



Antihypertensive Treatment Compliance in Stroke Patients with Hypertension

Hipertansiyonlu İnme Hastalarda Antihipertansif Tedavi Uyumu

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ABSTRACT

AIM: Stroke is responsible for approximately 6 millions of all the annual deaths worldwide. An effective method to prevent stroke and its comorbidities is the adequate control of the risk factors. This study aimed to evaluate the compliance of stroke patients in their antihypertensive treatment and the frequency of measuring blood pressure.

MATERIAL AND METHOD: Patient's files were retrieved from the hospital patients database using the ICD codes (I60-64, I67-69). In total, 5289 files were accessed. The age, sex, hypertension diagnosis, treatment compliance, the frequency of blood pressure measurements, and the presence of hypertensive crisis during admission were evaluated. Data about compliance with drug treatment and blood pressure monitoring was accepted only if it was received directly from the patient or their relatives. These parameters were also obtained from epicrisis retrospectively.

RESULTS: In this study, 478 files [female: male, 201 (42.1%):277 (57.9%)] with complete data were included. Among the patients, 76.3% had a good to very good treatment compliance and 29.8% had a good to very good frequency of blood pressure measurement. During admission, 23% of patients were in hypertensive crisis.

CONCLUSION: In patients with poor drug compliance and who did not have their blood pressure regularly measured, hypertensive crises occurred significantly more often. Strict blood pressure monitoring and regular doctor follow-ups are neglected by patients. Drug compliance is insufficient to prevent stroke and blood pressure monitoring and follow-ups are also important points to consider.

Key words: Blood pressure, Hypertension, Patient compliance, Stroke

ÖZET

AMAÇ: İnme, dünya çapında tüm yıllık ölümlerin yaklaşık 6 milyonundan sorumludur. İnmeyi ve eşlik eden hastalıklarını önlemenin en etkili yöntemi, risk faktörlerinin yeterli şekilde kontrol altına alınmasıdır. Bu çalışmada, inme hastalarının antihipertansif tedaviye uyumunu ve kan basıncı ölçüm sıklığını değerlendirmeyi amaçladık.

GEREÇ VE YÖNTEM: Hastane veri tabanından ICD kodları (I60-64, I67-69) kullanılarak toplam 5289 dosyaya erişildi. Bu dosyalardan yaş, cinsiyet, hipertansiyon tanısı, tedavi uyumu, kan basıncı ölçüm sıklığı ve başvuru sırasında hipertansif kriz varlığı bilgileri değerlendirildi. İlaç tedavisine uyum ve kan basıncı takibine ilişkin veriler epikrizlerden retrospektif olarak incelenerek doğrudan hasta veya yakınlarından alındığı takdirde kabul edildi.

BULGULAR: Bu çalışmaya, verileri eksiksiz olan 478 dosya (kadın: erkek, 201 (%42,1):277 (%57,9)) dahil edildi. Hastaların %76,3'ü iyi-çok iyi tedavi uyumuna ve %29,8'i iyi-çok iyi tansiyon ölçüm sıklığına sahipti. Başvuru sırasında hastaların %23'ü hipertansif krizdeydi.

SONUÇ: İlaç uyumsuzluğu olan ve kan basıncı düzenli olarak ölçülmeyen hastalarda, hipertansif krizler önemli ölçüde daha sık meydana geldiği gözlemlendi. Sıkı tansiyon takibi ve düzenli doktor takipleri hastalar tarafından ihmal edilmektedir. İlaç uyumu inmeyi önlemede yetersiz olarak görülmüş olup tansiyon takibi ve hastaların kontrolleri de dikkat edilmesi gereken önemli noktalar.

Anahtar kelimeler: Kan basıncı, Hipertansiyon, Hasta uyumu, İnme

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INTRODUCTION

Stroke is responsible for approximately 6 million of all the annual deaths throughout the world and constitutes a very important part of the health expenditures^{1,2}. In the UK, £100 million can be annually saved if 80% of patients affected by stroke can remain compliant with their antihypertensive treatment. Mennini in 2015 has reported that a 70% increase in antihypertensive treatment compliance would save more than £300 million in five European countries (Germany, Italy, France, Spain, United Kingdom)³.

