Increased Carbohydrate Antigen 19-9 (CA 19-9) Level Is Highly Associated with Low Skeletal Muscle Mass in Healthy Adults: A Population-Based Study

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Introduction

➢ **Carbohydrate antigen 19-9 (CA 19-9)** is commonly used serum tumor marker for pancreatic cancer diagnosis.

➢ However, several studies have reported its relationship with **benign, inflammatory conditions** such as systemic lupus erythematosus, rheumatoid arthritis ± and inflammatory diseases.

➢ Low muscle mass status including sarcopenia presents as subclinical inflammatory diseases

➡ We investigated the **relationship between high CA 19-9 levels and low skeletal muscle mass (LMM)** in healthy adults in a population-based study.

Method

➢ Participants who performed the evaluation of bioelectrical impedance analysis and CA-19-9 were included.

➢ **Skeletal muscle mass index (SMI)** was calculated based on **appendicular muscle mass (kg)/height (m)².**

➢ Participants with SMIs greater than -1 SD of the **sex-specific mean of young adults (age:18–39 years, n=139,255)** were categorized as **"normal"**, and within -1 to -2 SD (-2< SD ≤-1) and below -2 SD (SD ≤-2) were categorized as **"mild LMM"** and **"severe LMM"**, respectively.

•   In this study population, sex-specific cut-off values for mild and severe LMM were 6.78 kg/m² and 7.44 kg/m² in men, and 5.48 kg/m² and 4.86 kg/m² in women, respectively.

➢ Multivariable logistic regression analyses were conducted to assess the association of high CA 19-9 levels with mild LMM and severe LMM compared to normal muscle mass. (A high CA 19-9 level was defined as **≥30 U/mL**)

•   Confounding factors were age, sex, screening center, smoking status and drinking status, frequency of physical activity, SBP and serum glucose, TG, ALT, creatinine and CRP levels.

Results

Figure 1. Selection of study population

Table 1. Baseline characteristics of study subjects classified by skeletal muscle mass.

	Total	Normal	Mild LMM	Severe LMM	* p value
Number of subjects (n)	263,061	226,759	32,532	3,770	
Age (years)	41.0 ± 9.5	41.0 ± 9.0	41.1 ± 10.8	44.2 ± 13.5	<0.001 †,‡
Sex, Men (%)	50.8	49.6	56.9	73.5	<0.001
Secreenig center, Seoul (%)	48.3	48.3	48.5	47.4	0.456
Height (cm)	167.3 ± 8.6	167.6 ± 8.6	165.2 ± 8.1	164.3 ± 7.8	<0.001 †,‡,#
BMI (kg/m²)	23.5 ± 3.5	24.0 ± 3.4	20.7 ± 2.2	19.4 ± 2.2	<0.001 †,‡,#
Appendicular skeletal muscle mass (kg)	20.2 ± 5.0	20.7 ± 4.9	17.6 ± 4.1	16.5 ± 3.4	<0.001 †,‡,#
SMI (kg/m²)	7.1 ± 1.1	7.3 ± 1.1	6.4 ± 1.0	6.0 ± 0.8	<0.001 †,‡,#
Current smoker (%)	14.8	14.5	15.8	21.8	<0.001
Heavy drinking (%)	15.8	15.9	15.0	18.1	<0.001
SBP (mmHg)	109.6 ± 12.7	110.1 ± 12.7	106.5 ± 12.0	107.6 ± 13.1	<0.001 †,‡,#
DBP (mmHg)	70.4 ± 9.7	70.5 ± 9.8	69.2 ± 9.3	70.2 ± 9.4	<0.001 †,#
Hypertension (%)	8.5	8.6	7.6	10.5	<0.001
Diabetes mellitus (%)	2.4	2.4	2.7	5.1	<0.001
Insulin (IU/L)	7.1 ± 4.8	7.3 ± 4.9	5.7 ± 3.3	5.1 ± 3.1	<0.001 †,‡,#
Glucose (mg/dL)	96.7 ± 15.2	96.9 ± 15.1	95.4 ± 15.5	96.9 ± 20.0	<0.001 †,‡,#
Triglycerides (mg/dL)	112.9 ± 78.6	114.7 ± 80.6	101.4 ± 63.0	102.4 ± 65.1	<0.001 †,‡
Total cholesterol (mg/dL)	190.4 ± 33.9	190.4 ± 33.9	190.4 ± 33.9	190.6 ± 35.6	0.931
LDL-C (mg/dL)	125.6 ± 33.1	125.8 ± 33.0	124.3 ± 33.2	123.8 ± 34.4	<0.001 †,‡
HDL-C (mg/dL)	60.8 ± 16.2	60.3 ± 16.1	63.9 ± 16.3	64.1 ± 17.1	<0.001 †,‡
AST (IU/L)	22.2 ± 14.7	22.2 ± 14.8	21.6 ± 13.1	23.6 ± 21.1	<0.001 †,‡
ALT (IU/L)	23.6 ± 19.9	23.7 ± 20.3	20.9 ± 16.8	21.8 ± 18.3	<0.001 †,‡,#
Creatinine (mg/dL)	0.82 ± 0.22	0.82 ± 0.22	0.81 ± 0.19	0.83 ± 0.24	<0.001 †,‡,#
CRP (mg/dL)	0.11 ± 0.30	0.12 ± 0.29	0.10 ± 0.32	0.13 ± 0.43	<0.001 †,‡,#

