ORIGINAL ARTICLE

Impact of body mass index on outcome in stroke patients treated with intravenous thrombolysis

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Background and purpose: The impact of body mass index (BMI) on outcome in stroke patients treated with intravenous thrombolysis (IVT) was investigated.

Methods: In a multicentre IVT-register-based observational study, BMI with (i) poor 3-month outcome (i.e. modified Rankin Scale scores 3–6), (ii) death and (iii) symptomatic intracranial haemorrhage (sICH) based on criteria of the ECASS II trial was compared. BMI was used as a continuous and categorical variable distinguishing normal weight (reference group 18.5–24.9 kg/m^2) from underweight (<18.5 kg/m^2), overweight (25–29.9 kg/m^2) and obese (≥30 kg/m^2) patients. Univariable and multivariable regression analyses with adjustments for age and stroke severity were done and odds ratios with 95% confidence intervals [OR (95% CI)] were calculated.

Results: Of 1798 patients, 730 (40.6%) were normal weight, 55 (3.1%) were underweight, 717 (39.9%) overweight and 295 (16.4%) obese. Poor outcome occurred in 38.1% of normal weight patients and did not differ significantly from underweight (45.5%), overweight (36.1%) and obese (32.5%) patients. The same was true for death (9.5% vs. 14.5%, 9.6% and 7.5%) and sICH (3.9% vs. 5.5%, 4.3%, 2.7%). Neither in univariable nor in multivariable analyses did the risks of poor outcome, death or sICH differ significantly between BMI groups. BMI as a continuous variable was not associated with poor outcome, death or sICH in unadjusted [OR (95% CI) 0.99 (0.97–1.01), 0.98 (0.95–1.02), 0.98 (0.94–1.04)] or adjusted analyses [OR (95% CI) 1.01 (0.98–1.03), 0.99 (0.95–1.05), 1.01 (0.97–1.05)], respectively.

Conclusion: In this largest study to date, investigating the impact of BMI in IVT-treated stroke patients, BMI had no prognostic meaning with regard to 3-month functional outcome, death or occurrence of sICH.

Introduction

There is uncertainty whether body weight affects 3-month outcome or complication rates in stroke patients treated with intravenous thrombolysis (IVT). Previous studies revealed conflicting results. In some

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studies, obesity – defined by body mass index (BMI) >30 kg/m^2 [1–3] or body weight ≥95 [4] or >100 kg [5–7] – was associated with worse functional outcome [1,5,7], higher mortality [1,5,6] and increased risk of symptomatic intracranial haemorrhage (sICH) [4,6]. In contrast, other studies did not find any significant association between obesity and functional outcome [2,6], mortality [3] or bleeding complications [1,2,5,7].

The role of underweight has only been investigated in a single small study (14 underweight patients) which included both IVT-treated and intraarterially treated patients. This study did not reveal a significant association between underweight and mortality at 3 months [3].

Thus, it is controversial whether overweight or underweight is independently associated with functional outcome or complications in IVT-treated stroke patients. With these considerations in mind, our aim was to investigate the impact of BMI on functional 3-month outcome, mortality and sICH in a large population of IVT-treated stroke patients.

Methods

As a joint initiative of five European stroke centres, the Thrombolysis in Stroke Patients (TriSP) investigators performed a large collaborative explorative, register-based study in order to address the impact of BMI on outcomes in IVT-treated stroke patients. All participating centres treated patients with acute ischaemic stroke with IVT according to current guidelines at the relevant time (http://www.eso-stroke.org/eso-stroke/education/guidelines.html).

Data from individual patients were collected with a standardized form with predefined variables as was done in previous studies [8–10]. Local study investigators filled in the forms systematically using prospectively ascertained in-hospital intravenous ischaemic stroke thrombolysis registries. Completed forms from all centres were compiled in the coordinating centre Basel, where the analysis of the pooled data was performed, as done previously [8–10]. The study was approved by the ethics committee in Basel, Switzerland. The requirement for additional local ethical approval differed between participating centres and was obtained if required.

