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HIGH LIGHT

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Abstract—*Objective:* To study the association of previously unknown high blood pressure (HBP) during the acute phase of stroke (new-onset hypertension) with the inflammatory response and clinical outcome. *Methods:* We classified 844 patients with hemispheric ischemic stroke into three groups according to history of hypertension and presence of HBP within the first 24 hours after symptom onset: Group I (n = 412), normotensive patients; Group II (n = 265), chronic hypertensive patients; and Group III (n = 167), new-onset hypertensive patients. Interleukin 6 (IL-6), tumor necrosis factor α (TNF-α), intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1), and metalloproteinase 9 (MMP-9) were measured in blood samples obtained on admission. The influence of new-onset HBP and markers of inflammation on poor neurologic outcome at 3 months was evaluated by logistic regression analysis. *Results:* New-onset HBP was found in 19.9% of patients. Patients in this group had higher plasma concentrations of IL-6, TNF-α, ICAM-1, VCAM-1, and MMP-9 than the other two groups. New-onset HBP was associated with poor outcome at 3 months (odds ratio [OR] 2.10; 95% CI 1.54 to 3.52; $p < 0.0001$) after adjustment for other prognostic factors. However, when markers of inflammation were included in the model, IL-6 (OR 1.01; 95% CI 1.00 to 1.03; $p = 0.020$) and MMP-9 (OR 1.01; 95% CI 1.00 to 1.01; $p < 0.0001$), but not new-onset HBP, were independently associated with poor neurologic outcome. *Conclusions:* New-onset high blood pressure in acute ischemic stroke, but not chronic hypertension, is associated with an inflammatory response and poor neurologic outcome.

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Chronic inflammation is associated with an increased risk of acute vascular events, particularly myocardial infarction and ischemic stroke.[1,2] Cross-sectional evidence has demonstrated higher plasma levels of inflammatory markers among those individuals with high blood pressure (HBP).[3–6] HBP may bring about inflammation,[3] but inflammation plays a role in the development of HBP via a reduction in nitric oxide and changes in the renin–angiotensin system, these processes being associated with an endothelial dysfunction.[7–9] As a consequence, HBP may be considered, in part, an inflammatory disorder.[9]

More than half of patients present with HBP during the acute phase of stroke,[10–12] although its prognostic value has not been well established.[13] A large part of this variability may be attributed to the joint analysis of patients with clearly different HBP situations, such as the chronic HBP and the mainly transient HBP after acute stroke. Although acute stroke is associated with a marked inflammatory response,[14] few studies have investigated whether there is a causal relationship between HBP and inflammation during the acute phase of stroke.[15] Furthermore, neither the frequency nor the mechanism of this hypertensive response are well understood.

In this observational study, we investigated the frequency of previously unknown HBP during the acute phase of stroke ("new-onset" hypertension) and its potential association with the inflammatory response in the peripheral blood and clinical outcome.

Methods. We reviewed record of 1,122 patients with hemispheric ischemic stroke of less than 24 hours' duration from the onset of symptoms. These patients were prospectively included in three banks with the purposes of studying molecular markers for ischemia (249 patients),[14] the influence of blood pressure (BP) during the acute phase of cerebral ischemia (352 patients),[12] and the phenomenon of ischemic tolerance (521 patients).[16] These studies were approved by the institutional review boards. These three registers were pooled into a single database, because no patient appeared in more than one register, and the registers fulfilled the following criteria: they had a large number of common variables including neurologic and functional scales; the data were gathered by the same researchers at the same centers using similar clinical methodology; and frozen blood samples for molecular determination were stored using a common protocol. The three registers were carried out using a common standardized

