Supplementary Information

Dynamic Postoperative Skeletal Muscle Trajectories Predict Survival in Stage II–III Gastric Cancer

Jeong Eun Kim[1]*, Song Ee Park[2]*, Jin Hwa Choi[3,4†], In Gyu Hwang[3,5†]

[1]Department of Oncology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, South Korea

[2]Department of Oncology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea

[3]Chung-Ang University Integrated Oncology and Palliative Care Research Institute, Seoul, Korea

[4]Department of Radiation Oncology, Chung-Ang University College of Medicine, Seoul, South Korea

[5]Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, South Korea

*Jeong Eun Kim and Song Ee Park equally contributed to this study

[†]Corresponding authors

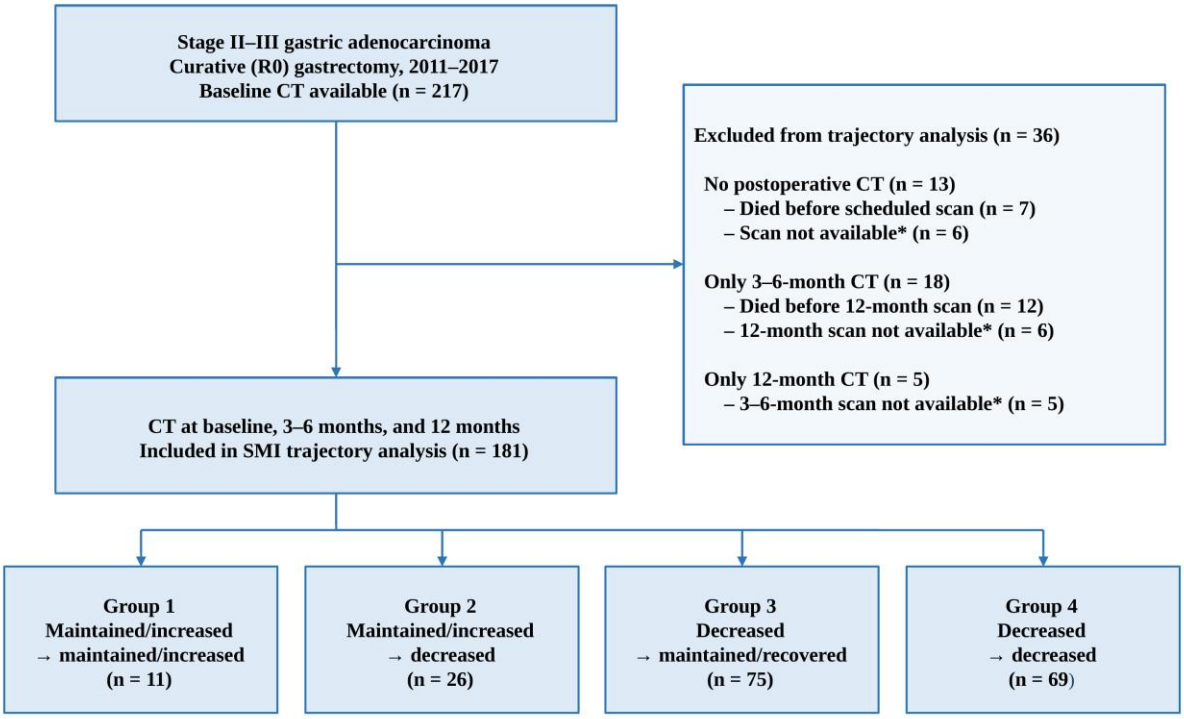
In Gyu Hwang, Division of Hemato-oncology, Department of Internal Medicine, Chung-Ang University College of Medicine, 84 Heukseok-ro, Dongjak-gu, Seoul 06973, Korea.

Phone: +82-2-6299-1403; Fax:+82-2-6299-2114; E-mail: oncology@cau.ac.kr

Jin Hwa Choi, Department of Radiation Oncology, Chung-Ang University College of Medicine, 84 Heukseok-ro, Dongjak-gu, Seoul 06973, Republic of Korea.

Tel: 82-2-6299-2676; E-mail: bonnybee@cau.ac.kr

Supplementary Fig. S1. Flow diagram of patient selection



CT, computed tomography; SMI, skeletal muscle index.

