

ORIGINAL ARTICLE

Influence of dehydration on collateral circulation and clinical outcome after endovascular therapy in patients with acute ischemic stroke



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KEYWORDS

Dehydration;
Collateral circulation;
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Outcome

Abstract

Introduction: Dehydration in patients with acute ischemic stroke (AIS) is associated with poor outcome. Our aim is to investigate whether dehydration is associated with collateral circulation (CC) and functional outcome in patients with AIS treated with mechanical thrombectomy (MT). **Methods:** Prospective multicenter study of patients with anterior circulation AIS treated with MT (January 2020–June 2021). Dehydration was assessed with two formulas: plasma osmolality and urea/creatinine (U/C) ratio. CC was quantified with an automated software (Brainomix Ltd.) on baseline computed tomography angiography. The primary outcome was the association between CC (expressed numerically as the percentage of change between hemispheres) and dehydration (osmolality ≥ 295 mmol/L, U/C ≥ 80). Secondary outcomes included disability at discharge and at three months of follow-up, assessed using the modified Rankin scale (poor outcome: 3–6). Multivariable logistic and ordinal regression analyses were performed.

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PALABRAS CLAVE

Deshidratación;
Circulación colateral;
Ictus isquémico;
Trombectomía
mecánica;
Pronóstico

Results: Two hundred sixty patients were included. 65.8% were dehydrated according to osmolality and 2.9% according to U/C. There was no association between CC score and dehydration [71% in dehydrated vs 73% in non-dehydrated; $P = .875$]. 64.3% of dehydrated patients vs. 46.7% of non-dehydrated patients had a poor outcome at discharge ($P = .026$). In multivariable logistic regression analysis, dehydration was an independent predictor of poor outcome at discharge (OR 2.50; $P = .011$) and at three months of follow-up (OR 2.27; $P = .046$).

Conclusions: Dehydration on admission is associated with poor outcome in patients with AIS treated with MT, but it is not related to CC.

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Deshidratación, circulación colateral y pronóstico funcional en pacientes con ictus isquémico tratados mediante trombectomía mecánica

Resumen

Introducción: La deshidratación en pacientes con ictus isquémico agudo (IIA) se relaciona con un mal pronóstico. Nuestro objetivo es investigar si la deshidratación se asocia con la circulación colateral (CC) y el pronóstico funcional en pacientes con IIA tratados mediante trombectomía mecánica (TM).

Método: Estudio prospectivo multicéntrico de pacientes con IIA de circulación anterior tratados con TM (enero 2020–junio 2021). La deshidratación se evaluó con dos fórmulas: osmolaridad plasmática y relación urea/creatinina (U/C). La CC se cuantificó con un software automatizado (Brainomix Ltd.) en la angio-tomografía computarizada basal. La medida de resultado principal fue la asociación entre CC (expresada numéricamente como el porcentaje de diferencia entre hemisferios) y deshidratación (osmolaridad ≥ 295 mmol/L, U/C ≥ 80). Las medidas secundarias incluyeron la discapacidad al alta y a los tres meses, evaluadas mediante la escala de Rankin modificada (mal pronóstico: 3–6). Se realizaron análisis multivariantes de regresión logística y ordinal.

Resultados: Se incluyeron 260 pacientes. El 65,8% presentaron deshidratación según la osmolaridad y el 2,9% según U/C. No hubo asociación entre CC y deshidratación [71% en deshidratados vs 73% en no deshidratados; $P = .875$]. Un 64,3% de los pacientes deshidratados frente a un 46,7% de los no deshidratados tuvieron un mal pronóstico al alta ($P = .026$). En el análisis de regresión logística multivariable, la deshidratación fue un predictor independiente de mal pronóstico al alta (OR 2,50; $P = .011$) y a los tres meses (OR 2,27; $P = .046$).

Conclusiones: La deshidratación al ingreso se asocia a un mal pronóstico en los pacientes con IIA tratados con TM, pero no se relaciona con la CC.

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Introduction

Dehydration, defined as a deficit in total body water, is frequent among hospitalised patients and has consistently been associated with increased rates of morbidity and mortality.^{1,2}

It is also common among patients with acute ischaemic stroke (AIS), with a highly variable prevalence (8.9%–70%),^{3,4} probably due to differences in diagnostic techniques and thresholds. In AIS, dehydration has been associated with more severe neurological deterioration,⁵ greater mortality, and poorer functional outcomes.^{3,4,6–9} However, no previous study has analysed whether the impact of dehydration persists in patients with AIS treated with mechanical thrombectomy (MT).

