# Ischemic stroke mortality is more strongly associated with anemia on admission than with underweight status

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**Abstract**

**Background:** Underweight patients were recently reported as a group with high risk of post-stroke death. Anemia also increases mortality rates in stroke patients. However, the causal associations between body weight and anemia resulting in stroke-related death remain unclear. We examined the association of weight status and hemoglobin levels with 3-month mortality after ischemic stroke.

**Methods:** The study enrolled all consecutive patients with acute ischemic stroke and no history of stroke, admitted to our hospital between January 2010 and December 2013. Patients were categorized into four body mass index (BMI) categories (underweight, normal-weight, overweight, and obese). Anemia was evaluated according to the World Health Organization criteria (men, <13 g/dl; women, <12 g/dl).

**Results:** A total of 1733 acute ischemic stroke patients (149 underweight, BMI<18.5 $kg/m^2$; 1076 normal-weight, BMI=18.5–24.9 $kg/m^2$; 436 overweight, BMI=25–29.9 $kg/m^2$; and 72 obese, BMI>30 $kg/m^2$) were included. Death within 3 months occurred in 65 patients (underweight, 10.1%; normal-weight, 3.4%; overweight, 2.3%; and obese, 5.6%). Compared to non-anemic patients, those with anemia (n=329, 19.0%) had lower BMI (21.8 vs. 23.7 $kg/m^2$, $P<0.001$) and higher mortality rates (9.1% vs. 2.5%, $P<0.001$). Underweight status was associated with 3-month mortality after adjusting for age, sex, comorbidities, and initial stroke severity. However, in the models that included laboratory findings, it was anemia status (odds ratio, 2.81; 95% confidence interval, 1.46–5.43), not underweight status, that was independently associated with 3-month mortality.

**Conclusion:** Anemia on admission was associated with stroke mortality independent of underweight status.

## Introduction

The risk of ischemic stroke is known to increase with excess body weight, independent of other vascular risk factors [1]. Obesity is also one of the causes of hypertension, diabetes mellitus, and dyslipidemia, which are among the classical vascular risk factors [2]. However, some reports have indicated that obesity may not increase the risk of stroke recurrence [3, 4]. On the other hand, the potential association between obesity and stroke-related mortality is still under debate. A few studies reported that being underweight also leads to poor stroke outcomes [5-8]. Therefore, the causal association between body mass index (BMI) and stroke mortality remains unclear.

Anemia has also been reported to worsen stroke outcomes [9, 10]. While there is yet no consensus regarding the potential association between anemia and BMI, anemia was shown to have higher incidence in underweight individuals [11, 12]. A recent meta-analysis found that anemia increased the mortality risk in patients with stroke [13]. However, few studies have investigated whether anemia remained associated with stroke mortality after adjusting for BMI or nutritional status. Indeed, it was reported that serum albumin levels are associated with stroke mortality [9, 14].

The aim of the present study was to elucidate the relationship among BMI status, anemia, and ischemic stroke mortality, and assess the influence of hypoalbuminemia on this relationship.

## Methods

This was a single-center, hospital-based, retrospective study that received approval from the hospital's institutional review board. The study included consecutive patients

with no history of stroke, who were admitted with acute ischemic stroke to the Brain Attack Center at Ota Memorial Hospital between January 2010 and December 2013. The patients with prior stroke history, as well as those admitted later than 7 days after stroke onset and those who received acute stroke management with intravenous recombinant tissue plasminogen activator treatment, endovascular therapy, or any operation, were excluded from this study. Ischemic strokes were classified according to the criteria laid down by the Trial of ORG 10172 in Acute Stroke Treatment [15]. The following baseline clinical characteristics were recorded at admission: age; sex; BMI; classical vascular risk factors including hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease (CKD), daily alcohol intake (>40 g), and smoking habit; laboratory findings including hemoglobin and serum albumin levels; and the National Institutes of Health Stroke Scale (NIHSS) score, as a measure of neurological severity. Hypertension was defined as the use of anti-hypertensive medications prior to admission, or as a confirmed blood pressure of ≥140/90 mmHg at rest 2 weeks after stroke onset. Diabetes mellitus was defined as glycated hemoglobin levels of ≥6.5%, fasting blood glucose levels of ≥126 mg/dl, or the use of anti-diabetic medication. Dyslipidemia was defined as total-cholesterol levels of ≥220 mg/dl, low-density lipoprotein cholesterol levels of ≥140 mg/dl, high-density lipoprotein cholesterol levels of <40 mg/dl, triglyceride levels of ≥150 mg/dl, or the use of anti-hyperlipidemia medication. CKD was defined as an estimated glomerular filtration rate (eGFR) of <60 ml/min/1.73 $m^2$. In the Japanese population, eGFR is calculated using the following equation:

$eGFR = 194 \times Cr^{-1.094} \times Age^{-0.287}$ ($\times 0.739$ for women) [16].

