SUPPLEMENTARY TABLES

Supplementary Table 1. Clinical parameters of human subjects.

	Sarcopenia (*N* = 6)	Non-Sarcopenia (*N* = 13)	95% CI of the difference	*P*-value	Reduced SMI (*N* = 11)	Control (*N* = 8)	95% CI of the difference	*p*-value
Age	85.0 ± 8.6	83.8 ± 6.3	–7.92 to 10.38	0.76	85.0 ± 8.6	83.8 ± 6.3	–7.92 to 10.38	0.76
Gender (Male; Female)	1;5	6;7			2;9	5;3		
SMI (kg/m^2)	5.0 ± 1.0	6.6 ± 1.2	–2.77 to –0.48	*0.01	5.2 ± 0.9	7.4 ± 0.8	–2.99 to –1.31	**0.0005
Handgrip(kg)	18.0 ± 4.0	23.0 ± 7.4	–10.53 to 0.66	0.08	21.1 ± 5.4	23.4 ± 8.4	–10.89 to 4.0	0.51
TUG(sec.)	23.5 ± 13.3	12.2 ± 6.5	–2.68 to 25.26	0.1	18.1 ± 11.4	12.6 ± 8.3	–4.10 to 14.95	0.27
Walking Speed (m/sec.)	1.07 ± 0.33	1.21 ± 0.40	–0.61 to 0.33	0.53	1.09 ± 0.26	1.27 ± 0.48	–0.57 to 0.21	0.37
BMI(kg/m^2)	20.0 ± 2.3	23.3 ± 3.6	–6.15 to –0.33	*0.03	20.7 ± 2.2	24.4 ± 4.0	–7.20 to –0.26	*0.04
Fat mass (kg)	12.7 ± 2.9	15.4 ± 5.7	–7.98 to 2.59	0.19	13.4 ± 2.7	16.0 ± 7.2	–7.60 to 2.33	0.35
Calf circumference(cm)	29.5 ± 4.1	33.5 ± 3.2	–7.65 to –0.42	*0.03	30.1 ± 3.1	35.3 ± 2.5	–8.12 to –2.42	**0.001
MoCA-J	18.2 ± 3.8	22.2 ± 4.8	–8.40 to 0.42	0.07	20.5 ± 4.3	21.5 ± 5.6	–6.17 to 4.08	0.66
Systolic BP(mmHg)	140.5 ± 10.4	136.5 ± 18.2	–9.95 to 18.03	0.55	143.9 ± 13.7	129.3 ± 14.2	0.40 to 28.92	*0.04
Diastolic BP(mmHg)	77.7 ± 6.8	77.3 ± 14.4	–9.89 to 10.61	0.94	77.2 ± 13.7	77.8 ± 10.1	–12.49 to 11.36	0.92
iADL	3.7 ± 3.1	2.0 ± 2.3	–1.05 to 4.38	0.28	2.7 ± 2.7	2.3 ± 2.7	–2.19 to 3.14	0.71
CRE□ mg/dl□	0.61 ± 0.22	0.92 ± 0.28	–0.57 to 0.06	*0.02	0.68 ± 0.23	1.03 ± 0.25	–0.59 to -0.11	**0.008
BUN□ mg/dl□	15.8 ± 4.8	19.7 ± 6.4	–9.67 to 1.75	0.16	15.6 ± 3.8	22.4 ± 6.6	–12.59 to –1.03	*0.025
CK□ U/L□	81.7 ± 24.6	124.4 ± 49.7	–77.50 to –7.33	*0.03	103.1 ± 54.2	121.3 ± 33.4	–59.69 to 23.62	0.39
AST （U/L□	20.8 ± 2.5	22.8 ± 4.8	–5.46 to 1.59	0.26	22.9 ± 4.7	21.1 ± 3.6	–2.20 to 5.77	0.36
ALT （U/L□	12.5 ± 4.5	14.6 ± 5.4	–7.27 to 3.04	0.39	13.8 ± 5.3	14.1 ± 5.3	–5.53 to 4.92	0.90
γGTP （U/L□	19.7 ± 5.9	32.3 ± 19.5	–25.21 to -0.07	*0.05	21.3 ± 5.4	38.0 ± 23.3	–36.32 to 2.87	0.08
HDL□ mg/dl□	77.0 ± 18.0	59.9 ± 17.4	–2.67 to 36.82	0.08	66.5 ± 18.9	63.8 ± 20.2	–16.82 to 22.23	0.77
LDL□ mg/dl□	113.5 ± 17.5	119.8 ± 28.9	–29.19 to 16.50	0.56	116.5 ± 21.6	119.6 ± 31.6	–31.36 to 25.21	0.82
Hba1c (%)	5.6 ± 0.4	5.9 ± 0.5	–0.72 to 0.12	0.15	5.7 ± 0.3	6.0 ± 0.6	–0.81 to 0.22	0.20
Alb□ g/dl□	3.9 ± 0.3	3.8 ± 0.2	–0.25 to 0.42	0.57	3.9 ± 0.3	3.8 ± 0.3	-0.18 to 0.34	0.53
Glu□ mg/dl□	96.7 ± 11.5	100.4 ± 17.6	–18.22 to 10.78	0.59	101.6 ± 18.5	95.9 ± 11.2	–8.70 to 20.22	0.41
TG□ mg/dl□	83.7 ± 53.9	134.4 ± 81.9	–118.38 to 16.94	0.13	118.9 ± 73.6	117.6 ± 85.8	–79.46 to 82.03	0.97
WBC□ 10^9/L□	4.4 ± 1.0	5.5 ± 1.6	–2.37 to 0.21	0.09	4.7 ± 1.2	5.7 ± 1.8	–2.61 to 0.62	0.20
RBC□ 10^{12}/L)	4.0 ± 0.2	4.2 ± 0.3	–0.43 to 0.15	0.31	4.2 ± 0.3	4.2 ± 0.4	–0.37 to 0.31	0.83
Hb□ g/dl□	12.7 ± 0.7	12.8 ± 0.8	–0.90 to 0.67	0.75	12.8 ± 0.7	12.7 ± 0.9	–0.68 to 0.99	0.70
HCT□ %□	39.3 ± 2.4	37.9 ± 2.9	–1.29 to 4.17	0.27	38.6 ± 2.6	38.0 ± 3.1	–2.27 to 3.48	0.66
Plt□ 10^9/L□	238.2 ± 24.9	206 ± 53.9	–5.99 to 70.32	0.09	217.5 ± 38.1	214.4 ± 62.9	–52.19 to 58.34	0.90

