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Risk Factors Control and Early Recurrent Cerebral Infarction in Patients with Symptomatic Intracranial Atherosclerotic Disease

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Abstract

Background: The risk of early recurrent cerebral infarction (RCI) is high in patients with symptomatic intracranial atherosclerotic disease (IAD). We sought to determine the relationship between risk factor control and early RCI risk among patients with symptomatic IAD.

Methods: We analyzed participants with symptomatic IAD in the multi-center prospective observational MYRIAD study. Risk factor control was assessed at 6–8-week follow-up. Optimal risk factor control was defined by target systolic blood pressure, being non-smoker, target physical activity, and antiplatelet and antilipidemic therapy compliance. Age-adjusted associations were calculated between risk factor control and RCI determined by MRI-evident new infarcts in the territory of the stenotic vessel at 6–8 weeks from the index event.

Results: Among 82 participants with clinical and brain MRI information available 6–8 weeks after the index event (mean age 63.5 ± 12.5 years, 62.2% men), RCI occurred in 21 (25.6%) cases. At 6–8-week follow-up, 37.8% had target systolic blood pressure, 92.7% were non-smokers, 51.2% had target physical activity, and 98.8% and 86.6% were compliant with antiplatelet and antilipidemic therapy, respectively. Optimal risk factor control increased from 4.9% at baseline to

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19.5% at 6–8-week follow-up (p=0.01). None of the participants with optimal risk factor control at follow-up had RCI (0% vs. 31.8%, p<0.01).

Conclusions: Only one-fifth of MYRIAD participants had optimal risk factor control during early follow-up. Approximately half and two-thirds had physical inactivity and uncontrolled systolic blood pressure, respectively. These risk factors may represent important therapeutic targets to prevent early RCI in patients with symptomatic IAD.

Keywords

Intracranial Atherosclerotic Disease; Stroke Recurrence; Vascular risk factors; Medication Compliance

Introduction

Stroke caused by intracranial atherosclerotic disease (IAD) has the highest risk of early recurrence when compared to other stroke subtypes.[1] Despite intensive medical management, the 1-year recurrence risk is as high as 15%.[2,3] Uncontrolled risk factors may substantially influence stroke recurrence in symptomatic IAD. In the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial, uncontrolled systolic blood pressure (SBP) (>140 mmHg) and elevated cholesterol (>200 mg/dL) were associated with increased recurrent stroke during follow-up.[4] Similarly, participants in the medical arm of the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial who did not achieve recommended targets for SBP, cholesterol levels, and physical activity were more likely to develop recurrent vascular events at 3 years.[5]

The Mechanisms of Early Recurrence in Intracranial Atherosclerotic Disease (MYRIAD) study was designed to evaluate pathogenic mechanisms of stroke in IAD and determine their role on stroke recurrence.[6] In this secondary analysis of MYRIAD, we sought to evaluate risk factor control during the early phase after an ischemic event and determine its relationship with recurrent cerebral infarction (RCI).

Methods

Study Design.

MYRIAD design has been previously described.[7] MYRIAD was a prospective observational study conducted across 10 sites in the US. Individuals aged ≥50 years were enrolled within 21 days of a stroke or transient ischemic attack (TIA) caused by moderate-to-severe IAD (50–99%). Individuals aged 30–49 years were eligible if they had ≥2 vascular risk factor or established atherosclerotic disease in order to avoid inclusion of non-atherosclerotic arteriopathies. In addition, exclusion criteria include other causes of stroke such as atrial fibrillation, myocardial infarction <30 days, mitral stenosis, mechanical valve, intracardiac thrombus or vegetation, dilated cardiomyopathy or ejection fraction <30%, and proximal extracranial carotid or vertebral stenosis >50%.

