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Associations between physical fitness, insulin resistance, and estimated glomerular filtration rate in individuals with spinal cord injury

Minjun Kim
Changwon National University
Chan Mi Jang
Changwon National University
Joonwoong Kim
Seowon University
Inhwan Lee
ansh00@changwon.ac.kr

Changwon National University

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Abstract

Purpose of in this study, to investigate the associations between physical fitness, insulin resistance, and estimated glomerular filtration rate (eGFR) in individuals with spinal cord injury (SCI). This cross-sectional study included 112 individuals with SCI (aged ≥ 30 years) who were receiving care at the disability welfare facilities in G and C Provinces. Physical fitness was assessed based on muscle strength, muscular endurance, flexibility, and cardiorespiratory fitness. Insulin resistance was determined using triglyceride-glucose index-body mass index, and eGFR was calculated using modification of diet in renal disease-spinal cord injury/disability. Odd ratios (ORs) and 95% confidence interval (CI) for exposure to insulin resistance and kidney dysfunction were calculated according to physical fitness. After adjusting for covariates, the low fitness groups showed a higher risk of insulin resistance (OR=5.61, 95% CI=1.01-31.04, p=0.048) and kidney function impairment (OR=6.22, 95% CI=1.01-38.21, p=0.048), compared to the high fitness group (reference, OR=1.00). In mediation analysis, after adjusting for covariates, physical fitness partially mediated the association between insulin resistance and eGFR (β=-0.042), explaining 19.9% of the total effect. Physical fitness may play a protective role against chronic kidney disease associated with high insulin resistance in individuals with SCI.

Introduction

Chronic kidney disease (CKD) is a progressive condition characterized by structural kidney fibrosis and decline in kidney function. CKD is typically diagnosed and monitored by evaluating indicators of kidney filtration function, such as estimated glomerular filtration rate (eGFR) and protein and albumin levels in urine [1–3]. CKD progresses silently in its early stages, with no noticeable symptoms observed until significant kidney function decline occurs. Symptoms such as uremia, anemia, electrolyte imbalances, and bone disorders begin to manifest in the middle stages of CKD [3–5]. If left untreated, CKD can lead to fatal outcomes [4, 6, 7]. Approximately 10% of the global adult population is affected by CKD [8], and an estimated 5–10 million people die annually due to CKD-related causes [9, 10].

For individuals with spinal cord injury (SCI), autonomic nervous system dysfunction caused by neurological damage weakens their immune responses, making them more vulnerable to chronic infections [11]. Additionally, bladder dysfunction increases their risk of recurrent urinary tract infections and kidney stones [12, 13], while a lack of physical activity led to increased insulin resistance, making them more susceptible to hypertension and diabetes [14–16]. As these are major risk factors for CKD [17–19], individuals with SCI may have a higher risk of developing CKD than those without disabilities. Notably, comprehensive studies on the prevalence of CKD in individuals with SCI are lacking. A study on U.S. veterans diagnosed with SCI indicated that more than one-third of the participants had CKD [20]. Additionally, several epidemiological studies have identified CKD as a major cause of mortality in individuals with SCI [21–23]. Despite these findings, considerably limitations exist in systematically understanding the risk of CKD in individuals with SCI and developing effective management strategies based on this understanding.

Insulin resistance, a pathological condition in which target tissues fail to respond normally to insulin, has been identified as a pathogenic factor for CKD [24, 25]. Although the molecular mechanisms underlying the association between insulin resistance and CKD have not been fully elucidated, hyperinsulinemia caused by

increased insulin resistance is reported to excessively activate the sympathetic nervous system and promote renal sodium reabsorption, leading to glomerular hyperfiltration and proteinuria, thereby contributing to kidney damage [24]. Additionally, insulin resistance induces changes in renal cell metabolism and electrolyte balance, which are established causes of kidney damage, while promoting kidney hypertrophy and hyaluronan deposition within the renal interstitium, acting as a major pathological mechanism driving kidney fibrosis and inflammation [24, 26].

Several epidemiological studies have indicated that a high level of physical fitness is an independent protective factor against the development of CKD [27–31]. Although the physiological mechanisms underlying the correlation between physical fitness and CKD remain unclear, regular physical activity is suggested to improve insulin resistance, thereby slowing the progression of CKD. Thus, increased physical fitness in individuals with SCI may mitigate insulin resistance and inhibit the key pathological mechanisms of CKD [32, 33]. Hence, analyzing whether physical fitness mediates the relationship between insulin resistance and CKD is critical for understanding its preventive role against CKD. This study aimed to examine the associations between physical fitness, insulin resistance, and CKD in individuals with SCI.

Results

Demographic characteristics of the participants

A total of 120 individuals with SCI who use manual wheelchairs were initially included in this study. Of these, eight participants were excluded from the analysis, including six who could not undergo physical fitness assessments, one who took hypoglycemic agents on the day of testing, and one with missing blood biomarker data. Therefore, 112 participants were included in the data analysis (Figure 1).

Comparison of variables according to sex

Comparison of variables according to sex showed that male had significantly higher height (*p<0.001*), weight (*p<0.001*), waist circumference (WC) (*p=0.027*), smoking (*p=0.028*), creatinine (*p<0.001*), muscular strength (*p<0.001*), muscular endurance (*p=0.023*), and cardiorespiratory fitness (CRF) (*p<0.001*) than female (Table 1). In contrast, women had a significantly higher body fat than male (*p<0.001*).

