Original Investigation

Body Mass Index and Death by Stroke
No Obesity Paradox

Christian Dehlendorff, MS, PhD; Klaus K. Andersen, MS, PhD; Tom S. Olsen, MD, PhD

CME Quiz at jamanetworkcme.com

IMPORTANCE Reports of an obesity paradox have led to uncertainty about secondary prevention in obese patients with stroke. The paradox is disputed and has been claimed to be an artifact due to selection bias.

OBJECTIVE To determine whether the obesity paradox in stroke is real or an artificial finding due to selection bias.

DESIGN, SETTING, AND PARTICIPANTS We studied survival after stroke in relation to body mass index (BMI, calculated as weight in kilograms divided by height in meters squared). To overcome selection bias, we studied only deaths caused by the index stroke on the assumption that death by stroke reported on a death certificate was due to the index stroke if death occurred within the first month poststroke. We used the Danish Stroke Register, containing information on all hospital admissions for stroke in Denmark from 2003 to 2012, and the Danish Registry of Causes of Death. The study included all registered Danes (n = 71 617) for whom information was available on BMI (n = 53 812), age, sex, civil status, stroke severity, stroke subtype, a predefined cardiovascular profile, and socioeconomic status.

MAIN OUTCOMES AND MEASURES The independent relation between BMI and death by the index stroke within the first week or month by calculating hazard ratios in multivariate Cox regression analysis and multiple imputation for cases for whom information on BMI was missing.

RESULTS Of the 71 617 patients, 7878 (11%) had died within the first month; of these, stroke was the cause of death of 5512 (70%). Of the patients for whom information on BMI was available, 9.7% were underweight, 39.0% were of normal weight, 34.5% were overweight, and 16.8% were obese. Body mass index was inversely related to mean age at stroke onset ($P < .001$). There was no difference in the risk for death by stroke in the first month among patients who were normal weight (reference), overweight (hazard ratio, 0.96; 95% CI, 0.88-1.04), and obese (hazard ratio, 1.0; 95% CI, 0.88-1.13). Analysis of deaths within 1 week gave similar results.

CONCLUSIONS AND RELEVANCE We found no evidence of an obesity paradox in patients with stroke. Stroke occurred at a significantly younger age in patients with higher BMI. Hence, obese patients with stroke should continue to aim for normal weight.

JAMA Neurol. 2014;71(8):978-984. doi:10.1001/jamaneurol.2014.1017
Published online June 2, 2014.

Author Affiliations: Danish Cancer Society Research Center, Copenhagen, Denmark (Dehlendorff, Andersen); The Stroke Unit, Frederiksberg University Hospital, Frederiksberg, Denmark (Olsen).

Corresponding Author: Tom S. Olsen, MD, PhD, The Stroke Unit, Frederiksberg University Hospital, DK-2000 Frederiksberg, Denmark (tso@dadlnet.dk).

Because obesity is associated with increased morbidity and mortality in the general population,[1] obese individuals are generally advised to strive for a normal weight (ie, a body mass index [BMI, calculated as weight in kilograms divided by height in meters squared] between 18.5 and 25.0).[2] However, many studies have shown that patients with a number of chronic diseases, including stroke,[3-7] who are overweight or obese have lower mortality rates than patients of normal weight and underweight.[8] This phenomenon is known as the *obesity paradox*[8] and has led to uncertainty about secondary prevention for overweight and obese patients with stroke[9,10] and other diseases.[11-13] Should striving for normal weight still be recommended if overweight and obesity constitute a survival advantage?

The obesity paradox still lacks an explanation. It might be the result of a balance between the disadvantages associated with obesity that lead to stroke and the benefits associated with obesity that promote survival after clinical illness. The paradox has also been explained as an artificial finding that is simply due to selection bias.[14-16] If stroke or any other disease in obese patients with stroke is less severe than in patients of normal weight, obese patients with stroke would have a lower risk for dying of any disease, leaving the false impression that obesity constitutes a survival advantage.

