

Cancer Patients' Symptom Burden and Health-related Quality of Life (HRQoL) at Tertiary Cancer Center from 2006 to 2013: A Cross-sectional Study

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Abstract. *Background/Aim:* To observe changes in symptoms and health-related quality of life (HRQoL) over 7 years among cancer patients at different stages of the disease. *Patients and Methods:* This prospective cross-sectional study at the Helsinki University Hospital Cancer Center, was carried out in 2006 and repeated in 2013. All participants filled in the EORTC-QLQ-C30 questionnaire. *Results:* Altogether, 581 patients responded (49% in 2006 and 54% in 2013). The disease was local in 51% and advanced in 49% of patients. The HRQoL was significantly lower, except for emotional and cognitive functions, and the symptom burden more severe in advanced cancer. The most prevalent symptoms were fatigue (93% and 85%; moderate/severe 22% and 9%), pain (65% and 47%; moderate/severe 16% and 5%), and insomnia (64% and 60%; moderate/severe 20 and 21%), respectively. No changes in HRQoL or symptoms were found at 7 years. *Conclusion:* There is a need for early integrated palliative care to improve HRQoL during cancer treatments.

Quality of life is a multi-dimensional concept. It reflects the ways in which a person's emotional, social, and physical aspects influence well-being in everyday life. Health-related quality of life (HRQoL) indicates how disease, disability, or

disorder affects the individual's well-being over time (1). Cancer and its treatments altogether affect patient's HRQoL in many ways.

In recent years, the survival of cancer patients has improved due to advances in cancer-specific therapies (2, 3). More patients are treated with intense protocols over extended periods of time. Alongside improvements in survival, it is important to maintain HRQoL (4). There is some evidence of cancer patients' symptom burden and decreasing HRQoL during oncological treatments (5-12). More than two-thirds of cancer patients with advanced disease are symptomatic (5, 6, 13). During the last decades, palliative care has been recognized as an elementary part of cancer care throughout the cancer disease trajectory in many cancer centers to improve quality of life of cancer patients (14-19). Already in the early stages of cancer, there is a need for palliative care and psycho-oncological follow-up (8, 9, 20).

Due to prolonged survival and various new treatment options, the symptom burden of cancer patients has changed. Previous data have mainly relied on clinical trials focusing on new cancer treatments and their adverse effects. The HRQoL related to the symptom burden has been the primary endpoint only in a few studies (1, 11). Real-life data concerning the symptom prevalence and HRQoL during cancer treatments are required to elucidate the need for earlier palliative and supportive care. The aims of this study were i) to observe the symptom burden and HRQoL among cancer patients in different stages of the disease treated at a tertiary cancer center in a prospective cross-sectional study design and ii) to investigate whether there is any change in the symptom burden or HRQoL over a 7-year period.

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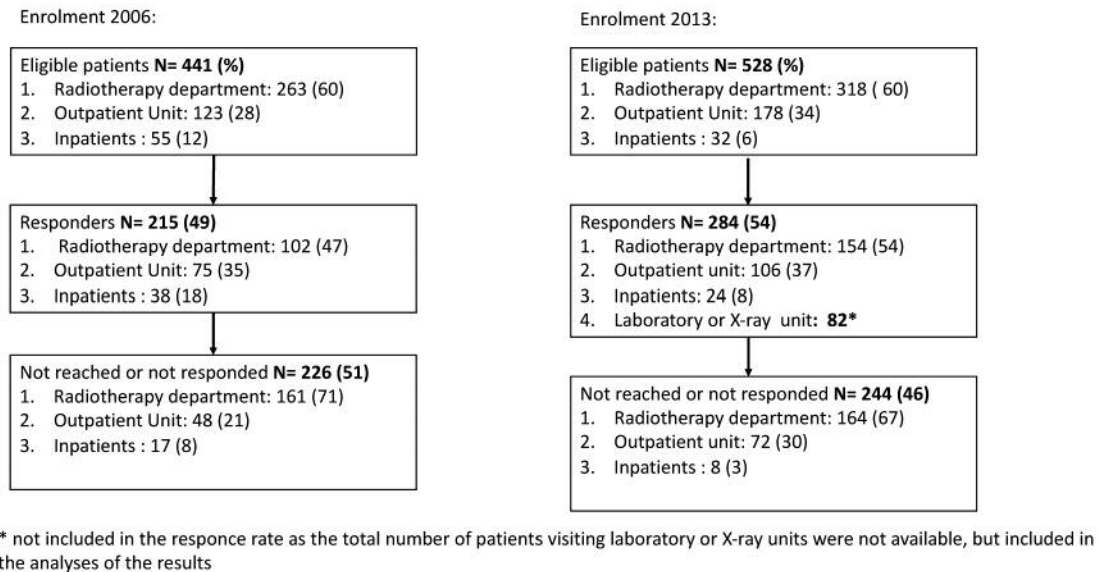


Figure 1. Flow diagram of the participants enrolment.

