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Sarcopenia and quality of life in Black South African women newly diagnosed with breast cancer living with and without HIV

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Abstract

Purpose: To examine associations between pre-treatment sarcopenia and quality of life during and after chemotherapy among Black South African women with stage I–III breast cancer, and whether these differed by HIV status.

Methods: Women with newly diagnosed stage I-III breast cancer between June 1, 2021 and August 31, 2024 at Chris Hani Baragwanath Academic Hospital, Soweto, were classified using revised European Working Group on Sarcopenia in Older People (EWGSOP2) criteria. They completed the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) at baseline, end of chemotherapy, and six months following the completion of chemotherapy. Scores range 0–100, with higher scores indicating better functioning or greater symptom burden, depending on the variable. Age-adjusted linear mixed-effects models included time, sarcopenia, HIV, and two-way interactions, with false-discovery-rate correction.

Results: Among 447 women, 106 (23.7%) had probable, confirmed, or severe sarcopenia. At baseline, unadjusted scores were poorer on eight scales among women with sarcopenia. No time × sarcopenia interaction remained significant after false-discovery-rate correction. Sarcopenia × HIV interactions remained significant for seven scales (q=0.034–0.046). For social functioning, sarcopenia was associated with a 21.0-point lower score among women living with HIV (95% CI −31.5 to −10.5) versus −2.7 points among HIV-negative women (95% CI −10.0 to 4.7). Only social functioning and constipation remained significant using laboratory HIV status where available.

Conclusion: Associations varied by HIV status, although only the interactions for social functioning and constipation remained significant when laboratory HIV status was used.

Keywords: Sarcopenia; Breast cancer; Health-related quality of life; HIV; Chemotherapy; South Africa.

Introduction

The 5-year overall survival rate for breast cancer is estimated to be 40% in sub-Saharan Africa, compared with 85–90% in high-income countries [1,2], with data from our group's South African Breast Cancer and HIV Outcomes (SABCHO) longitudinal study reporting a 5-year crude overall survival rate of 44% [3]. In this cohort, we identified high prevalences of cardiovascular disease and HIV-positive status among participants, both of which were associated with increased mortality risk [3]. These findings highlight the importance of identifying and managing co-existing conditions at the time of breast cancer diagnosis.

Sarcopenia, characterised by reduced muscle strength and reduced muscle quantity or quality [4], is associated with poorer overall survival in patients with cancer. A meta-analysis of 100 studies found that each standard deviation decrease in lean mass was associated with a 41% higher risk of all-cause mortality among patients with cancer [5], and Caan et al. (2018) [6] have shown that sarcopenia among women with stage II or III breast cancer is associated with higher all-cause mortality. Sarcopenia and lower lean mass have also been associated with greater chemotherapy toxicity and toxicity-related treatment modifications in women with breast cancer [7,8].

Across patients with a range of advanced cancers, sarcopenia has been linked to poorer health-related quality of life [9]. Beyond its impact on physical function, reduced muscle strength and mass may affect independence and emotional wellbeing [9]. Quality of life may also decline during chemotherapy in women with breast cancer, although the pattern and persistence of these changes differ among women [10,11]. It is not known whether sarcopenia is associated with quality of life at diagnosis, and whether quality of life changes are different during and after chemotherapy in women with and without sarcopenia.

This question is particularly relevant in South Africa, where human immunodeficiency virus (HIV) forms part of the broader burden of co-existing conditions among women with breast cancer [12]. Approximately one in five women with stage I–III breast cancer in the SABCHO cohort were living with HIV [13]. In a meta-analysis of 13 studies, sarcopenia was present in

24.1% of people living with HIV [14]. Whether the association between sarcopenia and quality of life in women with breast cancer differs by HIV status has not been established.

This study therefore investigated the association between sarcopenia and quality of life at breast cancer diagnosis, at the end of chemotherapy, and six months post-treatment among Black South African women with stage I–III breast cancer. A secondary aim was to determine whether these associations differed by HIV status.

Methods

Study population

Data were collected prospectively in a sub-cohort of women enrolled in the South African Breast Cancer and HIV Outcomes (SABCHO) study [15]. Since 2015, the SABCHO study has enrolled and followed more than 5,000 women newly diagnosed with breast cancer across six public hospitals in South Africa [16]. Institutional review boards at Columbia University (protocol AAAQ1359) and the University of the Witwatersrand (M200138) provided ethical approval for the study. Written informed consent was obtained from all participants.

Recruitment was restricted to women who received care at the Chris Hani Baragwanath Academic Hospital (Bara), a public tertiary hospital located in Soweto, Johannesburg [16], because dual-energy X-ray absorptiometry (DXA) for body composition assessment was available at the SAMRC/Wits Ageing African Adult Research Unit (A3RU) on the hospital campus [17].

Patient population

Women aged 18 years or older who were newly diagnosed with histologically confirmed stage I–III breast cancer at Bara between June 1, 2021 and August 31, 2024, and had no previous malignancies, were eligible for enrolment. At baseline, participants completed an interview with a study nurse that included information on socioeconomic characteristics and medical history. All baseline assessments were completed before initiation of systemic breast cancer treatment.

Quality of life assessment

Quality of life was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) at baseline, at the end of chemotherapy, and six months after completion of chemotherapy [18]. The questionnaire includes a global health status/quality of life scale, five functional scales (physical, role,

emotional, cognitive and social functioning), three symptom scales (fatigue, nausea and vomiting, and pain), and six single-item measures that assess dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties. Scores were transformed to a 0–100 scale according to the EORTC scoring manual, with higher scores indicating better global quality of life and functioning, and higher symptom scores indicating greater symptom burden [19].

Clinical characteristics

Body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared and categorised as normal weight (<25 kg/m^2), overweight (25.0–29.9 kg/m^2) or obesity (≥30 kg/m^2) [20]. Medical history included self-reported diabetes, hypertension, heart disease, stroke, tuberculosis and arthritis; tobacco and alcohol use data were also collected. Breast cancer characteristics included stage at diagnosis and receptor status, classified as hormone receptor-positive (HR+)/HER2−, HR−/HER2+, HR+/HER2+ or triple-negative (ER−/PR−/HER2−).