The following prospectively ascertained variables were used: age, sex, initial stroke severity as assessed by the National Institutes of Health Stroke Scale (NIHSS) score [11], data on weight (in kilograms) and height (in metres) at stroke onset measured or obtained from the patient or relatives or – if not available – from estimates made by the attending stroke physician, blood pressure prior to IVT, onset-to-treatment time, renal function as quantified by the estimated glomerular filtration rate (eGFR) (using the Chronic Kidney Disease Epidemiology Collaboration equation [9]) and glucose levels in blood serum, vascular risk factors according to predefined criteria [12] and prior treatment with antithrombotic agents (antiplatelet agents or anticoagulants). Functional outcome was assessed by outpatient visits or telephone calls using the modified Rankin Scale (mRS) at 3 months. There was monitoring for sICH by follow-up computed tomography or magnetic resonance imaging as done in prior research [8–10].

Each centre reported on the period for which they had prospectively collected data on consecutive patients up to 31 July 2014 (Table S1). All patients with available data on BMI were included and those with missing 3-month outcome data were excluded. BMI was calculated by dividing weight in kilograms by squared height in metres.

Outcome and complication measures were (i) poor functional 3-month outcome (defined as 3-month mRS 3–6), (ii) death and (iii) sICH according to the criteria of the ECASS II trial [13].

Statistical analyses

Statistical analyses were performed using SPSS (version 21.0 for Windows, SPSS Inc., Chicago, IL, USA). BMI was compared with outcome measures as a categorical variable and as a continuous variable. The categorical BMI groups were chosen according to prior research [2,14,15]: underweight (BMI <18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2) and obese (≥30 kg/m^2). Normal weight patients served as the reference group.

Demographic and clinical baseline characteristics were compared between patients in the BMI groups using Fisher's exact test or the chi-squared test for categorical variables and the Mann–Whitney U test for continuous variables. The association between BMI (both as a continuous variable and as a categorical variable as defined above) and each outcome was estimated by calculating the odds ratios (ORs) with 95% confidence intervals (CIs) using binary logistic regression models. In the multivariable analysis, the models were adjusted for all variables with $P < 0.1$ in the univariate analyses if the number of covariables did not exceed the number of outcome events (at least 1:10 ratio). Otherwise, those variables with established outcome-predictive value according to the literature were chosen (i.e. age, stroke severity, baseline glucose, atrial fibrillation and eGFR).

Post hoc, the association of body weight and outcomes was assessed. Body weight was dichotomized

into patients weighing ≤50 kg vs. >50 kg and >100 kg vs. ≤100 kg.

Furthermore, a meta-analysis was performed *post hoc* between obese and non-obese patients as well as between patients weighing >100 kg and ≤100 kg. The outcomes of interest were poor functional 3-month outcome, mortality and sICH (ECASS II criteria). ORs and their respective CIs were estimated for each study. The random effects model described by DerSimonian and Laird was used for the main analysis. Calculations were performed using the Review Manager (RevMan) Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Results

In total, 1798 of 1848 (97.3%) IVT-treated patients were suitable for analysis. Fifty (2.7%) patients were excluded because data on 3-month outcome were not available. Amongst eligible patients, 730 were normal weight (40.6%), 55 were underweight (3.1%), 717 overweight (39.9%) and 295 obese (16.4%). Baseline characteristics are summarized in Table 1. Results of the univariable and multivariable analyses for outcomes are presented in Tables 2 and 3. The distribution of mRS at 3 months depending on BMI is presented in Fig. S1.

Underweight versus normal weight

Underweight patients differed significantly from normal weight patients in terms of age, stroke severity, glucose and eGFR levels, current smoking and hypercholesterolaemia.

Amongst all BMI groups, the group of underweight patients had – numerically – the highest values for each of the primary outcomes (poor functional outcome 45.5%, mortality 14.5%, sICH 5.5%) (Fig. 1).

There were no significant differences in poor functional outcome (45.5% vs. 38.1%, $P = 0.280$), death (14.5% vs. 9.5%, $P = 0.236$) or sICH (5.5% vs. 3.9%, $P = 0.559$) between underweight and normal weight patients. Unadjusted (OR 1.36, 95% CI 0.78–2.35) and after adjustment (OR 1.34, 95% CI 0.71–2.54) the risk of poor functional outcome did not differ significantly. The same was true for the unadjusted odds for death (OR 1.44, 95% CI 0.42–4.89) and sICH (OR 1.63, 95% CI 0.74–3.59).

