

The Effect of Obesity on Functional Outcome at Six Months Post-Stroke in Korean Elderly: A Prospective Multicenter Study

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**The Effect of Obesity on Functional Outcome at Six Months Post-Stroke
in Korean Elderly: A Prospective Multicenter Study**

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4 **Objectives** We examined whether obesity based on body mass index (BMI) was a predictor
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6 of six-month functional independent measure (FIM) after ischemic stroke onset with
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8 adjustment for cardiovascular disease risk factors, education, smoking status, and National
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10 Institutes of Health Stroke Scale score by age group.
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14 **Design** This is an interim report of the Korean Stroke Cohort for Functioning and
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16 Rehabilitation as a nested case study with a nationwide hospital-based cohort.
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19 **Setting** We identified all patients of at least 18 years of age who were admitted to nine
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21 representative hospitals in Korea under a diagnosis of acute first-ever stroke, both ischemic
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23 and hemorrhagic, from 2012 until 2014. The hospitals were selected from the metropolitan
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25 district, mid-sized cities, and a small-sized city.
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29 **Participants** The sample included 2,057 acute ischemic stroke patients ≥ 20 years of age.
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32 **Primary and secondary outcome measures** We divided subjects into two age levels (< 65
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34 and ≥ 65 years old). Subjects were classified into three groups according to their baseline
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36 BMI at admission: normal ($18.5 \leq \text{BMI} < 23$), overweight ($23 \leq \text{BMI} < 25$), and obese (BMI
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38 ≥ 25).
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42 **Results** The proportions of overweight and obese patients were 29.6 % and 43.4 % in the
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44 patients less than 65 years of age and 27.9 % and 32.0 % in those over 65 years of age,
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46 respectively. The average six-month FIM was significantly higher in the obese group
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48 compared to the normal and overweight group in patients ≥ 65 years of age ($p < 0.05$). After
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4 adjustment for potential confounders, six-month FIM was found to be associated with obesity,
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6 especially in patients ≥ 65 years.
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10 **Conclusion** This nationwide hospital-based cohort study showed that obesity, as measured by
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12 BMI, is a predictor of good six-month FIM, especially in ischemic stroke patients ≥ 65 years.
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20 Keywords: obese, body mass index, elderly, ischemic stroke, functional independent measure
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24 25 **Article summary**

26 27 **Strengths and limitations of this study**

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29 - Obesity with stroke patient performed better activities of daily living than normal BMI in in
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31 patients 65 years of age and older.
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33 - Functional independent measurement (FIM) was evaluated as the activities of daily living.
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35 - Our study also showed associations between gender and chronic kidney disease and FIM.
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37 - Subject's height and weight were measured once at admission to our study.
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39 - We did not account for the proportions and distributions of muscle, bone, and adipose tissue
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41 in obese patients in this study.
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Introduction

Obesity is one of the leading risk factors for cardiovascular disease (CVD)¹. The China National Stroke Registry shows that severe obesity is independently associated with higher 3-month mortality². A suggested mechanism of post-stroke muscle atrophy is that inflammatory cytokines, such as catabolic cytokine tumor necrosis factor, cause tissue degradation³⁻⁵. Furthermore, inactivity and impaired feeding after stroke may lead to muscle wasting and weight loss⁶. In contrast, post-stroke mortality is inversely related to body mass index (BMI): overweight and obese stroke patients had a lower post-stroke mortality rate than normal-weight and underweight patients in a Denmark study⁷.

Functional outcome measurements in ischemic stroke patients, such as the functional independent measurement (FIM), evaluate the activities of daily living. Obesity is known as a good predictor of functional outcome in ischemic stroke patients⁸, especially elderly patients⁹. Functional outcome shows a sharp increase in the first 8 to 24 weeks after stroke and then plateaus¹⁰. The chronic stage of stroke begins at least six-month after stroke onset. However, few studies have analyzed functional outcome related to obesity at six-month post-stroke. We examined whether obesity based on BMI was predictive of six-month post-stroke FIM with adjustment for gender, education, smoking status, CVD risk factors, and National Institutes of Health Stroke Scale (NIHSS) score, after grouping the study cohort by age: less than 65 and greater than 65 years of age.

Methods

This is an interim report of the Korean Stroke Cohort for Functioning and Rehabilitation (KosCo). We identified all patients of at least 18 years of age who were admitted to nine representative hospitals in Korea under a diagnosis of acute first-ever stroke, both ischemic and hemorrhagic, from January 2012 until October 2014. The hospitals were selected from the metropolitan district (Samsung Medical Center, Yonsei University Hospital, and Konkuk University Hospital), mid-sized cities (Chungnam National University Hospital, Pusan National University Hospital, Chonnam National University Hospital, Wonkwang University Hospital, and Kyung-pook National University Hospital), and a small-sized city (Jeju University Hospital).

Acute stroke patients were defined as those experiencing ischemic and hemorrhagic stroke who were admitted within seven days of the onset of stroke symptoms. Patients with transient ischemic attack (TIA) or admission more than seven days after symptom onset were excluded. TIA was defined as symptoms resolving within 24 hours of onset and no evidence of acute infarction by brain CT or MRI. The medical records of all subjects were reviewed by well-trained rehabilitation specialists. The study protocol was approved by the Samsung Medical Center Institutional Review Board.

The nationwide hospital-based cohort study population included 2,057 ischemic stroke patients aged 20 years or older. We divided subjects into two age groups: less than 65 and greater 65 years old. Education level was classified into three categories: 1) elementary school: elementary school or six years or less of schooling, 2) middle/high school: middle school or 7–12 years of schooling, and 3) college, university: college or >12 years of

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4 schooling. Functional status was assessed at six months after stroke onset. FIM scale was
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6 assessed at six months after stroke onset, and consisted of 18 physical and three cognitive
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8 disability items such as self-eating, grooming, bathing/showering, dressing upper or lower
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10 body, toileting, control of bladder or bowel sphincters, mobility, communication,
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12 psychosocial function, and cognition. Each item was scored from 1 to 7 based on the level of
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14 independence, with 1 representing total dependence and 7 representing complete
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16 independence. Possible scores ranged from 18 to 126, with higher scores indicating greater
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18 independence. We assessed stroke severity using the NIHSS. NIHSS data were collected and
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20 assessed at seven days after stroke onset. NIHSS is composed of 11 items: level of
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22 consciousness, gage, visual activity, facial palsy, movement of arms or legs, limb ataxia,
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24 senses, language, dysarthria, extinction and inattention. The score of each specific ability
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26 ranges from 0 to 4. Possible scores range from 0 to 42, with higher scores indicative of some
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28 level of impairment.
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37 **Obesity**

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39 BMI was calculated as weight in kilograms divided by the square of the height in
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41 meters. We measured each subject's standing height using anthropometry. The patient stood
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43 with the heels together and toes apart and the back of the head, buttocks, and heels in contact
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45 with the backboard. The head was aligned in the Frankfort horizontal plane. We measured
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47 height to one decimal point (cm) with an anthropometric bar on the subject's head. Subjects
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49 were weighed in kilograms using a scale when gradation had stabilized after setting the scale
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51 to zero with no load. Subjects were classified into three groups based on their baseline BMI
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4 at admission: normal ($18.5 \leq \text{BMI} < 23$), overweight ($23 \leq \text{BMI} < 25$), and obese ($\text{BMI} \geq$
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6 25)^{11 12}.
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10 11 12 **Cardiovascular risk factors** 13

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15 We assessed CVD risk factors such as hypertension (HT), diabetes mellitus (DM),
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17 dyslipidemia, chronic kidney disease (CKD), and smoking status. Subjects were defined as
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19 having HT if they were taking an anti-hypertension drug, had been clinically diagnosed with
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21 hypertension, or had either a systolic blood pressure (SBP) ≥ 140 mmHg or a diastolic blood
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23 pressure (DBP) ≥ 90 mmHg. Subjects who met one of the following requirements were
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25 defined as having DM: taking an oral hyperglycemic agent, using insulin, clinical diagnosis
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27 of diabetes, or a fasting glucose level > 126 mg/dL. Subjects were defined as having
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29 dyslipidemia if they met one of the following requirements: diagnosis of
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31 hypercholesterolemia, medication history for hypercholesterolemia or total cholesterol (TC)
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33 > 200 mg/dL or low density lipoprotein (LDL) > 130 mg/dL. The estimated Glomerular
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35 Filtration Rate (eGFR), used as an indicator of kidney function, was calculated using the
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37 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation¹³. The CKD-EPI
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39 equation is as follows: $\text{GFR} = 141 \times \min(\text{serum Cr} / \kappa, 1)^\alpha \times \max(\text{serum Cr} / \kappa, 1)^{-1.209} \times$
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41 $0.993 \text{Age} \times 1.018$ [if female], where κ is 0.7 for females and 0.9 for males, α is -0.329 for
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43 females and -0.411 for males, min indicates the minimum serum Cr / κ or 1, and max indicates
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45 the maximum serum Cr / κ or 1. The National Kidney Foundation Kidney Disease Outcome
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47 Quality Initiative defines CKD as an eGFR < 60 mL/min/1.73m². A subject was identified as
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49 a current smoker if he/she had smoked within one year of the survey date.
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Statistical Analyses

Differences in general characteristics, clinical data, and covariate among obese patients were analyzed using one-way analysis of variance (ANOVA) for continuous variables and the χ^2 -test for categorical variables. Multiple linear regressions using general linear model for six-month FIM as a dependent variable and obesity classification, based on BMI, as the independent variable were performed by age group after adjusting for gender, HT, DM, dyslipidemia, CKD, education, smoking status, and seven-day NIHSS.