Comparison of variables according to TyG-BMI and MDRD-SCI/D levels

Comparison of variables according to triglyceride-glucose index-body mass index (TyG-BMI) levels is shown in Table 2. The results indicated that the group classified as normal exhibited significantly higher modification of diet in renal disease-spinal cord injury/disability (MDRD-SCI/D) (*p=0.017*), muscular strength (*p=0.004*), flexibility (*p=0.004*), and total physical fitness z-score (*p=0.005*) than the abnormal group. Conversely, the normal group showed significantly lower weight (*p<0.001*), body mass index (BMI) (*p<0.001*), body fat (*p<0.001*), WC (*p<0.001*), dyslipidemia (*p=0.011*), triglyceride (TG) (*p<0.001*), and creatinine (*p=0.035*) than the abnormal group. Comparison according to MDRD-SCI/D levels showed that the group classified as normal exhibited significantly higher muscular strength (*p=0.043*), CRF (*p=0.028*), and total physical fitness Z-score (*p=0.011*) than the abnormal group. Conversely, the normal group showed significantly lower TyG-BMI

(*p=0.047*), cervical injury (*p=0.011*), weight (*p=0.003*), BMI (*p=0.028*), and creatinine (*p<0.001*) than the abnormal group.

Analysis of trends in variables according to physical fitness levels

Results of the analysis of trends in variables according to physical fitness levels are shown in Table 3. The analysis showed that MDRD-SCI/D (*p=0.027*) and hypertension (*p=0.042*) tended to increase as physical fitness levels improved. Conversely, weight (*p=0.012*), BMI (*p=0.004*), body fat (*p=0.033*), WC (*p=0.015*), TyG-BMI (*p=0.006*), creatinine (*p=0.018*), and cervical injuries (*p=0.018*) tended to decrease as physical fitness levels increased.

Analysis of exposure to abnormal TyG-BMI and MDRD-SCI/D according to physical fitness levels

The odd ratios (ORs) for exposure to abnormal TyG-BMI and MDRD-SCI/D categorized according to physical fitness levels are presented in Table 4. Analysis of TyG-BMI indicated that in Models 1 and 2, the moderate fitness group (Model 1, OR=4.21, 95% confidence interval (CI)=1.12-15.76, *p=0.033*; Model 2, OR=4.16, 95% CI=1.10-15.60, *p=0.035*) and the low fitness group (Model 1, OR=6.09, 95% CI=1.44-25.66, *p=0.014*; Model 2, OR=5.74, 95% CI=1.32-24.99, *p=0.020*) showed significantly higher OR for exposure to high insulin resistance than the high fitness group (reference, OR=1.00). However, in Model 3, only the low fitness group (OR=5.61, 95% CI=1.01-31.04, *p=0.048*) had significantly higher OR for exposure to high insulin resistance than the high fitness group. For MDRD-SCI/D, the low fitness group (Model 1, OR=4.88, 95% CI=1.11-21.40, *p=0.035*; Model 2, OR=4.81, 95% CI=1.01-22.87, *p=0.048*; Model 3, OR=6.22, 95% CI=1.01-38.21, *p=0.048*) consistently showed significantly higher OR for exposure to kidney dysfunction than the high fitness group across all models.

Analysis of the mediation effect of physical fitness on the relationship between TyG-BMI and MDRD-SCI/D

The relationship between TyG-BMI and MDRD-SCI/D as mediated by physical fitness is shown in Table 5 and shown in Figure 2. The analysis conducted to verify the mediating effect of physical fitness on the relationship between TyG-BMI and MDRD-SCI/D revealed that TyG-BMI had a direct negative effect on MDRD-SCI/D (β=-0.169, *p=0.015*, c' path) and an indirect effect through its influence on physical fitness. Furthermore, TyG-BMI was positively associated with physical fitness (β=2.121, *p=0.022*, b path), which, in turn, was negatively associated with MDRD-SCI/D (β=-0.020, *p=0.009*, a path). Bootstrapping analysis of the mediation effect of physical fitness on the relationship between TyG-BMI and MDRD-SCI/D showed that the 95% CI (-0.108 to -0.002, ab path) did not include zero, indicating that physical fitness mediates the relationship between TyG-BMI and MDRD-SCI/D. Additionally, the results showed that 19.9% of the total effect of TyG-BMI on MDRD-SCI/D is explained through physical fitness.

Discussion

In this study, we analyzed the associations between physical fitness, insulin resistance, and eGFR in 112 individuals with SCI. The results showed that lower physical fitness levels were significantly associated with higher odds of high insulin resistance and kidney function impairment. Additionally, the results confirmed that physical fitness partially mediated the relationship between insulin resistance and eGFR.

Regular physical activity enhances the translocation and expression of the glucose transporter type 4 to the cell membrane, increasing glucose uptake by skeletal muscles and improving insulin sensitivity through insulin-independent pathways, thereby contributing to the alleviation of insulin resistance [34]. Based on this, physical fitness, which is a quantitative indicator of physical function and is influenced by physical activity, is considered a predictor of insulin resistance [35–37]. A recent study conducted in Australia revealed that CRF is an independent predictor of insulin resistance in adults, regardless of obesity or type 2 diabetes status [38]. Additionally, numerous epidemiological studies have identified grip strength, as an independent factor negatively associated with insulin resistance in adolescents, adults, and patients with type 2 diabetes [39–41]. Similarly, in the present study, analysis of the association between fitness levels and insulin resistance in individuals with SCI revealed that the group in the low fitness group had a significantly higher risk of exposure to high insulin resistance than the group in the high fitness group. Considering the results of the present study and the findings of previous research, physical fitness is strongly associated with insulin resistance, regardless of the presence of disability. Additionally, the findings of the present study suggest that the overall physical fitness index of individuals with SCI can be useful for predicting insulin resistance.

