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ORIGINAL ARTICLE

The impact of Body Mass Index on functional rehabilitation outcomes of working-age inpatients with stroke

Alejandro GARCÍA-RUDOLPH [1, 2, 3] *, John D. KELLEHER [4], Blanca CEGARRA [1, 2, 3, 5], Joan SAURÍ RUIZ [1, 2, 3], Vasudevan NEDUMPOZHIMANA [4], Eloy OPISSO [1, 2, 3], Josep M. TORMOS [1, 2, 3], Montserrat BERNABEU [1, 2, 3]

[1]Department of Research and Innovation, Institut Guttmann, Institut Universitari de Neurorehabilitació Adscrit a la UAB, Badalona, Spain; [2]Universitat Autònoma de Barcelona, Bellaterra, Spain; [3]Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Spain; [4]Information, Communication and Entertainment Research Institute, Technological University Dublin (TU), Dublin, Ireland; [5]Universitat de Barcelona, Barcelona, Spain

*Corresponding author: Alejandro García-Rudolph, Department of Research and Innovation, Institut Guttmann, Institut Universitari de Neurorehabilitació Adscrit a la UAB, Cami Can Ruti s/n, 08916 Badalona, Spain. E-mail: alejandropablogarcia@gmail.com

ABSTRACT

BACKGROUND: Stroke is the most relevant cause of acquired persistent disability in adulthood. The relationship between patient's weight during rehabilitation and stroke functional outcome is controversial, previous research reported positive, negative and no effects, with scarce studies specifically addressing working-age patients.
AIM: To evaluate the association between Body Mass Index (BMI) and the functional progress of adult (<65 years) patients with stroke admitted to a rehabilitation hospital.
DESIGN: Retrospective observational cohort study.
SETTING: Inpatient rehabilitation center.
POPULATION: 178 stroke patients (ischemic or hemorrhagic).
METHODS: Point-biserial and Spearman's correlations, multivariate linear regressions and analysis of covariance were used to describe differences in functional outcomes after adjusting for age, sex, severity, dysphagia, depression and BMI category. Functional Independence Measure (FIM), FIM gain, efficiency and effectiveness were assessed.
RESULTS: Participants were separated in 3 BMI categories: normal weight (47%), overweight (33%) and obese (20%). There were no significant differences between BMI categories in any functional outcome (total FIM [T-FIM], cognitive [C-FIM]), motor [M-FIM]) at discharge, admission, gain, efficiency or effectiveness. In regression models BMI (as continuous variable) was not significant predictor of T-FIM at discharge after adjusting for age, sex, severity, dysphagia, depression and ataxia (R^2=0.4813), significant predictors were T-FIM at admission (β=0.528) and NIHSS (β=-0.208). M-FIM efficiency did not significantly differ by BMI subgroups, neither did C-FIM efficiency. Length of stay (LOS) and T-FIM effectiveness were associated for normal (r=0.33) and overweight (r=0.43), but not for obese. LOS and T-FIM efficiency were strongly negatively associated only for obese (r=-0.50).
CONCLUSIONS: FIM outcomes were not associated to BMI, nevertheless each BMI category when individually considered (normal weight, overweight or obese) was characterized by different associations involving FIM outcomes and clinical factors.
CLINICAL REHABILITATION IMPACT: In subacute post-stroke working-age patients undergoing rehabilitation, BMI was not associated to FIM outcomes (no obesity paradox was reported in this sample). Distinctive significant associations emerged within each BMI category, (supporting their characterization) such as length of stay and T-FIM effectiveness were associated for normal weight and overweight, but not for obese. Length of stay and T-FIM efficiency were strongly negatively associated only for obese.

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KEY WORDS: Stroke; Body mass index; Independent living; Rehabilitation.

Stroke is a leading cause of acquired disability in adults worldwide[1] with excess body weight being an acknowledged risk factor for stroke.[2] Nevertheless, the effect of obesity on stroke clinical outcomes is unclear, with previous studies reporting lower levels of impairment and mortality in obese patients compared with normal weight patients.[1] In 2002, Gruberg *et al.* introduced the obesity paradox concept, in the context of coronary artery disease, for describing that overweight and obese patients had (paradoxically) better outcomes than normal weight patients.[3] Similar findings were reported in the context of other chronic diseases and, therefore, the use of the term has become widespread.[1] Nevertheless, stroke outcomes have been widely conflicting in that regard and explanations currently remain ambiguous.[4] A recent narrative review[1] supports the existence of the obesity paradox in stroke, concluding that most studies reported lower mortality levels and better functional outcomes in obese and overweight patients than in normal weight and underweight patients. However, authors remarked that this is still controversial and further higher quality evidence is needed.[1]

Specifically regarding functional recovery, in a recent systematic review MacDonald *et al.*[5] concluded that based on the current evidence it is unclear whether functional outcomes of adults undergoing inpatient stroke rehabilitation, are affected by obesity. All studies classified obesity using Body Mass Index (BMI) and most of them used the Functional Independence Measure (FIM) as outcome measure.

