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Quality of life of patients with gastrointestinal cancers undergoing chemotherapy

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Abstract

Purpose Findings regarding changes in the quality of life (QOL) of patients with gastrointestinal cancers (GI) undergoing chemotherapy (CTX) are inconclusive. Purpose was to evaluate for changes in QOL scores of patients with GI cancers over two cycles of CTX.

Methods Patients ($n = 397$) completed disease-specific [i.e., Quality of Life-Scale-Patient Version (QOL-PV)] and generic [12-item Medical Outcomes Study Short Form Survey (SF-12)] measures of QOL a total of six times over two cycles of CTX. Changes in these QOL scores were evaluated using bootstrapped multilevel regression with full information maximum likelihood estimation. Treatment group (i.e., with or without targeted therapy), age, number of metastatic sites, time from cancer diagnosis, number of prior cancer treatments, GI cancer diagnosis (i.e., colon/rectum/anal vs. other), and CTX regimen were evaluated as covariates in the conditional models for each of the QOL scores.

Results During the second cycle of CTX, QOL-PV scores decreased in the week following CTX administration, and then increased the following week. For both cycles of CTX, the physical component summary and mental component summary scores of the SF-12 decreased in the week following CTX administration and then increased the following week. Increased time from cancer diagnosis and a higher number of prior cancer treatments resulted in worse QOL-PV and SF-12 scores at enrollment.

Conclusions While changes in QOL scores over the two CTX cycles were statistically significant, the differences were not clinically meaningful. Future studies need to determine the optimal timing of QOL assessments to assess changes associated with cancer treatments.

Keywords Gastrointestinal cancer · Quality of life · Chemotherapy · Targeted therapy

Introduction

While overall and progression-free survival are important outcomes of cancer chemotherapy (CTX) [1], they do not provide information on patients' subjective well-being. Quality of life (QOL) has gained considerable importance as a primary endpoint to assist clinicians and patients to make treatment decisions [2]. Of note, assessments of QOL outcomes during cancer treatment are associated with decreased morbidity and increased patient–clinician communication about symptom burden [3].

While numerous definitions of QOL exist, most researchers agree that QOL measures should evaluate multiple domains (e.g., physical, psychological, social), as well as provide a global evaluation of QOL [4, 5]. In oncology, both generic [e.g., Medical Outcomes Study-36 Short Form

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(SF-36) [6], EuroQOL Instrument (EQ-5D) [7]] and disease-specific [e.g., European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaires (QLQ-C30) [8], Functional Assessment of Cancer Therapy—General (FACT-G) [9]] instruments are used to evaluate for changes in QOL during and following cancer treatment [10–12].

The development of targeted therapies (TT) has resulted in significant improvements in both survival and QOL in patients with gastrointestinal (GI) cancers, particularly for those with metastatic colorectal cancer (mCRC) [13]. However, the toxicities associated with CTX with or without TT can have a negative impact on patients' QOL [13]. Additional information is needed on how various treatment regimens, as well as pertinent demographic (e.g., age) and clinical (e.g., CTX treatment regimen) characteristics influence the QOL of patients with GI cancers during CTX treatment.

Findings regarding the changes in the QOL of patients with GI cancers during CTX are inconclusive. While some studies reported improvements in QOL [14, 15], others found that QOL scores remained stable or deteriorated during CTX [16, 17]. In addition, in recent studies that evaluated for differences in QOL in patients who received CTX alone and/or in combination with TT (e.g., bevacizumab, cetuximab), some studies found no differences regardless of treatment regimen (i.e., CTX alone or in combination with TT) [18–20] while others reported higher QOL in patients who received TT [21–23].

