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ORIGINAL ARTICLE

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The effectiveness of skeletal muscle evaluation at the third cervical vertebral level for computed tomography-defined sarcopenia assessment in patients with head and neck cancer

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Abstract

Background: Computed tomography (CT)-defined sarcopenia is a prognostic indicator in head and neck cancer (HNC), with the gold standard for muscle evaluation using cross-sectional area (CSA) at the third lumbar vertebra (L3). We compared methods using CSA at the third cervical vertebra (C3).

Methods: Muscle CSA was measured at L3, and CSA at C3 was used to estimate L3 CSA using a prediction model. Agreement and sarcopenia diagnosis were evaluated.

Results: Good correlation was found between measured and estimated CSA (101 scans; $r = 0.86$, $p < 0.001$). CSA mean difference (bias) 9.99 cm^2, (SD = 20.3 cm^2). Skeletal muscle index bias 5.85% (SD = 13.4%), 95% limits of agreement (LoA) (−20.4 to 32.1%, $r = 0.29$), exceeded clinically accepted limits of 5%. Sarcopenia was diagnosed in 26%-(L3), 45%-(C3), with weak agreement ($k = 0.368$, 95% confidence interval, 0.192–0.544, $p < 0.001$) (sensitivity 79.2%, specificity 66.7%).

Meetings at which this work has been presented: The Joint Congress on Head and Neck Oncology (ECHNO) and the International Congress on Innovative Approaches in Head and Neck Oncology (ICHNO) 2021—poster presentation July 2021.

Conclusion: Agreement between measures was weak. Widespread LoA, proportional bias, and sarcopenia misclassification indicates that estimates using C3 cannot replace actual measures at L3.

KEYWORDS
body composition, computed tomography, head and neck cancer, sarcopenia

1 | INTRODUCTION

Malnutrition in patients with head and neck cancer (HNC) continues to be a major concern, and has repeatedly been shown to be associated with poorer survival and treatment outcomes in this population.[1–4] The incidence of critical weight loss, especially during treatments including radiotherapy and chemotherapy, is high,[5–7] and is associated with reduced mortality, significant morbidity, and reduced quality of life.[8] However, diagnosing malnutrition, especially in patients who appear "well nourished" can be quite challenging for clinicians.

Sarcopenia is emerging as an independent prognostic indicator in patients with certain cancers,[9] including HNC.[10–14] Defined as depletion of muscle mass and the consequent decline in muscle function, sarcopenia can be influenced by malnutrition, however, may be present in its absence, or in the absence of any visible signs of wasting.[15,16] As a result, patients who are overweight or obese, may indeed have skeletal muscle mass depletion which may remain undiagnosed and untreated.[17]

Measurement of skeletal muscle using computed tomography (CT) images in a single abdominal cross-sectional image at the level of the third lumbar vertebra (L3) is the gold standard in muscle mass assessment, as images are considered the most accurate for body composition measure at the tissue-organ level.[15,18–20] CT-defined sarcopenia is a term now used to describe sarcopenia defined using this technique in cancer patients, usually without the measurement of muscle function and strength. Most patients will have a CT scan for diagnosis and staging, providing opportunistic use of these scans for skeletal muscle evaluation without additional burden or cost to the patient. The main limitation in the implementation of this method in the HNC population, is that diagnostic CT scans do not routinely extend to the abdomen. As a result, the use of alternate vertebral levels for sarcopenia assessment where L3 is not available, has been examined with varying results.[21]

The most common alternate method currently being used in patients with HNC was developed by Swartz et al., where the skeletal muscle cross-sectional area (CSA) at the level of the third cervical vertebra (C3) in head and neck CT scans is used to predict/estimate the muscle CSA at L3.[22] The present study aimed to apply this method in a larger cohort of patients with HNC presenting to our facility, to evaluate the agreement between actual skeletal muscle CSA at L3 and estimated CSA using C3 measures, and to investigate the accuracy of C3 in diagnosing CT-defined sarcopenia, when compared to the L3 gold standard.

2 | MATERIALS AND METHODS

This is an Ethics approved (2019/ETH13149), single center retrospective study conducted within the Nelune Comprehensive Cancer Centre at Prince of Wales Hospital, a large metropolitan tertiary referral Hospital in Sydney, Australia.

