Oral Oncology 95 (2019) 95–99

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Efficacy of head and neck computed tomography for skeletal muscle mass estimation in patients with head and neck cancer

Ah Ra Jung[a], Jong-Lyel Roh[a,*], Jae Seung Kim[b], Seung-Ho Choi[a], Soon Yuhl Nam[a], Sang Yoon Kim[a]

[a] Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea
[b] Department of Nuclear Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Keywords:
Head and neck squamous cell carcinoma
Skeletal muscle mass
Head and neck computed tomography
Cross-sectional area
Prediction
Survival

ABSTRACT

Objectives: Diminished skeletal muscle mass (SMM) is a reliable marker of poor survival outcomes in patients with cancer. SMM or body composition is generally assessed at the third lumbar vertebra (L3) by abdominal computed tomography (CT) scans, not routinely evaluated in patients with head and neck squamous cell carcinoma (HNSCC). Therefore, we evaluated the effectiveness of head and neck CT images to assess SMM in patients with HNSCC for predicting their overall survival.

Materials and Methods: SMM was assessed in 305 consecutive patients with stage III–IV HNSCC by measuring the cross-sectional area (CSA) at the third lumbar and cervical (C3) vertebrae levels. A formula for predicting the L3 SMM was established using linear regression analysis obtained from C3 CSA and other clinical factors. The actual SMM CSAs measured at L3 level and those obtained from the prediction model were compared using correlation analysis. The predictive power of our formula for estimating overall survival was compared using C-index.

Results: Median SMM CSAs at the L3 and C3 levels were 174.5 cm^2 and 56.3 cm^2, respectively, and were not strongly correlated (adjusted R^2 = 0.421). Prediction model 2 included the strongest predictive factors including sex, age, weight, and C3 SMM CSA, and significantly increased the L3 SMM correlation power (adjusted R^2 = 0.721). The C-index of the prediction model was 0.713 (95% confidence interval 0.692–0.747).

Conclusions: Head and neck CT imaging might be useful to estimate L3 SMM and predict overall survival in HNSCC patients.

Introduction

Multiple markers have been established to predict the clinical or treatment outcomes in patients with cancer. A change in body composition or diminished skeletal muscle mass (SMM) was recognized as a reliable outcome marker of poor survival in patients with various types of cancer or organ transplantation [1–3]. Patients with SMM depletion have higher rates of postoperative complications and post-treatment poor survival outcomes [4–7]. SMM depletion, additionally, is associated with increased treatment-related toxicity, with previous reports indicating thrice the risk of presenting chemotherapeutic toxicity in patients with depleted SMM as compared with non-depleted controls [8,9].

Computed tomography (CT) has been used to measure human body composition [10,11]. Cross-sectional areas (CSA) summating all SMM at specific regions can be computed from delineated CT images. A single abdominal skeletal muscle CSA has been reported to have a high correlation with the corresponding total body skeletal muscle volumes [12]. Patients with head and neck squamous cell carcinoma (HNSCC) undergo imaging workups including head and neck CT (hnCT), additionally, with chest CT for screening distant site metastasis, whereas, those are not routinely performed with abdominal CT. The CSA of SMM is commonly measured at the third lumbar vertebra (L3) level on abdominal CT scans.

A recent study suggested that the CSA measurement of SMM at the cervical vertebra (C3) level on hnCT scans is a feasible alternative to the actual L3 SMM CSA [13]. The previous study included 103 subjects (51 trauma patients and 52 HNSCC patients), which was a lack of proving its usefulness in terms of predicting the survival of HNSCC patients after treatment. Therefore, we hypothesized that the SMM CSA measurement at C3 level help predict the actual SMM CSA at L3 level and survival outcomes in HNSCC patients. In this study, we measured the SMM of

* Corresponding author at: Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 138-736, Republic of Korea.
E-mail address: rohjl@amc.seoul.kr (J.-L. Roh).

https://doi.org/10.1016/j.oraloncology.2019.06.009
Received 5 April 2019; Received in revised form 21 May 2019; Accepted 7 June 2019
Available online 11 June 2019
1368-8375/

both L3 and C3 levels, and established prediction models for estimating L3 SMM from C3 SMM measurements and several clinical factors, in a relatively large cohort of 305 HNSCC patients. Herein, we evaluated the feasibility and usefulness of hnCT images to assess SMM in HNSCC patients and predict their overall survival.