The independent effect of BMI on the risk for death after stroke can be estimated by multivariate statistics with adjustment for differences between groups in stroke severity and comorbid conditions; however, this is possible only for deaths caused by the index stroke. Differences between groups in the risks for death due to heart diseases, cancer, and other diseases, including subsequent recurrent stroke, cannot be adjusted for reliably by multivariate analysis mainly because the severity of these diseases has not been quantified. Nevertheless, the results of the available studies on the obesity paradox in patients with stroke[3-7] are based on death by any cause from the acute state to years after the index stroke. Therefore, the severity of the disease leading to death is usually not controlled for. Therefore, the validity of the conclusions about the obesity paradox drawn in these studies is questionable.

The aim of this study was to determine whether the obesity paradox in stroke is real or an artificial finding due to selection bias. We studied survival after stroke in relation to BMI among 71 617 patients with stroke admitted to Danish hospitals from 2003 to 2012 and in whom information on BMI was available in 53 812 patients. To avoid selection bias, we studied only deaths caused by the index stroke based on the assumption that death by stroke as recorded on the death certificate was due to the index stroke if the death occurred within the first week or first month after the stroke.

Methods

This study was based on data in the Danish Stroke Register (formerly the Danish National Indicator Project), which was started in 2001 and is described in detail elsewhere.[17,18] The register contains information on all stroke admissions in Denmark; coverage is currently estimated (by professional consensus) to be more than 80%.[19] All Danish hospitals report a defined set of data on all patients admitted to hospital for acute stroke including age, sex, civil status, admission stroke severity measured on the Scandinavian Stroke Scale (SSS),[20] stroke subtype (ischemic or hemorrhagic), and a predefined cardiovascular profile.

The SSS is a validated neurologic stroke scale for evaluating the level of consciousness; eye movement; power in the arm, hand, and leg; orientation; aphasia; facial paresis; and gait on a total score of 0 to 58, with lower scores indicating more severe stroke. Ischemic stroke was distinguished from primary intracerebral hematoma on computed tomography or magnetic resonance scans. The cardiovascular profile included information on alcohol consumption (over limit: >14 drinks per week for women and >21 drinks for men; under limit: ≤14 drinks per week for women and ≤21 drinks for men), smoking (current daily smoker, former smoker, or never a smoker), diabetes mellitus, atrial fibrillation (chronic or paroxysmal), arterial hypertension, intermittent arterial claudication, previous myocardial infarct, and previous stroke. Diabetes mellitus, atrial fibrillation, arterial hypertension, previous myocardial infarct, and previous stroke were diagnosed according to current Danish standards[18] and were either known before onset of stroke or diagnosed during hospitalization. Stroke was defined according to World Health Organization criteria.[21] Patients with subarachnoid hemorrhage were excluded from the study as were patients with transient ischemic attacks. For patients with multiple events, only the first event was included in the analysis. We excluded patients younger than 20 years of age and patients in whom computed tomography and magnetic resonance imaging were not performed (0.9%) or were unavailable (0.9%). Time was scaled from the day of hospital admission.

Inclusion of patients started on March 1, 2001, and the end of follow-up was December 1, 2011. Follow-up within the first month after stroke was complete. The study was approved by the institutional review board of the Danish Stroke Register and the Danish Data Protection Agency (journal No. 2012-41-0719); patient informed consent was waived.

For all patients in the study population, we obtained information on the level of education and disposable income by linkage to the registries of Statistics Denmark.[22] Education was grouped into 3 categories from basic to high: (1) basic or high school, defined as 7 to 12 years of primary, secondary, and grammar-school education; (2) vocational, defined as 10 to 12 years of education; and (3) higher, defined as 13 years or more of education. Patients for whom information on education was missing were not included (14%). Disposable income was defined as household income after taxation and interest per person, adjusted for the number of people in the household and deflated according to the 2000 value of the Danish crown (DKK). People with a high negative income owing to debt and interest on debt (>50 000 DKK per year) were excluded from all analyses. For the analyses, disposable income was categorized into the first, second, third, fourth, and fifth quintiles of income distribution.

Survival was followed through the Danish Central Person Registry. The cause of death was obtained from the Danish Registry of Causes of Death. We studied only deaths declared as being caused by stroke (*International Statistical Classification of Diseases, 10th Revision*[23] code I60-69) within the first month after the index stroke.

We present the distribution of the 4 BMI categories conditioned on each cardiovascular risk factor: age, sex, civil status, income, and education. We applied multiple linear regression to describe differences in mean BMI.