Several epidemiological studies have indicated that physical fitness plays a protective role against the development of CKD in the general population [30, 42]. A recent study conducted using data from the Kuopio Ischemic Heart Disease study, which was a Finnish study that followed adult men for an average of 25.8 years, showed that high cardiorespiratory fitness is independently associated with a reduced risk of developing CKD and offset the increased risk of CKD due to lower socioeconomic status [43]. Additionally, a study conducted using data from the Korea National Health and Nutrition Examination Survey, to examine the association between grip strength and CKD in adults, confirmed that lower grip strength is significantly and independently associated with an increased prevalence of CKD [30]. Considering the results of these previous studies, we analyzed the association between physical fitness and CKD in individuals with SCI. The results showed that the group with lower physical fitness levels had a significantly higher risk of exposure to CKD than the group with higher fitness levels, which is consistent with those of previous research. To the best of our knowledge, this is the first study to demonstrate the association between physical fitness and CKD in individuals with SCI, suggesting that improving physical fitness could be an effective strategy for preventing CKD in this population.

Considering that insulin resistance is a major cause of CKD [24, 25], and that physical fitness is negatively associated with insulin resistance [35-41]. physical fitness potentially mediates the relationship between insulin resistance and CKD. However, no previous study has investigated the role of physical fitness in the relationship between insulin resistance and CKD. Therefore, we conducted an analysis of the mediation effect of physical fitness on the relationship between insulin resistance and eGFR in individuals with SCI, who are particularly susceptible to CKD. Given the strong bidirectional relationship between metabolic syndrome and CKD [43], and the fact that both conditions share common risk factors, such as insulin resistance and hypertension [44,45], it is unsurprising that the findings of the present study align with those of Heiston et al. who found that regular exercise reduces the severity of metabolic syndrome by improving insulin resistance [46], and with those of Kim et al., who identified cardiorespiratory fitness as a modulating factor in the relationship between insulin resistance and metabolic syndrome [47]. The findings of the present study extend the existing knowledge regarding these associations to the population of individuals with SCI and

presents the first evidence of the effect of physical fitness on the relationship between insulin resistance and eGFR.

The primary limitation of this study was its cross-sectional design, which did not allow for inference of causal relationships. In addition, the insulin resistance and CKD markers used in this study were based on hematological surrogate indicators, which may have limited diagnostic accuracy. Furthermore, the possibility that some uninvestigated confounding variables may have influenced the study results cannot be completely excluded.

Considering these limitations, the results of this study should be interpreted with caution. Future longitudinal studies with larger sample sizes conducted using more comprehensive diagnostic methods are needed to validate the findings of this study. Nevertheless, to the best of our knowledge, this study is the first to demonstrate the mediation effect of physical fitness on the relationship between insulin resistance and CKD in individuals with SCI.

In conclusions, this study demonstrated that high physical fitness levels are independently associated with insulin resistance and eGFR in individuals with SCI. In addition, the results of this study showed that the relationship between insulin resistance and eGFR is partially mediated by physical fitness. This study provides important evidence that could facilitate the development of strategies targeted at improving physical fitness for the prevention of CKD in individuals with SCI.

Methods

Study participants

This was a cross-sectional study conducted from September 2022 to September 2024. The participants were adults aged ≥ 30 years with SCI who use manual wheelchairs and utilize sports and welfare facilities designed for individuals with disabilities. Only those who voluntarily consented to participate and provided written informed consent to participate were included in the study. This study was approved by the Institutional Review Board of Changwon National University (approval no.: 7001066-202401-HR-009).

Body composition and anthropometrics measurements

Body composition was assessed by measuring body fat percentage (S10, Inbody, Seoul, Republic of Korea). The anthropometric indices measured included height, weight, BMI, and WC. Height was measured using an anthropometric tape while the participant lay on a bed. Weight was measured using a wheelchair scale (AD-6105NP, AND, Bucheon, Republic of Korea). To determine the participant's body weight, the weight of the wheelchair was subtracted from the total weight measured. BMI was calculated using the following formula: weight (kg)/height (m^2). WC was measured using an anthropometric tape wrapped around the participant at the midpoint between the lowest rib and the iliac crest.

Blood analysis and calculation of TyG-BMI and MDRD-SCI/D

A 70 μL blood sample was collected from the tip of the left index finger after a minimum 12-h fasting period. The collected blood sample was placed in a cartridge and analyzed using a dry chemistry analyzer (Labgeo

PT10, Samsung Electronics, Seoul, Republic of Korea). The blood analysis device used in this study is capable of immediate analysis without preprocessing whole blood. The high precision and accuracy of the device and its strong correlations with various blood markers, including serum creatinine level, have been validated previously [48].

TyG-BMI, a surrogate marker considered the most reliable indicator of insulin resistance in Koreans, was calculated based on the participants' TG and fasting blood glucose (FBG) levels [49]. Additionally, MDRD-SCI/D, an eGFR formula used for the evaluation of individuals with SCI, was calculated based on the participants' creatinine levels [20]. For TyG-BMI, participants in the top 30% were considered to have high insulin resistance. For MDRD-SCI/D, values below the cut-off of 60, which indicates severe kidney function impairment, were considered indicative of kidney dysfunction [1].