Methods

Patients and study design

We prospectively included 305 consecutive patients, aged 18 years and above, with a diagnosis of stage III–IV HNSCC and underwent definitive treatments for previously untreated HNSCC at our tertiary referral hospital between January 2010 and December 2015. The inclusion criteria were an advanced stage of the cancer (III–IV), underwent whole-body ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT or hnCT and abdomen CT which measured the CSAs of SMM at both C3 and L3 levels. Tumors were staged as per clinical tumor-node-metastasis (TNM) staging as proposed by the American Joint Committee on Cancer (AJCC, 7th ed.). Our institutional research ethics board reviewed and approved the study proposal, and all patients gave written informed consent. Exclusion criteria involved patients with overall stage I–II cancer, history of HNSCC, palliative treatments, refusal to complete treatment, and lack of follow-up information. A total of 305 patients with confirmed treatment of overall stage III or IV HNSCC were included.

SMM measurement

The vertebral levels at L3 and C3 were selected as the standard landmarks for measuring the CSA of SMM [13]. The SMM CSA was manually delineated along the skeletal muscle outlines at both levels, from the CT images before treatment or whole body ^{18}F-FDG PET/CT or hnCT and abdominal CT [9]. The SMM measurement at L3 required abdominal CT scanning available from the whole body ^{18}F-FDG PET/CT images undertaken for cancer staging [14–16]. Delineation of the muscles was performed manually based on their anatomic landmarks, and features at the L3 and C3 levels were procured by CT Hounsfield unit thresholds of −29 to 150 for skeletal muscle (Supplementary Fig. S1) [15,17]. Images were viewed and analyzed using the workstation with the PetaVision (Seoul, Korea). After delineation, the CSA was automatically retrieved as the total sum of delineated pixels. At the C3 level, the CSAs of the paravertebral (PVM) and sternocleidomastoid (SCM) muscles were measured separately, owing to the possibility of the lymph nodes around the SCM muscles being invaded by metastatic invasion leading to complications in CSA measurement. Sum of the bilateral SCM areas was measured separately [18]. The duplicated value of normal or less affected side SCM area was used if the SCM was significantly affected by the enlarged metastatic lymph nodes. The main outcomes for SMM were the CSA of the PVM and SCM muscles at the C3 level and the sum of all skeletal muscles at the L3 level.

Statistical analyses

Continuous variables were expressed as median and interquartile range (IQR), and the categorical variables as number and percentage. Univariate and multivariate linear regression analyses were employed to establish the prediction models for L3 SMM from C3 SMM CSA and other clinical factors. Variables were selected based on the clinical parameters reported in HNSCC [19,20]. Univariate linear regression equation was made with the dependent variable being a linear function of one independent variable. The most important parameters included the statistical significance from the analysis of coefficient of regression, coefficient of correlation, adjusted coefficient of determination, standard error of the regression coefficient, t-distribution, and F-distribution. The F-value indicated the degree of fit of the regression equation with the data. The *t*-test was used to examine the significance of the variables in each model at 95% confidence level. The variable was considered to be significant to the prediction model when the t-value was < 0.05. Pearson correlation coefficients and linear regression analyses were used for assessing correlation between the actual L3 SMM and C3 SMM [21]. Statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC). To estimate the discriminatory ability of the actual L3 SMM from the prediction model, we calculated the C-index for a model containing the L3 SMM as the sole independent variable [22]. The null value for the C-index was 0.5, the maximum being 1.0; a large C-index is indicative of a better model for discriminating the outcome.