We used Cox regression models of the events of death by stroke within the first poststroke week and month by censuring for death by other causes, end of follow-up, or loss to follow-up, whichever came first. We used the time since admission as the time scale and adjusted for age, sex, civil status, income, education, and cardiovascular risk profile. Age and stroke severity were included as continuous variables by means of restricted cubic splines to account for potential nonlinear effects. Body mass index was included as a categorical variable in 4 groups. Furthermore, we estimated the effect of BMI using a restricted cubic spline.

We analyzed information for patients for whom the BMI was missing by logistic regression and applied multiple imputation (10 repetitions) for cases with information on BMI and for all cases, as described by Harrel.[24] We used R version 3.0.2 for all analyses[25] and accepted significance at 5%.

Results

The mean age of the 71 617 patients with stroke registered in the Danish Stroke Register was 71.8 years. Of all the patients, 47.2% were women, 8.3% had hemorrhagic stroke, and the mean SSS score was 42.3. Information on BMI was available for 53 812 patients. The mean BMI was 25.7. Of all the patients, 9.7% were underweight (mean age, 76.2 years), 39.0% were normal weight (mean age, 73.0 years), 34.5% were overweight (mean age, 70.7 years), and 16.8% were obese (mean age, 67.1 years). The mean age varied significantly between groups of BMI ($P < .001$).

Patients for whom BMI was not available were more often smokers (odds ratio [OR], 1.09; 95% CI, 1.05-1.13; $P < .001$); more often had a record of previous myocardial infarct (OR, 1.08; 95% CI, 1.02-1.13; $P = .005$), atrial fibrillation (OR, 1.09; 95% CI, 1.05-1.13; $P < .001$), or previous stroke (OR, 1.22; 95% CI, 1.18-1.27; $P < .001$); and more often had no record of hypertension (OR, 1.16; 95% CI, 1.12-1.20; $P < .001$). They had more severe stroke (OR, 1.20; SSS score per 10-point decrease; 95% CI, 1.19-1.21; $P < .001$), were older (OR, 1.06; 95% CI, 1.04-1.07; per 10 years' increase; $P < .001$), were more often women (OR, 1.06; 95% CI, 1.03-1.09; $P < .001$), were more often single (OR, 1.05; 95% CI, 1.02-1.08; $P < .001$), and more often had hemorrhagic stroke (OR, 2.09; 95% CI, 1.98-2.19; $P < .001$). Furthermore, they were more often in the lowest income group. Alcohol consumption, education, and the presence of diabetes mellitus or intermittent arterial claudication did not differ significantly between patients for whom BMI was available and unavailable.

Stroke Characteristics in Relation to BMI

Descriptive statistics of BMI in relation to sex, cardiovascular risk factors, stroke subtype, and socioeconomic status are shown in **Table 1**. In a multiple regression model with adjustment for age, sex, stroke severity (SSS score), stroke subtype, civil status, socioeconomic status, and cardiovascular risk factors, BMI was on average significantly higher in men (0.9 BMI units); in patients who were married or living with someone (0.4 BMI units); in nonsmokers (0.9 BMI units); in nondrinkers (0.6 BMI units); in patients with diabetes (1.9 BMI units), infarct (0.3 BMI units), hypertension (1.2 BMI units), previous infarct (0.2 BMI units), or atrial fibrillation (0.2 BMI units); and in patients with no previous stroke (0.4 BMI units) or no intermittent arterial claudication (0.8 BMI units). The group with the highest disposable income had significantly lower BMI than the group with the lowest income (0.5 BMI units), whereas groups with basic and vocational education had significantly higher BMI than those with higher education (0.9 and 0.5 BMI units, respectively). The relations between mean BMI and age and stroke severity (SSS score) are shown in **Figure 1**. The mean BMI decreased with increasing age ($P < .001$) from about 60 years, while patients with the most severe strokes had the lowest BMI ($P < .001$).