HIV status

Participants were asked to self-report their HIV status, and confirmatory testing was performed through the South African National Health Laboratory Service (NHLS) using an enzyme-linked immunosorbent assay. For the primary analyses, HIV status was based on self-report; where self-reported status was missing, an available laboratory result was used. In a sensitivity analysis, HIV status was defined using the laboratory result where available in preference to self-report. Women living with HIV were offered infectious disease specialty care and had baseline testing of CD4 count (reported in cells/μL) and HIV viral load (copies/mL). All women with HIV were confirmed to be on antiretroviral treatment prior to initiation of chemotherapy. Since 2019, the preferred first-line treatment in South Africa has been a once-daily, single-tablet fixed-dose combination of tenofovir disoproxil fumarate (TDF), lamivudine (3TC) and dolutegravir (DTG), commonly referred to as TLD [21,22].

DXA-derived body composition

Whole-body composition was assessed at baseline before initiation of systemic breast cancer treatment using a Hologic Discovery A dual-energy X-ray absorptiometry scanner (Hologic Inc., Bedford, MA, USA; Apex software version 13.4.2:3; serial number 83145). Scanner performance was monitored according to manufacturer quality-assurance procedures. Appendicular lean mass was calculated as the sum of the fat-free soft tissue mass of the upper and lower limbs.

Assessment of sarcopenia

Handgrip strength was measured using a Jamar hydraulic hand-held dynamometer (Sammons Preston, Bolingbrook, USA), with participants seated and the arm flexed at 90° alongside the body. The highest of three measurements of the non-dominant hand was used. Gait speed was measured over 6 meters, with participants instructed to walk at normal pace. Sarcopenia was classified according to the revised European Working Group on Sarcopenia in Older People (EWGSOP2) criteria [4]. Low muscle strength, defined as handgrip strength <16 kg, indicated probable sarcopenia. Sarcopenia was confirmed when low muscle strength was accompanied by an appendicular skeletal muscle index [ASMI; appendicular lean mass (ALM)/height^2] <5.5 kg/m^2. Severe sarcopenia was defined as confirmed sarcopenia with a gait speed <0.8 m/s. For analyses, participants with probable, confirmed or severe sarcopenia were classified as having sarcopenia; those with handgrip strength ≥16 kg were classified as not having sarcopenia. Participants without a valid handgrip measurement were excluded.

Statistical Analysis

Continuous variables were summarised using means and standard deviations (SDs) or medians and interquartile ranges (IQRs), as appropriate, and categorical variables using frequencies and percentages. Age was compared between participants with and without sarcopenia using an independent-samples *t*-test and body mass index using a Wilcoxon rank-sum test. Categorical characteristics were compared using chi-squared tests, with Fisher's exact tests used where cell counts were sparse. EORTC QLQ-C30 scores were compared between sarcopenia groups at baseline, at the end of chemotherapy and six months after completion of chemotherapy using Wilcoxon rank-sum tests. These time-specific comparisons were not adjusted for covariates or multiple testing.

In the primary analysis, QLQ-C30 scale scores were calculated only when all component items were available. Longitudinal associations with each of the 15 EORTC QLQ-C30 scales were examined separately using linear mixed-effects models fitted by restricted maximum likelihood with a participant-specific random intercept. Time was modelled categorically as baseline, end of chemotherapy and six months after completion of chemotherapy. Models included time, sarcopenia status, HIV status and age at diagnosis, together with time × sarcopenia, time × HIV and sarcopenia × HIV interaction terms. Baseline, no sarcopenia and HIV-negative status were the reference categories. Models used all available observations for each outcome; participants were not required to have quality-of-life data at all three assessments. Wald tests were used to assess model terms. Benjamini–Hochberg false-discovery-rate correction was

applied separately to each model term across the 15 quality-of-life scales, and both nominal *p* values and false-discovery-rate-adjusted q values were calculated.

Changes between baseline and the end of chemotherapy, the end of chemotherapy and six months, and baseline and six months were additionally estimated within each sarcopenia group using separate age-unadjusted linear mixed-effects models with participant-specific random intercepts. *P* values for the three pairwise time comparisons were Bonferroni-adjusted within each scale and sarcopenia group. Age-adjusted differences in QLQ-C30 scores associated with sarcopenia were also estimated separately by HIV status from the primary mixed-effects models and displayed with 95% confidence intervals.

Sensitivity analyses repeated the primary models without adjustment for age; with the participant whose three handgrip measurements were recorded as 0 kg retained and classified as having sarcopenia; using the EORTC QLQ-C30 missing-item scoring rule; and using laboratory HIV status where available. Two-sided $p<0.05$ was considered statistically significant for individual tests and Bonferroni-adjusted pairwise comparisons, while $q<0.05$ indicated statistical significance after false-discovery-rate correction. Analyses were performed using StataNow/SE version 19.5 (StataCorp LLC, College Station, TX, USA).

Results

General characteristics

Of 454 women with a sarcopenia assessment, seven were excluded from the primary analysis because handgrip strength was not measured (n=6) or all three handgrip trials were recorded as 0 kg (n=1), leaving 447 women in the analytic sample. Of these, 341 were classified as not having sarcopenia and 106 (23.7%) as having probable, confirmed or severe sarcopenia (Figure S1).

The mean age of the cohort was 48.7 (SD 11.7) years, and women with sarcopenia were older than women without sarcopenia (54.0 vs 47.0 years, $p<0.001$) (Table 1). Median BMI was 31.2 kg/m^2 (IQR 27.0–35.6), with 58.2% of participants living with obesity; neither BMI nor BMI category differed by sarcopenia status. Hypertension was more common among women with sarcopenia (46.7% vs 27.6%, $p<0.001$), while the other measured comorbidities and health behaviours did not differ significantly between groups. HIV prevalence was similar among women with and without sarcopenia (32.1% vs 32.6%, $p=0.927$). Among participants with available stage data, 98.0% had stage II or III breast cancer, and stage and receptor-status distributions did not differ significantly by sarcopenia status.

Quality of life by sarcopenia status

At baseline, unadjusted comparisons showed poorer physical, emotional, cognitive and social functioning among women with sarcopenia, together with greater fatigue, pain, constipation and financial difficulties (all $p<0.05$). The largest between-group differences were observed for social functioning (65.3 [SD 36.4] vs 77.8 [SD 29.9]) and financial difficulties (57.9 [SD 44.2] vs 41.1 [SD 42.6]). At the end of chemotherapy, social functioning was the only scale that differed significantly between groups (48.1 [SD 39.5] vs 59.6 [SD 34.8], $p=0.033$). None of the between-group comparisons reached statistical significance six months after chemotherapy. Quality-of-life data were available at six months for 218 of 341 women without sarcopenia (63.9%) and 42 of 106 women with sarcopenia (39.6%); retention differed by sarcopenia status ($p<0.001$) (Table S1).