The time-dependent area under the receiver operating characteristic curve (AUC) was used to examine the discriminatory ability and to find optimal cut-off values of L3 and C3 SMM for overall survival (OS). The analysis was conducted using the R package version.3.4.4. Univariate Cox proportional hazards regression analyses were used to identify associations between variables and OS. Significant variables in the univariate analyses with *P*-values of < 0.05 were included in multivariate analyses. In the multivariate model, variables with multi-collinearity were separately fit. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated. The Kaplan-Meier and log-rank tests were used to determine survival and statistical significance, respectively. *P*-values of < 0.05 were considered statistically significant, and all statistical tests were two-tailed. Statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC).

Table 1
Patient characteristics ($N = 305$).

	N	%
Sex, male/female	266/39	87.2/12.8
Age (years), median (IQR)	64 (56–73)	
Height (m), median (IQR)	1.66 (1.61–1.70)	
Weight (kg), median (IQR)	63.7 (56.7–70.5)	
Body mass index (kg/m^2), median (IQR)	23.0 (20.9–25.4)	
Charlson comorbidity index, 0/1/2/3/6	206/64/32/2/1	67.6/20.9/10.6/0.6/0.3
Tumor site		
Oropharynx	114	37.3
Oral cavity	69	22.6
Larynx	64	20.9
Hypopharynx	58	19.2
T classification, T1/T2/T3/T4	40/92/73/100	13.2/30.2/24.0/32.6
N classification, N0/N1/N2/N3	68/48/185/4	22.3/15.7/60.6/1.4
Overall TNM Stage, III/IV	84/221	27.5/72.5
Primary treatment (surgery/non-surgery)	211/94	69.2/30.8

Abbreviations: IQR, interquartile range; TNM, tumour-node-metastasis staging proposed by the AJCC (7th ed.).

Table 2
Summary of the statistical measures for the two predicted models of linear regression analysis.

Model no	Independent Variable	Coefficient	t-Value	t-Significant	F-Value	F-Significant	Standard error
Model 1							
	Constant	78.106	12.295	< 0.0001	222.479	< 0.0001	6.352
	C3 SMM	1.668	14.916	< 0.0001			0.111
Model 2							
	Constant	81.059	8.512	< 0.0001	196.929	< 0.0001	9.523
	C3 SMM	0.874	NA	NA	9.723	< 0.0001	0.090
	Weight	0.956	NA	NA	11.942	< 0.0001	0.080
	Sex	−28.127	NA	NA	−10.191	< 0.0001	2.760
	Age	−0.257	NA	NA	−3.249	< 0.0001	0.079

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; NA, not applicable; SMM, skeletal muscle mass.

Results

Patient characteristics

This study included 305 patients consisting 266 (87.2%) men and 39 (12.8%) women, with a median age of 64 years (IQR 56–73 years). Patient characteristics are presented in Table 1. Median height, weight, and body mass index (BMI) was 1.66 (1.61–1.70), 63.7 (56.7–70.5), and 23.0 (20.9–25.4), respectively. The Charlson's comorbidity index (CCI) value was 0 in 206 (67.6%) patients, 1 in 64 (20.9%) patients, and ≤2 in 35 (11.5%) patients. Karnofsky performance status ≤70 was found in 63 patients (20.7%). Frailty was found in 13 patients (4.3%). BMI < 18.5 kg/m^2 was found in 22 patients (7.2%). The most common site of tumor was the oropharynx (n = 114, 37.3%), followed by the oral cavity (n = 69, 22.6%), the larynx (n = 64, 20.9%), and the hypopharynx (n = 58, 19.2%). Advanced T classification was found in 173 patients (56.6%), nodal positivity in 237 patients (77.7%), and overall stage IV cancer in 221 patients (72.5%). The patients who underwent primary surgery alone (n = 76, 24.9%) or surgery plus radiotherapy (n = 92, 30.2%)/chemoradiotherapy (n = 43, 14.2%) were allocated to primary surgery group, whereas, those who underwent definitive radiotherapy alone (n = 3, 0.9%) or chemoradiotherapy (n = 91, 29.8%) were allocated to primary non-surgery group. The study patients were followed up to a median period of 40.5 (0.7–98.0) months. At last follow-up, 172 patients (56.4%) were alive without disease, 68 patients (22.3%) died of the disease, 29 patients (9.5%) died of other causes, and 36 patients (11.8%) were alive with the disease. The 2- and 5-year OS rates were 75.4% and 30.4%, respectively.