The deleterious effects of dehydration in stroke outcome have been attributed, on the one hand, to the increased risk of complications (infection, deep vein thrombosis, or delirium), and, on the other, to increased blood viscosity and decreased intravascular volume, both of which lead to haemoconcentration and decreased cerebral blood flow.^{4,7} Based on this pathophysiological mechanism, it has been hypothesised that dehydration decreases collateral circulation (CC).^{7,10}

Good CC maintains perfusion in the ischaemic penumbra and improves recanalisation rates, contributing to lower mortality and better functional prognosis in patients undergoing MT.^{10,11} Patients with AIS present a highly variable degree of CC. Ageing, elevated creatinine levels, and hyperglycaemia—all of which are associated with dehydration

—have also been linked to poorer CC,^{12,13} which suggests a potential relationship between dehydration and poor CC.

The purpose of this study is to examine the relationship between hydration status and CC in patients with AIS of the anterior circulation treated with MT. Our working hypothesis was that dehydrated patients would present poorer CC, which would in turn lead to poorer functional outcomes. Given that hydration status is an easily modifiable factor, it may represent a therapeutic target to improve and preserve CC in the acute phase of stroke.

Material and methods

Study design

We conducted a prospective, observational, multicentre study of patients with AIS of the anterior circulation treated with MT (a substudy of the COLISEUM project [PI19/00859], funded by the Carlos III Health Institute). Patients were recruited from 6 Spanish tertiary stroke hospitals between January 2020 and June 2021. The study was approved by the ethics committees of all participating hospitals. Written informed consent was obtained from all patients or their legal representatives.

Study population

Inclusion criteria were as follows: 1) age ≥ 18 years; 2) AIS secondary to occlusion of the middle cerebral artery (M1 and M2 segments) or the terminal internal carotid artery, with or without extracranial occlusion, confirmed by CT angiography; 3) CT angiography performed within 24 hours of stroke onset (including wake-up stroke); 4) baseline modified Rankin Scale (mRS) score of 0–2; 5) treatment with MT; and 6) written informed consent provided by the patient or their legal representative.

Exclusion criteria were as follows: 1) patients for whom laboratory test results were unavailable at hospital admission; and 2) inability to evaluate CC due to motion artefacts or any other technical issue preventing assessment.

The following data were collected at admission: demographic data (age and sex), vascular risk factors (arterial hypertension, diabetes mellitus, dyslipidaemia, previous history of stroke, atrial fibrillation), treatment (previous medications [antiplatelets, anticoagulants, diuretics], reperfusion therapy [direct MT or combined fibrinolysis and MT]), management times (time to admission, door-to-needle time), and stroke aetiology according to the modified TOAST criteria.¹⁴ Blood analyses were performed at admission to the emergency department. Baseline functional status and stroke severity were evaluated at admission by certified neurologists using the mRS and the National Institute of Health Stroke Scale (NIHSS), respectively.

The following outcome variables were gathered during follow-up: symptomatic intracerebral haemorrhage (defined as neurological deterioration ≥ 4 points on the NIHSS associated with intracerebral haemorrhage), and NIHSS and mRS scores at discharge and at 3 months, determined at

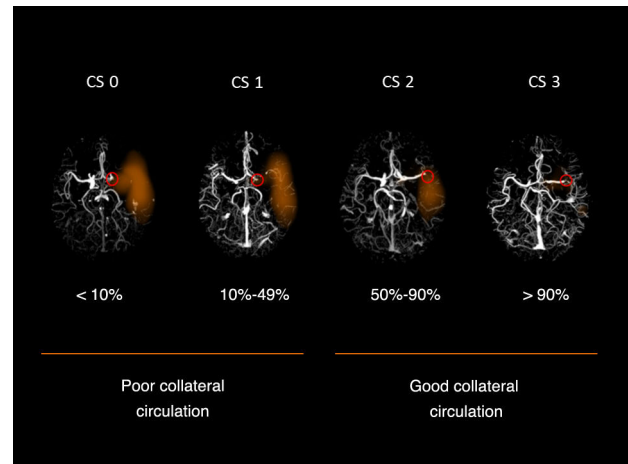


Figure 1 Categories of collateral circulation according to the automated software tool Brainomix Ltd.

