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Microembolic Signals Detected by Transcranial Doppler Predict Future Stroke and Poor Outcomes

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Abstract

Background and Purpose—Although transcranial Doppler detects microembolic signals (MES) in numerous settings, the practical significance of such findings remains unclear.

Methods—Clinical information from ischemic stroke or transient ischemic attack patients (n = 248) who underwent embolic monitoring from January 2015 to December 2018 was obtained.

Results—MES were found in 15% of studies and ischemic recurrence was seen in 11% of patients (over 7 ± 6 days). Patients with MES had more lacunes than those without MES (1 ± 3 vs. 1 ± 2 , $p = 0.016$), were more likely to have ischemic recurrence (37% vs. 6%, $p < 0.001$), undergo a future revascularization procedure (26% vs. 10%, $p = 0.005$), have a longer length of stay (9 vs. 4 days, $p = 0.043$), and have worse functional disability at discharge (modified Rankin Scale 3–6, 66% vs. 34%, $p < 0.001$). After controlling for several relevant cofactors, patients with MES were more likely to have ischemic recurrence (HR 4.90, 95% CI 2.16–11.09, $p < 0.001$), worse functional disability (OR 3.31, 95% CI 1.22–8.99, $p = 0.019$), and longer length of stays ($\beta = 0.202$, $p < 0.001$).

Conclusions—MES may help to risk stratify patients as their presence is associated with ischemic recurrence and worse outcomes.

Keywords

neurosonology; transcranial Doppler sonography; cerebral emboli; stroke; recurrence

Introduction:

Transcranial Doppler (TCD) with embolic monitoring has been used in numerous cerebrovascular settings to detect microembolic signals (MES), which are presumed to represent platelet-fibrinogen embolic particles.¹⁻⁴ Previous studies have suggested that these MES may predict recurrent stroke in patients with ischemic stroke or transient ischemic attack (TIA).^{5,6} However, beyond predicting stroke recurrence, the clinical and prognostic significance of MES remains unclear. It is uncertain whether MES are clinically silent, producing asymptomatic infarcts or minor strokes, or whether MES impact clinical outcomes, leading to increased morbidity and mortality. This ambiguity has likely deterred the widespread use of embolic monitoring among clinicians such that the use of TCD is omitted from current ischemic stroke management guidelines.⁷

Although embolic monitoring studies are often obtained during the time of the ischemic stroke, MES can be detected in asymptomatic patients prior to the development of a stroke.⁴ The chronic impact of these emboli is unclear; however, we hypothesize that MES produce covert infarcts, often manifested on MRI as either lacunes or white matter hyperintensities (WMH).⁸ In the current study, we sought to identify associations between MES and clinical outcomes, including recurrent stroke/TIA, discharge disability, mortality, and length of stay. Furthermore, we also aimed to identify whether patients with MES have higher burdens of chronic infarcts and WMH than those without MES.

Methods:

The data that support the findings of this study are available upon reasonable request.

Patient Selection

From January 2015 to December 2018, consecutive TCD studies (ordered at the discretion of the attending neurologist) at our institution that were performed on patients admitted for ischemic stroke (including both anterior and posterior circulation) or TIA were included. All patients that were diagnosed as having a stroke required a confirmatory CT or MRI lesion. Patients with mechanical heart valves were excluded since MES in this population carry limited prognostic value and are likely to be artifactual.^{9,10} All outpatient TCD studies and studies used for indications other than ischemic stroke were also excluded. Approval for this study was granted by our hospital's institutional review board. Informed consent was waived for this study given its retrospective nature.

Clinical and Demographic Variables

Demographic information and medical history including vascular risk factors such as hypertension, hyperlipidemia, diabetes mellitus, any history of smoking (present or past), coronary artery disease, atrial fibrillation, and previously reported ischemic stroke or transient ischemic attack were obtained from patient charts. Pre-morbid modified Rankin Scale (mRS) score,¹¹ discharge mRS, admission National Institutes of Health stroke scale (NIHSS) scores, admission ABCD² scores (for TIA patients only),¹² hospital length of stay, acute stroke therapies (such as tissue plasminogen activator (tPA) or endovascular thrombectomy), and antithrombotic usage at the time of the TCD study were also recorded.