Results

The proportions of overweight and obese patients were 29.6 % and 43.4 % in patients less than 65 years of age and 27.9 % and 32.0 % in those over 65 years of age, respectively. Generally, obese patients had HT more frequently than those in the normal weight group ($p<0.05$) for both age groups. In obese subjects, the mean values of triglyceride and six-month FIM were higher and seven-day NIHSS value was lower than those in normal and overweight subjects for the age group of 65 years and older ($p<0.05$) (Table 1).

As seen in Table 2, FIM at six months post-stroke was predicted at 3.13 (95% confidence interval (CI) 0.04, 6.21; $p<0.05$) in obesity, -4.00 (95% CI -7.22, -0.79; $p<0.05$) in females, -4.08 (95% CI -7.39, -0.77; $p<0.05$) in CKD, and -3.86 (95% CI -4.08, -3.64; $p<0.05$) in seven-day NIHSS in the 65 years and older age group. However, six-month FIM was not associated with obesity in the less than 65 years old age group.

Discussion

Higher FIM at six months after stroke onset was associated with obesity in the 65 years and older age group. Our finding corresponds well with those of the Telemedical Project for Integrative Stroke Care (TEMPiS) trial. The TEMPiS trial included 4,428 elderly patients with acute stroke or TIA and showed that overweight and obese patients improved survival and better combined outcomes of survival and non-fatal functional status compared with normal-weight patients¹⁴. Among 819 patients admitted to an acute rehabilitation hospital for stroke rehabilitation, overweight patients also had better FIM than patients in the other weight categories⁸. Onbiagele *et al.* showed that obese patients with stroke have a lower overall vascular risk than their leaner counterparts¹⁵. Furthermore, although the Atherosclerosis Risk in Communities (ARIC) study confirmed a positive and linear relationship between BMI and ischemic stroke incidence¹⁶, overweight and obese patients who survived the first event tended to have improved subsequent CVD^{17 18} and cerebrovascular disease burden^{19 20}. Previous studies have shown an association between obesity and FIM at discharge or three months after stroke. Stroke enters chronic stage at six month after onset. Our study results showed that obesity may predict six-month post-stroke outcomes in patients 65 years of age and older. Our findings are in contrast with those of the current American Stroke Association for Stroke Prevention recommendations for weight management after a stroke, which include weight reduction to a target BMI of 18.5 to 25 kg/m²²¹. Our results also differ from those of Strazzullo *et al.* who observed that overweight and obesity are associated with progressively increased risk of ischemic stroke, at least in part, and that this association is independent of age, lifestyle, and other cardiovascular risk factors²². Although Danish Stroke Register²³ had showed no relationship between mortality

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4 and obesity with stroke patients, our study showed obesity stroke patient performed better
5 activities of daily living than normal BMI in elderly. The obesity paradox²⁴ is that obese
6 patients receive better treatment and care because they are perceived to be at high risk²⁵. Ryu
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11 *et al.* have proposed that the obesity paradox phenomenon has limitations and that there
12 might not be a direct causal relationship between obesity and improved treatment and care
13 due to the association of long-term mortality with initial neurological severity in ischemic
14 stroke patients in Korea²⁶. However, our study showed that obesity might predict FIM at six
15 months after ischemic stroke onset after adjustment for NIHSS at seven days after stroke
16 onset as a stroke severity variable. Strength of this study is a high degree of representation of
17 Korean ischemic stroke patients. Our results, therefore, are applicable to the entire nation.
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27 Our study showed associations between gender and CKD and FIM. These results are
28 consistent with those of previous studies that reported that the functional outcome of females
29 after acute ischemic stroke is slightly poorer than that of males⁹ and that CKD may predict
30 poor functional outcome in elderly ischemic stroke patients²⁷.
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36 This study had several limitations. First, it was conducted prospectively with a multi-
37 center design, which may have impacted data reliability. To counteract this problem, the
38 KosCo committee leads a training course for rehabilitation specialists twice per year. Second,
39 height and weight were measured once at admission to our study. Third, we did not account
40 for the proportions and distributions of muscle, bone, and adipose tissue²⁸ in obese patients in
41 this study. Thus, further cardiovascular cohort studies that consider these variables are needed
42 to verify risk factors for CVA.
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Conclusion

This nationwide hospital-based cohort study showed that obesity is a predictor of good functional outcome in ischemic stroke patients, especially in the elderly.

Funding

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Conflicts of interest

The authors declare no conflicts of interest.

Table 1. Distribution of general characteristics, cardiovascular disease risk factors, socioeconomic position, and functional outcomes by age group and body mass index (n=2,057)

Variables	<65 years old (n=925)				≥65 years old (n=1,132)			
	Normal (n=249)	Overweight (n=274)	Obese (n=402)	p-value*	Normal (n=453)	Overweight (n=316)	Obese (n=363)	p-value*
Body mass index	20.6±1.50	23.5±0.50	27.2±2.55	<0.001	20.3±1.56	23.5±0.50	26.8±2.21	<0.001
Age, year-old	53.6±8.51	56.1±7.07	53.4±8.45	<0.001	76.2±6.26	74.3±5.57	73.5±5.63	<0.001
Gender, male	66.2	73.3	71.1	0.191	55.6	58.8	54.5	0.503
Smoking				0.004				0.543
Ex								
Current	11.2	12.4	14.1		16.7	18.6	18.1	
Drinking, current	45.3	47.0	33.8		19.4	16.1	15.1	
Education	47.7	50.7	51.9	0.578	29.5	24.0	31.6	0.078
College, University				0.038				0.194
Middle/high school	31.4	22.9	32.3		9.60	12.9	13.4	
Elementary	58.7	61.3	56.4		38.0	39.7	41.7	
Hypertension	9.9	15.8	11.3		52.4	47.4	44.8	
Diabetes mellitus	67.0	77.3	88.0	<0.001	86.9	86.7	93.3	0.004
Dyslipidemia	42.9	48.5	53.9	0.027	52.3	56.6	58.4	0.195
Chronic kidney disease	29.7	45.2	45.0	<0.001	27.8	31.3	32.7	0.281
SBP, mmHg	4.84	3.68	5.79	0.459	18.4	20.1	18.4	0.820
DBP, mmHg	143.5±27.0	147.9±27.8	154.8±29.0	<0.001	149.3±26.3	148.1±28.8	151.0±26.1	0.391
Fasting blood sugar, mg/dl	84.5±16.1	87.4±14.7	90.2±18.3	<0.001	81.9±13.9	82.0±14.4	83.0±14.3	0.484
Total cholesterol, mg/dl	140.8±78.9	137.3±56.8	145.7±63.5	0.269	141.7±66.0	144.3±65.7	142.7±55.5	0.857
Triglyceride, mg/dl	180.2±42.8	188.2±44.5	194.3±47.5	<0.001	174.6±39.7	176.0±37.0	175.4±42.4	0.888
High density lipoprotein, mg/dl	118.8±87.7	139.4±102	155.8±114	<0.001	102.7±61.2	111.6±60.8	126.0±76.1	<0.001
Low density lipoprotein, mg/dl	48.4±15.3	46.0±11.4	44.8±12.7	0.005	47.8±13.3	44.9±13.3	43.9±11.3	<0.001
Creatinine, mg/dl	107.6±35.2	122.2±44.5	123.7±47.4	<0.001	107.9±35.3	109.1±32.8	110.6±45.3	0.628
eGFR, mL/min/1.73m ²	0.91±1.23	0.87±0.62	0.88±0.53	0.828	10.8±1.51	0.95±0.57	0.94±0.39	0.094
FIM, six months	96.5±20.7	94.1±17.9	94.1±20.1	0.257	75.4±20.4	75.6±18.8	74.6±17.8	0.783
NIHSS, seven-day after onset	117.2±17.7	116.7±20.5	119.1±17.8	0.187	99.4±34.0	104.2±32.0	107.0±29.5	0.002
	3.28±5.08	2.94±4.80	2.53±4.27	0.128	4.71±6.03	4.08±6.08	3.52±5.75	0.018

SD standard deviation; SBP systolic blood pressure; DBP diastolic blood pressure; eGFR estimated Glomerular Filtration Rate; FIM functional independence measurement; NIHSS national institutes of health stroke scale

*Analysis of variance or χ^2 -test

Table 2. Multiple linear regressions for six months functional independence measurement (FIM) by age group*

Variables	<65 years old		≥65 years old	
	β (95% CI)	p-value	β (95% CI)	p-value
Obese grades				
Normal	1.0		1.0	
Overweight	-1.16 (-3.59, 1.27)	0.384	2.52 (-0.65, 5.70)	0.120
Obese	0.75 (-1.54, 3.05)	0.520	3.13 (0.04, 6.21)	0.046
Gender, female vs male	-1.19 (-3.55, 1.17)	0.322	-4.00 (-7.22, -0.79)	0.014
Education				
College, University	1.0		1.0	
Middle/high school	-2.08 (-4.13, -0.04)	0.045	1.91 (-2.07, 5.90)	0.346
Elementary	-2.58 (-5.71, 0.54)	0.105	0.08 (-4.01, 4.17)	0.969
Smoking, current	0.67 (-0.49, 1.83)	0.257	-0.22 (-2.16, 1.70)	0.818
Hypertension, yes	-1.05 (-3.33, 1.23)	0.365	-1.88 (-6.05, 2.27)	0.374
Diabetes mellitus, yes	-1.63 (-3.45, 0.17)	0.077	-0.31 (-2.93, 2.31)	0.816
Dyslipidemia, yes	-0.20 (-2.06, 1.65)	0.828	-1.08 (-3.93, 1.75)	0.453
Chronic kidney disease	-5.14 (-9.36, -0.92)	0.017	-4.08 (-7.39, -0.77)	0.015
NIHSS, seven-day	-2.59 (-2.79, -2.40)	<0.001	-3.86 (-4.08, -3.64)	<0.001

* Estimated by multiple linear regression models using the variables in the table

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**The Effect of Obesity on Functional Outcomes at Six Months Post-Stroke
among Elderly Koreans: A Prospective Multicenter Study**