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protocol for the detection of the history of hypertension. Inclusion and exclusion criteria were uniformly predefined. In summary, patients were over age 18 years, had a first episode of hemispheric ischemic stroke, and had no previous disability (modified Rankin scale score $\leq$ 1). Common reasons for exclusion were cerebral infarction unconfirmed by CT (n = 13), randomization in clinical trials (n = 80), thrombolytic therapy (n = 11), severe systemic diseases (n = 5), and absence of follow-up (n = 94). Although the three registers had some distinct exclusion criteria, only treatment with vasoactive drugs (n = 15), dementia or psychiatric disease (n = 15), and unstable cardiovascular problems (n = 45) were additional prospective exclusion criteria for this pooling analysis. A total of 844 patients were finally pooled in the database. For the purpose of this study, we used the following variables: age, sex, history of inflammatory or infectious diseases in the 15 days preceding admission or diagnosed at the moment of admission, history of diabetes and hypertension, atrial fibrillation, and time interval from onset to hospital admission. A positive history of hypertension was determined by the existence of a previous clinical diagnosis of arterial hypertension, electrocardiographic or retinoscopic evidence, regular treatment with antihypertensive drugs, or the existence of two or more readings prior stroke with figures above 140 and/or 90 mm Hg (Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure).[17]

On admission to the emergency department, systolic (SBP) and diastolic blood pressure (DBP) and body temperature were recorded; blood samples were taken for blood glucose, fibrinogen, and leukocyte count determination; and a cranial CT was performed. BP recorded in this study was the mean of all the BP measurements obtained before the administration of any antihypertensive drug during the first 24 hours after admission (median 2; range 1 to 4 measurements). Suspensions of plasma were centrifuged at 3,000*g* for 5 minutes and stored at −80 °C for further molecular determinations. Interleukin-6 (IL-6), tumor necrosis factor α (TNF-α), vascular cell adhesion molecule 1 (VCAM-1), and intercellular adhesion molecule 1 (ICAM-1) were measured with commercially available quantitative sandwich ELISA kits (Quantikine, R & D Systems, Minneapolis, MN); for the determination of matrix metalloproteinase 9 (MMP-9), the same technique was used with kits obtained from Biotrack (Amersham Pharmacia, UK). Determinations of markers were made regularly during the studies, at intervals not longer than 4 months from obtaining samples.

Infarct volume was measured in a cranial CT performed between the fourth and seventh days of evolution, in accordance with the formula $0.5 \times a \times b \times c$ (a and b = greatest perpendicular diameters, c = number of sections of 10 mm where the cerebral infarct was apparent).

Only patients with an SBP $\geq$ 220 mm Hg or a DPB $\geq$ 120 mm Hg received antihypertensive drugs within the first 48 hours after admission. Treatment with insulin for hyperglycemia (blood glucose $>$ 160 mg/dL) and with IV metamizol or paracetamol for hyperthermia (tympanic temperature $>$ 37 °C) was initiated early after hospitalization. Subcutaneous low-dose heparin as prophylaxis against pulmonary thromboembolism and antiplatelet drugs was prescribed. Anticoagulants were given to patients with a major cardioembolic source but not as a treatment for early neurologic deterioration.

Stroke subtype was classified as atherothrombotic (ipsilateral arterial stenosis $>$ 50% and absence of cardioembolic diseases), cardioembolic (major cardioembolic source and absence of ipsilateral arterial stenosis $>$ 50%), small vessel disease (lacunar syndrome with normal CT or showing lacunar infarction, in the absence of proximal ipsilateral stenosis $>$ 50% and of cardioembolic source), or cryptogenic (patients who did not fulfil any of the preceding criteria).[18] Transcranial and carotid ultrasound studies were performed in all patients, whereas echocardiography and magnetic resonance angiography or conventional angiography were performed on selected patients.

Stroke severity was evaluated by an experienced neurologist using the Canadian Stroke Scale (CSS) assessed on admission, at 48 $\pm$ 6 hours and at 3 months $\pm$ 15 days. The CSS score was equalized to 0 in patients who died during the follow-up. The CSS ranges from 1.5 (maximum deficit) to 10 (absence of deficit).[19] Patients in whom the modified Rankin scale (mRS) was $\geq$3 points at 3 months were classified in the poor outcome group.