The best method of preventing stroke and its associated complications is the elimination or control of the risk factors. Hypertension plays a significant role in stroke risk factors. In the USA, deaths associated with hypertension have increased up to 61.8% between 2000 and 2013⁴. Other studies have shown that hypertension control can reduce the incidence of stroke by 30%–40%^{5,6}. Therefore, national, and international guidelines recommend the screening, treatment, and control of hypertension^{7,8}.

Several agents, such as calcium channel blockers, diuretics, beta blockers, angiotensin-converting enzyme inhibitors and receptor blockers are used for controlling blood pressure. However, it is estimated that approximately 50% of the patients have poor treatment compliance. Treatment compliance is proportional to the improvement in blood pressure, decrease in hospitalization rate and mortality, and lower treatment costs^{9,10}. Various studies have evaluated the incidence of stroke and treatment compliance^{5,6,11-16}.

The aim of the present study was to evaluate antihypertensive treatment compliance and the frequency of measuring blood pressure in stroke patients and their relationship with hypertensive crisis.

MATERIAL AND METHOD

Patients treated in our service between 2011 and 2016 were selected from the hospital system using the stroke ICD codes (I60–64, I67–69). In total, 5289 files were accessed. The parameters evaluated included age, sex, the presence of hypertension prior to stroke, compliance with antihypertensive treatment, the frequency of blood pressure measurements, and the presence or absence of hypertension during admission. Only 478 patients with the complete data of these parameters were included. Data about compliance with drug treatment and blood pressure monitoring was accepted only if it was received directly from the patient or their relatives. These parameters were obtained from epicrisis retrospectively. A scale of 0–4 (0: None-Patient never uses drugs, 1: Bad-Use only if patient feels bad, 2: Moderate-Use half of what is prescribed, 3: Good- Forgets only a few doses monthly, and 4: Very Good-Use exactly as prescribed) was used to assess the level of treatment compliance. For assessing the frequency of tension measurement, the scale of 0–4 (0: None-No controls, 1: Bad- Checks only if patient feels bad, 2: Moderate-1-2 checks monthly, 3: Good- 1-2 checks weekly, and 4: Very good- Checks everyday) was used. For evaluating hypertension attacks, systolic blood pressure >180 mmHg and diastolic blood pressure > 110 mmHg were used.

Descriptive statistics were used to define continuous variables (mean, standard deviation, minimum, median, and maximum). More than two groups that are independent and not compatible with normal distribution were compared using the Kruskal–Wallis test. Comparison of two groups that were independent and not compatible with normal distribution was performed using the Mann–Whitney U test. The chi-square (or Fisher's exact test in appropriate situations) was used for the relationship between categorical variables. Statistical significance level was set at $p > 0.05$. MedCalc Statistical Software version 12.7.7 was used for analyses (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2013).

This study was approved by the ethics committee of the Haydarpaşa Training and Research Hospital (1491-137-15/1539).

RESULTS

Files of 5289 stroke patients were reviewed, and 478 patients with complete information of all parameters were included. The mean age of patients was 76.5 ± 9.9 years, and 201 (42.1%) were females and 277 (57.9%) were males (Table 1).

Table 1: Distribution of parameters

		N	%
Sex	Female	201	42.1
	Male	277	57.9
Hypertension	None	160	33.5
	Yes	318	66.5
Treatment compliance	None	12	3.8
	Poor	10	3.2
	Moderate	21	6.7
	Good	47	14.9
	Very Good	225	71.4
Tension controls	None	40	12.7
	Poor	78	24.8
	Moderate	103	32.7
	Good	69	21.9
	Very Good	25	7.9
Arrival hypertension crisis	None	368	77.0
	Yes	110	23.0

Only 76.3% of patients reported good to very good treatment compliance and 29.8% reported good to very good frequency of blood pressure measurement. Among the 478 stroke patients, 23% had a systolic blood pressure of >180 mmHg and a diastolic blood pressure of >110 mmHg.