Table S1. Baseline clinical and body composition characteristics according to postoperative skeletal muscle index change groups

Characteristics	Group 1 (N = 11)	Group 2 (N = 26)	Group 3 (N = 75)	Group 4 (N = 69)	p-value
Age (years), median (range)	65.0 (45.0–83.0)	71.0 (36.0–88.0)	62.0 (33.0–88.0)	65.0 (30.0–84.0)	0.272
Sex					0.102
Male	9 (81.8%)	13 (50.0%)	54 (72.0%)	51 (73.9%)	
Female	2 (18.2%)	13 (50.0%)	21 (28.0%)	18 (26.1%)	
Stage					0.467
II	6 (54.5%)	10 (38.5%)	42 (56.0%)	34 (49.3%)	
III	5 (45.5%)	16 (61.5%)	33 (44.0%)	35 (50.7%)	
Surgery type					
Total	3 (27.3%)	6 (23.1%)	24 (32.0%)	27 (39.1%)	0.494
Subtotal	8 (72.7%)	20 (76.9%)	51 (68.0%)	42 (60.9%)	
Height (cm), mean ± SD	164.1 ± 6.3	158.7 ± 7.5	163.0 ± 8.7	163.7 ± 7.9	0.052
Weight (kg), mean ± SD	58.1 ± 11.9	57.4 ± 8.3	62.6 ± 11.9	63.4 ± 10.5	0.065
BMI					0.557
Underweight (BMI<18.5)	2 (18.2%)	1 (3.8%)	5 (6.7%)	5 (7.2%)	
Normal weight (18.5≤BMI<23)	6 (54.5%)	13 (50.0%)	31 (41.3%)	26 (37.7%)	
	3 (27.3%)	12 (46.2%)	39 (52.0%)	38 (55.1%)	

Overweight (BMI≥23)					
Baseline SMI (cm^2/m^2), mean ± SD	44.8 ± 6.7	45.4 ± 7.6	49.2 ± 8.0	49.8 ± 8.0	0.034
Baseline Sarcopenia	6 (54.5%)	8 (30.8%)	18 (24.0%)	20 (29.0%)	0.224
Hemoglobin (g/dL), median (range)	12.4 (5.1–16.0)	12.2 (8.0–14.9)	12.3 (5.6–17.3)	12.7 (7.3–15.9)	0.609
Albumin (g/dL), median (range)	3.9 (3.0–4.7)	3.8 (2.8–4.7)	4.0 (1.4–4.8)	4.0 (2.7–5.0)	0.646
Chemotherapy Regimen					0.974
5FL	1 (9.1%)	4 (15.4%)	10 (13.3%)	7 (10.1%)	
TS-1	4 (36.4%)	9 (34.6%)	29 (38.7%)	31 (44.9%)	
CAPOX	5 (45.5%)	8 (30.8%)	23 (30.7%)	20 (29.0%)	
FOLFOX	0 (0%)	0 (0%)	1 (1.3%)	2 (2.9%)	
SOX	0 (0%)	1 (3.8%)	6 (8.0%)	3 (4.3%)	
Others	0 (0%)	1 (3.8%)	0 (0%)	2 (2.9%)	
None	1 (9.1%)	3 (11.5%)	6 (8.0%)	4 (5.8%)	

5FL, 5-fluorouracil plus leucovorin; BMI, body mass index; FOLFOX, 5-fluorouracil/leucovorin plus oxaliplatin; SD, standard deviation; SMI, skeletal muscle index; SOX, S-1 plus oxaliplatin; TS-1, tegafur/gimeracil/oteracil; CAPOX, capecitabine plus oxaliplatin.

Table S2. Nature of DFS events according to SMI change groups

SMI change group	Event type	n (%)
Group 1	Recurrence	4 (80.0)
	Death without documented recurrence	1 (20.0)
Group 2	Recurrence	11 (91.7)
	Death without documented recurrence	1 (8.3)
Group 3	Recurrence	20 (83.3)
	Death without documented recurrence	4 (16.7)
Group 4	Recurrence	25 (67.6)
	Death without documented recurrence	12 (32.4)

Recurrence includes patients with documented recurrence, regardless of subsequent death. Percentages are calculated among DFS events in each group. DFS, disease-free survival; SMI, skeletal muscle index.

Table S3. Sex-stratified associations between skeletal muscle index changes and survival outcomes

(A) Disease-Free Survival (DFS)

Variable	Sex	HR (95% CI)	p-value
Baseline Low SMI	All	1.809 (1.229–2.664)	0.003
	Male	1.930 (1.198–3.108)	0.007
	Female	1.600 (0.824–3.109)	0.165
Interval* 1 SMI decrease	All	1.396 (0.927–2.103)	0.111
	Male	1.467 (0.882–2.438)	0.140
	Female	1.263 (0.630–2.532)	0.510
Interval 2 SMI decrease	All	1.705 (1.085–2.680)	0.021
	Male	2.264 (1.289–3.976)	0.004
	Female	0.929 (0.422–2.041)	0.854
Interval 3 SMI decrease	All	0.936 (0.607–1.444)	0.766
	Male	1.079 (0.636–1.831)	0.778
	Female	0.691 (0.320–1.489)	0.345

*Interval definitions: Interval 1, SMI change from baseline to 3–6 months; interval 2, SMI change from 3–6 months to 12 months; interval 3, overall SMI change from baseline to 12 months. Baseline low SMI, baseline SMI below the sex-specific median; CI, confidence interval; HR, hazard ratio; SMI, skeletal muscle index.