Patients and Methods

This study was carried out at the Cancer Center of Helsinki University Central Hospital (HUCH) as a one-day cross-sectional study performed on 31.11.2006 and 15.5.2013. The same study design was in both study sections. The study was open to all inpatients hospitalized in the oncology department and to all ambulatory patients who visited the outpatient unit or radiotherapy department during the predefined days. The exclusion criteria in 2006 were age under 16 years, trial patients, patients visiting the palliative care unit, or cancer survivors, and in 2013, age under 16 years, patient visiting the palliative care unit, and trial patients. The study protocol was approved by the Ethics Committee of the Helsinki and Uusimaa district, and each patient gave written informed consent prior to study inclusion.

The primary outcome measurements were main symptoms and HRQoL measured by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30). The questionnaire was delivered together with an informed consent form to be filled out by the participant. This 30-item questionnaire produces a global health status, five functional scales (physical, role, social, emotional, and cognitive functions), three symptom scales (fatigue, nausea/vomiting, and pain), and six single-symptom items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties) (21). All nine EORTC QLQ-C30 multi-item dimension scales produce a score from 0 (=lowest) to 100 (=highest). The higher scores on the global and functioning scales indicate better HRQoL and functioning, while the higher scores on symptom items represent more intense symptom burden (21, 22). A clinically significant difference is a 10-point change in the score (23). For single-symptom items, symptoms are scaled in the following manner: no symptoms=0, mild symptoms ≤ 33.33 , moderate symptoms ≤ 66.66 , and severe symptoms ≤ 100 . For pain, fatigue, and nausea/vomiting, which are

multi-item symptoms, 0=no symptoms, 0.01-66.65=mild symptoms, 66.66-99.99=moderate symptoms, and 100=severe symptoms. Medical history and demographic data of the patients were obtained from patient records.

Statistical analysis. The characteristics of the study population were presented as means with standard deviations (SD) or as counts with percentages. The statistical significance between groups were evaluated by *t*-test, Mann-Whitney test and chi-square test. Adjusted hypothesis was evaluated using generalized linear models with appropriate distribution and link function. Models included gender and age as covariates. The normality of variables was evaluated by the Shapiro-Wilk *W* test. Stata 15.1, StataCorp LP (College Station, TX, USA) statistical package was used for the analyses.

Results

The enrollments in 2006 and 2013 are described in a flowchart (Figure 1). The total response rate was 51% (499/969), being 49% (215/441) in 2006 and 54% (284/528) in 2013. In 2013, the 82 patients who visited the clinic only for investigations (x-ray, laboratory units) were not included in the response rate, as the total number of patients visiting these units was not available. But they were included in the analysis since they returned the questionnaire. Thus, the total number of patients in this study was 581. The disease was local in 298 patients (51.3%) and advanced in 283 patients (48.7%). The main diagnoses were breast cancer in 229 (39%), prostate cancer in 100 (17%), gastrointestinal cancer in 74 (13%), lymphoma in 53 (9%), and other malignancies in 125 (22%) of the patients. However, there were more

Table I. Patient characteristics.

	Local disease			Advanced disease		
	2006 N=117 (%)	2013 N=181(%)	<i>p</i> -Value	2006 N=98 (%)	2013 N=185 (%)	<i>p</i> -Value
Female, n (%)	65 (56)	126 (70)	0.014	64 (65)	102 (55)	0.098
Age, mean (SD)	61 (12)	62 (13)	0.43	62 (12)	63 (14)	0.57
Diagnosis, n (%)			0.14			0.074
1. Breast cancer	58 (50)	100 (55)		29 (30)	42 (23)	
2. Prostate cancer	35 (30)	34 (19)		10 (10)	21 (11)	
3. Gastrointestinal cancer	7 (6)	9 (5)		26 (27)	32 (17)	
4. Lymphoma	4 (3)	5 (3)		9 (9)	35 (19)	
5. Other	13 (11)	33 (18)		24 (24)	55 (30)	
Bone metastases (%)	0 (0)	0 (0)		34 (35)	54 (29)	0.34
Radiotherapy, n (%)	77 (66)	103 (57)	0.12	27 (28)	62 (34)	0.30
Endocrine therapy, n (%)	45 (38)	73 (40)	0.75	11 (11)	36 (19)	0.077
Targeted therapy, n (%)	9 (8)	19 (10)	0.42	13 (13)	17 (9)	0.29
Chemotherapy line, n (%)			0.42			0.043
None	88 (75)	143 (79)		28 (29)	94 (51)	
1	28 (24)	38 (21)		47 (48)	43 (23)	
2	0 (0)	0 (0)		13 (13)	19 (10)	
3	0 (0)	0 (0)		7 (7)	13 (7)	
≥4	1 (1)	0 (0)		3 (3)	16 (9)	