According to the lowest BP therapeutic target levels (160/90 mm Hg) recommended by the European Stroke Initiative (EUSI) in the acute phase of ischemic stroke,[20] we classified patients into three groups, depending on the existence or absence of a history of arterial hypertension ($>$140 and or $>$90 mm Hg) and the presence or absence of HBP ($>$160 and or $>$90 mm Hg) within the first 24 hours' evolution from stroke onset: Group I, normotensives (n = 412): patients without a history of HBP, or with a history of HBP but with pressure lower than 140/90 mm Hg in recent readings, including those within the first 24 hours of stroke; Group II, chronic hypertensives (n = 265): patients with HBP in the acute phase and with a history of HBP; and Group III, new-onset hypertensives (n = 167): patients with HBP ($>$160 and or $>$ 90 mm Hg) in the acute phase and without a history of HBP.

Statistical analyses. The results are expressed as percentages for categorical variables and as mean (SD) or median [quartiles] for the continuous variables. Proportions were compared using the χ^2 test, and the *t* test or analysis of variance and Mann–Whitney or Kruskal–Wallis tests were used to compare continuous variables between two groups, or three or more groups, as appropriate.

The correlation between SBP and DBP on admission and the levels of the inflammatory markers in blood was determined using the Spearman coefficient. We used a general linear model to asses the influence of the acute inflammatory reaction on SBP and DBP levels in the acute phase in the three groups of the study separately. Likewise, the influence of chronic or new-onset HBP on poor neurologic outcome was evaluated by logistic regression analysis. Models were adjusted for factors related to SBP, DBP, or poor neurologic outcome in the bivariate analyses. We fitted the models in a customized way by means of the Enter method. Values of *p* below 0.05 were considered to be significant in all tests.

Results. One hundred seventy-seven patients (19.9%) developed new-onset HBP during the first 24 hours after admission (Group III), which represents 38.6% of patients who had HBP during this time frame. Baseline clinical characteristics and outcome variables in the three groups are shown in table 1. Patients in Group III had a more frequent history of atrial fibrillation, greater stroke severity, higher body temperature, and higher leukocyte count in comparison with the other two groups. The frequency of cardioembolic infarction was greater in Group III, whereas lacunar infarctions were more frequent in Group II. Patients in Group III showed a larger infarct volume and poorer neurologic outcome at 3 months. HBP at the end of follow-up was found in 6.6% of patients in Group III and 5.3% of patients in Group I, compared with 31.6% of those in Group II.

Plasma concentrations of IL-6, TNF-α, ICAM-1, VCAM-1, and MMP-9 were significantly higher in Group III than in the other two groups (table 2). There was no correlation between SBP levels and the markers of inflammation in Group I, a moderate correlation in Group II, and a very significant correlation in Group III (figure). The values were similar for DBP. Generalized linear model showed an independent association between the molecular markers of inflammation and SBP and DBP in patients of Group III (table 3). In patients of Group II, the association was only significant for MMP-9, whereas no markers were associated in Group I (data not shown).

History of diabetes, atrial fibrillation, delay from stroke onset to admission, greater baseline stroke severity, higher body temperature, leukocyte count, serum glucose and fibrinogen levels, and stroke subtype were associated with poor outcome in the bivariate analyses (table 4). After adjusting for these potential confounders, new-onset HBP was independently associated with poor outcome at 3

