The added value of geriatric assessment in evaluating a patient's Health Related Quality of Life: a study in ≥ 70-year-old early stage invasive breast cancer patients

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Disclosures and Conflict of Interest Statements

All authors declare no conflicts of interest.

Acknowledgement

We thank all the hospitals, their clinical investigators and all the patients who participated in the study. Hans Wildiers is a recipient of funding from the 'Fonds voor Wetenschappelijk Onderzoek' (FWO). The study was supported by a grant from the Belgian 'Stichting tegen Kanker' (B32220096117). We also would like to thank Michael Kennedy-Scanlon for proofreading and editing.

Abstract

Objective

The objective of this study was to assess the relationship between Geriatric Assessment (GA) to Health-Related Quality Of Life (HRQOL) in older breast cancer patients.

Methods

Patients were assigned either to adjuvant chemotherapy (CTG) or to a control group (CG). Spearman rank coefficients (ρ) calculated correlations between HRQOL and GA at baseline, three months and one year. Multivariate regressions modelled the prognostic value of GA in evaluating of a patient's HRQOL and the accuracy of baseline GA in predicting HRQOL decline (change of ≥ 10 points).

Results

The analysis included 57 patients in the CTG and 52 in the CG. Strong correlations ($\rho \geq 0.5$) were reported between the EORTC QLQ-C30 Physical Functioning scale and Activities of Daily Living (ADL), Instrumental ADL (iADL) and Leuven Oncogeriatric Frailty Score Scale (LOFS) in both groups. Multivariate models demonstrated that poor iADL, ADL and LOFS (CG) and ADL and iADL (CTG) contributed to a statistically (all $p < 0.05$) worse HRQOL. The relative gain in predicting three-month and one-year HRQOL decline was 24.1% and 4.7% (CG) and 6.1% and 18.3% (CTG).

Conclusion

Our results show that the functional measures in the GA are strongly correlated with patient self-reported functioning. Poor baseline GA has a modest probability of predicting HRQOL deterioration.

Key words: breast cancer, older patients, adjuvant chemotherapy, geriatric assessment, quality of life, patient reports

1. Introduction

Most cancer treatments centre around extending a cancer patient's life expectancy. However, when older adults with cancer are asked about their expectations for treatment, most will focus on Health-Related Quality Of Life (HRQOL) as an important goal (Wedding, Pientka, & Höffken, 2007). Therefore the field of geriatric oncology research is increasingly focused on maintaining a patient's quality of life (Fitzsimmons, 2004), especially when survival benefits become less achievable due to increased treatment-related toxicity burdens and comorbidities inherent to ageing.

HRQOL is captured through patients' self-reported questionnaires. The general purpose of HRQOL assessment in clinical research is to provide an accurate evaluation of the patient's well-being that can support clinical decision-making (Lemieux, Goodwin, Bordeleau, Luazier, & Théberge, 2011) and HRQOL assessment is frequently included as a (co)endpoint in clinical breast studies (Ghislain et al., 2016). The European Organisation for Research and Treatment of Cancer quality-of-life questionnaire (EORTC QLQ-C30) is one of the most frequently used HRQOL questionnaires in patients with cancer.

When such patients are older, because the traditional clinical oncology assessment instruments fail to capture a variety of important age-related changes (Owusu & Berger, 2014), a specific geriatric assessment (GA) comprising several measures is widely implemented (Wildiers et al., 2014; Owusu & Berger, 2014). Unlike HRQOL measures, which are Patient-Reported Outcomes (PROs), these GA measures are mainly done by oncologists, geriatricians or other health care professionals.

Whereas a number of studies have reported a correlation between HRQOL and other assessment instruments, notably the Karnofsky Performance Score (KPS) and the Eastern Cooperative Oncology Group Performance Status (ECOG-PS) (Quinten et al., 2009; Ediebah et al., 2018), only a few studies have investigated the correlation between HRQOL and GA. This would be logical because several scales in GA and the EORTC QLQ-C30 questionnaire address the same issues. For example, both the EORTC QLQ-C30 Physical Functioning (PF) scale and two of the GA measures, the Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (iADL), can be used to assess the physical functioning of a patient with cancer. In a previous study involving a group of older patients with cancer (Quinten et al., 2018), a strong correlation was reported between baseline ADL and iADL on the one hand and

the EORTC QLQ-C30 scales related to not only Physical Functioning but also Global Health Status (GHS) and Role Functioning on the other. Similarly, an earlier study (Wedding, Röhrig, Klippstein, Brix, Pientka, & Höffken, 2007) reported that the EORTC GHS scale was significantly associated with iADL in a heterogeneous group of older patients with cancer when prognostic clinical and socio-demographic variables were adjusted for. By the same token, Cognitive Functioning scale of the EORTC QLQ-C30 and the Mini Mental State Examination (MMSE) can both measure the cognitive impairment of a patient with cancer. However, previous studies have yielded conflicting results regarding statistically significant correlations between the two measures (Mystakidou, Tsilika, Parpa, Galanos, & Vlahos, 2007; Iconomou, Vasilki, Koutras, Iconomou, & Kalofonos, 2004). Finally, the 15-item version of the Geriatric Depression Scale (GDS-15), another component of the GA, is widely used to screen depression among older persons, but little is known about its correlation with the EORTC QLQ-C30's Emotional Functioning scale.