Changes in quality of life over time

Among women without sarcopenia, significant deterioration from baseline to the end of chemotherapy was observed for 14 of the 15 quality-of-life scales, with global health status/quality of life the only exception (Figure 1; Table S2). The largest declines in functioning were observed for role functioning (mean change −20.56, $p<0.001$), social functioning (−18.38, $p<0.001$) and cognitive functioning (−15.32, $p<0.001$). Seven scales improved significantly between the end of chemotherapy and six months: global health status/quality of life, physical and role functioning, fatigue, nausea and vomiting, appetite loss and diarrhoea. Despite this improvement, physical, role, cognitive and social functioning, fatigue, pain, constipation and financial difficulties remained significantly worse at six months than at baseline.

Among women with sarcopenia, physical (mean change −7.07, $p=0.029$), cognitive (−13.52, $p=0.001$) and social functioning (−17.49, $p=0.009$) worsened significantly from baseline to the end of chemotherapy; the change in role functioning did not reach statistical significance after Bonferroni adjustment (−10.40, $p=0.075$). No scale changed significantly between the end of chemotherapy and six months or between baseline and six months (Table S2).

Longitudinal associations of time, sarcopenia and HIV with quality of life

In the age-adjusted mixed-effects models, the time term, representing change over time among HIV-negative women without sarcopenia, remained significant after false-discovery-rate correction for 14 of the 15 quality-of-life scales, with insomnia the only exception ($q=0.066$) (Table S3). No sarcopenia or HIV main-effect terms remained significant after false-discovery-rate correction. Time × sarcopenia interactions were observed for role functioning ($p=0.032$), fatigue ($p=0.018$) and financial difficulties ($p=0.013$), but none remained significant after false-

discovery-rate correction (q=0.161, 0.133 and 0.133, respectively). No time × HIV interaction was statistically significant.

Sarcopenia × HIV interactions remained significant after false-discovery-rate correction for seven quality-of-life scales: global health status/quality of life, emotional and social functioning, fatigue, insomnia, appetite loss and constipation (q=0.034–0.046; Table S3; Figure 2). The magnitude and direction of the sarcopenia-associated differences varied by HIV status. Among women living with HIV, sarcopenia was associated with a 21.0-point lower social functioning score (95% CI −31.5 to −10.5) and a 14.3-point higher constipation score (95% CI 5.5 to 23.0), averaged across the three assessments. The corresponding differences among HIV-negative women were −2.7 points (95% CI −10.0 to 4.7) and −0.2 points (95% CI −6.3 to 5.9), respectively (Figure 2).

Sensitivity analyses

No sarcopenia main-effect or time × sarcopenia interaction remained significant after false-discovery-rate correction in any sensitivity analysis (Table S4). For the sarcopenia × HIV interaction, eight scales remained significant after false-discovery-rate correction when age was omitted from the models, five when the participant with handgrip values recorded as 0 kg was retained as having sarcopenia, and six when QLQ-C30 scores were calculated using the EORTC missing-item rule. When laboratory HIV status was used where available, significant sarcopenia × HIV interactions remained for social functioning and constipation.

Discussion

Women with sarcopenia at breast cancer diagnosis reported poorer quality of life across several functional and symptom domains than women without sarcopenia, although these baseline comparisons were unadjusted. During chemotherapy, quality of life deteriorated across more domains among women without sarcopenia, and the between-group differences apparent at diagnosis became less evident over follow-up. However, evidence that quality-of-life trajectories differed by sarcopenia status did not persist after false-discovery-rate correction. In contrast, sarcopenia × HIV interactions remained significant across seven quality-of-life domains in the primary analysis, although the pattern was less extensive in sensitivity analyses.

The poorer quality of life observed among women with sarcopenia at diagnosis is consistent with broader observational evidence. A meta-analysis of 43 observational studies, almost all cross-sectional, showed lower health-related quality of life among people with sarcopenia,

although there was substantial heterogeneity between studies [23]. Cross-sectional studies have similarly linked sarcopenia with poorer physical and mental components of quality of life, while lower handgrip strength has been associated with poorer general health and physical functioning [24,25]. In this study, differences were evident not only in physical functioning but also in emotional functioning, concentration and memory, family and social activities, and several symptom domains. Because sarcopenia and quality of life were assessed concurrently at diagnosis, the direction of these associations cannot be determined.

Quality of life deteriorated during chemotherapy and partially recovered thereafter, a pattern reported in longitudinal studies in women treated for early breast cancer. Chemotherapy has been associated with poorer physical and cognitive functioning, dyspnoea, and financial difficulties during follow-up [10]. In the CANTO cohort, longer-term quality-of-life trajectories varied considerably, with persistent deterioration more common among women with obesity, comorbidities, lower income and current smoking [11]. In the current study, the baseline differences between women with and without sarcopenia became less apparent during follow-up. For role functioning, the nominal interaction reflected poorer scores among women with sarcopenia at diagnosis and a larger decline during chemotherapy among women without sarcopenia, followed by some recovery in both groups. Similar declines in role functioning during chemotherapy, followed by recovery after treatment, have been reported in other breast cancer studies [26,27]. A recent study also found deterioration in health-related quality of life during breast cancer treatment among women with better baseline muscle quality but not among those with poorer muscle quality, although muscle quality and sarcopenia represent different constructs [28]. The smaller change among women with sarcopenia may therefore partly reflect their poorer quality of life at diagnosis, leaving less scope for further measurable deterioration. Nevertheless, none of the time × sarcopenia interactions remained significant after correction for multiple testing, so these patterns should be interpreted descriptively rather than as robust evidence of different trajectories.

In contrast, sarcopenia × HIV interactions remained significant after correction for multiple testing across seven quality-of-life domains. Across these domains, the estimated differences associated with sarcopenia were consistently adverse among women living with HIV, with poorer global quality of life and emotional and social functioning and greater fatigue, insomnia, appetite loss, and constipation, whereas corresponding differences among women without HIV were attenuated and in several domains were in the opposite direction. There was no evidence that quality-of-life trajectories differed by HIV status, consistent with findings from the prospective Thabatse Cancer Cohort in Botswana, where improvement in physical and mental

quality of life did not differ significantly by HIV status among women treated for stage I–III breast cancer [29]. Evidence from people living with HIV nevertheless suggests that sarcopenia itself may be relevant to quality of life: in a cross-sectional study of 150 adults living with HIV in Hong Kong, sarcopenia was associated with poorer mobility and physical functioning and lower physical-component quality-of-life scores after adjustment for age and sex [30]. Sarcopenia is also more prevalent among people living with HIV than among HIV-negative populations [14]. Comparable studies examining sarcopenia and HIV together in women with breast cancer are lacking, and the mechanisms underlying the observed interaction cannot be determined from the present study. The interaction pattern was broadly reproduced in sensitivity analyses of age adjustment, sarcopenia classification and QLQ-C30 scoring, but when laboratory HIV status was used where available, only social functioning and constipation remained significant after false-discovery-rate correction. Together with the small number of women with both sarcopenia and HIV, this limits confidence in the domain-specific pattern and warrants confirmation in larger studies.