Stroke or TIA subtype was obtained from discharge reports and was based on TOAST classification schema¹³ although four specific categories were discriminated for practical purposes: dissection, vasculopathy (including both inflammatory causes such as primary/secondary cerebral vasculitis and non-inflammatory causes such as moyamoya disease), hypercoagulability, and cryptogenic.

Carotid stenosis was graded using NASCET criteria¹⁴ and divided according to four categories as described elsewhere: mild (0% to 29%), moderate (30% to 69%), severe (70% to 99%), and complete occlusion.¹⁵ If more than one modality was performed, CT angiography (CTA) was used preferentially over MR angiography (MRA), and carotid ultrasound was used when no other modality was performed. CTA was the most commonly used modality to grade stenosis and was available in 64% of patients. Significant stenosis was defined as any stenosis greater than moderate stenosis (> 69%).

Clinical End Points

Ischemic event recurrence was defined as either a new sudden focal neurological deficit of vascular origin, worsening of the initial neurological deficit,⁶ or radiographic worsening/progression (silent stroke included) that occurred within the hospitalization.⁶

Surgical or endovascular procedures including carotid endarterectomy (CEA), carotid stenting, carotid angioplasty, or carotid bypass were also noted. Length of stay was defined as the time from admission to discharge from the neurology service. If a patient was transferred to another service, e.g. for CEA, the duration of that stay was not included in the length of stay (described previously).⁶

Neuroimaging Analysis

To test the hypothesis that MES result in the accumulation of WMH and lacunes (defined elsewhere¹⁶⁻²⁰), brain CT or MRI scans were analyzed by an experienced grader (ASD) blinded to MES data. Fazekas score was used to grade WMH severity.²¹ To evaluate whether asymmetric MES resulted in asymmetric accumulation of WMH, each brain hemisphere was graded separately. A score (0–3) was provided for both deep and periventricular WMH,²¹ and the highest score was selected as the total Fazekas score for the hemisphere. If the difference in Fazekas score between hemispheres was ≥ 1 , the patient was classified as having WMH asymmetry. The highest score between the left and right hemispheres was taken as the total WMH grade for the patient. The number of lacunes in each hemisphere as well as the sum total lacunes in the entire brain were recorded. A difference of ≥ 1 lacune between each hemisphere was considered as having asymmetric lacunes. Diffusion-weighted imaging (DWI) sequences were reviewed to classify the infarct pattern according to an established classification scheme.²²

TCD Studies

TCD studies were performed by experienced technologists (SL or ADM) anytime during the patient's hospitalization at the discretion of the treating physician. If multiple TCD studies were performed to track the progression of MES, only the first study was included in the analysis (as performed previously).²³ Embolic signals were recorded from a single TCD

machine with bilateral 2-MHz monitoring probes calibrated with standardized settings (Doppler Box X, Compumedics DWL, San Juan Capistrano, CA) and equipped with software for emboli detection (QL Monitoring Software, Compumedics, Germany). The filter was set at 150 Hz and the detection threshold was set at 9 dB. Vessels were measured distal to any focal stenoses and all recordings were attempted for 60 minutes (as per guidelines^{24,25}), unless the study was terminated prematurely because of patient-specific reasons (in 17% of cases). At the onset of each study, the probes were positioned adjacent to the temporal bone windows and immobilized using a probe fixation head frame (Marc 500, Spencer Technologies, Seattle, WA). The middle cerebral artery (MCA) was insonated at depths of 50 mm to 65 mm, the anterior cerebral artery (ACA) was insonated at depths of 60 mm to 80 mm, and the posterior cerebral artery was insonated at depths of 55 mm to 75 mm. The arteries that were monitored were chosen based on the infarct location or presumed TIA localization. Gains were kept low enough for visual observation of MES. The following definitions for MES were used: typical visible and audible signal confirmed by technologist (click, chirp, whistle), unidirectional from the baseline, short-duration (around 25 to 100 milliseconds), high intensity signal within the Doppler flow spectrum with its occurrence at random in the cardiac cycle, and an intensity increase of at least 9 dB above the background signal as reported previously.^{23,24} MES at a rate 1/hr were interpreted as positive study. TCD studies were reviewed by neurologists with training in neurosonology.