(B) Overall Survival (OS)

Variable	Sex	HR (95% CI)	p-value
Baseline Low SMI	All	2.003 (1.320–3.040)	0.001
	Male	2.216 (1.320–3.721)	0.003
	Female	1.658 (0.818–3.361)	0.161
Interval* 1 SMI decrease	All	1.504 (0.970–2.332)	0.068
	Male	1.655(0.960–2.851)	0.070
	Female	1.242 (0.590–2.613)	0.569
Interval 2 SMI decrease	All	2.620 (1.569–4.373)	<0.001
	Male	3.266 (1.715–6.221)	<0.001
	Female	1.735 (0.724–4.154)	0.216
Interval 3 SMI decrease	All	1.219 (0.762–1.949)	0.409
	Male	1.455 (0.818–2.589)	0.202
	Female	0.842 (0.368–1.922)	0.682

*Interval definitions: Interval 1, SMI change from baseline to 3–6 months; interval 2, SMI change from 3–6 months to 12 months; interval 3, overall SMI change from baseline to 12 months. Baseline low SMI, baseline SMI below the sex-specific median; CI, confidence interval; HR, hazard ratio; SMI, skeletal muscle index.

Table S4. Interval 1 skeletal muscle index change according to chemotherapy-related factors and scan timing (n = 181)

Comparison (A vs. B)	A, n	A, % change (mean ± SD)	B, n	B, % change (mean ± SD)	p value
Adjuvant chemotherapy (yes vs. no)	167	−6.1 ± 10.0	14	−11.4 ± 13.7	0.282
First follow-up CT during chemotherapy (yes vs. no)*	143	−6.4 ± 10.2	24	−4.3 ± 8.3	0.233
Oxaliplatin-based vs. non-oxaliplatin regimen*	69	−6.3 ± 9.7	98	−6.0 ± 10.2	0.839
Early discontinuation or regimen change (yes vs. no)*	29	−7.1 ± 8.7	138	−5.9 ± 10.2	0.592

Spearman's correlation between interval 1 SMI change and the number of chemotherapy cycles: $\rho = -0.02$, $p = 0.774$; between interval 1 SMI change and the time from surgery to the first follow-up CT: $\rho = 0.13$, $p = 0.080$. Distribution of trajectory groups according to adjuvant chemotherapy: $p = 0.819$ (chi-square test). P values for group comparisons were obtained using the Mann–Whitney U test. *Among patients who received adjuvant chemotherapy (n = 167). CT, computed tomography; SD, standard deviation; SMI, skeletal muscle index.

Table S5. Competing-risk analysis of recurrence according to postoperative skeletal muscle index trajectory (n = 181)

(A) Cumulative incidence of recurrence and death without recurrence

Group	n	Recurrence, n	Death without recurrence, n	5-year CIR, %	5-year CID, %
Group 1	11	4	1	36.4	9.1
Group 2	26	11	1	47.3	3.8
Group 3	75	20	4	28.1	3.4
Group 4	69	25	12	36.5	19.5
Gray's test, p				0.405	0.058
SMI-resilient (groups 1 and 3)	86	24	5	29.2	4.1
SMI non-resilient (groups 2 and 4)	95	36	13	39.3	15.2
Gray's test, p				0.124	0.065

(B) Fine–Gray multivariate model for recurrence (death without recurrence as a competing event)

Variable	sHR (95% CI)	p value
SMI trajectory (overall)		0.660
Group 1 vs. group 4	0.667 (0.182–2.448)	0.540
Group 2 vs. group 4	0.981 (0.463–2.081)	0.960
Group 3 vs. group 4	0.709 (0.378–1.327)	0.280
Age > 65	1.201 (0.706–2.042)	0.500
Stage III	4.853 (2.621–8.988)	< 0.001
BMI < 18.5	1.978 (0.752–5.200)	0.170
Chemotherapy	1.119 (0.337–3.713)	0.850
Subtotal gastrectomy	0.780 (0.442–1.377)	0.390
Hb < 10	2.343 (1.334–4.118)	0.003
Albumin < 3.5	0.802 (0.393–1.639)	0.550
Baseline sarcopenia	1.688 (0.986–2.891)	0.056

Cumulative incidence was estimated with death without recurrence treated as a competing event and compared using Gray's test. The Fine–Gray model was adjusted for the same covariates as the multivariate Cox model (Table 3); the overall p value for SMI trajectory was obtained from a Wald test. In the corresponding Fine–Gray model for death without recurrence, the sHR for group 3 vs. group 4 was 0.281 (95% CI 0.084–0.934; p = 0.038); this estimate should be interpreted with caution given the small number of events (n = 18). BMI, body mass index; CI, confidence interval; CID, cumulative incidence of death without recurrence; CIR, cumulative incidence of recurrence; Hb, hemoglobin; sHR, subdistribution hazard ratio; SMI, skeletal muscle index.