2.1 | Study population

All adult patients (≥18 years) who presented to the Head and Neck Clinic between January 2013 and December 2020 with newly diagnosed head and neck squamous cell carcinoma of the larynx, hypopharynx, nasopharynx, oropharynx, or oral cavity, who had a diagnostic positron emission tomography-computed tomography (PET-CT) scan were included. Patients were excluded if they had a previous cancer diagnosis or treatment, or if the PET-CT scan was incomplete or unclear enough for analysis. Patient's height and weight were recorded at presentation to the clinic, and within 2 weeks of the PET-CT. Other demographic data collected were: age, sex, TNM staging, and tumor site.

2.2 | PET-CT scan analysis

Diagnostic PET-CT scans were acquired from patient medical records and anonymized for analysis. Slice-O-Matic version 5.0 (TomoVision, Montreal, QC, Canada) software was used to quantify the CSA of muscle at both L3 and C3 from the same PET-CT scan in each patient. Skeletal muscle was measured using the standard predetermined Hounsfield unit (HU) threshold of −29 to +150 HU[23,24] and delineated manually by a single researcher trained in CT scan muscle analysis (training program devised by Prof Vickie Baracos et al., with $a < 2\%$ interrater variation achieved) (BV) and supervised and cross-checked by a Senior Radiologist (DM).

CSA at C3 was landmarked using the previously described method by Swartz et al. by selecting a single axial slice when scrolling from caudal to cephalad direction that has the first entire vertebral arc, and transverse and spinous processes visible.[22] Both the sternocleidomastoid muscles (SCM) and the paravertebral muscles were measured together. The method of doubling the SCM if there was tumor invasion unilaterally, was employed as necessary. The CSA at C3 for each patient was then used to estimate CSA at L3 using the equation below defined by the same group.[22] This includes grouping of patients by sex:

$$\begin{aligned}\text{CSA at L3}\,(\text{cm}^2) = {} & 27.304 + 1.363 \\ & * \text{CSA at C3}\,(\text{cm}^2) - 0.671 \\ & * \text{age}\,(\text{years}) + 0.640 * \text{weight}\,(\text{kg}) \\ & + 26.442 \\ & * \text{sex}\,(\text{sex} = 1 \text{ for female}, 2 \text{ for male}).\end{aligned}$$

The CSA at L3 was measured using the skeletal muscle in the entire axial slice approximately mid-way through the vertebra with both transverse processes clearly visible. Muscles in this area include the psoas, erector spinae, transverse abdominis, internal and external obliques, quadratus lumborum and rectus abdominus. CSA at L3 was compared to the predicted CSA of the converted value at C3.

2.3 | Sarcopenia assessment

CSA data was normalized for stature (height^2) and presented as skeletal muscle index (SMI) (cm^2/m^2) to enable sarcopenia assessment comparison. SMI values were reported to three significant figures to avoid misclassification from rounding up or down (height and CSA measures were to three significant figures also). Body mass index (BMI) was calculated in kg/m^2, and patients were categorized as being underweight (BMI <20), healthy weight (BMI 20.0–24.9), overweight (BMI 25.0–29.9) or obese (BMI ≥30). Each patient was classified as sarcopenic or not by applying the sex and BMI-specific threshold values at L3 (defined by Martin et al.[25]). Sarcopenia was subsequently defined as SMI <41 cm^2/m^2 in females, regardless of BMI, and in males <43 cm^2/m^2 (underweight or healthy weight) and <53 cm^2/m^2 (overweight or obese). Sarcopenia diagnosis based on the L3 measure was compared to that of the estimated L3 value.

2.4 | Statistical analysis

Descriptive statistics were calculated and presented as frequencies and percentages, with continuous variables presented as the mean (standard deviation, SD and range) or median (interquartile range, IQR). Normality of data was investigated using the Shapiro–Wilk test and a quantile–quantile (QQ) plot.

Values for the two methods of skeletal muscle measurement were separated into groups: Group 1—actual CSA measured at L3, and Group 2—the estimated measure for L3 using CSA at C3. Measurements were directly compared for each patient. A linear regression model was used to determine correlation between the two methods, providing a coefficient of determination (R^2) value to represent the proportion of variance explained by the model.