Overweight versus normal weight

Overweight patients differed from those with normal weight in frequency of hypertension, hypercholesterolaemia and diabetes mellitus. Poor functional outcome (36.1% vs. 38.1%, $P = 0.447$), death (9.6% vs. 9.5%, $P = 0.912$) and sICH (4.3% vs. 3.9%, $P = 0.647$)

Table 1 Clinical characteristics of IVT-treated stroke patients divided into groups depending on their BMI at stroke onset

	Normal weight[a]	Underweight[a]		Overweight[a]		Obese[a]	
	n = 730	*n* = 55	*P* value[b]	*n* = 717	*P* value[b]	*n* = 295	*P* value[b]
Age, years, median (IQR)	74 (63–80)	66 (55–76)	0.014	73 (62–79)	0.200	69 (60–77)	<0.001
Weight, kg, median (IQR)	65 (60–72)	50 (45–55)	<0.001	79 (71–84)	<0.001	95 (85–102)	<0.001
Men, *n* (%)	426 (58.4)	28 (50.9)	0.322	436 (61.0)	0.325	177 (60.0)	0.674
Stroke severity, NIHSS, median (IQR)	10 (6–17)	14 (9–18)	0.01	10 (6–16)	0.426	10 (6–15)	0.030
Systolic blood pressure, mmHg, median (IQR)	152 (136–170)	150 (132–172)	0.50	153 (139–171)	0.152	155 (140–170)	0.253
Onset-to-treatment time, min, median (IQR)	150 (120–180)	135 (118–172)	0.192	150 (120–185)	0.662	158 (120–196)	0.066
eGFR, ml/min/1.73 m^2, median (IQR)	78 (61–92)	86 (71–97)	0.033	76 (60–90)	0.103	76 (60–90)	0.099
Glucose on admission, mmol/l, median (IQR)	6.4 (5.7–7.7)	6.0 (5.0–6.8)	0.004	6.6 (5.8–7.8)	0.091	6.8 (5.9–8.9)	0.001
Atrial fibrillation, *n* (%)	199 (27.3)	15 (27.3)	0.992	186 (25.9)	0.549	75 (25.4)	0.585
Hypertension, *n* (%)	459 (62.9)	32 (58.2)	0.564	502 (70.0)	0.040	235 (79.7)	<0.001
Smoking, *n* (%)	152 (20.9)	21 (38.9)	0.004	139 (19.5)	0.488	62 (21.4)	0.865
Hypercholesterolaemia, *n* (%)	334 (45.8)	15 (27.3)	0.008	373 (52.2)	0.015	171 (59.0)	<0.001
Diabetes mellitus, *n* (%)	92 (12.6)	9 (16.4)	0.406	129 (18.0)	0.050	80 (27.1)	<0.001
Coronary artery disease, *n* (%)	121 (16.6)	9 (16.4)	0.957	108 (15.1)	0.411	51 (17.3)	0.854
Prior stroke, *n* (%)	111 (15.2)	7 (13.0)	0.844	103 (14.5)	0.653	40 (13.7)	0.559
Prior antithrombotics, *n* (%)	346 (47.5)	21 (38.2)	0.208	351 (49.2)	0.535	165 (55.9)	0.016

BMI, body mass index; eGFR, estimated glomerular filtration rate; IQR, interquartile range; IVT, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale.

[a]Underweight (BMI < 18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2) and obese (≥30 kg/m^2); [b]the normal weight subgroup served as reference group.