Each patient was assigned to one of four BMI categories (underweight, BMI<18.5 $kg/m^2$; normal weight, BMI=18.5–24.9 $kg/m^2$; overweight, BMI=25.0–29.9 $kg/m^2$; or obese, BMI ≥30.0 $kg/m^2$), according to the classification laid down by the World Health Organization (WHO). Anemia was also defined according to the WHO criteria as a hemoglobin concentration of <13 g/dl in men and <12 g/dl in women [17]. Statistical analysis was performed using the JMP v12.0.1 software (SAS Institute, Inc., Cary, NC). For continuous variables, the data are expressed either as the means ± standard deviations (SD) or medians (25th and 75th percentiles). Discrete variables are expressed as frequencies and percentages. The statistical significance of inter-group differences was assessed by $\chi^2$, unpaired *t*, Mann-Whitney *U* and Kruskal-Wallis tests, as appropriate. Multivariate logistic analyses were performed to identify the indicators (model 1; age, sex, underweight, hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, daily alcohol intake, smoking habit, cardioembolic stroke and NIHSS scores, and model 2; anemia and serum albumin added to the indicators of model 1) for stroke mortality using a backward selection procedure with P>0.10 as the exclusion criterion for the likelihood ratio test.

## Results

### Baseline characteristics according to BMI categories or anemia status

A total of 1733 patients (age, 72±12 years; women, 37.6%) were included. The mean BMI was 23.3±3.7 $kg/m^2$, and 149 patients (8.6%) were underweight. Demographic and clinical characteristics including age, sex, history hypertension, diabetes mellitus, dyslipidemia, hemoglobin levels, serum albumin levels, and NIHSS score were significantly different among BMI categories (Table 1). Underweight patients were

older and more often female, had higher NIHSS scores, and had lower incidence of hypertension, diabetes mellitus, and dyslipidemia. The levels of hemoglobin and serum albumin were the lowest in underweight patients. The incidence of anemia was also significantly different among BMI categories (Figure 1A), and was the highest (36.9%) in underweight patient. Patients with anemia (n=329, 19.0%) were older and more often underweight, with a higher incidence of CKD and cardioembolic stroke, but with a lower incidence of dyslipidemia, lower daily alcohol intake, less frequent smoking habit, higher NIHSS scores, and lower levels of serum albumin (Supplemental Table 1).

**Indicators for stoke mortality at 3 months**

Death within 3 months occurred in 65 patients (underweight, 10.1%; normal-weight, 3.4%; overweight, 2.3%; and obese, 5.6%; Figure 1B). Table 2 shows the baseline characteristics among patients with 3-month mortality and those without. The patients with 3-month mortality were older and more often female and underweight, with a higher incidence of CKD and cardioembolic stroke, but with a lower incidence of dyslipidemia, less frequent smoking habit, higher NIHSS scores, and lower levels of serum albumin. In addition, the patient with 3-month mortality had higher incidence of anemia than those without (46.2% vs. 17.9%, $P<0.001$, Table 2). The causes of death are listed in Supplemental Table 2. Most patients died of stroke, cardiovascular disease, or infection. Multivariate logistic regression analysis revealed that age, cardioembolic stroke, NIHSS at admission and underweight status was independently associated with 3-month mortality (Table 3, model 1). When including laboratory findings (anemia and serum albumin levels) in the model, we found that anemia, but not underweight status or serum albumin levels, was independently associated with 3-month mortality (odds ratio, 2.81; 95% confidence interval, 1.46–5.43) (Table 3, model 2).

## Discussion

In the present study, we found that the incidence of anemia and the rate of 3-month mortality were higher in underweight patients than in those with other BMI categories. In addition, we found that anemia status, but not underweight status, was independently associated with 3-month mortality.