Table 1 *Baseline clinical characteristics and outcome variables by group*

	Group I: Normotensives, n = 412	Group II: Chronic hypertensives, n = 265	Group III: New-onset hypertensives, n = 167	*p*
Age, years	68.9 (10.6)	71.8 (8.6)	70.7 (8.2)	<0.0001
Men, n (%)	232 (56.3)	139 (52.2)	97 (58.1)	0.459
History of diabetes, n (%)	98 (23.8)	68 (25.7)	35 (21.0)	0.536
History of atrial fibrillation, n (%)	95 (23.1)	89 (33.6)	66 (39.5)	<0.0001
History of infection or inflammation, n (%)	8 (1.9)	5 (1.9)	5 (2.9)	0.172
Time from onset, hours	7 [4.5–11.5]	6 [4.5–9]	7 [4.5–13]	0.220
CSS on admission	5.5 [4–7]	5 [3–6.5]	5 [3–6]	<0.0001
Body temperature on admission, ºC	37.1 (0.7)	36.9 (0.7)	37.4 (0.7)	<0.0001
SBP on admission, mm Hg	140 [120–150]	181 [170–200]	180 [170–208]	<0.0001
DBP on admission, mm Hg	76 [65–86]	100 [90–112]	98 [90–110]	<0.0001
Glycemia on admission, mg/dL	140 [123–205]	143 [115–194]	146 [123–181]	0.618
Fibrinogen on admission, mg/dL	442 [352–550]	416 [368–481]	412 [394–467]	0.074
Leukocyte count admission, $\times 10^3/mm^3$	6.2 [4.7–8.3]	6.5 [5.1–8.1]	6.6 [5.1–8.9]	0.007
Statins intake, n (%)	34 (15.0)	49 (14.4)	50 (18.1)	0.416
Stroke subtype				<0.0001
Atherothrombotic, n (%)	191 (46.4)	106 (40)	57 (34.1)	
Cardioembolic, n (%)	190 (46.1)	103 (38.9)	89 (53.3)	
Small vessel disease, n (%)	23 (5.6)	53 (20)	19 (11.4)	
Cryptogenic, n (%)	8 (1.9)	3 (1.1)	2 (1.2)	
Infarct volume, cc	23 [14–97]	66 [41–122]	81 [54–133]	<0.0001
Poor outcome at 3 months, n (%)	71 (17.2)	119 (44.9)	138 (82.6)	<0.0001
HBP at 3 months (%)				<0.0001
Without antihypertensives, n (%)	15 (3.6)	19 (7.1)	2 (1.2)	
With antihypertensives, n (%)	7 (1.7)	65 (24.5)	9 (5.4)	

CSS = Canadian Stroke Scale; SBP = systolic blood pressure; DBP = diastolic blood pressure; HBP = high blood pressure.

months (odds ratio [OR] 2.10; 95% CI 1.54 to 3.52; $p < 0.0001$). The OR for new-onset HBP did not change when the ultimate infarct volume was forced into the model. In a further logistic regression analysis including the molecular markers, high IL-6 (OR 1.01; 95% CI 1.00 to 1.03; $p = 0.020$) and MMP-9 concentrations (OR 1.01; 95% CI 1.00 to 1.01; $p < 0.0001$), but not new-onset HBP, were independently associated with poor neurologic outcome (table 5).

Discussion. Patients without history of arterial hypertension who develop HBP within the first 24 hours after the onset of stroke (new-onset HBP) have poorer neurologic outcome and greater acute inflammatory response. Interestingly, these patients had higher concentrations of proinflammatory markers in blood (IL-6, TNF-α, ICAM-1, and VCAM-1) vs

Table 2 *Plasma concentrations of molecular markers of inflammation*

	Group I: Normotensives, n = 412	Group II: Chronic hypertensives, n = 265	Group III: New-onset hypertensives, n = 167	*p*
IL-6, pg/mL	12.4 [7.7–20.2]	15.5 [7.1–27.1]	33.5 [21.6–46.2]	<0.0001
TNF-α, pg/mL	11.7 [6.5–18.6]	13.4 [3.7–19.7]	29.6 [18.8–35.8]	<0.0001
ICAM-1, ng/mL	234.3 [166.3–362.2]	283.1 [194.4–573.2]	688 [446.8–915.6]	<0.0001
VCAM-1, ng/mL	419.8 [348.6–529.2]	478.9 [395.9–583.2]	634.2 [475.3–894.3]	<0.0001
MMP-9, ng/mL	36.3 [25.5–55.4]	57 [27.8–108.8]	115.4 [78.8–153.6]	<0.0001

IL-6 = interleukin 6; TNF-α = tumor necrosis factor α; ICAM-1 = intercellular adhesion molecule 1; VCAM-1 = vascular cell adhesion molecule 1; MMP-9 = matrix metalloproteinase 9.