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4 **Objectives** We examined whether obesity based on body mass index (BMI) was a predictor
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6 of functional independence measure (FIM) at 6 months after ischemic stroke onset while
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8 adjusting for stroke risk factors and covariates and stratifying by age group.
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11 **Design** This is an interim report of the Korean Stroke Cohort for Functioning and
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13 Rehabilitation that was designed as a nested case study within a nationwide hospital-based
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15 cohort.
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18 **Setting** We identified all patients who were admitted to nine representative hospitals in Korea
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20 from 2012 until 2014 under a diagnosis of acute first-ever ischemic stroke. The hospitals
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22 were selected from the metropolitan district, mid-sized cities, and a small-sized city.
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26 **Participants** The sample included 2,057 acute ischemic stroke patients who were at least 18
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28 years old.
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31 **Primary and secondary outcome measures** We divided subjects into two age levels (<65
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33 and ≥65 years old). Subjects were classified into five groups according to their baseline BMI
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35 at admission: underweight (BMI<18.5), normal (18.5≤BMI<23), overweight (23≤BMI<25),
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37 obese (25≤BMI<30), and extremely obese (30≤BMI).
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41 **Results** The proportion of patients who were ≥65 years old was 55.0%. The proportions of
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43 underweight, normal, overweight, obese, and extremely obese patients were 2.6%, 24.3%,
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45 29.6 %, 37.2% and 6.3%, respectively, in the <65 years old group and 5.5%, 34.5%, 27.9 %,
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47 28.8%, and 3.3 %, respectively, in the ≥65 years old group. In a multiple linear regression,
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49 the six-month FIM after stroke in the elderly group was significantly associated with being
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51 extremely obese (7.95, $p<0.05$) after adjusting for confounding variables. In the <65 years old
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53 group, the six-month FIM was not associated with any weight category.
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7 **Conclusion** This nationwide hospital-based cohort study showed that extreme obesity is a
8
9 predictor of a good six-month FIM, especially in ischemic stroke patients who are at least 65
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11 years of age.
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18 Keywords: obese, body mass index, elderly, ischemic stroke, functional independence
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20 measure
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22 23 24 25 **Article summary**

26 27 **Strengths and limitations of this study**

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29 - Stroke patients who were extremely obese better performed activities of daily living than
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31 did patients with a normal BMI among patients 65 years of age or older. However, the six-
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33 month FIM was not associated with any weight category in the under 65 age group.
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37 - The Functional independence measurement was evaluated for daily living activities.
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40 - Subjects' heights and weights were measured once upon admission to our study.
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43 - We did not account for the proportions and distributions of muscle, bone, and adipose tissue
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45 in obese patients in this study.
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Introduction

The prevalence of obesity in Korea was shown to be 32.5% among individuals aged 20 years or older (32.2% in those 20-64 years old and 34.3% in those over 65 years old) in the 2013 Korea National Health and Nutrition Examination Survey¹. Obesity is one of the leading risk factors for cardiovascular disease (CVD)². However, obese and overweight patients undergoing acute rehabilitation showed higher functional outcomes than did patients in a normal weight range based on body mass index (BMI)³. Obesity is also known to be a good predictor of functional outcomes in ischemic stroke patients⁴, especially elderly patients⁵. Furthermore, post-stroke mortality is inversely related to BMI: overweight and obese stroke patients had a lower post-stroke mortality rate than normal-weight and underweight patients in a study from Denmark⁶.

Functional outcomes such as the functional independence measurement (FIM) are used to evaluate the ability of individuals to perform activities of daily living. Functional outcomes in ischemic stroke patients sharply increase from 2 to 6 months after the stroke, and ability of daily living (ADL) were recovered slowly in the chronic stage 6 months after the stroke⁷. However, few studies have analyzed functional outcomes in relation to obesity at six months post-stroke. We examined whether obesity based on BMI was predictive of the six-month post-stroke FIM after adjustment for gender, education, smoking, drinking, hypertension (HT), diabetes mellitus (DM), dyslipidemia, chronic kidney disease (CKD), discharge FIM, and 7-day National Institutes of Health Stroke Scale (NIHSS) score and stratification by two age groups: less than 65 years and greater than or equal to 65 years.

Methods

This is an interim report of the Korean Stroke Cohort for Functioning and Rehabilitation (KosCo). We identified all patients of at least 18 years of age who were admitted to nine representative hospitals in Korea under a diagnosis of acute first-ever stroke, either ischemic or hemorrhagic, from January 2012 until October 2014. The hospitals were selected from the metropolitan district (Samsung Medical Center, Yonsei University Hospital, and Konkuk University Hospital), mid-sized cities (Chungnam National University Hospital, Pusan National University Hospital, Chonnam National University Hospital, Wonkwang University Hospital, and Kyung-pook National University Hospital), and a small-sized city (Jeju University Hospital). Acute stroke patients were defined as those experiencing ischemic or hemorrhagic stroke who were admitted within seven days of the onset of stroke symptoms. Patients experiencing a transient ischemic attack (TIA) or who were admitted more than seven days after symptom onset were excluded. TIA was defined as symptoms resolving within 24 hours of onset and no evidence of acute infarction by brain CT or MRI. The medical records of all subjects were reviewed by well-trained rehabilitation specialists. The study protocol was approved by the Samsung Medical Center Institutional Review Board.

The nationwide hospital-based cohort study population included 2,057 ischemic stroke patients aged 18 years or older. We divided subjects into two age groups: less than 65 (young and middle aged; 45%) and greater than or equal to 65 years old (elderly; 55.0%). The mean age was 54.2 (± 8.16) years in the young and middle aged patients and 74.8 (± 5.98) years in the elderly patients. The proportions of males in these groups were 70.5% and 56.1%, respectively (Supplementary table 1). Education level was classified into three categories: 1) elementary school: elementary school or six years or less of schooling, 2) middle/high school:

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4 middle school or 7–12 years of schooling, and 3) college/university: college or >12 years of
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6 schooling. A subject was defined as a current drinker if he/she had consumed an alcoholic
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8 drink within one year of the survey date. Functional status was assessed at discharge and at
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10 six months after stroke onset in the Kosco study. In a multiple linear regression analysis, we
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12 used the FIM at discharge to assess the initial ADL status. The FIM scale consisted of 13
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14 physical and 5 cognitive disability items, such as independent eating; grooming;
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16 bathing/showering; dressing the upper or lower body; using the toilet; bladder or bowel
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18 control; 5 different mobility abilities; communication including expression and
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20 comprehension; psychosocial ability; and cognition including problem solving and memory.
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22 Each item was scored from 1 to 7 based on the patient's level of independence, with 1
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24 representing total dependence and 7 representing complete independence. Possible total
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26 scores ranged from 18 to 126, with higher scores indicating greater independence. We
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28 assessed stroke severity using the NIHSS at 7 days after stroke onset. The NIHSS is
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30 composed of 11 items: level of consciousness, gaze, visual field, facial palsy, movement of
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32 arms and legs, limb ataxia, sensory loss, language, dysarthria, and extinction and inattention.
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34 The score of each specific ability ranges from 0 to 4. Possible total scores range from 0 to 42,
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36 with higher scores indicative of some level of impairment.
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46 **Obesity**

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48 BMI was calculated as weight in kilograms divided by the square of height in meters.
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50 We measured each subject's standing height using anthropometry. The patient stood with the
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52 heels together and toes apart and the back of the head, buttocks, and heels in contact with the
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backboard. The head was aligned in the Frankfort horizontal plane. We measured height to one decimal point (cm) with an anthropometric bar on the subject's head. Subjects were weighed in kilograms using a scale when gradation had stabilized after setting the scale to zero with no load. Subjects were classified into five groups based on their baseline BMI at admission: underweight ($\text{BMI} < 18.5$), normal ($18.5 \leq \text{BMI} < 23$), overweight ($23 \leq \text{BMI} < 25$), obese ($25 \leq \text{BMI} < 30$), and extremely obese ($30 \leq \text{BMI}$)^{8 9}.

Stroke risk factors

We assessed stroke risk factors such as HT, DM, dyslipidemia, CKD, and smoking status. Subjects were defined as having HT if they were taking an anti-hypertension drug, had been clinically diagnosed with hypertension, or had either a systolic blood pressure (SBP) ≥ 140 mmHg or a diastolic blood pressure (DBP) ≥ 90 mmHg. Subjects who met one of the following requirements were defined as having DM: taking an oral hyperglycemic agent, using insulin, having received a clinical diagnosis of diabetes, or having a fasting glucose level > 126 mg/dL. Subjects were defined as having dyslipidemia if they met one of the following requirements: diagnosis of hypercholesterolemia, medication history for hypercholesterolemia, total cholesterol (TC) > 200 mg/dL, or low density lipoprotein (LDL) > 130 mg/dL. The estimated glomerular filtration rate (eGFR), used as an indicator of kidney function, was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation¹⁰. The CKD-EPI equation is as follows: $\text{GFR} = 141 \times \min(\text{serum Cr} / \kappa, 1)^\alpha \times \max(\text{serum Cr} / \kappa, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018$ [if female], where κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the smaller value of

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4 serum Cr / κ or 1, and max indicates the larger value of serum Cr / κ or 1. The National Kidney
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6 Foundation Kidney Disease Outcome Quality Initiative defines CKD as an eGFR <60
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8 mL/min/1.73m². A subject was identified as a current smoker if he/she had smoked within
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10 one year of the survey date.
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14 15 16 17 18 19 20 **Statistical Analyses** 21

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23 Differences in general characteristics, clinical data, and covariates among obese
24 patients were analyzed using Student's *t*-test or one-way analysis of variance (ANOVA) for
25 continuous variables and the χ^2 -test for categorical variables. Multiple linear regressions
26 using general linear models with the six-month FIM as the dependent variable and obesity
27 classification, based on BMI, as the independent variable were performed by age group after
28 adjusting for gender, HT, DM, dyslipidemia, CKD, education, smoking, drinking, FIM on
29 discharge, and 7-day NIHSS score.
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Results

The proportions of underweight, normal, overweight, obese, and extremely obese patients were 2.6%, 24.3%, 29.6 %, 37.2% and 6.3%, respectively, in the under 65 age group and 5.5%, 34.5%, 27.9 %, 28.8%, and 3.3 %, respectively, in the 65 or older group. Among young and middle aged patients, the mean FIMs at six months after a stroke for underweight, normal, overweight, obese, and extremely obese individuals were 108.4 (± 27.3), 118.1 (± 16.2), 116.7 (± 20.5), 118.9 (± 18.1), and 120.6 (± 16.1), respectively ($p < 0.05$). Among elderly patients, the mean FIMs at six months after a stroke for the same weight categories were 93.0 (± 38.4), 100.4 (± 33.2), 104.2 (± 32.0), 106.5 (± 29.7), and 111.6 (± 27.8), respectively ($p = \text{non-significant}$) (Table 1).