The findings have implications for the assessment of supportive-care needs before and during breast cancer treatment. The widespread deterioration in quality of life during chemotherapy, together with the absence of robust differences in trajectories by sarcopenia status, suggests that sarcopenia status alone does not distinguish women with different quality-of-life trajectories during treatment. Its potential relevance may instead lie in characterising the greater burden of impaired functioning and symptoms already present at diagnosis, with the primary analysis also suggesting that these associations may differ according to HIV status. However, the present study does not establish the predictive or clinical utility of sarcopenia assessment, either alone or in combination with HIV status. Further studies should determine whether measures of muscle strength and mass provide clinically useful information beyond direct assessment of quality of life and routinely available clinical characteristics, and whether such information can meaningfully inform supportive-care decisions.

Strengths of this study include prospective assessment of quality of life before chemotherapy, at the end of chemotherapy and six months later, classification of muscle strength and sarcopenia status using EWGSOP2 criteria, and correction for multiple testing in the longitudinal analyses. The baseline comparisons between women with and without sarcopenia were unadjusted for covariates and were not corrected for multiple testing. Because sarcopenia and quality of life were assessed concurrently at diagnosis, these comparisons cannot establish the direction of the observed associations. Women with sarcopenia were older at diagnosis, so age and other differences between the groups may have contributed to

the baseline associations. Although the longitudinal models were adjusted for age, residual confounding by other clinical and social factors remains possible. Loss to follow-up was substantial and differed by sarcopenia status; by six months, quality-of-life data were available for 63.9% of women without sarcopenia and 39.6% of women with sarcopenia. Although the mixed-effects models incorporated all available observations, they do not eliminate bias if loss to follow-up was related to unobserved quality of life or other factors not captured by the models; the direction and magnitude of any resulting bias cannot be determined. Sarcopenia was assessed only at diagnosis, so it was not possible to examine whether changes in muscle status during treatment accompanied changes in quality of life. Finally, the study was conducted at a single public-sector hospital among Black South African women with predominantly stage II–III breast cancer, and only 34 women had both sarcopenia and HIV, limiting the precision of the interaction estimates and the generalisability of the findings to other populations and treatment settings.

Among Black South African women with stage I–III breast cancer, women with sarcopenia at diagnosis reported poorer quality of life across several domains, although evidence that quality-of-life trajectories differed by sarcopenia status did not persist after correction for multiple testing. The association between sarcopenia and quality of life differed by HIV status in the primary analysis, although the domain-specific pattern was sensitive to HIV classification. These findings require confirmation in larger studies before the clinical utility of sarcopenia assessment can be established.

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Consent to participate

Written informed consent was obtained from all participants.

Conflicts of interest

The authors declare no competing interests.

Data availability

Data access is subject to approval. Requests for new collaborations and data access may also be directed to the principal investigator.

Author contributions

Contributors L.K.M., W.C.C., L.Q., M.J., A.I.N. – conceptualisation; W.C.C., L.Q. - statistical analysis; L.K.M, M.L. - writing draft; All authors – review and editing of final manuscript.

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Tables

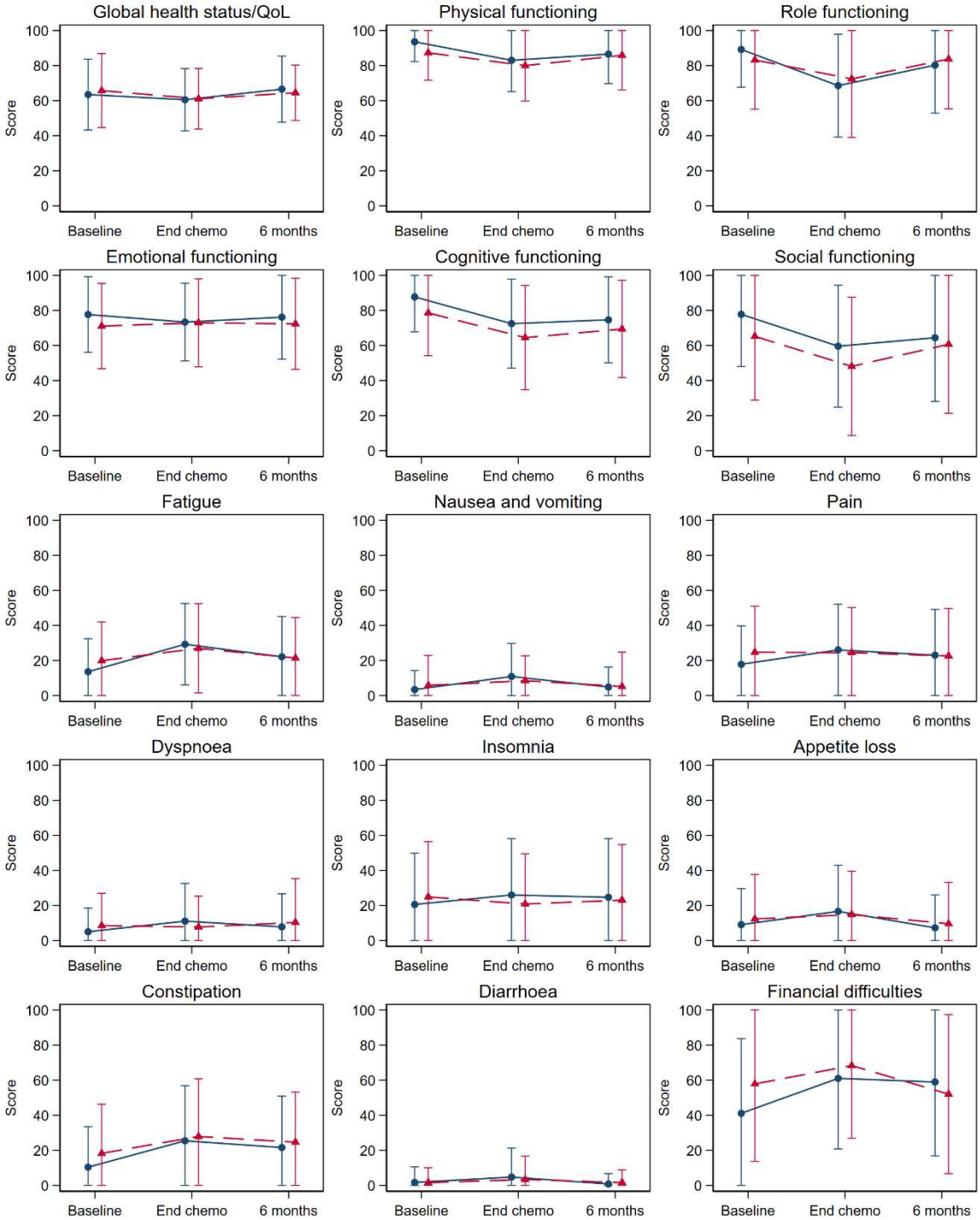
Table 1. Baseline demographic and clinical characteristics (n=447)