Patients with lower BMI were reported to have a higher risk of mortality after stroke, while the opposite was reported for patients with higher BMI [5-8, 18]. In Japan, several epidemiological studies found that lower BMI represented a significant risk factor for long-term stroke mortality, especially among men [19, 20]. While these large-scale studies evaluated the long-term outcomes of stroke patients (over the course of 10 or even 19 years of follow-up), Kawase et al. have recently reported that, in Japanese ischemic stroke patients, lower BMI might be associated with not only long-term but also short-term outcomes [21]. Similarly, in our study, underweight patients showed significantly higher mortality at 3 months after stroke compared to that noted among normal-weight patients, while this was not the case for obese patients. The present study evaluated the causal association among BMI, anemia, and stroke mortality, and found that anemia status, but not underweight status, was independently associated with stroke mortality, which represents a novel finding.

In the present study, the prevalence of anemia was 19.0%, which is similar to the prevalence reported in a recent meta-analysis for acute ischemic stroke patients (21.9%) [13]. In fact, several studies have showed that anemia or lower hemoglobin levels were associated with stroke mortality [13]. Unlike these previous studies, we considered the concomitant influence of BMI (weight status) and serum albumin levels. Our findings

provided further evidence for the associations between anemia status and stroke mortality in consideration of these indicators. Nevertheless, we were not able to fully clarify the reason why anemia was associated with stroke mortality. One possible cause for our observation is related to the complications due to anemia. In general, the pathological mechanisms of congestive heart failure, CKD, and anemia are thought to be interconnected, acting in a vicious circle in which each condition causes or exacerbates the other [22]. Indeed, our univariate analysis showed that CKD was associated with mortality, even though this association was not significant in the multivariate analysis. Although we reanalyzed the multivariate logistic regression analysis adding the severe renal dysfunction (eGFR<30 ml/min/1.73 $m^2$) instead of CKD, severe renal dysfunction was also not associated with mortality (data not shown). The details regarding the severity of heart failure could not be evaluated in the present study. Further studies whether the combination of interactions between anemia and renal failure or heart failure contributes to stroke mortality will be needed. Second, some patients with anemia have active cancer. Indeed, five patients died of cancer within 3 months after stroke. Third, the oxygen supply of the brain depends on hemoglobin levels and blood viscosity [13]. Therefore, impaired oxygen and energy supply might contribute to the progression of stroke and occurrence of stroke-related death in anemic patients. Anemia has also been suggested to be related to inflammatory response and endothelial dysfunction [13]. The above-described factors might account for at least part of the increased stroke mortality noted among patients with anemia.

Previous reports found that underweight status, anemia, and low albumin levels were associated with increased mortality after stroke, but these studies only accounted for the individual effect of each factor, and not for their interaction [5-8, 10, 23-25]. In our

study, we showed that anemia status was associated with mortality after ischemic stroke, independent of underweight status and low albumin levels; moreover, we showed that underweight status and low albumin levels did not remain statistically significant predictors of mortality when adjusting for anemia status. Our results thus suggest that anemia may account for the high post-stroke mortality rates noted in underweight patients. It remains unclear whether the treatment of anemia at admission could reduce the mortality after ischemic stroke. Further interventional treatment to correct low hemoglobin levels may clarify the therapeutic value of treating anemia to reduce mortality risk after ischemic stroke.

There are several limitations to our study. First, this was a single-center study, and we cannot exclude the possibility of selection bias. However, ours is a large-volume stroke center, and the analysis was based on a large study sample (1733 patients). Moreover, the baseline characteristics of our patients did not deviate from those reported in large Japanese stroke-registry studies [26, 27]. Therefore, we expect that selection bias does not play a major role. Second, this retrospective cross-sectional study depended on the quality of data collection and thoroughness of recording of the results from laboratory examinations performed upon admission; therefore, it was not possible to investigate the cause of low hemoglobin levels. It was reported that patients with anemia have a higher incidence of malnutrition, and nutrition status early after stroke was independently associated with poor outcome [28, 29]. In our study, we were not able to evaluate nutrition status because of the type of data that were recorded, and therefore, potential bias related to malnutrition was not accounted for. Finally, other laboratory findings such as initial glucose levels or lipid profiles were not evaluated in the present study. Indeed, initial glucose levels were thought to be associated with

stroke mortality [30]. In addition, lipid profiles might be also associated with the underweight or anemia status.

