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Effect of obesity on functional outcomes at 6 months post-stroke among elderly Koreans: a prospective multicentre 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 ischaemic 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 ischaemic stroke. The hospitals were selected from the metropolitan district, mid-sized cities and a small-sized city.

Participants: The sample included 2057 patients with acute ischaemic stroke who were at least 18 years old.

Primary and secondary outcome measures: We divided participants into two age levels (<65 and ≥65 years). Participants were classified into five groups according to their baseline BMI at admission: underweight (BMI<18.5), normal (18.5≤BMI<23), overweight (23≤BMI<25), obese (25≤BMI<30) and extremely obese (30≤BMI).

Results: The proportion of patients who were aged ≥65 years 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 group and 5.5%, 34.5%, 27.9%, 28.8% and 3.3%, respectively, in the ≥65 years group. In a multiple linear regression, the 6-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 group, the 6-month FIM was not associated with any weight category.

Conclusions: This nationwide hospital-based cohort study showed that extreme obesity is a predictor of a good 6-month FIM, especially in patients with ischaemic stroke who are at least 65 years of age.

Strengths and limitations of this study

- Patients with stroke who were extremely obese performed activities of daily living better than did patients with a normal body mass index among patients aged 65 years or older. However, the 6-month functional independence measure (FIM) was not associated with any weight category in the under 65 age group.
- The FIM was evaluated for daily living activities.
- Participants' heights and weights were measured once on admission to our study.
- We did not account for the proportions and distributions of muscle, bone and adipose tissue in obese patients in this study.

INTRODUCTION

The prevalence of obesity in Korea was shown to be 32.5% among individuals aged 20 years or older (32.2% in those aged 20–64 years and 34.3% in those over 65 years) in the 2013 Korea National Health and Nutrition Examination Survey.[1] Obesity is one of the leading risk factors for cardiovascular disease.[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 patients with ischaemic stroke,[4] especially elderly patients.[5] Furthermore, post-stroke mortality is inversely related to BMI: overweight and obese patients with stroke had a lower post-stroke mortality rate than normal-weight and underweight patients in a study from Denmark.[6]

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 patients with ischaemic stroke sharply increase from 2 to

6 months after the stroke, and ability of daily living (ADL) was recovered slowly in the chronic stage 6 months after the stroke.[7] However, few studies have analysed functional outcomes in relation to obesity at 6 months post-stroke. Therefore, we examined whether obesity based on BMI was predictive of the 6-month post-stroke FIM after adjustment for gender, education, smoking, drinking, hypertension (HT), diabetes mellitus (DM), dyslipidaemia, 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 ischaemic or haemorrhagic, 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). Patients with acute stroke were defined as those experiencing ischaemic or haemorrhagic stroke who were admitted within 7 days of the onset of stroke symptoms. Patients experiencing a transient ischaemic attack (TIA) or who were admitted more than 7 days after symptom onset were excluded. TIA was defined as symptoms resolving within 24 h of onset and no evidence of acute infarction by brain CT or MRI. The medical records of all participants 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 2057 patients with ischaemic stroke aged 18 years or older. We divided participants into two age groups: less than 65 years (young and middle-aged; 45%) and greater than or equal to 65 years (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 (see online supplementary table S1). Education level was classified into three categories: (1) elementary school: elementary school or 6 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 schooling. A participant was defined as a current drinker if he/she had consumed an alcoholic drink within 1 year of the survey date. Functional status was assessed at discharge and at 6 months after stroke onset in the KOSCO study. In a multiple linear regression analysis, we used the FIM at discharge to assess the initial ADL status. The FIM scale consisted of 13 physical and 5 cognitive disability items, such as independent eating; grooming; bathing/showering; dressing the upper or lower body; using the toilet; bladder or bowel control; 5 different mobility abilities; communication including expression and comprehension; psychosocial ability; and cognition, including problem-solving and memory. Each item was scored from one to seven based on the patient's level of independence, with one representing total dependence and seven representing complete independence. Possible total scores ranged from 18 to 126, with higher scores indicating greater independence. We assessed stroke severity using the NIHSS at 7 days after stroke onset. The NIHSS is composed of 11 items: level of consciousness, gaze, visual field, facial palsy, movement of arms and legs, limb ataxia, sensory loss, language, dysarthria, and extinction and inattention. The score of each specific ability ranges from 0 to 4. Possible total scores range from 0 to 42, with higher scores indicative of some level of impairment.