CS: collateral score.

an in-person interview by local researchers blinded to the patients' hydration and CC status.

Assessment of hydration status

Hydration status was evaluated with 2 different formulae using blood samples obtained at admission.

- 1 Plasma osmolality. Osmolality was calculated using the formula proposed by Khajuria and Krahn,¹⁵ as recommended in a recent multidisciplinary consensus document on dehydration¹:

$$\text{pOsm} = 1.86 \times ([\text{Na}^+] + [\text{K}^+]) + 1.15 \times [\text{glucose}] + [\text{urea}] + 14(\text{all in mmol/L})$$

Individuals with plasma osmolality ≥ 295 mmol/L were classified as dehydrated.

- 2 Urea/creatinine (U/C) ratio. Patients with U/C ratio ≥ 80 were considered to be dehydrated, as proposed in previous studies.^{1,3,6}

Neuroimaging studies

Patients underwent single-phase CT angiography study. Baseline CT, CT angiography, CT perfusion (in some patients), and conventional angiography studies were evaluated by local neuroradiologists blinded to the patients' hydration status.

The degree of CC in the territory of the middle cerebral artery was quantified using an automated program from the e-STROKE SUITE software (Brainomix Ltd.; Oxford, United Kingdom). The resulting value reflects the difference in CC between the affected and unaffected cerebral hemispheres, and ranges from 0% to 100%. CC was also assigned a collateral score from 0 to 3, which was further classified as poor CC (0–1) or good CC (2–3) (Fig. 1).

The following radiological data were also gathered: Alberta Stroke Program Early CT Score (ASPECTS), the occluded artery in the CT angiography study, ischaemic core volume (defined as relative cerebral blood flow < 30% of normal tissue on CT perfusion), mismatch ratio (defined as the ratio of hypoperfused tissue [time to maximum tissue residue function > 6 seconds] to core volume), and Thrombolysis In Cerebral Infarction (TICI) scale score.

Outcome measures

The primary outcome measure was CC on baseline CT angiography, expressed numerically as the percentage difference between the affected and unaffected hemispheres (0%–100%). Secondary outcome measures included dichotomised CC (poor [collateral scores 0–1] vs good [collateral scores 2–3]) and functional status at discharge and at 3 months of follow-up (mRS scores 3–6 indicate poor outcomes).

Statistical analysis

Continuous variables are expressed as means and standard deviation (SD) or medians and quartiles 1 and 3 (Q_1 – Q_3), depending on data distribution. Categorical variables are expressed as frequencies and percentages. Differences in CC between dehydrated and non-dehydrated patients were compared with the *t* test. Differences in the distribution of collateral scores were evaluated with the chi-square test.

Regarding secondary outcome measures, functional outcome was classified as good (mRS 0–2) or poor (mRS 3–6). We also evaluated the association between study variables and the likelihood of presenting poor functional outcome at discharge and at 3 months of follow-up. Univariate analyses were performed using the *t* test or the Wilcoxon rank-sum test (when a non-parametric test was required) for continuous variables, and the chi-square test for categorical variables. Multivariate logistic regression analysis was subsequently performed to identify predictors of poor functional outcome using a stepwise backward regression model, based on an initial model including all the variables showing at least a trend toward statistical significance ($P < .1$).

We also conducted a shift analysis using the Wilcoxon rank-sum test to evaluate differences in the distribution of mRS scores at discharge and at 3 months of follow-up between patients with and without dehydration. We also calculated the common odds ratio (OR) of worsening 1 point on the mRS due to dehydration. Multivariate ordinal regression analysis was subsequently performed using the same approach as in the previous logistic regression analysis.

Multivariate models were adjusted for potential confounders. A confounding effect was defined as an absolute change > 10% in regression coefficients when the variable was added to the model.

The threshold for statistical significance was set at $P = .05$ (two-tailed). All analyses were performed using Stata v.15 (Texas, USA).

Results

We recruited 301 patients with AIS due to large-vessel occlusion in the anterior circulation, 260 of whom were treated with MT. Hydration status was evaluated using plasma osmolality in 181 patients and the U/C ratio in 208 (see Fig. S1 in Supplementary Material).