TABLE 1 Patient characteristics

	Whole cohort $N = 101$ (%)
Sex	
Male	84 (83)
Female	17 (17)
Age (years)	
Mean ± SD	60.6 ± 10.2
Range	33–85
Tumor site	
Larynx	8 (8)
Hypopharynx	1 (1)
Oropharynx	72 (71)
Nasopharynx	10 (10)
Oral cavity	6 (6)
Unknown primary	4 (4)
TNM classification	
T-classification	
Tis	1 (1)
T1	41 (40)
T2	26 (26)
T3	12 (12)
T4	15 (15)
Tx	6 (6)
N-classification	
N0	10 (10)
N1	31 (31)
N2	53 (53)
N3	6 (6)
M-classification	
M0	97 (96)
M1	4 (4)
BMI (kg/m^2)	
Mean ± SD	27.4 ± 5.4

Abbreviations: BMI, body mass index; SD, standard deviation; Tis, tumor in situ.

The Bland–Altman method was used to visualize the level of agreement between the two methods.[26] The difference between CSA measurements in the two groups, and the means of each pair of results were calculated. A one-sample *t*-test was conducted using the difference values of each pair to determine the mean difference (bias), standard deviation (SD), and 95% confidence intervals (CI). A plot was constructed to visually demonstrate the level of agreement between the two measurements methods, including the 95% limits of agreement (LoA), (mean difference (bias) ±1.96 SD). The difference and mean values were then applied to a linear regression model to determine proportional bias.

Patients were categorized as having sarcopenia or not in both groups (SMI at L3 vs estimated SMI using C3), using the application of previously described thresholds as mentioned above.[25] Cohen's Kappa ($\hat{k}$) measurement of agreement was used to compare the two. Sensitivity and specificity of diagnosing sarcopenia using the estimated L3 SMI compared to actual SMI measured at L3 was also reported. The Bland–Altman method was applied on SMI measurements in both groups to determine LoA, with differences plotted in both cm^2/m^2 and percentage difference for additional clinical applicability. Patients were also analyzed based on sex and level of agreement compared. The limit of clinically acceptable difference was set as a defined a priori of <5% (equating to ±2.65 cm^2/m^2 in sarcopenia cut off, based on upper threshold of 53 cm^2/m^2). The a priori limit of clinically acceptable difference should be defined based on relevant clinical/biological and analytical criteria.[26] However, as there is currently no set criteria in the literature, the 5% a priori in this study was determined based on clinical judgment that a small degree of error was acceptable, as patients would also have full nutritional assessments to determine appropriate intervention.

Statistically significant results were defined as $p < 0.05$. All statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), (version 26.0. IBM Corp., Armonk, NY).

3 | RESULTS

3.1 | Demographics

A total of 110 patients who met the inclusion criteria presented to the head and neck clinic and had a diagnostic PET-CT. Three patients had poor quality scans and six scans were unsuitable for C3 analysis due to patients having significant curvature in the cervical spine with unclear muscle area, therefore, nine patients were excluded. Two patients had extensive unilateral nodal involvement in the SCM deeming this muscle unmeasurable and required doubling of one side. The total study population consisted of 101 subjects (mean age 60.6 ± 10.2 (SD) years, range 33–85 years), of whom 83% were male, and the majority presenting with cancer of the oropharynx (71%) and early-stage disease. Patient characteristics are shown in Table 1.

3.2 | Correlation and level of agreement between measures

A linear regression model demonstrated good correlation between actual and estimated muscle CSA in this cohort ($r = 0.858$, $p < 0.001$) (Figure 1). The mean percentage