Across all of the longitudinal studies of changes in QOL in patients with GI cancers receiving CTX [14–23], the inconsistent findings may be related to a number of factors including differences in the instruments used to evaluate QOL, timing of the assessments, failure to control for clinically meaningful covariates, and the "context" of the assessments (e.g., randomized clinical trial, community settings). Given these inconsistent findings, the purpose of this study was to evaluate for changes in QOL scores in a sample of patients with GI cancers who were assessed six times over two cycles of CTX using a disease-specific and a generic measure of QOL. In addition, the effect of select demographic and clinical characteristics that are known to influence cancer patients' QOL [i.e., treatment group (CTX alone or in combination with TT) [22, 23], age [24, 25], number of metastatic sites [26], time from cancer diagnosis [27, 28], number of prior cancer treatments [29, 30], GI cancer diagnosis (i.e., colon/rectum/anal vs. pancreatic/liver, gall bladder/esophageal/small intestine) [17], CTX regimen [31]] on patients' enrollment scores, as well as on changes in QOL scores were evaluated. We hypothesized that QOL scores would change over time and that each of these covariates would influence patients' enrollment, as well as the trajectories of each of the QOL outcomes that were evaluated in this study.

Methods

Patients and settings

This study is part of a larger, longitudinal study of the symptom experience of oncology outpatients who received CTX [32, 33]. For the larger study, patients were eligible if they were ≥ 18 years of age; had a diagnosis of breast, GI, lung, or gynecological cancer; had received CTX within the preceding 4 weeks; were scheduled to receive at least two additional cycles of CTX; were able to read, write, and understand English; and provided written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veterans Affairs hospital, and four community-based oncology programs. A total of 2234 patients were approached and 1343 consented to participate (60.1% response rate) in the larger study. The major reason for refusal was being overwhelmed with their cancer treatment. For this study, only patients with GI cancers were included ($n = 397$).

Study procedures

The study was approved by the Committee on Human Research at the University of California at San Francisco and by the Institutional Review Board at each of the study sites. Eligible patients were approached by a research staff member in the infusion unit to discuss participation in the study. Written informed consent was obtained from all patients. Based on the length of the CTX cycle, GI cancer patients completed questionnaires in their homes, three times during each cycle of CTX for two consecutive cycles. During the first cycle, questionnaires were completed: before CTX administration [i.e., assessment of symptoms and QOL outcomes during recovery from previous CTX cycle, Time 1 (*T*1)], approximately 1 week after CTX administration [i.e., assessment of acute symptoms and associated QOL outcomes, Time 2 (*T*2)], and approximately 2 weeks after CTX administration [i.e., assessment of symptoms and associated QOL outcomes during the potential nadir from the CTX, Times (*T*3)]. During the second consecutive cycle of CTX, these assessments were repeated (i.e., *T*4, *T*5, and *T*6, respectively).

Instruments

A demographic questionnaire obtained information on age, sex, ethnicity, marital status, living arrangements, education, employment status, and income. Medical records were reviewed for information on stage of disease and CTX regimen. Functional status was assessed using the Karnofsky

Performance Status (KPS) scale [34], which is widely used in patients with cancer and has well-established validity and reliability [34]. Patients rated their functional status using the KPS scale that ranged from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms) [34].

Self-Administered Comorbidity Questionnaire (SCQ) [35] consists of 13 common medical conditions simplified into language that can be understood without prior medical knowledge [35]. Patients indicated if they had the condition; if they received treatment for it (proxy for disease severity); and if it limited their activity (indication of functional limitations). For each condition, patients can receive a maximum of 3 points. The total SCQ score ranges from 0 to 39. The SCQ has well-established validity and reliability [35].

The disease-specific QOL measure used in this study was the Quality of Life-Scale-Patient Version (QOL-PV). This 41-item instrument measures four domains of QOL (i.e., physical, psychological, social, and spiritual well-being), as well as a total QOL score. Each item is rated on a 0–10 numeric rating scale (NRS) with higher scores indicating a better QOL. The QOL-PV has well-established validity and reliability [36–39]. In the current study, the Cronbach's alpha for the QOL-PV total score was 0.92.

The generic measure of QOL used in this study was the 12-item Medical Outcomes Study Short Form Survey (SF-12). This instrument consists of 12 questions about physical and mental health as well as overall health status. The individual items on the SF-12 are evaluated and the instrument is scored into two components that measure physical [i.e., physical component summary (PCS) score] and mental [i.e., mental component summary (MCS) score] domains of QOL. These scores can range from 0 to 100. Higher PCS and MCS scores indicate a better QOL. The SF-12 has well-established validity and reliability [40].