Furthermore, to our best knowledge, existing studies have scarcely considered potential confounders previously related to functional outcomes, such as diabetes,[6] depression,[7] atrial fibrillation,[8] ataxia,[9] dysphagia,[10] hypertension[11] or recurrent stroke.[12]

Besides, associations between factors for ischemic or hemorrhagic stroke and clinical outcomes have been analyzed predominantly in older rather than younger patients, *e.g.* the mean age across studies included in McDonalds'[5] review ranged from 63 to 82. Nevertheless, the incidence of any stroke in the young (18–44 years) has increased by 23% during the past ten years.[13] Ischemic stroke is no longer a disease affecting just elderly people with an estimated 3.6 million young people (age <55 years) affected each year.[14]

As reported in previous research, in elderly patients (age >70 years), excess body weight might have a protective effect.[15] Furthermore, age and stroke severity are the most powerful predictors of stroke outcome.[1]

In this study we propose to evaluate the influence of the patient's weight, measured as BMI, on rehabilitation functional outcomes, measured using the FIM, in first event or recurrent stroke, working-age (mostly severe) patients in sub-acute rehabilitation. To that aim we are using variables identified in previous research such as stroke severity, measured using the National institute of Health Stroke Scale (NIHSS), gender, age, total FIM (T-FIM), motor FIM (M-FIM) and cognitive FIM (C-FIM), further extending them with specific clinical factors (diabetes, atrial fibrillation, dysphagia, ataxia and depression) scarcely addressed in previous research.

Materials and methods

Study design

The data that support the findings of this study are available from the corresponding author upon reasonable request. We conducted a retrospective observational cohort study enrolling subacute ischemic or hemorrhagic patients with stroke admitted to the Rehabilitation Unit of the Acquired Brain Injury Department of Institut Guttmann hospital. Recruitment period was from March 2012 to October 2019.

This study conforms to the STROBE Guidelines (Strengthening the Reporting of Observational Studies in Epidemiology).[16]

Participants

Eligible participants were adult patients (≥18 and ≤64 y.o.) with the diagnosis of first-time or recurrent stroke, receiving inpatient subacute rehabilitation and with electronical health records including complete data within 10 days of admission.

Patients were excluded for the following reasons: major musculoskeletal problems, more than 3 weeks of the onset of symptoms since admission to inpatient subacute rehabilitation, cases of transient ischemic attack or subarachnoid hemorrhage, diagnosis of stroke in the context of another concomitant comorbidity (*e.g.* traumatic brain injury) and a previous history of another disabling condition.

Functional assessments

A physician assessed functional status using the FIM. The FIM Scale includes 18 items structured in 2 domains: the motor domain, including 13 items, and the cognitive domain, including 5 items. The total score is obtained by adding the motor score (range: 3-91) to the cognitive score (range: 5-5) and ranges from 18 to 126 with a higher score indicating a higher degree of independence.

FIM gain is defined as the difference between FIM at admission and FIM at discharge. FIM efficiency is defined as FIM gain divided by LOS.

Effectiveness is defined as: (final score-initial score)/(maximum score-initial score)×100.[17]

The RPG (Rehabilitation Patient Groups) benchmark[18] is used in this work to stratify patients based on age and functional ability measured using the M-FIM at admission and C-FIM at admission. The RPG classifies stroke severity as mild-RPG, moderate-RPG or severe-RPG (details of the RPG algorithm are presented in Supplementary Digital Material 1: Supplementary Figure 1).

Clinical variables

At hospital admission, stroke severity was assessed using the NIHSS. Medical complications and comorbidities (reported using ICD9 codes) were collected from the participants' electronical health records (EHRs). The following were included as predictor variables: diabetes, dysphagia, depression, hypertension, smoking habits and atrial fibrillation (all of them recorded as yes/no). Missing values were completed by means of the specific internal or external reports.

Demographics (age, sex, education), stroke characteristics (type, and location), time since stroke onset to rehabilitation admission after discharge from an acute stroke care facility (in days), were also obtained from EHRs, as well as BMI at admission.

Patients were separated into 4 groups according to their BMI at admission using the World Health Organization (WHO) classification system:[5] underweight: <18.5 kg/m^2; normal weight: 18.51 to 25 kg/m^2; overweight: 25.1 to 30 kg/m^2 and obese >30 kg/m^2.

Rehabilitation program

All patients were admitted to the Rehabilitation Unit of our Acquired Brain Injury Department and underwent motor and cognitive rehabilitation – starting usually the day after admission and lasting until discharge. The rationale for motor and cognitive rehabilitation was based on currently available knowledge[19] and hospital protocols.

Statistical analysis

All statistical analyses were performed in R-v3.5.1 (64 bits), level of significance was set at P=0.05. Patients were stratified into four groups according to their BMI as described in clinical variables section. Descriptive statistics were used for demographic and clinical characteristics of participants as well as functional assessments. The four groups were compared using the χ^2 test for categorical variables and the Kruskal-Wallis test for continuous and ordered variables.

FIM at discharge and FIM efficiency were analyzed using two different approaches (for comparison with previous research).

The bivariate (Spearman's) correlation was used to evaluate the association between FIM outcomes (efficiency and FIM at discharge) and BMI (as continuous variable). Correlated variables (P<0.05) were submitted as independent variables to the multivariate analysis (T-FIM at discharge as dependent variable). Categorical variables were dichotomized (yes =1, no=0; woman =0, man =1; current smoker =1, former smoker and nonsmoker =0; less than 12 years of education =0, more than 12 years of education =1).

Multicollinearity of independent variables is tested by the variance inflation factor (VIF) and the tolerance (1/VIF). Tolerance is associated with each independent variable and ranges from 0 to 1. A tolerance below 0.40 and/or a VIF of 5 and above indicates a multicollinearity problem.[20] The assumption of independent errors is evaluated using the Durbin-Watson. The closer to 2 that the value is, the better. As a conservative rule it is suggested that for values less than 1 or greater than 3 the assumption of independence is not met.[20]

Analysis of covariance was used to describe differences in FIM scores after adjusting for age, sex, and weight group. A FIM efficiency adjusted mean was estimated for each of the 4 weight categories. The pairwise comparisons between the 4 weight groups were completed using the Tukey honestly significant difference test. An adjusted FIM efficiency mean for the 4 weight categories was defined as the predicted response value obtained by evaluating the regression equation for each weight category at the mean for the other covariates included in the regression model. Multivariable regression analysis of FIM efficiency scores was performed by regressing the FIM efficiency discharge score on the FIM admission score adjusted for BMI as a continuous covariate and adjusted for sex, age, and length of hospital stay.