Cause of Death Related to BMI

Of the total sample of 71 617 patients, 4373 (6.1%) died within the first week after the stroke; of the total sample, 3334 (4.7%) died of stroke. Within the first month, 7878 (11.0%) died and of the total sample, 5512 (7.7%) died of stroke. Hence, according to death certificates, stroke was the cause of death in 76% of the deaths within the first week and in 70% of the deaths within the first month poststroke. The risk for death by stroke within 1 week and 1 month of the index stroke stratified by the 4 BMI groups is shown in **Tables 2** and **3**. Results are shown for the 32 743 cases with complete information on all variables and after applying multiple imputation for 53 812 cases with information on BMI and for all 71 617 cases. Adjustments were made for age, sex, stroke severity (SSS score), stroke subtype, civil status, cardiovascular risk factors, duration of education, and income. The risk of obese patients with stroke for death by stroke did not differ significantly from that of patients of normal weight in any of the 3 analyses. The risk of overweight patients for death by stroke was slightly lower than that of normal-weight patients in the analysis of the 32 743 cases with complete information on all variables; however, the difference disappeared in the analysis based on applying multiple imputation for all 71 617 cases. Underweight status was associated with a higher risk for death in all 3 analyses.

The relations between BMI as a continuous variable and risk for death by stroke within the first month after the stroke, adjusted for age, sex, stroke severity, cardiovascular risk factors, civil status, and socioeconomic status, are shown in **Figure 2** and are in line with the results of the analyses based on BMI categories. Analyses for death by stroke within the first week gave similar results (data not shown).

Discussion

This study was unable to confirm the existence of an obesity paradox in stroke. The risk of obese patients with stroke for death did not differ from that of normal-weight patients with

Table 1. Descriptive Statistics of BMI in Relation to Sex, Cardiovascular Risk Factors, Stroke Subtype, Civil Status, and Socioeconomic Status

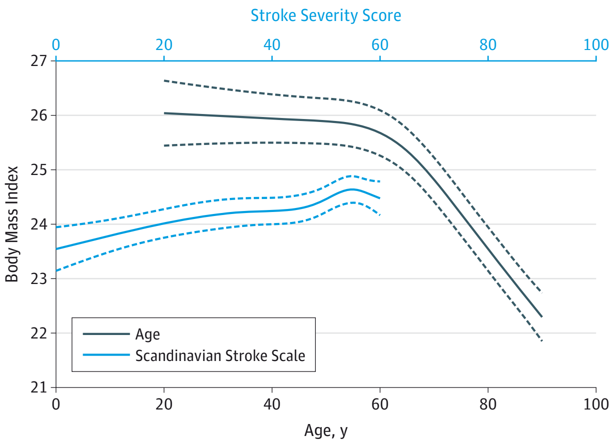
	All		Underweight (BMI < 18.5)		Normal Weight (BMI = 18.5-25.0)		Overweight (BMI = 25-30)		Obese (BMI > 30)	
Characteristic	No.	Death From Stroke[a]	No.	Death From Stroke[a]	No.	Death From Stroke[a]	No.	Death From Stroke[a]	No.	Death From Stroke[a]
All	53 812	1795	5220	382	20 985	742	18 544	462	9063	209
Sex										
Female	25 134	992	3750	287	10 402	401	6935	197	4047	107
Male	28 678	803	1470	95	10 583	341	11 609	265	5016	102
Alcohol[b]										
Above limit	4152	78	400	16	1598	29	1465	27	689	6
Below limit	43 569	1207	3983	249	16 865	495	15 218	312	7503	151
Smoking										
Never	16 331	516	1309	111	6198	211	5845	127	2979	67
Ever	30 381	687	2984	144	11 845	277	10 484	179	5068	87
Civil status										
Single	23 516	1054	3152	266	9816	452	7093	232	3455	104
Not single	29 143	671	1926	100	10 741	258	11 060	216	5416	97
Diabetes mellitus										
Yes	7302	273	363	30	2063	95	2722	96	2154	52
No	45 311	1446	4703	334	18 453	615	15 432	349	6723	148
Atrial fibrillation										
Yes	8748	499	1044	110	3600	220	2823	113	1281	56
No	43 587	1193	3982	239	16 816	490	15 239	320	7550	144
Previous myocardial infarct										
Yes	4907	230	425	45	1787	92	1824	65	871	28
No	46 981	1429	4542	302	18 413	594	16 127	364	7899	169
Hypertension										
Yes	27 727	894	2228	167	9923	357	9972	235	5604	135
No	24 051	772	2722	188	10 210	334	7941	187	3178	63
Previous stroke										
Yes	10 299	439	1182	102	4056	155	3439	129	1622	53
No	42 005	1243	3829	251	16 286	546	14 663	305	7227	141
Intermittent arterial claudication										
Yes	1606	53	189	16	655	26	532	7	230	4
No	40 345	1166	3753	228	15 632	475	14 084	320	6876	143
Severity score										
0-34	11 757	1376	1737	307	4865	568	3518	340	1637	161
35-49	15 547	305	1719	59	6173	133	5202	80	2453	33
50-55	13 620	85	1090	15	5174	31	4864	31	2492	8
56-60	12 888	29	674	1	4773	10	4960	11	2481	7
Quintile of disposable income distribution										
1	14 272	620	1559	139	5609	238	4800	178	2304	65
2	17 297	682	1888	154	6734	291	5757	153	2918	84
3	8877	254	804	46	3462	108	3065	64	1546	36
4	6571	132	511	24	2490	60	2414	38	1156	10
5	6647	106	448	19	2640	44	2446	29	1113	14
Education										
Higher	6450	135	507	21	2746	58	2331	40	866	16
Vocational	21 863	451	1765	67	8237	184	7876	133	3985	67
Basic	6729	586	1186	171	3102	251	1804	126	637	38
Unknown	18 622	622	1752	123	6850	248	6471	163	3549	88