Qualifying stroke was defined as symptoms lasting ≥24 hours and associated with imaging evidence of brain ischemia in the distribution of a stenotic vessel, whereas qualifying TIA was defined as transient neurological symptoms accompanied by either MRI-DWI abnormalities in the distribution of the stenotic vessel, or multiple (≥2), stereotyped events associated with unequivocal ischemic symptoms (i.e., aphasia, hemiparesis, diplopia, but not dizziness). IAD causing stenosis of 50–99% was quantified by digital subtraction angiography (DSA) or non-invasive testing: CT-angiography (CTA) or MR-angiography (MRA). Degree of stenosis was measured by WASID criteria (percent stenosis = 1 − [diameter stenosis/diameter normal] × 100),[8] or by presence of a flow gap on MRA. DSA was not required, but used if obtained as part of clinical care. Non-invasive testing was considered appropriate based on CTA excellent diagnostic accuracy with sensitivity and specificity >97% compared to DSA,[10,11] and MRA good negative predictive value to diagnose IAD with stenosis >50%.[9] Nevertheless, MRA was considered an inferior diagnostic modality based on previously reported suboptimal positive predictive value (59%).[9] Therefore, our study protocol prioritized DSA, then CTA, then MRA.

Baseline demographics collected at enrolment include participant's age at the time of the qualifying event, sex, and self-reported race/ethnicity. Clinical information collected at enrolment include history of hypertension, diabetes, hyperlipidemia, stroke or TIA previous to the index event, and history of coronary artery disease. Hypertension, diabetes, and hyperlipidemia were defined as patient's self-report of such a history, or use of antihypertensive therapy, hypoglycemic drugs, or antilipidemic therapy, respectively. Similarly, history of previous stroke or TIA and coronary artery disease were self-reported. Body mass index was calculated as kg/m^2 and obesity was defined as body mass index ≥30 kg/m^2. Smoking status was considered as a baseline risk factor in those participants who were current smokers or had quit less than 2 years before enrolment.

Study protocol included clinical follow-up at 6–8 weeks from the qualifying event, as well as brain MRI with FLAIR and DWI sequences at the same time period to evaluate new ischemic lesions (NIL) in the territory of the affected vessel. For the current subanalysis, only participants with complete clinical and brain MRI information at 6–8-week follow-up were included. MYRIAD was funded by the National Institutes of Health/National Institute of Neurological Disorders and Stroke (R01-NS084288). MYRIAD protocol was approved by each study site's ethics board and all participants provided informed consent. Anonymized data of the current analysis is available upon reasonable request to MYRIAD steering committee.

Stroke prevention management.

MYRIAD participants were advised to follow intensive medical management based on the SAMMPRIS regimen,[12] and were not planned to have IAD endovascular therapy during the study period. Recommended medical therapy for stroke prevention management were provided to the study investigators at each site. However, MYRIAD did not mandate specific protocols or time-line algorithms to address risk factors, and in contrast to SAMMPRIS,[12] no lifestyle coaching was provided. Recommended treatment included dual-antiplatelet therapy for 90 days followed by antiplatelet monotherapy, antilipidemic therapy titrated

to achieve low-density-lipoprotein <70 mg/dL, antihypertensive therapy initiated at the time of study enrollment to achieve SBP <140 mmHg (<130 mmHg for diabetics), and counseling on smoking cessation and regular physical activity. Although study investigators recommended specific targets for SBP control, whether blood pressure (BP) was controlled aggressively or conservatively was based on treating physician decision.

Risk factor control assessment.

Risk factor control was assessed at baseline and during 6–8-week follow-up by site investigators based on data gathered from direct patient encounters. To evaluate optimal control of risk factors, the stroke prevention guidelines considered were: 1) target SBP, 2) being non-smoker, 3) target physical activity, 4) antiplatelet therapy, and 5) antilipidemic therapy. For BP measurement, trained personnel obtained 3 consecutive measurements 1–2 minutes apart and averaged them to determine a final BP value. BP was considered at target when SBP <140 mmHg (<130 mmHg for diabetics). Non-smoker was defined as complete absence of smoking at the time of the index event or during follow-up. Physical activity was self-reported and considered at target when the participant performed moderate-to-vigorous exercise for 30 minutes or more at least three times a week. Antiplatelet and antilipidemic therapy use was self-reported and dichotomized as complete or inadequate. Participants who met to all these five criteria were considered to have optimal stroke prevention risk factor control.

Recurrent cerebral ischemia.

