Utility of Transesophageal Echocardiography in the Identification and Treatment of Occult Mechanisms of Cerebral Infarction

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Abstract

Purpose

To evaluate the diagnostic utility of TEE in identifying cardiac sources of embolism (CSE) in cryptogenic stroke patients and to determine whether the identification of these CSE results in clinically significant management changes.

Methods

A prospective registry of consecutively admitted patients with acute ischemic stroke (1/1/2015-8/10/2020) was retrospectively queried. Patients 18 to 60 years of age with stroke due to mechanisms other than large or small vessel disease, or atrial fibrillation were eligible for inclusion. The primary outcome was any high-risk CSE identified on TEE following unrevealing TTE. Secondary outcomes included a composite of individual CSEs and subsequent management changes.

Results

Of the 2,404 consecutive stroke patients evaluated during the study period, 263 (11%) met inclusion criteria; 103 (39%) were women and the median age was 53 (IQR 46-57). TEE was performed in 108 patients (41%). A high-risk CSE was identified in 36 patients (33%), the majority of which were PFOs (n=29). TEE led to a clinical management change in 14 patients (39%) after identification of a high-risk CSE; 6 underwent PFO closure and 8 had adjustment to their antithrombotic therapy.

Conclusion

In our single-center study of cryptogenic stroke patients, the addition of TEE to the comprehensive stroke evaluation led to the identification of a high-risk CSE in one in three patients resulting in significant management changes. Most high-risk CSEs were PFOs, which likely underestimates the likelihood of management change given the publication of successful PFO closure trials in the middle of our study period.

Background

Cryptogenic stroke comprises approximately 25% of all patients with ischemic stroke [1], with an annualized risk of recurrence between 5–7% [2, 3]. Although the clinical construct of embolic stroke of undetermined source (ESUS) was introduced in 2014 to better define this population of stroke patients (1), the heterogeneity of the condition likely explains why a single targeted treatment is no more advantageous than aspirin and risk-factor modification [2, 3].

Following a standard ischemic stroke evaluation for large artery atherosclerotic disease, small vessel disease, and cardioembolism with an electrocardiogram (ECG), 24-hour cardiac rhythm monitoring, a transthoracic echocardiogram (TTE), and CT or MR angiography [4], a substantial proportion of patients

have no identifiable source of cerebral embolism. The best available evidence suggests that the most common occult mechanisms of ESUS include non-stenotic atherosclerotic disease in 20–30% of patients [5], paroxysmal atrial fibrillation in 10–20% of patients [6], suspected atrial cardiopathy without atrial fibrillation (AF) or atrial flutter [7], occult thrombophilia, and other mechanisms. Among these less common etiologies of ESUS, patent foramen ovale (PFO), valvular disease, aortic arch atheroma, and intracardiac thrombus are better visualized using transesophageal echocardiography (TEE) when compared to transthoracic echocardiography (TTE) [8]. Awareness of each of these sources of embolism has the potential to influence clinical management–with unique treatment recommendations–which can reduce the risk of subsequent cerebrovascular events. Additionally, recognition of these occult sources of cardiac embolism can provide clarity to patients regarding their stroke mechanism and risk of recurrence, as well as deter unnecessary additional testing for other stroke etiologies.

In the present investigation, we sought to confirm the increased diagnostic yield of TEE in patients with cryptogenic stroke, describe relevant echocardiographic findings, and to determine whether TEE, in addition to routine TTE, is associated with changes in clinical management.