In addition to clinical features derived from sarcopenia diagnosis, 19 participants were statistically analyzed by SMI. Comparison between the sarcopenia and non-sarcopenia groups detected significant decreases in SMI (5.0 ± 1.0 vs 6.6 ± 1.2 kg/m^2, $p < 0.05$), Body Mass Index (BMI) (20.0 ± 2.3 U/L vs 23.3 ± 3.6 kg/m^2, $p < 0.05$), serum creatinine (0.61 ± 0.22 vs 0.92 ± 0.28 mg/dl, $p < 0.05$), serum creatine kinase (CK) (81.7 ± 24.6 vs 124.4 ± 49.7 U/L, $p < 0.05$) and serum γGTP (19.7 ± 5.9 vs 32.3 ± 19.5 U/L, $p < 0.05$) in sarcopenia. A comparison between decreased and normal SMI groups detected significant decreases in SMI (5.2 ± 0.9 vs 7.4 ± 0.8 kg/m^2, $p < 0.01$, BMI (20.7 ± 2.2 vs 24.4 ± 4.0 kg/m^2, $p < 0.05$), serum creatinine (0.68 ± 0.23 vs 1.03 ± 0.25 mg/dl, $p < 0.01$) and serum BUN (15.6 ± 3.8 vs 22.4 ± 6.6 mg/dl, $p < 0.05$) and a significant increase in systolic blood pressure (143.9 ± 13.7 vs 129.3 ± 14.2 mmHG, $p < 0.05$). Asterisks indicate significant differences ($^*p < 0.05$). Asterisks indicate significant differences ($^{**}p < 0.01$). Abbreviation: SMI: skeletal muscle mass index; MoCA-J: Japanese version of Montreal Cognitive Assessment; TUG: Timed up and go test; BMI: Body mass index; BP: Blood pressure; CRE: creatinine; BUN, Blood urea nitrogen; CK: creatine kinase; HCT: hematocrit; CI: Confidence Interval.

Supplementary Table 2. List of 22 metabolites involved in sarcopenia.