Statistical analysis

All analyses were done using SPSS Version 23 (IBM, Armonk, NY) and Stata Version 14 (StataCorp LP, College Station, TX). Descriptive statistics as means and standard deviations (SD) for quantitative variables and frequencies and percentages for categorical variables were calculated. Based on a review of the literature of characteristics that are known to influence the QOL of patients with cancer, treatment group (i.e., CTX alone or in combination with TT) [22, 23], age [24, 25], number of metastatic sites [26], time from cancer diagnosis [27, 28], number of prior cancer treatments [29, 30], GI cancer diagnosis [17], CTX regimen [31] were evaluated as covariates in our longitudinal analyses.

For the three QOL scores (i.e., QOL-PV, PCS, MCS), multilevel regression analysis was used to estimate changes over time in QOL (i.e., a total of six assessments over two cycles of CTX). Estimation with multilevel regression provided an important advantage over a traditional method such as repeated measures analysis of variance (RMANOVA). Cases are not dropped in multilevel regression if one or more assessments are missing, as is the case with RMANOVA. With multilevel regression, unbiased estimates are possible as long as the missingness is ignorable (i.e., missing completely at random, missing at random, or covariate-dependent missingness) [41–47]. Missingness is handled with the use of full information maximum likelihood (FIML) [42, 47] with the expectation–maximization (EM) algorithm [42, 48]. Even if patients only provided data at the initial assessment, their data contributed to the estimation of the intercept (e.g., estimated mean at enrollment, when the intercept is modeled as the first assessment) and intercept variance. Patients contributed information to the analysis for as many times as they provided data.

Unconditional models were examined first to estimate the linear change in each QOL score without regard to treatment or other covariates. Given the possibility that the growth trajectory might not be linear, quadratic effects were examined. In addition, because the length of treatment and two treatment cycles invited the examination of shifts in the growth trajectories (also called "discontinuities") [49], piecewise models were examined. The piecewise model had four segments: enrollment ($T1$) to the $T2$, $T2$ to $T3$, $T4$ to $T5$, and $T5$ to $T6$. After identifying the best fitting growth trajectory for each QOL score (i.e., linear, linear plus quadratic, or piecewise) based on the smallest Akaike information criterion (AIC) [49], conditional models were fit to examine the association between each of the covariates (i.e., CTX alone and/or in combination with TT, age, number of metastatic sites, time from cancer diagnosis, number of prior cancer treatments, GI cancer diagnosis, and CTX regimen) on each of the QOL scores at enrollment and on the change trajectories in each of the QOL scores over time (i.e., cross-level interaction) [49].

The distributions of the three QOL scores examined in these models did not meet the assumption of normality required for multilevel regression estimation with FIML [49, 50]. Therefore, estimation was carried out using bootstrapped multilevel regression of the FIML estimates [46, 51–55]. The bootstrap was carried out with 1000 repetitions for each model. With this approach, inference regarding statistical significance was possible by inspecting the non-parametric bootstrapped bias-corrected confidence intervals [i.e., if zero was not in the 95% bias-corrected confidence interval (BC CI), the effect was significant]. A two-sided alpha of 0.05 was considered statistically significant for the CI.

Results

Demographic and clinical characteristics

Of the 397 patients with GI cancers who consented to participate, 98.0% ($n=395$) completed the QOL-PV and 97.0% ($n=392$) completed the SF-12 at *T*1. As shown in Table 1, the majority of the patients were male (55.2%), married/partnered (67.5%), and had a diagnosis of colon, rectal, or anal cancer (63.6%). The patients had a mean age of 58.0 (± 11.8) years, reported an average of 5.4 (± 2.9) comorbidities, and had a KPS score of 80.8 (± 12.5).