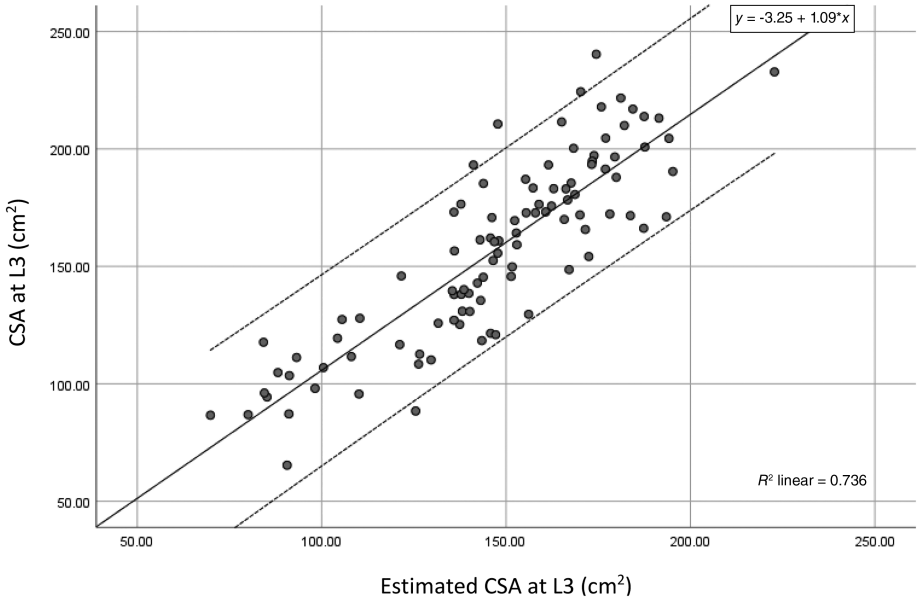

FIGURE 1 CSA comparison at L3 with predicted value using C3 including linear regression line with equation and 95% prediction interval

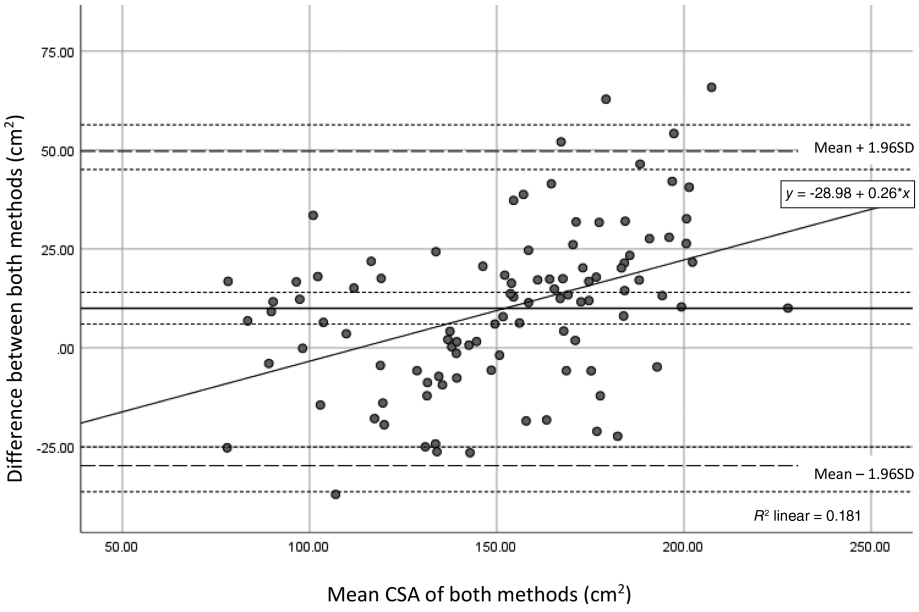

FIGURE 2 Bland–Altman plot of agreement between the two methods with limits of agreement (dashed lines), 95% confidence Intervals (dotted lines), and linear regression line with equation

TABLE 2 Sarcopenia assessment cross-comparison

		Sarcopenia using C3	
		No sarcopenia	**Sarcopenia**
Sarcopenia at L3	No sarcopenia	46 (66.7%)	23 (20.8%)
	Sarcopenia	5 (33.3%)	19 (79.2%)

Note: Population with SMI measure ($n = 93$).

