Title

Lipid Levels and Short-Term Risk of Recurrent Brain Infarcts in Symptomatic Intracranial Stenosis.

Journal

Journal of Stroke & Cerebrovascular Diseases, 31(1)

Authors

Prabhakaran, Shyam
Liebeskind, David
Cotsonis, George
et al.

Publication Date

2022

DOI

10.1016/j.jstrokecerebrovasdis.2021.106141

Peer reviewed

HHS Public Access

Author manuscript

J Stroke Cerebrovasc Dis. Author manuscript; available in PMC 2023 January 01.

Published in final edited form as:

J Stroke Cerebrovasc Dis. 2022 January ; 31(1): 106141. doi:10.1016/j.jstrokecerebrovasdis.2021.106141.

Lipid levels and short-term recurrent brain infarcts in symptomatic intracranial stenosis

Shyam Prabhakaran, MD, MS[1], **David S. Liebeskind, MD**[2], **George Cotsonis, MA**[3], **Azhar Nizam, MS**[3], **Edward Feldmann, MD**[4], **Rajbeer S. Sangha, MD**[5], **Iszet Campo-Bustillo, MD, MPH**[6], **Jose G. Romano, MD**[6] **on behalf of MYRIAD Investigators**

[1]The University of Chicago, Chicago, IL, USA

[2]University of California at Los Angeles, Los Angeles, CA, USA

[3]Emory University, Atlanta, GA, USA

[4]The University of Massachusetts Medical School-Baystate, Springfield, MA, USA

[5]University of Alabama at Birmingham, Birmingham, AL, USA

[6]University of Miami, Miami, FL, USA

Abstract

Objectives: Hyperlipidemia is a strong risk factor for intracranial atherosclerotic disease (ICAD) and clinical stroke recurrence. We explored the effect of serum lipid levels on subclinical infarct recurrence in the Mechanisms of earlY Recurrence in Intracranial Atherosclerotic Disease (MYRIAD) study.

Materials and Methods: We included enrolled MYRIAD patients with lipid measurements and brain MRI at baseline and brain MRI at 6–8 weeks. Infarct recurrence was defined as new infarcts in the territory of the symptomatic artery on brain MRI at 6–8 weeks compared to baseline brain

Corresponding author information: Shyam Prabhakaran, MD, MS, 5841 S. Maryland Ave. MC 2030, A-223, Chicago, IL 60637, Tel: 773-702-0080, shyam1@uchicago.edu.

AUTHOR CONTRIBUTIONS

Study design and conduct: SP, DSL, JGR

Study coordination: ICB

Data management: GC, AN

Statistical analysis: SP

Manuscript drafting: SP

Critical revisions: All

David S. Liebeskind, MD, University of California at Los Angeles, Neuroscience Research Building, 635 Charles E Young Drive South, Suite 225, Los Angeles, CA, USA 90095-7334

George Cotsonis, MA, Emory University School of Public Health, Dept. of Biostatistics and Bioinformatics, 1518 Clifton Road NE, GCR 234, Atlanta, GA 30322

Azhar Nizam, MS, Emory University School of Public Health, Dept. of Biostatistics and Bioinformatics, 1518 Clifton Road NE, GCR 234, Atlanta, GA 30322

Edward Feldmann, MD, Department of Neurology at UMMS-Baystate, 759 Chestnut Street, Springfield MA 01199

Rajbeer S. Sangha, MD, University of Alabama Birmingham, 350 1720 7th Ave, Birmingham, AL 35233

Iszet Campo-Bustillo, MD, MPH, University of Miami, Clinical Research Building, 1120 NW 14th St. Suite# 1364, Miami, FL 33136

Jose G. Romano, MD, University of Miami, Clinical Research Building, 1120 NW 14th St. Suite# 1362, Miami, FL 33136

MRI. We assessed the association between baseline total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels and recurrent infarct at 6–8 weeks using multivariable logistic regression.