RCI outcome was determine by NIL in the territory of the symptomatic stenotic artery on brain MRI performed at 6–8 weeks from the qualifying event. NIL were defined as new DWI/ADC or FLAIR sequence lesions compared to baseline MRI. Two independent vascular neurologists blinded to participants' characteristics adjudicated outcomes centrally. In case of any disagreement, case was reviewed for consensus.

Statistical analysis.

Data analysis was carried out by SAS v9.4 (SAS Institute, Cary, NC). Descriptive statistics are presented as means with standard deviations or medians with interquartile ranges (IQR) for continuous variables and as percentages for categorical variables. Continuous variables were compared by linear models and categorical variables by x^2 or the Fisher exact test as appropriate. Risk factor control at follow-up was determined by comparing the fraction of each parameter at target between baseline and 6–8-week follow-up using the McNemar test. Age-adjusted associations with RCI were explored by binary logistic regression modeling. A two-sided p-value <0.05 was considered statistically significant.

Results

Of 105 participants enrolled in MYRIAD, 7 had incomplete clinical information on risk factor control, 6 had no brain MRI at 6–8 weeks, and 10 had both incomplete clinical information and no brain MRI at 6–8 weeks, thus resulting in 82 participants included in the analysis (mean age 63.5 ± 12.5 years, 62.2% men). The median time from index event to enrollment was 14.5 days, with only 10 participants enrolled during the first week after

stroke, and only 1 participant enrolled before 48 hours after stroke. The following were used to determine stenosis: CTA in 54, DSA in 16, and MRA in 12. MRI-defined RCI outcome was determined in 21 (25.6%) participants, two of whom had a clinical stroke before 6–8 weeks translating into 2.4% rate of clinical stroke recurrence. Table 1 summarizes study population baseline characteristics. As noted, participants who had RCI were younger (mean age 57.6 ± 12.5 years vs. 65.9 ± 11.9 years, p=0.01). Otherwise, no significant differences were found between participants with and without RCI.

At 6–8-week follow-up, the proportion of non-smokers and participants with target physical activity increased (92.7% vs. 82.9%, p<0.01 and 51.2% vs. 24.4%, p<0.01, respectively), as well as the proportion of participants compliant with antiplatelet and antilipidemic therapy (98.8% vs. 89.0%, p<0.01 and 86.6% vs. 57.3%, p<0.01, respectively). In contrast, the proportion of participants with target SBP between baseline and follow-up remained low and unchanged (37.8% vs. 31.7%, p=0.49) despite 79.3% of participants being compliant with prescribed antihypertensive therapy at follow-up. Moreover, the majority of participants (88.2%) who had out-of-target SBP were on antihypertensive therapy.

Optimal risk factor control increased from 4.9% to 19.5% during follow-up (p=0.01; Figure 1). There were no significant differences between individual risk factors and RCI. When BP was analyzed continuously, systolic and diastolic BP did not vary significantly according to RCI occurrence. However, delta SBP showed a trend toward lower values among those without RCI (−5.3 ± 24.2 mmHg vs. 6.2 ± 20.8 mmHg, p=0.06; Supplemental material). RCI occurred in 31.8% of participants with suboptimal risk factor control compared to 0% among those with optimal risk factor control (p<0.01; Table 2). Participants of Hispanic origin and those with history of diabetes were less likely to have optimal risk factor control at follow-up (Table 3).

Discussion

During the first 2 months after index event, only one-fifth of patients with symptomatic IAD had optimal stroke risk factor control defined by SBP at target, smoking cessation, regular physical activity, and antiplatelet and antilipidemic therapy compliance. Although smoking cessation and medication compliance were frequently achieved, SBP control and physical activity targets were infrequently achieved. None of the participants with optimal stroke risk factor control had MRI-defined RCI, thus suggesting that lifestyle modifications and pharmacotherapy are important in reducing the already heightened risk of subsequent ischemia in symptomatic IAD.