## Conclusion

Our study found that the 3-month mortality after acute ischemic stroke was higher among underweight patients than among patients who were not underweight. The incidence of anemia was also higher among underweight patients, and anemia status was associated with stroke mortality, independent of the underweight status and serum albumin levels.


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## Contributors' statement

Satoshi Kubo, Naohisa Hosomi, Hirofumi Maruyama, Masaru Kuriyama, and Masayasu Matsumoto contributed to the study design, data analysis, data interpretation, and manuscript preparation. Satoshi Kubo, Naoyuki Hara, Shuichiro Neshige, Takahiro

Himeno, Shinichi Takeshima, Kazuhiro Takamatsu, Yutaka Shimoe, Taisei Ota, and Masaru Kuriyama contributed in data collection. All authors revised and approved the manuscript.

**Conflicts of interest**

Dr. Hosomi reports an honorarium from Mochida Pharmaceutical Co., LTD., which is outside the scope of the submitted work. Prof. Matsumoto reports grants from Takeda Pharmaceutical Co., LTD., Sanofi K.K., Mochida Pharmaceutical Co., LTD., Otsuka Pharmaceutical, and Daiichi Sankyo Co., LTD. and honoraria from Sanofi K.K., Bayer Health Care, and Daiichi Sankyo Co., LTD., which are outside the scope of the submitted work. The other authors declare no conflicts of interest.

## References

1. Strazzullo P, D'Elia L, Cairella G, et al. Excess body weight and incidence of stroke: meta-analysis of prospective studies with 2 million participants. Stroke. 2010;41:e418-26.

2. Wilson PW, D'Agostino RB, Sullivan L, et al. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. Arch Intern Med. 2002;162:1867-72.

3. Ovbiagele B, Bath PM, Cotton D, et al. Obesity and recurrent vascular risk after a recent ischemic stroke. Stroke. 2011;42:3397-402.

4. Andersen KK, Olsen TS. Body mass index and stroke: overweight and obesity less often associated with stroke recurrence. J Stroke Cerebrovasc Dis. 2013;22:e576-81.

5. Kim BJ, Lee SH, Ryu WS, et al. Paradoxical longevity in obese patients with intracerebral hemorrhage. Neurology. 2011;76:567-73.

6. Vemmos K, Ntaios G, Spengos K, et al. Association between obesity and mortality after acute first-ever stroke: the obesity-stroke paradox. Stroke. 2011;42:30-6.

7. Doehner W, Schenkel J, Anker SD, et al. 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;34:268-77.

8. Andersen KK, Olsen TS. The obesity paradox in stroke: lower mortality and lower risk of readmission for recurrent stroke in obese stroke patients. Int J Stroke. 2015;10:99-104.

9. Famakin B, Weiss P, Hertzberg V, et al. Hypoalbuminemia predicts acute stroke mortality: Paul Coverdell Georgia Stroke Registry. J Stroke Cerebrovasc Dis. 2010;19:17-22.

10. Hao Z, Wu B, Wang D, et al. Acohort study of patients with anemia on admission and fatality after acute ischemic stroke. J Clin Neurosci. 2013;20:37-42.

11. Qin Y, Melse-Boonstra A, Pan X, et al. Anemia in relation to body mass index and waist circumference among Chinese women. Nutr J. 2013;12:10.

12. Ugwuja EI, Ogbonnaya LU, Obuna AJ, et al. Anaemia in relation to body mass index (BMI) and socio-demographic characteristics in adult Nigerians in Ebonyi state. J Clin Diagn Res. 2015;9:LC04-7.

13. Li Z, Zhou T, Li Y, et al. Anemia increases the mortality risk in patients with stroke: A meta-analysis of cohort studies. Sci Rep. 2016;6:26636.

14. Gillum RF, Ingram DD, Makuc DM. Relation between serum albumin concentration and stroke incidence and death: the NHANES I Epidemiologic Follow-up Study. Am J Epidemiol. 1994;140:876-88.

15. Adams HP, Jr., Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993;24:35-41.

16. Matsuo S, Imai E, Horio M, et al. Revised equations for estimated GFR from serum

creatinine in Japan. Am J Kidney Dis. 2009;53:982-92.