Statistical Analysis

Mean and standard deviation were reported for continuous variables, median and interquartile range were reported for ordinal variables, and percent and counts were reported for categorical variables. Baseline characteristics were assessed using student t tests, χ^2 tests, and Mann-Whitney U tests where appropriate. Univariate analyses were performed to explore all potential associations between relevant covariates and outcome measures. Variables included age, sex, vascular risk factors, atrial fibrillation, previous stroke or TIA, acute stroke therapies, antithrombotic therapies, carotid stenosis, presence of MES, lacunes, total Fazekas score, ischemic recurrence, or procedure type. Variables with $p < 0.10$ were entered into a multivariable logistic regression model along with discharge disability. Discharge mRS was dichotomized into favorable (mRS 0–2) or unfavorable (mRS 3–6).²⁶ A Cox proportional hazard regression model was used to determine the association of MES on ischemic recurrence. This model included the following *a priori* variables hypothesized to be related to the stroke recurrence: age, sex, vascular risk factors, presence of carotid stenosis, acute stroke therapies, admission NIHSS, and antithrombotic therapies at the time of study. Lastly, a multivariable linear regression model was constructed using length of stay as the dependent variable and included the following related *a priori* variables: age, sex, previous stroke/TIA, baseline mRS, admission NIHSS, acute stroke therapies, and recurrence. Two-tailed p values < 0.05 and 95% confidence interval (CI) that did not include unity were interpreted as statistically significant. All analyses were performed with SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA).

Results:

832 consecutive TCD studies were performed between January 2015 and December 2018. The following studies were excluded: 330 performed for indications other than stroke, 200 outpatient studies, and 54 repeat studies on the same patient. A total of 248 studies (478 arteries) were ultimately included. At least one vessel per hemisphere was insonated in 89% of cases (Table 1), and only one patient had ACAs insonated.

15% of patients had MES, with a mean of 6 ± 10 MES/hr. MES were detected at 14.4 ± 3.1 dB. Vasculopathy was strongly associated with the development of MES ($p < 0.001$) (Table 1). A stroke was found on the side of MES in 97% of patients. 18% of patients with MES had bilateral strokes despite only having unilateral MES, and 16% had a unilateral stroke despite having bilateral MES. There were no differences in stroke subtype between unilateral vs. bilateral MES (data not shown); however, there was a trend toward an increased proportion of cardioembolic strokes in patients with bilateral MES compared to unilateral MES (33% vs. 10%; $p = 0.098$). Recurrent stroke was seen in 10.9% of patients (monitored over 6.5 ± 5.8 days). In a univariate analysis, the number of MES was associated with recurrence (OR 1.128, 95% CI 1.13–1.24; $p = 0.011$).

Patients with MES were more likely to have recurrent stroke (37% vs. 6%, $p < 0.001$), undergo a carotid revascularization procedure (26% vs. 10%, $p = 0.005$), have a longer length of stay (9 vs. 4 days, $p = 0.043$), and have a discharge mRS 3–6 (66% vs. 34%, $p < 0.001$) compared to those without MES in univariate analyses (Table 2). Patients with MES were confirmed more likely to have recurrent stroke (HR 4.895, 95% CI 2.16–11.09; $p < 0.001$) in a multivariate model controlling for potential confounders. The event rate of those without MES was 1.16 per 100 patient-days and for those with MES was 5.09 per 100 patient-days (Figure 1). In multivariate analyses, MES were independently associated with discharge mRS 3–6 (OR 3.312, 95% CI 1.220–8.993, $p = 0.019$) (Table 3, Figure 2) and were also independently associated with length of stay (Table 4). The presence of MES increased the length of stay by approximately 3 days ($p = 0.001$).