In a multiple linear regression, the six-month FIM after stroke in elderly group was significantly associated with being extremely obese (7.95, $p < 0.05$) after adjusting for confounding variables. The six-month FIM was not associated with any weight category in the young and middle aged group (Table 2).

Discussion

A higher FIM at six months after stroke onset was associated with extreme obesity in the 65 years and older age group. Our finding is similar to that of the Telemedical Project for Integrative Stroke Care (TEMPiS) trial. The TEMPiS trial included 4,428 elderly patients with acute stroke or TIA and showed that overweight and obese patients had improved survival and better combined outcomes of survival and non-fatal functional status than did with normal-weight patients¹¹. Among the 819 patients admitted to an acute rehabilitation hospital for stroke rehabilitation, overweight patients also had better FIMs than did patients in the other weight categories⁴. Onbiagele *et al.* showed that obese patients with stroke have a lower overall vascular risk than do their leaner counterparts¹². Furthermore, the Atherosclerosis Risk in Communities (ARIC) study confirmed a positive and linear relationship between BMI and ischemic stroke incidence¹³, and overweight and obese patients who survived the first event tended to subsequently have improved CVD^{14 15} and cerebrovascular disease burdens^{16 17}.

Although the obesity paradox¹⁸ indicates that obese patients receive better treatment and care because they are perceived to be at high risk¹⁹, Ryu *et al.* have proposed that the obesity paradox phenomenon has limitations and that there might not be a direct causal relationship between obesity and improved treatment and care due to the association of long-term mortality with initial neurological severity in ischemic stroke patients in Korea²⁰. Obesity increases the bone mineral density and decreases osteoporosis and hip fractures in the elderly²¹. Bamia *et al.* showed that the body weight of elderly individuals was reported to be an independent protecting factor against femoral osteoporosis²². Furthermore, among the 1,077 patients admitted to an acute rehabilitation hospital in the United States, motor FIM

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4 scores increased from admission to discharge in the obese (BMI 30.0-34.9) group³. Our
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6 results also showed that the 6-month FIMs gradually increased as weight category increased
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8 from underweight to extremely obese in both age groups. For this reason, the finding that
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10 obesity is a good predictor for the six-month FIM was not surprising in this study.
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14 Strazzullo *et al.* observed that being overweight or obese is associated, at least in part,
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16 with a progressively increasing risk of ischemic stroke and that this association is
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18 independent of age, lifestyle, and other cardiovascular risk factors²³. Additionally, the China
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20 National Stroke Registry shows that severe obesity is independently associated with higher 3-
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22 month mortality²⁴. However, Jee *et al.* showed that the mortality rate did not increase for
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24 elderly Korean individuals with BMI of 25 or higher. The effect of obesity on mortality in the
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26 elderly can be influenced by various parameters such as existing diseases²⁵. These results do
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28 not indicate that obesity is less harmful to the elderly than to younger people. We believe that
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30 if elderly stroke patients utilize resistance exercises and proper diets, increased muscle mass
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32 and reduced body fat could be expected during a successful stroke rehabilitation.
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37 This study had several limitations. First, it was conducted prospectively with a multi-
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39 center design, which may have impacted data reliability. To counteract this problem, the
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41 KosCo committee leads a training course for rehabilitation specialists twice per year. Second,
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43 height and weight were measured once at admission to our study. Third, we did not account
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45 for the proportions and distributions of muscle, bone, and adipose tissue²⁶ in obese patients in
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47 this study. Thus, further cardiovascular cohort studies that consider these variables are needed
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49 to verify the risk factors for CVA.
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52 53 **Conclusion** 54 55

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4 Our study showed that extreme obesity is a predictor of good functional outcomes in
5 ischemic stroke patients, especially elderly patients. Strength of this study is the high degree
6 of representation of Korean ischemic stroke patients that was achieved. Our results are thus
7 applicable to the entire nation.
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13 14 15 16 17 **Contributorship statement**

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19 Shin Yi Jang, She had made study design, analyzed statistic and discussed interpretation and
20 wrote this paper. Yun-Hee Kim, She had made study design, discussed interpretation and
21 taken all responsibility for this paper. Min Kyun Sohn, He had discussed interpretation.
22
23 Jongmin Lee, He had discussed interpretation. Deog Young Kim, He had discussed
24 interpretation. Sam-Gyu Lee, He had discussed interpretation. Yong-Il Shin, He had discussed
25 interpretation. Gyung-Jae Oh, He had discussed interpretation. Yang-Soo Lee, He had
26 discussed interpretation. Min Cheol Joo, He had discussed interpretation. Eun Young Han,
27 She had discussed interpretation. Won Hyuk Chang, He had discussed interpretation. Ahee
28 Lee, She had discussed interpretation. Jeong Hyun Kim, She had discussed interpretation.
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42 **Competing interest**

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45 The authors declare no competing interest.
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51 **Funding**

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5
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7
8 Korea government (MSIP) (NRF-2014R1A2A1A01005128).
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11 12 13 14 **Data sharing statement**

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17 We will release this study data with the permission of Korea Centers for Disease Control and
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19 Prevention and National Research Foundation of Korea after the study has been completed.
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Table 1. Distribution of general characteristics, stroke risk factors, and covariates by age group and weight group based on body mass index (n=2,057)*

Variables	Underweight (n=86)	Normal (n=616)	Overweight (n=590)	Obese (n=670)	Extremely obese (n=95)
<65 years old (n=925)	n=24	n=225	n=274	n=344	n=58
Body mass index†	17.2±1.12	21.0±1.01	23.5±0.50	26.4±1.29	32.0±2.87
Age, years†	52.0±9.18	53.7±8.44	56.1±7.07	53.9±8.04	50.5±10.1
Gender, male	54.1	67.5	73.3	70.6	74.1
Smoking					
Ex	4.2	12.0	12.4	13.9	15.5
Current	54.1	44.4	47.0	33.3	36.2
Drinking, current	54.1	47.1	50.7	52.3	50.0
Education					
College/university	33.3	31.2	23.0	32.7	29.8
Middle/high school	58.3	58.8	61.2	56.8	54.4
Elementary	8.4	10.0	15.8	10.5	15.8
Hypertension†	58.3	68.0	77.3	88.6	84.4
Diabetes mellitus	50.0	42.2	48.5	52.9	60.3
Dyslipidemia†	25.0	30.2	45.2	43.3	55.1
CKD‡	16.6	3.5	3.6	5.3	8.6
SBP, mmHg†	131.9±23.8	144.7±27.0	147.9±27.8	154.4±27.4	156.8±37.2
DBP, mmHg†	79.5±14.9	85.1±16.1	87.4±14.7	90.1±17.1	90.8±24.6
FBS, mg/dl	139.9±68.1	140.9±80.2	137.3±56.8	143.5±60.5	158.3±78.6
TC, mg/dl‡	172.1±36.0	181.1±43.4	188.2±44.5	193.7±47.6	197.7±47.4
TG, mg/dl‡	128.9±152.4	117.8±79.4	139.4±102.6	154.5±112.4	163.4±124.1
HDL, mg/dl‡	47.5±18.5	48.4±15.0	46.0±11.4	45.0±12.9	43.4±10.9
LDL, mg/dl†	95.9±25.0	108.8±35.9	122.2±44.5	121.6±37.2	136.4±85.9
Creatinine, mg/dl	1.06±1.10	0.90±1.24	0.87±0.62	0.86±0.45	0.99±0.86
eGFR, mL/min/1.73 m ²	93.2±32.1	96.8±19.1	94.1±17.9	94.1±19.6	93.9±23.3
FIM, discharge	94.8±31.6	105.7±22.3	105.6±23.3	106.7±23.0	106.4±26.1
FIM, six months‡	108.4±27.3	118.1±16.2	116.7±20.5	118.9±18.1	120.6±16.1
NIHSS, 7-day	4.38±5.68	3.16±5.01	2.94±4.80	2.55±4.36	2.40±3.74
≥65 years old (n=1,132)	n=62	n=391	n=316	n=326	n=37
Body mass index†	17.4±0.90	20.8±1.05	23.5±0.50	26.2±1.26	31.7±2.67
Age, years†	79.1±5.65	75.7±6.20	74.3±5.57	73.6±5.66	72.6±5.35
Gender, male‡	35.4	58.8	58.8	55.5	45.9
Smoking					
Ex	14.5	17.1	18.6	18.7	13.5
Current	19.3	19.4	16.1	16.2	5.4
Drinking, current	19.3	31.2	24.0	32.2	27.0
Education					
College/university	1.6	10.8	12.9	12.8	18.9
Middle/high school	47.5	36.5	39.7	42.8	32.4
Elementary	50.9	52.7	47.4	44.4	48.7
Hypertension‡	85.4	87.2	86.7	92.9	97.3
Diabetes mellitus	46.7	53.2	56.6	57.6	67.5
Dyslipidemia	20.9	28.9	31.3	32.2	37.8
CKD	29.5	16.7	20.1	18.6	16.6
SBP, mmHg	152.2±32.0	148.9±25.4	148.1±28.8	151.2±26.2	148.6±25.9
DBP, mmHg	81.0±18.9	82.0±12.9	82.0±14.4	83.2±14.5	81.0±12.9
FBS, mg/dl	138.7±67.2	142.2±65.8	144.3±65.7	143.4±56.6	136.5±44.6
TC, mg/dl	176.5±43.0	174.3±39.2	176.0±37.0	175.7±41.7	172.9±49.1
TG, mg/dl†	88.1±41.8	104.8±63.2	111.6±60.8	127.3±77.6	113.6±60.1

