

## Supplementary Information

Table S1. Clinicopathologic variables, biochemical and nutrition-inflammation data, anthropometric and body composition characteristics, serum HLOP metabolite and treatment-related factors of 44 patients with LAHNSCC completing CCRT course stratified by the status of CRP change during the treatment course

Variables expressed as Numbers (%) or mean $\pm$ SD	ALL	$\Delta$ CRP increase <sup>§</sup>	$\Delta$ CRP decrease <sup>§</sup>	p value*
Included patient number	44 (100.0)	29 (65.9)	15 (34.1)	
Treatment interruption (no : yes)	35 (79.5) : 9 (20.5)	20 (69.0) : 9 (31.0)	15 (100.0) : 0 (0.0)	0.016*
<i>Clinicopathologic</i>				
Age (years)	54.7 $\pm$ 9.2	56.1 $\pm$ 8.8	53.0 $\pm$ 9.6	0.189
$\geq$ 65 : <65	6 (13.6) : 38 (86.4)	5 (17.2) : 24 (82.8)	1 (6.7) : 14 (93.3)	0.333
Sex (male: female)	42 (95.5) : 2 (4.5)	28 (96.6) : 1 (3.4)	14 (93.3) : 1 (6.7)	0.627
Tumor location (oral cavity/non-oral cavity)				0.754
Buccal mucosa/Tonsil	3 (6.8) / 3 (6.8)	2 (6.9) / 2 (6.9)	1 (6.7) / 1 (6.7)	
Tongue/Tongue base	12 (27.2) / 1 (2.2)	9 (31.0) / 0 (0.0)	3 (20.1) / 1 (6.7)	
Gingiva/Soft palate	5 (11.4) / 0 (0.0)	3 (10.3) / 0 (0.0)	2 (13.3) / 0 (0.0)	
Retromolar /Hypopharynx	2 (4.5) / 10 (22.7)	2 (6.9) / 7 (24.1)	0 (0.0) / 3 (20.0)	
Hard palate / Larynx	1 (2.2) / 5 (6.7)	0 (0.0) / 3 (10.3)	1 (6.7) 2 (13.3)	
Lip/--	2 (4.5) / --	1 (3.4) / --	1 (6.7) / ---	
TNM stage				0.191
III : IVA : IVB	5 (11.4) : 25 (56.8) : 14 (31.8)	5 (17.2):16 (55.2) : 8 (27.6)	0 (0.0) : 8 (53.3) : 7 (46.7)	
T status				0.359
T0-2 : T3-4	11 (25.0) : 33 (75.0)	6 (20.7) : 23 (79.3)	5 (33.3) : 10 (66.7)	
N status				0.939
N0-1 : N2-3	15 (34.1) : 29 (65.9)	10 (34.5) : 19 (65.5)	5 (33.3) : 10 (66.7)	