Data are presented as mean ± SD, median (IQR), or percentage. * p values for between-group difference by one-way ANOVA in continuous variables or by χ2 test in categorical variables. Group comparisons by Bonferroni post hoc analysis were conducted after one-way ANOVA. †: Bonferroni post hoc p < 0.05 for group comparison of normal vs. mild LMM. ‡: Bonferroni post hoc p < 0.05 for group comparison of normal vs. severe LMM. #: Bonferroni post hoc p < 0.05 for group comparison of mild LMM vs. severe LMM.

Table 2. Proportion of high CA 19-9 level for subjects classified by skeletal muscle mass (n = 263,061).

	Normal	Mild LMM	Severe LMM	p for trend
Classification according to CA 19-9 level				<0.0001
High CA 19-9 level (≥30 U/mL) (%)	1.4	1.9	2.3	
Normal CA 19-9 level (<30 U/mL) (%)	98.6	98.1	97.7	

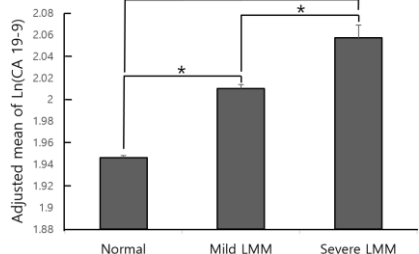CA 19-9: carbohydrate antigen 19-9; LMM: low muscle mass.

Figure 2. Comparison of adjusted mean of ln(CA 19-9) between normal, mild LMM, and severe LMM group. Adjusted means (±SE) of natural-log-transformed CA 19-9 levels in the groups were estimated from ANCOVA after adjustments for age, sex, SBP, glucose, triglyceride, ALT, creatinine and CRP. *: Group difference by Bonferroni post hoc p ≤ 0.001.

Table 3. Multivariate regression analyses showing association of increased CA 19-9 with LMM

	Mild LMM, OR (95% CI)	Severe LMM, OR (95% CI)
Model 1		
Normal (<30 U/mL)	1 (reference)	1 (reference)
High CA 19-9 level (≥30 U/mL)	1.531 (1.403-1.672)	2.280 (1.835-2.835)
Model 2		
Normal (<30 U/mL)	1 (reference)	1 (reference)
High CA 19-9 level (≥30 U/mL)	1.522 (1.394-1.662)	2.248 (1.807-2.795)
Model 3		
Normal (<30 U/mL)	1 (reference)	1 (reference)
High CA 19-9 level (≥30 U/mL)	1.668 (1.525-1.824)	2.638 (2.115-3.290)

ORs were calculated as the risks of having mild, low or severely low skeletal muscle mass according to the presence of high CA 19-9 level. Model 1: adjusted for age, sex, screening center. Model 2: adjusted for age, sex, screening center, smoking status, heavy drinker and frequency of physical activity. Model 3: adjusted for age, sex, screening center, smoking status, heavy drinker, frequency of physical activity, SBP, glucose, triglyceride, ALT, creatinine and CRP.

Table 4. Subgroup analyses for age and sex for associations of increased CA 19-9 with LMM

	Mild LMM, OR (95% CI)	Severe LMM, OR (95% CI)	p for interaction
Age			0.839
<40 (n=134,353)	1.429 (1.265-1.615)	2.048 (1.456-2.879)	
40~59 (n=117,388)	1.756 (1.508-2.044)	2.414 (1.591-3.662)	
≥60 (n=11,320)	1.410 (1.062-1.872)	2.005 (1.286-3.126)	
Sex			0.002
Men (n=133,685)	1.959 (1.607-2.390)	3.475 (2.491-4.847)	
Women (n=129,376)	1.571 (1.419-1.738)	2.092 (1.545-2.832)	

Adjusted ORs were calculated as the risks of having mild and severe low skeletal muscle mass (LMM) according to the presence of high CA 19-9 level in each subgroup after adjustments for age, sex, screening center, smoking status, heavy drinker, frequency of physical activity, SBP, glucose, triglyceride,

Conclusion

➢**Elevated CA 19-9 levels were independently associated with a higher prevalence of LMM** in apparently healthy adults without cancer.

➢Therefore, **increased CA 19-9** could be used as a novel biomarker for detecting **sarcopenia status.**