Table 1 Demographic and clinical characteristics of patients with gastrointestinal cancers who received chemotherapy ($n=397$)

Characteristics	Mean (SD)
Age (years)	58.0 (11.8)
Education (years)	16.1 (3.1)
Karnofsky Performance Status score	80.8 (12.5)
Self-Administered Comorbidity Questionnaire score	5.4 (2.9)
Time since cancer diagnosis (years)	1.4 (2.9)
Time since diagnosis (median)	0.42
Number of prior cancer treatments	1.4 (1.3)
Number of metastatic sites including lymph node involvement	1.5 (1.1)
	% (*n*)
Female	44.8 (181)
Married/partnered (% yes)	67.5 (270)
Lives alone (% yes)	19.0 (76)
Currently employed (% yes)	34.3 (136)
Type of prior cancer treatment	
No prior treatment	29.0 (113)
Only surgery, CTX, or RT	38.3 (149)
Surgery & CTX, or surgery & RT, or CTX & RT	21.9 (85)
Surgery & CTX & RT	10.8 (42)
Cancer diagnosis	
Colon/rectum/anal	63.6 (252)
Pancreatic/liver/gall bladder/esophageal/gastric/small intestine/and other	36.4 (144)
Genetic testing (% yes)	
BRAF detected	2.3 (9)
KRAS detected	12.7 (50)
Metastatic sites	
No metastasis	19.3 (77)
Only lymph node metastasis	19.6 (78)
Only metastatic disease in other sites	28.6 (114)
Metastatic disease in lymph nodes/and other sites	32.4 (129)
CTX regimen	
FOLFIRI	13.9 (56)
FOLFOX	43.6 (176)
FOLFIRINOX	10.9 (44)
Other	31.7 (128)
Targeted therapy	
Yes	23.4 (93)
No	76.6 (304)

BRAF B-Raf proto-oncogene, serine/threonine kinase, *CTX* chemotherapy, *FOLFIRI* leucovorin/5-fluorouracil/irinotecan, *FOLFIRINOX* leucovorin/5-fluorouracil/irinotecan/oxaliplatin, *FOLFOX* leucovorin/5-fluorouracil/oxaliplatin, *KRAS* Kristen rat sarcoma viral oncogene homolog, *RT* radiation therapy, *SD* standard deviation

Changes in QOL-PV scores

As illustrated in the piecewise model in Fig. 1a, a significant decrease in QOL-PV scores (−0.15) occurred from piecewise segment *T*4 to *T*5, followed by a significant increase (0.11) from piecewise segment *T*5 to *T*6 (Table 2). Age, time from cancer diagnosis, and number of prior cancer treatments were associated with QOL-PV scores at enrollment. A 1-year increase in age was associated with a 0.02 U increase in the reported total QOL-PV score. Each additional year from the patients' cancer diagnosis was associated with a −0.04 U decrease in total QOL-PV score. Each additional number of prior cancer treatments was associated with a −0.14 U decrease in total QOL-PV score.

Changes in PCS scores

As illustrated in the piecewise model in Fig. 1b, a significant increase in PCS scores (0.89) occurred from piecewise segment *T*2 to *T*3, followed by a significant decrease in PCS scores (−1.83) from piecewise segment *T*4 to *T*5, followed by a significant increase in PCS scores (2.34) from piecewise segment *T*5 to *T*6 (Table 3). Only time from cancer diagnosis and number of prior cancer treatments were associated with PCS scores at enrollment. Each additional year from the patients' cancer diagnosis was associated with a −0.45 U decrease in PCS scores. Each additional prior cancer treatment was associated with a −0.83 U decrease in PCS scores.

Changes in MCS scores

As illustrated in the piecewise model in Fig. 1c, a significant increase in MCS scores (1.78) occurred from piecewise segment *T*2 to *T*3, followed by a significant decrease in MCS scores (−2.63) from piecewise segment *T*4 to *T*5, followed by a significant increase in MCS scores (2.42) from piecewise segment *T*5 to *T*6 (Table 3). Age and number of prior cancer treatments were associated with MCS scores at enrollment. Each 1-year increase in age was associated with a 0.11 U increase in MCS scores. Each additional prior cancer treatment was associated with a −0.78 U decrease in MCS scores. In addition, the overall cross-level interaction with number of metastatic sites was significant. However, the effect of number of metastatic sites was not significant for any of the piecewise segments.