If the two measures provide similar information, the question arises as to whether they provide complementary or overlapping information. As collecting information for both measures can be quite time-consuming and increases the burden on both the patient and health care professionals, a careful selection of measures is important. Our study aims to analyse the correlation between GA and HRQOL and, if highly correlated domains are detected, to explore whether GA can optimize the assessment of a patient's HRQOL evaluation at baseline and over time. In addition, as within this group of older patients life expectancy is often greater than 6 months and maintaining HRQOL is regarded as a key outcome, we felt it important to carry out a responder analysis to assess the predictive accuracy of GA at baseline, alongside clinical and socio-demographic information, for estimating the probability of a decline in a patient's HRQOL.

2. Methods

2.1 Patients and Data

This prospective, multicentre, non-interventional study accrued patients in two academic and three regional hospitals in Belgium from 2009 until 2012. Eligible patients were women ≥ 70 years of age who had just undergone surgery for early stage invasive breast cancer. Once enrolled, participants were assigned to a chemotherapy group (CTG) or control group (CG) according to their planned adjuvant treatment as decided upon by their physicians. For CG, all patients received an aromatase inhibitor. For CTG, the scheduled therapy consisted of docetaxel at a dose of 75 mg/m^2 and cyclophosphamide at 600 mg/m^2 every 3 weeks for a total of 4 cycles (TC scheme). In our study, patients either received or not received adjuvant radiotherapy according to institution policy. In the chemotherapy group, patients with hormone sensitive tumours also received an endocrine therapy after completion of chemotherapy. Trastuzumab was associated to the adjuvant chemotherapy if the tumour was HER2 positive. More details are reported elsewhere (Brouwers et al., 2016). The study was approved by the Ethics Committees of the respective hospitals and prior written consent was obtained provided. Besides standard clinical variables, patient-reported outcomes as assessed with the EORTC QLQ-C30 questionnaire and frailty as assessed by geriatric assessment (GA) were collected.

EORTC QLQ-C30 Questionnaire

HRQOL was assessed using the EORTC QLQ-C30 questionnaire. The EORTC QLQ-C30 incorporates 15 scales: a GHS scale; five scales measuring respectively physical, role, cognitive, emotional and social functioning; three symptom scales measuring fatigue, pain and nausea and vomiting; and six individual items focusing on dyspnoea, appetite loss, sleepiness, constipation, diarrhoea and the perceived financial effect of disease and treatment (Aaronson et al., 1993). All scores are converted linearly into scores ranging from 0 to 100. Our study focuses on only the five functioning scales and the GHS scale. For these scales, a high score represents a good level of functioning.

Geriatric Assessment

GA was performed as recommended by the International Society of Geriatric Oncology (SIOG) (Wildiers et al., 2014; Decoster et al., 2014). The following GA measures were included: the Charlson Comorbidity Index (CCI) (Charlson, Pompei, Ales, & MacKenzie, 1987), Katz's Activities of Daily Living (ADL) (Katz, 1983), Lawton's instrumental Activities of Daily Living (iADL) (Lawton & Brody, 1969), the Mini Mental State Examination (MMSE)

(Folstein, Folstein, & Mchugh, 1975), the Mini Nutritional Assessment – Short Form (MNA-SF) (Vellas et al., 1999) and the Geriatric Depression Scale (GDS-15) (Sheikh & Yesavage, 1986). The CCI categorizes comorbidities of patients on a scale from 0 to 37, where a score of zero indicates no comorbidities. Scores on the ADL range from 6 (fully independent) to 24 (fully dependent) with dependency defined as a score > 6. The iADL summary score ranges from 0 to 8 for women and 0 to 5 for men, with the top scores indicating full independence. The Activities measured by the iADL differ from those measured by the ADL because the former require more complex cognitive and motor skills and also measure a different level of independence. The MMSE is a 30-point questionnaire measuring cognitive impairment, where a score ≥ 24 points indicates normal cognition, 18-23 points mild impairment and ≤ 18 points significant impairment. The MNA-SF (score 0–14) is a validated screening tool that identifies geriatric patients age 65 and above who are malnourished or at risk of malnutrition (< 12). Risk for depression is measured by the 15-item GDS–15 (score 0–15), with scores > 4 indicating some degree of risk. Additionally, two summary scales were included, the Balducci Frailty Criteria (BFC) (Balducci & Extermann, 2000) and Leuven Oncogeriatric Frailty Score (LOFS) (Brouwers et al., 2016). The BFC is a system for classifying older patients with cancer as 'fit', 'vulnerable' or 'frail', based on their GA findings. Scores on the LOFS, which integrates results from the ADL, iADL, MMSE, MNS-SF and CCI, range from 0 (frail) to 10 (fit). A high score indicates a high level of fitness.