Parameters	Peak area (10^6 AU)		*T* test	
	Sarcopenia	Non-sarcopenia	95% CI of the dif.	*p*-value
	(*N* = 6)	(*N* = 13)		
Acetyl-carnitine	337.73 ± 76.94	433.23 ± 99.79	–186.23 to – 4.77	*0.040
Dimethyl-proline	186.23± 91.05	313.38 ± 102.26	–230.09 to –24.20	*0.020
Phenylalanine	225.19 ± 55.70	287.35 ± 40.46	–121.27 to –3.07	*0.042
Dimethyl-arginine	38.92± 4.67	50.22 ± 13.03	–19.94 to –2.66	*0.013
N1-Methyl-histidine	21.75 ± 8.25	37.39 ± 12.08	–25.82 to –5.44	**0.005
Isovaleryl-carnitine	14.24 ± 3.85	20.57 ± 7.7	–11.95 to –0.71	*0.033
Aspartate (↑)	22.91 ± 5.65	13.64 ± 7.84	2.44 to 16.09	*0.011
myo-Inositol	13.95 ± 1.58	20.30 ± 7.43	–10.98 to –1.72	*0.011
Creatinine	15.60 ± 4.82	21.48 ± 6.64	–11.70 to –0.08	*0.047
Pantothenate	10.14 ± 3.09	17.20 ± 8.03	–12.47 to –1.65	*0.013
Hypoxanthine	4.11 ± 1.36	7.58± 4.95	–6.62 to –0.31	*0.033
Dimethyl-guanosine	2.50 ± 0.74	3.95 ± 0.81	–2.29 to –0.62	**0.003
N1-Methyl-adenosine	2.36 ±1.07	3.64 ± 1.08	–2.47 to –0.10	*0.036
2-Oxoglutarate	2.01 ± 0.49	3.01 ±1.1	–1.76 to –0.23	*0.018
Pentose-phosphate	2.13 ±0.24	2.71 ± 0.75	–1.07 to –0.09	*0.022
Succinate	1.33 ± 0.18	1.74 ± 0.45	–0.71 to –0.10	*0.012
N-Acetyl-glutamate	0.42 ± 0.14	0.58 ± 0.12	–0.31 to –0.01	*0.037
Quinolinic acid	0.26 ± 0.14	0.50 ± 0.24	–0.43 to –0.06	*0.013
4-Guanidinobutanoate	0.16 ± 0.06	0.55 ± 0.60	–0.76 to –0.03	*0.035
N1-Methyl-guanosine	0.21 ±0.09	0.32 ± 0.10	–0.21 to –0.01	*0.038
Trimethyl-tyrosine	0.05 ± 0.04	0.17 ± 0.17	–0.23 to –0.02	*0.027
cis-Aconitate	0.05 ± 0.02	0.12 ± 0.05	–0.10 to –0.04	**0.000

Metabolite peak area. High > 10^8 AU. Medium 10^7–10^8 AU. Low < 10^7 AU. 21 sarcopenia markers (acetyl-carnitine, dimethyl-proline, phenylalanine, dimethyl-arginine, N1-methyl-histidine, isovaleryl-carnitine, myo-inositol, creatinine, pantothenate, hypoxanthine, dimethyl-guanosine, N1-methyl-adenosine, 2-oxoglutarate, pentose-phosphate, succinate, N-acetyl-glutamate, quinolinic acid, 4-guanidinobutanoate, N1-methyl-guanosine, trimethyl-tyrosine, and cis-aconitate) decreased significantly. However, aspartate increased significantly in sarcopenia. Abbreviations: SMI: skeletal muscle index; CI: Confidence Interval. (↑) indicates upregulated metabolite in sarcopenia. Asterisks indicate significant differences ($^*p < 0.05$). Asterisks indicate significant differences ($^{**}p < 0.01$).

Supplementary Table 3. List of ten metabolites involved in muscle mass.