Table 2 Univariable analysis of clinical characteristics

	Outcome measures		
Putative predicting variables	Poor outcome[a]	Death	sICH
Age (each year)	1.04 (1.03–1.05), <0.001	1.06 (1.04–1.08), <0.001	1.02 (0.99–1.04), 0.113
Gender	1.41 (1.16–1.71), 0.001	1.21 (0.88–1.66), 0.254	1.11 (0.68–1.80), 0.675
NIHSS (each point)	1.17 (1.15–1.19), <0.001	1.15 (1.11–1.18), <0.001	1.08 (1.04–1.11), <0.001
Glucose (each mg/dl)	1.06 (1.02–1.09), 0.001	1.08 (1.04–1.12), <0.001	1.02 (0.97–1.07), 0.412
eGFR (each ml/min/1.73 m^2)	1.02 (1.01–1.02), <0.001	1.03 (1.02–1.04), <0.001	1.00 (0.99–1.01), 0.458
Systolic blood pressure (each mmHg)	1.01 (0.99–1.01), 0.205	1.01 (0.99–1.01), 0.467	0.99 (0.98–1.01), 0.723
Onset-to-treatment time (each min)	0.99 (0.99–1.00), 0.312	1.01 (0.99–1.02), 0.421	1.01 (0.99–1.02), 0.976
Atrial fibrillation	2.15 (1.74–2.67), <0.001	2.54 (1.84–3.52), <0.001	1.47 (0.89–2.44), 0.320
Diabetes mellitus	1.56 (1.22–2.00), <0.001	1.75 (1.21–2.54), 0.003	1.32 (0.74–2.27), 0.353
Hypertension	1.59 (1.28–1.96), <0.001	1.93 (1.31–2.85), 0.001	1.01 (0.60–1.69), 0.972
Hypercholesterolaemia	1.06 (0.87–1.28), 0.571	1.02 (0.74–1.41), 0.893	0.84 (0.52–1.36), 0.486
Current smoking	0.66 (0.51–0.84), 0.001	0.40 (0.24–0–68), 0.001	0.89 (0.48–1.64), 0.698
Coronary artery disease	1.66 (1.28–2.14), <0.001	2.71 (1.91–3.87), <0.001	1.71 (0.974–2.99), 0.062
Prior ischaemic stroke	1.14 (0.87–1.49), 0.330	1.09 (0.70–1.70), 0.695	1.54 (0.84–2.81), 0.163
Prior antithrombotic treatment	1.67 (1.38–2.03), <0.001	2.57 (1.82–3.62), <0.001	1.78 (1.08–2.91), 0.023
Underweight versus normal weight	1.36 (0.78–2.35), 0.280	1.63 (0.74–3.59), 0.225	1.44 (0.42–4.89), 0.559
Overweight versus normal weight	0.92 (0.74–1.14), 0.441	1.02 (0.72–1.45), 0.912	1.13 (0.67–1.90), 0.647
Obese versus normal weight	0.78 (0.59–1.04), 0.096	0.77 (0.67–1.27), 0.311	0.70 (0.32–1.55), 0.373
BMI continuous (each point)	0.99 (0.97–1.01), 0.358	0.98 (0.95–1.02), 0.419	0.98 (0.94–1.04), 0.633
Obese versus underweight	0.58 (0.32–1.04), 0.067	0.47 (0.20–1.13), 0.091	0.48 (0.12–1.88), 0.294
>100 kg vs. ≤100 kg	1.11 (0.71–1.75), 0.643	1.71 (0.91–3.23), 0.096	0.60 (1.50–2.51), 0.488
>95 kg vs. ≤95 kg	0.91 (0.65–1.28), 0.579	1.09 (0.64–1.88), 0.746	0.61 (0.22–1.71), 0.348
≤50 kg vs. >50 kg	1.75 (0.94–3.29), 0.079	2.92 (1.37–6.24), 0.006	0.63 (0.09–4.62), 0.646

BMI, body mass index; eGFR, estimated glomerular filtration rate; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracerebral haemorrhage (ECASS II definition).
Odds ratio (95% confidence interval), *P* value.
[a]Poor outcome: modified Rankin Scale 3–6.

Table 3 Multivariable analysis of outcomes

	Outcome measures		
Putative predicting variables	Poor outcome[a]	Death	sICH[b]
Underweight versus normal weight	1.34 (0.71–2.54), 0.373[c]	1.44 (0.42–4.89), 0.559[d]	1.63 (0.74–3.59), 0.225[d]
Overweight versus normal weight	0.90 (0.70–1.15), 0.386[e]	0.95 (0.65–1.40), 0.783[f]	1.12 (0.66–1.89), 0.679[c]
Obese versus normal weight	0.95 (0.68–1.31), 0.740[f]	1.00 (0.59–1.70), 0.993[c]	0.70 (0.32–1.55), 0.373[d]
BMI continuous (each point)	1.01 (0.98–1.03), 0.353[c]	1.01 (0.97–1.05), 0.596[c]	0.99 (0.95–1.05), 0.891[c]

Odds ratio (95% confidence interval), *P* value.
[a]Poor outcome: modified Rankin Scale 3–6; [b]sICH, symptomatic intracerebral haemorrhage (ECASS II definition); [c]adjusted for age and National Institutes of Health Stroke Scale; [d]no adjustment because of the small number of sICH; [e]adjusted for all variables with $P < 0.1$ in univariable analysis; [f]adjusted for age, National Institutes of Health Stroke Scale, baseline glucose, estimated glomerular filtration rate, atrial fibrillation.

occurred similarly often in both groups and the adjusted odds of poor functional outcome (OR 0.90, 95% CI 0.70–1.15), death (OR 0.95, 95% CI 0.65–1.40) and sICH (OR 1.12, 95% CI 0.66–1.89) did not differ significantly.