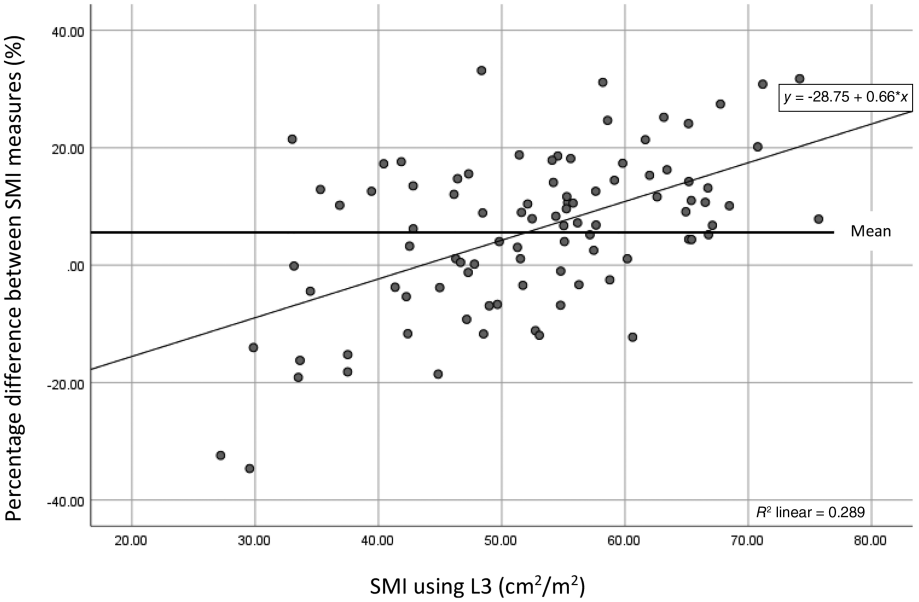

FIGURE 3 Plot of difference between SMI measures (%) against measured SMI at L3

difference in CSA measures as a percentage of L3 CSA was 4.6% (range −41.9% to 28.4%). The mean difference (bias) in CSA between the methods was 9.99 cm^2 (SD 20.3, 95% CI 6.0–14.0), with 95% LoA (−29.8 to 49.7 cm^2) (95% CI lower LoA −36.4 to −25.1, upper LoA 45.1–56.4 cm^2) and indicating poor agreement. A Bland–Altman plot was constructed to demonstrate this graphically (Figure 2). A significant level of proportional bias was discovered via linear regression with most measurements found above the mean ($r = 0.43$, $p < 0.001$).

3.3 | Sarcopenia diagnosis

Ninety-three (92%) patients had a documented height, and therefore had both BMI and SMI calculated. Sixty-

three percent of patients were either overweight or obese ($n = 59$). Mean SMI in the measured L3 group was 52.42 cm^2/m^2 (SD 10.92, range 27.20–75.71) and in the estimated group was 49.10 cm^2/m^2 (SD 8.72, range 26.61–69.99). When the sarcopenia thresholds were applied to the SMI values, 26% of the cohort were found to be sarcopenic using the measured L3 SMI. A higher proportion of patients (45%) were deemed sarcopenic in the estimated group. Thirty percent of patients ($n = 28$) had differing sarcopenia assessment with the two measurements. Five percent of patients assessed at L3 as having sarcopenia were misclassified with the C3 method (Table 2). Weak agreement was subsequently determined ($\hat{k} = 0.368$, 95% CI 0.192–0.544, $p < 0.001$), with the number of patients with sarcopenia being correctly identified with a sensitivity of 79.2%, and specificity of 66.7%.

Actual percentage difference between the SMI using measured CSA at L3 and estimated CSA, [(L3 measure – estimated measure)/L3 measure) × 100], differed significantly, with a mean of 5.6% difference between measures in each patient (range −34.7% to 33.1%, $r = 0.548$, $p < 0.001$) (Figure 3).

The Bland–Altman plot further demonstrates the weak agreement (Figure 4), with the mean difference (bias) SMI 3.32 cm^2/m^2 (SD 6.57, 95% CI 1.97–4.67) with 95% LoA (−9.56 to 16.20 cm^2/m^2, $r = 0.35$). When

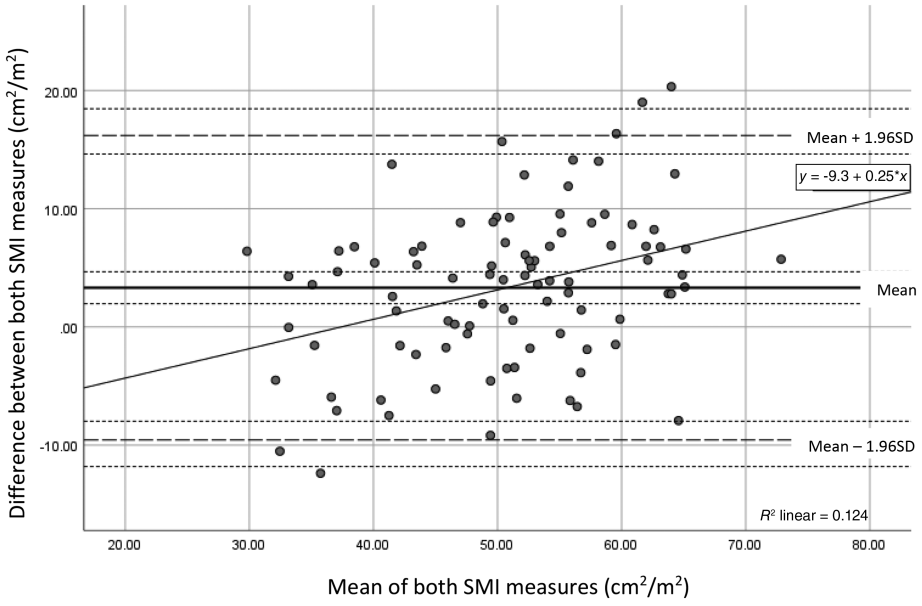

FIGURE 4 Bland–Altman plot of agreement between SMI measures using both methods. Limits of agreement (dashed lines), 95% confidence Intervals (dotted lines), and linear regression line with equation