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

[a] Deaths from stroke are deaths within the first month after stroke.

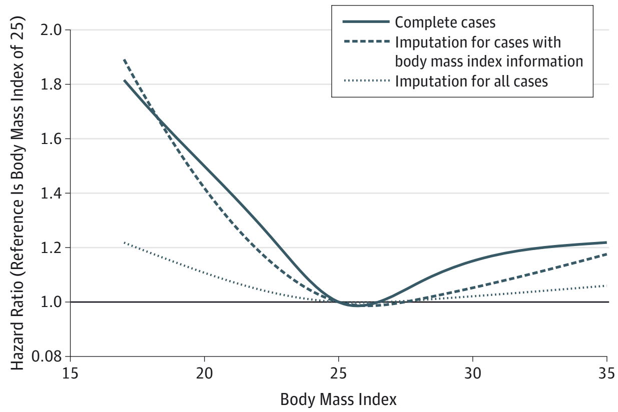
[b] Over limit: more than 14 drinks/week for women and more than 21 for men. Under limit: 14 or fewer drinks/week for women and 21 or fewer for men.

Figure 1. Relationships Between Mean Body Mass Index and Age and Stroke Severity



Adjusted for age, sex, stroke severity (Scandinavian Stroke Scale score), stroke subtype, cardiovascular risk factors, civil status, and socioeconomic status. Body mass index is calculated as weight in kilograms divided by height in meters squared.

Figure 2. Relation Between Body Mass Index as a Continuous Variable and Risk for Death by Stroke Within the First Month After the Stroke



Adjusted for age, sex, stroke severity (Scandinavian Stroke Scale score), stroke subtype, cardiovascular risk factors, civil status, and socioeconomic status. Body mass index is calculated as weight in kilograms divided by height in meters squared.

Table 2. BMI Related to Risk for Death by Stroke Within 1 Week of the Index Stroke

BMI	Hazard Ratio (95% CI)[a] Unadjusted: All Cases (n = 32 743)	Adjusted[b]: All Complete Cases (n = 32 743)[c]	Adjusted[b]: Multiple Imputation for Cases With Information on BMI (n = 53 812)	Adjusted[b]: Multiple Imputation for All Cases (n = 79 617)
Underweight	1.92 (1.54-2.39)	1.17 (0.81-1.69)	1.41 (1.13-1.76)	1.07 (0.93-1.24)
Overweight	0.69 (0.57-0.84)	0.78 (0.58-1.07)	0.85 (0.69-1.04)	0.97 (0.86-1.09)
Obese	0.83 (0.65-1.06)	1.09 (0.75-1.59)	1.19 (0.92-1.52)	1.05 (0.88-1.24)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

[a] Hazard ratios for complete cases and for imputed data.

[b] Adjusted for age, sex, stroke type, stroke severity (Scandinavian Stroke Scale score), cardiovascular risk factors, civil status, and socioeconomic status. Reference is normal weight.