In the imaging analysis, multiple lesions confined to either the bilateral anterior or posterior circulation were associated with MES ($p = 0.011$). There were no differences in the severity of WMH in patients with MES or without MES (Fazekas grade 2 vs. Fazekas grade 1, $p = 0.625$). Furthermore, there were no differences in WMH asymmetry in patients with asymmetric MES vs. those with symmetric or no MES (22% vs 12%, $p = 0.108$). However, patients with MES were observed to have more lacunes than those without MES (1.2 ± 2.7 vs. 0.7 ± 1.8 , $p = 0.016$). There was a trend toward an increased number of lacunes in patients with MES in a multivariable model controlling for age and other vascular risk factors ($\beta = 0.119$, $p = 0.054$).

Discussion:

The present study shows that MES are associated with stroke recurrence, unfavorable discharge disability, and increased length of stay. While previous studies have reported an elevated risk of future stroke in patients with carotid stenosis or MCA stenosis who have

MES detected by TCD,²⁷⁻³¹ in our study incorporating all stroke subtypes, we observed a strong association between MES and ischemic recurrence. While several earlier studies excluded patients with cardioembolic sources of stroke,^{5,6,15} this study detected MES in all stroke subtypes with the exception of small vessel disease (according to TOAST criteria), which is concordant with previous reports.³² The recurrence rate in our study was 11%, identical to the recurrence rate of a symptomatic carotid stenosis study which monitored patients for 10 ± 8 days.⁶ Although our monitoring time for recurrence was shorter, our recurrence rate was also similar to the recurrence rate of 12% in a study of patients with MCA stenosis (which monitored patients for an average of 13.6 months).⁵ In that study, the majority (58%) of recurrent events occurred within the first month after the index stroke.

Our study demonstrates that MES are an independent predictor of worsened clinical outcomes such as poor discharge disability and increased hospital length of stay in a cohort of patients comprised of all stroke subtypes. These findings are similar to a previous study of patients with large artery anterior circulation occlusions, in which the presence of MES after endovascular thrombectomy was associated with worse functional outcome and increased mortality.³³ However, these findings have not been reproduced in other studies. In a study of anterior circulation ischemic stroke patients, MES did not predict neurological outcome at 3 months after stroke.³⁴ Furthermore, in a recent study of prospective enrolled patients with anterior circulation stroke, the presence of MES was not associated with favorable outcomes (mRS < 3) at 6 months or mortality.³⁵ These studies, however, recruited a small number of patients and may have been underpowered to detect any significant differences in clinical outcomes. In our study, despite controlling for ischemic recurrence in our multivariate model, MES independently correlated with poor discharge outcome. Therefore, MES portend increased disability through mechanisms beyond additional stroke burden. Consistent with this notion, in a study of early ischemic recurrence after finding MES, 6 out of 8 patients achieved a full recovery of their deficits after a recurrent ischemic event.⁶

Our study reported a lower prevalence and frequency of MES compared to other studies.^{5,6,15} Reasons for this include using a less enriched population of patients with probable MES, since we included all ischemic stroke patients including patients with small vessel disease. Furthermore, although performed in the majority of cases, we did not monitor patients immediately after their index event in all cases. Previous studies have demonstrated an inverse correlation between MES/hour and the time elapsed after stroke symptoms,³⁶ although this has not been replicated universally.³⁷ We also used a criteria of 9.0 dB in our study, one of the highest thresholds of the recommended threshold ranges,²⁴ whereas other studies that reported a higher rate of MES and used a lower threshold may have captured an increased number of smaller particles.^{5,6} In addition, in our study, 56% of the patients without MES were on either dual antiplatelet therapy or anticoagulation at the time of the study. This may have potentially reduced the prevalence of MES (as well as recurrent stroke⁶) in our population as suggested elsewhere.^{15,38-41} Although we did not assess statin pretreatment or statin dosage, statins also appear to have a dose-dependent reduction in the presence and burden of MES.⁴² In the present study, 16 out of 17 patients that had escalation of antithrombotic therapy (either the addition of a second antiplatelet agent or addition/switch to anticoagulation) in response to MES had a decreased number of MES on repeat

studies (data not shown). Lastly, MES may be affected by the time of day a study occurs; this factor is difficult to control for, even prospectively.²⁵