Characteristic	No sarcopenia (n=341)	Probable, confirmed or severe sarcopenia (n=106)	Full cohort (N=447)	p-value
Age, years, mean (SD)	47.0 (11.2)	54.0 (11.9)	48.7 (11.7)	**<0.001**[a]
BMI, kg/m^2, median (IQR)	31.1 (27.0–35.6)	31.8 (25.8–35.2)	31.2 (27.0–35.6)	0.840[b]
BMI category, n (%)				0.153[c]
Normal weight (<25 kg/m^2)	44 (12.9)	20 (18.9)	64 (14.3)	
Overweight (25.0–29.9 kg/m^2)	100 (29.3)	23 (21.7)	123 (27.5)	
Obesity (≥30 kg/m^2)	197 (57.8)	63 (59.4)	260 (58.2)	
Comorbidities, n (%)[d]				
Diabetes	20 (5.9)	12 (11.4)	32 (7.2)	0.053[c]
Hypertension	94 (27.6)	49 (46.7)	143 (32.1)	**<0.001**[c]
Heart disease	2 (0.6)	0 (0.0)	2 (0.4)	1.000[e]
Stroke	2 (0.6)	2 (1.9)	4 (0.9)	0.237[e]
Tuberculosis	15 (4.4)	6 (5.7)	21 (4.7)	0.578[c]
Arthritis	4 (1.2)	1 (1.0)	5 (1.1)	1.000[e]

Characteristic	No sarcopenia (n=341)	Probable, confirmed or severe sarcopenia (n=106)	Full cohort (N=447)	p-value
Tobacco use	16 (4.7)	5 (4.8)	21 (4.7)	0.976[c]
Alcohol use	79 (23.2)	32 (30.5)	111 (24.9)	0.130[c]
Living with HIV, n (%)	111 (32.6)	34 (32.1)	145 (32.4)	0.927[c]
Breast cancer stage, n (%)[f]				0.757[c]
I	6 (1.9)	2 (2.3)	8 (2.0)	
II	110 (34.7)	34 (38.6)	144 (35.6)	
III	201 (63.4)	52 (59.1)	253 (62.5)	
Receptor status, n (%)[g]				0.561[c]
HR+/HER2−	160 (50.3)	49 (51.0)	209 (50.5)	
HR−/HER2+	26 (8.2)	10 (10.4)	36 (8.7)	
HR+/HER2+	86 (27.0)	20 (20.8)	106 (25.6)	
Triple negative (ER−/PR−/HER2−)	46 (14.5)	17 (17.7)	63 (15.2)	

Notes: [a] Independent-samples t-test. [b] Wilcoxon rank-sum test. [c] Chi-squared test. [d] Comorbidity data missing for 1 participant; percentages use denominators of 341 and 105. [e] Fisher's exact test (expected cell count <5). [f] Stage available for 405/447 (42 missing); percentages use denominators of 317 and 88. [g] Receptor status available for 414/447 (33 missing); percentages use denominators of 318 and 96.

Figures



Blue circles, solid line: no sarcopenia. Red triangles, dashed line: sarcopenia.
Error bars: ±1 SD (truncated at 0 and 100).
Global health status and functional scales: higher = better.
Symptom scales and single items: higher = worse.

Figure 1. Quality-of-life trajectories according to sarcopenia status.
Points show observed mean EORTC QLQ-C30 scores at baseline, end of chemotherapy and 6 months after completion of chemotherapy; error bars indicate ±1 SD and are truncated at the 0–100 scale limits. Higher scores indicate better quality of life or functioning for global health status and functional scales, and greater symptom burden for symptom scales and financial difficulties.

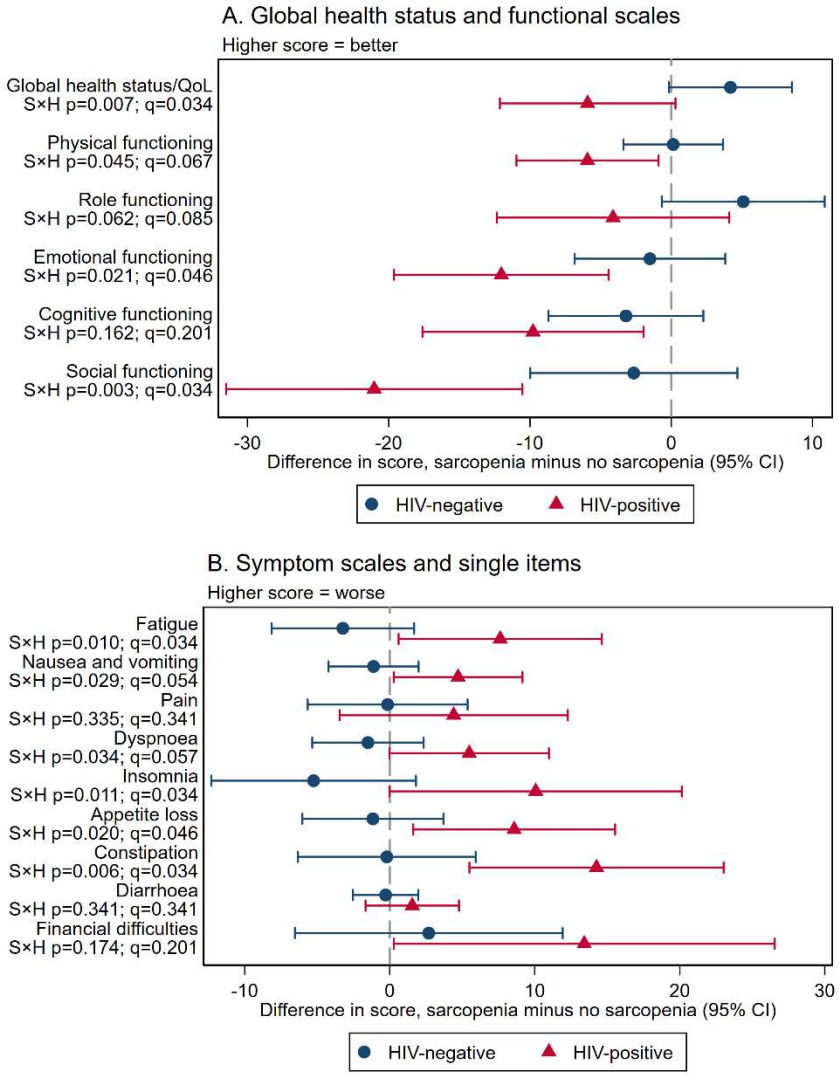


Figure 2. Age-adjusted association between sarcopenia and EORTC QLQ-C30 scores according to HIV status.