Results: Among 74 patients (mean age 64.2±12.9 years, 59.5% were white, 60.8% men), 20 (27.0%) had new or recurrent infarcts. Mean HDL-C (37.2 vs. 43.9 mg/dL, *P*=0.037) was lower and TG (113.5 vs. 91.3 mg/dL, P=0.008) was higher while TC (199.8 vs. 174.3 mg/dL, *P*=0.061) and LDL-C (124.3 vs. 101.2 mg/dL, *P*=0.053) were nominally higher among those with recurrent infarcts than those without. LDL-C (adj. OR 1.022, 95% CI 1.004–1.040, *P*=0.015) and TG (adj. OR 1.009, 95% CI 1.001–1.016, *P*=0.021) were predictors of recurrent infarct at 6–8 weeks adjusting for other clinical and imaging factors.

Conclusions: Baseline cholesterol markers can predict early infarct recurrence in patients with symptomatic ICAD. More intensive and rapid lipid lowering drugs may be required to reduce risk of early recurrence.

Keywords

cholesterol; stroke; statin; magnetic resonance imaging

INTRODUCTION

Hyperlipidemia is known risk factor for intracranial atherosclerotic disease (ICAD); in prior trials of symptomatic ICAD, lipid levels were associated with clinical stroke and vascular event recurrence.[1–3] However, it is unknown whether lipid levels influence subclinical events in the form of infarct recurrence on brain imaging.

Given the even greater risk of subclinical infarct recurrence on brain magnetic resonance imaging (MRI) in patients with symptomatic ICAD,[4] we explored the effect of baseline lipid levels on infarct recurrence at 6–8 weeks in the Mechanisms of earlY Recurrence in Intracranial Atherosclerotic Disease (MYRIAD) study. Prior publications from MYRIAD has noted a 5-fold greater risk of subclinical recurrence than clinical recurrence,[4] identified imaging predictors subclinical recurrence,[5] and assessed risk factor control from baseline to 6–8 weeks.[6]

In this post-hoc analysis of MYRIAD, we hypothesized that lipid levels, particularly low-density lipoprotein cholesterol (LDL-C), at time of index ischemic stroke or transient ischemic attack (TIA) in patients with moderate or severe intracranial atherosclerotic stenosis are associated with early subclinical infarct recurrence.

MATERIAL AND METHODS

Eligibility criteria for MYRIAD have been previously reported.[7] Patients with ischemic stroke or TIA within 21 days from onset and caused by 50–99% atherosclerotic stenosis of the intracranial carotid artery, middle cerebral artery M1 segment, basilar artery, or vertebral artery V4 segment based on magnetic resonance angiography, computerized tomographic angiography, or digital subtraction angiography were recruited with informed consent. Those with contraindications to MRI, MR contrast agents, including allergy, creatinine >1.5

or GFR <30 mL/min/1.73 m^2, planned endovascular treatment for ICAD, or co-existing atrial fibrillation or proximal extracranial atherosclerotic stenosis >50% were excluded. De-identified data will be provided upon reasonable request to the corresponding author.

In this analysis, we included only those MYRIAD participants with baseline lipid levels collected during index stroke or TIA hospitalization and in whom brain MRI at 6–8 weeks was obtained. All sites and treating physicians agreed to follow current practice guidelines for aggressive medical management for patients with symptomatic ICAD.[8]

Lipid measurements were collected at time of index hospitalization and included total cholesterol (TC), LDL-C, high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels. We also collected demographics (age, sex, race), risk factors (hypertension, diabetes, hyperlipidemia, prior stroke, physical activity, current smoking), and index stroke characteristics including baseline National Institutes of Health Stroke Scale (NIHSS) score, degree of stenosis categorized as 50–69% vs. 70–99% stenosis, location (anterior vs. posterior circulation), and systolic and diastolic blood pressure (SBP, DBP) at enrollment, which occurred within 21 days of index event (median 15 days).[4] Recurrent infarct on 6–8 week MRI was the primary outcome of interest. Definitions and methods for index and 6–8 week MRI reading and adjudication have been previously reported.[9]