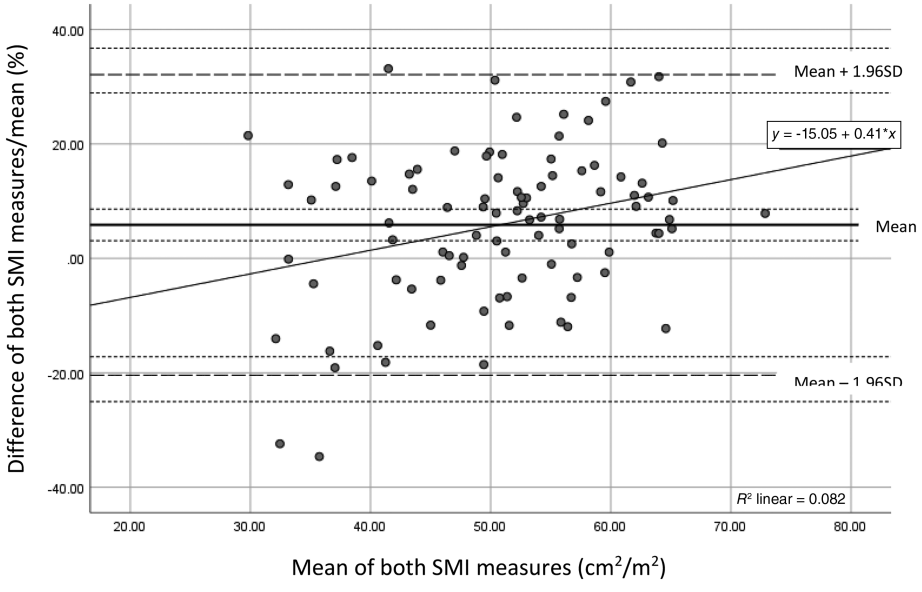

FIGURE 5 Bland–Altman plot of differences between both methods expressed as percentages of SMI measures against the mean of the measures, with limits of agreement (dashed lines), 95% confidence intervals (dotted lines), linear regression line and equation

demonstrated in percentages of difference in SMI compared to the mean, [(L3 measured SMI – estimated SMI)/mean SMI) × 100], the mean difference (bias) was 5.85% (SD 13.40, 95% CI 3.09–8.61) and LoA (−20.42% to 32.11%, $r = 0.29$), (95% CI lower LoA −25.0 to −17.2, upper LoA 28.9%–36.7%), indicating that the set a priori of 5% was exceeded (Figure 5). Sex-based analysis found the a priori for clinically acceptable difference was also exceeded in both groups with widespread LoA. Mean difference (bias) in males = 5.94% (SD 12.8, 95% CI 3.0–8.8, LoA −19.0% to 31.0%, $r = 0.43$, $p < 0.001$) and in females = 5.41% (SD 16.6, 95% CI -3.4-14.3, LoA −27.1% to 38.0%, $r = 0.19$, $p = 0.48$). A Bland–Altman plot was not included as the female cohort was too small ($n = 17$).

4 | DISCUSSION

This study has demonstrated that estimated CSA at L3 using the C3 vertebral landmark is unsuitable for use in our HNC population at both the individual and group level due to the SMI bias exceeding the clinically set a priori, wide LoA, and significant level of proportional bias. There was also weak agreement for identification of sarcopenia, deeming the prediction equation developed by Swartz et al.[22] nontransferable to our Australian HNC population.

The use of CT scans to measure skeletal muscle mass and diagnose sarcopenia has emerged as an important tool in the nutritional assessment of patients with cancer, especially as the measurement of weight loss alone does not indicate the level of lean tissue lost.[19] This is especially important in patients with HNC, as many do not present as malnourished or having lost weight at the time of diagnosis, however, are likely to experience significant nutritional issues during and immediately after the various treatment modalities used.[27–29] The accuracy and clinical reproducibility of methods to assess sarcopenia are therefore important in this population to ensure appropriate and timely nutritional interventions.