HRQOL and GA were collected at three time points: at baseline, defined as 3 to 6 weeks after surgery, but before first chemotherapy administration in the CTG group; at approximately 3 months after baseline (T1) (for CTG, day of last chemotherapy, but before last chemotherapy administration); and at around one year after baseline (T2).

2.2 Statistical Analysis

The correlation between the five EORTC QLQ-C30 functioning scales and GHS scale and the eight GA measures was analysed at three time points using the Spearman rank correlation coefficient (ρ) (Wayne, 1990). The ρ can take values from +1 (perfect positive correlation) to -1 (perfect negative correlation). According to Cohen (1988), strong correlation is ≥ 0.5, medium is < 0.5 and ≤ 0.3, and small is < 0.3 and ≥ 0.1.

For those measures with a strong correlation ($\rho \geq 0.5$), multivariate linear regression models adjusted for three clinical variables, namely number of nodes (N = 0 versus N = 1–3), tumour size (T = 1 'small tumour' versus T = 2 'large tumour') and phenotype, and two socio-

demographic variables, namely age and ECOG Performance Status (ECOG PS = 0–1 versus ECOG PS = 2–4), were performed for the chemotherapy and control groups separately to assess the relative value of GA to a patient's HRQOL. Time was included as a random effect. The assessment was established with the least mean square difference (β), its 95% confidence interval (CI) and the p-value of the Wald $\chi 2$ statistic. The level of significance was set at $p < 0.05$.

Multivariate logistic regression models were used to investigate the added gain provided by geriatric information, alongside clinical and socio-demographic variables, to correctly classify patients with short-term (3 months) and long-term (one year) HRQOL decline. A dummy variable 'HRQOL decline' was created to categorize patients whose HRQOL declined versus patients whose HRQOL remained stable or improved (i.e., no decline) at three months and one year. HRQOL decline was defined as a point difference of ≥ 10 points on the EORTC QLQ-C30 scale (Osoba, Rodrigues, Myles, Zee, & Pater, 1998). The accuracy of classification was assessed in terms of sensitivity (correctly classifying true positives), specificity (correctly classifying true negatives) and classification coefficients showing how many cases were correctly categorized by the model. The assessment was established with the odds ratio (OR), its 95% CI and the p-value of the Wald $\chi 2$ statistic. The level of significance was set at $p < 0.05$.

Missing values for the clinical variables, GA measures and HRQOL scales were imputed using chained equations (MICE) (Jolani, Debray, Koffijberg, van Buuren, & Moons, 2015). This method is based on fully conditional specification where each incomplete variable is imputed by a separate model. For those patients that died during the study, we replaced the missing HRQOL and GA scale data during follow-up with their "last" reported value. All analyses were performed using Stata software.

3. Results

In total, 109 patients were included in the study, of whom 57 were in the CTG and 52 in the CG. Further patient details have been reported previously [9]. Three patients (one in CTG and two in CG) died before the end of the study. Returned and completed EORTC QLQ-C30 questionnaires and GA measures varied at different time points and among the scales (see Table 1). Although EORTC QLQ-C30 questionnaires were completed by all 109 patients at baseline, the number of questionnaires received dropped to 104 at T1 and 97 at T2, although at all time points some of the completed questionnaires were missing scores for some of the scales. Completed individual GA measures fell from 109 at baseline, to between 101 and 105 at T1, and between 94 and 99 at T2, depending on the measure.

INSERT Table 1.

3.1 Correlation between HRQOL and GA

The correlation between the EORTC QLQ-C30's GHS scale and five functioning scales and the eight GA measures are displayed in Table 1. Correlations were calculated for those patients who reported a value for both the QLQ-C30 scale and geriatric assessment measure at a specified time point. As a result, the number of observations varied across comparisons. A strong positive correlation (≥ 0.5) at baseline and over time was reported between the EORTC QLQ-C30 Physical Functioning scale and the ADL, iADL and LOFS scales. These correlations were present for both the control and the chemotherapy group (see Appendix A). At follow-up GDS became strongly correlated with the EORTC QLQ-C30 GHS and emotional functioning scale in the control group only.

The multivariate models in Table 2 show that in the control group, besides tumour size and ECOG PS, the association of geriatric measures ADL, iADL and LOFS with the EORTC QLQ-C30 PF score was statistically significant. For the CTG group, only ADL and iADL was significantly associated with the EORTC QLQ-C30 PF score, in addition to tumour size.

INSERT Table 2.

To demonstrate with an example the relationship between GA and HRQOL accounted for clinical prognostic variables, mean Physcial Functioning scores for the three time points were calculated separately for two subgroups of CTG group patients. Scores were calculated for those with small (T = 1) tumours and those with large (T = 2) tumours, as our model showed a statistically significant difference in HRQOL depending on whether the tumour in patients

undergoing chemotherapy was small (solid line in Figure 1) or large (solid line in Figure 2). Figure 1 also shows mean QLQ-C30 Physical Functioning scores for the small tumour subgroup taking into consideration whether patients had a good iADL score (= 8; short-dash line) or poor iADL score (< 8; long-dash line). Patients with a good iADL score reported a clinically better HRQOL (>10 points) than those with a poor iADL at baseline (97 versus 65), at three months (96 versus 60) and at one year (96 versus 58). A similar pattern was present in the CTG subgroup of patients with large tumours (T=2), as can be seen in Figure 2.