Impact of dehydration (evaluated with plasma osmolality) on collateral circulation and outcomes

A total of 119 patients (65.8%) met criteria for dehydration at admission. Mean age was 74.2 years (11.6), and 52 patients (43.7%) were women. Table 1 summarises the patients' baseline demographic, clinical, treatment, and prognostic characteristics, by hydration status.

Dehydration and collateral circulation

CC assessment was available for 107 patients. The median degree of CC was 71% in the group of dehydrated patients, vs 73% among those without dehydration ($P = .875$). The proportion of patients with good CC (collateral score 2–3) was similar in dehydrated and non-dehydrated patients (74.0% vs 70.6%; $P = .714$). Furthermore, 26.0% of dehydrated patients and 23.5% of non-dehydrated patients presented excellent CC (collateral score 3) ($P = .782$).

No significant differences were observed in cerebral perfusion parameters (ischaemic core or mismatch ratio).

Dehydration and prognosis

The mRS score at discharge was available for 172 patients. A total of 64.3% of dehydrated patients presented poor outcomes (mRS 3–6) at discharge, vs 46.7% of non-dehydrated patients ($P = .026$).

The comparison between patients with good vs poor functional outcomes at discharge is shown in the Supplementary Material (table 1).

According to the multivariate logistic regression analysis, dehydration was significantly associated with poor outcome at discharge, with an OR of 2.5 ($P = .011$) (Table 2). In the shift analysis, dehydrated patients scored higher on the mRS at discharge than non-dehydrated patients (median of 3 vs 2; $P = .012$) (Fig. 2). According to the multivariate ordinal logistic regression analysis adjusted for baseline mRS and NIHSS scores, the common OR of worsening by 1 point on the mRS at discharge was 2.27 among dehydrated patients ($P = .005$).

At 3 months, dehydration remained independently associated with poor outcomes in the multivariate logistic regression analysis, with an OR of 2.27 ($P = .046$) (Table 2). Dehydrated patients also presented a non-significant trend towards poorer functional outcomes in the shift analysis (median mRS score of 3, vs 2 among patients with normal hydration status; $P = .113$).

Table 1 Variables associated with dehydration (diagnosis of dehydration is established when plasma osmolality ≥ 295 mmol/L).

	Dehydration (n = 119)	Normal hydration (n = 62)	P
<i>Baseline demographic, clinical, and treatment characteristics</i>			
Age in years, mean (SD)	74.2 (11.6)	73.1 (11.9)	.533
Sex (female), n (%)	52 (43.7)	29 (46.7)	.693
Hypertension, n (%)	93 (78.2)	34 (56.7)	.003
Diabetes mellitus, n (%)	30 (25.4)	7 (11.5)	.029
Atrial fibrillation, n (%)	25 (21.4)	21 (33.9)	.069
Diuretic treatment, n (%)	47 (39.5)	22 (37.3)	.776
Previous mRS score, median (Q ₁ –Q ₃)	0 (0–1)	0 (0–1)	.600
Baseline NIHSS score, median (Q ₁ –Q ₃)	16 (8–20)	16 (10–20)	.363
Stroke onset < 6 hours, n (%)	79 (71.2)	39 (70.9)	.972
Fibrinolytic treatment, n (%)	32 (28.8)	19 (34.5)	.455
Door-to-needle time (minutes), mean (SD)	71.8 (60.1)	74.3 (62.2)	.798
<i>TOAST</i>			
Large-artery atherosclerosis, n (%)	22 (21.4)	9 (15.0)	.573
Cardioembolic stroke, n (%)	50 (48.5)	35 (58.3)	
Stroke of other determined aetiology, n (%)	6 (5.8)	2 (3.3)	
Stroke of undetermined aetiology, n (%)	25 (24.3)	14 (23.3)	
<i>Radiological characteristics</i>			
ASPECTS, median (Q ₁ –Q ₃)	9 (8–10)	9 (8–10)	.575
<i>Occlusion site</i>			
M1, n (%)	54 (46.9)	30 (49.2)	.895
M2, n (%)	25 (21.7)	15 (24.6)	
TICA, n (%)	21 (18.3)	10 (16.4)	
Tandem, n (%)	15 (13.0)	6 (9.8)	
Ischaemic core volume (mL), median (Q ₁ –Q ₃) ^a	7.0 (2–14)	9.5 (5–25)	.623
Mismatch ratio, median (Q ₁ –Q ₃) ^a	16.4 (7.9–23.1)	6.6 (4.6–13.9)	.115
Percentage of CC, median (Q ₁ –Q ₃)	71 (44–92)	73 (41–89)	.875
Good CC, n (%) ^b	54 (74.0)	24 (70.6)	.714
TICI 2b-3, n (%)	110 (94.0)	58 (96.7)	.448
<i>Prognostic characteristics</i>			
siCH, n (%)	15 (14.0)	6 (6.6)	.616
mRS score at discharge, median (Q ₁ –Q ₃)	3 (2–5)	2 (1–4)	.012
Poor prognosis at discharge, n (%) ^c	72 (64.3)	28 (46.7)	.026
Mortality at discharge, n (%)	15 (12.6)	2 (3.3)	.031
mRS score at 3 months, median (Q ₁ –Q ₃)	3 (1–5)	2 (1–4)	.113
Poor prognosis at 3 months, n (%) ^c	64 (57.1)	24 (42.1)	.064
Mortality at 3 months, n (%)	21 (17.6)	7 (11.3)	.289