	Peak area (10^6 AU)		*T* test	
	Decreased SMI ($N = 11$)	Normal SMI ($N = 8$)	95% CI of the dif.	*p*-value
Urate	95.24 ± 21.23	114.54 ± 1.64	–38.18 to –0.41	*0.046
Butyro-betaine	88.02 ± 19.93	108.91± 19.46	–40.32 to –1.47	*0.037
Dimethyl-arginine	40.23 ±11.17	55.48 ± 7.04	–24.09 to –6.40	**0.002
N1-Methyl-histidine	24.73 ± 9.48	43.07 ± 9.55	–27.77 to –8.93	**0.001
Isovaleryl-carnitine	14.47 ±3.12	24.21 ± 7.76	–16.34 to –3.14	**0.009
Creatinine	16.89 ± 6.31	23.38 ± 5.27	–12.12 to –0.86	*0.026
Hippurate	12.92 ± 8.00	26.70 ± 13.19	–25.37 to –2.19	*0.020
Dimethyl-guanosine	2.98 ± 0.92	4.20 ± 0.74	–2.03 to –0.41	**0.005
2-Oxoglutarate	2.15 ± 0.53	3.45 ± 1.14	–2.27 to –0.32	*0.014
cis-Aconitate	0.07 ± 0.04	0.14 ± 0.05	–0.11 to –0.27	**0.004

Metabolite peak area. High > 10^8 AU, Medium 10^7–10^8 AU, Low < 10^7 AU. 10 metabolites (urate, butyro-betaine, dimethyl-arginine, N1-methyl-histidine, isovaleryl-carnitine, creatinine, hippurate, dimethyl-guanosine, 2-oxoglutarate, cis-aconitate) decreased significantly in sarcopenia. Abbreviations: SMI: skeletal muscle index; CI: Confidence Interval. Asterisks indicate significant differences (*$p < 0.05$). Asterisks indicate significant differences (**$p < 0.01$).

Supplementary Table 4. Correlation analysis between 25 sarcopenia-related markers and SMI or EFS.

Parameters	SMI			EFS		
	R	95% CI	*p* value	R	95% CI	*p* value
Isovaleryl-carnitine	0.70	0.37 to 0.88	**0.001	–0.55	–0.80 to -0.12	*0.015
Urate	0.58	0.18 to 0.82	**0.008	–0.54	0.10 to 0.79	*0.02
Hippurate	0.60	0.21 to 0.83	**0.006	–0.46	–0.76 to -0.01	*0.05
Phenylalanine	0.40	–0.07 to 0.72	0.09	–0.45	–0.75 to 0.00	0.05
Butyro-betaine	0.5	0.06 to 0.78	*0.029	–0.44	–0.75 to 0.01	0.05
Acetyl-carnitine	0.55	0.12 to 0.80	*0.02	–0.43	–0.74 to 0.03	0.06
N1-Methyl-guanosine	0.65	0.27 to 0.85	**0.003	–0.39	–0.71 to 0.08	0.10
Pantothenate	0.62	0.23 to 0.84	**0.005	–0.36	–0.70 to 0.11	0.13
N1-Methyl-histidine	0.58	0.17 to 0.82	**0.009	–0.3	–0.66 to 0.18	0.22
Hypoxanthine	0.52	0.09 to 0.79	*0.02	–0.29	–0.65 to 0.18	0.22
Dimethyl-guanosine	0.62	0.23 to 0.84	**0.005	–0.28	–0.65 to 0.20	0.25
Dimethyl-arginine	0.55	0.12 to 0.80	*0.02	–0.27	–0.64 to 0.20	0.26
Creatinine	0.69	0.35 to 0.87	**0.001	–0.25	–0.63 to 0.23	0.31
Dimethyl-proline	0.24	–0.24 to 0.63	0.32	–0.25	–0.63 to 0.23	0.31
N-Acetyl-glutamate	0.41	–0.05 to 0.73	0.08	–0.21	–0.60 to 0.26	0.38
Quinolinic acid	0.36	–0.11 to 0.70	0.13	–0.19	–0.59 to 0.28	0.44
2-Oxoglutarate	0.65	0.27 to 0.85	**0.003	–0.17	–0.58 to 0.31	0.49
Trimethyl-tyrosine	0.28	–0.20 to 0.65	0.24	–0.17	–0.58 to 0.30	0.47
Aspartate [(1)]	-0.45	–0.75 to –0.001	0.05	–0.17	–0.30 to 0.58	0.48
cis-Aconitate	0.57	0.16 to 0.82	*0.01	–0.16	–0.57 to 0.32	0.52
Succinate	0.59	0.19 to 0.82	**0.008	–0.12	–0.54 to 0.36	0.63
Pentose-phosphate	0.31	–0.17 to 0.67	0.20	–0.11	–0.53 to 0.36	0.65
4-Guanidinobutanoate	0.20	–0.27 to 0.60	0.41	–0.1	–0.53 to 0.37	0.68
N1-Methyl-adenosine	0.37	–0.10 to 0.71	0.12	–0.07	–0.52 to 0.40	0.76
myo-Inositol	0.52	0.09 to 0.79	*0.02	–0.04	–0.48 to 0.42	0.88