INSERT Figure 1 and Figure 2.

3.2 The accuracy of baseline GA to estimate HRQOL decline

Patient baseline characteristics, including GA information, might aid in predicting the evolution of a patient's HRQOL. By performing a responder analysis, we aimed to assess whether baseline GA, in combination with clinical and socio-demographic information, would be useful for classifying patients into those who would most likely experience a HRQOL decline and those whose HRQOL would most likely remain stable or improve. The results of our analysis showed that 46.2% and 55.8% of the patients in the CG group reported a HRQOL decline at three months and at one year respectively, with all other patients remaining stable or reporting an improved HRQOL. In the CTG group, 40.4% and 45.6% of the patients reported a HRQOL decline at three months and one year respectively, while the remaining patients remained stable or reported improvement. Table 3 shows the multivariate linear regression assessing the association between short term (Table 3a) and long term (Table 3b) HRQOL decline and socio-demographic and clinical variables alone on the one hand and, on the other, the association between short- and long-term decline and socio-demographic and GA measures taken together.

INSERT Table 3a and 3b

Table 4 shows the diagnostics of the multivariate models assessing the improved accuracy in predicting short-term and long-term HRQOL decline when baseline GA information is used in conjunction with the clinical and socio-demographic characteristics of a patient.

INSERT Table 4.

Normally for any model with no information about the patient, the accuracy in predicting the outcome would be 50% (~ random guess). The accuracy will most likely increase as more

characteristics of the patient, including GA information, are accounted for. In our analysis, for the CG group, when we combined information about ADL, iADL and LOFS with baseline socio-demographic and clinical information, we noticed that the relative accuracy of short-term (3 months) outcome prediction (i.e., HRQOL decline as measured with the EORTC QLQ-C30 Physical Functioning scale) increased by 24.1% (from 69.6% to 86.4%) and the accuracy of long term (one year) outcome prediction increased by 4.7% (77.3% to 81.0%). When the same process was applied to the CTG group data, the relative accuracy increased by 6.1% (from 72.5% to 76.9%) for short-term prediction and by 18.3% (from 65.0% to 76.9%) for long-term prediction.

4. Discussion

Our analysis showed a strong correlation between HRQOL, as assessed with the EORTC QLQ-C30 Physical Functioning scale, and geriatric measures ADL, iADL and LOFS at baseline and over time, within both the control and chemotherapy group. The high correlation indicates that the above measures assess similar aspects of a patient's quality of life, more specifically a patient's physical functioning. Notwithstanding the high correlation, and possible duplication in patient information, our models demonstrated that ADL, iADL and LOFS, alongside prognostic clinical and socio-demographic data, will complement our understanding of an older patient's HRQOL. More specifically, GA allows us to separate older patients into those who have a clinically better or worse HRQOL before and during treatment. Finally, GA improves accuracy when it comes to assessing which breast cancer patient's HRQOL is most likely to deteriorate over time. This observation holds both at three months and at one year and is independent of treatment.

No correlations were identified between other GA and EORTC QLQ-C30 scales addressing similar aspect of a patient's quality of life. Lack of correlation between similar measures might indicate that they are measuring different things. Similar to Iconomou et al. (2004), we found no correlation between MMSE and the EORTC QLQ-C30's Cognitive Functioning scale. This might be related to the fact that the EORTC scale is self-reported and can be evaluated differently than the objective MMSE screening test for cognitive deficits used by health care professionals. A previous study by Philips et al. (2003) also suggests that the EORTC Cognitive Functioning scale measures more emotional distress than cognitive function given its high correlation with the EORTC Emotional Functioning scale. A study by Decoster et al. (2019) reported a correlation between GDS and HRQOL, as measured with the EORTC GHS scale. A correlation which our study did not confirm. This might be explained by differences in the statistical methods used or the study population. Our study included patients who had undergone previous treatment (i.e. surgery) and less frail patients (G8>14) who might cope differently with their anxiety than newly diagnosed frail patients studied by Decoster et al.

In our multivariate models assessing the association between HRQOL and GA, LOFS was dropped as being significantly correlated with the EORTC QLQ-C30 Physical Functioning scale in the chemotherapy group. This was most likely due to the overlapping information obtained by LOFS on the one hand and ADL ($\rho = 0.57$) and iADL ($\rho = 0.73$) on the other. This phenomenon is called multicollinearity and occurs when two independent variables are

strongly correlated. As a result, the least strong indicator is removed by the multivariate model or, if retained, its strength of association becomes smaller compared to the univariate model.