The formulas used for calculating TyG-BMI and MDRD-SCI/D in this study are as follows:

TyG-BMI = Ln [TG (mg/dL) × FBG (mg/dL)/2] × BMI

MDRD-SCI/D = 186 × (creatinine)^-1.154 × (age)^-0.203 × (0.742, if female) × 0.69

Physical fitness

We analyzed four components of physical fitness based on the fitness assessment methods for individuals with SCI provided by the Physical Fitness Certification Center under the Korea Paralympic Committee [50]. Muscular strength was measured using a digital grip dynamometer (TKK-5401, Takei, Tokyo, Japan). The highest value obtained was divided by body weight to calculate relative grip strength, which was expressed as a percentage (%). Muscular endurance was assessed by counting the number of times participants could lift a dumbbell (4 kg for men, 2 kg for women) within 2 min. Flexibility was measured using a back scratch test. CRF was evaluated by measuring the total distance the participants covered within 5 min as they propelled their wheelchairs back and forth along a 20-m course. The standardized scores for the four fitness components were calculated based on sex and age and summed to produce a comprehensive fitness score. The total fitness scores were categorized into three groups based on sex- and age-specific quartiles: the top 25% were classified as 'high fitness', the middle 50% as 'moderate fitness,' and the bottom 25% as 'low fitness'.

Covariates

For disability characteristics, the survey included questions on the location of spinal pathology and the duration of disability. Household monthly income was calculated by dividing the total household income earned over the past year by 12. Educational level was categorized into three groups: elementary school graduate or below, middle and high school graduate, and college graduate or higher. Marital status was classified as married, divorced/widowed, and single. Smoking was defined as a lifetime history of smoking at least five packs of cigarettes [51]. Heavy drinking was defined as consuming at least seven drinks per occasion for men and five drinks for women [52]. Physical activities were assessed using the physical activity scale for individuals with physical disabilities (PASIPD), with the results recorded in MET-hours/day [53]. Additionally, the survey included questions on whether participants had been diagnosed with hypertension, hyperlipidemia, or diabetes by a physician.

Data analysis

Independent t-tests were conducted to compare continuous variables according to sex and TyG-BMI or MDRD-SCI/D classifications, whereas chi-square tests were used to compare categorical variables. Trends in variables were analyzed according to fitness levels using polynomial contrasts in one-way analysis of variance and linear-by-linear association in chi-square tests. Binary logistic regression analysis was performed to calculate ORs and 95% CI for exposure to abnormal TyG-BMI and MDRD-SCI/D status according to fitness levels. Mediation effects of fitness on the relationship between TyG-BMI and MDRD-SCI/D were analyzed using Process macro model 4 by Andrew F. Hayes, and applying a bootstrapping method with repeated random sampling. All analyses were conducted using SPSS-PC statistics software (version 28.0, IBM, New York, USA). The statistical significance level for hypothesis testing was set at $\alpha=0.05$.

Declarations

Authors' contributions

Conceptualization: MK and IL. Methodology: MK, CMJ, and IL. Formal analysis: MK, JK, and IL. Investigation: MK and IL. Data curation: CMJ, JK, and IL. Writing-original draft preparation: MK and I.L. Writing-review and editing: MK and IL. Funding acquisition: IL. All authors contributed to the manuscript equally and approved the submitted version.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Institutional Review Board of Changwon National University (IRB-7001066-202401-HR-009). All participants provided written informed consent prior to participation.

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Tables

Table 1. Characteristics of the study participants

Variables	Total (n=112)	Male (n=86)	Female (n=26)	*p*-value
Socio-demographic status				
Age (years)	57.5±7.9	56.9±7.9	59.3±7.8	0.167
Location of spinal pathology, n (%)				0.158
Cervical	26 (23.2)	20 (23.3)	6 (23.1)	
Thoracic	60 (53.5)	47 (54.6)	13 (50.0)	
Lumbar	19 (17.0)	16 (18.6)	3 (11.5)	
Myelitis	7 (6.3)	3 (3.5)	4 (15.4)	
Duration of injury (years)	25.3±11.9	24.2±10.8	28.9±14.7	0.080
Anthropometric parameters				
Height (cm)	165.0±7.9	167.6±6.4	156.4±5.8	<0.001
Weight (kg)	66.2±11.6	68.7±10.8	58.2±10.8	<0.001
BMI (kg/m^2)	24.3±3.9	24.5±3.9	23.8±3.9	0.398
Body fat (%)	39.0±8.1	37.6±7.9	44.0±6.9	<0.001
WC (cm)	92.3±11.4	93.6±10.9	88.0±12.0	0.027
Socio-economic status				
Income (10,000 won/month)	301.8±229.1	304.4±218.7	293.2±265.3	0.827
Education, n (%)				0.087
Lower than elementary school	7 (6.3)	3 (3.5)	4 (15.4)	
Middle/high school	84 (75.0)	66 (76.7)	18 (69.2)	
College or higher	21 (18.2)	17 (19.8)	4 (15.4)	
Marital status, n (%)				0.198
Married/cohabitation	76 (67.9)	57 (66.3)	19 (73.1)	
Widowed/divorced	20 (17.9)	14 (16.3)	6 (23.1)	
Unmarried	16 (14.2)	15 (17.4)	1 (3.8)	
Health-related factors				
Smoking, n (%)	32 (28.6)	29 (33.7)	3 (11.5)	0.028
Binge drinking, n (%)	28 (25.0)	23 (26.7)	5 (19.2)	0.438
Physical activity (METs-hr/day)	22.9±12.0	22.9±12.7	22.9±9.4	0.997