Interestingly, 62% of patients with vasculopathy had MES, a finding that is consistent with a recent report of positive MES in 23% of moyamoya disease patients.⁴³ Similar to previous studies showing that multiple infarcts are more common than single infarcts,^{44,45} our analysis also demonstrated that multiple punctate lesions confined to the anterior circulation or posterior circulation were associated with MES. MES were not associated with WMH severity or asymmetry using the Fazekas scale, which is a crude estimate of WMH burden. Perhaps quantitative volumetric WMH analysis may be more accurate in detecting any subtle differences attributable to MES. However, there was a trend toward more lacunes, which are readily detected on CT or MRI, in patients with MES. Although small vessel disease strokes were not associated with MES, as suggested elsewhere, this may be due to sampling error.³² Furthermore, it is conceivable that patients with positive MES were unlikely to be diagnosed as having small vessel strokes by the treating neurologist. Patients with lacunar strokes were seldom monitored using TCD because of the *a priori* assumption that lacunar stroke is rarely embolic in nature. However, lacunar stroke is due to heterogenous causes including embolism (not captured by TOAST),^{17,18,20} and the current study showing that MES is associated with lacunes serves as proof-of-concept. Given that lacunes contribute to vascular cognitive impairment, it is likely that patients with MES are at increased risk of cognitive dysfunction as has been suggested in the setting of cardiac surgery.⁴⁶

This study had some limitations, largely driven by its retrospective design. There may be a component of selection bias given that TCD studies were performed at the discretion of the treating physician. It is likely that patients with a high-pretest probability of ischemic stroke were selected to undergo monitoring, since it is not performed indiscriminately among patients at our institution. This may have also contributed to the finding of an increased length of stay, such that patients with MES were monitored for a longer duration. Furthermore, since our study focused on ischemic recurrence limited to the patient's hospitalization, we may have not captured patients who were discharged from our facility but presented to another facility with another stroke. MRI was not available for all of the studies (94%) or performed for every stroke/TIA recurrence, which may have affected the results of our study in a minor way. Our study used the TOAST classification¹³ although the use of a newer classification system, such as ASCOD, may have been more accurate as it allows for multiple contributing stroke etiologies instead of only one causative factor.⁴⁷ Incorporating heterogenous strokes types allows for the possibility that several additional factors that are difficult to account for may contribute to morbidity outcomes. However, it should be emphasized that our broad enrollment criteria closely mimic real-world embolic monitoring. Lastly, several different imaging modalities were used to measure the degree of carotid stenosis, which may have introduced some inequality into our assessments.

In a cohort of ischemic stroke/TIA patients who underwent embolic monitoring with TCD, MES predicted ischemic recurrence, worsened disability, and prolonged hospital stays. MES may also contribute to asymptomatic stroke and cerebral small vessel disease burden. Given

that MES can provide important prognostic information, TCD with embolic monitoring may be clinically useful in the workup of ischemic stroke or TIA.

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Figure 1:

This figure demonstrates the ischemic recurrence-free probability stratified by the presence of microembolic signals (MES). Patients with MES had an increased recurrence-free probability compared to those without MES ($p < 0.0001$).

Figure 2:

This figure depicts the breakdown of modified Rankin Scale (mRS) scores of patients without microembolic signals (MES –) and patients with MES (MES +). Scores increase from left to right (ranging from 0 to 6), and the numbers within each box represent the percentage of patients with that particular mRS score.

Table 1.

Baseline Characteristics of Patients With and Without Microembolic Signals.