Discussion

To our knowledge, this study is the first to evaluate for changes in QOL in patients with a variety of GI cancers who were evaluated six times over two cycles of CTX. While the changes in QOL within each cycle were

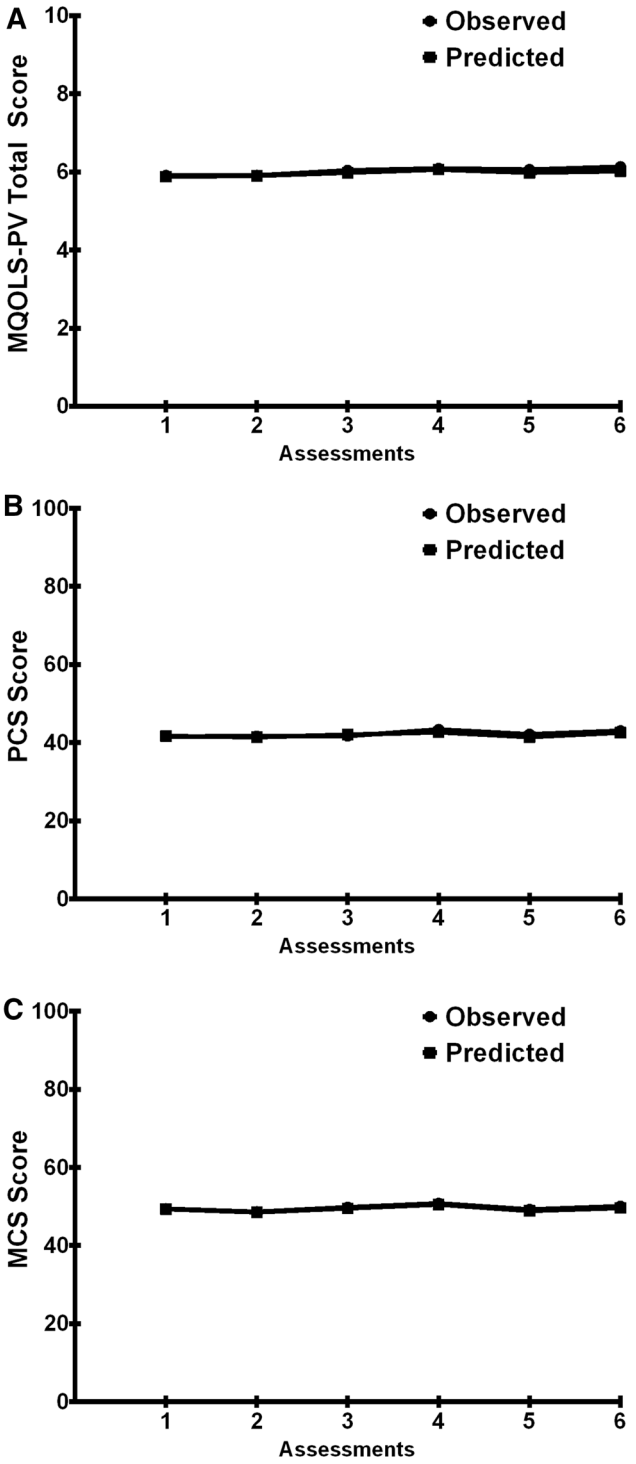

Fig. 1 **a** Observed (filled circles) and predicted (filled squares) trajectories of QOL-PV scores across the six assessments. **b** Observed (filled circles) and predicted (filled squares) trajectories of PCS scores across the six assessments. **c** Observed (filled circles) and predicted (filled squares) trajectories of MCS scores across the six assessments

Table 2 Results of the multilevel regression analyses of the Quality Of Life-Scale-Patient Version scores reported by patients with gastrointestinal cancers who received chemotherapy