When the ages of patients were examined according to their sex, females were found to have stroke 4.5 years later than males (Mann–Whitney U-test, $p < 0.001$). With regard to the presence of hypertension, there was a statistically significant difference in terms of age distribution (Mann–Whitney U test, $p < 0.05$). Thus, the incidence of hypertension was higher in elderly patients. With regard to the drug compliance and blood pressure control, there was no statistically significant difference in terms of age distribution (Kruskal–Wallis test, both $p > 0.05$).

Table 2: Significancy of age

	Sex	n	Mean	Min.	Maks.	p
Age	Female	201	79,1	50	101	<0,001*
	Male	277	74,6	28	97	
	Hypertension					
	No	160	74,9	28	96	0,026**
	Yes	318	77,3	51	101	
	Drug compliance					
	No	12	71,1	58	87	0,192***
	Bad	10	80,1	61	94	
	Moderate	21	77,9	60	92	
	Good	47	77,8	58	95	
	Very good	225	77,3	51	97	
	Blood pressure control					
	No	40	78,8	61	94	0,634****
	Bad	78	76,8	58	95	
	Moderate	103	77,2	56	96	
	Good	69	76,6	57	97	
	Very good	25	78,6	51	97	

*Statistically significant (Mann-Whitney U p<0.001)

** Statistically significant (Mann-Whitney U p<0.05)

*** Statistically NOT significant (Kruskal Wallis p>0,05)

**** Statistically NOT significant (Kruskal Wallis p>0,05)

Hypertension was more frequent in women with stroke than in men (chi-square test, p < 0.05). There was no statistically significant difference between sex and drug compliance (Fisher's exact test, p > 0.05) and between sex and treatment controls (Fisher's exact test, p > 0.05)

Table 3: Significancy of sex

		Female	Male	p
Hypertension	No	57 (28,4)	103 (37,2)	0,044*
	Yes	144 (71,6)	174 (62,8)	
Drug compliance	No	5 (3,5)	7 (4,0)	0,722**
	Bad	4 (2,8)	6 (3,5)	
	Moderate	10 (7,0)	11 (6,4)	
	Good	17 (12,0)	30 (17,3)	
	Very good	106 (74,6)	119 (68,8)	
Blood pressure control	No	21 (14,8)	19 (11,0)	0,405***
	Bad	29 (20,4)	49 (28,3)	
	Moderate	47 (33,1)	56 (32,4)	
	Good	35 (24,6)	34 (19,7)	
	Very good	10 (7,0)	15 (8,7)	

* Statistically significant (Chi-square test, p < 0.05)

** Statistically NOT significant (Fisher's Exact p>0,05)

*** Statistically NOT significant (Fisher's Exact p>0,05)

Hypertensive crisis was more frequently detected in patients with previous hypertension diagnosis (Fisher's exact test, p < 0.05)

Table 4: Hypertension and Hypertensive crisis

		Hypertension		p
		No	Yes	
Hypertensive crisis	No	136 (85,0)	232 (73,0)	0,002*
	Yes	24 (15,0)	86 (27,0)	

* Statistically significant (Fisher's Exact p<0,05)

In the analysis of drug compliance and blood pressure control, the p-value was not calculated because the number of subgroup patients was low

Table 5: Drug compliance vs Blood pressure control

		Drug compliance				
		None	Poor	Moderate	Good	Very Good
Blood pressure controls	None	9 (75.0)	8 (80.0)	4 (19.0)	4 (8.5)	15 (6.7)
	Poor	3 (25.0)	2 (20.0)	14 (66.7)	22 (46.8)	37 (16.4)
	Moderate	0 (0.0)	0 (0.0)	3 (14.3)	17 (36.2)	83 (36.9)
	Good	0 (0.0)	0 (0.0)	0 (0.0)	4 (8.5)	65 (28.9)
	Very Good	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	25 (11.1)

Since the number of patients was low, the p value could not be calculated.