Analyses were performed using SPSS software, version 25 (IBM, Armonk, NY). Categorical variables were presented as counts and percentages, and the difference between groups was tested using Pearson chi-square tests or Fisher's exact tests, as appropriate. Continuous variables were presented as means and standard deviations (SD) or medians with 25^{th} and 75^{th} percentiles and the difference between groups was tested using the Mann-Whitney U test. We assessed the association between lipid levels on recurrent infarct risk using multivariable logistic regression adjusting for other clinical and imaging factors previously identified: age, SBP, infarct pattern (borderzone vs. non-borderzone), location of stenosis (anterior vs. posterior), and degree of stenosis (severe vs. moderate).[5] Goodness of fit of models was evaluated using the Hosmer-Lemeshow test. *P*-value <0.05 was considered significant in final models.

RESULTS

Among 74 included MYRIAD patients (mean age 64.2±12.9 years, 59.5% were white, 60.8% men), 20 (27.0%) had new or recurrent infarcts. The mean times from qualifying event to enrollment and 6–8 week MRI were 14.2±6.9 days and 52.8±18.8 days, respectively. At time of index hospitalization, mean cholesterol, LDL-C, HDL-C, and median TG were 181.2±51.9, 107.4±45.6, 42.1±12.3, and 126.5 (IQR 90.5–207.3) mg/dL, respectively. Mean SBP was 145.3±18.3 mm Hg at enrollment. TC was highly correlated with LDL-C (r=0.925, P<0.001) and modestly with TG (r=0.275, P=0.018), and TG and HDL-C were modestly correlated (r=−0.373, P=0.001). While mean cholesterol and HDL-C and median TG levels were similar between white and non-white groups, LDL-C was significantly higher in non-whites (121.5 vs. 99.3 mg/dL, P=0.017). Use of anti-lipidemic drugs was 39.2% at index hospitalization, 94.6% at enrollment, and 89.2% at 6–8 weeks. Sensitivity analyses showed no significant differences in age, sex, race, index NIHSS score,

or past medical history between included (n=74) and excluded (n=31) MYRIAD patients (Table 1; Supplemental Table).

Mean HDL-C (37.2 vs. 43.9 mg/dL, *P*=0.037) was lower and TG (113.5 vs. 91.3 mg/dL, *P*=0.008) was higher while TC (199.8 vs. 174.3 mg/dL, *P*=0.061) and LDL-C (124.3 vs. 101.2 mg/dL, *P*=0.053) were nominally higher among those with recurrent infarcts than those without. Other bivariate comparisons between demographic, clinical, and imaging factors and recurrent infarct are shown in Table 2.

In a multivariable model (Table 3) including LDL-C and HDL-C, LDL-C (adj. OR 1.020, 95% CI 1.004–1.036, *P*=0.016) was predictor of recurrent infarct at 6–8 weeks adjusting for other clinical and imaging factors. There was a trend towards significance for HDL-C level (adj. OR 0.932, 95% CI 0.868–0.1001, *P*=0.053). In a separate model including TG instead of HDL-C, LDL-C (adj. OR 1.022, 95% CI 1.004–1.040, *P*=0.015) and TG (adj. OR 1.009, 95% CI 1.001–1.016, *P*=0.021) were both predictors of recurrent infarct.

DISCUSSION

In this analysis of a multi-center cohort of patients with symptomatic ICAD, we found that LDL-C, TG, and, to a lesser degree, HDL-C levels at the time of index stroke or TIA are modest predictors of cerebral infarct recurrence in the territory of the stenosis at 6–8 weeks. These findings extend the known effects of lipid levels on clinical stroke recurrence to early subclinical infarct recurrence. Our data provide further support for aggressive lipid lowering therapy in the medical management of symptomatic ICAD, particularly among non-white patients whose baseline LDL-C levels were higher than white patients.