Obese versus normal weight

Compared with normal weight, obese patients were younger, had higher glucose levels, higher prevalence of hypertension, hypercholesterolaemia and diabetes mellitus, and more common use of antithrombotics. Poor functional outcome (32.5% vs. 38.1%, $P = 0.096$), death (7.5% vs. 9.5%, $P = 0.311$) and sICH (2.7% vs. 3.9%, $P = 0.373$) occurred similarly often in obese and normal weight patients. The adjusted risk of poor functional outcome (OR 0.95, 95% CI 0.68–1.31), death (OR 1.01, 95% CI 0.59–1.70) and sICH (OR 0.70, 95% CI 0.32–1.55) did not differ significantly.

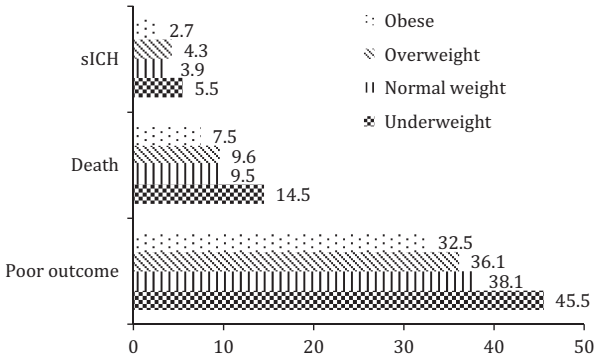

Figure 1 Frequency (%) of symptomatic intracranial hemorrhage, death and poor outcome at 3 months depending on the BMI-group. Underweight = BMI < 18.5 kg/m^2, normal weight = 18.5–24.9 kg/m^2, overweight = 25.0–29.9 kg/m^2, obesity = ≥ 30kg/m^2. sICH = symptomatic intracranial hemorrhage. Poor outcome = modified Rankin Scale 3–6.

Body mass index as a continuous variable

Body mass index as a continuous variable had no significant impact on any outcome either in univariable analyses (poor functional outcome OR 0.99, 95% CI 0.97–1.01; death OR 0.98, 95% CI 0.95–1.02; sICH OR 0.98, 95% CI 0.94–1.04) or after adjustment for age and NIHSS (poor functional outcome OR 1.01, 95% CI 0.98–1.03; death OR 0.99, 95% CI 0.95–1.05; sICH OR 1.01, 95% CI 0.97–1.05).

Body weight (≤50 kg vs. >50 kg and >100 kg vs. ≤100 kg)

Post hoc the impact of body weight on outcomes was investigated. In univariate analysis, patients weighing >100 kg did not differ significantly from patients weighing ≤100 kg with regard to risk of poor functional outcome, death and sICH (Table 2). Patients with body weight ≤50 kg were not at increased risk either of poor outcome or of sICH. However, there was a significant association between body weight <50 kg and death [$OR_{unadjusted}$ 2.92 (1.37–6.24)] in univariate analysis, which lost significance after adjustment for age and NIHSS [$OR_{adjusted}$ 2.20 (0.95–5.06), $P = 0.064$].

Meta-analysis of studies comparing obese with non-obese patients and patients weighing >100 kg with ≤100 kg

Including the current study, three studies comparing obese with non-obese patients and four studies comparing body weight >100 kg with ≤100 kg were identified as being eligible for meta-analysis. The observational period was 3 months in all studies. Except for two studies [1,7] (mRS 2–6) all studies used mRS 3–6 as favourable functional outcome and, except for one study [7] (which used NINDS criteria), all studies applied the ECASS II criteria to define sICH. Overall, the risk of each outcome did not differ significantly between obese and non-obese patients or between patients weighing >100 kg and ≤100 kg (Figs 2 and S2).

Discussion

This large prospective cohort study indicates that BMI – neither as a categorical nor as a continuous variable – had a prognostic meaning for 3-month functional outcome, mortality and the risk of sICH in stroke patients treated with IVT.