In our multivariate models assessing the predictive accuracy of baseline GA to estimate HRQOL decline, we reported that almost none of the baseline clinical, socio-demographic and GA variables were prognostic for HRQOL. Nevertheless, despite this lack of prognostic value of these baseline measures in identifying subgroups most likely to experience a HRQOL decline or not, an increase in classification accuracy clearly demonstrated the incremental value of combining GA measures with clinical and socio-demographic variables.

Our study presents several limitations. The sample size of our study was relatively small, and this dilutes the strength of our findings. For example, a previous study by Decoster et al. (2019) and Quinten et al. (2019) conducted on a larger cohort of older cancer patients demonstrated the prognostic value of GA, in addition to clinical and socio-demographic variables, in HRQOL decline, a finding that we were not able to replicate in our study. In addition, our data set was missing values for several of the EORTC QLQ-C30 scales and the GA measures at follow-up, but we imputed the missing values for our inferential analysis with a method suitable for the observed missingness pattern. Another limitation is that our findings are derived from an observational study, where patients were allocated to the chemotherapy group or control group based on clinical factors and judgement rather than randomization, which would have preserved the balanced allocation of patients to treatment groups. This lack of randomization most likely also influences the fact that the HRQOL decline was higher in the control group than in the chemotherapy group, as the control group included more patients with a poor ECOG performance status, and it was mainly those patients that reported a HRQOL decline. As a result of the above limitations, more research needs to be done on a bigger and more general older population to support our results, preferably in a randomized clinical trial setting.

Notwithstanding these limitations, we believe this study lends support to the added value of GA information, used in conjunction with socio-demographic and clinical patient data, in evaluating an older breast cancer patient's HRQOL regardless of treatment. More specifically, our study demonstrates that these separate measures, which are designed to assess aspects of functional capacities, in fact complement one another, and should be considered together when assessing the functional status of an older patient with cancer.

In conclusion, our findings provide further evidence and support the recommendations (Extermann et al., 2005) that GA in an older population with early breast cancer should be

taken into account as it has the ability to improve the assessment of a patient's HRQOL. In this way, clinicians could have a sounder footing when making decisions about which intervention is optimal (Reimer & Gerber, 2010).

Author Contributions

CQ, HW, UW and CK were responsible for the conception and design of this study. CQ, HW, UW and CK designed the statistical aspects of this study. HW, MH, AC, BB, LDL, PN, PV, GD, HVDB, AS, PS and CK provided study materials or patients. HW and CK collected and assembled data and CQ analysed the data. All authors interpreted the data and contributed to the writing of the report. All authors approved the final version.

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Tables

TABLE 1.

Table 1. Spearman rank correlation between the EORTC QLQ-C30's GHS scale and five functioning scales and the eight GA measures at baseline, T1 and T2. Bold values represent strong correlations. Italic/underlined boxes represent correlations of major interest.

			Geriatric Measures							
			MNA	**CCI**	**ADL**	**iADL**	**MMSE**	**Balducci**	**LOFS**	**GDS**
QLQ-C30 Scales	Global Health Status	Baseline	N = 108 0.09	N = 102 0.04	N = 108 0.22	N = 108 0.27	N = 109 0.22	*N = 108* *-0.03*	*N = 107* *0.17*	N = 101 -0.36
		T1	N = 103 0.40	N = 101 -0.09	N = 104 0.25	N = 104 0.53	N = 104 0.44	*N = 101* *-0.33*	*N = 101* *0.47*	N = 103 -0.46
		T2	N = 95 0.44	N = 93 -0.11	N = 96 0.24	N = 96 0.36	N = 96 0.32	*N = 93* *-0.18*	*N = 93* *0.35*	N = 94 -0.60
	Physical Functioning	Baseline	N = 108 0.26	N = 102 -0.24	**N = 108** **0.78**	**N = 108** **0.81**	N = 109 0.22	N = 108 -0.12	**N = 107** **0.70**	N = 101 -0.14
		T1	N = 103 0.34	N = 101 -0.32	**N = 104** **0.74**	**N = 104** **0.78**	N = 104 0.43	N = 101 -0.04	**N = 101** **0.76**	N = 103 -0.37
		T2	N = 96 0.48	N = 94 -0.33	**N = 97** **0.69**	**N = 97** **0.79**	N = 97 0.30	N = 94 -0.12	**N = 94** **0.71**	N = 95 -0.40
	Role Functioning	Baseline	N = 108 0.19	N = 101 0.02	N = 107 0.38	N = 108 0.40	N = 109 0.03	N = 108 -0.08	N = 107 0.33	N = 101 -0.15
		T1	N = 103 0.36	N = 101 -0.24	N = 104 0.51	N = 104 0.62	N = 104 0.42	N = 101 -0.12	N = 101 0.55	N = 103 -0.43
		T2	N = 96 0.51	N = 94 0.02	N = 97 0.40	N = 97 0.31	N = 97 0.22	N = 94 0.04	N = 94 0.31	N = 95 -0.30
	Emotional Functioning	Baseline	N = 107 0.35	N = 101 0.01	N = 107 0.00	N = 107 0.06	N = 108 0.18	N = 107 0.02	N = 106 0.11	*N = 101* *-0.39*
		T1	N = 103 0.32	N = 101 -0.05	N = 104 0.30	N = 104 0.30	N = 104 0.20	N = 101 -0.08	N = 101 0.26	*N = 103* *-0.54*
		T2	N = 96 0.54	N = 94 0.01	N = 97 0.13	N = 97 0.18	N = 97 0.28	N = 94 -0.13	N = 94 0.23	*N = 95* *-0.56*
	Cognitive Functioning	Baseline	N = 108 0.08	N = 102 -0.11	N = 108 0.20	N = 108 0.14	*N = 109* *0.26*	N = 108 -0.05	N = 107 0.17	N = 101 -0.31