Despite high adherence to medical therapy in MYRIAD,[4] we noted a very high risk of subclinical recurrence in the first 6–8 weeks after stroke or TIA, arguing for more aggressive measures to prevent early subclinical and clinical recurrence. Prior studies have shown that subclinical infarcts increase the risk of dementia and cognitive decline.[10] Thus, the accumulation of subclinical infarcts likely has clinical consequences over time and its prevention merits further study.

Aggressive plaque stabilization with dual antiplaletet therapy (DAPT) and high-intensity statin therapy is the current standard of care for stroke prevention in patients with symptomatic ICAD. Prior studies have suggested that DAPT can reduce the risk of atherothrombotic embolism in ICAD.[11, 12] Furthermore, the reduced risk of recurrent stroke in SAMMPRIS compared to WASID has been hypothesized to be due, in part, to DAPT despite no randomized controlled trial of DAPT versus single antiplatelet therapy in symptomatic ICAD patients.[13] The role of novel antithrombotic agents and combinations is actively being investigated as potential therapeutic approaches that may be superior to combination aspirin and clopidogrel.

High-intensity statin therapy has also been recommended with a goal LDL-C <70 mg/dL in patients with ischemic stroke or TIA of atherosclerotic origin.[14] Several studies have noted the direct benefits of lipid lowering therapy on plaque characteristics in ICAD. In asymptomatic patients, rosuvastatin was associated with regression of plaques at 6 months

using CT angiography[15] while another study using transcranial color-coded sonography for serial follow-up over 2 years showed intensive statin therapy was superior to standard statin therapy in reducing plaque burden and stenosis.[16] Given it may take months to years to lead to statin-mediated protective effects on intracranial plaque biology, it is not surprising that we observed a high rate of subclinical recurrence at 6–8 weeks. Our data on early infarct recurrence suggests even more rapid and aggressive lipid lowering may be warranted. For example, PCSK-9 inhibitors have been shown to reduce LDL-C levels to < 70 mg/dL at 8 weeks in over 95% of patients with acute coronary syndrome compared to statin therapy alone.[17] An ongoing study, Reducing Intracranial Atherosclerosis with Repatha (RISER) study (ClinicalTrials.gov Identifier: NCT04573777), is evaluating this approach in patients with ICAD.

Our data also suggest a modest effect of TG and, to a lesser extent, HDL-C levels on recurrent infarct risk extending the evidence beyond the well-established clinical stroke risk associated with these factors.[18, 19] Though low HDL-C and elevated TG respond to high-intensity statin therapy, alternative approaches such as fibrates and omega-3-fatty acid drugs should also be considered. Icosapent, in particular, may be a useful adjunctive therapy in addition to high-intensity statins to lower TG levels and reduce risk of recurrent events.[20] In addition, the benefits of weight loss and physical activity,[1] which are recommended stroke prevention interventions in patients with symptomatic ICAD, may be mediated by their known effects on reducing TG levels.[21]

There are several limitations to this study. First, as an exploratory study of limited sample size, further prospective validation in larger cohorts is needed. Second, we did not mandate fasting lipid measurements though this is standard clinical practice in hospitalized stroke patients. Some participants may have also been referred by outside physicians or transferred from outside hospitals and, therefore, lipids done elsewhere may not be available for abstraction. Third, we did not require or systematically collect follow-up lipid measurements; thus, we are unable to assess whether change in lipid levels correlate with infarct recurrence. Fourth, we did not mandate high-intensity lipid lowering therapy but participating sites were asked to follow current practice guidelines which include high-intensity statin therapy after stroke or TIA due to ICAD. We also did not capture the type or dose of lipid-lowering therapy and cannot analyze drug or dose effects. Fifth, while predictors of subclinical recurrence, the focus of our study, and clinical recurrence are likely overlapping, there may be important differences. Finally, since we did not include vessel wall imaging MRI in MYRIAD, we are unable to correlate lipid levels with characteristics such as intra-plaque enhancement or hemorrhage.