HDL, mg/dl†	50.6±13.7	47.4±13.2	44.9±13.3	43.4±11.2	48.7±11.6
LDL, mg/dl	110.2±46.2	107.6±33.4	109.1±32.8	110.4±46.2	112.5±36.5
Creatinine, mg/dl	1.09±1.72	1.08±1.48	0.95±0.57	0.94±0.40	0.86±0.29
eGFR, mL/min/1.73 m ²	72.4±21.3	75.9±20.3	75.6±18.8	74.3±17.9	77.4±16.8
FIM, discharge	81.8±32.8	89.3±31.4	93.1±31.2	95.4±29.3	93.1±31.7
FIM, six months	93.0±38.4	100.4±33.2	104.2±32.0	106.5±29.7	111.6±27.8
NIHSS, 7-day‡	4.95±5.89	4.67±6.06	4.08±6.08	3.49±5.48	3.76±7.82

*Analysis of variance or χ^2 -test

†p<0.001 ‡p<0.05

SD standard deviation;

CKD chronic kidney disease; SBP systolic blood pressure; DBP diastolic blood pressure; FBS fasting blood sugar; TC total cholesterol; TG triglyceride; HDL high density lipoprotein; LDL low density lipoprotein; eGFR estimated glomerular filtration rate; NIHSS National Institutes of Health Stroke Scale; FIM functional independence measure

Table 2. Multiple linear regressions for six months FIM by age group*

Variables	<65 years old		≥65 years old	
	β (95% CI)	p-value	β (95% CI)	p-value
Weight categories				
Underweight	-3.81 (-8.93, 1.31)	0.145	-2.53 (-7.74, 2.67)	0.340
Normal	1.0		1.0	
Overweight	-1.19 (-3.35, 0.97)	0.280	1.17 (-1.67, 4.02)	0.420
Obese	0.05 (-2.05, 2.15)	0.962	0.76 (-2.07, 3.61)	0.596
Extremely obese	1.66 (-1.87, 5.20)	0.355	7.95 (1.41, 14.4)	0.017
Gender, female vs male	0.27 (-1.86, 2.41)	0.800	-1.00 (-3.92, 1.91)	0.501
Education				
College/university	1.0		1.0	
Middle/high school	-1.61 (-3.39, -0.16)	0.074	1.79 (-1.67, 5.26)	0.310
Elementary	-0.38 (-3.12, 2.35)	0.783	1.65 (-1.89, 5.20)	0.360
Smoking, current	0.38 (-0.65, 1.42)	0.467	0.64 (-1.10, 2.38)	0.469
Drinking, current	1.37 (-0.42, 3.17)	0.133	1.34 (-1.51, 4.20)	0.356
Hypertension, yes	-0.20 (-2.19, 1.78)	0.841	-0.03 (-3.65, 3.58)	0.984
Diabetes mellitus, yes	-0.73 (-2.31, 0.85)	0.364	-0.68 (-2.96, 1.59)	0.556
Dyslipidemia, yes	-0.42 (-2.04, 1.19)	0.610	-0.33 (-2.80, 2.14)	0.792
Chronic kidney disease	-3.35 (-7.03, 0.33)	0.075	-3.48 (-6.37, -0.62)	0.017
FIM, discharge	0.36 (0.31, 0.41)	<0.001	0.53 (0.47, 0.58)	<0.001
NIHSS, seven-day	-1.33 (-1.56, -1.10)	<0.001	-1.82 (-2.10, -1.58)	<0.001

* Estimated by multiple linear regression models using the variables in the table

NIHSS National Institutes of Health Stroke Scale; FIM functional independence measure

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Supplementary table 1. Distribution of FIMs at 6 months post-stroke by general characteristics, stroke risk factors, and covariates by age group (n=2,057)

Variables	<65 years old (n=925)		p-value*	≥65 years old (n=1,132)		p-value*
	Mean±SD or %	FIM, 6 month		Mean±SD or %	FIM, 6 month	
Overall	-	117.9±18.6	-	-	103.2±32.2	-
Body mass index	24.3±3.30	-	0.046	23.3±3.18	-	0.003
Underweight	2.6	108.4±27.3		5.5	93.0±38.4	
Normal	24.3	118.1±16.2		34.5	100.4±33.2	
Overweight	29.6	116.7±20.5		27.9	104.2±32.0	
Obese	37.2	118.9±18.1		28.8	106.5±29.7	
Extremely obese	6.3	120.6±16.1		3.3	111.6±27.8	
Age, years	54.2±8.16	-	-	74.8±5.98	-	-
Gender			0.240			<0.001
Male	70.5	118.3±18.3		56.1	89.9±23.2	
Female	29.5	116.8±19.4		43.8	82.1±30.4	
Education			<0.001			<0.001
College	29.3	121.8±12.0		11.8	97.3±17.1	
Middle or High school	58.5	116.4±20.0		39.7	88.3±25.1	
Elementary or under	12.2	115.3±23.4		48.5	80.8±30.7	
Smoking			0.624			0.031
Non	46.2	117.5±19.3		65.1	84.6±28.6	
Ex-	12.9	119.4±16.7		17.8	89.3±23.7	
Current	40.9	117.8±18.5		17.1	90.5±22.5	
Drinking			0.048			0.012
Non	49.5	116.6±20.4		71.3	84.6±28.5	
Current	50.5	119.1±16.7		28.7	90.8±22.2	
Hypertension			0.531			0.197
No	20.7	118.6±17.5		11.0	90.5±22.1	
Yes	79.3	117.7±18.9		89.0	86.3±27.1	
Diabetes mellitus			0.015			0.203
No	50.6	119.3±16.3		44.5	88.6±25.0	
Yes	49.4	116.4±20.7		55.5	85.5±27.5	
Dyslipidemia			0.480			0.381
No	59.0	117.5±19.2		69.6	86.5±27.0	
Yes	41.0	118.4±17.8		30.4	87.8±25.2	
CKD			0.049			0.011
No	95.0	118.2±18.0		81.0	88.2±25.1	
Yes	5.0	112.7±25.4		19.0	78.5±33.1	
SBP, mmHg	149.7±28.5	-	-	149.5±27.0	-	-
DBP, mmHg	87.9±16.9	-	-	82.3±14.2	-	-
FBS, mg/dl	141.9±66.3	-	-	142.7±62.7	-	-
TC, mg/dl	188.7±45.7	-	-	175.3±39.8	-	-
TG, mg/dl	141.2±105.2	-	-	112.7±66.9	-	-
HDL, mg/dl	46.1±13.1	-	-	45.7±12.8	-	-
LDL, mg/dl	119.0±44.1	-	-	109.1±38.1	-	-
Creatinine, mg/dl	0.89±0.80	-	-	1.00±1.03	-	-
eGFR, mL/min/1.73 m ²	94.7±18.7	-	-	75.2±19.2	-	-
FIM, discharge	105.8±23.4	-	-	91.8±31.0	-	-
NIHSS, 7 days	2.85±4.67	-	-	4.15±5.97	-	-
Median (IQR)	1 (0, 3)	-	-	2 (0, 5)	-	-

*Student's *t*-test or analysis of variance for FIM at 6 months post-stroke within categories of general characteristics, stroke risk factors, and covariates

SD standard deviation, IQR interquartile range

CKD chronic kidney disease; SBP systolic blood pressure; DBP diastolic blood pressure; FBS fasting blood sugar; TC total cholesterol; TG triglyceride; HDL high density lipoprotein; LDL low density lipoprotein; eGFR estimated glomerular filtration rate; NIHSS National Institutes of Health Stroke Scale; FIM functional

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independence measure

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The Effect of Obesity on Functional Outcomes at Six Months Post-Stroke among Elderly Koreans: A Prospective Multicenter Study

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**The Effect of Obesity on Functional Outcomes at Six Months Post-Stroke
among Elderly Koreans: A Prospective Multicenter Study**

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ABSTRACT

Objectives We examined whether obesity based on body mass index (BMI) was a predictor of functional independence measure (FIM) at 6 months after ischemic stroke onset while adjusting for stroke risk factors and covariates and stratifying by age group.

Design This is an interim report of the Korean Stroke Cohort for Functioning and Rehabilitation that was designed as a nested case study within a nationwide hospital-based cohort.

Setting We identified all patients who were admitted to nine representative hospitals in Korea from 2012 until 2014 under a diagnosis of acute first-ever ischemic stroke. The hospitals were selected from the metropolitan district, mid-sized cities, and a small-sized city.

Participants The sample included 2,057 acute ischemic stroke patients who were at least 18 years old.

Primary and secondary outcome measures We divided subjects into two age levels (<65 and ≥ 65 years old). Subjects were classified into five groups according to their baseline BMI at admission: underweight (BMI<18.5), normal ($18.5 \leq \text{BMI} < 23$), overweight ($23 \leq \text{BMI} < 25$), obese ($25 \leq \text{BMI} < 30$), and extremely obese ($30 \leq \text{BMI}$).