<i>Histological differentiation grade</i>				
well : moderately : poorly	6 (13.6): 32 (72.8) : 6 (13.6)	5 (17.2): 19 (65.6) : 5 (17.2)	1 (6.7): 13 (86.7) : 1 (6.7)	0.328
ECOG performance status (0 : 1 : 2)	3 (6.9) : 39 (88.6) : 2 (4.5)	2 (6.9) : 25 (86.2) : 2 (6.9)	1 (6.7) : 14 (93.3) : 0 (0.0)	0.579
Tracheostomy (no vs. yes)	27 (61.4) : 17 (38.6)	17 (58.6) : 12 (41.4)	10 (66.6) : 5 (33.4)	0.603
Smoking exposure (no vs. yes)	7 (15.9) : 37 (84.1)	5 (17.2) : 24 (82.8)	2 (13.3) : 13 (86.7)	0.737
Alcohol consumption (no vs. yes)	12 (27.3) : 32 (72.7)	8 (27.6) : 21 (72.4)	4 (26.7) : 11 (73.3)	0.948
Betel nut use (no vs. yes)	16 (36.4) : 28 (63.6)	11 (37.9) : 18 (62.1)	5 (33.4) : 10 (66.6)	0.764
HN-CCI (0 : $\geq$ 1)	0 (0.0) : 44 (100.0)	0 (0.0) : 29 (100.0)	0 (0.0) : 15 (100.0)	----
<i>PG-SGA assessment before CCRT</i>				
Malnutrition none: moderate : severe	9 (20.5): 26 (59.0) : 9 (20.5)	6 (20.7): 17 (58.6) : 6 (20.7)	3 (20.0): 9 (60.0) : 3 (20.0)	0.996
<i>Biochemical data</i>				
Before CCRT				
eGFR (mL/min/1.73 m <sup>2</sup> )	105.4 $\pm$ 28.8	104.8 $\pm$ 31.2	106.3 $\pm$ 24.5	0.878
ALT (U/L, normal $\leq$ 36)	22.5 $\pm$ 10.8	25.6 $\pm$ 16.9	22.4 $\pm$ 9.4	0.516
Total bilirubin (mg/dL, normal $\leq$ 1.3)	0.8 $\pm$ 0.4	0.5 $\pm$ 0.4	0.4 $\pm$ 0.1	0.434
Uric acid (mg/dL, normal $<$ 7.0)	5.2 $\pm$ 1.7	5.2 $\pm$ 1.7	5.1 $\pm$ 2.1	0.885
Sugar (AC, mg/dL)	115.2 $\pm$ 16.5	111.1 $\pm$ 546.6	123.1 $\pm$ 51.8	0.445
Treatment-interval change (%)				
$\Delta$ eGFR%*	-11.3 $\pm$ 26.7	-6.6 $\pm$ 29.5	-20.4 $\pm$ 24.8	0.128
$\Delta$ ALT%*	-22.5 $\pm$ 28.5	-18.0 $\pm$ 18.8	-31.4 $\pm$ 44.6	0.747
$\Delta$ Total bilirubin%*	-2.2 $\pm$ 8.5	-1.0 $\pm$ 11.6	-8.6 $\pm$ 10.9	0.597