Ethical considerations

The study follows the Declaration of Helsinki and this study was approved by the Ethics Committee of Clinical Research of Institut Guttmann. The participants are anonymized and non-identifiable.

Results

The source population was the total number of stroke patients admitted to the rehabilitation unit of the Institut Guttmann hospital during the whole period under study (March 2012 to October 2019).

A total of 1217 patients with stroke composed such population. After excluding 158 patients with more than 3 weeks since stroke onset to admission and 137 patients with more than one week since admission to FIM assessment, 922 were analyzed for FIM at discharge. After excluding 198 patients with more than one week since discharge to FIM assessment 724 were included for FIM gain calculation.

After excluding 97 with missing T-FIM, 193 with missing C-FIM, 189 with missing M-FIM, 34 were removed in relation to demographics or clinical data (*e.g.* the total number of underweight participants was 3 therefore they were removed and this BMI category was excluded from the analysis) 251 patients were analyzed in relation to acute NIHSS, 73 of them were not available, leaving 178 patients (The patient selection flowchart is presented in Supplementary Digital Material 2: Supplementary Figure 2).

All participants included in our study have been admitted in a stroke unit receiving appropriate acute treatment, most of them supported by the Stroke Code System in Catalonia. As shown in Supplementary Digital Material 3: Supplementary Table I, 96% of participants in this study come from Catalonia. The Stroke Code System (SCI-Cat) implemented since 2006, is set in motion when a person suffers a stroke and the same patient or someone in their environment alerts the healthcare system. The SCI-Cat guarantees the urgent and priority transfer of the patient to the nearest hospital with the appropriate diagnostic and therapeutic capacity.

Table I summarizes the demographic and clinical characteristics at admission by BMI categories, these data demonstrate that 47% were normal weight, 33% were overweight, and 20% were obese. The mean BMIs for the same categories were 22.3 kg/m^2, 27.0 kg/m^2, and 32.1 kg/m^2, respectively.

The participant's mean age was 49.6 with no significant differences between them (mean age was 48.5, 50.7 and 50.6 respectively), 31.5% were women (34.5%, 16.9% and 48.66%) (P=0.004).

The average number of days since stroke onset to rehabilitation admission was 17.76±4.59.

As shown in Table I, there is a majority of ischemic stroke participants (71.3%) and according to Oxfordshire Community Stroke Project (OCSP) classification, more than half of them were total anterior circulation infarcts (TACI) in all three BMI categories.

There were no statistically significant differences between groups in the admission NIHSS total score (mean values were 12.96±5.49, 12.40±5.44 and 13.08±5.05 respectively).

There were no statistically significant differences between groups either when considering RPG severity, nevertheless as shown in Table I, in all three BMI categories half of the participants are classified as RPG-severe. In particular in the obese BMI category 57.1% of participants are RPG-severe. Only 14.6% of all participants are classified as RPG-mild.

The percentage of RPG-severe patients across BMI categories was 51.7%.

Functional assessments

There were no statistically significant differences between groups at admission in the T-FIM (P=0.592), C-FIM (P=0.105), M-FIM (P=0.557); either at discharge T-FIM (P=0.857), C-FIM (P=0.229), M-FIM (P=0.436). Neither regarding FIM gain, efficiency, effectiveness for T-FIM, C-FIM, M-FIM, as shown in Table II.

However some tendencies can be seen, as illustrated in Supplementary Digital Material 4: Supplementary Figure 3, the highest C-FIM at admission and discharge can be seen in the obese group, intermmediate values correspond to the overweight group and lowest to the normal group. Similar behaviour can be seen in the C-FIM effectiveness, though any of them is statistically signifficant (noted using "NS").

Correlations analyses

We performed the bivariate Spearman's correlation analysis to evaluate the association between BMI (as a continuous variable) and T-FIM at discharge, C-FIM efficiency and M-FIM efficiency. As shown in Table III, BMI was not significantly associated to any of them.

We further explored Spearman's correlations between BMI and the following FIM assessments: T-FIM at admission, T-FIM at discharge, TGIM gain, T-FIM efficiency, T-FIM effectiveness, M-FIM at admission, M-FIM at discharge, MGIM gain, M-FIM efficiency, M-FIM effectiveness, C-FIM at admission, C-FIM at discharge, CGIM gain, C-FIM efficiency, C-FIM effectiveness.

None of them was significant, details are presented in Supplementary Digital Material 5: Supplementary Figure 4.

Table III also shows the associations between T-FIM Dis, M-FIM efficienciy and C-FIM efficiency with other potential predictors, for dichotomous variables (*e.g.* diabetes) we used point-biserial correlation. Such significant associations were entered as independent variables into the multiple regression model (T-FIM at discharge as dependent variable) presented in multivariant analysis section.

