)	3.732	0.001	0.194
Financial difficulties	16.5 (30.1)	18.1 (32.8)	15.6 (28.6)	1.496	0.135	-
FUNCTIONAL scale	76.0 (19.6)	69.7 (22.6)	79.4 (16.9)	-9.140	0.001	-0.486
SYMPTOM scale	21.9 (17.8)	29.0 (20.5)	18.1 (14.8)	11.663	0.001	0.609
HEALTH	66.5	59.7 (25.6)	70.2 (20.1)	-8.571	0.001	-0.456

STATUS Scale	(22.7)					
Satisfaction with life (SWLS)^b	26.8 (6.2)	25.8 (6.8)	27.0 (5.8)	-3.471	0.001	-0.189
Psychological distress (BSI-18)	64.8 (7.2)	66.9 (7.4)	63.7 (6.8)	8.161	0.001	0.450

Bold values indicate significance at the 5% level.

Table 4 Changes in quality of life and psychological distress between pre-treatment and post-treatment in patients with a resected non-metastatic cancer (n=627)

Scales	Pre Mean (SD)	Post Mean (SD)	t	p	Effect size
EORTC QLQ- C30					
Physical function	86.1 (15.3)	83.5 (18.0)	3.502	0.001	0.155
Emotional function	72.1 (25.0)	75.9 (25.4)	-3.746	0.001	-0.150
Cognitive function	85.7 (20.9)	82.6 (23.1)	3.409	0.001	0.140
Social function	77.5 (25.5)	76.5 (27.1)	0.905	0.366	–
Fatigue	8.7 (17.0)	35.8 (27.6)	-22.182	0.001	-1.182
Nausea/vomiting	28.6 (24.0)	10.9 (20.0)	14.891	0.001	0.801
Pain	17.3 (23.3)	20.1 (26.3)	-2.545	0.012	-0.112
Dyspnea	4.6 (15.1)	6.6 (19.0)	-2.544	0.011	-0.115
Insomnia	30.8 (31.9)	32.2 (33.4)	-0.990	0.322	–
Appetite loss	19.8 (29.5)	20.5 (30.2)	-0.562	0.575	–
Constipation	20.9 (30.0)	23.0 (31.4)	-1.583	0.114	–
Diarrhea	12.6 (22.5)	15.6 (26.4)	-2.529	0.012	-0.122
Financial difficulties	15.2 (27.4)	13.7 (27.4)	1.380	0.168	–
FUNCTIONAL scale	79.5 (17.2)	78.9 (19.6)	0.903	0.367	–
SYMPTOM scale	17.6 (14.1)	19.8 (17.2)	-3.3460	0.001	-0.139
HEALTH STATUS Scale	71.2 (19.4)	69.2 (23.5)	1.988	0.047	–
Psychological distress (BSI-18)	63.8 (6.9)	64.8 (7.1)	-3.651	0.001	-0.142

Abbreviations: *EORTC-QLQ-C30*, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; *BSI-18*, Brief Symptom Inventory 18; *Pre*, before systemic treatment; *Post*, after

treatment; *SD*, Standard Deviation.

Bold values indicate significance at the 5% level.