Regression analysis

Median SMM values were 174.5 cm^2 (IQR 157.1–188.1) at L3 level and 56.3 cm^2 (IQR 49.9–64.5) at C3 level. Table 2 summarizes the regression models used in linear regression analysis and lists the statistical parameters calculated at 95% confidence level. Two prediction models of L3 SMM are as follows:

Model 1 = 78.106 + 1.668 * C3 SMM

Model 2 = 81.059 + 0.874 * C3 SMM + 0.956 * Weight − 28.127 * Sex − 0.257 * Age

The correlation coefficient of Model 1 including C3 SMM alone was in an intermediated range (R^2 = 0.423). Model 2 included several significant clinical covariates introduced into the regression model such as: sex, age, and weight. Model 2 was observed to significantly increase the correlation coefficient of model 1 (R^2 = 0.724) Age, sex, and weight were identified as the independent predictors of L3 SMM, whereas, the C3 SMM was the strongest predictor of L3 SMM.

The adjusted correlation coefficient was 0.421 between the actual L3 and C3 SMM (P < 0.001). Multivariate regression analysis showed a strong correlation between the actual L3 SMM and that obtained using the prediction model (adjusted R^2 = 0.721, P < 0.001) (Fig. 1).

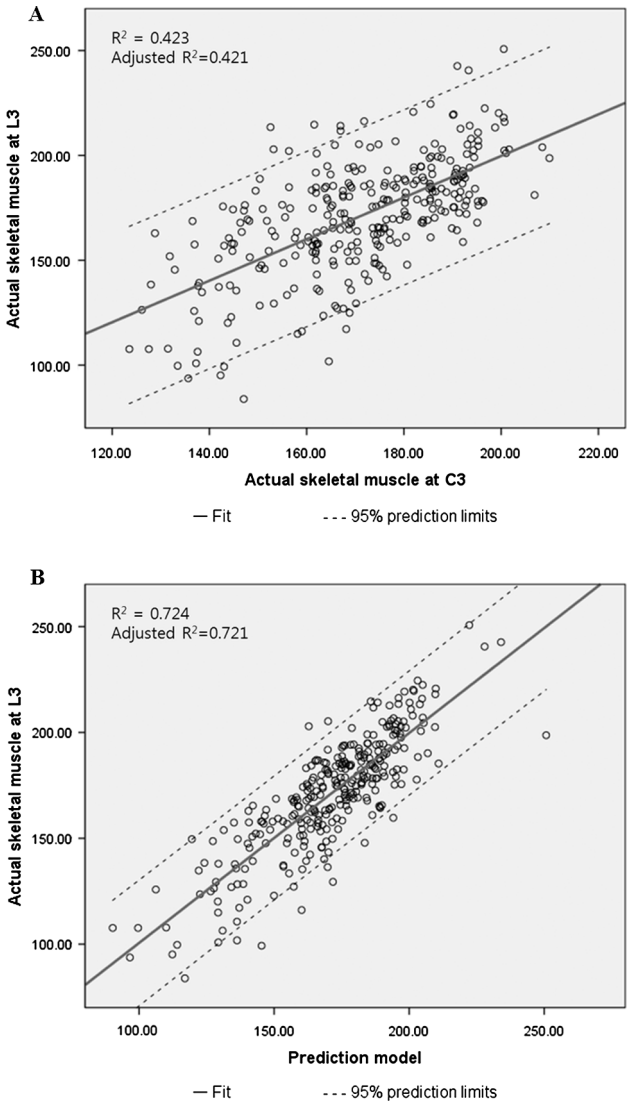

Fig. 1. Correlation between the actual and predicted models for skeletal muscle mass. (A) Comparison between the actual skeletal muscle mass (SMM) at C3 and L3 levels (adjusted R^2 = 0.421). (B) Comparison of the SMM between the actual L3 and the prediction model (adjusted R^2 = 0.721).