TABLE I.—*Characteristics at admission.*

Parameters	Normal (N.=84)	Overweight (N.=59)	Obese (N.=35)	Total (N.=178)	P
Sex (females)	29 (34.5%)	10 (16.9%)	17 (48.6%)	56 (31.5%)	0.004
Age in years, mean (SD)	48.47 (10.65)	50.71 (7.74)	50.59 (8.18)	49.63 (9.32)	0.663
Type of stroke					0.593
ischemic	63 (75.0%)	40 (67.8%)	24 (68.6%)	127 (71.3%)	
hemorrhagic	21 (25.0%)	19 (32.2%)	11 (31.4%)	51 (28.7%)	
OCSP Classification					0.294
LACI	1 (1.2%)	1 (1.7%)	1 (2.9%)	3 (1.7%)	
POCI	9 (10.7%)	1 (1.7%)	0 (0.0%)	10 (5.6%)	
TACI	46 (54.8%)	33 (55.9%)	19 (54.3%)	98 (55.1%)	
PACI	7 (8.3%)	5 (8.5%)	4 (11.4%)	16 (9.0%)	
Hemorrhagic subtypes					0.294
primary	14 (16.7%)	10 (16.9%)	9 (25.7%)	33 (18.5%)	
secondary	7 (8.3%)	9 (15.3%)	2 (5.7%)	18 (10.1%)	
NIHSS, mean (SD)	12.96 (5.49)	12.40 (5.44)	13.08 (5.05)	12.80 (5.37)	0.846
RPG stroke Severity					0.237
mild-RPG	12 (14.3%)	6 (10.2%)	8 (22.9%)	26 (14.6%)	
moderate-RPG	29 (34.5%)	24 (40.7%)	7 (20.0%)	60 (33.7%)	
severe-RPG	43 (51.2%)	29 (49.2%)	20 (57.1%)	92 (51.7%)	
Time since onset to Adm	17.50 (4.84)	18.06 (4.22)	17.94 (4.50)	17.76 (4.59)	0.925
BMI Adm	22.33 (1.76)	27.06 (1.34)	32.15 (1.65)	25.83 (4.09)	<0.001
Smoking habits					0.078
current	20 (23.8%)	10 (16.9%)	5 (14.3%)	35 (19.7%)	
former	3 (3.6%)	9 (15.3%)	6 (17.1%)	18 (10.1%)	
non	61 (72.6%)	40 (67.8%)	24 (68.6%)	125 (70.2%)	
Hypertension	50 (59.5%)	41 (69.5%)	27 (77.1%)	118 (66.3%)	0.147
Hyperlipidemia	26 (31.0%)	21 (35.6%)	13 (37.1%)	60 (33.7%)	0.754
Dysphagia	29 (34.5%)	15 (25.4%)	10 (28.6%)	54 (30.3%)	0.491
Medication for depression	43 (51.2%)	33 (55.9%)	22 (62.9%)	98 (55.1%)	0.500
Diabetes	9 (10.7%)	18 (30.5%)	9 (25.7%)	36 (20.2%)	0.01
Atrial Fibrillation	6 (7.1%)	9 (15.3%)	2 (5.7%)	17 (9.6%)	0.184
Ataxia	7 (8.3%)	2 (3.4%)	0 (0.0%)	9 (5.1%)	0.130
Recurrent stroke	6 (7.1%)	3 (5.1%)	3 (8.6%)	12 (6.7%)	0.792
Falls	24 (28.6%)	16 (27.1%)	17 (48.6%)	57 (32.0%)	0.063
Educational level					0.118
primary	46 (54.8%)	24 (40.7%)	15 (42.9%)	85 (47.8%)	
intermediate	18 (21.4%)	21 (35.6%)	15 (42.9%)	54 (30.3%)	
higher	20 (23.8%)	14 (23.7%)	5 (14.3%)	39 (21.9%)	
LOS in days	61.19 (27.38)	59.56(24.81)	61.31 (28.99)	60.67 (26.74)	0.906

All characteristics are presented as frequencies and percentages, N. (%), unless otherwise indicated.
SD: standard deviation; OCSP: Oxfordshire Community Stroke Project; TACI: total anterior circulation infarcts; PACI: partial anterior circulation infarcts; LACI: lacunar infarcts; POCI: posterior circulation infarcts; NIHSS: National Institutes of Health Stroke Scale; FIM: functional independence; LOS: length of stay; BMI: Body Mass Index; RPG: rehabilitation patient groups.

Multivariant analysis

Results of regression analyses with T-FIM at discharge as dependent variable is presented in Table IV model 2 (after adjustment for age, sex and T-FIM-admission) and BMI was not significantly associated with T-FIM at discharge ($P=0.264$; $R^2=0.4427$).

Table IV model 1 uses potential predictors of T-FIM at discharge obtained from Table III, outperforming model 2 ($R^2=0.4813$) and identifying the following significant predictors: T-FIM at admission ($\beta=0.528$, $P<0.0001$) and NIHSS ($\beta=-0.208$, $P=0.003$). When including BMI as independent variable in model 1 it was not found significant either.

Table IV shows VIF for all predictors (are all well below 5), none of them close to 3. Based on these measures we can safely conclude that there is no collinearity within our data.

ANCOVA analyses

Tables V provides adjusted means for the M-FIM efficiency and C-FIM efficiency cognitive by weight category. Af-

TABLE II.—*Functional assessments at admission and discharge between individuals in different BMI groups.*