Points show the estimated difference in score between women with and without sarcopenia (sarcopenia minus no sarcopenia), separately for HIV-negative and HIV-positive women, averaged equally across baseline, end of chemotherapy and 6 months; horizontal bars indicate 95% confidence intervals. Estimates were derived from linear mixed-effects models including time, sarcopenia, HIV status, age at diagnosis, and time×sarcopenia, time×HIV and sarcopenia×HIV interactions. Panel A shows global health status/quality of life and functional scales; Panel B shows symptom scales and financial difficulties. Higher scores indicate better health status or functioning for the global and functional scales, and greater symptom or financial burden for the symptom scales and financial difficulties. Sarcopenia×HIV interaction P values and Benjamini–Hochberg–adjusted q values are reported in Table S3.

Supplementary tables

Table S1. Quality of life by sarcopenia status at each assessment

Quality-of-life indicator	Baseline: No sarcopenia (n=341)	Baseline: Sarcopenia (n=106)	*P* value	End of chemotherapy: No sarcopenia (n=248)	End of chemotherapy: Sarcopenia (n=61)	*P* value	6 months: No sarcopenia (n=218)	6 months: Sarcopenia (n=42)	*P* value
Global health status/QoL	63.5 (20.2)	65.7 (21.1)	0.136	60.5 (17.7)	61.1 (17.3)	0.751	66.6 (18.8)	64.5 (15.8)	0.300
Functional scales									
Physical functioning	93.6 (11.3)	87.3 (15.7)	**<0.001**	83.0 (17.9)	80.0 (20.2)	0.390	86.5 (16.8)	85.9 (19.7)	0.870
Role functioning	89.2 (21.6)	83.2 (28.1)	0.073	68.5 (29.3)	72.4 (33.5)	0.218	80.2 (27.3)	83.7 (28.4)	0.216
Emotional functioning	77.7 (21.6)	71.1 (24.3)	**0.015**	73.4 (22.1)	73.0 (25.1)	0.818	76.2 (23.9)	72.4 (26.0)	0.363
Cognitive functioning	87.7 (20.0)	78.6 (24.4)	**<0.001**	72.5 (25.3)	64.5 (29.7)	0.066	74.7 (24.5)	69.4 (27.8)	0.289
Social functioning	77.8 (29.9)	65.3 (36.4)	**0.001**	59.6 (34.8)	48.1 (39.5)	**0.033**	64.4 (36.4)	60.7 (39.4)	0.640
Symptom scales and single-item measures									
Fatigue	13.6 (18.8)	19.9 (22.1)	**0.004**	29.3 (23.2)	27.0 (25.5)	0.319	22.1 (22.9)	21.4 (23.1)	0.787

Quality-of-life indicator	Baseline: No sarcopenia (n=341)	Baseline: Sarcopenia (n=106)	*P* value	End of chemotherapy: No sarcopenia (n=248)	End of chemotherapy: Sarcopenia (n=61)	*P* value	6 months: No sarcopenia (n=218)	6 months: Sarcopenia (n=42)	*P* value
Nausea and vomiting	3.4 (10.9)	5.8 (17.1)	0.209	10.9 (18.9)	8.5 (14.1)	0.544	4.9 (11.4)	5.2 (19.6)	0.099
Pain	17.9 (21.9)	24.7 (26.4)	**0.016**	26.0 (26.1)	24.4 (25.8)	0.658	23.0 (26.1)	22.6 (27.0)	0.891
Dyspnoea	5.0 (13.5)	8.5 (18.4)	0.076	11.0 (21.5)	7.7 (17.6)	0.271	7.8 (18.8)	10.3 (25.0)	0.726
Insomnia	20.5 (29.3)	24.8 (31.6)	0.227	25.9 (32.1)	20.8 (28.7)	0.269	24.6 (33.4)	23.0 (31.7)	0.907
Appetite loss	9.0 (20.6)	12.3 (25.3)	0.347	16.6 (26.4)	14.8 (24.7)	0.621	7.2 (18.8)	9.5 (23.6)	0.690
Constipation	10.4 (23.1)	18.2 (28.0)	**0.003**	25.4 (31.4)	27.9 (32.9)	0.649	21.6 (29.3)	24.6 (28.6)	0.366
Diarrhoea	1.7 (8.9)	1.6 (8.5)	0.983	4.7 (16.5)	3.3 (13.3)	0.523	0.8 (5.9)	1.6 (7.2)	0.254
Financial difficulties	41.1 (42.6)	57.9 (44.2)	**<0.001**	61.0 (40.3)	68.3 (41.5)	0.140	59.0 (42.2)	52.0 (45.4)	0.396

Note: Values are mean (SD). *P* values are from Wilcoxon rank-sum tests comparing participants with and without sarcopenia at each assessment. Bold indicates $P<0.05$. Participants contributing quality-of-life data were 341/341 (100%) without sarcopenia and 106/106 (100%) with sarcopenia at baseline; 248/341 (72.7%) and 61/106 (57.5%), respectively, at the end of chemotherapy; and 218/341 (63.9%) and 42/106 (39.6%), respectively, at 6 months after chemotherapy. Retention to 6 months differed by sarcopenia status ($P<0.001$, χ^2 test). Higher EORTC QLQ-C30 global health status/QoL and functional-scale scores indicate better quality of life or functioning; higher symptom-scale and financial-difficulties scores indicate greater burden. Abbreviation: QoL, quality of life.