Quality of life ($n=395$)				
Piecewise model				
	Unconditional model		Conditional model	
	Coefficient	BC 95% CI	Coefficient	BC 95% CI
P1 assessments	0.02	−0.048 to 0.087		
P2 assessments	0.06	−0.030 to 0.149		
P3 assessments	−0.15	−0.229 to −0.075		
P4 assessments	0.11	0.024 to 0.201		
Treatment group				
Enrollment			NS	
Cross-level interaction			NS	
Age				
P1 assessments			0.02	−0.048 to 0.087
P2 assessments			0.06	−0.030 to 0.148
P3 assessments			−0.15	−0.229 to −0.075
P4 assessments			0.11	0.024–0.201
Enrollment			0.02	0.014–0.036
Cross-level interaction			NS	
Number of metastatic sites				
Enrollment			NS	
Cross-level interaction			NS	
Time from cancer diagnosis				
P1 assessments			0.02	−0.051 to 0.083
P2 assessments			0.06	−0.023 to 0.150
P3 assessments			−0.16	−0.238 to −0.084
P4 assessments			0.12	0.035–0.212
Enrollment			−0.04	−0.096 to −0.006
Cross-level interaction			NS	
Number of prior cancer treatments				
P1 assessments			0.02	−0.051 to 0.083
P2 assessments			0.06	−0.023 to 0.150
P3 assessments			−0.16	−0.238 to −0.084
P4 assessments			0.12	0.034–0.212
Enrollment			−0.14	−0.256 to −0.022
Cross-level interaction			NS	
Cancer diagnosis				
Enrollment			NS	
Cross-level interaction			NS	
Chemotherapy regimen				
Enrollment			NS	
Cross-level interaction			NS	

BC 95% CI non-parametric bootstrapped bias-corrected confidence interval (if zero is not in the interval, the effect is significant), *NS* not significant, *P1* enrollment to time 2, *P2* time 2 to time 3, *P3* time 4 to time 5, *P4* time 5 to time 6

relatively subtle, the pattern of change in all three QOL outcomes was similar. In this study, age, time from cancer diagnosis, and number of prior cancer treatments were associated with differences in QOL scores at enrollment. Statistically significant changes in QOL scores were identified for both the disease-specific and generic measures of QOL. However, these increases and decreases in the three QOL outcomes do not represent clinically meaningful differences [56]. Our findings suggest that weekly assessments of QOL are not necessary. Future studies need to determine the optimal timing for QOL assessments during CTX [57, 58].

Table 3 Results of the multilevel regression analyses of physical component summary and mental component summary scores from the SF-12 reported by patients with gastrointestinal cancers who received chemotherapy

Physical component summary score ($n = 392$)				
	Unconditional model		Conditional model	
	Coefficient	BC 95% CI	Coefficient	BC 95% CI
P1 assessments	− 0.26	− 0.979 to 0.423		
P2 assessments	0.89	0.006–1.795		
P3 assessments	− 1.83	− 2.655 to − 0.988		
P4 assessments	2.34	1.320–3.362		
Treatment group				
Enrollment			NS	
Cross-level interaction			NS	
Age				
Enrollment			NS	
Cross-level interaction			NS	
Number of metastatic sites				
Enrollment			NS	
Cross-level interaction			NS	
Time from cancer diagnosis				
P1 assessments			− 0.26	− 0.984 to 0.467
P2 assessments			0.88	− 0.051 to 1.799
P3 assessments			− 1.83	− 2.664 to − 0.978
P4 assessments			2.34	1.287–3.391
Enrollment			− 0.45	− 0.713 to − 0.133
Cross-level interaction			NS	
Number of prior cancer treatments				
P1 assessments			− 0.25	− 0.979 to 0.470
P2 assessments			0.87	− 0.053 to 1.798
P3 assessments			− 1.83	− 2.665 to − 0.978
P4 assessments			2.34	1.287–3.388
Enrollment			− 0.83	− 1.610 to − 0.111
Cross-level interaction			NS	
Cancer diagnosis				
Enrollment			NS	
Cross-level interaction			NS	
Chemotherapy regimen				
Enrollment			NS	
Cross-level interaction			NS	
Mental component summary score ($n = 392$)				
Piecewise model				
P1 assessments	− 0.79	− 1.561 to 0.014		
P2 assessments	1.78	0.681–2.834		
P3 assessments	− 2.63	− 3.718 to − 1.596		
P4 assessments	2.42	1.138–3.779		
Treatment group				
Enrollment			NS	
Cross-level interaction			NS	
Age				
P1 assessments			− 0.79	− 1.559 to 0.015
P2 assessments			1.77	0.677–2.825