[c] Information on all variables was complete.

Table 3. BMI Related to Risk for Death by Stroke Within 1 Month of the Index Stroke

BMI	Hazard Ratio (95% CI)[a] Unadjusted: All Cases (n = 32 743)	Adjusted[b]: All Complete Cases (n = 32 743)[c]	Adjusted[b]: Multiple Imputation for Cases With Information on BMI (n = 53 812)	Adjusted[b]: Multiple Imputation for All Cases (n = 79 617)
Underweight	2.13 (1.88-2.41)	1.45 (1.18-1.78)	1.55 (1.37-1.76)	1.16 (1.06-1.26)
Overweight	0.70 (0.62-0.78)	0.83 (0.69-0.99)	0.88 (0.78-0.98)	0.96 (0.88-1.04)
Obese	0.65 (0.55-0.75)	1.03 (0.82-1.29)	0.98 (0.84-1.15)	1.00 (0.88-1.13)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

[a] Hazard ratios for complete cases and for imputed data.

[b] Adjusted for age, sex, stroke type, stroke severity (Scandinavian Stroke Scale score), cardiovascular risk factors, civil status, and socioeconomic status. Reference is normal weight.

[c] Information on all variables was complete.

stroke nor was there evidence of a survival advantage associated with being overweight.

Previous studies, including those by our group,[3-7] have all shown that mortality after a stroke is lower in obese than in normal-weight patients with stroke, giving an impression of a survival advantage associated with obesity (ie, the obesity stroke paradox). However, in none of these studies was adjustment made for the severity of the diseases leading to death after the stroke. In the present study, we included only patients who died of stroke within the first week and month and adjusted for stroke severity on admission, thereby adjusting for the severity of the disease that led to death. That it is essential to determine whether there is an obesity paradox appears from our study. Stroke severity was related to BMI, with patients with the most severe strokes having the lowest BMI. As stroke severity is closely associated with the risk for death after a stroke,[26] a lower BMI is also associated with a higher risk for death. This failure to adjust for disease severity leads to selection bias and possible false conclusions. It is not unlikely that the severity of other diseases that lead to death after a stroke (such as heart disease, cancer, and recurrent stroke) is also related to BMI. Because we had no information on the severity of other diseases (such as cancer and heart diseases) leading to death, we could not estimate an independent effect of BMI on the risk for death by these diseases. Thus, our study provides no evidence for the existence of an obesity paradox in stroke.

Overweight status was associated with a slightly lower risk for death by stroke in our analyses of all cases with complete information on all variables; however, in the analysis with multiple imputation for patients for whom information on BMI was missing, the association between overweight status and death disappeared. In our study, BMI was inversely associated with age at admission for stroke. Thus, in comparison with normal-weight patients, stroke occurred 3 years earlier in overweight patients and 6 years earlier in obese patients. Therefore, our study supports the recommendation to strive for normal weight[2] because overweight status and obesity, while associated with premature stroke, do not carry a significant survival advantage.

Underweight status was associated with an increased risk for death by stroke. This does not mean that having a BMI below that of the average population is associated with a higher risk for death in stroke as our study was a hospital-based study of sick people. Underweight status may be an expression of dissatisfaction for reasons ranging from physical and mental illness to poor quality of life because of existential reasons, for which we could not control in our statistical analyses. These factors could reduce the capacity for survival in case of severe illness. Thus, otherwise healthy underweight people who have a stroke might not be at increased risk for death. This notion might find support in the observation that the underweight patients with stroke were 3 years older than their normal-weight counterparts when hospitalized for stroke.

Our study had strengths and weaknesses. Its strength is its large sample size, which allowed for sufficient statistical power. We included patients without limitation on age (>20 years), sex, or stroke severity. Stroke severity was measured on admission to hospital on a well-validated neurologic scale, and height and weight were recorded by nursing staff. Survival data up to 1 month poststroke, including causes of death recorded on death certificates, were complete. We studied only deaths that were caused by stroke, according to death certificates. According to population-based studies, two-thirds of deaths after stroke are reported to be caused by the index stroke.[27-29] These findings are in line with the findings in our study in which death within 1 month, according to death certificates, were due to stroke in 70%. Because we limited our study to only include early deaths within 1 month after the stroke, we believe that it is probable that the deaths studied were caused by the index stroke. Therefore, we were able to focus on the BMI of patients who died of stroke and to correct for the severity of their stroke using the admission SSS score. To our knowledge, this was not done in previous studies of the obesity paradox.[3-7] The results for deaths within 1 week after stroke further strengthen the validity of conclusions drawn from our study (ie, obesity and overweight status were not associated with a survival advantage).