CT-defined sarcopenia using muscle CSA at the lumbar L3 landmark was first established by Shen et al.[18] in healthy adults and by Mourtzakis et al.[20] in cancer patients, as the most appropriate for skeletal muscle evaluation, and researchers have used this method to investigate the impact on survival outcomes in HNC populations.[13] Due to the L3 landmark not being visible in a typical head and neck CT scan, Swartz et al.[22] developed an equation to convert CSA measures at C3 to an estimated L3 value. This has been applied in several studies to assess sarcopenia in various HNC populations where CT-defined sarcopenia using CSA at C3 has been demonstrated to be prognostic of morbidity and mortality in the HNC population.[11,30–34] A recent meta-analysis investigating survival in CT-defined sarcopenia in HNC included three studies that used the C3 prediction formula, and subgroup analysis found that these studies demonstrated sarcopenia to have a significant effect on reducing overall survival.[12] The results of the present study indicate that this method, however, may not be transferable across varied HNC populations, and may be inaccurate for actual sarcopenia diagnosis. To our knowledge, this is the first study to not only investigate the agreement between these two methods, but also the differences in sarcopenia assessment in HNC.

Swartz et al.[22] demonstrated good correlation between measured skeletal CSA at L3 and predicted measures using C3 ($r = 0.891$) in 52 patients with HNC, however, as correlation measures the relationship between the two variables and not the differences, it is not an indication of agreement.[26] "Reasonable" agreement was implied with this method as there were only a few patients outside the two standard deviations of the difference between measurements. Jung et al. defined their own prediction models for estimating muscle area at L3 using C3 in a larger population of 305 Korean HNC patients, and also demonstrated good correlation (adjusted $R^2 = 0.721$), however, did not define the level of agreement between the two methods.[35] Similarly, Muresan et al. demonstrated good correlation between measures at the two vertebral landmarks in a small population ($n = 37$), using CT planning scans, but did not investigate agreement.[36] In our population, a good correlation was also found, however, agreement was shown to be weak, with a significant level of proportional bias. This in turn translated into major differences in SMI values and ultimately sarcopenia diagnosis.

Thresholds for sarcopenia diagnosis vary between studies. This study used the sex-specific and BMI thresholds to classify patients, as described by Martin et al.,[25] as these were considered to be clinically the most similar to the population we investigated. (ie, taking into account BMI and sex differences, and formulated from a similar Canadian population). There is currently paucity of evidence for sarcopenia cut off thresholds that include both sex and BMI-specific values established in patients with HNC. Several studies have previously recommended sex-specific threshold values based on outcomes in HNC populations, however, do not include BMI stratification.[37–40] Although the Martin et al.[25] thresholds were derived using a large population of patients with either lung or gastrointestinal cancers ($n = 1473$), they have been applied to HNC populations by several authors.[32,41–43] Ideally, sarcopenia thresholds using both sex and BMI-specific values should be derived specifically using a large population of HNC patients. Although this

has not been established to our knowledge to date, the use of the Martin et al.[25] thresholds has been demonstrated in an Australian population, with Findlay et al. investigating the impact of depleted skeletal muscle on outcomes in a large cohort of 277 patients with HNC.[42]

As there is not currently a set standard threshold for classifying sarcopenia in cancer patients in general, or specifically patients with HNC, comparison between studies is difficult. In Australia, an estimated 67% of adults were overweight or obese in 2017–2018,[44] and as the majority of patients in the present study were overweight or obese (63%), using the thresholds that included BMI classification was appropriate. The median BMI of the population of 52 Dutch HNC patients used for the development of the C3 prediction equation by Swartz et al.[22] was 24.3 kg/m^2 compared to a median of 27 kg/m^2 in the present study. This may have been a contributing factor to the lack of agreement seen in our population, as most had higher BMIs. A third of the cohort in this study were misclassified using the predicted C3 method. The difference in weight distribution of the two populations (Dutch and Australian), may have impacted on this, and the concern is with patients being misclassified as not being sarcopenic when in fact they are. The application of different threshold measures may also change these results.

The use of sex-specific sarcopenia cut offs is also important as there can be notable differences in muscle proportion between sexes.[45] This, however, enables direct comparison only where studies have used the same thresholds. In the present study, both groups exceeded the a priori when analyzed for percentage mean difference (bias) in SMI. As our female population was small ($n = 17$), this needs to be interpreted with caution and further studies in larger populations are required to explore this further.