$\Delta$ Uric acid%*	-3.5 ± 46.7	-11.2 ± 7.4	12.5 ± 6.9	0.038*
$\Delta$ Sugar (AC)*	-9.1 ± 36.7	-7.4 ± 46.8	-12.1 ± 26.5	0.697
<b>Anthropometric data and blood</b>				
<b>NIB data</b>				
Before CCRT				
BW (kg)	63.9 ± 12.4	63.7 ± 11.4	64.3 ± 14.4	0.899
BMI (kg/m <sup>2</sup> )	23.1 ± 3.9	23.2 ± 3.7	22.8 ± 4.2	0.782
< 18.5 : ≥ 18.5	10 (22.7) : 34 (77.3)	7 (24.1) : 22 (75.9)	3 (20.0) : 12 (80.0)	0.594
Hb (g/dL)	12.0 ± 1.8	11.9 ± 1.4	12.0 ± 2.4	0.963
WBC (x10 <sup>3</sup> cells/mm <sup>3</sup> )	6.6 ± 2.8	6.6 ± 3.2	6.5 ± 1.7	0.920
Platelet count (x10 <sup>3</sup> /mm <sup>3</sup> )	260.1 ± 91.4	244.3 ± 82.2	290.6 ± 103.1	0.111
TLC (x10 <sup>3</sup> cells/mm <sup>3</sup> )	1.8 ± 0.6	1.8 ± 0.6	1.7 ± 0.7	0.761
< 1.5 : ≥ 1.5	14 (31.8) : 30 (68.2)	8 (27.6) : 21 (72.4)	6 (40.0) : 9 (60.0)	0.402
TNC (x 10 <sup>3</sup> /mm <sup>3</sup> )	4.0 ± 0.3	4.0 ± 0.4	4.0 ± 1.2	0.941
TMC (x 10 <sup>3</sup> /mm <sup>3</sup> )	0.5 ± 0.3	0.5 ± 0.3	0.4 ± 0.1	0.389
Albumin (g/dL)	3.9 ± 0.4	3.9 ± 0.4	3.9 ± 0.3	0.827
< 3.5 : ≥ 3.5	5 (11.4) : 39 (88.6)	3 (10.3) : 26 (89.7)	2 (13.3) : 13 (86.7)	0.767
Prealbumin (g/dL, normal: 20–40)	25.3 ± 5.4	25.3 ± 5.7	25.4 ± 5.1	0.941
Transferrin (g/dL normal: 200–360)	208.0 ± 34.6	208.9 ± 36.3	206.2 ± 32.1	0.807
Total cholesterol (mg/dL, normal < 200)	169.3 ± 41.8	167.8 ± 96.5	172.4 ± 42.0	0.760
Triglyceride (mg/dL, normal < 150)	160.5 ± 15.4	152.5 ± 17.2	175.8 ± 116.3	0.483
CRP (mg/dL)	6.3 ± 7.7	3.5 ± 4.0	11.7 ± 10.2	0.009*
Treatment-interval change (%)				
$\Delta$ BW%*	-4.9 ± 5.7	-6.2 ± 5.9	-2.6 ± 4.6	0.041*
$\Delta$ BMI%*	-4.9 ± 6.4	-6.5 ± 6.4	-1.8 ± 5.2	0.018*
$\Delta$ Hb%*	-13.3 ± 14.1	-13.5 ± 2.5	-12.6 ± 3.9	0.836
$\Delta$ WBC%*	-25.9 ± 51.6	-20.8 ± 10.8	-36.0 ± 18.6	0.359
$\Delta$ Platelet%*	-15.5 ± 37.8	-13.6 ± 40.4	-19.1 ± 32.9	0.654
$\Delta$ TLC%*	-24.8 ± 8.5	-34.7 ± 32.6	-17.5 ± 21.4	0.211
$\Delta$ TNC%*	16.4 ± 3.0	18.1 ± 3.6	11.7 ± 5.6	0.249
$\Delta$ TMC%*	-4.0 ± 10.9	-5.9 ± 11.7	-1.3 ± 23.3	0.813
$\Delta$ Albumin%*	-1.0 ± 14.1	-2.6 ± 15.2	6.8 ± 6.4	0.031*
$\Delta$ Prealbumin%*	-9.7 ± 28.2	-9.7 ± 23.8	10.8 ± 31.7	0.020*
$\Delta$ Transferrin%*	-13.1 ± 13.3	-6.2 ± 21.5	6.9 ± 20.4	0.041*
$\Delta$ Cholesterol%*	0.9 ± 21.1	-1.2 ± 22.0	4.9 ± 19.3	0.366
$\Delta$ Triglyceride%*	-3.1 ± 41.6	2.8 ± 43.3	-14.4 ± 36.7	0.198
$\Delta$ CRP%*	609.5 ± 30.6	955.1 ± 454.9	-58.6 ± 7.9	0.034*
<b>DXA-related measurements</b>				
Before CCRT				
LBM (kg)	43.8 ± 5.9	43.8 ± 5.6	43.9 ± 6.6	0.925
TFM (kg)	17.5 ± 7.3	17.5 ± 7.0	17.7 ± 8.2	0.914
ASM (kg)	18.5 ± 3.3	18.6 ± 3.1	18.5 ± 3.9	0.969
Treatment-interval change (%)				
$\Delta$ LBM%*	-7.1 ± 6.0	-9.2 ± 5.1	-3.6 ± 1.1	0.001*
$\Delta$ TFM%*	-3.4 ± 13.2	-3.4 ± 20.2	-3.1 ± 18.1	0.908
$\Delta$ ASM%*	-7.8 ± 8.5	-10.8 ± 8.0	-2.0 ± 6.4	0.027*
<b>HLOP Metabolites</b>				
Before CCRT				
Histidine (μM)	78.8 ± 16.2	78.9 ± 15.4	78.4 ± 18.3	0.917
Leucine (μM)	128.7 ± 40.2	120.4 ± 36.5	144.9 ± 43.1	0.054