Results The proportion of patients who were ≥ 65 years old was 55.0%. The proportions of underweight, normal, overweight, obese, and extremely obese patients were 2.6%, 24.3%, 29.6 %, 37.2% and 6.3%, respectively, in the <65 years old group and 5.5%, 34.5%, 27.9 %, 28.8%, and 3.3 %, respectively, in the ≥ 65 years old group. In a multiple linear regression, the six-month FIM after stroke in the elderly group was significantly associated with being extremely obese (7.95, $p < 0.05$) after adjusting for confounding variables. In the <65 years old

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4 group, the six-month FIM was not associated with any weight category.
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10 **Conclusion** This nationwide hospital-based cohort study showed that extreme obesity is a
11 predictor of a good six-month FIM, especially in ischemic stroke patients who are at least 65
12 years of age.
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20 Keywords: obese, body mass index, elderly, ischemic stroke, functional independence
21 measure
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28 **Article summary**

29 **Strengths and limitations of this study**

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32 - Stroke patients who were extremely obese better performed activities of daily living than
33 did patients with a normal BMI among patients 65 years of age or older. However, the six-
34 month FIM was not associated with any weight category in the under 65 age group.
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38 - The functional independence measurement was evaluated for daily living activities.
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41 - Subjects' heights and weights were measured once upon admission to our study.
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44 - We did not account for the proportions and distributions of muscle, bone, and adipose tissue
45 in obese patients in this study.
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Introduction

The prevalence of obesity in Korea was shown to be 32.5% among individuals aged 20 years or older (32.2% in those 20-64 years old and 34.3% in those over 65 years old) in the 2013 Korea National Health and Nutrition Examination Survey¹. Obesity is one of the leading risk factors for cardiovascular disease². However, obese and overweight patients undergoing acute rehabilitation showed higher functional outcomes than did patients in a normal weight range based on body mass index (BMI)³. Obesity is also known to be a good predictor of functional outcomes in ischemic stroke patients⁴, especially elderly patients⁵. Furthermore, post-stroke mortality is inversely related to BMI: overweight and obese stroke patients had a lower post-stroke mortality rate than normal-weight and underweight patients in a study from Denmark⁶.

Functional outcomes such as the functional independence measurement (FIM) are used to evaluate the ability of individuals to perform activities of daily living. Functional outcomes in ischemic stroke patients sharply increase from 2 to 6 months after the stroke, and ability of daily living (ADL) were recovered slowly in the chronic stage 6 months after the stroke⁷. However, few studies have analyzed functional outcomes in relation to obesity at six months post-stroke. Therefore, we examined whether obesity based on BMI was predictive of the six-month post-stroke FIM after adjustment for gender, education, smoking, drinking, hypertension (HT), diabetes mellitus (DM), dyslipidemia, chronic kidney disease (CKD), discharge FIM, and 7-day National Institutes of Health Stroke Scale (NIHSS) score and stratification by two age groups: less than 65 years and greater than or equal to 65 years.

Methods

This is an interim report of the Korean Stroke Cohort for Functioning and Rehabilitation (KOSCO). We identified all patients of at least 18 years of age who were admitted to nine representative hospitals in Korea under a diagnosis of acute first-ever stroke, either ischemic or hemorrhagic, from January 2012 until October 2014. The hospitals were selected from the metropolitan district (Samsung Medical Center, Yonsei University Hospital, and Konkuk University Hospital), mid-sized cities (Chungnam National University Hospital, Pusan National University Hospital, Chonnam National University Hospital, Wonkwang University Hospital, and Kyung-pook National University Hospital), and a small-sized city (Jeju University Hospital). Acute stroke patients were defined as those experiencing ischemic or hemorrhagic stroke who were admitted within seven days of the onset of stroke symptoms. Patients experiencing a transient ischemic attack (TIA) or who were admitted more than seven days after symptom onset were excluded. TIA was defined as symptoms resolving within 24 hours of onset and no evidence of acute infarction by brain CT or MRI. The medical records of all subjects were reviewed by well-trained rehabilitation specialists. The study protocol was approved by the Samsung Medical Center Institutional Review Board.

The nationwide hospital-based cohort study population included 2,057 ischemic stroke patients aged 18 years or older. We divided subjects into two age groups: less than 65 (young and middle aged; 45%) and greater than or equal to 65 years old (elderly; 55.0%). The mean age was 54.2 (± 8.16) years in the young and middle aged patients and 74.8 (± 5.98) years in the elderly patients. The proportions of males in these groups were 70.5% and 56.1%, respectively (Supplementary table 1). Education level was classified into three categories: 1) elementary school: elementary school or six years or less of schooling, 2) middle/high school:

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4 middle school or 7–12 years of schooling, and 3) college/university: college or >12 years of
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6 schooling. A subject was defined as a current drinker if he/she had consumed an alcoholic
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8 drink within one year of the survey date. Functional status was assessed at discharge and at
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10 six months after stroke onset in the KOSCO study. In a multiple linear regression analysis,
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12 we used the FIM at discharge to assess the initial ADL status. The FIM scale consisted of 13
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14 physical and 5 cognitive disability items, such as independent eating; grooming;
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16 bathing/showering; dressing the upper or lower body; using the toilet; bladder or bowel
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18 control; 5 different mobility abilities; communication including expression and
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20 comprehension; psychosocial ability; and cognition, including problem solving and memory.
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22 Each item was scored from 1 to 7 based on the patient's level of independence, with 1
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24 representing total dependence and 7 representing complete independence. Possible total
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26 scores ranged from 18 to 126, with higher scores indicating greater independence. We
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28 assessed stroke severity using the NIHSS at 7 days after stroke onset. The NIHSS is
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30 composed of 11 items: level of consciousness, gaze, visual field, facial palsy, movement of
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32 arms and legs, limb ataxia, sensory loss, language, dysarthria, and extinction and inattention.
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34 The score of each specific ability ranges from 0 to 4. Possible total scores range from 0 to 42,
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36 with higher scores indicative of some level of impairment.
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46 **Obesity**

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48 BMI was calculated as weight in kilograms divided by the square of height in meters.
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50 We measured each subject's standing height using anthropometry. The patient stood with the
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52 heels together and toes apart and the back of the head, buttocks, and heels in contact with the
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backboard. The head was aligned in the Frankfort horizontal plane. We measured height to one decimal point (cm) with an anthropometric bar on the subject's head. Subjects were weighed in kilograms using a scale when gradation had stabilized after setting the scale to zero with no load. Subjects were classified into five groups based on their baseline BMI at admission: underweight ($\text{BMI} < 18.5$), normal ($18.5 \leq \text{BMI} < 23$), overweight ($23 \leq \text{BMI} < 25$), obese ($25 \leq \text{BMI} < 30$), and extremely obese ($30 \leq \text{BMI}$)^{8 9}.

Stroke risk factors

We assessed stroke risk factors such as HT, DM, dyslipidemia, CKD, and smoking status. Subjects were defined as having HT if they were taking an anti-hypertension drug, had been clinically diagnosed with hypertension, or had either a systolic blood pressure (SBP) ≥ 140 mmHg or a diastolic blood pressure (DBP) ≥ 90 mmHg. Subjects who met one of the following requirements were defined as having DM: taking an oral hyperglycemic agent, using insulin, having received a clinical diagnosis of diabetes, or having a fasting glucose level > 126 mg/dL. Subjects were defined as having dyslipidemia if they met one of the following requirements: diagnosis of hypercholesterolemia, medication history for hypercholesterolemia, total cholesterol (TC) > 200 mg/dL, or low density lipoprotein (LDL) > 130 mg/dL. The estimated glomerular filtration rate (eGFR), used as an indicator of kidney function, was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation¹⁰. The CKD-EPI equation is as follows: $\text{GFR} = 141 \times \min(\text{serum Cr} / \kappa, 1)^\alpha \times \max(\text{serum Cr} / \kappa, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018$ [if female], where κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the smaller value of

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4 serum Cr / κ or 1, and max indicates the larger value of serum Cr / κ or 1. The National Kidney
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6 Foundation Kidney Disease Outcome Quality Initiative defines CKD as an eGFR <60
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8 mL/min/1.73m². A subject was identified as a current smoker if he/she had smoked within
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10 one year of the survey date.
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14 15 16 17 18 19 20 **Statistical Analyses** 21

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23 Differences in general characteristics, clinical data, and covariates among obese
24 patients were analyzed using Student's *t*-test or one-way analysis of variance (ANOVA) for
25 continuous variables and the χ^2 -test for categorical variables. Multiple linear regressions
26 using general linear models with the six-month FIM as the dependent variable and obesity
27 classification, based on BMI, as the independent variable were performed by age group after
28 adjusting for gender, HT, DM, dyslipidemia, CKD, education, smoking, drinking, FIM on
29 discharge, and 7-day NIHSS score.
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Results

The proportions of underweight, normal, overweight, obese, and extremely obese patients were 2.6%, 24.3%, 29.6 %, 37.2% and 6.3%, respectively, in the under 65 age group and 5.5%, 34.5%, 27.9 %, 28.8%, and 3.3 %, respectively, in the 65 or older group. For drinking, the proportion by obese classification was about 50% in young and middle aged patients and about 20-30% in elderly patients. The proportions of anti-hypertensive agent, anti-DM agent, and lipid lowering agent were about 20-40%, 10-20%, and 0-10%, respectively, in young and middle aged patients and about 30-80%, 20-40%, and 5-20%, respectively, in elderly patients. Among young and middle aged patients, the mean FIMs at six months after a stroke for underweight, normal, overweight, obese, and extremely obese individuals were 108.4 (± 27.3), 118.1 (± 16.2), 116.7 (± 20.5), 118.9 (± 18.1), and 120.6 (± 16.1), respectively ($p < 0.05$). Among elderly patients, the mean FIMs at six months after a stroke for the same weight categories were 93.0 (± 38.4), 100.4 (± 33.2), 104.2 (± 32.0), 106.5 (± 29.7), and 111.6 (± 27.8), respectively ($p = \text{non-significant}$) (Table 1).