Obesity

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

Stroke risk factors

We assessed stroke risk factors such as HT, DM, dyslipidaemia, CKD and smoking status. Participants were defined as having HT if they were taking an anti-HT drug, had been clinically diagnosed with hypertension, or had either a systolic blood pressure (SBP) ≥140 mm Hg or a diastolic blood pressure (DBP) ≥90 mm Hg. Participants who met one of the following requirements were defined as having DM: taking an oral hyperglycaemic agent, using insulin, having received a clinical diagnosis of diabetes, or having a fasting glucose level >126 mg/dL. Participants were defined as having dyslipidaemia if they met one of the following requirements: diagnosis of hypercholesterolaemia, medication history for hypercholesterolaemia, total cholesterol (TC) >200 mg/dL, or low density lipoprotein (LDL)

Table 1 Distribution of general characteristics, stroke risk factors and covariates by age group and weight group based on body mass index (n=2057)*

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
Dyslipidaemia†	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, mm Hg†	131.9±23.8	144.7±27.0	147.9±27.8	154.4±27.4	156.8±37.2
DBP, mm Hg†	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, 6 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=1132)	**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
Dyslipidaemia	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, mm Hg	152.2±32.0	148.9±25.4	148.1±28.8	151.2±26.2	148.6±25.9
DBP, mm Hg	81.0±18.9	82.0±12.9	82.0±14.4	83.2±14.5	81.0±12.9

Continued

Table 1 Continued

≥65 years old (n=1132)	n=62	n=391	n=316	n=326	n=37
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, 6 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

†p<0.001; ‡p<0.05.
*Analysis of variance or χ^2 test.
CKD, chronic kidney disease; DBP, diastolic blood pressure; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FBS, fasting blood sugar; FIM, functional independence measure; HDL, high density lipoprotein; LDL, low density lipoprotein; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

>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) equation.[10] The CKD-EPI equation is as follows: $GFR=141\times\min(\text{serum Cr}/\kappa, 1)^{\alpha}\times\max(\text{serum Cr}/\kappa, 1)^{-1.209}\times0.993^{Age}\times1.018$ (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 serum Cr/κ or 1, and max indicates the larger value of serum Cr/κ or 1. The National Kidney Foundation Kidney Disease Outcome Quality Initiative defines CKD as an eGFR <60 mL/min/1.73 m^2. A participant was identified as a current smoker if he/she had smoked within 1 year of the survey date.

Statistical analyses

Differences in general characteristics, clinical data and covariates among obese patients were analysed using Student's t test or one-way analysis of variance for continuous variables and the χ^2 test for categorical variables. Multiple linear regressions using general linear models with the 6-month FIM as the dependent variable and obesity classification, based on BMI, as the independent variable were performed by age group after adjusting for gender, HT, DM, dyslipidaemia, CKD, education, smoking, drinking, FIM on discharge and 7-day NIHSS score.

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 years 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 antihypertensive 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 6 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 6 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=non-significant) (table 1).

In a multiple linear regression, the 6-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. The 6-month FIM was not associated with any weight category in the young and middle-aged group (table 2).

DISCUSSION

A higher FIM at 6 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 4428 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 normal-weight patients.[11] 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 categories.[4] Ovbiagele *et al*[12] showed that obese patients with stroke have a lower overall vascular risk than do their leaner counterparts. Furthermore, the Atherosclerosis Risk in Communities (ARIC) study confirmed a positive and linear relationship between BMI and ischaemic stroke incidence,[13] and overweight and