Ornithine ( $\mu$ M)	122.5 $\pm$ 35.4	122.3 $\pm$ 39.2	122.6 $\pm$ 27.8	0.983
Phenylalanine ( $\mu$ M)	63.1 $\pm$ 10.4	63.6 $\pm$ 16.4	65.5 $\pm$ 17.1	0.705
Treatment-interval change (%)				
$\Delta$ Histidine%*	-1.4 $\pm$ 28.2	-6.2 $\pm$ 15.3	7.6 $\pm$ 11.5	0.038*
$\Delta$ Leucine%*	-7.5 $\pm$ 27.2	-3.5 $\pm$ 24.0	-15.3 $\pm$ 23.4	0.076
$\Delta$ Ornithine%*	-7.0 $\pm$ 23.4	-11.7 $\pm$ 27.6	-12.1 $\pm$ 22.9	0.963
$\Delta$ Phenylalanine%*	13.9 $\pm$ 33.3	8.6 $\pm$ 28.4	5.9 $\pm$ 33.0	0.785
Mean daily calorie intake during CCRT †	26.9 $\pm$ 6.6	27.2 $\pm$ 7.1	26.5 $\pm$ 5.7	0.738
$\geq$ 25 and < 30 : $\geq$ 30	31 (70.5) : 13 (29.5)	19 (65.5) : 10 (34.5)	12 (80.0) : 3 (20.0)	0.318
Mean daily protein intake during CCRT ††	1.0 $\pm$ 0.3	1.0 $\pm$ 0.2	1.0 $\pm$ 0.3	0.751
Mean daily CHO intake during CCRT ††	3.7 $\pm$ 0.9	3.7 $\pm$ 0.7	3.7 $\pm$ 0.9	0.738
Mean daily fat intake during CCRT ††	0.8 $\pm$ 0.2	0.9 $\pm$ 0.2	0.8 $\pm$ 0.2	0.739
Feeding tube placement (no vs. yes)	22 (50.0) : 22 (50.0)	16 (55.2) : 13 (44.8)	6 (40.0) : 9 (60.0)	0.340
Mean days of feeding tube placement during CCRT	20.3 $\pm$ 3.7	19.6 $\pm$ 4.7	21.7 $\pm$ 5.8	0.792
<b>CCRT data</b>				
Radiotherapy				
Dose (Gy)	66.6 $\pm$ 3.9	65.9 $\pm$ 3.9	67.7 $\pm$ 4.0	0.154
Fractions	32.6 $\pm$ 1.3	32.3 $\pm$ 1.3	32.9 $\pm$ 1.2	0.146
Duration (days)	48.4 $\pm$ 5.1	48.6 $\pm$ 5.8	47.8 $\pm$ 3.5	0.648
Cisplatin dose (mg/m <sup>2</sup> )	233.4 $\pm$ 22.2	238.1 $\pm$ 14.6	215.0 $\pm$ 35.7	0.004*
Grade 3/4 toxicity during CCRT				
Non-hematologic				
Dermatitis (no vs. yes)	43 (97.7) : 1 (2.3)	28 (96.6) : 1 (3.4)	15 (100) : 0 (0.0)	0.608
Pharyngitis (no vs. yes)	42 (95.5) : 2 (4.5)	27 (93.1) : 2 (6.9)	15 (100) : 0 (0.0)	0.298
Infection (no vs. yes)	30 (68.2) : 14 (31.8)	20 (69.0) : 9 (31.0)	10 (66.7) : 5 (33.3)	0.877
Mucositis (no vs. yes)	33 (75.0) : 11 (25.0)	19 (65.5) : 10 (34.5)	14 (93.3) : 1 (6.7)	0.043*
Emesis (no vs. yes)	41 (93.2) : 3 (6.8)	27 (93.1) : 2 (6.9)	14 (93.3) : 1 (6.7)	0.977
Hematologic				
Anemia (no vs. yes)	41 (93.2) : 3 (6.8)	27 (93.1) : 2 (6.9)	14 (93.3) : 1 (6.7)	0.977
Neutropenia (no vs. yes)	29 (65.9) : 15 (34.1)	20 (69.0) : 9 (31.0)	9 (60.0) : 6 (40.0)	0.552
Thrombocytopenia (no vs. yes)	38 (86.4) : 6 (13.6)	25 (86.2) : 4 (13.8)	13 (86.7) : 2 (13.3)	0.801
Number of grade 3/4 toxicity	1.2 $\pm$ 1.1	1.4 $\pm$ 1.2	1.0 $\pm$ 1.0	0.338