CONCLUSIONS

Despite high level of adherence to standard anti-lipidemic medications, lipid levels at time of index stroke or TIA predicted early infarct recurrence in the territory of the stenotic artery in patients with symptomatic ICAD. More intensive and rapid lipid lowering drugs may be required to reduce risk of recurrence further.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Grant Support: MYRIAD is supported through a grant by the NIH/NINDS (R01 NS084288). The institutional review board/ethics committee at each participating institution approved this study, which is registered at ClinicalTrials.gov (NCT02121028).

CONFLICTS OF INTEREST

Dr. Prabhakaran reports grants from NIH during the conduct of the study; grants from AHRQ, personal fees from Abbvie, and personal fees from UpToDate outside the submitted work.

Dr. Liebeskind reports grants from NIH during the conduct of the study; other from Cerenovus, other from Genentech, other from Medtronic, and other from Stryker outside the submitted work.

Mr. Cotsonis reports grants from NIH during the conduct of the study.

Mr. Nizam reports grants from NIH during the conduct of the study.

Dr. Feldmann reports grants from NIH during the conduct of the study; and expert witness case reviews.

Dr. Sangha reports no conflicts of interest.

Ms. Campo-Bustillo reports grants from NIH during the conduct of the study.

Dr. Romano reports grants from NIH during the conduct of the study.

REFERENCES

1. Turan TN, Nizam A, Lynn MJ, Egan BM, Le NA, et al. Relationship between risk factor control and vascular events in the SAMMPRIS trial. Neurology. 2017;88(4):379–385. [PubMed: 28003500]
2. Ma YH, Leng XY, Dong Y, Xu W, Cao XP, et al. Risk factors for intracranial atherosclerosis: A systematic review and meta-analysis. Atherosclerosis. 2019;281:71–77. [PubMed: 30658194]
3. Chaturvedi S, Turan TN, Lynn MJ, Kasner SE, Romano J, et al. Risk factor status and vascular events in patients with symptomatic intracranial stenosis. Neurology. 2007;69(22):2063–2068. [PubMed: 18040012]
4. Romano JG, Prabhakaran S, Nizam A, Feldmann E, Sangha R, et al. Infarct recurrence in intracranial atherosclerosis: Results from the MyRIAD study. J Stroke Cerebrovasc Dis. 2020;30(2):105504. [PubMed: 33276302]
5. Prabhakaran S, Liebeskind DS, Cotsonis G, Nizam A, Feldmann E, et al. Predictors of Early Infarct Recurrence in Patients With Symptomatic Intracranial Atherosclerotic Disease. Stroke. 2021;52(6):1961–1966. [PubMed: 33866818]
6. Del Brutto VJ, Liebeskind DS, Romano JG, Campo-Bustillo I, Cotsonis G, et al. Risk Factors Control and Early Recurrent Cerebral Infarction in Patients with Symptomatic Intracranial Atherosclerotic Disease. J Stroke Cerebrovasc Dis. 2021;30(9):105914. [PubMed: 34217065]
7. Liebeskind DS, Prabhakaran S, Azhar N, Feldmann E, Campo-Bustillo I, et al. Mechanisms of early Recurrence in Intracranial Atherosclerotic Disease (MyRIAD): Rationale and design. J Stroke Cerebrovasc Dis. 2020;29(10):105051. [PubMed: 32912558]
8. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(7):2160–2236. [PubMed: 24788967]