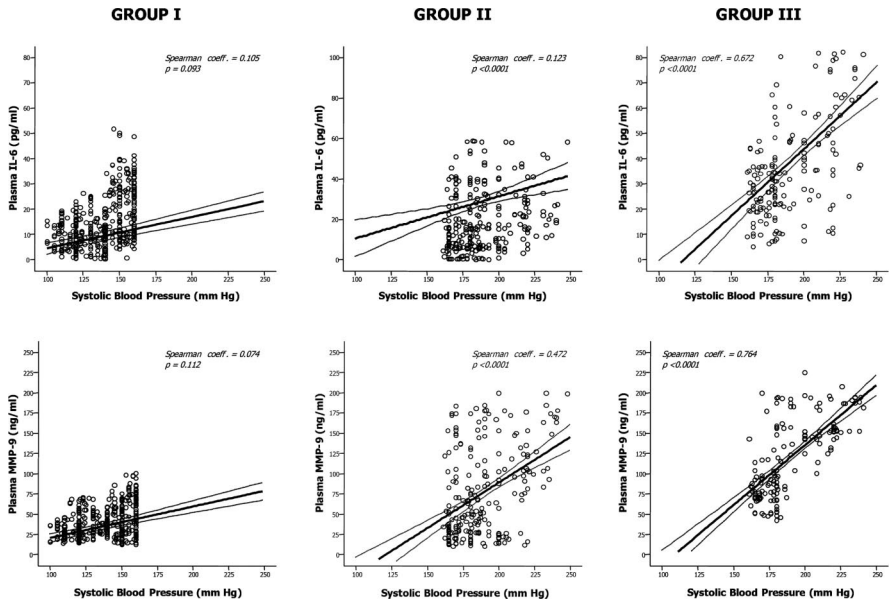

Figure. Scatter plot of the relationship between systolic blood pressure and interleukin 6 (IL-6) and matrix metalloproteinase 9 (MMP-9) in blood pressure groups (Group I, normotensives; Group II, chronic hypertensives; Group III, new-onset hypertensives). Similar results were found for plasma tumor necrosis factor α (TNF)-α, intercellular adhesion molecule 1 (ICAM-1), and vascular cell adhesion molecule 1 (VCAM-1).

patients with chronic HBP and normotensive patients. MMP-9 levels were higher in patients with new-onset hypertension and, to a lesser extent, in those with chronic HBP in comparison with normotensive patients. This finding may be explained because MMP genes are activated by increased levels of proinflammatory cytokines, but also by the mechanical stimulation of HBP on the vessel's wall and by angiotensin II.[21] These effects were independent of infarct size and other potential confounders in multivariate models, so our results suggest a direct relationship between the inflammatory reaction and emergent HBP. However, the design of the present study does not permit us to provide any evidence of causality between inflammation and HBP.

New-onset HBP, but not chronic HBP, was associated with poor neurologic outcome after adjusting for other factors of poor prognosis. Although HBP in the acute phase of stroke might be the result of a greater brain injury, the OR did not change when the ultimate infarct volume was included in the logistic model. We may speculate about whether new-onset HBP led to a proinflammatory reaction in the ischemic brain or vice versa. However, whatever the primary event, our results suggest that elevated concentrations of some molecular markers such as IL-6 and MMP-9 have a greater influence than new-onset HBP on poor outcome.