Table 3 (continued)

Mental component summary score ($n=392$)		
P3 assessments	−2.63	−3.719 to −1.598
P4 assessments	2.42	1.139–3.780
Enrollment	0.11	0.032–0.189
Cross-level interaction	NS	
Number of metastatic sites		
P1 assessments	−0.95	−2.258 to 0.346
P2 assessments	2.58	0.832–4.306
P3 assessments	−3.25	−4.859 to −1.605
P4 assessments	1.76	−0.366 to 3.793
Enrollment	NS	
Cross-level interaction: omnibus test[a]	$X^2=11.11$; $p=0.025$	
P1 by number of metastatic sites	0.11	−0.629 to 0.841
P2 by number of metastatic sites	−0.56	−1.519 to 0.424
P3 by number of metastatic sites	0.41	−0.478 to 1.373
P4 by number of metastatic sites	0.48	−0.726 to 1.813
Number of prior cancer treatments		
P1 assessments	−0.81	−1.601 to 0.257
P2 assessments	1.80	0.680–2.862
P3 assessments	−2.66	−3.729 to −1.617
P4 assessments	2.47	1.177–3.854
Enrollment	−0.78	−1.489 to −0.008
Cross-level interaction	NS	
Cancer diagnosis		
Enrollment	NS	
Cross-level interaction	NS	
Chemotherapy regimen		
Enrollment	NS	
Cross-level interaction	NS	

BC 95% CI non-parametric bootstrapped bias-corrected confidence interval (if zero is not in the interval, the effect is significant), *FOLFIRI* leucovorin/5-fluorouracil/irinotecan, *FOLFIRINOX* leucovorin/5-fluorouracil/irinotecan/oxaliplatin, *NS* not significant, *P1* enrollment to time 2, *P2* time 2 to time 3, *P3* time 4 to time 5, *P4* time 5 to time 6

[a]Omnibus test is significant, but no segment is significant for the cross-level interaction

Disease-specific measure of QOL

In terms of the disease-specific measure of QOL, changes in QOL-PV scores were found only during the second cycle of CTX. However, the pattern to the changes within the second cycle is what one would expect to occur during CTX. Compared to *T*4 (i.e., recovery from previous cycle of CTX), QOL-PV scores decreased in the week following the administration of CTX (*T*4 to *T*5). This decrease was followed by an increase in QOL scores in the week following treatment (i.e., *T*5 to *T*6). While no studies were found that assessed for changes in QOL scores within and across multiple cycles of CTX, our findings are consistent with previous reports that identified a decrease in QOL 1 week after CTX administration [58, 59]. Compared to other studies that evaluated mean QOL-PV scores in oncology patients [60, 61], our findings were generally similar. For example, in one study that evaluated QOL in patients with colon cancer [60], the mean QOL-PV score was 5.20 (±1.43), which is similar to our mean QOL-PV score of 6.02 (±0.34). In another study that evaluated QOL in women with non-small cell lung cancer [61], the mean QOL-PV score was 6.27 (±1.42). One potential explanation for the small decrease in QOL-PV in the period following the administration of CTX (*T*4 to *T*5) is that patients were experiencing a relatively high symptom burden.