		T1	N = 103 0.11	N = 101 -0.11	N = 104 0.25	N = 104 0.23	*N = 104* *0.42*	N = 101 0.18	N = 101 0.24	N = 103 -0.32
		T2	N = 96 0.30	N = 94 -0.17	N = 97 0.24	N = 97 0.33	*N = 97* *0.41*	N = 94 -0.10	N = 94 0.34	N = 95 -0.38
	Social Functioning	Baseline	N = 108 0.12	N = 102 -0.04	N = 108 0.15	N = 108 0.01	N = 109 0.12	N = 108 0.09	N = 106 0.10	N = 101 -0.23
		T1	N = 103 0.47	N = 101 -0.04	N = 104 0.28	N = 104 0.33	N = 104 0.30	N = 101 -0.06	N = 101 0.32	N = 103 -0.45
		T2	N = 96 0.41	N = 94 -0.11	N = 97 0.28	N = 97 0.06	N = 97 0.07	N = 94 0.10	N = 94 0.23	N = 95 -0.44

¶ N represents the number of patients who reported a value for both the QLQ-C30 scale and geriatric measure at the defined time point.

TABLE 2

Table 2. Univariate and multivariate linear regression analyses to assess the association between EORTC QLQ-C30 Physical Functioning and GA measures ADL, iADL and LOFS adjusted for socio-demographic and clinical variables.

	Control group (N = 52)				**Chemotherapy group (N = 57)**			
	Univariate Analysis		Multivariate Analysis		Univariate Analysis		Multivariate Analysis	
	$\beta^{\ddagger}$ (95% CI) ∏	*p*-value	β (95% CI)	*p*-value	β (95% CI)	*p* -value	β (95% CI)	*p*-value
Socio-demographic and clinical variables								
Nodes N = 0 vs N = 1-3	-12.96 (-27.27;1.34)	$p = 0.076$			-7.74 (-20.62;5.14)	$p = 0.238$		
Tumour T = 1 vs T = 2	-21.68 (-35.75;-7.61)	***p* = 0.003**	-5.86 (-10.78;-0.95)	***p* = 0.019**	-16.83 (-29.67;-3.99)	***p* = 0.010**	-8.01 (-15.19;-0.83)	***p* = 0.029**
Phenotype	-7.19 (-21.42;7.03)	$p = 0.322$			-2.97 (-7.12;1.19)	$p = 0.162$		
Age	-1.18 (-2.61;0.24)	$p = 0.103$			-1.25 (-3.78;1.28)	$p = 0.331$		
ECOG PS PS = 0-1 vs PS=2-5	-56 (-70.95;-42.69)	***p* < 0.001**	-9.12 (-16.42;-1.80)	***p* = 0.015**	-19.11 (-35.60;-2.61)	***p* = 0.023**	-6.26 (-16.92;4.40)	$p = 0.249$
Geriatric variables								
ADL (higher better)	7.25 (5.83;8.67)	***p* < 0.001**	2.39 (1.13;3.65)	***p* < 0.001**	5.76 (3.97;7.56)	***p* < 0.001**	2.13 (0.46;3.81)	***p* = 0.013**
iADL (higher better)	9.55 (7.99;11.11)	***p* < 0.001**	7.59 (3.78;6.41)	***p* < 0.001**	9.43 (7.83;11.03)	***p* < 0.001**	6.07 (4.17;7.97)	***p* < 0.001**
LOFS (higher better)	9.44 (7.86;11.01)	***p* < 0.001**	2.45 (1.04;3.85)	***p* = 0.001**	7.73 (5.97;9.48)	$p < 0.001$	1.94 (-0.01;3.90)	$p = 0.051$

‡ β = Least mean square difference

∏ CI = Confidence Interval

TABLE 3

Table a. Multivariate linear regression analyses to assess the association between short-term HRQOL decline versus no HRQOL decline