In a multiple linear regression, the six-month FIM after stroke in elderly group was significantly associated with being extremely obese (7.95, $p < 0.05$) after adjusting for confounding variables. The six-month FIM was not associated with any weight category in the young and middle aged group (Table 2).

Discussion

A higher FIM at six months after stroke onset was associated with extreme obesity in the 65 years and older age group. Our finding is similar to that of the Telemedical Project for Integrative Stroke Care (TEMPiS) trial. The TEMPiS trial included 4,428 elderly patients with acute stroke or TIA and showed that overweight and obese patients had improved survival and better combined outcomes of survival and non-fatal functional status than did with normal-weight patients¹¹. Among the 819 patients admitted to an acute rehabilitation hospital for stroke rehabilitation, overweight patients also had better FIMs than did patients in the other weight categories⁴. Onbiagele *et al.* showed that obese patients with stroke have a lower overall vascular risk than do their leaner counterparts¹². Furthermore, the Atherosclerosis Risk in Communities (ARIC) study confirmed a positive and linear relationship between BMI and ischemic stroke incidence¹³, and overweight and obese patients who survived the first event tended to subsequently have improved cardiovascular disease^{14 15} and cerebrovascular disease burdens^{16 17}.

Although the obesity paradox¹⁸ indicates that obese patients receive better treatment and care because they are perceived to be at high risk¹⁹, Ryu *et al.* have proposed that the obesity paradox phenomenon has limitations and that there might not be a direct causal relationship between obesity and improved treatment and care due to the association of long-term mortality with initial neurological severity in ischemic stroke patients in Korea²⁰. Obesity increases the bone mineral density and decreases osteoporosis and hip fractures in the elderly²¹. Bamia *et al.* showed that the body weight of elderly individuals was reported to be an independent protecting factor against femoral osteoporosis²². Furthermore, among the 1,077 patients admitted to an acute rehabilitation hospital in the United States, motor FIM

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4 scores increased from admission to discharge in the obese (BMI 30.0-34.9) group³. Our
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6 results also showed that the 6-month FIMs gradually increased as weight category increased
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8 from underweight to extremely obese in both age groups. For this reason, the finding that
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10 obesity is a good predictor for the six-month FIM was not surprising in this study.
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14 Strazzullo *et al.* observed that being overweight or obese is associated, at least in part,
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16 with a progressively increasing risk of ischemic stroke and that this association is
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18 independent of age, lifestyle, and other cardiovascular risk factors²³. Additionally, the China
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20 National Stroke Registry shows that severe obesity is independently associated with higher 3-
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22 month mortality²⁴. However, Jee *et al.* showed that the mortality rate did not increase for
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24 elderly Korean individuals with BMI of 25 or higher. The effect of obesity on mortality in the
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26 elderly can be influenced by various parameters such as existing diseases²⁵. These results do
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28 not indicate that obesity is less harmful to the elderly than to younger people. We believe that
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30 if elderly stroke patients utilize resistance exercises and proper diets, increased muscle mass
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32 and reduced body fat could be expected during a successful stroke rehabilitation.
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37 This study had several limitations. First, it was conducted prospectively with a multi-
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39 center design, which may have impacted data reliability. To counteract this problem, the
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41 KOSCO committee leads a training course for rehabilitation specialists twice per year.
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43 Second, height and weight were measured once at admission to our study. Third, we did not
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45 account for the proportions and distributions of muscle, bone, and adipose tissue²⁶ in obese
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47 patients in this study. Thus, further cardiovascular cohort studies that consider these variables
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49 are needed to verify the risk factors for cerebrovascular accident.
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52 53 **Conclusion**

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4 Our study showed that extreme obesity is a predictor of good functional outcomes in
5 ischemic stroke patients, especially elderly patients. Strength of this study is the high degree
6 of representation of Korean ischemic stroke patients that was achieved. Our results are thus
7 applicable to the entire nation.
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14 15 16 17 **Contributorship statement**

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19 Shin Yi Jang, She had made study design, analyzed statistic and discussed interpretation and
20 wrote this paper. Yong-Il Shin, He had discussed interpretation. Deog Young Kim, He had
21 discussed interpretation. Min Kyun Sohn, He had discussed interpretation. Jongmin Lee, He
22 had discussed interpretation. Min Kyun Sohn, He had discussed interpretation. Jongmin Lee, He
23 had discussed interpretation. Sam-Gyu Lee, He had discussed interpretation. Gyung-Jae Oh,
24 He had discussed interpretation. Yang-Soo Lee, He had discussed interpretation. Min Cheol
25 Joo, He had discussed interpretation. Eun Young Han, She had discussed interpretation. Won
26 Hyuk Chang, He had discussed interpretation. Chung Kang, She had discussed interpretation.
27 And Yun-Hee Kim, she had made study design, discussed interpretation and taken all
28 responsibility for this paper.
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42 **Competing interest**

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45 The authors declare no competing interest.
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51 **Funding**

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5
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7
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11 12 13 14 **Data sharing statement** 15

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Table 1. Distribution of general characteristics, stroke risk factors, and covariates by age group and weight group based on body mass index (n=2,057)*

Variables	Underweight (n=86)	Normal (n=616)	Overweight (n=590)	Obese (n=670)	Extremely obese (n=95)
<65 years old (n=925)	n=24	n=225	n=274	n=344	n=58
Body mass index†	17.2±1.12	21.0±1.01	23.5±0.50	26.4±1.29	32.0±2.87
Age, years†	52.0±9.18	53.7±8.44	56.1±7.07	53.9±8.04	50.5±10.1
Gender, male	54.1	67.5	73.3	70.6	74.1
Smoking					
Ex	4.2	12.0	12.4	13.9	15.5
Current	54.1	44.4	47.0	33.3	36.2
Drinking, current	54.1	47.1	50.7	52.3	50.0
Education					
College/university	33.3	31.2	23.0	32.7	29.8
Middle/high school	58.3	58.8	61.2	56.8	54.4
Elementary	8.4	10.0	15.8	10.5	15.8
Hypertension†	58.3	68.0	77.3	88.6	84.4
Diabetes mellitus	50.0	42.2	48.5	52.9	60.3
Dyslipidemia†	25.0	30.2	45.2	43.3	55.1
CKD‡	16.6	3.5	3.6	5.3	8.6
Taking a medicine, yes					
Anti-hypertensive agent†	29.1	22.2	35.4	37.7	37.9
Anti-DM agent	20.8	11.1	13.8	17.4	17.2
Lipid lowering agent	0.0	4.4	8.0	8.7	8.6
SBP, mmHg†	131.9±23.8	144.7±27.0	147.9±27.8	154.4±27.4	156.8±37.2
DBP, mmHg†	79.5±14.9	85.1±16.1	87.4±14.7	90.1±17.1	90.8±24.6
FBS, mg/dl	139.9±68.1	140.9±80.2	137.3±56.8	143.5±60.5	158.3±78.6
TC, mg/dl‡	172.1±36.0	181.1±43.4	188.2±44.5	193.7±47.6	197.7±47.4
TG, mg/dl‡	128.9±152.4	117.8±79.4	139.4±102.6	154.5±112.4	163.4±124.1
HDL, mg/dl‡	47.5±18.5	48.4±15.0	46.0±11.4	45.0±12.9	43.4±10.9
LDL, mg/dl†	95.9±25.0	108.8±35.9	122.2±44.5	121.6±37.2	136.4±85.9
Creatinine, mg/dl	1.06±1.10	0.90±1.24	0.87±0.62	0.86±0.45	0.99±0.86
eGFR, mL/min/1.73 m ²	93.2±32.1	96.8±19.1	94.1±17.9	94.1±19.6	93.9±23.3
FIM, discharge	94.8±31.6	105.7±22.3	105.6±23.3	106.7±23.0	106.4±26.1
FIM, six months‡	108.4±27.3	118.1±16.2	116.7±20.5	118.9±18.1	120.6±16.1
NIHSS, 7-day	4.38±5.68	3.16±5.01	2.94±4.80	2.55±4.36	2.40±3.74
≥65 years old (n=1,132)	n=62	n=391	n=316	n=326	n=37
Body mass index†	17.4±0.90	20.8±1.05	23.5±0.50	26.2±1.26	31.7±2.67
Age, years†	79.1±5.65	75.7±6.20	74.3±5.57	73.6±5.66	72.6±5.35
Gender, male‡	35.4	58.8	58.8	55.5	45.9
Smoking					
Ex	14.5	17.1	18.6	18.7	13.5
Current	19.3	19.4	16.1	16.2	5.4
Drinking, current	19.3	31.2	24.0	32.2	27.0
Education					
College/university	1.6	10.8	12.9	12.8	18.9
Middle/high school	47.5	36.5	39.7	42.8	32.4
Elementary	50.9	52.7	47.4	44.4	48.7
Hypertension‡	85.4	87.2	86.7	92.9	97.3
Diabetes mellitus	46.7	53.2	56.6	57.6	67.5
Dyslipidemia	20.9	28.9	31.3	32.2	37.8
CKD	29.5	16.7	20.1	18.6	16.6
Taking a medicine, yes					