Menopause, n (%)	22 (196)	0 (0.0)	22 (84.6)	<0.001
Hypertension, n (%)	32 (28.6)	27 (31.4)	5 (19.2)	0.229
Dyslipidemia, n (%)	23 (20.5)	17 (19.8)	6 (23.1)	0.714
Diabetes, n (%)	21 (18.8)	18 (20.9)	3 (11.5)	0.282
Laboratory parameters				
TG (mg/dL)	163.5±78.8	161.0±80.9	172.0±72.0	0.534
FBG (mg/dL)	111.7±24.6	113.2±26.1	106.9±18.5	0.174
TyG-BMI	219.4±38.4	220.8±38.7	214.8±37.5	0.483
Creatinine (mg/dL)	0.7±0.2	0.7±0.2	0.5±0.2	<0.001
MDRD-SCI/D (mL/min/1.73m^2)	80.7±23.9	79.8±23.1	83.7±26.5	0.470
Physical fitness				
Muscular strength (%)	53.0±18.0	57.1±16.7	39.5±15.7	<0.001
Muscular endurance (rep/2 min)	87.5±26.9	90.7±26.9	77.1±24.5	0.023
CRF (m/5min)	403.2±132.4	434.3±117.2	300.1±129.0	<0.001
Flexibility (cm)	-19.6±11.1	-20.7±10.8	-15.8±11.6	0.050

BMI: body mass index, WC: waist circumference, MET: metabolic equivalent of task, TG: triglyceride, FBG: fasting blood glucose, TyG-BMI: triglyceride-glucose index-body mass index, MDRD-SCI/D: modification of diet in renal disease-spinal cord injury/disability, CRF: cardiorespiratory fitness

Table 2. Comparison of variables according to TyG-BMI and MDRD-SCI/D values

Variables	TyG-BMI		*p*-value	MDRD-SCI/D		*p*-value
	Normal (n=78)	Abnormal (n=34)		Normal (n=92)	Abnormal (n=20)	
TyG-BMI	199.3±22.5	265.6±24.6	<0.001	216.1±38.5	234.8±34.8	0.047
MDRD-SCI/D (mL/min/1.73m^2)	84.2±23.8	72.5±22.3	0.017	86.9±21.4	51.9±9.4	<0.001
Socio-demographic status						
Age (years)	57.7±7.7	57.0±8.4	0.665	56.9±7.7	59.9±8.5	0.137
Female, n (%)	18 (23.1)	8 (23.5)	0.958	24 (26.1)	2 (10.0)	0.122
Location of spinal pathology, n (%)			0.051			0.011
Cervical	15 (19.2)	11 (32.3)		17 (18.5)	9 (45.0)	
Thoracic	43 (55.2)	17 (50.0)		54 (58.7)	6 (30.0)	
Lumbar	17 (21.8)	2 (5.9)		17 (18.5)	2 (10.0)	
Myelitis	3 (3.8)	4 (11.8)		4 (4.3)	3 (15.0)	
Duration of injury (years)	25.7±11.8	24.5±12.4	0.632	25.9±12.2	22.5±10.4	0.241
Anthropometric parameters						
Height (cm)	165.9±7.6	163.0±8.2	0.078	164.4±8.4	167.7±3.9	0.091
Weight (kg)	61.8±8.7	76.3±11.1	<0.001	64.7±11.3	73.2±10.3	0.003
BMI (kg/m^2)	22.4±2.5	28.6±2.8	<0.001	23.9±3.9	26.0±3.4	0.028
Body fat (%)	37.3±7.9	43.0±7.3	<0.001	39.2±8.3	38.4±7.2	0.715
WC (cm)	88.4±8.8	101.3±11.8	<0.001	91.4±11.4	96.5±10.9	0.074
Socio-economic status						
Income (10,000 won/month)	329.1±239.3	239.1±192.9	0.056	309.9±238.9	264.5±177.8	0.424
Education, n (%)			0.384			0.189
Lower than elementary school	4 (5.1)	3 (8.8)		5 (5.4)	2 (10.0)	
Middle/high school	57 (73.1)	27 (79.4)		67 (72.8)	17 (85.0)	