Parameters	Normal (N.=84)	Overweight (N.=59)	Obese (N.=35)	TOTAL (N.=178)	P
T-FIM Adm	60.69 (28.02)	64.712 (21.733)	61.45 (26.36)	62.174 (25.688)	0.592
C-FIM Adm	20.893 (10.516)	23.966 (7.697)	24.714 (9.596)	22.663 (9.583)	0.105
M-FIM Adm	39.798 (21.470)	40.746 (18.083)	36.743 (19.440)	39.511 (19.949)	0.557
T-FIM Dis	95.786 (22.343)	96.712 (16.833)	93.743 (23.919)	95.691 (20.927)	0.857
C-FIM Dis	25.988 (8.789)	28.186 (6.482)	28.943 (7.211)	27.298 (7.848)	0.229
M-FIM Dis	69.798 (16.066)	68.525 (14.311)	64.800 (19.888)	68.393 (16.359)	0.436
T-FIM Gain	35.095 (21.952)	32.000 (16.806)	32.286 (19.769)	33.517 (19.896)	0.722
C-FIM Gain	5.095 (6.156)	4.220 (4.602)	4.229 (4.544)	4.635 (5.373)	0.967
M-FIM Gain	30.000 (17.842)	27.780 (15.546)	28.057 (18.096)	28.882 (17.103)	0.667
T-FIM Efficiency median (P_{25}–P_{75})	0.518 (0.311, 0.881)	0.568 (0.351, 0.709)	0.569 (0.408, 0.834)	0.551 (0.345, 0.813)	0.936
T-FIM Efficiency mean	0.639 (0.455)	0.575 (0.299)	0.611 (0.378)	0.612 (0.393)	0.936
C-FIM Efficiency median (P_{25}–P_{75})	0.043 (0.000, 0.129)	0.062 (0.018, 0.109)	0.060 (0.000, 0.111)	0.054 (0.000, 0.125)	0.948
C-FIM Efficiency mean	0.084 (0.101)	0.073 (0.080)	0.075 (0.084)	0.078 (0.091)	0.948
M-FIM Efficiency median (P_{25}–P_{75})	0.452 (0.276, 0.802)	0.515 (0.305, 0.660)	0.506 (0.358, 0.726)	0.481 (0.292, 0.729)	0.907
M-FIM Efficiency mean	0.555 (0.413)	0.503 (0.284)	0.536 (0.344)	0.534 (0.360)	0.907
C-FIM Effectiveness median (P_{25}–P_{75})	26.50 (0.00, 61.16)	31.818 (8.33, 66.73)	34.78 (0.00, 65.15)	31.534 (0.00, 63.35)	0.591
C-FIM Effectiveness mean	34.028 (35.497)	37.647 (39.509)	39.206 (32.782)	36.246 (36.243)	0.591
M-FIM Effectiveness median (P_{25}–P_{75})	62.12 (44.07, 76.99)	56.25 (39.05, 75.00)	54.16 (35.18, 72.12)	58.27 (38.97, 75.38)	0.314
M-FIM Effectiveness mean	58.255 (26.323)	55.917 (25.128)	50.868 (27.562)	56.027 (26.179)	0.314

All assessments are presented as mean (SD), unless otherwise indicated.
FIM gain definition: difference between FIM admission and FIM discharge; FIM efficiency definition: FIM gain divided by LOS; FIM: Functional Independence Measure; T-FIM: total FIM; M-FIM: motor FIM; C-FIM: cognitive FIM; T-FIM: M-FIM+C-FIM; LOS: length of stay.

TABLE III.—*Correlation analysis (BMI as continuous variable).*

Parameters	T-FIM Dis		C-FIM Effi		M-FIM Effi	
	rho	P	rho	P	rho	P
Age in years	-0.165	0.027	0.102	0.174	-0.154	0.039
Sex	0.020	0.786	-0.094	0.211	0.063	0.398
NIHSS Acute	-0.543	<0.001	0.169	0.023	-0.021	0.780
TSO	-0.074	0.321	0.040	0.595	-0.009	0.896
Hypertension	-0.124	0.097	-0.003	0.966	-0.009	0.899
Dysphagia	-0.183	0.014	0.189	0.011	-0.033	0.659
Depression	-0.163	0.028	0.135	0.071	0.031	0.674
Diabetes	-0.072	0.337	0.044	0.556	-0.066	0.377
Hyperlipidemia	0.008	0.912	0.068	0.364	0.010	0.890
Ataxia	0.158	0.034	0.003	0.967	0.034	0.651
Atrial fibrillation	-0.015	0.839	0.072	0.337	0.091	0.226
Recurrent stroke	-0.006	0.928	-0.087	0.246	-0.011	0.879
Smoking habits	-0.042	0.570	0.065	0.383	-0.028	0.708
BMI Adm	-0.085	0.256	-0.008	0.915	-0.007	0.916
Years of education	0.070	0.35	0.029	0.692	-0.110	0.140
T-FIM Adm	0.636	<0.001	-0.334	<0.001	-0.211	0.004
C-FIM Adm	0.569	<0.001	-0.538	<0.001	0.068	0.366
M-FIM Adm	0.560	<0.001	-0.205	0.006	-0.285	0.0001
Length of stay	-0.324	<0.001	0.0367	0.626	-0.308	<0.001

NIHSS: National Institutes of Health Stroke Scale; FIM: Functional Independence Measure; T-FIM: total FIM; M-FIM: motor FIM; C-FIM: cognitive FIM; T-FIM: M-FIM+C-FIM.

ter adjusting for age and sex, the M-FIM efficiency did not significantly differ by BMI subgroups (P=0.949) (Table V model 1).

After adjusting for age and LOS, the M-FIM efficiency did not significantly differ by BMI subgroups (P=0.890) (Table V model 2).