Prediction power of models for overall survival

The time-dependent area under the receiver operating characteristic curve was used to examine the discriminatory ability of the models for estimating the overall survival (Fig. 2). The C-index for predicting the overall survival was 0.751 and 0.742 for actual estimations of L3 SMM

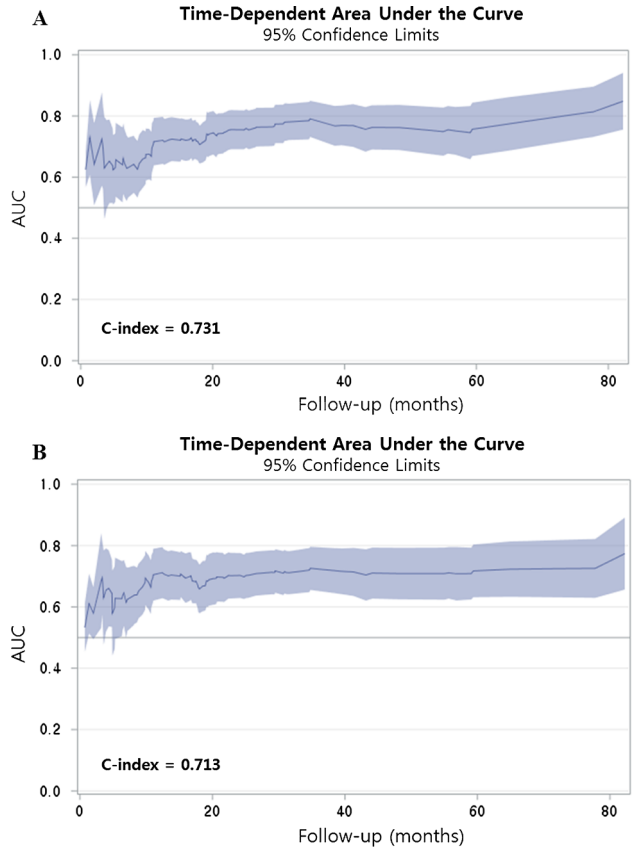

Fig. 2. Time-dependent areas under the curve of two prediction models for overall survival. (A) The univariate model including the C3 skeletal muscle mass (SMM) alone (C-index = 0.731). (B) The multivariate model including the predictive factors of sex, age, and weight in addition to the C3 SMM (C-index = 0.713).

and C3 SMM, respectively. The C-index for predicting the overall survival was 0.731 (95% CI, 0.701–0.759) for model 1 and 0.713 (0.692–0.747) for model 2 (all $P < 0.001$). These observations support the predictive ability of the models for estimating the overall survival after definitive treatments in patients with advanced stages of HNSCC.

The receiver operating characteristic curve analyses provided optimal cut-off values for L3 and C3 SMM for OS around these median values: 174.5 cm^2 for L3 SMM (AUC = 0.809 [95% CI 0.724–0.833], $P < 0.001$) and 56.3 cm^2 for C3 SMM (AUC = 0.830 [95% CI 0.817–0.853], $P < 0.001$). Univariate Cox proportional regression analysis showed that age (≥65 years), Karnofsky performance status (≤70), CCI (≥1), frailty, low L3 SMM (< 174.5 cm^2), low C3 SMM (< 56.3 cm^2), tumor sites (oral cavity and hypopharynx), and advanced T classification were significantly associated with poor OS outcomes (all $P < 0.005$) (Supplementary Table S1). Multivariate Cox proportional hazard regression analysis showed that L3 SMM and C3 SMM remained the independent variables predictive of OS outcomes ($P < 0.001$). Five-year OS rates of low and high L3 SMM were 43.6% and 90.6%, respectively ($P < 0.001$) (Fig. 3). Five-year OS rates of low and high C3 SMM were 46.3% and 87.6%, respectively ($P < 0.001$).