Previous trials have demonstrated risk factor control reduces stroke risk among patients with IAD.[4,5,13] Particularly, uncontrolled BP has been associated with increased stroke recurrence in the territory of the stenotic vessel.[14] We found that only one-third of MYRIAD participants had controlled SBP and the proportion did not increase considerably during early follow-up. In our study, clinical follow-up occurred within 2 months after enrolment. Therefore, is plausible that treating physicians chose not to treat BP aggressively due to concerns of IAD-related hypoperfusion during the early phase or participants did not have enough time to adjust their antihypertensive regimen to achieve optimal BP control.[15]

Moreover, the current analysis found a trend towards higher RCI in participants with uncontrolled SBP at follow-up. The latter may be the result of deleterious effects of elevated BP and its influence on atherosclerotic disease, or, alternatively, either due to BP being refractory to treatment in those with critical IAD or treating physicians being more conservative in lowering BP in those with more severe IAD as aforementioned. Larger studies with detailed information on early BP management are warranted to clarify the benefit (or not) of strict BP control in the early phase after symptomatic IAD.

Nonetheless, our study highlights the sizable fraction of patients with IAD who had uncontrolled BP in the first weeks after an ischemic event despite antihypertensive therapy. In the WASID trial, the prevalence of target SBP was nearly 50% and did not vary during two years of follow-up.[4] Contrarily, SAMMPRIS implemented a protocol-driven program and achieved an increase in target SBP from 34% at baseline to 70% at one year.[16] Similarly, another trial among patients with carotid stenosis applied antihypertensives titration algorithms resulting in improvements in target from 43% at baseline to 61% at 24 months.[17] The latter denotes the efficacy of protocol-driven BP management in clinical trials and supports its application in clinical practice.

Engagement in regular physical activity was also suboptimal in our study. Physical activity likely contributes to other vascular risk factors control (i.e., hypertension and diabetes) and may decrease the risk of stroke itself.[18] In SAMMPRIS, greater physical activity was the only factor independently associated with a lower risk of vascular events at 3 years.[5] In our study, nearly half of participants were not physically active according to guidelines-based recommendations during early follow-up. Other trials have reported similar prevalence of physical inactivity in stroke patients with atherosclerosis.[5,16] Common barriers for physical activity participation after stroke include neurological deficits, fatigue, depression, and limited access to parks and gyms.[18] In MYRIAD, most patients had mild neurological deficits at enrollment (median NIHSS 1, IQR 3). However, low NIHSS scores may underestimate neurological deficits that preclude participation in physical activity such as leg mono-paresis or gait ataxia. In addition, absence of individualized regular coaching along with other psychological or socioeconomic factors may have influenced physical activity participation.

Lastly, we found that Hispanic ethnicity and history diabetes were associated with suboptimal risk factor control. Racial and ethnic disparities in stroke prevention measure compliance are likely associated to cultural barriers that include denial of disease, concern for side effects of medications, hierarchy of needs, and socioeconomic barriers.[19] On the other hand, diabetes may interfere with blood pressure control and restricts physical activity due to limitations associated to medical complications of the disease. Additionally, participants without optimal risk factors control had a trend towards higher baseline prevalence of hypertension, obesity and being smokers. It is likely that baseline characteristics of the study population influenced optimal risk factors control at follow-up.

Study strengths include its prospective design and systematic data capture. Our study is novel as we analyzed early risk factor control according to stroke prevention guidelines, as well as MRI-evident early RCI. Limitations include the small sample size which restricted

power to detect associations between risk factors control and stroke recurrence. Based on the known low positive predictive value of MRA for IAD >50%,[9] it is possible that some false positive stenoses were included among participants who qualified based on MRA only. Medication compliance was self-reported and subject to recall bias. Serum markers such as low-density-lipoprotein and glycohemoglobin were not included due to scarce available data. Finally, our findings may not be generalizable to routine practice due to Hawthorne effect.