College or higher	17 (21.8)	4 (11.8)		20 (21.8)	1 (5.0)	
Marital status, n (%)			0.173			0.431
Married/cohabitation	56 (71.8)	20 (58.8)		60 (65.2)	16 (80.0)	
Widowed/divorced	14 (17.9)	6 (17.6)		18 (19.6)	2 (10.0)	
Unmarried	8 (10.3)	8 (23.6)		14 (15.2)	2 (10.0)	
Health-related factors						
Smoking, n (%)	22 (28.2)	10 (29.4)	0.897	28 (30.4)	4 (20.0)	0.349
Binge drinking, n (%)	21 (26.9)	7 (20.6)	0.477	26 (28.3)	2 (10.0)	0.087
Physical activity (METs-hr/day)	23.4±13.2	22.0±8.6	0.585	23.0±12.4	22.9±10.3	0.982
Menopause, n (%)	14 (17.9)	8 (23.5)	0.494	20 (21.7)	2 (10.0)	0.231
Hypertension, n (%)	21 (26.9)	11 (32.4)	0.559	24 (26.1)	8 (40.0)	0.212
Dyslipidemia, n (%)	11 (14.1)	12 (35.3)	0.011	17 (18.5)	6 (30.0)	0.248
Diabetes, n (%)	16 (20.5)	5 (14.7)	0.469	17 (18.5)	4 (20.0)	0.874
Laboratory parameters						
TG (mg/dL)	143.5±67.4	209.5±84.5	<0.001	162.8±81.1	166.9±68.5	0.837
FBG (mg/dL)	111.9±27.2	111.2±17.5	0.442	112.6±25.7	107.5±18.6	0.399
Creatinine (mg/dL)	0.7±0.2	0.8±0.2	0.035	0.6±0.1	1.0±0.2	<0.001
Physical fitness						
Muscular strength (%)	56.2±16.8	45.6±18.8	0.004	54.6±17.2	45.6±20.2	0.043
Muscular endurance (rep/2 min)	89.2±25.3	83.7±30.3	0.325	89.8±224.8	77.2±34.0	0.057
CRF (m/5min)	409.6±130.7	388.4±137.0	0.439	416.0±121.3	344.5±165.6	0.028
Flexibility (cm)	-17.6±11.6	-24.1±8.4	0.004	-19.0±11.5	-22.1±8.7	0.256
Total physical fitness Z-score	0.489±2.571	-1.121±3.130	0.005	0.405±2.517	-1.863±3.502	0.011

TyG-BMI: triglyceride-glucose index–body mass index, MDRD-SCI/D: modification of diet in renal disease-spinal cord injury/disability, BMI: body mass index, WC: waist circumference, MET: metabolic equivalent of task, TG: triglyceride, FBG: fasting blood glucose, CRF: cardiorespiratory fitness

Table 3. Comparison of variables according to physical fitness level

Variables	Low fitness (n=26)	Moderate fitness (n=59)	High fitness (n=27)	*p* for linear trend
Physical fitness				
Total physical fitness Z-score	-3.595±1.570	0.170±1.086	3.089±1.366	<0.001
Muscular strength (%)	35.9±17.1	54.8±14.7	65.5±12.6	<0.001
Muscular endurance (rep/2 min)	61.0±24.0	89.6±20.9	108.6±19.6	<0.001
CRF (m/5 min)	297.2±126.7	409.3±112.8	491.9±107.1	<0.001
Flexibility (cm)	-25.2±8.4	-20.5±9.6	-12.0±12.6	<0.001
Socio-demographic status				
Age (years)	58.2±8.7	57.7±8.1	56.3±6.7	0.378
Female, n (%)	6 (23.1)	14 (53.8)	6 (22.2)	0.940
Location of spinal pathology, n (%)				0.018
Cervical	13 (50.0)	10 (16.9)	3 (11.1)	
Thoracic	9 (34.7)	35 (59.3)	16 (59.3)	
Lumbar	3 (11.5)	9 (15.3)	7 (25.9)	
Myelitis	1 (3.8)	5 (8.5)	1 (3.7)	
Duration of injury (years)	24.1±14.8)	25.2±11.3	26.6±10.6	0.448
Anthropometric parameters				
Height (cm)	165.5±6.1	164.6±8.1	165.5±9.0	0.990
Weight (kg)	69.1±10.9	67.3±12.0	61.2±9.9	0.012
BMI (kg/m^2)	25.2±3.9	24.9±4.0	22.2±2.6	0.004
Body fat (%)	40.4±7.3	40.0±7.8	35.7±8.8	0.033
WC (cm)	95.8±13.3	92.7±11.2	88.2±8.9	0.015
Socio-economic status				
Income (10,000 won/month)	306.9±275.4	287.9±208.0	327.2±231.5	0.749
Education, n (%)				0.168
Lower than elementary school	3 (11.5)	4 (6.8)	0 (0.0)	
Middle/high school	19 (73.1)	44 (74.6)	21 (77.8)	

College or higher	4 (15.4)	11 (18.6)	6 (22.2)	
Marital status, n (%)				0.307
Married/cohabitation	17 (65.4)	37 (62.8)	22 (81.5)	
Widowed/divorced	6 (23.1)	11 (18.6)	3 (11.1)	
Unmarried	3 (11.5)	11 (18.6)	2 (7.4)	
Health-related factors				
Smoking, n (%)	7 (26.9)	119 (32.2)	6 (22.2)	0.697
Binge drinking, n (%)	6 (23.1)	16 (27.1)	6 (22.2)	0.937
Physical activity (METs-hr/day)	23.8±15.6	22.5±10.2	23.2±12.2	0.852
Menopause, n (%)	5 (19.2)	13 (22.0)	4 (14.8)	0.680
Hypertension, n (%)	5 (19.2)	15 (25.4)	12 (44.4)	0.042
Dyslipidemia, n (%)	6 (32.1)	11 (18.6)	6 (22.2)	0.945
Diabetes, n (%)	6 (23.1)	11 (18.6)	4 (14.8)	0.443
Laboratory parameters				
TG (mg/dL)	170.5±86.0	161.3±76.3	161.7±79.4	0.685
FBG (mg/dL)	109.8±21.0	112.5±24.7	111.9±28.1	0.765
TyG-BMI	228.6±39.5	224.3±40.3	199.9±25.1	0.006
Creatinine (mg/dL)	0.8±0.3	0.7±0.2	0.7±0.2	0.018
MDRD-SCI/D (mL/min/1.73m^2)	70.8±23.4	82.9±22.5	85.2±25.6	0.027