ASPECTS: Alberta Stroke Program Early CT Score; CC: collateral circulation; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; Q₁–Q₃: quartiles 1 and 3; siCH: symptomatic intracranial haemorrhage; SD: standard deviation; TICA: terminal internal carotid artery; TICI: Thrombolysis in Cerebral Infarction scale; TOAST: Trial of Org 10172 in Acute Stroke Treatment.

^a Data available for 50 patients.

^b Good collateral circulation: $\geq 50\%$.

^c Poor prognosis: mRS 3–6.

Impact of dehydration (evaluated with urea/creatinine ratio) on collateral circulation and prognosis

Six patients (2.9%) met criteria for dehydration. Mean age was 75.3 (7.3) years; 3 patients (50.0%) were women.

Dehydration and collateral circulation

The median degree of CC was 64% in the group of patients with dehydration, vs 72% (43%–91%) among non-dehydrated

patients ($P = .897$). No statistically significant differences were observed between patients with and without dehydration in the percentage of patients with good or excellent CC.

Dehydration and prognosis

The median mRS score at discharge was 5 (4–5) among dehydrated patients vs 3 (1–4) among non-dehydrated patients ($P = .144$), and 5 (1–5) vs 2 (1–4) at 3 months ($P = .324$). Only one dehydrated patient presented a good outcome at dis-

Table 2 Multivariate logistic regression analysis of predictors of poor prognosis (mRS 3–6).*Predictors of poor prognosis at discharge^a*

	OR	95% CI	P
Dehydration ^b	2.50	1.23–5.00	.011
Baseline NIHSS score	1.14	1.08–1.20	< .001
Baseline mRS score	1.67	1.08–2.56	.023

Predictors of poor prognosis at 3 months of follow-up^c

	OR	95% CI	P
Dehydration ^b	2.27	1.02–5.00	.046
Baseline NIHSS score	1.16	1.09–1.25	< .001
Baseline mRS score	2.56	1.56–4.35	< .001
sICH	16.67	3.03–100	.001

CI: confidence interval; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; OR: odds ratio; sICH: symptomatic intracranial haemorrhage.

Results from a stepwise selection model based on an initial model including all the variables showing a trend toward statistical significance ($P < .1$) in the bivariate analysis; the variables showing a P -value $> .1$ in each iteration were subsequently removed.

^a After additional adjustment for hypertension and diabetes (these variables were not distributed equitably between groups), dehydration persisted with an OR of presenting poor outcome at discharge of 2.63 (95% CI, 1.27–5.55; $P = .010$).

^b Dehydration: plasma osmolality ≥ 295 mmol/L.

^c After additional adjustment for hypertension and diabetes (variables unequally distributed between groups), we observed a strong trend toward an association between dehydration and a poor outcome at 3 months of follow-up (OR = 2.22; 95% CI, 0.96–5.26; $P = .063$).