The incidence of hypertensive crises was significantly higher in patients with poor drug compliance and in those who did not have their blood pressure regularly measured (Fisher's exact test, p < 0.001)

Table 6: Blood pressure control vs Hypertension crisis

		Hypertension crisis		p
		No	Yes	
Blood pressure control	None	19 (8.3)	21 (24.7)	<0.001*
	Poor	31 (13.5)	47 (55.3)	
	Moderate	86 (37.4)	17 (20.0)	
	Good	69 (30.0)	0 (0.0)	
	Very Good	25 (10.9)	0 (0.0)	

*Fisher's Exact p<0.001

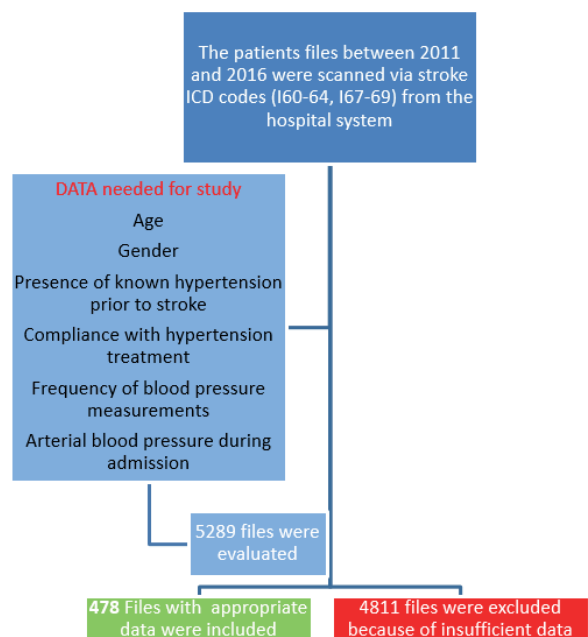


Figure 1: Flowchart of the study

DISCUSSION

In this retrospective clinical study, 478 patients with the diagnosis of stroke within a period of 6 years were evaluated. The results revealed an increase in the incidence of hypertension in proportion to age. Female patients had a stroke at younger ages than the male patients, and hypertension was more frequently monitored in females with a stroke than males. Hypertensive crisis was more frequent in patients with a previous diagnosis of hypertension and in those who did not have any regular blood pressure measurements and had poor anti-hypertensive treatment compliance.

Hypertension is an important risk factor for stroke, and attempts have been made to develop adequate treatment strategies for the regulation of hypertension. In that regard, regular doctor appointment to follow-up antihypertensive treatment, frequent blood pressure monitoring, and drug compliance are the most common methods.

High blood pressure is a very important and controllable risk factor in stroke. Similarly, other studies have revealed a direct relationship between patient compliance and antihypertensive treatment with the prevention of stroke¹⁷⁻¹⁹. In these studies, a decrease in the incidence of stroke was shown to correlate with health expenditures, hospital admission rates, reductions in emergency admission, and mortality rates^{6, 13, 14, 16, 20}.

In the meta-analysis by Abegaz et al., 45.2% of hypertensive patients had poor treatment compliance and females had lower drug compliance than males²¹. In another study by Kettani et al., a treatment compliance of >80% was shown to reduce the risk of cerebrovascular diseases by 22%⁶. Other studies have suggested that treatment compliance is suboptimal in >50% of patients with uncontrolled hypertension²². In the cohort study by Blaschke et al., 16907 patients were examined; 40% of these patients did not follow any treatment in the first year and 4% of these patients did not receive any treatment in the first year²³. It is determined that decreasing the systolic blood pressure by 10 mmHg decreases the cardiovascular disease risk by 20%, stroke risk by 27%, and mortality risk related to all reasons by 13%²⁴.

Bruno et al declared that adherence to HTN medications was significantly lower among black patients and those without health insurance²⁵. Additionally, as a result of the study conducted by Bawand et al. involving 530 patients, it was concluded that stroke-related mortality and morbidity rates could be significantly altered by persuading individuals to regularly monitor their blood pressure and maximize adherence to antihypertensive medications. The same study also indicated that increasing health literacy and reducing smoking rates would play a crucial role in achieving these goals²⁶.