Generic measures of QOL

Across the two cycles of CTX, the PCS and the MCS scores exhibited the same expected pattern of change. For both QOL outcomes, compared to the assessments done prior to the next dose of CTX (i.e., *T*1 and *T*4, "recovery from previous cycle"), PCS and MCS scores decreased in the week

following CTX (i.e., *T*1 to *T*2, *T*4 to *T*5, "acute" symptoms) and then increased in the week following the administration of CTX (i.e., *T*2 to *T*3, *T*5 to *T*6).

Compared to previous studies that used the SF-12 to evaluate QOL in oncology patients [62, 63], our mean PCS scores at enrollment was similar. However, in our study this mean PCS score (42.19 ± 10.35) was below the United States population mean of 50 [40]. This relatively low PCS score that persisted across the two cycles of CTX suggests that oncology patients undergoing CTX have deficits in general health as well as physical and role functioning, and increases in bodily pain.

Again, no studies were found that evaluated for changes in MCS scores across two cycles of CTX. However, compared to other studies that used the SF-12 [62, 64], our mean MCS score at enrollment (49.62 ± 10.11) was similar to the population norm of 50 [40]. One possible explanation for why PCS, but not MCS scores were below the population norm of 50 is that physical symptoms associated with CTX have a more immediate effect on patients' ability to function.

Age

Consistent with previous reports [24, 65], younger age was associated with lower QOL-PV and MCS scores at enrollment. In terms of the QOL-PV scores, one possible explanation for this association may be that younger patients continue to work during CTX, which may have a negative impact on their overall QOL [25]. In addition, younger patients are more likely to receive higher doses of CTX, which may result in increased toxicities and associated decrements in QOL [24]. In terms of the MCS scores, younger patients may have lower scores because they have fewer coping strategies and resources to manage a life-threatening illness like cancer [66]. In addition, compared to older patients, younger patients may view their cancer as a greater threat to their overall survival [67].

Time from cancer diagnosis

Consistent with previous reports [27, 28, 68–72], increased time from cancer diagnosis was associated with lower QOL-PV and PCS scores at enrollment. For both of these scores, it is possible that patients who had cancer longer had received a variety of treatments that had cumulative effects. These adverse effects had a negative impact on patients' physical and psychological well-being [73]. In our study, time from cancer diagnosis had a wide range (i.e., 1–30 years; median = 0.42). While previous studies found that oncology patients may experience a "response shift" in their appraisal of their QOL (i.e., they adjust their internal standard and QOL improves), the exact time from the diagnosis may influence this response shift [27, 68].

Number of prior cancer treatments

Across all three QOL outcomes, a higher number of prior treatments was associated with lower QOL scores at enrollment. This finding is consistent with previous studies that found that patients who received multiple types of CTX reported more treatment-related adverse effects, which can negatively impact their QOL [29, 30]. In addition, and consistent with our findings regarding length of time from cancer diagnosis, patients are more likely to receive additional treatments as a result of disease progression which could result in cumulative toxicities [31].

Limitations and conclusions

Several limitations warrant consideration. First, QOL was not assessed prior to the initiation of CTX. Second, while the sample size was large, the numbers of patients diagnosed with pancreatic, esophageal, and gastric cancers were relatively small. In addition, only 23.4% of these patients received a TT with their CTX. Therefore, our findings may not generalize to all GI cancer patients receiving CTX with or without TT. Future studies are warranted that evaluate the impact of other factors that are known to influence QOL (e.g., social support, life style factors), on initial levels as well as the trajectories of various domains of QOL.

Despite these limitations, this study is the first to evaluate for changes in QOL six times over two cycles of CTX, as well as the effect of a number of demographic and clinical characteristics on QOL outcomes. Clinicians can use the findings regarding significant predictors to identify patients who are at greater risk for poorer QOL outcomes. In addition, while our findings support the evaluation of QOL during CTX treatment, the optimal timing of these assessments warrants additional investigation. Future studies should be carried out to identify appropriate timing of QOL assessments to be able to identify patients who warrant interventions to improve their QOL.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

Ethical approval All procedures performed in this study are in accordance with ethical standards of the Institutional Review Board at the University of California, San Francisco, and with the Declaration of Helsinki.

Informed consent Written informed consent was obtained from all study participants.

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