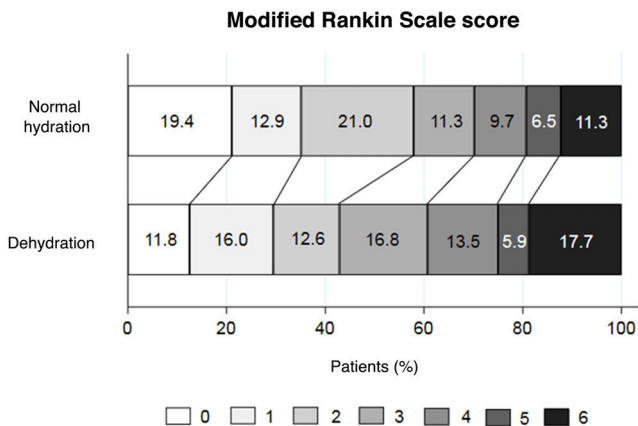


Figure 2 Distribution of modified Rankin Scale scores at 3 months of follow-up, by hydration status.

charge. However, the shift analysis identified no significant association between dehydration and mRS score at discharge or at 3 months.

Discussion

The results of this multicentre prospective study confirm an association between dehydration and poor functional outcomes in patients with AIS of the anterior circulation treated with MT. Dehydrated patients were 2.5 times more likely to present poor outcome at discharge; this association remained significant at 3 months of follow-up. However, the poorer outcomes in these patients were not found to be associated with poorer CC.

Using the plasma osmolality formula, 65.8% of patients with stroke and treated with MT met criteria for dehydration; the U/C ratio, in contrast, identified dehydration in only 2.9% of patients. The percentage of patients with dehydration according to the plasma osmolality formula in our sample is comparable to those reported in previous studies on the frequency of dehydration in patients with stroke (8.9%–70%), which used different techniques and diagnostic thresholds, with highly variable precision.^{3,4} A recent multidisciplinary consensus statement determined that plasma osmolality is the main homeostatic parameter for the measurement of hydration status.¹ However, the U/C ratio and the blood urea nitrogen (BUN)/creatinine ratio are the laboratory markers most extensively used in previous studies; only 4 of these studies have evaluated dehydration in patients with stroke using plasma osmolality.^{9,16–18} The U/C ratio is not a specific marker of hydration status, and may increase in patients with hypercatabolic states (sepsis, major surgery), high protein intake, upper gastrointestinal bleeding, or following corticosteroid administration.¹ Consequently, assessment of hydration status using the U/C ratio is imprecise. Plasma osmolality results provide more reliable information on the frequency of dehydration at admission in patients with AIS treated with MT. The high percentage of dehydrated patients observed in our study may be explained by the high mean age of our sample, the widespread use of diuretic treatments, and the high proportion of patients with diabetes.

In our study, no correlation was observed between dehydration and the degree of CC. A previous, single-centre retrospective study including 87 patients with M1 occlusion stroke found an inverse association between dehydration and CC.¹⁹ Unlike our study, the study by Chang et al.¹⁹ measured dehydration upon arrival at the hospital, whereas CC was evaluated on day 3 after stroke onset in patients with

persistent M1 occlusion. Furthermore, the study excluded patients treated with reperfusion therapy, and dehydration was determined using the BUN/creatinine ratio. Therefore, the reported association may be questioned based on the delay between the assessment of the 2 variables. In the context of AIS, CC maintains perfusion in the ischaemic penumbra, temporarily preserving cell integrity.¹⁰ Thus, the greatest impact on CC occurs during the acute phase of stroke, and any theoretical association with dehydration should be evaluated at this stage.

The negative impact of dehydration on the functional outcome and mortality of stroke has been demonstrated in multiple studies, even in patients receiving fibrinolytic therapy.²⁰ However, no prior studies have analysed the association between dehydration and functional outcome in patients with AIS treated with MT. Our study found a stronger association between dehydration and functional outcome at discharge than at 3 months of follow-up. These findings are consistent with those of a previous study,⁹ which found that dehydration influenced mortality in the short term, but not at one year of follow-up. This association may be explained by the relationship with in-hospital complications and longer mean hospital stay.⁸

The mechanisms underlying the deleterious effects of dehydration on stroke outcome have also been attributed to increased blood viscosity and decreased cerebral blood flow.⁷ In our study, no association was found between dehydration and baseline collateral blood flow measured on CT angiography. One plausible explanation is that the efficacy of CC in tissue perfusion depends not only on macrocirculation but also on microcirculation.¹⁰ Although CT angiography is widely used to evaluate collaterality (mainly due to its availability) and has repeatedly demonstrated an association between CC and prognosis,^{11,21} it is unable to evaluate microvascular CC. We may therefore hypothesise that the effect of dehydration on cerebral blood flow is due to its role in microcirculation and, therefore, cannot be evaluated with such techniques as CT angiography. In line with this hypothesis, we compared infarct core volume and mismatch ratio between patients with and without dehydration, observing no statistically significant differences. However, only a small subset of patients were studied with CT perfusion ($n = 50$).