Table S2. Pairwise comparisons between assessment time points within each sarcopenia group

Panel A. No sarcopenia (n=341)

EORTC QLQ-C30 scale	Baseline → end of chemotherapy, mean change	*P* value	End of chemotherapy → 6 months, mean change	*P* value	Baseline → 6 months, mean change	*P* value
Global health status/QoL	−2.57	0.159	5.64	**<0.001**	3.06	0.083
Functional scales						
Physical functioning	−10.55	**<0.001**	3.63	**0.008**	−6.93	**<0.001**
Role functioning	−20.56	**<0.001**	11.82	**<0.001**	−8.74	**<0.001**
Emotional functioning	−4.35	**0.013**	2.60	0.366	−1.75	0.823
Cognitive functioning	−15.32	**<0.001**	1.86	0.857	−13.46	**<0.001**
Social functioning	−18.38	**<0.001**	4.65	0.300	−13.74	**<0.001**
Symptom scales and single-item measures						
Fatigue	15.59	**<0.001**	−7.27	**<0.001**	8.32	**<0.001**
Nausea and vomiting	7.46	**<0.001**	−6.02	**<0.001**	1.44	0.661
Pain	8.12	**<0.001**	−2.89	0.471	5.24	**0.020**
Dyspnoea	6.06	**<0.001**	−3.27	0.115	2.80	0.178
Insomnia	5.40	**0.043**	−1.71	1.000	3.69	0.330

Appetite loss	7.50	**<0.001**	−9.10	**<0.001**	−1.60	1.000
Constipation	15.41	**<0.001**	−4.25	0.168	11.17	**<0.001**
Diarrhoea	3.05	**0.002**	−3.98	**<0.001**	−0.93	0.972
Financial difficulties	20.13	**<0.001**	−2.05	1.000	18.08	**<0.001**

Panel B. Sarcopenia (n=106)

EORTC QLQ-C30 scale	**Baseline → end of chemotherapy, mean change**	**P value**	**End of chemotherapy → 6 months, mean change**	**P value**	**Baseline → 6 months, mean change**	**P value**
Global health status/QoL	−4.71	**0.306**	3.59	0.948	−1.12	**1.000**
Functional scales						
Physical functioning	−7.07	**0.029**	6.17	0.210	−0.90	**1.000**
Role functioning	−10.40	**0.076**	11.12	0.162	0.72	**1.000**
Emotional functioning	1.83	**1.000**	−1.00	1.000	0.82	**1.000**
Cognitive functioning	−13.52	**0.001**	4.30	1.000	−9.22	**0.102**
Social functioning	−17.49	**0.009**	12.62	0.255	−4.86	**1.000**
Symptom scales and single-item measures						
Fatigue	6.53	**0.160**	−6.26	0.402	0.26	**1.000**
Nausea and vomiting	2.77	**0.651**	−3.81	0.502	−1.04	**1.000**

Pain	−0.50	**1.000**	−2.48	1.000	−2.99	**1.000**
Dyspnoea	−0.87	**1.000**	1.46	1.000	0.59	**1.000**
Insomnia	−3.87	**1.000**	1.52	1.000	−2.35	**1.000**
Appetite loss	3.03	**1.000**	−6.87	0.393	−3.83	**1.000**
Constipation	9.63	**0.130**	−3.27	1.000	6.36	**0.719**
Diarrhoea	1.76	**0.814**	−1.75	1.000	0.01	**1.000**
Financial difficulties	10.32	**0.327**	−14.42	0.223	−4.10	**1.000**

Note: Values are estimated mean changes in EORTC QLQ-C30 scores from age-unadjusted linear mixed-effects models fitted separately within each sarcopenia group. Mean change represents the later assessment minus the earlier assessment. P values are Bonferroni-adjusted for the three pairwise comparisons within each scale and sarcopenia group; bold indicates $P<0.05$. For global health status/QoL and functional scales, negative values indicate worsening and positive values indicate improvement. For symptom scales and financial difficulties, positive values indicate worsening and negative values indicate improvement. Models used all available observations at each assessment. Abbreviation: QoL, quality of life.

Table S3. Associations of time, sarcopenia status and HIV status with EORTC QLQ-C30 scales

Scale	Time p	Time q	Sarcopenia p	Sarcopenia q	HIV p	HIV q	Time × sarcopenia p	Time × sarcopenia q	Time × HIV p	Time × HIV q	Sarcopenia × HIV p	Sarcopenia × HIV q
Global health status/QoL	**0.001**	**0.002**	**0.011**	0.088	0.587	0.880	0.465	0.581	0.543	0.815	**0.007**	**0.034**
Functional scales												
Physical functioning	**<0.001**	**<0.001**	0.103	0.310	0.210	0.631	0.056	0.186	0.382	0.766	**0.045**	0.067
Role functioning	**<0.001**	**<0.001**	0.627	0.784	0.127	0.508	**0.032**	0.161	0.413	0.766	0.063	0.085
Emotional functioning	**0.037**	**0.039**	0.151	0.378	0.464	0.801	0.257	0.429	0.742	0.906	**0.021**	**0.046**
Cognitive functioning	**<0.001**	**<0.001**	0.087	0.310	0.968	0.968	0.563	0.604	0.868	0.924	0.163	0.201
Social functioning	**<0.001**	**<0.001**	0.184	0.395	0.481	0.801	0.322	0.482	0.076	0.766	**0.004**	**0.034**
Symptom scales												
Fatigue	**<0.001**	**<0.001**	0.376	0.626	0.134	0.508	**0.018**	0.133	0.707	0.906	**0.010**	**0.034**
Nausea and vomiting	**<0.001**	**<0.001**	0.517	0.739	0.136	0.508	0.195	0.366	0.331	0.766	**0.029**	0.054
Pain	**0.002**	**0.003**	0.088	0.310	0.824	0.960	0.062	0.186	0.785	0.906	0.336	0.342

Scale	Time p	Time q	Sarcopenia p	Sarcopenia q	HIV p	HIV q	Time × sarcopenia p	Time × sarcopenia q	Time × HIV p	Time × HIV q	Sarcopenia × HIV p	Sarcopenia × HIV q
Dyspnoea	**0.001**	**0.002**	0.542	0.739	0.832	0.960	0.106	0.264	0.148	0.766	**0.034**	0.057
Insomnia	0.066	0.066	0.971	0.971	0.374	0.801	0.169	0.361	0.242	0.766	**0.011**	**0.034**
Appetite loss	**<0.001**	**<0.001**	0.742	0.856	0.804	0.960	0.558	0.604	0.924	0.924	**0.020**	**0.046**
Constipation	**<0.001**	**<0.001**	0.364	0.626	0.899	0.963	0.420	0.573	0.287	0.766	**0.006**	**0.034**
Diarrhoea	**0.001**	**0.002**	0.874	0.937	0.369	0.801	0.691	0.691	0.459	0.766	0.342	0.342
Single item												
Financial difficulties	**<0.001**	**<0.001**	**0.012**	0.088	0.126	0.508	**0.013**	0.133	0.426	0.766	0.174	0.201