\*unit: Kcal /kg/day †unit: g/kg/day

\* Comparing the value difference between treatment interruption and treatment with no interruption for each variable;  
 $p < 0.05$ , statistically significant

§ $\Delta$ CRP increase was defined as a positive value obtained by subtracting the pre-treatment CRP value from the post-treatment CRP value.  $\Delta$ CRP decrease was defined as a negative value obtained by subtracting the pre-treatment CRP value from the post-treatment CRP value.

The Mann–Whitney test was used for  $\Delta$ Hb%, CRP,  $\Delta$  uric acid%, total bilirubin, mean days for feeding tube placement, dose, fraction and days of radiotherapy, cisplatin dose, all DXA-related measurements, all metabolites, and the number of grade 3/4 toxicities. Independent *t* test was used for other continuous variables. The chi-square test was used for all categorical data.

\* $\Delta$  indicates the value obtained by subtracting the pretreatment value from the post-treatment value; % indicates

( $\Delta$  value/ the pretreatment value)  $\times 100\%$

Abbreviations: LAHNSCC, locally advanced head and neck squamous cell carcinoma; CCRT, concurrent chemoradiotherapy; SD, standard deviation; HN-CCI, Charlson comorbidity index; ECOG, Eastern Cooperative Oncology Group; CHO, carbohydrate; PG-SGA, patient-generated subjective global assessment; BW, body weight; BMI, body mass index; eGFR, estimated glomerular filtration rate; ALT, alanine aminotransferase; Hb, hemoglobin; WBC, white blood cell; TLC, total lymphocyte count; TNC, total neutrophil count; TMC, total monocyte count; CRP, C-reactive protein; DXA, dual-energy X-ray absorptiometry; LBM, lean body mass; TFM, total fat mass; ASM, appendicular skeletal mass; HLOP, histidine, leucine, ornithine, and phenylalanine.

Table S2. Associations of clinicopathologic variables, NIBs, body composition parameters, treatment-related factors, and serum metabolites with treatment interval changes of leucine and ornithine over the CCRT course in 44 patients with LAHNSCC completing CCRT

Variables	$\Delta$ Leucine%		$\Delta$ Ornithine%		
	Univariate	Multivariate	Univariate	Multivariate	
	p-value*	Coefficient (95% CI)	p-value*	Coefficient (95% CI)	p-value*
<i>Clinicopathologic factors</i>					
Age	0.779		0.965		
Sex (male vs female)	0.803		0.803		
Tumor location (OC vs NOC)	0.859		0.281		
TNM stage (III vs IVA vs IVB)	0.602		0.068		
T status (T1-2 vs T3-4)	0.007*		0.376		
N status (N0-1 vs N2-3)	0.732		0.892		
Histologic grade (well vs moderately vs poorly)	1.00		1.00		
Smoking (no vs yes)	0.550		0.032*		
Alcohol (no vs yes)	0.067		0.271		
Betel nut (no vs yes)	0.884		0.079		
ECOG performance status (0 : 1 : 2)	0.163		0.547		
Tracheostomy (no vs yes)	0.206		0.138		
PG-SGA before CCRT (none : moderate : severe)	0.385		0.247		
<i>Biochemical data</i>					
Before CCRT					
eGFR (mL/min/1.73 m <sup>2</sup> )	0.930		0.840		
ALT (U/L)	0.069		0.953		
Total bilirubin (mg/dL)	0.437		0.931		
Uric acid (mg/dL)	0.756		0.182		
Sugar (AC)( (mg/dL)	0.810		0.112		
Treatment-interval change (%)					
$\Delta$ eGFR%*	0.640		0.237		
$\Delta$ ALT%*	0.114		0.261		
$\Delta$ Total bilirubin%*	0.066		0.334		
$\Delta$ Uric acid%*	0.573		0.495		

$\Delta$ Sugar (AC)*	0.745		0.783
<i>Anthropometric data and blood NIBs data</i>			
<b>Before CCRT</b>			
BW (kg)	0.441		0.850
BMI (kg/m <sup>2</sup> )	0.466		0.905
Hb (g/dL)	0.016*		0.189
WBC (x10 <sup>3</sup> cells/mm <sup>3</sup> )	0.025*		0.176
Platelet count (x10 <sup>3</sup> /mm <sup>3</sup> )	0.194		0.794
TLC (x10 <sup>3</sup> cells/mm <sup>3</sup> )	0.036*	13.108 (6.210 ~ 19.990)	<0.001*
TNC (x 10 <sup>3</sup> /mm <sup>3</sup> )	0.086		0.151
TMC (x 10 <sup>3</sup> /mm <sup>3</sup> )	0.032*		0.368
Albumin (g/dL)	0.113		0.720
Prealbumin (g/dL)	0.072		0.425
Transferrin (g/dL)	0.311		0.199
Total cholesterol (mg/dL)	0.313		0.363
Triglyceride (mg/dL)	0.475		0.892
CRP (mg/dL)	0.486		0.498
<b>Treatment-interval change (%)</b>			
$\Delta$ BW%*	0.747		0.597
$\Delta$ BMI%*	0.387		0.510
$\Delta$ Hb%*	0.002*	0.470 (0.127 ~ 0.816)	0.009*
$\Delta$ WBC%*	0.630		0.185
$\Delta$ Platelet%*	0.092		0.756
$\Delta$ TLC%*	0.179		0.414
$\Delta$ TNC%*	0.307		0.876
$\Delta$ TMC%*	0.508		0.923
$\Delta$ Albumin%*	0.305		0.146
$\Delta$ Prealbumin%*	0.769		0.162
$\Delta$ Transferrin%*	0.658		0.103
$\Delta$ Cholesterol%*	0.021		0.003
$\Delta$ Triglyceride%*	0.343	0.430 (0.054 ~ 0.807)	0.026*