In summary, a large fraction of individuals with recent symptomatic IAD had suboptimal stroke risk factor control, mainly due to poor SBP control and physically inactivity. The absence of infarct recurrence in participants with optimal risk factor control points to an important therapeutic target for secondary stroke prevention. Our study underscores the value of intensive medical management on reducing stroke recurrence in patients with IAD and extends it to subclinical infarct recurrence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflict of interest:

V.J. Del Brutto has salary support from the Florida Regional Coordinating Center for the NINDS Stroke Trials Network; S. Prabhakaran has research salary support for role as PI (MPI) of MYRIAD from NIH/NINDS (1R01NS084288). Receives compensation from AHRQ/NIH grants, Abbvie consulting, and UpToDate royalties; D.S. Liebeskind has research salary support for role as PI (MPI) of MYRIAD from NIH/NINDS (1R01NS084288); I. Campo-Bustillo has salary support from R01 grant NIH/NINDS (1R01NS084288) to the University of Miami for role as MyRIAD Project Manager; G. Cotsonis has research salary support for role as biostatistician of MYRIAD from NIH/NINDS (1R01NS084288); A. Nizam has research salary support for role as biostatistician of MYRIAD from NIH/NINDS (1R01NS084288); J.G. Romano has research salary support for role as PI (MPI) of MYRIAD from NIH/NINDS (1R01NS084288)

References

[1]. Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: a population-based study of functional outcome, survival, and recurrence. Stroke. 20005;31(5):1062–8. [PubMed: 10797166]

[2]. Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, Frankel MR, Levine SR, Chaturvedi S, Kasner SE, Benesch CG, Sila CA, Jovin TG, Romano JG; Warfarin-Aspirin Symptomatic Intracranial Disease Trial Investigators. Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis. N Engl J Med. 2005331;352(13):1305–16. [PubMed: 15800226]

[3]. Chimowitz MI, Lynn MJ, Derdeyn CP, Turan TN, Fiorella D, Lane BF, Janis LS, Lutsep HL, Barnwell SL, Waters MF, Hoh BL, Hourihane JM, Levy EI, Alexandrov AV, Harrigan MR, Chiu D, Klucznik RP, Clark JM, McDougall CG, Johnson MD, Pride GL Jr, Torbey MT, Zaidat OO, Rumboldt Z, Cloft HJ; SAMMPRIS Trial Investigators. Stenting versus aggressive medical therapy for intracranial arterial stenosis. N Engl J Med. 2011915;365(11):993–1003. [PubMed: 21899409]

[4]. Chaturvedi S, Turan TN, Lynn MJ, Kasner SE, Romano J, Cotsonis G, Frankel M, Chimowitz MI; WASID Study Group. Risk factor status and vascular events in patients with symptomatic intracranial stenosis. Neurology. 20071127;69(22):2063–8. [PubMed: 18040012]

[5]. Turan TN, Nizam A, Lynn MJ, Egan BM, Le NA, Lopes-Virella MF, Hermayer KL, Harrell J, Derdeyn CP, Fiorella D, Janis LS, Lane B, Montgomery J, Chimowitz MI. Relationship between risk factor control and vascular events in the SAMMPRIS trial. Neurology. 2017124;88(4):379–385. [PubMed: 28003500]

[6]. Romano JG, Prabhakaran S, Nizam A, Feldmann E, Sangha R, Cotsonis G, Campo-Bustillo I, Koch S, Rundek T, Chimowitz MI, Liebeskind DS; MyRIAD Investigators. Infarct Recurrence in Intracranial Atherosclerosis: Results from the MyRIAD Study. J Stroke Cerebrovasc Dis. 20212;30(2):105504. [PubMed: 33276302]

[7]. Liebeskind DS, Prabhakaran S, Azhar N, Feldmann E, Campo-Bustillo I, Sangha R, Koch S, Rundek T, Ostergren L, Chimowitz MI, Romano JG; MyRIAD Investigators. Mechanisms of early Recurrence in Intracranial Atherosclerotic Disease (MyRIAD): Rationale and design. J Stroke Cerebrovasc Dis. 202010;29(10):105051. [PubMed: 32912558]

[8]. Samuels OB, Joseph GJ, Lynn MJ, Smith HA, Chimowitz MI. A standardized method for measuring intracranial arterial stenosis. AJNR Am J Neuroradiol. 20004;21(4):643–6. [PubMed: 10782772]

[9]. Feldmann E, Wilterdink JL, Kosinski A, Lynn M, Chimowitz MI, Sarafin J, Smith HH, Nichols F, Rogg J, Cloft HJ, Wechsler L, Saver J, Levine SR, Tegeler C, Adams R, Sloan M; Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA) Trial Investigators. The Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA) trial. Neurology. 2007612;68(24):2099–106. [PubMed: 17409371]