Another issue may have been the small cohort used to derive the original equation. Larger population studies may be required for such prediction equations for estimating CSA at L3 to be appropriately validated across populations. In addition, population-specific equations are likely necessary where ethnicity, obesity incidence, and sex differences are taken into account.

The present study demonstrated weak agreement between SMI measures, and of concern is the range of difference between SMI values using the two methods. A certain percentage of error is likely, and a clinically set a priori is necessary, however, the large discrepancies between the methods in our population is concerning (up to 42%), and beyond the limits of clinical acceptability. Our group decided on a 5% a priori for SMI, as measures need to be as accurate as possible for sarcopenia diagnosis. We acknowledge that 5% is a subjective figure, based on the clinical judgment of the authors, as there is currently no set value for acceptable difference between measures. Ideally this should be investigated further, potentially utilizing for example the Delphi method[46] to reach a clinical consensus based on expert opinion, however, any difference in measures may result in a proportion of patients being misclassified as not having sarcopenia. Clinically, patients should be assessed for nutritional interventions holistically, and a 5% (± 2.65 cm^2/m^2) difference is acceptable in the context of delivering patient care. The results of the present study showed a mean difference (bias) of 5.85% in SMI measurements, indicating the a priori was exceeded beyond our acceptable measures. This is of concern, as it equates to misclassification of sarcopenia status in a large proportion of patients in this cohort.

The rounding up or down of SMI values can change sarcopenia status, hence the reason to use three significant figures in our data. The absolute values therefore were compared using both methods for true comparison. As mentioned, patients should be assessed using not only SMI values, but also with clinical judgment when deciding on nutritional interventions. This is especially important when assessing sarcopenia status at the time of diagnosis, as identification of patients at highest risk would allow for earlier and more targeted nutritional intervention. For the purposes of morbidity and mortality prediction, the method of assessing SMI status should be an accurate one, and strong agreement with CSA measures at L3 (or ideally with whole body muscle mass) should be sought before an alternate vertebral landmark can be used for sarcopenia assessment. A recent meta-analysis of studies investigating CT-defined sarcopenia in HNC concluded that sarcopenia significantly reduced overall survival in studies that had used L3 measures, and also those using the C3 prediction equation.[12] Researchers, however, do not have standardized cut off thresholds to use and results should be interpreted with caution, especially in light of potential misclassification as identified in this study.

The need for an alternate vertebral landmark for muscle mass assessment is important to consider, especially in patients with HNC, as routine diagnostic CT scans do not always extend to the level of L3. The use of C3 is a controversial one, not only due to the limitations around tumor involvement in the area, but also the question of whether muscles in the neck waste in the same degree as those in the abdomen, and whether assessment of muscle in this area translates appropriately. Measurement of muscle taken at L3 is a surrogate measure of whole body skeletal muscle, and there may be issues in using C3 as a proxy of a surrogate measure. Nevertheless, measures using the C3 landmark have been shown to impact on overall survival in HNC in several studies. Therefore on a

population-based level where outcomes are investigated, muscle measurements using C3 may be suitable, however, our findings demonstrate that it is not suitable to be substituted for L3 evaluation in this Australian HNC cohort. This prediction model did not fit our cohort, and future use of the C3 landmark in prediction model development may need to be population specific.

This is a retrospective, single institution study, and therefore has limitations. Patient selection was based on a diagnostic PET-CT scan being undertaken as part of cancer staging. Patients will only have a scan if required by their treating Oncologist, and therefore creating a bias, as not all patients who presented to the clinic were included. Unclear scans were deemed unusable due to the difficulty to analyze muscle mass, reducing cohort number. Not all patients had a height measure taken in the clinic ($n = 8$), therefore were not included in the SMI comparisons. Our cohort though was larger than the original study using C3, was a reasonable size at 101, and representative of the usual Australian heterogeneous cohort of patients with HNC. One prediction model is unlikely to be universally applicable to all cohorts of patients with HNC. Larger studies, that consider sex-specific thresholds, obesity incidence, and ethnicity, are likely to be required before alternative vertebral landmarks can be effectively used in place of L3 for CT-defined sarcopenia analysis in this group of patients.

5 | CONCLUSION

Agreement between CSA and SMI estimates from C3 and actual L3 measures was weak in this cohort of patients with HNC. The widespread LoA, proportional bias, and clinically significant discrepancies in sarcopenia identification, indicate that CT-defined sarcopenia measured at the L3 landmark cannot accurately be replaced with an estimated measure[22] using CSA at C3 in this Australian population.

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CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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