	Control group (N = 52)				**Chemotherapy group (N = 57)**			
	Multivariate model including only clinical and socio-demographic variables‡		Multivariate model including clinical and socio-demographic and geriatric variables¶		Multivariate model including only clinical and socio-demographic variables‡		Multivariate model including clinical and socio-demographic and geriatric variables¶	
	OR‡ (95% CI∏)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Socio-demographic and clinical variables								
Nodes N = 0 N = 1-3	 1.00 1.86 (0.44;7.84)	 0.397	 1.00 4.23 (0.35;50.12)	 0.253	 1.00 0.21 (0.04;1.12)	 0.068	 1.00 1.67 (0.03;1.06)	 0.057
Tumour T = 1 T = 2	 1.00 4.17 (0.96;18.13)	 0.056	 1.00 12.69 (1.67;96.27)	 0.014	 1.00 10.86 (1.31;90.32)	 0.027	 1.00 16.97 (0.81;352.86)	 0.067
Phenotype	2.88 (0.72;11.49)	0.133	4.56 (0.85;24.31)	0.075	0.67 (0.39;1.16)	0.152	0.59 (0.55;1.16)	0.167
Age	1.09 (0.94;1.25)	0.213	1.14 (0.93;1.41)	0.206	0.98 (0.75;1.27)	0.909	0.80 (0.55;1.16)	0.251
ECOG PSρ PS = 0-1 PS = 2-5								
Geriatric variables								
ADL			2.25 (0.95;5.35)	0.066			0.68 (0.23;2.01)	0.494
iADL			0.67 (0.37;1.21)	0.189			0.53 (0.21;1.30)	0.166
LOFS			1.04 (0.51;2.09)	0.920			0.86 (0.38;1.93)	0.721

‡OR = Odds Ratio

∏ CI = Confidence Interval

‡ Multivariate logistic regression modelling the association between HRQOL decline and clinical variables number of nodes, tumour size, phenotype, socio-demographic variables age and ECOG PS

¶ Multivariate logistic regression modelling the association between HRQOL decline and clinical variables number of nodes, tumour size, phenotype, socio-demographic variables age and ECOG PS and geriatric variables ADL, iADL and LOFS

ρ No model fit as all patients who had poor ECOG PS reported a HRQOL decline in both groups

Table b. Multivariate linear regression analyses to assess the association between long-term HRQOL decline versus no HRQOL decline

	Control group (N = 52)				Chemotherapy group (N = 57)			
	Multivariate model including only clinical and socio-demographic variables‡		Multivariate model including clinical and socio-demographic and geriatric variables¶		Multivariate model including only clinical and socio-demographic variables‡		Multivariate model including clinical and socio-demographic and geriatric variables¶	
	OR‡ (95% CI∏)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Socio-demographic and clinical variables								
Nodes N = 0 (Ref) N = 1-3	 1.00 1.29 (0.35;4.85)	 0.698	 1.00 0.59 (0.09;3.58)	 0.570	 1.00 0.56 (0.13;2.49)	 0.453	 1.00 0.57 (0.08;3.72)	 0.558
Tumour T = 1 (Ref) T = 2	 1.00 2.05 (0.54;7.73)	 0.290	 1.00 1.91 (0.43;8.63)	 0.396	 1.00 4.14 (0.72;23.14)	 0.105	 1.00 14.31 (1.25;163.61)	 0.032
Phenotype	0.86 (0.23;3.19)	0.827	0.90 (0.21;3.92)	0.893	1.47 (0.89;2.41)	0.125	2.57 (1.08;6.09)	0.031
Age	1.20 (1.03;1.40)	0.016	1.12 (0.93;1.35)	0.220	1.10 (0.85;1.42)	0.440	1.53 (1.01;2.34)	0.044
ECOG PSρ PS = 0-1 PS = 2-5	 1.00 6.06 (0.57;64.11)	 0.134	 1.00 0.53 (0.04;87.71)	 0.746				
Geriatric variables								
ADL			0.95 (0.46;1.96)	0.891			0.34 (0.11;1.03)	0.057
iADL			0.53 (0.27;1.04)	0.066			3.42 (1.04;11.21)	0.043
LOFS			0.87 (0.49;1.53)	0.640			2.04 (0.82;5.06)	0.120

‡ OR = Odds Ratio

∏ CI = Confidence Interval

‡ Multivariate logistic regression modelling the association between HRQOL decline and clinical variables number of nodes, tumour size, phenotype, socio-demographic variables age and ECOG PS

¶ Multivariate logistic regression modelling the association between HRQOL decline and clinical variables number of nodes, tumour size, phenotype, socio-demographic variables age and ECOG PS and geriatric variables ADL, iADL and LOFS

ρ No model fit as all patients in chemotherapy group who had poor ECOG PS reported a HRQOL decline

TABLE 4

Table 4. Diagnostic accuracy of geriatric assessment when used in combination with clinical and socio-demographic variables, to predict short-term (baseline to 3 months) and long-term (baseline to 1 year) HRQOL decline versus no HRQOL decline (stable or improved)