[10]. Bash S, Villablanca JP, Jahan R, Duckwiler G, Tillis M, Kidwell C, Saver J, Sayre J. Intracranial vascular stenosis and occlusive disease: evaluation with CT angiography, MR angiography, and digital subtraction angiography. AJNR Am J Neuroradiol. 20055;26(5):1012–21. [PubMed: 15891154]

[11]. Nguyen-Huynh MN, Wintermark M, English J, Lam J, Vittinghoff E, Smith WS, Johnston SC. How accurate is CT angiography in evaluating intracranial atherosclerotic disease?Stroke. 20084;39(4):1184–8. [PubMed: 18292376]

[12]. Turan TN, Lynn MJ, Nizam A, Lane B, Egan BM, Le NA, Lopes-Virella MF, Hermayer KL, Benavente O, White CL, Brown WV, Caskey MF, Steiner MR, Vilardo N, Stufflebean A, Derdeyn CP, Fiorella D, Janis S, Chimowitz MI; SAMMPRIS Investigators. Rationale, design, and implementation of aggressive risk factor management in the Stenting and Aggressive Medical Management for Prevention of Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial. Circ Cardiovasc Qual Outcomes. 201291;5(5):e51–60. [PubMed: 22991350]

[13]. Chang KC, Chuang IC, Huang YC, Wu CY, Lin WC, Kuo YL, Lee TH, Ryu SJ. Risk factors outperform intracranial large artery stenosis predicting unfavorable outcomes in patients with stroke. BMC Neurol. 201981;19(1):180. [PubMed: 31370812]

[14]. Turan TN, Cotsonis G, Lynn MJ, Chaturvedi S, Chimowitz M; Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) Trial Investigators. Relationship between blood pressure and stroke recurrence in patients with intracranial arterial stenosis. Circulation. 2007612;115(23):2969–75. [PubMed: 17515467]

[15]. Bulwa Z, Gomez CR, Morales-Vidal S, Biller J. Management of Blood Pressure After Acute Ischemic Stroke. Curr Neurol Neurosci Rep. 2019429;19(6):29. [PubMed: 31037389]

[16]. Derdeyn CP, Chimowitz MI, Lynn MJ, Fiorella D, Turan TN, Janis LS, Montgomery J, Nizam A, Lane BF, Lutsep HL, Barnwell SL, Waters MF, Hoh BL, Hourihane JM, Levy EI, Alexandrov AV, Harrigan MR, Chiu D, Klucznik RP, Clark JM, McDougall CG, Johnson MD, Pride GL Jr, Lynch JR, Zaidat OO, Rumboldt Z, Cloft HJ; Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis Trial Investigators. Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomised trial. Lancet. 2014125;383(9914):333–41. [PubMed: 24168957]

[17]. Turan TN, Voeks JH, Chimowitz MI, Roldan A, LeMatty T, Haley W, Lopes-Virella M, Chaturvedi S, Jones M, Heck D, Howard G, Lal BK, Meschia JF, Brott TG. Rationale, Design, and Implementation of Intensive Risk Factor Treatment in the CREST2 Trial. Stroke. 202010;51(10):2960–2971. [PubMed: 32951538]

[18]. Billinger SA, Arena R, Bernhardt J, Eng JJ, Franklin BA, Johnson CM, MacKay-Lyons M, Macko RF, Mead GE, Roth EJ, Shaughnessy M, Tang A; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Lifestyle and Cardiometabolic Health; Council on Epidemiology and Prevention; Council on Clinical Cardiology. Physical activity and exercise recommendations for stroke survivors: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 20148;45(8):2532–53. [PubMed: 24846875]

[19]. Cruz-Flores S, Rabinstein A, Biller J, Elkind MS, Griffith P, Gorelick PB, Howard G, Leira EC, Morgenstern LB, Ovbiagele B, Peterson E, Rosamond W, Trimble B, Valderrama AL; American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Epidemiology and Prevention; Council on Quality of Care and Outcomes Research. Racial-ethnic disparities in stroke care: the American experience: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 20117;42(7):2091–116 [PubMed: 21617147]

Highlights

- Only one-fifth on patients with symptomatic intracranial atherosclerosis (IAD) had optimal stroke risk factors control during early follow-up.
- Uncontrolled systolic blood pressure and physical inactivity were frequent during early follow-up in patients with symptomatic IAD.
- None of the participants with optimal risk factors control had early recurrent cerebral infarction, thus suggesting that lifestyle modifications and pharmacotherapy are important in reducing risk of recurrent ischemia in patients with symptomatic IAD.