The studies conducted thus far have investigated whether patients use antihypertensive drugs using several different methods. The effects of treatment compliance on stroke, complications, and health expenditures are also examined. However, in our daily practice, although some patients have very good compliance, they do not have their blood pressure regularly measured and have high blood pressures because of insufficient treatments received. However, other studies have reported such patients to have very good treatment compliance. However, because their blood pressure values are high, they should be accepted as high risk in terms of complications due to hypertension. Therefore, patients who had stroke for the first time in our study were examined for the presence of hypertension, treatment compliance, frequency of blood pressure measurements, and hypertensive crisis.

CONCLUSION

Hypertension control is very important in the etiology of stroke, and it has been determined that this control can be achieved via regular doctor appointments, strict blood pressure monitoring, and drug compliance. It has been observed that treatment compliance is independent of age and sex. Therefore, there is a need for prospective, randomized, double-blind, multi-center, and long-term follow-up studies involving a larger number of patients to demonstrate the efficacy and strength of these strategies in controlling hypertension.

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REFERENCES

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019 [published correction appears in *Lancet*. 2020 Nov 14;396(10262):1562]. *Lancet* 2020;396(10258):1204-1222. doi:10.1016/S0140-6736(20)30925-9
2. Goldstein, L. B., Adams, R., Alberts, M. J., Appel, L. J., Brass, L. M., Bushnell, C. D. et al. Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2006;113:e873–e923.
3. Mennini, F. S., Marcellusi, A., von der Schulenburg, J. M., Gray, A., Levy, P., Sciattella, P et al. Cost of poor adherence to anti-hypertensive therapy in five European countries. *Eur. J. Health Econ* 2015;16:65–72. doi:10.1007/s10198-013-0554-4
4. Kung HC, Xu J. Hypertension-related Mortality in the United States, 2000–2013. *NCHS Data Brief*. 2015;(193):1-8
5. Mazzaglia, G., Ambrosioni, E., Alacqua, M., Filippi, A., Sessa, E., Immordino, Vet al. Adherence to antihypertensive medications and cardiovascular morbidity among newly diagnosed hypertensive patients. *Circulation* 2009;120:1598–605. doi: 10.1161/CIRCULATIONAHA.108.830299.
6. Kettani, F. Z., Dragomir, A., Côté, R., Roy, L., Bérard, A., Blais, Let al. Impact of a better adherence to antihypertensive agents on cerebrovascular disease for primary prevention. *Stroke* 2009;40:213–20. doi: 10.1161/STROKEAHA.108.522193
7. James, P. A., Oparil, S., Carter, B. L., Cushman, W. C., Dennison-Himmelfarb, C., Handler et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 2014;311:507–20. doi: 10.1001/jama.2013.284427
8. Whitworth JA. World Health Organization, International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society of hypertension (ISH) statement on management of hypertension. *J Hypertens* 2003;21:1983–92. doi: 10.1097/00004872-200311000-00002.
9. Bramley TJ, Gerbino PP, Nightengale BS, Feride Frech-Tamas. Relationship of blood pressure control to adherence with antihypertensive monotherapy in 13 managed care organizations. *J Manag Care Pharm*. 2006;12:239–45. doi: 10.18553/jmcp.2006.12.3.239.
10. Sokol MC, McGuigan KA, Verbrugge RR, Robert S Epstein. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43:521–30. doi: 10.1097/01.mlr.0000163641.86870.af.
11. Herttua K, Tabák AG, Martikainen P, Jussi Vahtera, Mika Kivimäki. Adherence to antihypertensive therapy prior to the first presentation of stroke in hypertensive adults: population-based study. *Eur Heart J* 2013;34:2933–9 . doi: 10.1093/eurheartj/eh219. Epub 2013 Jul 16.
12. Wu, P. H., Yang, C. Y., Yao, Z. L., Lin, W. Z., Wu, L. W., Chang, C. C. Relationship of blood pressure control and hospitalization risk to medication adherence among patients with hypertension in Taiwan. *Am J Hypertens* 2010;23:155–60. doi: 10.1038/ajh.2009.210. Epub 2009 Nov 19
13. Degli Esposti, L., Saragoni, S., Benemei, S., Batacchi, P., Gepetti, P., Di Bari, M. et al. Adherence to antihypertensive medications and health outcomes among newly treated hypertensive patients. *Clinicoecon Outcomes Res* 2011;3:47–54. doi: 10.2147/CEOR.S15619. Epub 2011 Mar 7
14. Shin, S., Song, H., Oh, S. K., Choi, K. E., Kim, H., Jang, S. Effect of antihypertensive medication adherence on hospitalization for cardiovascular disease and mortality in hypertensive patients. *Hypertens Res* 2013;36:1000–5. doi: 10.1038/hr.2013.85. Epub