	Control group (N = 52)		**Chemotherapy group (N = 57)**	
	A model including only clinical and socio-demographic variables‡	A model including clinical and socio-demographic and geriatric variables¶	A model including only clinical and socio-demographic variables‡	A model including clinical and socio-demographic and geriatric variables¶
Short-term (3 month evolution)				
Number of patients showing HRQOL decline versus no HRQOL decline	24 (46.2%) versus 28 (53.8%)		23 (40.4%) versus 34 (59.6%)	
Classification	69.6%	86.4%	72.5%	76.9%
Sensitivity	66.7%	77.8%	83.3%	83.3%
Specificity	68.3%	82.5%	56.3%	66.7%
Long-term (1 year evolution)				
Number of patients showing HRQOL decline versus no HRQOL decline	29 (55.8%) versus 23 (44.2%)		26 (45.6%) versus 31 (54.4%)	
Classification	77.3%	81.0%	65.0%	76.9%
Sensitivity	77.8%	81.5%	80.0%	68.4%
Specificity	77.6%	81.3%	72.5%	85.0%

‡ Multivariate logistic regression modelling the association between HRQOL decline (versus no decline) and clinical variables number of nodes, tumour size, phenotype, socio-demographic variables age and ECOG PS

¶ Multivariate logistic regression modelling the association between HRQOL decline (versus no decline) and clinical variables number of nodes, tumour size, phenotype, socio-demographic variables age and ECOG PS and geriatric variables ADL, iADL and LOFS

Figures

FIGURE 1.

Figure 1. Mean score on the EORTC QLQ-C30 Physical Functioning scale over time in chemotherapy (CTG) group patients with small tumour size (T = 1) without iADL information and stratified by those patients with good iADL scores (= 8) versus poor iADL scores (< 8).

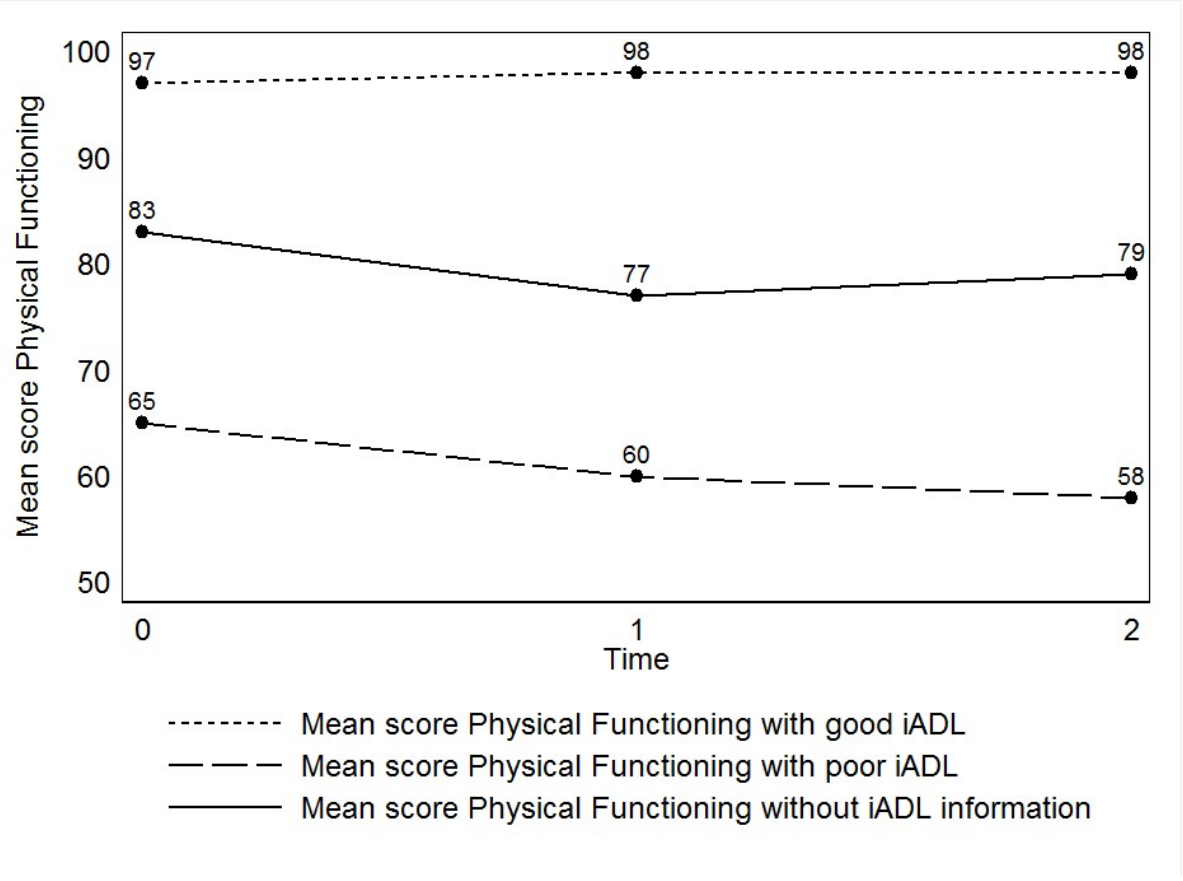

FIGURE 2.

Figure 1. Mean score on the EORTC QLQ-C30 Physical Functioning scale over time in chemotherapy (CTG) group patients with large tumour size (T = 2) without iADL information and stratified by those patients with good iADL (score=8) versus poor iADL (score<8).