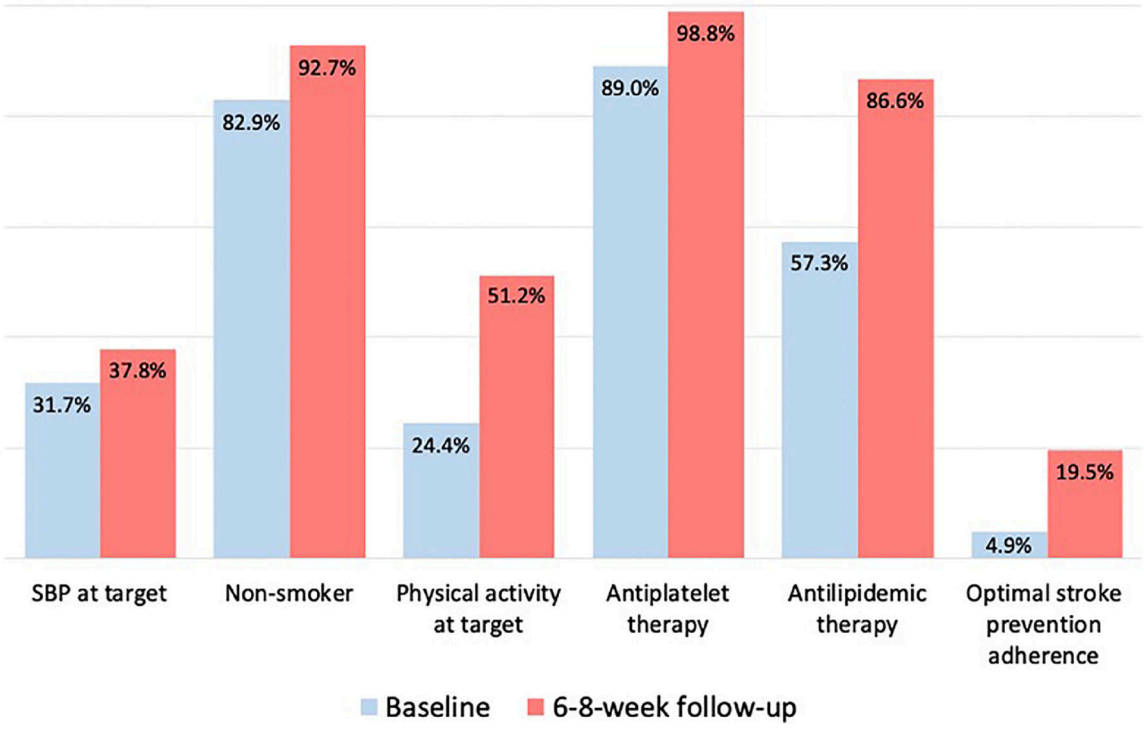

Figure 1.
Stroke risk factor control between baseline and 6–8-week follow-up.

Table 1.

Baseline clinical characteristics of the study population and its relationship with MRI-defined recurrent cerebral ischemia during follow-up.