The impact of BMI and body weight on functional outcome and mortality in the general stroke population has been investigated and discussed intensively. Several studies assumed an inverse relationship between BMI and functional outcome and mortality and have coined the term 'obesity paradox' [15,17]. However, little is known about whether this is also true in IVT-treated stroke patients. Three studies with relatively small sample sizes (n = 169 [2], n = 304 [1], n = 321 [3]) used the BMI to define overweight and obesity. In one of these three studies, obesity (BMI ≥30 kg/m^2 vs. BMI <30 kg/m^2) was an independent predictor both for unfavourable outcome (i.e. mRS 2–6) and mortality [1]. In contrast, the second study did not observe any differences in functional outcome between obese (BMI ≥30 kg/m^2) and normal weight (BMI 18.5–24.9 kg/m^2) as well as between overweight (BMI 25.0–29.9 kg/m^2) and normal weight patients [2]. The third study, which included also patients treated with intraarterial thrombolysis, did not reveal any differences in mortality between obese (BMI ≥25 kg/m^2) and normal weight patients (BMI 18.5–22.9 kg/m^2) [3]. Our study included more patients than the total of the aforementioned three BMI studies together [1–3]. No evidence that overweight or obese IVT-treated stroke patients differed from normal weight patients with regard to functional 3-month outcome or mortality was observed. A meta-analysis across these studies (including the current study) did not show significant differences in the risk of poor outcome and death between obese and non-obese patients.

In our *post hoc* analysis, patients with body weight >100 kg did not differ from those ≤100 kg with regard to poor functional outcome or death in our cohort. Previous studies have shown conflicting results. In two studies, patients with >100 kg more often had

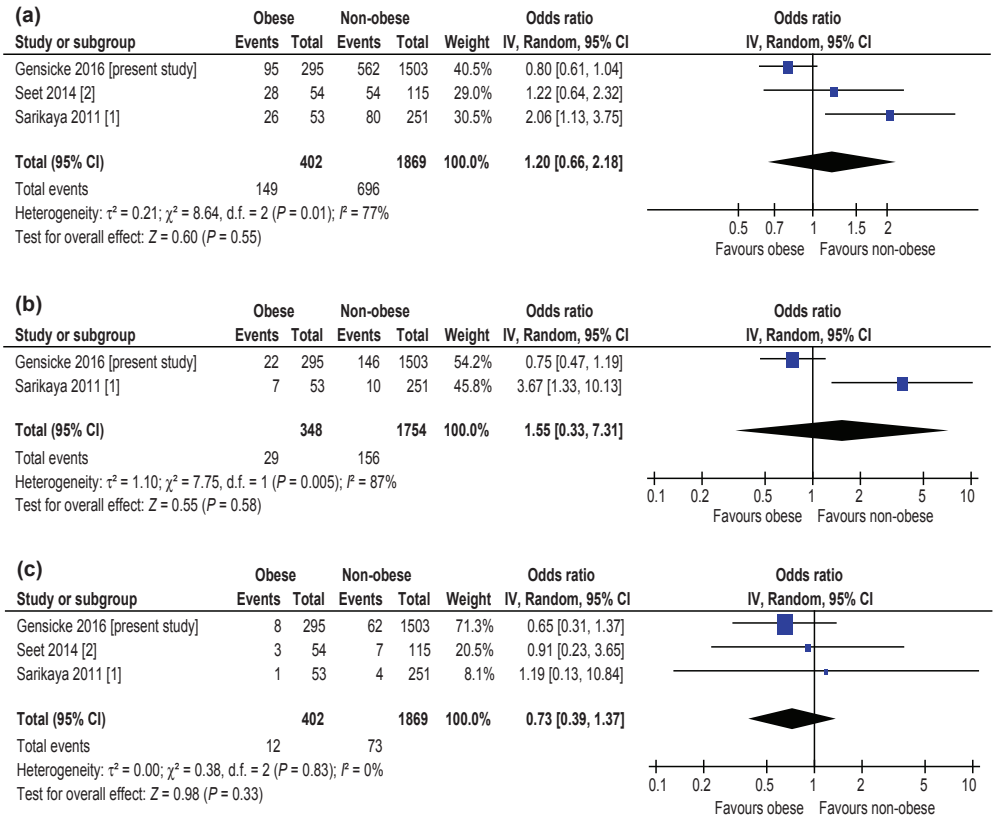

Figure 2 Forest plots comparing obese (BMI ≥30 kg/m^2) versus non-obese (BMI <30 kg/m^2) for (a) poor outcome, (b) mortality and (c) sICH.

unfavourable functional outcome [5,7] and higher mortality [5,6] than patients ≤100 kg. Another study did not find differences with regard to poor functional outcome [6]. Our meta-analysis across these aforementioned four studies also showed no significant difference between the two weight groups.