CRF: cardiorespiratory fitness, BMI: body mass index, WC: waist circumference, MET: metabolic equivalent of task, TG: triglyceride, FBG: fasting blood glucose, TyG-BMI: triglyceride-glucose index–body mass index, MDRD-SCI/D: modification of diet in renal disease-spinal cord injury/disability

Table 4. Odd ratios and 95% confidence intervals for TyG–BMI and MDRD–SCI/D according to fitness level

	High fitness	Moderate fitness		Low fitness	
		OR (95% CI)	*p*–value	OR (95% CI)	*p*–value
TyG–BMI					
Model 1	1 (reference)	4.21 (1.12–15.76)	0.033	6.09 (1.44–25.66)	0.014
Model 2	1 (reference)	4.16 (1.10–15.60)	0.035	5.74 (1.32–24.99)	0.020
Model 3	1 (reference)	3.26 (0.68–15.62)	0.139	5.61 (1.01–31.04)	0.048
MDRD–SCI/D					
Model 1	1 (reference)	0.99 (0.23–4.31)	0.996	4.88 (1.11–21.40)	0.035
Model 2	1 (reference)	0.97 (0.22–4.28)	0.976	4.81 (1.01–22.87)	0.048
Model 3	1 (reference)	1.30 (0.25–6.76)	0.675	6.22 (1.01–38.21)	0.048

OR: odd ratio, CI: confidence interval, TyG-BMI: triglyceride-glucose index–body mass index, MDRD-SCI/D: modification of diet in renal disease-spinal cord injury/disability

Model 1: adjusted for age and sex.

Model 2: Model 1 + location of spinal pathology and duration of injury.

Model 3: Model 2 + body fat, income, education, marital status, smoking, binge drinking, physical activity, menopause, hypertension, dyslipidemia, and diabetes.

Table 5. Association between TyG-BMI and MDRD-SCI/D, mediated by physical fitness, in individuals with spinal cord injury

Path	ß	SE	t	95% CI		*p*-value
				LLCI	ULCI	
TyG-BMI → Physical fitness, a	-0.020	0.007	-2.681	-0.034	-0.005	0.009
Physical fitness → MDRD-SCI/D, b	2.121	0.913	2.324	0.309	3.933	0.022
Total effect, c	-0.211	0.068	-3.118	-0.345	-0.077	0.002
Direct effect, c`	-0.169	0.068	-2.466	-0.305	-0.033	0.015
Indirect effect, ab	-0.042	0.028		-0.108	-0.002	
Indirect to total effect	19.9%					

SE: standard error, CI: confidence interval, LLCI: lower limit of confidence interval, ULCI: upper limit confidence interval, TyG-BMI: triglyceride-glucose index–body mass index, MDRD-SCI/D: modification of diet in renal disease-spinal cord injury/disability

Adjusted for age, sex, location of spinal pathology, duration of injury, body fat, income, education, marital status, smoking, binge drinking, physical activity, menopause, hypertension, dyslipidemia, and diabetes.

In the mediation model, the indirect effect is the product of path coefficients a (TyG-BMI → physical fitness) and b (physical fitness → MDRD-SCI/D). The direct effect is the coefficient c

$. The \rightarrow tale ffect(c) isequal \rightarrow the \sum of the direct \text{and} \in direct(c$+ ab).