	Total (n=82)		Recurrent cerebral infarction				Age-adjusted p-value
			No (n=61)		Yes (n=21)		
Age, mean (SD)	63.5	(12.5)	65.9	(11.9)	57.6	(12.5)	0.01 *
Men, n (%)	51	(62.2)	38	(62.3)	13	(61.9)	0.98
Race/Ethnicity							
Non-Hispanic White	34	(41.5)	26	(42.6)	8	(38.1)	-
Non-Hispanic Blacks	29	(35.4)	21	(34.4)	8	(38.1)	0.60
Hispanic	16	(19.5)	12	(19.7)	4	(19.1)	0.97
Asian	3	(3.7)	2	(3.3)	1	(4.8)	0.87
Vascular Risk Factors							
Hypertension, n (%)	69	(84.2)	49	(80.3)	20	(95.2)	0.14
Diabetes, n (%)	42	(51.2)	28	(45.9)	14	(66.7)	0.23
Hyperlipidemia, n (%)	55	(67.1)	43	(70.5)	12	(57.1)	0.48
Smoker current or recent (<2y), n (%)	19	(23.2)	13	(21.3)	6	(28.6)	0.92
Obesity (BMI >30 kg/m2), n (%) **	28	(39.4)	20	(37.4)	8	(44.4)	0.99
Prior stroke or TIA, n (%)	21	(25.6)	17	(27.8)	4	(19.1)	0.43
Coronary artery disease, n (%)	13	(15.9)	10	(16.4)	3	(14.3)	1.00
Days from index event to baseline brain MRI, median (IQR)	1	(3)	1	(2)	1	(6)	0.26
Days from index event to enrolment, median (IQR)	14.5	(9)	14	(10)	16	(8)	0.35
NIHSS >3, n (%)	16	(19.5)	11	(18.0)	5	(23.1)	0.51

Abbreviations BMI body-mass index, NIHSS National Institutes of Health Stroke Scale, TIA transient ischemic attack

* Unadjusted analysis

** Missing values were excluded (n=71)

Table 2.

Stroke risk factors control at 6–8-week follow-up and risk of MRI-defined recurrent cerebral ischemia.

	Recurrent cerebral ischemia	Age-adjusted p-value
SBP at target, n (%)		0.13
yes	5/31 (16.1)	
no	16/51 (31.4)	
Non-smoker, n (%)		0.83
yes	19/68 (25.0)	
no	2/6 (33.3)	
Physically activity at target, n (%)		0.48
yes	9/42 (21.4)	
no	12/40 (30.0)	
Antiplatelet therapy, n (%)		0.99
yes	21/81 (25.9)	
no	0/1 (0.0)	
Antilipidemic therapy, n (%)		0.49
yes	19/71 (26.8)	
no	2/11 (18.2)	
Optimal stroke risk factors control, n (%)		<0.01 *
yes	0/16 (0.0)	
no	21/66 (31.8)	

* Unadjusted analysis

Abbreviations SBP systolic blood pressure

Table 3.

Relationship between baseline clinical characteristics of the study population and optimal stroke risk factors control during follow-up.

	No (n=66)		Yes (n=16)		
Age, mean (SD)	62.9	(11.8)	66.0	(15.2)	0.39
Men, n (%)	41	(62.1)	10	(62.5)	0.98
Race/Ethnicity					
Non-Hispanic White	24	(36.4)	10	(62.5)	-
Non-Hispanic Blacks	24	(36.4)	5	(31.3)	0.38
Hispanic	16	(24.2)	0	(0.0)	0.02
Asian	2	(3.0)	1	(6.3)	1.0
Vascular Risk Factors					
Hypertension, n (%)	58	(87.9)	11	(68.8)	0.12
Diabetes, n (%)	38	(57.6)	4	(25.0)	0.02
Hyperlipidemia, n (%)	42	(63.7)	13	(81.3)	0.18
Smoker current or recent (<2y), n (%)	17	(25.8)	2	(12.5)	0.33
Obesity (BMI >30 kg/m2), n (%) *	24	(42.9)	4	(26.7)	0.25
Prior stroke or TIA, n (%)	17	(25.8)	4	(25.0)	1.0
Coronary artery disease, n (%)	9	(13.6)	4	(25.0)	0.27
NIHSS >3, n (%)	14	(21.2)	2	(12.5)	0.72
Baseline SBP, mean (SD)	145.5	(18.3)	140.1	(22.2)	0.32
Baseline DBP, mean (SD)	80.1	(13.3)	81.6	(12.2)	0.68

Abbreviations BMI body-mass index, DBP diastolic blood pressure, NIHSS National Institutes of Health Stroke Scale, SBP systolic blood pressure, TIA transient ischemic attack

* Missing values were excluded (n=71)