Our observation that there was no prognostic impact of BMI and body weight amongst IVT-treated stroke patients appears to be in contrast to findings in stroke in general. However, these seemingly discrepant observations might be explained by differences in lengths of follow-up, which was 3 months in our study and 1 year or longer in most of the studies which found a beneficial prognostic impact of a higher BMI on outcomes. Thus, the observational period of 3 months after stroke onset might be too short to detect prognostic effects of BMI on functional outcome and mortality. This assumption might be supported by the analogy of observational studies of general stroke populations. One study reported on a J-shaped relation between BMI and mortality both (i) at 1 year and (ii) at long-term follow-up visits (average 1.3 years). However, at the 1- and 3-month follow-ups such an association was absent [16]. A second study showed a reduced mortality of obese patients compared to normal weight patients after a median of 2.6 years [18], whilst no association between BMI and mortality was found in a third study 1 month after stroke onset [14].

In IVT-treated stroke patients only one smaller study (n = 321) provided long-term follow-up data [3]. In underweight patients there was no significant association between BMI and mortality after 3 months. However, after 2 years of follow-up underweight patients had an increased risk of death compared to normal weight patients [OR 3.49 (1.44–8.46)]. In contrast, overweight and obese patients did not differ significantly from normal weight patients during either short-term or long-term follow-up [3].

With regard to sICH, neither overweight nor obesity (compared to normal weight) nor body weight >100 kg was associated with sICH after IVT in our study. Consistent with our findings, in two other studies neither BMI ≥30 kg/m^2 [1,2] nor body weight >100 kg [5] were independently associated with sICH. However, the definition of sICH used seems to have a crucial role. In one large study, body weight >100 kg independently increased the risk of sICH when using

the SITS-MOST definition but not when using the ECASS II definition [6]. One other study using the SITS-MOST definition showed a significant association between body weight ≥95 kg and higher frequency of sICH [4]. In this situation, our meta-analyses across the aforementioned studies clarified the situation, as it revealed no significant association either between BMI and sICH or between body weight and sICH.

As a novelty, whether there was an association between underweight and functional outcome, mortality and sICH compared to normal weight patients was investigated. Despite numerically higher percentages in the underweight group, the odds were comparable between the two groups, although the 95% CIs were wide. Thus, given the small number of underweight patients included in our study, a negative impact of underweight on outcomes after IVT cannot be ruled out. One previous study including IVT and intraarterially treated patients did not find significant differences in risk of mortality after 3 months between underweight (n = 14) and normal weight patients [3].

The strengths of this study include (i) the relatively large sample size addressing the impact of BMI on outcome in IVT-treated patients, which reduces the odds for false-positive or false-negative results and allows adjustment for potential confounding variables, (ii) the few missing data on 3-month outcome (2.7%) which reduces the risk of bias and (iii) the systematic and standardized assessment of data collection. All variables and outcomes have been collected prospectively according to standardized criteria irrespective of the present research question.

Nevertheless, there are several limitations. (i) Data came from registries that were not monitored and non-randomized. Because observational studies have a higher risk of bias, a cautious interpretation is advised. (ii) In most patients, data about weight and height were obtained from patients, relatives or were based on estimates made by the stroke team. Thus, how much these data deviated from the actual values is not known. Interestingly, according to recent research estimated weights were not significantly different from actual weights in IVT patients [19]. (iii) The number of underweight patients in the present study population is larger than in any other study reported yet but still relatively low. Therefore, a cautious interpretation of the observed absence of an association between underweight and poor outcome, death or sICH is urged. These results need to be confirmed by studies including a larger number of underweight patients.

In conclusion, this large study addressing the impact of BMI in IVT-treated stroke patients showed that BMI had no prognostic meaning with regard to 3-month functional outcome, death or occurrence of sICH.

Disclosure of conflicts of interest

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Scatter plot of modified Rankin Scale (mRS) score at 3 months against body mass index (BMI) at stroke onset.

Figure S2. Forest plots comparing patients with body weight >100 kg versus ≤100 kg for (a) poor outcome, (b) mortality and (c) sICH.

Table S1. Participating centres, period and patient number of inclusion (alphabetical order).

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