The main strengths of this study are its multicentre, prospective design, and the fact that analysis of dehydration and CC was blind and performed centrally. Among its limitations, we should underscore the fact that although plasma osmolality is the recommended hydration biomarker, hydration status was estimated using a formula rather than measured directly. However, the formula used has been shown to have 85% sensitivity and 59% specificity.²² Secondly, CC was evaluated with baseline CT angiography, which is not considered the most accurate imaging technique and cannot assess microcirculation. However, CC was measured with a validated, automated software tool (Brainomix Ltd.) that has shown excellent sensitivity and specificity.²³ Furthermore, no data were gathered on fluid intake or hydration status during hospitalisation; changes in these 2 parameters during the hospital stay may have affected outcomes.^{3,17} Lastly, no data were gathered on dehydration-associated complications that may have influenced outcomes, such as infections or deep vein thrombosis.

These results further confirm the role of dehydration as a modifiable risk factor for poor outcome after stroke. In spite of this, the impact of hydration therapy on AIS is not well established. Hydration therapy with saline solution following AIS in patients presenting dehydration, as determined with the BUN/creatinine ratio, has shown a significant association with less severe early neurological deterioration,²⁴ lower infection rates, and shorter hospital stays.²⁵ However, a study into its role in stroke prognosis only found a trend toward better outcomes in patients with lacunar strokes compared to historical controls.²⁶ Further studies with better identification of dehydration are needed to determine the role of hydration therapy in stroke outcome.

In conclusion, our results suggest that dehydration at admission is a frequent risk factor associated with poorer functional outcomes in patients with AIS treated with MT, and that this association is unrelated to CC.

Ethical standards

This study was reviewed and approved by the ethics committee of Hospital de la Santa Creu i Sant Pau (IIBSP-COL-2019-120).

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jnrl.2023.04.007>.

Declaration of competing interest

Brainomix provided their software free of cost to the stroke unit of Hospital de la Santa Creu i Sant Pau, in accordance with the regulations of the Sant Pau Biomedical Research Institute and exclusively for research purposes.

The authors have no conflicts of interest to declare.

References

1. Lacey J, Corbett J, Forni L, Hooper L, Hughes F, Minto G, et al. A multidisciplinary consensus on dehydration: defini-