	MES Negative (n = 210)	MES Positive (n = 38)	p Value
Age (years), mean $\pm$ SD	63 ($\pm$ 16)	60 ($\pm$ 15)	0.849
Male sex	136 (65)	20 (53)	0.154
Hypertension	138 (66)	19 (50)	0.064
Hyperlipidemia	129 (61)	20 (53)	0.308
Diabetes	48 (23)	8 (21)	0.807
Coronary artery disease	48 (23)	11 (29)	0.417
Atrial fibrillation	35 (17)	5 (13)	0.588
Previous ischemic event	48 (23)	10 (26)	0.643
Smoking	97 (46)	15 (39)	0.444
Baseline mRS, median (IQR)	1 (1, 2)	0 (0,1)	0.364
Admission NIHSS, median (IQR)	3 (2, 5)	4 (3, 10)	0.468
ABCD ² scores, ¹² median (IQR)	5 (1, 5)	5 (4, 5)	0.389
tPA received	38 (18)	4 (11)	0.252
Endovascular therapy	26 (12)	3 (8)	0.428
Transient ischemic attack	10 (5)	3 (8)	0.425
Significant carotid stenosis	73 (35)	15 (40)	0.576
Time to study (days), mean $\pm$ SD	2 ($\pm$ 2)	1 ($\pm$ 2)	0.473
Anticoagulation at time of study	70 (33)	15 (39)	0.463
Antiplatelet at time of study	156 (74)	24 (63)	0.157
Study duration (minutes), median (IQR)	60 (60, 60)	60 (60, 60)	0.952
Insonated vessels			
Right MCA	192 (91)	34 (90)	0.697
Left MCA	190 (91)	36 (95)	0.395
Right PCA	9 (4)	4 (11)	0.112
Left PCA	8 (4)	3 (8)	0.260
Etiologies			
Large artery atherosclerosis	89 (42)	15 (39)	0.783
Cardioembolic	58 (28)	6 (16)	0.125
Small vessel disease	9 (4)	0 (0)	0.194
Dissection	17 (8)	1 (3)	0.232
Cryptogenic	16 (8)	2 (5)	0.606
Vasculopathy	5 (2)	8 (21)	< 0.001
Hypercoagulability	16 (8)	5 (13)	0.259
Other (fat embolism)	0 (0)	1 (3)	0.018
Affected Territories			
MCA	168 (80)	31 (82)	0.822
PCA	5 (2)	1 (3)	0.926
ACA	2 (1)	0 (0)	0.546
Basilar	5 (2)	0 (0)	0.337

	MES Negative (n = 210)	MES Positive (n = 38)	<i>p</i> Value
PICA	5 (2)	0 (0)	0.337
SCA	1 (0)	0 (0)	0.670
Anterior choroidal	1 (0)	0 (0)	0.670
Retinal	7 (3)	1 (3)	0.822
Multiple territories	16 (8)	5 (13)	0.259

Data are counts (*n*) and percentages (%), means and standard deviations (SD), or medians and interquartile ranges (IQR). NIHSS: National Institutes of Health stroke scale; MCA: middle cerebral artery; SCA: superior cerebellar artery; PICA: posterior inferior cerebellar artery; ACA: anterior cerebral artery; PCA: posterior cerebral artery

Table 2.

Outcomes of Patients With and Without Embolic Signals.