Figures

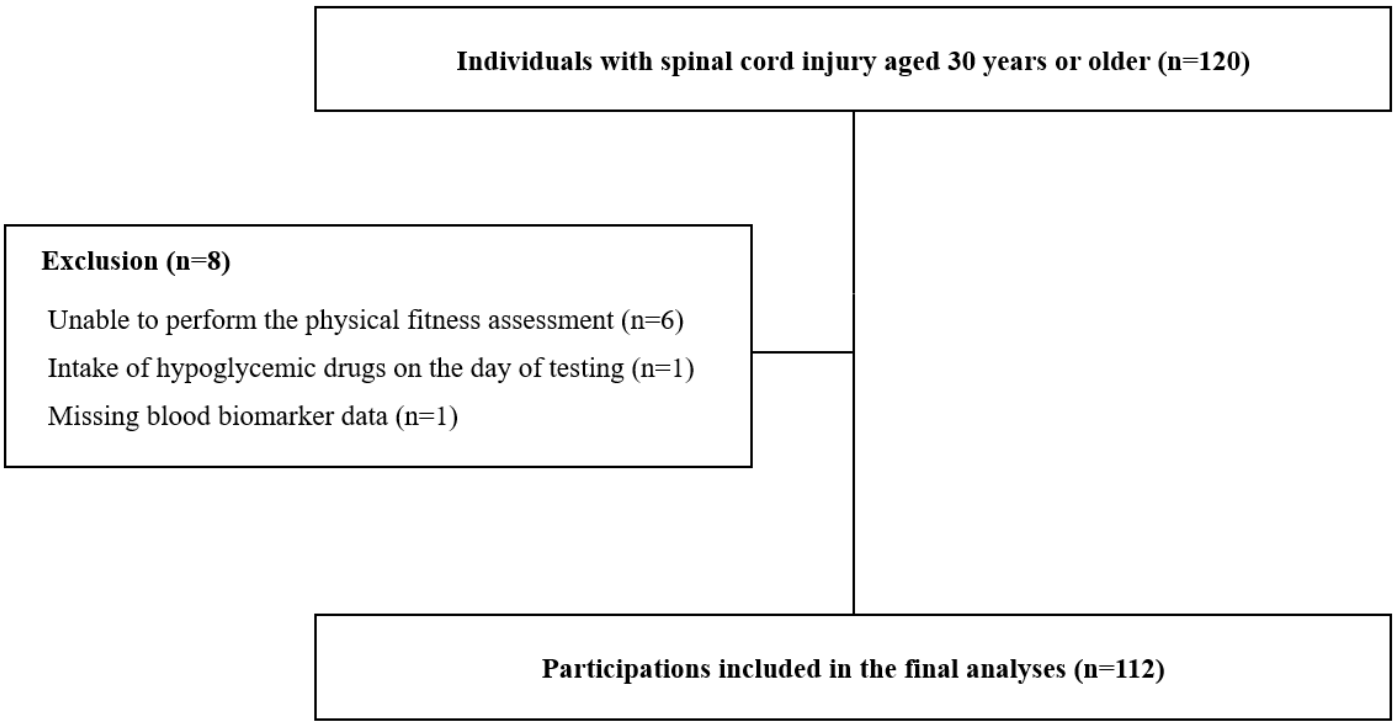


Figure 1

Flow chart of eligible participants in the study

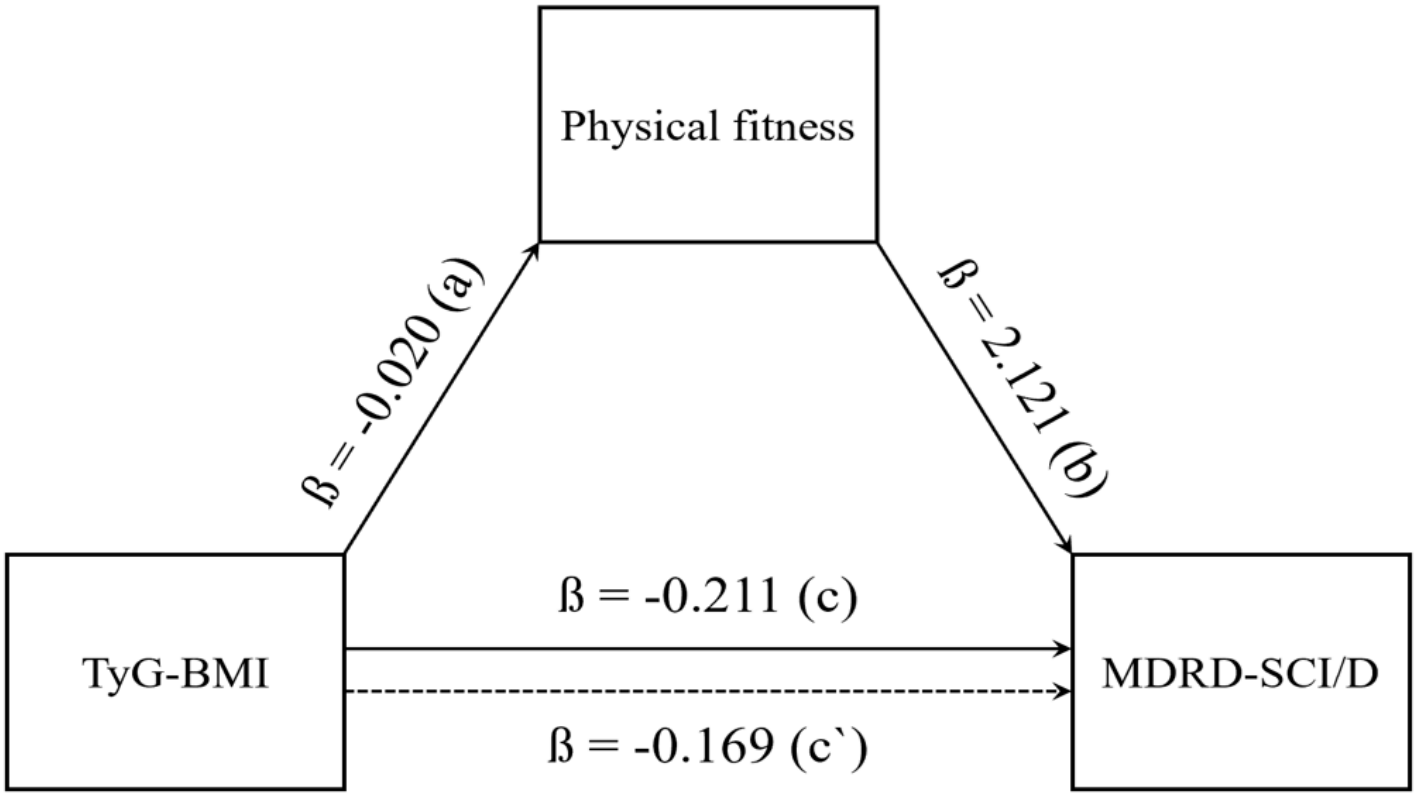


Figure 2

Mediation analysis. Path coefficients of triglyceride-glucose index-body mass index (TyG-BMI) on modification of diet in renal disease-spinal cord injury/disability (MDRD-SCI/D) through physical fitness.

Path a, estimated coefficient for the regression with TyG-BMI predicting physical fitness; Path b, estimated coefficient for the regression with physical fitness predicting MDRD-SCI/D; Path c, total effects for the regression with TyG-BMI predicting MDRD/SCI-D; Path c`, direct effects for the regression with TyG-BMI predicting MDRD-SCI/D independent of physical fitness