After adjusting for age and sex, the C-FIM efficiency did not significantly differ by BMI subgroups (P=0.771)

TABLE IV.—*Multivariate lineal regressions, nonstandard beta 95% CIs, standard beta, Durbin test, VIF, R^2 and adjusted R^2.*

Model	Variables	β (95% CI)	Std β	VIF	Tol	P	R^2	Adj R^2	10FCVR10
1	NIHSS	-0.810 (-1.348, -0.272)	-0.208	1.60	0.62	0.003	0.4813	0.46	0.4802
T-FIM Dis	Age	-0.221 (-0.471, 0.027)	-0.098	1.03	0.96	0.080			
	Dysphagia	0.406 (-4.847, 5.660)	0.008	1.12	0.88	0.878			
	Depression	3.053 (-1.891, 7.998)	0.072	1.16	0.85	0.224			
	Ataxia	10.252 (-0.403, 20.907)	0.107	1.05	0.94	0.059			
	LOS	-0.017 (-0.117, 0.083)	-0.022	1.38	0.72	0.733			
	T-FIM Adm	0.430 (0.305, 0.555)	0.528	1.97	0.50	<0.001			
	Durbin test		D-W=1.965; P=0.768						
2 T-FIM Dis	Age	-0.223 (-0.483, 0.036)	-0.099	1.06	0.93	0.091	0.4427	0.4298	0.4412
	Sex	-0.203 (-5.299, 4.893)	-0.004	1.02	0.97	0.937			
	BMI	-0.331 (-0.914, 0.252)	-0.064	1.04	0.96	0.264			
	T-FIM Adm	0.525 (0.433, 0.616)	0.644	1.00	0.99	<0.001			
	Durbin test		D-W=1.943; P=0.636						

NIHSS: National Institutes of Health Stroke Scale; FIM: Functional Independence Measure; C-FIM: Cognitive FIM; T-FIM: M-FIM+C-FIM; BMI: Body Mass Index; LOS: Length of Stay; 10FCVR10: 10-fold cross validation repeated 10 times.

TABLE V.—*Motor and cognitive FIM efficiency by BMI categories.*

Models	BMI Categories	N.	Mean M-FIM Efficiency	95% CI lr	95% CI upr	se
Model 1	Normal	84	0.541	0.465	0.617	0.038
Adj:	Overweight	59	0.521	0.429	0.613	0.046
age and sex	Obese	35	0.536	0.417	0.655	0.060
			P=0.949			
Model 2	Normal	84	0.540	0.476	0.605	0.032
Adj:	Overweight	59	0.518	0.441	0.595	0.038
age and LOS	Obese	35	0.542	0.443	0.642	0.0502
			P=0.890			
Model 3	Normal	84	0.083	0.064	0.102	0.009
Adj:	Overweight	59	0.072	0.049	0.095	0.011
Age and sex	Obese	35	0.077	0.047	0.107	0.015
			P=0.771			
Model 4	Normal	84	0.081	0.062	0.100	0.009
Adj:	Overweight	59	0.075	0.053	0.098	0.014
NIHSS and dysphagia	Obese	35	0.075	0.046	0.104	0.011
			P=0.902			

NIHSS: National Institutes of Health Stroke Scale; M-FIM: motor FIM; C-FIM: cognitive FIM; FIM: Functional Independence Measure; BMI: Body Mass Index; LOS: length of stay.

(Table V model 3). After adjusting for NIHSS and dysphagia, the M-FIM efficiency did not significantly differ by BMI subgroups (P=0.902) (Table V model 4).

Correlation analysis within each BMI category

We performed Spearman's correlation analyses separately for normal weight (presented in Table VI overweight (Table VII) and obese (Table VIII) patients, to identify associations existing in one BMI category that do not exist in the others, for T-FIM.

Significant correlations involving our main continuous variables (BMI, NIHSS, Age, LOS) and T-FIM outcomes (T-FIM gain, T-FIM efficiency and T-FIM effectiveness) are highlighted in Table VI, VII, VIII, showing different associations between them for the different BMI categories.

For example, LOS is significantly correlated to T-FIM gain for the normal (r=0.33, P=0.01) and overweight (r=0.43, P<0.001) BMI categories, but it is non-significant for the obese category. LOS is also significantly correlated to T-FIM effectiveness for the normal (r=0.33, P=0.01) and overweight (r=0.43, P<0.001) BMI categories, but it is non-significant for the obese category.

As shown in Table VI, VII, VIII, T-FIM at admission is the only variable correlated to T-FIM gain for obese patients. This correlation between T-FIM at admission and T-FIM gain is stronger in normal (r=-0.63, P<0.001) and in overweight patients (r=-0.62, P<0.001) than in obese (r=-0.43, P=0.01) as shown in Table VI, VII, VIII.

TABLE VI.—*Spearman's correlations for normal weight group.*

Parameters	NIHSS	Age	TSO	BMI	LOS	T-FIM Adm	T-FIM Dis	T-FIM gain	T-FIM effi	T-FIM Effe
NIHSS	1									
Age	ns	1								
TSO	ns	ns	1							
BMI	ns	0.41b	ns	1						
LOS	0.31b	0.22a	ns	ns	1					
T-FIM Adm	-0.62b	ns	ns	ns	-0.47b	1				
T-FIM Dis	-0.56b	ns	ns	ns	-0.22a	0.63b	1			
T-FIM gain	0.26a	ns	ns	ns	0.33b	-0.63b	ns	1		
T-FIM Effi	ns	-0.26a	ns	ns	-0.25a	-0.33b	0.23a	0.79b	1	
T-FIM Effe	0.26a	ns	ns	ns	0.33b	-0.63b	ns	1b	0.79b	1

aP<0.05; bP<0.01; ns: non-significant.
NIHSS: National Institutes of Health Stroke Scale; TSO: time since stroke onset to rehabilitation admission; BMI: Body Mass Index; LOS: length of stay; FIM: Functional Independence Measure; T-FIM Adm: total FIM at admission; T-FIM Dis: total FIM at discharge; T-FIM gain: total FIM gain; T-FIM Effi: total FIM efficiency; T-FIM Effe: total FIM effectiveness.