gastrointestinal cancers (75%) in the advanced group and breast (69%) and prostate cancers (69%) in the local group. Of the patients with advanced disease, 88 (31%) had bone metastases.

Differences between the years 2006 and 2013. The patient characteristics are presented separately for local and advanced disease in Table I. No significant changes occurred in the prevalence of moderate or severe symptoms, except dyspnea, which was slightly more prevalent among patients with local disease in 2006 ($p=0.002$).

No significant changes were seen in the HRQoL or main functional scales in local or advanced stages of the disease between 2006 and 2013 (Figure 2).

Differences between local and advanced cancer (pooled data of 2006 and 2013). All symptoms, except insomnia and diarrhea, were more prevalent in patients with advanced disease. The overall intensity of symptoms was low in patients with local disease, although moderate or severe insomnia occurred in 21% of the patients. Fatigue, pain, and insomnia were the most prevalent and severe symptoms in advanced disease (Table II, Figure 2).

Pain was more prevalent in patients with bone metastases [67/87 (77%)] than in those without metastases [117/194 (60%)] ($p=0.007$). The pain was moderate or severe in 21/87 patients (24%) with and in 23/194 patients (12%) without bone metastases, respectively.

The HRQoL was significantly impaired in patients with advanced disease relative to those with local disease in global health status ($p<0.001$), physical functioning ($p<0.001$), role functioning ($p<0.001$), and social functioning ($p<0.001$). No differences were found in emotional ($p=0.065$) or cognitive ($p=0.31$) functioning (Table III; Figure 2).

Financial difficulties. In pooled analysis for the years 2006 and 2013, financial difficulties were more prevalent in patients with advanced disease than in those with local disease ($p=0.044$) (Table II; Figure 2). Financial difficulties were reported by 33.0% and 26.9% (moderate or severe difficulties in 8.4% and 5.1%) of patients with advanced and local disease, respectively (Table II). No significant changes were found between the study years (Figure 2).

Discussion

This was a cross-sectional study describing the symptom burden and HRQoL among the unselected cancer population treated at the tertiary Cancer Center at two different time-points spaced seven years apart. In line with previous research on patients receiving active cancer treatments, fatigue, insomnia, and pain were found to be the most prevalent symptoms in both the advanced and early stages of disease (5). Likewise, the symptom burden in the present and earlier studies has been more severe among patients with advanced cancer (5, 7, 8, 20).