Note: Values are from linear mixed-effects models with a participant-specific random intercept, adjusted for age at diagnosis. Models included time as a categorical variable, sarcopenia status, HIV status, age at diagnosis, and time × sarcopenia, time × HIV and sarcopenia × HIV interaction terms. *p* indicates the nominal Wald *p* value; *q* indicates the Benjamini–Hochberg false-discovery-rate-adjusted *q* value, calculated separately within each model term across the 15 EORTC QLQ-C30 scales. Because interaction terms were included, the time *p* value tests change over time among HIV-negative women without sarcopenia; the sarcopenia *p* value tests the sarcopenia difference at baseline among HIV-negative women; and the HIV *p* value tests the HIV difference at baseline among women without sarcopenia. Bold values indicate $p<0.05$ or $q<0.05$, as applicable. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QoL, quality of life.

Table S4. Sensitivity analyses of associations of sarcopenia status and HIV status with EORTC QLQ-C30 scales

Sensitivity analysis	N women	Sarcopenia, $p<0.05$ / $q<0.05$	Time × sarcopenia, $p<0.05$ / $q<0.05$	Sarcopenia × HIV, $p<0.05$ / $q<0.05$	Sarcopenia × HIV scales with $q<0.05$
Primary analysis	447	2 / 0	3 / 0	10 / 7	Global health status/QoL; emotional functioning; social functioning; fatigue; insomnia; appetite loss; constipation
Not adjusted for age	447	4 / 0	3 / 0	9 / 8	Global health status/QoL; emotional functioning; social functioning; fatigue; nausea and vomiting; insomnia; appetite loss; constipation
Participant with handgrip strength recorded as 0 kg retained and classified as having sarcopenia	448	2 / 0	3 / 0	9 / 5	Global health status/QoL; social functioning; fatigue; insomnia; constipation
QLQ-C30 scored using the EORTC missing-item rule	447	2 / 0	3 / 0	9 / 6	Global health status/QoL; social functioning; fatigue; insomnia; appetite loss; constipation
HIV status defined using the laboratory result where available	447	2 / 0	3 / 0	8 / 2	Social functioning; constipation

Note: Values in the sarcopenia, time × sarcopenia and sarcopenia × HIV columns indicate the number of the 15 EORTC QLQ-C30 scales with a nominal $p<0.05$ / Benjamini–Hochberg false-discovery-rate-adjusted $q<0.05$. The primary analysis used age-adjusted linear mixed-effects models with a participant-specific random intercept and included categorical time, sarcopenia status, HIV status, age at diagnosis, and time × sarcopenia, time × HIV and sarcopenia × HIV interaction terms. Each sensitivity analysis repeated the primary model while changing only the feature specified in the first column. False-discovery-rate adjustment was applied separately within each model term across the 15 quality-of-life scales. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QoL, quality of life.

Supplementary figures

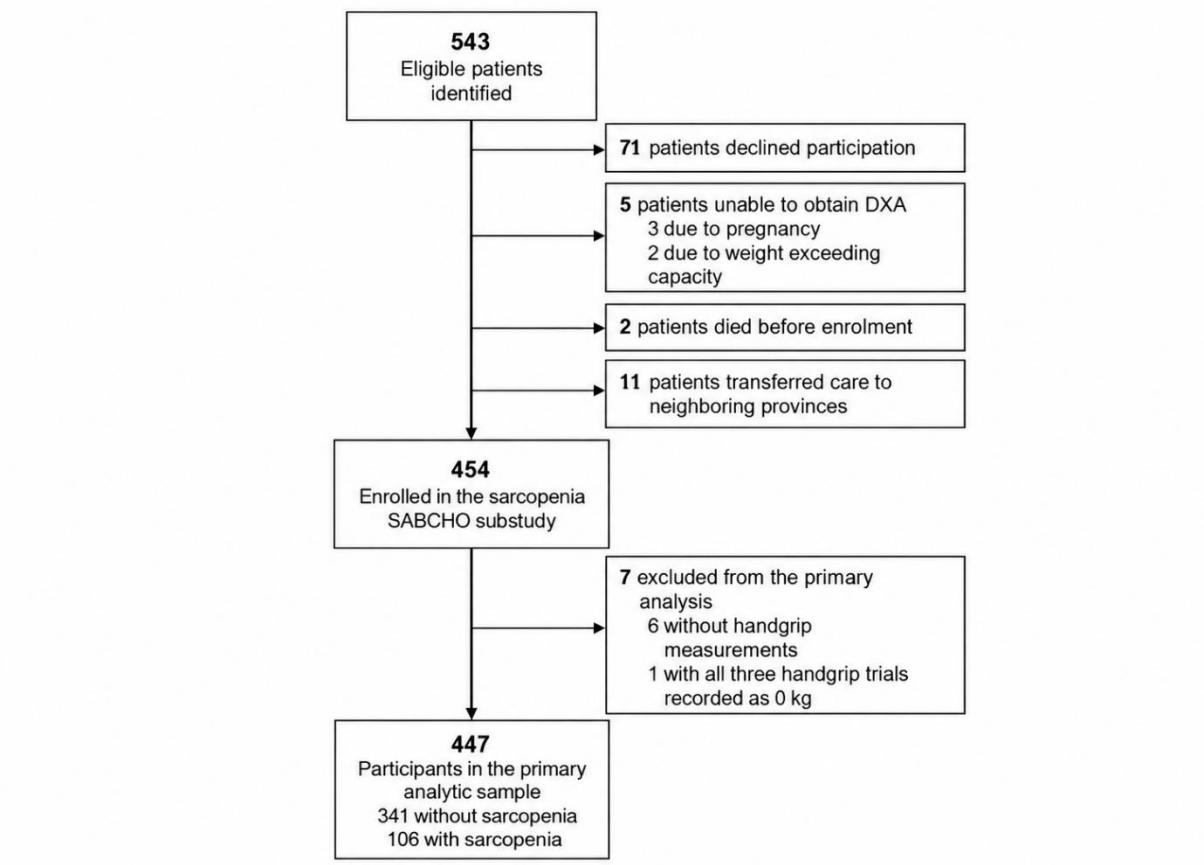


Figure S1. Flow of participants into the SABCHO sarcopenia sub study and analytic sample