9. Sangha RS, Prabhakaran S, Feldmann E, Honda T, Nizam A, et al. Imaging Patterns of Recurrent Infarction in the Mechanisms of Early Recurrence in Intracranial Atherosclerotic Disease (MyRIAD) Study. Front Neurol. 2020;11:615094. [PubMed: 33551972]
10. Azeem F, Durrani R, Zerna C, Smith EE. Silent brain infarctions and cognition decline: systematic review and meta-analysis. J Neurol. 2020;267(2):502–512. [PubMed: 31691021]
11. Wang X, Lin WH, Zhao YD, Chen XY, Leung TW, et al. The effectiveness of dual antiplatelet treatment in acute ischemic stroke patients with intracranial arterial stenosis: a subgroup analysis of CLAIR study. Int J Stroke. 2013;8(8):663–668. [PubMed: 22883712]
12. Markus HS, Droste DW, Kaps M, Larrue V, Lees KR, et al. Dual antiplatelet therapy with clopidogrel and aspirin in symptomatic carotid stenosis evaluated using doppler embolic signal detection: the Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial. Circulation. 2005;111(17):2233–2240. [PubMed: 15851601]
13. Chaturvedi S, Turan TN, Lynn MJ, Derdeyn CP, Fiorella D, et al. Do Patient Characteristics Explain the Differences in Outcome Between Medically Treated Patients in SAMMPRIS and WASID? Stroke. 2015;46(9):2562–2567. [PubMed: 26251251]
14. Amarenco P, Kim JS, Labreuche J, Charles H, Abtan J, et al. A Comparison of Two LDL Cholesterol Targets after Ischemic Stroke. N Engl J Med. 2020;382(1):9. [PubMed: 31738483]
15. Kim BS, Lim JS, Jeong JU, Mun JH, Kim SH. Regression of asymptomatic intracranial arterial stenosis by aggressive medical management with a lipid-lowering agent. J Cerebrovasc Endovasc Neurosurg. 2019;21(3):144–151. [PubMed: 31886149]
16. Miao H, Yang Y, Wang H, Huo L, Wang M, et al. Intensive Lipid-Lowering Therapy Ameliorates Asymptomatic Intracranial Atherosclerosis. Aging Dis. 2019;10(2):258–266. [PubMed: 31011477]
17. Koskinas KC, Windecker S, Pedrazzini G, Mueller C, Cook S, et al. Evolocumab for Early Reduction of LDL Cholesterol Levels in Patients With Acute Coronary Syndromes (EVOPACS). J Am Coll Cardiol. 2019;74(20):2452–2462. [PubMed: 31479722]
18. Sacco RL, Benson RT, Kargman DE, Boden-Albala B, Tuck C, et al. High-density lipoprotein cholesterol and ischemic stroke in the elderly: the Northern Manhattan Stroke Study. JAMA. 2001;285(21):2729–2735. [PubMed: 11386928]
19. Labreuche J, Touboul PJ, Amarenco P. Plasma triglyceride levels and risk of stroke and carotid atherosclerosis: a systematic review of the epidemiological studies. Atherosclerosis. 2009;203(2):331–345. [PubMed: 18954872]
20. Bhatt DL, Steg PG, Miller M, Brinton EA, Jacobson TA, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med. 2019;380(1):11–22. [PubMed: 30415628]
21. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73(24):3168–3209. [PubMed: 30423391]

Highlights

- Recurrent infarcts on brain magnetic resonance imaging are common 6–8 weeks after index presentation in patients with symptomatic intracranial stenosis despite relatively high adherence to aggressive medical management.
- Low-density lipoprotein and triglyceride levels at time of index stroke or transient ischemic attack predict recurrent infarcts independent of other clinical and imaging factors.
- More aggressive and rapid reduction of lipid levels may be required to reduce the burden of early clinical and subclinical recurrence in patients with symptomatic intracranial stenosis.

Table 1:

Sensitivity analysis of included versus excluded patients in this analysis from total MYRIAD participants (n=105)

	Included (n=74)	**Excluded (n=31)**	***P*-value**
Age in years, mean (SD)	64.2 (12.9)	62.8 (8.9)	0.585
Male, n (%)	45 (60.8)	15 (48.4)	0.241
White, n (%)	44 (59.5)	15 (48.4)	0.297
Hypertension, n (%)	65 (87.8)	25 (80.6)	0.337
Diabetes mellitus, n (%)	41 (55.4)	16 (51.6)	0.722
Hyperlipidemia, n (%)	50 (67.6)	21 (67.7)	0.986
Prior stroke, n (%)	14 (18.9)	8 (25.8)	0.429
Current smoking, n (%)	17 (23.0)	10 (32.3)	0.321
Optimal physical activity, n (%)	17 (23.0)	7 (22.6)	0.965
NIHSS score, median (IQR)	2 (0–3)	1 (0–4)	0.777
SBP at enrollment, mean (SD)	145.0 (18.0)	147.1 (24.6)	0.616
DBP at enrollment, mean (SD)	80.6 (13.1)	79.5 (11.8)	0.698

Table 2.