$\Delta$ CRP%*	0.951	0.053
<b><i>DXA-related measurements</i></b>		
<b>Before CCRT</b>		
LBM (kg)	0.694	0.664
TFM (kg)	0.385	0.990
ASM (kg)	0.920	0.917
<b>Treatment-interval change (%)</b>		
$\Delta$ LBM%*	0.388	0.633
$\Delta$ TFM%*	0.326	0.105
$\Delta$ ASM%*	0.849	0.915
<b>HLOP Metabolites</b>		
<b>Before CCRT</b>		
Histidine ( $\mu$ M)	<0.001*	0.052
Leucine ( $\mu$ M)	<0.001*	-0.462 (-0.536 ~ -0.309)
Ornithine ( $\mu$ M)	0.001*	0.005*
Phenylalanine ( $\mu$ M)	<0.001*	0.303
<b>Treatment-interval change (%)</b>		
$\Delta$ Histidine%*	0.015*	0.022*
$\Delta$ Leucine%*	----	0.004*
$\Delta$ Ornithine%*	0.004*	0.006*
$\Delta$ Phenylalanine%*	0.001*	0.102
<i>Mean daily calorie intake during CCRT †</i>	0.764	0.697
<i>Mean daily protein intake during CCRT††</i>	0.723	0.409
<i>Mean daily CHO intake during CCRT†††</i>	0.864	0.029
<i>Mean daily fat intake during CCRT†††</i>	0.959	0.686
<i>Feeding tube placement (no vs. yes)</i>	0.583	
<i>Mean days of feeding tube placement during CCRT</i>	0.750	0.083
<b>CCRT factor</b>		
RT dose (Gy)	0.710	0.647
RT fractions	0.296	0.851
RT duration (days)	0.439	0.709

Cisplatin dose (mg/m <sup>2</sup> )	0.153	0.119
<i>CCRT-induced grade 3/4 toxicity</i>		
<b>Non-hematologic</b>		
Dermatitis (no vs yes)	0.318	0.091
Pharyngitis (no vs yes)	0.013*	0.211
Mucositis (no vs yes)	0.979	0.391
Infection (no vs yes)	0.880	0.705
Emesis (no vs yes)	0.563	0.596
<b>Hematologic</b>		
Anemia (no vs yes)	0.221	0.394
Neutropenia (no vs yes)	0.594	0.450
Thrombocytopenia (no vs yes)	0.777	0.777

\*indicates a significant *p*-value < 0.05.

Univariate analysis: simple linear regression model for all continuous variables; Mann–Whitney test for sex, T status, N status, smoking, alcohol, betel nut, tracheostomy, and feeding tube placement; Kruskal–Wallis test for TNM stage, histological grade, ECOG performance status, and PG-SGA

‡Δ indicates the value obtained by subtracting the pretreatment value from the post-treatment value; % indicates ( $\Delta$  value/ the pretreatment value) ×100%

Abbreviations: NIBs, nutritional and inflammatory biomarkers; LAHNSCC, locally advanced head and neck squamous cell carcinoma; CCRT, concurrent chemoradiotherapy; CI, confidence interval; OC, oral cavity; NOC, non-oral cavity; TNM, tumor node metastasis; ECOG, Eastern Collaboration Oncology Group; RT, radiotherapy; PG-SGA, patient-generated subjective global assessment; eGFR, estimated glomerular filtration rate; ALT, alanine transaminase; NIBs, nutritional/inflammatory biomarkers; BMI, body mass index; BW, body weight; Hb, hemoglobin; WBC, white cell count; TLC, total lymphocyte count; TNC, total neutrophil count; TMC, total monocyte count; CRP, C-reactive protein; DXA, dual-energy X-ray absorptiometry; LBM, lean body mass; TFM, total fat mass; ASM, appendicular skeletal mass; HLOP, histidine, leucine, ornithine, and phenylalanine.