Metabolite peak area. High > 10^8 AU. Medium 10^7–10^8 AU. Low < 10^7 AU. Metabolites are ordered according to its correlation coefficient to EFS. Abbreviations: SMI: skeletal muscle index; Pearson: Pearson's correlation coefficient between a metabolite and SMI; CI: Confidence Interval; EFS: Edmonton frail scale. Asterisks indicate correlation (*$p < 0.05$). Asterisks indicate correlation (**$p < 0.01$).

Supplementary Table 5. Correlation analysis between 22 frailty-related markers and SMI or EFS.

	SMI			EFS		
	R	**95% CI**	***p* value**	**R**	**95% CI**	***p* value**
Isovaleryl-carnitine	0.70	0.37 to 0.88	**0.001	–0.54	–0.80 to –0.12	*0.015
Acetyl-carnosine	0.69	0.35 to 0.87	**0.001	–0.51	0.07 to 0.78	*0.03
Hippurate	0.60	0.21 to 0.83	**0.006	–0.46	0.01 to 0.76	*0.05
Urate	0.58	0.18 to 0.82	**0.009	–0.54	0.11 to 0.80	*0.02
1,5-anhydroglucitol	0.52	0.08 to 0.79	*0.02	–0.56	0.14 to 0.80	*0.01
Proline	0.49	0.05 to 0.77	*0.03	–0.54	0.11 to 0.80	*0.02
Methionine	0.46	0.01 to 0.76	*0.046	–0.56	0.14 to 0.80	*0.01
Leucine	0.46	0.01 to 0.75	*0.046	–0.46	0.01 to 0.75	*0.04
N3-methyl-histidine	0.45	–0.01 to 0.74	0.05	–0.19	–0.59 to 0.29	0.43
Trimethyl-histidine	0.44	–0.01 to 0.75	0.057	–0.39	–0.08 to 0.71	0.10
Isoleucine	0.42	–0.04 to 0.74	0.07	–0.45	0.14 to 0.80	*0.04
Tryptophan	0.37	–0.09 to 0.71	0.12	–0.57	0.15 to 0.82	*0.01
Arginine	0.36	–0.11 to 0.70	0.13	–0.32	–0.15 to 0.67	0.17
Ergothioneine	0.33	–0.14 to 0.69	0.16	–0.45	0.01 to 0.75	0.05
Adenine	0.23	–0.25 to 0.62	0.34	–0.45	–0.001 to 0.75	0.05
S-methyl-ergothioneine	0.22	–0.26 to 0.61	0.37	–0.51	0.07 to 0.78	*0.02
Ophthalmic acid	0.14	–0.34 to 0.56	0.56	–0.41	–0.06 to 0.73	0.08
2-ketobutyrate	0.14	–0.33 to 0.56	0.56	–0.29	–0.19 to 0.66	0.24
UDP-glucose (↑)	0.04	–0.41 to 0.49	0.86	–0.12	–0.55 to 0.34	0.60
Creatine (↑)	–0.08	–0.51 to 0.38	0.73	0.44	–0.74 to 0.02	0.06
N-acetyl-aspartate (↑)	–0.09	–0.52 to 0.38	0.71	0.16	–0.32 to 0.57	0.51
UDP-glucuronate (↑)	–0.15	–0.56 to 0.32	0.54	0.47	–0.76 to -0.02	*0.04

Metabolite peak area. High > 10^8 AU. Medium 10^7–10^8 AU. Low < 10^7 AU. Metabolites are ordered according to its correlation coefficient to SMI. Abbreviations: SMI: skeletal muscle index; Pearson: Pearson's correlation coefficient between a metabolite and SMI; CI: Confidence Interval. Asterisks indicate correlation ($^{*}p < 0.05$). Asterisks indicate correlation ($^{**}p < 0.01$).