High BP in the acute phase of stroke is usually considered to be a transient and beneficial physiologic response to ischemia that does not require treatment.[22,23] In some instances, however, it has been associated with poor outcome[10,11,13,24] and with development of cerebral edema in the ischemic tissue.[25] A variety of mechanisms have been implicated in HBP in the acute phase of stroke, but they are not necessarily involved in all patients. As an example, it is difficult to consider HBP as a physiologic response to cerebral ischemia in lacunar infarcts,[10] even though changes in cerebral vasoregulation have been demonstrated in patients with minor stroke.[26] HBP in acute stroke has also been associated with increased cortisol levels, a biologic marker of stress[27] that positively correlates with infarct volume.[28] How-

Table 3 *Adjusted increase in mean (95% CI) systolic and diastolic blood pressures in the acute phase for molecular markers of inflammation in patients with new-onset hypertension (Group III)*

	Systolic blood pressure			Diastolic blood pressure		
	B	95% CI	*p*	B	95% CI	*p*
IL-6	0.22	(0.09 to 0.35)	<0.0001	0.14	(0.02 to 0.27)	0.023
TNF-α	0.32	(0.14 to 0.50)	0.001	0.17	(0.00 to 0.35)	0.040
ICAM-1	0.01	(0.00 to 0.02)	<0.0001	0.02	(0.00 to 0.35)	0.027
VCAM-1	0.01	(0.00 to 0.02)	0.003	0.00	(−0.00 to 0.00)	0.706
MMP-9	0.16	(0.10 to 0.22)	<0.0001	0.11	(0.05 to 0.17)	<0.0001

The models included all the molecular markers and were adjusted for age, history of atrial fibrillation, Canadian Stroke Scale score on admission, body temperature, fibrinogen levels, leukocyte count and infarct volume.

IL-6 = interleukin 6; TNF-α = tumor necrosis factor α; ICAM-1 = intercellular adhesion molecule 1; VCAM-1 = vascular cell adhesion molecule 1; MMP-9 = matrix metalloproteinase 9.

Table 4 *Baseline clinical characteristics by neurologic outcome*

	Good outcome: mRS < 3, n = 516	Poor outcome: mRS ≥ 3, n = 328	*p*
Age, years	69.8 (9.8)	70.8 (9.4)	0.221
Men, n (%)	299 (57.9)	169 (51.5)	0.076
History of diabetes, n (%)	105 (20.3)	96 (29.3)	0.004
History of atrial fibrillation, n (%)	108 (20.9)	142 (43.3)	<0.0001
History of infection or inflammation, n (%)	8 (1.6)	7 (2.1)	0.500
Time from onset, hours	6 [4.5–9.4]	7.5 [5–13]	<0.0001
CSS on admission	6 [5–7]	3.5 [2.5–5]	<0.0001
Body temperature on admission, ºC	37.0 (0.7)	37.3 (0.7)	<0.0001
Glycemia on admission, mg/dL	138 [119–180]	158 [123–206]	0.004
Fibrinogen on admission, mg/dL	411 [359–499]	440 [379–531]	0.007
Leukocytes on admission, $\times 10^3/mm^3$	6.3 [4.8–8.5]	6.7 [5.1–9]	0.001
Statins intake, n (%)	74 (14.3)	59 (18.0)	0.175
Stroke subtype			<0.0001
Atherothrombotic, n (%)	229 (44.4)	125 (38.1)	
Cardioembolic, n (%)	186 (36.0)	196 (59.8)	
Small vessel disease, n (%)	92 (17.8)	3 (0.9)	
Cryptogenic, n (%)	9 (1.7)	4 (1.2)	
HBP groups			<0.0001
Group I, n (%)	156 (30.2)	71 (21.6)	
Group II, n (%)	222 (43.0)	119 (36.3)	
Group III, n (%)	138 (26.7)	138 (42.1)	

mRS = modified Rankin scale; CSS = Canadian Stroke Scale; HBP = high blood pressure.

ever, it is difficult to support the stress reaction as a mechanism for HBP in lacunar infarctions and in those of small size. Cross-sectional data have shown the association between increased BP and a range of biologic markers of inflammation,[3,9] and that they have a positive interaction on stroke risk.[15] Some research have suggested that HBP can provoke an inflammatory response,[1,3] whereas others found that increased levels of markers of inflammation are associated with the risk of developing hypertension,[29,30] this latter mechanism perhaps owing to the stimulation of angiotensin type I receptors.[31]