Table S3. Clinicopathologic variables, biochemical and nutrition-inflammation data, anthropometric and body composition characteristics, and serum HLOP metabolite of 50 patients with LAHNSCC stratified by the status of complete and incomplete CCRT

14  
15  
16

Variables expressed as Numbers (%) or mean $\pm$ SD	Complete CCRT	Incomplete CCRT <sup>§</sup>	p value*
Included patient number	44 (88.0)	6 (12.0)	
<i>Clinicopathologic</i>			
Age (years)	54.7 $\pm$ 9.1	56.5 $\pm$ 7.4	0.645
Sex (male: female)	42 (95.5) : 2 (4.5)	6 (100.0) : 0 (0.0)	0.594
Tumor location (oral cavity/non-oral cavity)			0.133
Buccal mucosa/Tonsil	3 (6.8) / 3 (6.8)	1 (16.7) / 1 (16.7)	
Tongue/Tongue base	12 (27.2) / 1 (2.2)	1 (16.7) / 0 (0.0)	
Gingiva/Soft palate	5 (11.4) / 0 (0.0)	1 (16.7) / 0 (0.0)	
Retromolar /Hypopharynx	2 (4.5) / 10 (22.7)	0 (0.0) / 1 (16.7)	
Hard palate / Larynx	1 (2.2) / 5 (6.7)	0 (0.0) / 1 (16.7)	
Lip/-	2 (4.5) / --	0 (0.0)/ ---	
TNM stage			0.149
III : IVA : IVB	4 (9.1):22 (50.0) : 18 (40.9)	0 (0.0) : 1 (16.7) : 5 (83.3)	
T status			0.849
T0-2 : T3-4	13 (29.5) : 31 (70.5)	2 (33.3) : 4 (66.7)	
N status			0.941
N0-1 : N2-3	14 (31.8) : 30 (68.2)	2 (33.3) : 4 (66.7)	
<i>Histological differentiation grade</i>			
well : moderately : poorly	5 (11.4): 32 (72.7) : 7 (15.9)	1 (16.7) : 5 (83.3) : 0 (0.0)	0.583
ECOG performance status (0 : 1 : 2)	3 (6.8) : 39 (88.6) : 2 (4.5)	2 (33.3) : 4 (66.7) : 0 (0.0)	0.358
Tracheostomy (no vs. yes)	27 (61.4) : 17 (38.6)	3 (50.0) : 3 (50.0)	0.594
Smoking exposure (no vs. yes)	7 (15.8) : 37 (84.1)	1 (16.7) : 5 (83.3)	0.962
Alcohol consumption (no vs. yes)	12 (27.3) : 32 (72.7)	2 (33.3) : 4 (66.7)	0.756
Betel nut use (no vs. yes)	11 (37.9) : 18 (62.1)	3 (50.0) : 3 (50.0)	0.519
HN-CCI (0 : $\geq$ 1)	18 (40.9) : 26 (59.1)	2 (33.3) : 4 (66.7)	0.722
<i>PG-SGA assessment before CCRT</i>			
Malnutrition none : moderate : severe	9 (20.5): 26 (59.0) : 9 (20.5)	0 (20.0): 4 (66.7) : 2 (33.3)	0.433
<i>Biochemical data</i>			
eGFR (mL/min/1.73 m <sup>2</sup> )	104.2 $\pm$ 32.2	105.0 $\pm$ 29.5	0.910
ALT (U/L, normal $\leq$ 36)	24.6 $\pm$ 14.7	33.7 $\pm$ 21.2	0.188
Total bilirubin (mg/dL, normal $\leq$ 1.3)	0.7 $\pm$ 0.4	0.9 $\pm$ 1.0	0.502
Uric acid (mg/dL, normal < 7.0)	5.2 $\pm$ 1.8	5.1 $\pm$ 1.3	0.948
Sugar (AC, mg/dL)	115.2 $\pm$ 48.2	110.0 $\pm$ 34.2	0.799
<i>Anthropometric data and blood NIB data</i>			
BW (kg)	63.9 $\pm$ 12.3	64.6 $\pm$ 7.2	0.900
BMI (kg/m <sup>2</sup> )	23.0 $\pm$ 3.9	21.9 $\pm$ 2.6	0.517
Hb (g/dL)	12.0 $\pm$ 1.7	11.6 $\pm$ 2.4	0.637
WBC ( $\times 10^3$ cells/mm <sup>3</sup> )	6.6 $\pm$ 2.8	6.6 $\pm$ 1.9	0.975
Platelet count ( $\times 10^3$ /mm <sup>3</sup> )	260.1 $\pm$ 91.4	270.3 $\pm$ 71.0	0.794
TLC ( $\times 10^3$ cells/mm <sup>3</sup> )	1.8 $\pm$ 0.6	1.6 $\pm$ 0.3	0.480
TNC ( $\times 10^3$ /mm <sup>3</sup> )	4.0 $\pm$ 2.0	4.2 $\pm$ 1.9	0.855
TMC ( $\times 10^3$ /mm <sup>3</sup> )	0.5 $\pm$ 0.1	0.4 $\pm$ 0.2	0.329
Albumin (g/dL)	3.9 $\pm$ 0.4	3.8 $\pm$ 0.8	0.576
Prealbumin (g/dL, normal: 20–40)	25.3 $\pm$ 5.4	23.5 $\pm$ 6.6	0.249
Transferrin (g/dL normal: 200–360)	208.0 $\pm$ 34.6	196.2 $\pm$ 412.1	0.747