Discussion

This study highlights the usefulness of hnCT images for predicting the overall survival of patients with HNSCC by analyzing SMM correlation between the actual and predicted values of SMM. The prediction model based on C3 SMM measurement correlates strongly with the actual L3 SMM, suggesting that C3 SMM estimation may be a reliable alternative to L3 SMM for the diagnosis of skeletal muscle depletion in patients with HNSCC.

Sarcopenia and skeletal mass depletion are documented independent predictors of poor survival in patients with HNSCC [23]. Patients are at a higher risk for malnutrition and sarcopenia at diagnosis, and during and after treatment for HNSCC. A previous study reported that weight loss of more than 30% were observed in patients with advanced stage HNSCC, owing to pain and swallowing difficulty [24]. Therefore, proper evaluation of body composition or skeletal muscle change in cancer patients may help predict the clinical course of cancer, treatment response, and survival outcomes. Accordingly, we conducted this study for estimating skeletal muscle depletion in patients with advanced-stage HNSCC.

CT scans at the L3 level have been recognized as a reliable method of SMM assessment for diagnosing skeletal muscle depletion. Grossberg et al. [25] measured SMM at the L3 level from the CT component of whole-body ^{18}F-FDG PET/CT scans and abdominal CT scans in 190 patients with HNSCC, before and after curative radiotherapy. Their results indicated that low SMM index, before and after radiotherapy. That was independently associated with decreased overall survival after treatment. Weight loss after radiotherapy initiation was not a predictor of skeletal mass loss or overall survival of patients. However, the abdominal CT scan for measuring L3 SMM is commonly not performed in patients with HNSCC.

hnCT, alternative to abdominal CT, was recently validated for its effectiveness in measuring SMM at C3 for predicting L3 SMM. Swartz et al. [13] measured the SMM CSA at both L3 and C3 levels in 51 and 52 patients with trauma and HNSCC, respectively, who underwent whole body CT ^{18}F-FDG PET/CT, respectively. In this study, patients with HNSCC had lower SMM than those with trauma, suggesting the increased prevalence of sarcopenia in patients with cancer. This might be

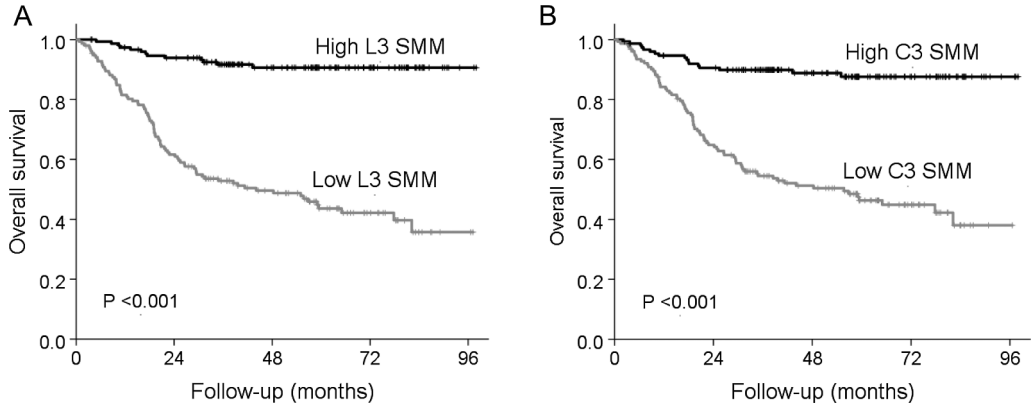

Fig. 3. Kaplan-Meier curves comparing overall survival according to the cutoff values of L3 SMM (174.5 cm^2, A) and C3 SMM (56.3 cm^2, B). Log-rank test, $P < 0.001$.