17. Nutritional anaemias. Report of a WHO scientific group. World Health Organ Tech Rep Ser. 1968;405:5-37.

18. Kim BJ, Lee SH, Jung KH, et al. Dynamics of obesity paradox after stroke, related to time from onset, age, and causes of death. Neurology. 2012;79:856-63.

19. 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;34:2343-7.

20. Oki I, Nakamura Y, Okamura T, et al. Body mass index and risk of stroke mortality among a random sample of Japanese adults: 19-year follow-up of NIPPON DATA80. Cerebrovasc Dis. 2006;22:409-15.

21. Kawase S, Kowa H, Suto Y, et al. Association between body mass index and outcome in Japanese ischemic stroke patients. Geriatr Gerontol Int. 2016.

22. Silverberg D, Wexler D, Blum M, et al. The association between congestive heart failure and chronic renal disease. Curr Opin Nephrol Hypertens. 2004;13:163-70.

23. Abubakar S, Sabir A, Ndakotsu M, et al. Low admission serum albumin as prognostic determinant of 30-day case fatality and adverse functional outcome following acute ischemic stroke. Pan Afr Med J. 2013;14:53.

24. Babu MS, Kaul S, Dadheech S, et al. Serum albumin levels in ischemic stroke and its

subtypes: correlation with clinical outcome. Nutrition. 2013;29:872-5.

25. Milionis H, Papavasileiou V, Eskandari A, et al. Anemia on admission predicts short- and long-term outcomes in patients with acute ischemic stroke. Int J Stroke. 2015;10:224-30.

26. Kimura K, Minematsu K, Kazui S, et al. Mortality and cause of death after hospital discharge in 10,981 patients with ischemic stroke and transient ischemic attack. Cerebrovasc Dis. 2005;19:171-8.

27. Kamouchi M, Matsuki T, Hata J, et al. Prestroke glycemic control is associated with the functional outcome in acute ischemic stroke: the Fukuoka Stroke Registry. Stroke. 2011;42:2788-94.

28. Mitrache C, Passweg JR, Libura J, et al. Anemia: an indicator for malnutrition in the elderly. Ann Hematol. 2001;80:295-8.

29. FOOD Trial Collaboration. Poor nutritional status on admission predicts poor outcomes after stroke: observational data from the FOOD trial. Stroke. 2003;34:1450-6.

30. Roquer J, Giralt-Steinhauer E, Cerda G, et al. Glycated Hemoglobin Value Combined with Initial Glucose Levels for Evaluating Mortality Risk in Patients with Ischemic Stroke. Cerebrovasc Dis. 2015;40:244-50.

**Figure legends**

Figure 1. Prevalence of anemia according to body mass index category (A). Three-month mortality rates according to body mass index category (B).

**Table 1. Baseline characteristics at admission, by BMI category**

| Factors | Underweight (n = 149) | Normal weight (n = 1076) | Overweight (n = 436) | Obese (n = 72) | *p*-value (Among the groups) |
|---|---|---|---|---|---|
| Age, years | 76±11 | 73±12 | 69±11 | 64±15 | <0.001 |
| Female, n (%) | 81 (54.4) | 386 (35.9) | 151 (34.8) | 33 (45.1) | <0.001 |
| Body mass index, kg/m$^2$ | 17.2±1.1 | 22.1±1.8 | 26.9±1.3 | 32.4±2.5 | <0.001 |
| Vascular risk factors | | | | | |
| Hypertension, n (%) | 103 (69.1) | 772 (71.8) | 352 (80.6) | 63 (88.7) | <0.001 |
| Diabetes mellitus, n (%) | 37 (24.8) | 331 (30.8) | 192 (43.9) | 30 (42.3) | <0.001 |
| Dyslipidemia, n (%) | 54 (36.2) | 557 (51.8) | 284 (65.0) | 50 (70.4) | <0.001 |
| Chronic kidney disease, n (%) | 47 (31.5) | 349 (32.4) | 142 (32.5) | 16 (22.5) | 0.379 |
| Daily alcohol intake, n (%) | 21 (14.1) | 166 (15.4) | 72 (16.5) | 9 (12.7) | 0.806 |
| Smoking habit, n (%) | 36 (24.2) | 275 (25.6) | 122 (27.9) | 24 (33.8) | 0.348 |
| Subtype of ischemic stroke | | | | | 0.088 |