TABLE VII.—*Spearman's correlations for overweight group.*

Parameters	NIHSS	Age	TSO	BMI	LOS	T-FIM Adm	T-FIM Dis	T-FIM gain	T-FIM effi	T-FIM Effe
NIHSS	1									
Age	ns	1								
TSO	ns	ns	1							
BMI	ns	ns	ns	1						
LOS	0.39b	ns	ns	ns	1					
T-FIM Adm	-0.51b	ns	ns	ns	-0.72b	1				
T-FIM Dis	-0.39b	ns	-0.27a	ns	-0.43b	0.61b	1			
T-FIM gain	ns	ns	ns	ns	0.43b	-0.62b	ns	1		
T-FIM Effi	ns	ns	-0.30a	ns	ns	ns	0.39b	0.72b	1	
T-FIM Effe	ns	ns	ns	ns	0.43b	-0.62b	ns	1b	0.72b	1

aP<0.05; bP<0.01; ns: non-significant.
NIHSS: National Institutes of Health Stroke Scale; TSO: time since stroke onset to rehabilitation admission; BMI: Body Mass Index; LOS: length of stay; FIM: Functional Independence Measure; T-FIM Adm: total FIM at admission; T-FIM Dis: total FIM at discharge; T-FIM gain: total FIM gain; T-FIM Effi: total FIM efficiency; T-FIM Effe: total FIM effectiveness.

In the normal weight patients, NIHSS is correlated to T-FIM gain (r=0.26, P<0.05) and T-FIM effectiveness (r=0.26, P<0.05) meanwhile for overweight and obese patients none of them are significant.

In Supplementary Digital Material 6: Supplementary Figure 5, Supplementary Figure 6, we included the analysis for C-FIM showing similar results.

Discussion

The relationship between patient's weight during rehabilitation and stroke functional outcome is controversial. MacDonald *et al.*[5] recently published a systematic review of the impact of obesity on stroke inpatient rehabilitation functional outcomes (2765 titles and abstracts were screened, and 64 articles were reviewed in full text). A total of seven studies (involving 3070 participants) met the inclusion criteria. Of the seven studies, two reported a positive association between obesity and functional outcome,[21, 22] two did not find an association[23, 24,] and three reported a negative association.[25-27] Five of the seven studies used FIM as their outcome measure.

Therefore, our results are in keeping with those of Hagii *et al.*[23] and Karaahmet *et al.*[24] However, they did not use a BMI categorization and instead examined all individuals who were classified as overweight (BMI≥25 kg/m2). Hagii *et al.*[23] reported results using the Modified Rankin Scale (mRS).[28] Nevertheless, mRS and FIM are highly correlated as reported in previous research.[29]

Karaahmet *et al.*[24] was one of the smallest studies included in MacDonald's review,[5] with 85 participants.

In this study we followed the WHO categorization, which has been also used in studies such as Burke *et al.*[25] and Kalichman *et al.*,[27] who did find associations between BMI and functional outcomes.

In relation to the studies that reported a positive relation, Nishioka *et al.*[21] used a 2-level categorical variable (obesity - yes/no) (BMI≥27.5 kg/m2). Their multivariate linear regression adjusted by sex, LOS, TSO and T-FIM at

TABLE VIII.—*Spearman's correlations for obesity group.*

Parameters	NIHSS	Age	TSO	BMI	LOS	T-FIM Adm	T-FIM Dis	T-FIM gain	T-FIM effi	T-FIM Effe
NIHSS	1									
Age	ns	1								
TSO	ns	ns	1							
BMI	ns	ns	ns	1						
LOS	0.34[b]	ns	ns	ns	1					
T-FIM Adm	-0.69[b]	-0.35[a]	ns	ns	-0.53[b]	1				
T-FIM Dis	-0.69[b]	ns	ns	ns	-0.48[b]	0.70[b]	1			
T-FIM gain	ns	ns	ns	ns	ns	-0.43[b]	ns	1		
T-FIM Effi	ns	ns	ns	ns	-0.50[b]	ns	0.34[a]	0.73	1	
T-FIM Effe	ns	ns	ns	ns	ns	-0.43[b]	ns	1[b]	0.73	1

[a]P<0.05; [b]P<0.01; ns: non-significant.
NIHSS: National Institutes of Health Stroke Scale; TSO: time since stroke onset to rehabilitation admission; BMI: Body Mass Index; LOS: length of stay; FIM: Functional Independence Measure; T-FIM Adm: total FIM at admission; T-FIM Dis: total FIM at discharge; T-FIM gain: total FIM gain; T-FIM Effi: total FIM efficiency; T-FIM Effe: total FIM effectiveness.

admission, when using T-FIM at discharge as dependent variable, reported an R^2=0.66. In our case using the same variables except TSO and sex (which were not significantly correlated to T-FIM at discharge as presented in Table III) and further including NIHSS, dysphagia, depression and ataxia (significantly correlated to T-FIM at discharge) our reported R^2= 0.4813. Nishioka *et al.* did not adjust the model for stroke severity (NIHSS not reported).[21]

The other study that reported a positive relation, Morone *et al.*[22] concluded that increased BMI was correlated with improved rehabilitation effectiveness as reflected by the Barthel Index. Effectiveness of rehabilitation was significantly correlated with BMI at discharge (Spearman's *r*=0.111). NIHSS was not reported.[22] In our case we did not assess participants using Barthel Index, nevertheless Barthel Index and FIM are highly correlated.[29]

In our study we have 68% men and only 32% women, meanwhile when comparing with both studies with a positive relation between BMI and functionality, the mean age of participants in Morone *et al.* study was 68 years old[22] and 72 years old[21] in Nishioka *et al.* Besides, in both studies the proportion of women and men is quite similar (46% and 54%). (Details are presented in Supplementary Digital Material 7: Supplementary Table II). After the age of 60, average body weight and muscle mass tend to decrease. As physical activity and energy expenditure also decrease there is a tendency to fat accumulation and fat redistribution.[30]

Kalichman *et al.*[27] reported a statistically significant negative correlation between T-FIM gain and BMI in the total sample. In Supplementary Digital Material 8: Supplementary Figure 7 we present correlations analysis in the total sample, in our case BMI was not correlated to any FIM outcome, in particular T-FIM gain, C-FIM gain neither M-FIM gain.