The recognition of patients with a hypertensive response linked to the acute phase of stroke is difficult. Most patients with ischemic stroke show high BP levels during the acute phase (51.2% in this series).[10-12] However, HBP is the most important risk factor for stroke[32] and, consequently, it is not reasonable to assume that the entire increase in BP in the acute phase of cerebral ischemia is due to the stroke itself, nor that it is transient. Furthermore, although in the majority of cases the BP values decrease during the first days,[12,24,25,33] this does not exclude previous unknown chronic HBP, because the decrease may simply be the result of rest, tranquility, diet, and hydroelectrolytic control after admission. In this study, we used the concept of HBP within the first 24 hours from the onset of ischemic stroke in the absence of previous diagnosis and of supporting clinical data for arterial hypertension. This definition allows correct identification of 85% to 99% of patients with new-onset HBP.[30,34,35] Accordingly, only 6.6% of patients classified in Group III in our study had HBP 3 months after stroke, a proportion similar to that observed in normotensive patients and much lower than the 31.6% found in patients with chronic HBP.

Our study presents some limitations owing to its retrospective nature, particularly the variability in the number of BP determinations during the first 24 hours and the absence of some data, such as the number of patients receiving therapy with antihypertensive drugs, which could affect the levels of molecular markers of inflammation. Consequently, one factor to bear in mind when interpreting the results is that the percentage of atherothrombotic strokes is greater among the patients in Group II (chronic hypertensives), in whom the potential use of statins could exert a reduction of the inflammatory response. However, the effect of the inflammatory response on neurologic outcome remained significant after adjusting for stroke subtype.

Another limitation of this study is the lack of consensus for the definition of hypertension in the acute phase of ischemic stroke. In the present study, the lowest therapeutic target recommended by the EUSI in previously normotensive patients has been used to define new-onset HBP. However, the logistic regression analysis using the therapeutic target accepted

Table 5 *Adjusted odds ratios (95% CIs) of poor neurologic outcome (mRS >3) at 3 months for prognostic variables*

	OR	95% CI	*p*
History of diabetes	1.94	1.18–3.19	0.009
History of atrial fibrillation	1.56	1.01–2.41	0.041
Time from onset	1.01	0.98–1.05	0.307
CSS score	0.48	0.42–0.54	<0.0001
Temperature	0.98	0.72–1.33	0.931
Glycemia	0.99	0.99–1.00	0.636
Fibrinogen	1.00	0.99–1.00	0.426
Leukocytes	1.05	0.97–1.14	0.199
Group			
Normal BP	1.00		
Chronic HBP	0.69	0.39–1.19	0.189
New-onset HBP	2.13	0.91–4.19	0.127
Stroke subtype			
Lacunar	1.00		
Atherothrombotic	1.79	0.67–5.73	0.768
Cardioembolic + cryptogenic	1.17	1.02–3.60	0.005
IL-6	1.01	1.00–1.03	0.020
TNF-α	0.97	0.95–1.99	0.132
ICAM-1	1.00	0.99–1.00	0.539
VCAM-1	1.00	0.99–1.00	0.731
MMP-9	1.01	1.00–1.01	<0.0001

mRS = modified Rankin scale; OR = odds ratio; CSS = Canadian Stroke Scale; BP = blood pressure; HBP = high blood pressure; IL-6 = interleukin 6; TNF-α = tumor necrosis factor α; ICAM-1 = intercellular adhesion molecule 1; VCAM-1 = vascular cell adhesion molecule 1; MMP-9 = matrix metalloproteinase 9.

in patients who receive thrombolytic therapy (185/105 mm Hg; Group III, 86 patients) yielded the same result, as new-onset HBP remained independently associated with poor outcome at 3 months (OR 4.15; 95% CI 1.13 to 7.24; $p < 0.0001$).

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