Total cholesterol (mg/dL, normal < 200)	$169.3 \pm 41.8$	$175.7 \pm 54.2$	0.736
Triglyceride (mg/dL, normal < 150)	$152.5 \pm 17.2$	$175.8 \pm 116.3$	0.483
CRP (mg/dL)	$6.3 \pm 7.7$	$10.4 \pm 13.3$	0.267
<b>DXA-related measurements</b>			
LBM (kg)	$43.8 \pm 5.9$	$46.7 \pm 2.4$	0.294
TFM (kg)	$17.5 \pm 7.3$	$15.6 \pm 5.8$	0.576
ASM (kg)	$18.2 \pm 3.7$	$18.4 \pm 3.2$	0.911
<b>HLOP Metabolites</b>			
Histidine ( $\mu\text{M}$ )	$78.8 \pm 16.2$	$76.7 \pm 17.4$	0.770
Leucine ( $\mu\text{M}$ )	$128.7 \pm 40.2$	$120.7 \pm 29.5$	0.641
Ornithine ( $\mu\text{M}$ )	$122.4 \pm 35.4$	$118.6 \pm 26.4$	0.802
Phenylalanine ( $\mu\text{M}$ )	$64.3 \pm 16.5$	$61.4 \pm 17.3$	0.698

\* Comparison of the value difference between complete CCRT and incomplete CCRT for each variable;  $p < 0.05$ , 17  
statistical significance.

§ Incomplete CCRT group included drop-outs and incomplete data collection. 18

The Mann-Whitney test was used for CRP, total bilirubin, all DXA-related measurements, and all metabolites. 20  
Independent  $t$  test was used for other continuous variables. The chi-square test was used for all categorical data. 21

Abbreviations: LAHNSCC, locally advanced head and neck squamous cell carcinoma; CCRT, concurrent 22  
chemoradiotherapy; SD, standard deviation; HN-CCI, Charlson comorbidity index; ECOG, Eastern Cooperative 23  
Oncology Group; PG-SGA, patient-generated subjective global assessment; BW, body weight; BMI, body mass index; 24  
eGFR, estimated glomerular filtration rate; ALT, alanine aminotransferase; Hb, hemoglobin; WBC, white blood cell; 25  
TLC, total lymphocyte count; TNC, total neutrophil count; TMC, total monocyte count; CRP, C-reactive protein; DXA, 26  
dual-energy X-ray absorptiometry; LBM, lean body mass; TFM, total fat mass; ASM, appendicular skeletal mass; HLOP, 27  
histidine, leucine, ornithine, phenylalanine. 28

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