Anti-hypertensive agent†	32.2	51.9	51.5	60.7	83.7
Anti-DM agent	19.3	23.7	21.5	27.6	40.5
Lipid lowering agent‡	4.8	8.4	14.8	12.8	18.9
SBP, mmHg	152.2±32.0	148.9±25.4	148.1±28.8	151.2±26.2	148.6±25.9
DBP, mmHg	81.0±18.9	82.0±12.9	82.0±14.4	83.2±14.5	81.0±12.9
FBS, mg/dl	138.7±67.2	142.2±65.8	144.3±65.7	143.4±56.6	136.5±44.6
TC, mg/dl	176.5±43.0	174.3±39.2	176.0±37.0	175.7±41.7	172.9±49.1
TG, mg/dl†	88.1±41.8	104.8±63.2	111.6±60.8	127.3±77.6	113.6±60.1
HDL, mg/dl†	50.6±13.7	47.4±13.2	44.9±13.3	43.4±11.2	48.7±11.6
LDL, mg/dl	110.2±46.2	107.6±33.4	109.1±32.8	110.4±46.2	112.5±36.5
Creatinine, mg/dl	1.09±1.72	1.08±1.48	0.95±0.57	0.94±0.40	0.86±0.29
eGFR, mL/min/1.73 m ²	72.4±21.3	75.9±20.3	75.6±18.8	74.3±17.9	77.4±16.8
FIM, discharge	81.8±32.8	89.3±31.4	93.1±31.2	95.4±29.3	93.1±31.7
FIM, six months	93.0±38.4	100.4±33.2	104.2±32.0	106.5±29.7	111.6±27.8
NIHSS, 7-day‡	4.95±5.89	4.67±6.06	4.08±6.08	3.49±5.48	3.76±7.82

*Analysis of variance or χ^2 -test

†p<0.001 ‡p<0.05

SD standard deviation;

CKD chronic kidney disease; DM Diabetes mellitus, SBP systolic blood pressure; DBP diastolic blood pressure; FBS fasting blood sugar; TC total cholesterol; TG triglyceride; HDL high density lipoprotein; LDL low density lipoprotein; eGFR estimated glomerular filtration rate; NIHSS National Institutes of Health Stroke Scale; FIM functional independence measure

Table 2. Multiple linear regressions for six months FIM by age group*

Variables	<65 years old		≥65 years old	
	β (95% CI)	p-value	β (95% CI)	p-value
Weight categories				
Underweight	-3.81 (-8.93, 1.31)	0.145	-2.53 (-7.74, 2.67)	0.340
Normal	1.0		1.0	
Overweight	-1.19 (-3.35, 0.97)	0.280	1.17 (-1.67, 4.02)	0.420
Obese	0.05 (-2.05, 2.15)	0.962	0.76 (-2.07, 3.61)	0.596
Extremely obese	1.66 (-1.87, 5.20)	0.355	7.95 (1.41, 14.4)	0.017
Gender, female vs male	0.27 (-1.86, 2.41)	0.800	-1.00 (-3.92, 1.91)	0.501
Education				
College/university	1.0		1.0	
Middle/high school	-1.61 (-3.39, -0.16)	0.074	1.79 (-1.67, 5.26)	0.310
Elementary	-0.38 (-3.12, 2.35)	0.783	1.65 (-1.89, 5.20)	0.360
Smoking, current	0.38 (-0.65, 1.42)	0.467	0.64 (-1.10, 2.38)	0.469
Drinking, current	1.37 (-0.42, 3.17)	0.133	1.34 (-1.51, 4.20)	0.356
Hypertension, yes	-0.20 (-2.19, 1.78)	0.841	-0.03 (-3.65, 3.58)	0.984
Diabetes mellitus, yes	-0.73 (-2.31, 0.85)	0.364	-0.68 (-2.96, 1.59)	0.556
Dyslipidemia, yes	-0.42 (-2.04, 1.19)	0.610	-0.33 (-2.80, 2.14)	0.792
Chronic kidney disease	-3.35 (-7.03, 0.33)	0.075	-3.48 (-6.37, -0.62)	0.017
FIM, discharge	0.36 (0.31, 0.41)	<0.001	0.53 (0.47, 0.58)	<0.001
NIHSS, seven-day	-1.33 (-1.56, -1.10)	<0.001	-1.82 (-2.10, -1.58)	<0.001

* Estimated by multiple linear regression models using the variables in the table

NIHSS National Institutes of Health Stroke Scale; FIM functional independence measure

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Supplementary table 1. Distribution of FIMs at 6 months post-stroke by general characteristics, stroke risk factors, and covariates by age group (n=2,057)

Variables	<65 years old (n=925)		p-value*	≥65 years old (n=1,132)		p-value*
	Mean±SD or %	FIM, 6 month		Mean±SD or %	FIM, 6 month	
Overall	-	117.9±18.6	-	-	103.2±32.2	-
Body mass index	24.3±3.30	-	0.046	23.3±3.18	-	0.003
Underweight	2.6	108.4±27.3		5.5	93.0±38.4	
Normal	24.3	118.1±16.2		34.5	100.4±33.2	
Overweight	29.6	116.7±20.5		27.9	104.2±32.0	
Obese	37.2	118.9±18.1		28.8	106.5±29.7	
Extremely obese	6.3	120.6±16.1		3.3	111.6±27.8	
Age, years	54.2±8.16	-	-	74.8±5.98	-	-
Gender			0.240			<0.001
Male	70.5	118.3±18.3		56.1	89.9±23.2	
Female	29.5	116.8±19.4		43.8	82.1±30.4	
Education			<0.001			<0.001
College	29.3	121.8±12.0		11.8	97.3±17.1	
Middle or High school	58.5	116.4±20.0		39.7	88.3±25.1	
Elementary or under	12.2	115.3±23.4		48.5	80.8±30.7	
Smoking			0.624			0.031
Non	46.2	117.5±19.3		65.1	84.6±28.6	
Ex-	12.9	119.4±16.7		17.8	89.3±23.7	
Current	40.9	117.8±18.5		17.1	90.5±22.5	
Drinking			0.048			0.012
Non	49.5	116.6±20.4		71.3	84.6±28.5	
Current	50.5	119.1±16.7		28.7	90.8±22.2	
Hypertension			0.531			0.197
No	20.7	118.6±17.5		11.0	90.5±22.1	
Yes	79.3	117.7±18.9		89.0	86.3±27.1	
Diabetes mellitus			0.015			0.203
No	50.6	119.3±16.3		44.5	88.6±25.0	
Yes	49.4	116.4±20.7		55.5	85.5±27.5	
Dyslipidemia			0.480			0.381
No	59.0	117.5±19.2		69.6	86.5±27.0	
Yes	41.0	118.4±17.8		30.4	87.8±25.2	
CKD			0.049			0.011
No	95.0	118.2±18.0		81.0	88.2±25.1	
Yes	5.0	112.7±25.4		19.0	78.5±33.1	
SBP, mmHg	149.7±28.5	-	-	149.5±27.0	-	-
DBP, mmHg	87.9±16.9	-	-	82.3±14.2	-	-
FBS, mg/dl	141.9±66.3	-	-	142.7±62.7	-	-
TC, mg/dl	188.7±45.7	-	-	175.3±39.8	-	-
TG, mg/dl	141.2±105.2	-	-	112.7±66.9	-	-
HDL, mg/dl	46.1±13.1	-	-	45.7±12.8	-	-
LDL, mg/dl	119.0±44.1	-	-	109.1±38.1	-	-
Creatinine, mg/dl	0.89±0.80	-	-	1.00±1.03	-	-
eGFR, mL/min/1.73 m ²	94.7±18.7	-	-	75.2±19.2	-	-
FIM, discharge	105.8±23.4	-	-	91.8±31.0	-	-
NIHSS, 7 days	2.85±4.67	-	-	4.15±5.97	-	-
Median (IQR)	1 (0, 3)	-	-	2 (0, 5)	-	-

*Student's *t*-test or analysis of variance for FIM at 6 months post-stroke within categories of general characteristics, stroke risk factors, and covariates

SD standard deviation, IQR interquartile range

CKD chronic kidney disease; SBP systolic blood pressure; DBP diastolic blood pressure; FBS fasting blood sugar; TC total cholesterol; TG triglyceride; HDL high density lipoprotein; LDL low density lipoprotein; eGFR estimated glomerular filtration rate; NIHSS National Institutes of Health Stroke Scale; FIM functional

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independence measure

For peer review only

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract → Page 1,2 (b) Provide in the abstract an informative and balanced summary of what was done and what was found → Page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported → Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses → Page 4
Methods		
Study design	4	Present key elements of study design early in the paper → Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection → Page 5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up → Page 5 <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls → Non applicable (NA) <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants → NA (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case → NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable → Page 5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group → Page 5
Bias	9	Describe any efforts to address potential sources of bias → Page 11
Study size	10	Explain how the study size was arrived at → Page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,

		describe which groupings were chosen and why → Page 5-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding → Page 8
		(b) Describe any methods used to examine subgroups and interactions → NA
		(c) Explain how missing data were addressed → No missing data in this study, because we used follow up data post stroke 6 months. We stated it page 6 as the following: “Functional status was assessed at discharge and at six months after stroke onset in the KOSCO study.”
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy → NA
		(e) Describe any sensitivity analyses → NA

Continued on next page

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed → Page 5
		(b) Give reasons for non-participation at each stage → NA
		(c) Consider use of a flow diagram → NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders → Page 9
		(b) Indicate number of participants with missing data for each variable of interest → No missing data in this study, because we used follow up data post stroke 6 months. We stated it page 6 as the following: “Functional status was assessed at discharge and at six months after stroke onset in the KOSCO study.”
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount) → Page 6
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time → Page 9
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure → NA
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures → NA
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included → Page 9
		(b) Report category boundaries when continuous variables were categorized → Page 9
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period → NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses → NA
Discussion		
Key results	18	Summarise key results with reference to study objectives → Page 10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias → Page 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence → Page 10-12

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2 Generalisability 21 Discuss the generalisability (external validity) of the study results

3 → Page 12

4 **Other information**

5
6 Funding 22 Give the source of funding and the role of the funders for the present study and, if applicable,
7 for the original study on which the present article is based

8 → Page 12-13

9
10
11 *Give information separately for cases and controls in case-control studies and, if applicable, for exposed and
12 unexposed groups in cohort and cross-sectional studies.

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14 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and
15 published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely
16 available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at
17 <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is
18 available at www.strobe-statement.org.
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