Bivariate analysis of clinical and imaging characteristics in those with and without infarct recurrence at 6–8 weeks (n=74)

	New infarct (n=20)	No new infarct (n=54)	*P*-value
Age in years, mean (SD)	58.3 (12.5)	66.4 (12.4)	0.015
Male, n (%)	13 (65.0)	32 (59.3)	0.653
White, n (%)	12 (60.0)	32 (59.3)	0.954
Hypertension, n (%)	20 (100.0)	45 (83.3)	0.102
Diabetes mellitus, n (%)	14 (70.0)	27 (50.0)	0.125
Hyperlipidemia, n (%)	12 (60.0)	38 (70.4)	0.397
Prior stroke, n (%)	2 (10.0)	12 (22.2)	0.233
Current smoking, n (%)	5 (25.0)	12 (22.2)	0.766
Optimal physical activity, n (%)	3 (15.0)	14 (25.9)	0.373
NIHSS score, median (IQR)	2 (0–4)	2 (0–3)	0.534
70–99% stenosis or flow gap, n (%)	19 (95.0)	43 (79.6)	0.162
Anterior circulation, n (%)	18 (90.0)	38 (70.4)	0.126
Borderzone infarct pattern, n (%)	7 (35.0)	4 (7.4)	0.007
Total cholesterol, mean (SD)	199.8 (56.1)	174.3 (49.0)	0.061
LDL-C, mean (SD)	124.3 (52.3)	101.2 (41.7)	0.053
HDL-C, mean (SD)	37.2 (10.1)	43.9 (12.6)	0.037
Triglyceride, median (IQR)	162.0 (113.5–251.5)	122.5 (91.3–181.0)	0.008
SBP at enrollment, mean (SD)	140.0 (16.5)	146.8 (18.4)	0.155
DBP at enrollment, mean (SD)	81.2 (12.2)	80.4 (13.5)	0.822

Table 3.

Multivariable logistic regression models of infarct recurrence at 6–8 weeks. Model 1 includes age, LDL-C, HDL-C, SBP, infarct pattern, stenosis location, and degree of stenosis. Model 2 includes same variables but replaces HDL-C with TG (not included together as they were collinear).

Model 1	**Adjusted Odds Ratio**	**95% CI**	***P*-value**
LDL-C, per 1 mg/dL	1.020	1.004–1.036	0.016
HDL-C, per 1 mg/dL	0.932	0.868–1.001	0.053
SBP at enrollment, per 1 mm Hg	0.948	0.905–0.994	0.027
Borderzone infarct pattern	3.773	0.689–20.667	0.126
Age, per 1 year	0.966	0.913–1.023	0.240
Anterior location	0.391	0.062–2.460	0.317
Severe stenosis	4.486	0.434–46.369	0.208
Hosmer-Lemeshow test: Chi-square=13.215, df=8, *P*=0.105			
Model 2	**Adjusted Odds Ratio**	**95% CI**	***P*-value**
LDL-C, per 1 mg/dL	1.022	1.004–1.040	0.015
TG, per 1 mg/dL	1.009	1.001–1.016	0.021
SBP at enrollment, per 1 mm Hg	0.935	0.884–0.989	0.020
Age, per 1 year	0.938	0.884–0.997	0.039
Borderzone infarct pattern	3.889	0.717–21.093	0.115
Anterior location	0.622	0.092–4.217	0.627
Severe stenosis	3.611	0.324–40.182	0.296
Hosmer-Lemeshow test: Chi-square=10.118, df=8, *P*=0.257			