- 2013 Aug 22.
15. Bailey, J. E., Wan, J. Y., Tang, J., Ghani, M. A., Cushman, W. C. Antihypertensive medication adherence, ambulatory visits, and risk of stroke and death. *J Gen Intern Med* 2010;25:495–503. doi: 10.1007/s11606-009-1240-1
 16. Lee HJ, Jang S-I, Park E-C. Effect of adherence to antihypertensive medication on stroke incidence in patients with hypertension: a population-based retrospective cohort study. *BMJ Open* 2017;7:e014486. doi: 10.1136/bmjopen-2016-014486.
 17. Xu, T., Yu, X., Ou, S., Liu, X., Yuan, J., Tan, X. et al. Adherence to Antihypertensive Medications and Stroke Risk: A Dose-Response Meta-Analysis. *J Am Heart Assoc.* 2017;6(7):e006371 doi: 10.1161/JAHA.117.006371.
 18. Herttua, K., Martikainen, P., Batty, G. D., Kivimäki, M. Poor adherence to statin and antihypertensive therapies as risk factors for fatal stroke. *J Am Coll Cardiol.* 2016;67:1507–15. doi: 10.1016/j.jacc.2016.01.044
 19. Krousel-Wood, M., Holt, E., Joyce, C., Ruiz, R., Dornelles, A., Webber, L. S. et al. Differences in cardiovascular disease risk of medication adherence among older adults (cosmo). *J Hypertens.* 2015;33:412–20 doi:10.1097/HJH.0000000000000382
 20. Pittman, D. G., Tao, Z., Chen, W., Stettin, G. D. Antihypertensive medication adherence and subsequent healthcare utilization and costs. *Am J Manag Care* 2010;16:568–76.
 21. Abegaz, T. M., Shehab, A., Gebreyohannes, E. A., Bhagavathula, A. S., Elnour, A. A. Nonadherence to antihypertensive drugs: A systematic review and meta-analysis. *Medicine (Baltimore).* 2017 Jan;96(4):e5641. doi: 10.1097/MD.00000000000005641.
 22. Egan BM. Treatment resistant hypertension. *Ethn Dis* 2015;25:495–8. doi:10.18865/ed.25.4.495
 23. Blaschke, T. F., Osterberg, L., Vrijens, B., Urquhart, J. Adherence to medications: insights arising from studies on the unreliable link between prescribed and actual drug dosing histories. *Annu. Rev. Pharmacol. Toxicol.* 2012;52:275–301. doi:10.1146/annurev-pharmtox-011711-113247
 24. Ettehad, D., Emdin, C. A., Kiran, A., Anderson, S. G., Callender, T., Emberson, J. et al. Blood pressure lowering for prevention of cardiovascular diseases and death: a systematic review and meta-analysis. *Lancet* 2016;387:957–67. doi:10.1016/S0140-6736(15)01225-8
 25. Bruno, A., Muppa, J., & Cabahug, I. N. K.. Pre-stroke Adherence to Hypertension Medications in a Bi-racial United States Stroke Belt. *High blood pressure & cardiovascular prevention : the official journal of the Italian Society of Hypertension* 2023;30(4):333–6. doi:10.1007/s40292-023-00581-6
 26. Bawand, R., Ghiasian, M., Khazaei, M., Samadyan, M., & Moradi, A.. Effects of blood pressure unawareness and poor adherence to antihypertensive drugs on outcomes of cerebrovascular accidents among patients with their first-ever stroke. *Journal of hypertension* 2023;41(3):459–69. doi:10.1097/HJH.0000000000003358