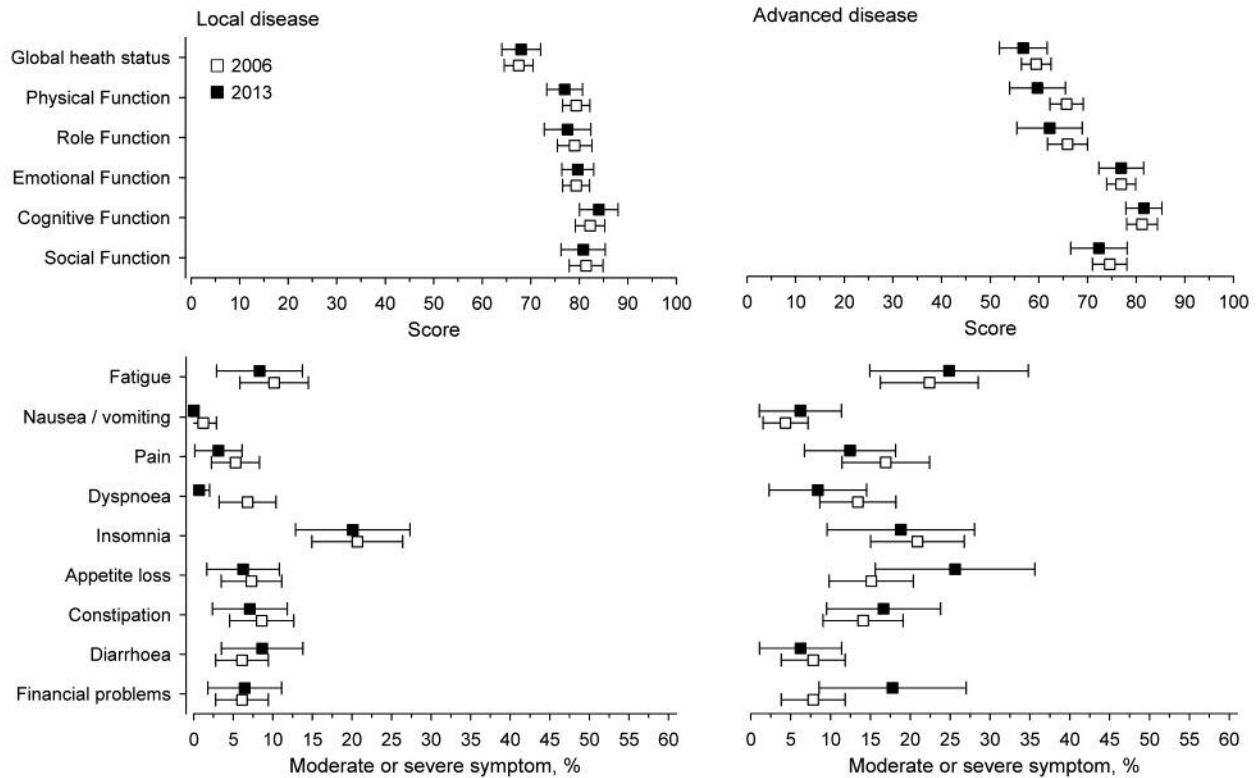


Figure 2. Health-related quality of life and prevalence of moderate or severe symptoms in patients with local and advanced disease in 2006 and 2013.

Table II. The severity of the symptoms in local and advanced disease (pooled data of year 2006 and 2013).

Symptoms	Local n (%)				Advanced n (%)				p-Value*
	None	Mild	Moderate	Severe	None	Mild	Moderate	Severe	
Fatigue	44 (15)	227 (76)	23 (8)	4 (1)	19 (7)	198 (71)	55 (20)	7 (2)	<0.001
Nausea	242 (81)	54 (18)	0 (0)	2 (1)	180 (64)	87 (31)	11 (4)	2 (1)	<0.001
Pain	159 (53)	124 (42)	14 (5)	0 (0)	97 (34)	140 (50)	31 (11)	13 (5)	<0.001
Dyspnea	199 (67)	85 (29)	13 (4)	1 (0)	164 (59)	85 (30)	18 (6)	13 (5)	0.015
Insomnia	118 (40)	116 (39)	54 (18)	10 (3)	101 (36)	123 (44)	46 (16)	11 (4)	0.52
Appetite loss	230 (78)	49 (16)	11 (4)	7 (2)	159 (57)	71 (25)	30 (11)	19 (7)	<0.001
Constipation	206 (70)	68 (23)	18 (6)	3 (1)	168 (60)	69 (25)	32 (12)	9 (3)	0.006
Diarrhea	211 (71)	65 (22)	14 (5)	5 (2)	195 (70)	66 (24)	10 (4)	6 (2)	0.74
Financial difficulties	215 (73)	64 (22)	10 (3)	5 (2)	184 (67)	68 (25)	17 (6)	6 (2)	0.044

*Adjusted for gender and age.

Fatigue was the most prevalent symptom in our study, reported by 89% of patients, although it was mild in the majority of patients. Fatigue has been related to cancer treatments like chemotherapy (24, 25), but a high prevalence of fatigue has also been reported irrespectively of the therapy received. In our study, the prevalence of fatigue was

significantly higher in patients with advanced disease than in those with local disease. This was probably related to the higher tumor burden and psychosocial distress among patients with advanced cancer, rather than to cancer treatments.

In our study, 56% of the patients reported pain (47% with local and 65% with advanced disease) compared to a

Table III. *Quality of life in local and advanced disease (pooled data from years 2006 and 2013).*

	Local mean (SD)	Advanced mean (SD)	p-Value*
Global health status	68 (20)	58 (22)	<0.001
Physical function	78 (20)	64 (25)	<0.001
Role function	78 (25)	64 (30)	<0.001
Emotional function	79 (19)	77 (21)	0.065
Cognitive function	83 (20)	82 (21)	0.31
Social function	81 (24)	73 (26)	<0.001

*Adjusted for gender and age.