| | | | | | |
|---|---|---|---|---|---|
| Cardioembolic stroke, n (%) | 41 (27.5) | 235 (21.8) | 83 (19.0) | 20 (27.8) | |
| Large-artery atherosclerosis, n (%) | 42 (28.2) | 342 (31.8) | 151 (34.6) | 27 (37.5) | |
| Small-vessel occlusion, n (%) | 42 (28.2) | 326 (30.3) | 145 (33.3) | 19 (26.4) | |
| Other determined etiology, n (%) | 7 (4.7) | 41 (3.8) | 7 (1.6) | 1 (1.4) | |
| Undetermine, n (%) | 17 (11.4) | 132 (12.3) | 50 (11.4) | 5 (6.9) | |
| Hemoglobin, g/dl | 12.9±2.0 | 13.8±1.9 | 14.5±1.7 | 14.9±1.5 | <0.001 |
| Serum albumin, g/dl | 4.0±0.4 | 4.2±0.4 | 4.3±0.4 | 4.3±0.4 | <0.001 |
| NIHSS score at admission | 3 (2–7) | 2 (1–5) | 2 (1–4) | 3 (1–4) | <0.001 |

NIHSS, National Institutes of Health Stroke Scale

**Table 2. Univariate analysis to determine factors associated with 3-month mortality.**

| Factors | Death (n=65) | Alive (n=1668) | p-value |
|---|---|---|---|
| Age, years | 80±11 | 71±12 | <0.001 |
| Female, n (%) | 34 (52.3) | 617 (37.0) | 0.012 |
| Body mass index, kg/m$^2$ | 21.8±4.8 | 23.4±3.6 | <0.001 |
| Underweight, n (%) | 15 (23.1) | 134 (8.0) | <0.001 |
| Vascular risk factors | | | |
| Hypertension, n (%) | 46 (70.8) | 1244 (74.6) | 0.490 |
| Diabetes mellitus, n (%) | 23 (35.4) | 567 (34.0) | 0.816 |
| Dyslipidemia, n (%) | 25 (38.5) | 920 (55.2) | 0.008 |
| Chronic kidney disease, n (%) | 36 (55.4) | 518 (31.1) | <0.001 |
| Daily alcohol intake, n (%) | 5 (7.7) | 263 (15.8) | 0.077 |
| Smoking habit, n (%) | 9 (13.9) | 448 (26.9) | 0.020 |
| Cardioembolic stroke, n (%) | 38 (58.5) | 341 (20.4) | <0.001 |
| Hemoglobin, g/dl | 12.3±3.0 | 14.0±1.8 | <0.001 |
| Anemia, n (%) | 30 (46.2) | 299 (17.9) | <0.001 |
| Serum albumin, g/dl | 3.8±0.4 | 4.2±0.4 | <0.001 |

| | | | |
|---|---|---|---|
| NIHSS score at admission | 20 (8–27) | 2 (1–4) | <0.001 |

NIHSS, National Institutes of Health Stroke Scale

**Table 3. Indicators associated with 3-month mortality after acute ischemic stroke**

| Indicators | Model 1 | | Model 2 | |
|---|---|---|---|---|
| | Odds ratio (95%CI) | P | Odds ratio (95%CI) | P |
| Age (per 1 year) | 1.04 (1.01-1.07) | 0.003 | 1.03 (1.00-1.06) | 0.032 |
| Cardioembolic stroke | 2.04 (1.06-3.92) | 0.034 | 1.98 (1.02-3.82) | 0.043 |
| NIHSS (per 1 score) | 1.15 (1.11-1.18) | <0.001 | 1.15 (1.12-1.18) | <0.001 |
| Underweight status | 2.39 (1.06-5.07) | 0.036 | 2.06 (0.90-4.44) | 0.083 |
| Anemia | - | - | 2.81 (1.46-5.43) | 0.002 |

CI, confidence interval and NIHSS, National Institutes of Health Stroke Scale

Multivariate logistic analyses were performed to identify the indicators (model 1; age, sex, underweight, hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, daily alcohol intake, smoking habit, cardioembolic stroke and NIHSS scores, and model 2; anemia and serum albumin added to the indicators of model 1) for multiple lesions using a backward selection procedure with P>0.10 as the exclusion criterion for the likelihood ratio test.

Figure(s)
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