caused due to the differences between the present and previous studies in terms of inclusion patients, covariates, and statistical methods. Another recent study assessed the relationship between L3 skeletal muscle index and PVM or SCM at C2, C3, and C4 levels [18]. All values of C2, C3, and C4 PVM and SCM indices strongly correlated with L3 skeletal muscle index, though the study did not establish any prediction model for estimating L3 SMM. However, these previous studies have not commented on the prognostic role of the C3 SMM or prediction model for estimating the overall survival after definitive treatment for HNSCC.

The relationship between SMM depletion and clinical outcomes is rarely assessed in patients with HNSCC. A prior study examined the role of low SMM at C3 level to predict chemotherapy dose-limiting toxicity (CDLT) observed in 34 of 112 (30.4%) patients with locally advanced HNSCC [26]. A low skeletal muscle index (cutoff $\leq 43.2\,cm^2/m^2$) was found in 61 (54.5%) patients who had more frequent incidences of adverse effects resulting from chemotherapy, suggesting a reliable adverse prognostic ability of skeletal muscle index for predicting CDLT. Our study showed high predictability of C3 SMM alone or the prediction model for estimating the OS after curative treatment for advanced stage HNSCC. High C-index values were observed in our multivariate models. The results from the present and previous studies suggest that C3 SMM measured by hnCT may serve as an alternative to L3 SMM measurement, and may be used for the prognosis of treatment toxicity, response, or survival outcomes. Therefore, the assessment of body composition including skeletal muscle mass, during routine staging hnCT for HNSCC, may be efficacious for measuring the C3 level, and may aid in stratifying high risk patients with unfavorable prognosis.

Conclusion

The present study suggests that hnCT imaging is useful for estimating L3 SMM, and predicting the overall survival in patients with advanced stage HNSCC. Assessment of C3 SMM may identify SMM-depleted patients, further signifying its performance in routine, pre-treatment hnCT scans in patients with HNSCC.

Acknowledgment

The authors acknowledge the kind support provided to this study by the National Research Foundation of Korea (NRF) grant, funded by the Ministry of Science and ICT (MSIT), The Government of Korea (No. 2019R1A2C2002259) (J.-L.R.).

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.oraloncology.2019.06.009.