Although the Danish Stroke Registry is a nationwide register of all patients admitted to hospital for acute stroke, its coverage is not yet complete (presently about 80%).[19] Of the 71 617 patients in the register, BMI was available for 53 812 patients; nevertheless, the completeness of all other variables was high, exceeding 85% for all individual variables. The relatively high rate of missing data on BMI is a well-known problem in studies of BMI and stroke survival. In the FOOD (Feed Or Ordinary Diet) Trial,[3] the TEMPIiS (Telemedical Project for Integrative Stroke Care) Trial,[6] and the Korean Stroke Registry,[7] information on BMI was not available for 80%, 66%, and 15% of patients, respectively, probably reflecting the fact that the clinical usefulness of this information is still not generally accepted. Our analysis showed that patients for whom information on BMI was missing had more severe strokes and a higher prevalence of hemorrhagic stroke and a number of stroke risk factors. Hence, patients in whom BMI was missing had higher death rates. However, even when we applied multiple imputation for cases with nonmissing BMI and for all the cases in our data set, our conclusion was sustained. Obesity remained unrelated to death, and no survival advantage was observed. We cannot exclude the possibility of bias due to variables not recorded in the register, including treatment and interventions that might have influenced survival, but we consider it unlikely that such information would change the conclusions of this study.

Conclusions

We found no evidence for the existence of an obesity paradox in stroke. Obesity was not associated with a lower risk for death after a stroke. The obesity paradox reported in previous studies[3-7] appears to be the result of selection bias due to lack of control for the severity of the diseases leading to death after a stroke. Furthermore, a higher BMI was significantly associated with younger age at the time of hospitalization for stroke. Hence, our study supports the recommendation that obese patients with stroke should strive for normal weight.

ARTICLE INFORMATION

Accepted for Publication: April 4, 2014.

Published Online: June 2, 2014. doi:10.1001/jamaneurol.2014.1017.

Author Contributions: Dr Olsen had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Andersen, Olsen.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Olsen.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Dehlendorff, Andersen.

Obtained funding: Olsen.
Study supervision: Olsen.

Conflict of Interest Disclosures: None reported.

Funding/Support: Jascha Fonden provided funding for this study.

Role of the Sponsor: Jascha Fonden had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

REFERENCES

1. Poirier P, Giles TD, Bray GA, et al; American Heart Association; Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation*. 2006;113(6):898-918.

2. Sacco RL, Adams R, Albers G, et al; American Heart Association; American Stroke Association Council on Stroke; Council on Cardiovascular Radiology and Intervention; American Academy of Neurology. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke*. 2006; 37(2):577-617.

3. FOOD Trial Collaboration. Poor nutritional status on admission predicts poor outcomes after stroke: observational data from the FOOD Trial. *Stroke*. 2003;34(6):1450-1456.

4. Olsen TS, Dehlendorff C, Petersen HG, Andersen KK. Body mass index and poststroke mortality. *Neuroepidemiology*. 2008;30(2):93-100.

5. Vemmos K, Ntaios G, Spengos K, et al. Association between obesity and mortality after acute first-ever stroke: the obesity-stroke paradox. *Stroke*. 2011;42(1):30-36.

6. Doehner W, Schenkel J, Anker SD, Springer J, Audebert HJ. Overweight and obesity are associated with improved survival, functional outcome, and stroke recurrence after acute stroke or transient ischaemic attack: observations from the TEMPiS trial. *Eur Heart J*. 2013;34(4):268-277.

7. Kim BJ, Lee S-H, Jung K-H, Yu KH, Lee B-C, Roh J-K; For Korean Stroke Registry investigators. Dynamics of obesity paradox after stroke, related to time from onset, age, and causes of death. *Neurology*. 2012;79(9):856-863.