	MES Negative (n = 210)	MES Positive (n = 38)	p Value
Infarct Patterns			
Single lesions			
Corticocortical	20 (10)	3 (8)	0.750
Cortical	36 (17)	4 (11)	0.308
Subcortical 15 mm	11 (5)	1 (3)	0.491
Subcortical < 15 mm	17 (8)	2 (5)	0.546
Small scattered lesions in one vascular territory	46 (22)	9 (24)	0.808
Multiple lesions in multiple territories			
Confluent with additional lesions in one vascular territory	38 (18)	5 (13)	0.459
Unilateral anterior circulation	1 (0)	1 (3)	0.172
Unilateral posterior circulation	1 (0)	0 (0)	0.670
Bilateral anterior circulation	8 (4)	4 (11)	0.076
Bilateral posterior circulation	5 (2)	3 (8)	0.077
Unilateral anterior and posterior circulation	4 (2)	0 (0)	0.391
Bilateral anterior and posterior circulation	7 (3)	2 (5)	0.558
Confined to either bilateral anterior or posterior circulation	13 (6)	7 (18)	0.011
Neuroimaging Markers			
Presence of white matter hyperintensities	153 (73)	28 (74)	0.916
Fazekas score, median (IQR)	1 (1, 2)	2 (2, 3)	0.625
White matter hyperintensity asymmetry	26 (12)	8 (21)	0.153
Lacunes, mean $\pm$ SD	1 ($\pm$ 2)	1 ($\pm$ 3)	0.016
Presence of lacunes	62 (30)	13 (34)	0.563
Lacune asymmetry	54 (26)	10 (26)	0.938
Clinical Outcomes			
Ischemic recurrence	13 (6)	14 (37)	< 0.001
Procedure received	21 (10)	10 (26)	0.005
Carotid procedure type			
Endarterectomy	16 (8)	4 (11)	0.545
Stenting	4 (2)	3 (8)	0.040
Bypass	1 (0)	2 (5)	0.013
Angioplasty	0 (0)	1 (3)	0.018
Poor discharge outcome (mRS 3)	71 (34)	25 (66)	< 0.001
In-hospital fatality	7 (3)	3 (8)	0.188
Length of stay, mean $\pm$ SD	6 ($\pm$ 5)	10 ($\pm$ 6)	0.043

Data are counts (n) and percentages (%), means and standard deviations (SD), or medians and interquartile ranges (IQR). mRS: modified Rankin score; MES: microembolic signals

Table 3.

Associations with discharge disability

	Univariate		Multivariate	
	OR (95% CI)	<i>p</i> Value	OR (95% CI)	<i>p</i> Value
MES positive	3.765 (1.817–7.802)	<0.001	3.312 (1.220–8.993)	0.019
Admission NIHSS	1.201 (1.138–1.267)	<0.001	1.181 (1.096–1.273)	<0.001
Baseline mRS	1.836 (1.345–2.505)	<0.001	2.341 (1.528–3.584)	<0.001
Carotid stenosis	1.792 (1.053–3.049)	0.031	1.796 (0.882–3.658)	0.107
Endovascular therapy	0.285 (0.126–0.644)	0.002	0.993 (0.270–3.218)	0.913
Ischemic recurrence	3.667 (1.573–8.548)	0.002	1.316 (0.394–4.398)	0.656
Length of stay	1.391 (1.259–1.536)	<0.001	1.242 (1.116–1.382)	<0.001

MES: microembolic signals; NIHSS: National Institutes of Health stroke scale; OR: odds ratio; CI: confidence interval; mRS: modified Rankin score

Table 4.

Associations with length of stay

	Coefficient (SE)	β	<i>p</i> Value
<i>MES present</i>	3.254 (0.958)	0.202	0.001
<i>Age</i>	−0.002 (0.021)	−0.005	0.937
<i>Sex</i>	0.193 (0.684)	0.016	0.283
<i>Previous ischemic event</i>	0.750 (0.802)	0.055	0.351
<i>Baseline mRS</i>	0.041 (0.402)	0.006	0.919
<i>Admission NIHSS</i>	0.447 (0.063)	0.488	<0.001
<i>tPA received</i>	−0.141 (0.934)	−0.009	0.881
<i>Endovascular therapy</i>	−2.840 (1.243)	−0.157	0.023
<i>Ischemic recurrence</i>	3.196 (1.099)	0.171	0.004

Microembolic signals (MES) were associated with an increased hospital length of stay. The regression model above represents a good fit of the data such that the independent variables included in this model significantly predict length of stay, $F(9, 238) = 10.561$, $p < 0.0001$, $R^2 = .258$. mRS: modified Rankin scale; NIHSS: National Institutes of Health stroke scale; tPA: tissue plasminogen activator; SE: standard error