- tions, diagnostic methods and clinical implications. *Ann Med*. 2019;51:232–51.
2. El-Sharkawy AM, Watson P, Neal KR, Ljungqvist O, Maughan RJ, Sahota O, et al. Hydration and outcome in older patients admitted to hospital (The HOOP prospective cohort study). *Age Ageing*. 2015;44:943–7.
3. Cortés-Vicente E, Guisado-Alonso D, Delgado-Mederos R, Camps-Renom P, Prats-Sánchez L, Martínez-Domeño A, et al. Frequency, risk factors, and prognosis of dehydration in acute stroke. *Front Neurol*. 2019;10:305.
4. Bahouth MN, Gottesman RF, Szanton SL. Primary 'dehydration' and acute stroke: a systematic research review. *J Neurol*. 2018;265:2167–81.
5. Lin LC, Yang JT, Weng HH, Hsiao CT, Lai SL, Fann WC. Predictors of early clinical deterioration after acute ischemic stroke. *Am J Emerg Med*. 2011;29:577–81.
6. Rowat A, Graham C, Dennis M. Dehydration in hospital-admitted stroke patients: detection, frequency, and association. *Stroke*. 2012;43:857–9.
7. Schrock JW, Glasenapp M, Drogell K. Elevated blood urea nitrogen/creatinine ratio is associated with poor outcome in patients with ischemic stroke. *Clin Neurol Neurosurg*. 2012;114:881–4.
8. Liu CH, Lin SC, Lin JR, Yang JT, Chang YJ, Chang CH, et al. Dehydration is an independent predictor of discharge outcome and admission cost in acute ischaemic stroke. *Eur J Neurol*. 2014;21:1184–901.
9. Liu M, Deng Y, Cheng Y, Hao Z, Wu S, Liu M. Association between plasma osmolality and case fatality within 1 year after severe acute ischemic stroke. *Yonsei Med J*. 2021;62:600–7.
10. Shuaib A, Butcher K, Mohammad AA, Saqqur M, Liebeskind DS. Collateral blood vessels in acute ischaemic stroke: a potential therapeutic target. *Lancet Neurol*. 2011;10:909–21.
11. Leng X, Fang H, Leung TW, Mao C, Miao Z, Liu L, et al. Impact of collaterals on the efficacy and safety of endovascular treatment in acute ischaemic stroke: a systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry*. 2016;87:537–44.
12. Menon BK, Smith EE, Coutts SB, Welsh DG, Faber JE, Goyal M, et al. Leptomeningeal collaterals are associated with modifiable metabolic risk factors. *Ann Neurol*. 2013;74:241–8.
13. Nannoni S, Sirimarco G, Cereda CW, Lambrou D, Strambo D, Eskandari A, et al. Determining factors of better leptomeningeal collaterals: a study of 857 consecutive acute ischemic stroke patients. *J Neurol*. 2019;266:582–8.
14. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, 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.
15. Khajuria A, Krahn J. Osmolality revisited-deriving and validating the best formula for calculated osmolality. *Clin Biochem*. 2005;38:514–9.
16. O'Neill PA, Davies I, Fullerton KJ, Bennett D. Fluid balance in elderly patients following acute stroke. *Age Ageing*. 1992;21:280–5.
17. Bhalla A, Sankaralingam S, Dundas R, Swaminathan R, Wolfe CD, Rudd AG. Influence of raised plasma osmolality on clinical outcome after acute stroke. *Stroke*. 2000;31:2043–8.
18. Rodriguez GJ, Cordina SM, Vazquez G, Suri MF, Kirmani JF, Ezzedine MA, et al. The hydration influence on the risk of stroke (THIRST) study. *Neurocrit Care*. 2009;10:187–94.
19. Chang SW, Huang YC, Lin LC, Yang JT, Weng HH, Tsai YH, et al. Effect of dehydration on the development of collaterals in acute middle cerebral artery occlusion. *Eur J Neurol*. 2016;23:494–500.
20. Wu FF, Hung YC, Tsai YH, Yang JT, Lee TH, Liow CW, et al. The influence of dehydration on the prognosis of acute ischemic stroke for patients treated with tissue plasminogen activator. *BMC Cardiovasc Disord*. 2017;17:154.
21. Jansen IG, Mulder MJ, Goldhoorn RB, Boers AM, van Es AC, Yo LS, et al. Impact of single phase CT angiography collateral status on functional outcome over time: results from the MR CLEAN Registry. *J Neurointerv Surg*. 2019;11:866–73.
22. Hooper L, Abdelhamid A, Ali A, Bunn DK, Jennings A, John WG, et al. Diagnostic accuracy of calculated serum osmolality to predict dehydration in older people: adding value to pathology laboratory reports. *BMJ Open*. 2015;5:e008846.
23. Grunwald IQ, Kulikovski J, Reith W, Gerry S, Namias R, Politi M, et al. Collateral automation for triage in stroke: evaluating automated scoring of collaterals in acute stroke on computed tomography scans. *Cerebrovasc Dis*. 2019;47:217–22.
24. Lin LC, Lee JD, Hung YC, Chang CH, Yang JT. Bun/creatinine ratio-based hydration for preventing stroke-in-evolution after acute ischemic stroke. *Am J Emerg Med*. 2014;32:709–12.
25. Lin WC, Shih HM, Lin LC. Preliminary prospective study to assess the effect of early blood urea nitrogen/creatinine ratio-based hydration therapy on poststroke infection rate and length of stay in acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2015;24:2720–7.
26. Lin CJ, Yang JT, Huang YC, Tsai YH, Lee MH, Lee M, et al. Favorable outcome of blood urea nitrogen/creatinine-based hydration therapy 3 months after acute ischemic stroke. *Am J Emerg Med*. 2016;34:2414–8.