References

[1] Tan BH, Birdsell LA, Martin L, Baracos VE, Fearon KC. Sarcopenia in an overweight or obese patient is an adverse prognostic factor in pancreatic cancer. Clin Cancer Res 2009;15:6973–9.
[2] Van Vledder M, Levolger S, Ayez N, Verhoef C, Tran T, Ijzermans J. Body composition and outcome in patients undergoing resection of colorectal liver metastases. Br J Surg 2012;99:550–7.
[3] Englesbe MJ, Patel SP, He K, Lynch RJ, Schaubel DE, Harbaugh C, et al. Sarcopenia and mortality after liver transplantation. J Am Coll Surg 2010;211:271–8.
[4] Joglekar S, Nau PN, Mezhir JJ. The impact of sarcopenia on survival and complications in surgical oncology: a review of the current literature. J Surg Oncol 2015;112:503–9.
[5] Lieffers J, Bathe O, Fassbender K, Winget M, Baracos V. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Cancer 2012;107:931.
[6] Harada K, Ida S, Baba Y, Ishimoto T, Kosumi K, Tokunaga R, et al. Prognostic and clinical impact of sarcopenia in esophageal squamous cell carcinoma. Dis Esophagus 2016;29:627–33.
[7] Harimoto N, Shirabe K, Yamashita YI, Ikegami T, Yoshizumi T, Soejima Y, et al. Sarcopenia as a predictor of prognosis in patients following hepatectomy for hepatocellular carcinoma. Br J Surg 2013;100:1523–30.
[8] Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol 2008;9:629–35.
[9] Prado CM, Baracos VE, McCargar LJ, Reiman T, Mourtzakis M, Tonkin K, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. Clin Cancer Res 2009;15:2920–6.
[10] Mitsiopoulos N, Baumgartner R, Heymsfield S, Lyons W, Gallagher D, Ross R. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol 1998;85:115–22.
[11] Heymsfield SB, Wang Z, Baumgartner RN, Ross R. Human body composition: advances in models and methods. Annual Rev Nutrit 1997;17:527–58.
[12] Shen W, Punyanitya M, Wang Z, Gallagher D, St-Onge M-P, Albu J, et al. Total body skeletal muscle and adipose tissue volumes: estimation from a single abdominal cross-sectional image. J Appl Physiol 2004.
[13] Swartz JE, Pothen AJ, Wegner I, Smid EJ, Swart KM, de Bree R, et al. Feasibility of using head and neck CT imaging to assess skeletal muscle mass in head and neck cancer patients. Oral Oncol 2016;62:28–33.
[14] Chong A, Ha JM, Han YH, Kong E, Choi Y, Hong KH, et al. Preoperative lymph node staging by FDG PET/CT With contrast enhancement for thyroid cancer: a multicenter study and comparison with neck CT. Clin Exp Otorhinolaryngol 2017;10:121–8.
[15] Doyle SL, Bennett AM, Donohoe CL, Mongan AM, Howard JM, Lithander FE, et al. Establishing computed tomography–defined visceral fat area thresholds for use in obesity-related cancer research. Nutr Res 2013;33:171–9.
[16] Lee Y, Park M. Relationships among factors relevant to abdominal fat and age-related hearing loss. Clin Exp Otorhinolaryngol 2017;10:309–14.
[17] Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab 2008;33:997–1006.
[18] Ufuk F, Herek D, Yüksel D. Diagnosis of sarcopenia in head and neck computed tomography: cervical muscle mass as a strong indicator of sarcopenia. Clin Exp Otorhinolaryngol [Epub ahead of print] 2019.
[19] Ahn SH, Hong HJ, Kwon SY, Kwon KH, Roh JL, Ryu J, et al. Guidelines for the surgical management of laryngeal cancer: korean society of thyroid-head and neck surgery. Clin Exp Otorhinolaryngol 2017;10:1–43.
[20] Kim BH, Park SJ, Jeong WJ, Ahn SH. Comparison of treatment outcomes for T3 glottic squamous cell carcinoma: a meta-analysis. Clin Exp Otorhinolaryngol 2018;11:1–8.
[21] Williams BA. Finding optimal cutpoints for continuous covariates with binary and time-to-event outcomes. 2006.
[22] Harrell FE, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med 1996;15:361–87.
[23] O'Sullivan B, Huang SH, Su J, Garden AS, Sturgis EM, Dahlstrom K, et al. Development and validation of a staging system for HPV-related oropharyngeal cancer by the International Collaboration on Oropharyngeal cancer Network for Staging (ICON-S): a multicentre cohort study. Lancet Oncol 2016;17:440–51.
[24] Jager-Wittenaar H, Dijkstra PU, Vissink A, van der Laan BF, van Oort RP, Roodenburg JL. Critical weight loss in head and neck cancer—prevalence and risk factors at diagnosis: an explorative study. Support Care Cancer 2007;15:1045–50.
[25] Grossberg AJ, Chamchod S, Fuller CD, Mohamed AS, Heukelom J, Eichelberger H, et al. Association of body composition with survival and locoregional control of radiotherapy-treated head and neck squamous cell carcinoma. JAMA oncology. 2016;2:782–9.
[26] Wendrich AW, Swartz JE, Bril SI, Wegner I, de Graeff A, Smid EJ, et al. Low skeletal muscle mass is a predictive factor for chemotherapy dose-limiting toxicity in patients with locally advanced head and neck cancer. Oral Oncol. 2017;71:26–33.