Stroke severity at admission in Kalichman *et al.*[27] was NIHSS: 8.03±4.38, meanwhile in our case NIHSS severity was higher (12.80±5.37). In our sample, when categorizing stroke severity using RPG benchmark, half of participants were categorized as RPG-severe (the percentage of RPG-severe patients across BMI categories was 51.7% as presented in Table I). In the case of obese patients, almost 60% of them were RPG-severe in our sample.

In relation to mean age, Kalichman *et al.*[27] reported 63.07±10.47, in our case it was 49.63±9.32.

Kalichman[27] performed adjustments using linear regression for age, but not for severity.

Burke *et al.*[25] provide adjusted means for the M-FIM efficiency and C-FIM efficiency subscores by weight category. After adjusting for age and sex, the M-FIM efficiency did not significantly differ by BMI subgroups (P=0.17). These results are similar to ours, as reported in Table V model 1 (P=0.949). Nevertheless, after adjusting for age and sex, C-FIM efficiency differed by BMI subgroups according to Burke results (P=0.01)[25] but not in our case Table V model 3 (P=0.771). In our case we further adjusted by NIHSS severity and dysphagia but did not significantly differ either (Table V model 4).

We performed Bivariate Spearman's correlation analysis considering each BMI category separately and identified different associations within BMI categories. Aside from those presented in Table VI, VII, VIII for T-FIM, further associations are detailed in Supplementary Digital Material 9: Supplementary Table III for M-FIM. For example, there was no significant association for overweight patients between NIHSS and M-FIM discharge, M-FIM gain, neither M-FIM effectiveness, but NIHSS was strongly associated to M-FIM discharge in obese and normal weight patients.

Similarly, LOS was strongly associated to M-FIM efficiency for obese patients, but there was no association for overweight patients and the association is weak for normal weight patients.

M-FIM at admission is not associated to M-FIM efficiency for obese patients, but it is for normal and overweight patients. Similar behavior is observed for the C-FIM subscale.

Finally, it is important to remark that BMI assessment as the sole indicator of stroke functional recovery may present some limits as this parameter does not allow a proper evaluation of the distribution of fat mass and fat free mass, and thus makes the evaluation of body composition too simplistic.[31]

As reported in recent previous research underweight patients with type 2 diabetes mellitus (T2DM) consistently showed poor outcomes when compared to obese patients.[32] Previous studies also showed poor outcomes in underweight T2DM patients. The patients who have a greater genetic susceptibility to T2DM have a greater chance of developing T2DM at lower BMI, which will consequently lead to a poor prognosis[33] In relation to participants with T2DM in our study (20% of our included patients) we found significant differences when comparing overweight and normal weight participants in relation to their total FIM efficiency (0.342 [0.153] in normal weight and 0.656 [0.315] in overweight patients, P=0.032) but these results must be interpreted with caution because in our study normal weight patients with T2DM were only N.=9 and overweight patients with T2DM were only N.=18.

In relation to recurrent stroke, lower mortality and lower risk of readmission for recurrent stroke has been previously reported in obese patients,[34] the contribution of our study in this direction is limited because only 6.7% of participants had a second stroke.

Risk of death by stroke has been also associated to BMI in previous research[35] but only 3.43% of our sample died in the period under study. A reason for this can be found in the young mean age of our sample.

Limitations of the study

The data for this study was collected in one single tertiary center, suggesting that the generalization of these results should be considered carefully. Nevertheless, patients' severity assessed by means of NIHSS, the BMI categories determined following WHO classification, the RPG benchmark used to assess functional severity and the focus on working-age population, allows for similar comparative studies.

A large number of stroke patients were not eligible for this study due to missing assessments, no data imputation was performed in this study, if any assessment was missing the patient was not included in the final analysis.

The specific manner in which stroke rehabilitation services are delivered (locally and internationally) may also impact outcomes. Therefore, the relationship between obesity and functional recovery after stroke could have been impacted by these changes along time, in the center where this study took place and similarly in related clinical rehabilitation centers, as also remarked in previous research (*e.g.* MacDonald *et al.*[5]).

Adjusted R^2 was confirmed by means of 10-fold cross validation repeated ten times, in a test set, we independently partitioned initial data in training set (65%) and test set (35%), nevertheless results may require an external validation.

A further limitation is the measurement of body weight using BMI. It has been criticized for being unable to discriminate between fat and lean mass[36] and also because its diagnostic performance worsened with increasing age.[36] Nevertheless, our analysis is focused on working-age adults (about twenty year younger in mean age than related research presented in MacDonald's *et al.* systematic review[5]).

Conclusions

Several variables were analyzed in this work to assess their potential impact regarding the association between BMI and the functional progress of working-age, mostly severe, first-ever or recurrent patients with stroke, admitted to a rehabilitation hospital. We found no associations between BMI and FIM measures (at discharge, admission, gain, efficiency or effectiveness). BMI was not found as significant predictor of FIM at discharge, either of FIM efficiency, even after adjusting using state-of-the art variables neither when using variables (diabetes, depression, dysphagia, or stroke severity) that have scarcely been used in previous studies addressing BMI and functionality. We performed Spearman's correlation analyses separately for normal weight, overweight and obese patients and in that case, we were able to identify associations that exist in one BMI category that do not exist in the others, for T-FIM and also for C-FIM and M-FIM.

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