Table 2 Multiple linear regressions for 6 months FIM by age group*

Variables	<65 years old β (95% CI)	p Value	≥65 years old β (95% CI)	p Value
Weight categories				
Underweight	−3.81 (−8.93 to 1.31)	0.145	−2.53 (−7.74 to 2.67)	0.340
Normal	1.0		1.0	
Overweight	−1.19 (−3.35 to 0.97)	0.280	1.17 (−1.67 to 4.02)	0.420
Obese	0.05 (−2.05 to 2.15)	0.962	0.76 (−2.07 to 3.61)	0.596
Extremely obese	1.66 (−1.87 to 5.20)	0.355	7.95 (1.41 to 14.4)	0.017
Gender, female vs male	0.27 (−1.86 to 2.41)	0.800	−1.00 (−3.92 to 1.91)	0.501
Education				
College/university	1.0		1.0	
Middle/high school	−1.61 (−3.39 to −0.16)	0.074	1.79 (−1.67 to 5.26)	0.310
Elementary	−0.38 (−3.12 to 2.35)	0.783	1.65 (−1.89 to 5.20)	0.360
Smoking, current	0.38 (−0.65 to 1.42)	0.467	0.64 (−1.10 to 2.38)	0.469
Drinking, current	1.37 (−0.42 to 3.17)	0.133	1.34 (−1.51 to 4.20)	0.356
Hypertension, yes	−0.20 (−2.19 to 1.78)	0.841	−0.03 (−3.65 to 3.58)	0.984
Diabetes mellitus, yes	−0.73 (−2.31 to 0.85)	0.364	−0.68 (−2.96 to 1.59)	0.556
Dyslipidaemia, yes	−0.42 (−2.04 to 1.19)	0.610	−0.33 (−2.80 to 2.14)	0.792
Chronic kidney disease	−3.35 (−7.03 to 0.33)	0.075	−3.48 (−6.37 to −0.62)	0.017
FIM, discharge	0.36 (0.31 to 0.41)	<0.001	0.53 (0.47 to 0.58)	<0.001
NIHSS, 7-day	−1.33 (−1.56 to −1.10)	<0.001	−1.82 (−2.10 to −1.58)	<0.001

*Estimated by multiple linear regression models using the variables in the table.
FIM, functional independence measure; NIHSS, National Institutes of Health Stroke Scale.

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 paradox[18] indicates that obese patients receive better treatment and care because they are perceived to be at high risk,[19] Ryu *et al*[20] 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 patients with ischaemic stroke in Korea. Obesity increases the bone mineral density and decreases osteoporosis and hip fractures in the elderly.[21] Bamia *et al*[22] showed that the body weight of elderly individuals was reported to be an independent protecting factor against femoral osteoporosis. Furthermore, among the 1077 patients admitted to an acute rehabilitation hospital in the USA, motor FIM scores increased from admission to discharge in the obese (BMI 30.0–34.9) group.[3] Our results also showed that the 6-month FIMs gradually increased as weight category increased from underweight to extremely obese in both age groups. For this reason, the finding that obesity is a good predictor for the 6-month FIM was not surprising in this study.

Strazzullo *et al*[23] observed that being overweight or obese is associated, at least in part, with a progressively increasing risk of ischaemic stroke and that this association is independent of age, lifestyle and other cardiovascular risk factors. Additionally, the China National Stroke Registry shows that severe obesity is independently associated with higher 3-month mortality.[24] However, Jee *et al* showed that the mortality rate did not increase for elderly Korean individuals with a BMI of 25 or higher. The effect of obesity on mortality in the elderly can be influenced by various parameters such as existing diseases.[25] These results do not indicate that obesity is less harmful to the elderly than to younger people. We believe that if elderly patients with stroke utilise resistance exercises and proper diets, increased muscle mass and reduced body fat could be expected during a successful stroke rehabilitation.

This study has several limitations. First, it was conducted prospectively with a multicentre design, which may have impacted data reliability. To counteract this problem, the KOSCO committee leads a training course for rehabilitation specialists twice a year. Second, height and weight were measured once at admission to our study. Third, we did not account for the proportions and distributions of muscle, bone and adipose tissue[26] in obese patients in this study. Thus, further cardiovascular cohort studies that consider these variables are needed to verify the risk factors for cerebrovascular accident.

CONCLUSION

Our study shows that extreme obesity is a predictor of good functional outcomes in patients with ischaemic stroke, especially elderly patients. The strength of this study is the high degree of representation of Korean patients with ischaemic stroke that was achieved. Our results are thus applicable to the entire nation.

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Contributors SYJ made the study design, analysed the statistics and discussed the interpretation, and wrote this paper. Y-IS, DYK, MKS, JL, S-GL, G-JO, Y-SL, MCJ, EYH, WHC, CK: discussed the interpretation. Y-HK: made the study design, discussed the interpretation and takes all responsibility for this paper.

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