8. McAuley PA, Blair SN. Obesity paradoxes. *J Sports Sci*. 2011;29(8):773-782.

9. Scherbakov N, Dirnagl U, Doehner W. Body weight after stroke: lessons from the obesity paradox. *Stroke*. 2011;42(12):3646-3650.

10. Kernan WN, Inzucchi SE, Sawan C, Macko RF, Furie KL. Obesity: a stubbornly obvious target for stroke prevention. *Stroke*. 2013;44(1):278-286.

11. Anker SD, von Haehling S. The obesity paradox in heart failure: accepting reality and making rational decisions. *Clin Pharmacol Ther*. 2011;90(1): 188-190.

12. Kato J. Obesity paradox in peripheral vascular disease. *Atherosclerosis*. 2013;229(2):509-510.

13. Florez H, Castillo-Florez S. Beyond the obesity paradox in diabetes: fitness, fatness, and mortality. *JAMA*. 2012;308(6):619-620.

14. Ferreira I, Stehouwer CD. Obesity paradox or inappropriate study designs? time for life-course epidemiology. *J Hypertens*. 2012;30(12):2271-2275.

15. Banack HR, Kaufman JS. The "obesity paradox" explained. *Epidemiology*. 2013;24(3):461-462.

16. Lajous M, Bijon A, Fagherazzi G, et al. Body mass index, diabetes, and mortality in French women: explaining away a "paradox". *Epidemiology*. 2014;25(1):10-14.

17. Olsen TS, Dehlendorff C, Andersen KK. Sex-related time-dependent variations in post-stroke survival: evidence of a female stroke survival advantage. *Neuroepidemiology*. 2007;29 (3-4):218-225.

18. Mainz J, Krog BR, Bjørnshave B, Bartels P. Nationwide continuous quality improvement using clinical indicators: the Danish National Indicator Project. *Int J Qual Health Care*. 2004;16(suppl 1): i45-i50.

19. Det Nationale Indikatorprojekt. National auditrapport 2010: version 3.2011. https://www.sundhed.dk/content/cms/69/4669_2010_apopleksi_nat_sfa.pdf. Accessed October 23, 2013.

20. Lindenstrøm E, Boysen G, Christiansen LW, á Rogvi-Hansen B, Nielsen BW. Reliability of Scandinavian Stroke Scale. *Cerebrovasc Dis*. 1991;1: 103-107.

21. Stroke--1989: recommendations on stroke prevention, diagnosis, and therapy: report of the WHO Task Force on Stroke and other Cerebrovascular Disorders. *Stroke*. 1989;20(10): 1407-1431.

22. Dalton SO, Steding-Jessen M, Gislum M, Frederiksen K, Engholm G, Schüz J. Social inequality and incidence of and survival from cancer in a population-based study in Denmark, 1994-2003: background, aims, material and methods. *Eur J Cancer*. 2008;44(14):1938-1949.

23. World Health Organization. *International Statistical Classification of Diseases, 10th Revision (ICD-10).* Geneva, Switzerland: World Health Organization; 1992.

24. Harrel FE Jr. *Regression Modeling Strategies With Applications to Linear Models, Logistic Regression and Survival Analysis.* Berlin, Germany: Springer; 2001:47-50.

25. R Development Core Team. *R: A Language and Environment for Statistical Computing.* Vienna, Austria: R Foundation for Statistical Computing; 2011.

26. Andersen KK, Andersen ZJ, Olsen TS. Predictors of early and late case-fatality in a nationwide Danish study of 26,818 patients with first-ever ischemic stroke. *Stroke*. 2011;42(10): 2806-2812.

27. Hankey GJ, Jamrozik K, Broadhurst RJ, et al. Five-year survival after first-ever stroke and related prognostic factors in the Perth Community Stroke Study. *Stroke*. 2000;31(9):2080-2086.

28. Kiyohara Y, Kubo M, Kato I, et al. Ten-year prognosis of stroke and risk factors for death in a Japanese community: the Hisayama Study. *Stroke*. 2003;34(10):2343-2347.

29. Lavados PM, Sacks C, Prina L, et al. Incidence, 30-day case-fatality rate, and prognosis of stroke in Iquique, Chile: a 2-year community-based prospective study (PISCIS project). *Lancet*. 2005; 365(9478):2206-2215.