Norwegian study, where the prevalence of pain among inpatients with either local or advanced cancer varied between 53% and 55% and among outpatients between 35% and 39% (26). In the present study, moderate or severe pain was reported by 5% of patients with local disease and 16% of patients with advanced disease. The pain was more prevalent and intense among the patients with bone metastases (77% vs. 60%; moderate or severe pain 24% vs. 12%, respectively). Thus, recent studies, including our own, show that pain remains a significant symptom among patients receiving anticancer therapies. This warrant's systematic evaluation of pain, especially in patients with bone metastases, to provide early and effective pain treatment, including palliative radiotherapy (27).

Interestingly, insomnia was frequently reported by patients, with no significant difference between individuals with local or advanced disease. Likewise, in line with previous studies of different cancer populations (8, 10, 28, 29), emotional and cognitive function did not differ in different stages of the disease. Thus, insomnia and emotional well-being could be related to individual coping strategies for psychosocial distress caused by cancer and treatments rather than to the stage of the disease. This highlights the need for early interventions, providing psychosocial support already in the early stage of the disease.

In our study, HRQoL was lower in patients with advanced disease than in those with local disease. The most impaired functions were the physical, role, and social domains, which is consistent with previous research (9, 12, 29). In our earlier study on women with advanced breast cancer, pain was shown to be one of the main activity-limiting symptoms together with fatigue and depression. These three symptoms combined had a major influence on functional capacity and HRQoL (10). In addition, a previous study found fatigue, depression, and physical inactivity to be the most significant factors associated with breast cancer survivors' impaired HRQoL (28). Thus, the high prevalence and intensity of fatigue, pain, and insomnia in our study could explain the significant impairment in physical, role, and social functions, especially in patients with

advanced disease. Activity-limiting symptoms and functional impairment may cause physical inactivity, triggering a vicious cycle with generalized weakness and impaired HRQoL (10, 30, 31). There is solid evidence of the benefits of cancer patients' rehabilitation during and after adjuvant treatments in terms of improved HRQoL (28, 32-36), but also some evidence among patients with advanced phase disease (10, 37). Our results highlight the need for active rehabilitation programs to be integrated into cancer center care to maintain physical and emotional well-being during ongoing treatments and follow-up.

Unexpectedly, we failed to show any significant improvement in symptom control or HRQoL during 2006-2013. Our findings are partly in line with a Norwegian study describing pain intensity in cancer patients treated at a tertiary cancer unit. The authors had concluded that no significant change occurred in experienced pain from 2008 to 2014 (26). There are several possible explanations for the lack of improvement in HRQoL and symptom control in our study. Firstly, even though outpatient palliative care clinics located in cancer centers play an important role in cancer patient care (14), patients are still introduced to the palliative care team at a late stage of the disease, after oncological treatments have been terminated, rather than concurrently with the cancer-centered care. However, an international consensus highlights the early introduction of patients with advanced cancer or patients with severe symptoms or suffering to the palliative care team to improve HRQoL of the patients already during the cancer-directed treatments (38). This early integration of palliative care has been shown to improve cancer patients' QoL and overall satisfaction with care (18, 19, 39-41). Yet, during the study period there were no standards in the study center for referral to the palliative care unit early in the course of the disease. Secondly, the symptoms were not routinely assessed during the cancer treatments. This might have left patients' symptoms hidden and possibly insufficiently treated in clinical practice. Similarly, there was no systematic assessment of emotional distress or any standard procedure for referral to the psycho-oncological team for consultation.

Strengths of our study were the cancer-specific, commonly used and validated questionnaire and equivalent study groups in terms of sample size and the main characteristics (*e.g.* cancer types, ages). Thus, comparing the local and advanced disease groups was possible within the combined population. In addition, we present non-selected patient populations, thus representing the real-life situation in the cancer center. However, some limitations in our investigation must also be noted. First, the study method was cross-sectional, which prevented us from identifying any changes in symptoms or HRQoL over time. Second, the study population included heterogeneous cancer types and the total response rate remained relatively low (49/54%).

Conclusion

The symptom load was higher in patients with advanced disease during the oncological treatments, but also patients with local disease suffered from symptoms of moderate or severe intensity. No significant changes were seen during seven years in the main functional components used to assess HRQoL or in the total symptom burden of the patients treated at the tertiary cancer center. This survey highlights the need for systematic assessment of symptoms, psychological distress, and functional impairment of cancer patients in all phases of the disease. There is an ongoing need for early integrated palliative care, rehabilitation, and psycho-oncological support in order to maintain HRQoL during cancer-directed treatments.

Conflicts of Interest

The Authors declare no conflicts of interest regarding this study.

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