Methods

Study Design and Participants

We retrospectively queried a prospectively maintained registry of consecutively admitted patients with acute ischemic stroke 18 to 60 years of age at Cooper University Hospital (CUH) from January 1, 2015 to August 10, 2020 and supplemented these data with review of electronic medical records and imaging studies. Patients were excluded from the analysis if they opted to receive comfort care during the index hospitalization. Stroke etiology was classified according to the modified Trial of Org 10172 Acute Stroke Trial criteria [9] and patients with strokes due to large or small vessel disease, or AF were excluded from the study. For the purposes of this investigation, patients with PFO, aortic arch atheroma > 4mm or ulcerated plaque, aortic arch thrombus, or left atrial enlargement of any severity were classified as having a cryptogenic infarction. Patients with paroxysmal AF identified on subsequent outpatient telemetry were classified as having a cryptogenic infarction during their index hospitalization. Patients with multiple possible etiologies of stroke were included if a non-AF cardioembolic source (e.g., severe systolic dysfunction with ejection fraction < 40%, left ventricular thrombus, endocarditis) were identified. To optimize sensitivity of capturing relevant TEE findings, and because TEE findings could have contributed to a classification of stroke mechanism as cardioembolic, patients with non-AF CSE and cryptogenic stroke were consolidated into a single patient group for all analyses. Furthermore, the designation of stroke mechanism as cryptogenic or cardioembolic in patients with severe systolic dysfunction, PFO, or other intracardiac pathologies or variants remains controversial [10–12]; therefore, suspected non-AF CSE and cryptogenic patients were consolidated. (Subgroup analyses of findings based on non-AF CSE and cryptogenic stroke are also presented for the sake of transparency.) At our center, each TEE is first interpreted by a senior cardiology fellow using standard TEE windows, and then confirmed by a board-certified cardiologist. The use of agitated saline or Definity® contrast was made at the discretion of the

cardiology attending. Abnormalities including PFO (identified by color flow doppler, visual examination, and/or agitated saline injection in the bicaval view), left atrial appendage thrombus or spontaneous echo contrast, mobile or aneurysmal interatrial septum, grade IV or greater atheroma of the aortic arch, valvular pathology including stenosis, regurgitation or vegetation, visible thrombus, and ejection fraction (measured in the transgastric short axis view) were identified. Echocardiographic findings were abstracted from the medical record, confirmed by the secondary read (EC), and then included in the study analysis. At our center, transcranial doppler with agitated saline is not routinely performed to evaluate for PFO as it cannot identify other CSE such as valvular disease, intracardiac thrombus, aortic arch plaque, or other pathologies. Acute ischemic stroke was diagnosed clinically by a vascular neurologist or if there was radiographic evidence of acute infarction on unenhanced computed tomography (CT) or diffusion-weighted imaging magnetic resonance imaging (DWI-MRI). Infarctions were categorized as cortical, subcortical/infratentorial, and/or involving multiple vascular distributions based on CT and/or MRI findings. Subcortical/infratentorial infarctions were documented if their maximal diameter exceeded 1.5cm or if there were multiple, and therefore could not be categorized as lacunar infarcts.

Data Collection

The baseline demographics, comorbidities, National Institutes of Health Stroke Scale (NIHSS) scores, imaging characteristics, high-risk cardiac sources of embolism (CSEs) on TEE, cardiac event monitoring data, and clinical management changes were captured among included patients. High-risk CSEs were defined as cardiac abnormalities or variants that have been previously associated with stroke etiology in otherwise cryptogenic stroke and included PFO, atrial septal aneurysm (ASA), aortic arch atheroma > 4mm and/or ulceration [13], valvular lesion(s), intracardiac tumors, and intracardiac thrombus. Excess atrial mobility (5-10mm atrial excursion) was also captured, but was not considered a singular high-risk CSE unless it occurred in conjunction with a PFO. Subsequent cerebrovascular events were also evaluated, including recurrent ischemic stroke, hemorrhagic stroke, or death. Cardiac event monitoring data were obtained from Holter monitor and implantable loop recorder (ILR) interrogation reports.

Statistical Analysis

Descriptive statistics were used to summarize continuous and categorical variables. Continuous variables were reported as medians with interquartile range or means with standard deviation. Chi-squared test was used for between-group comparisons for categorical data, or Fisher's exact test when the contingency table cell counts were less than five. The Wilcoxon Rank-Sum test was used for between-group comparisons of continuous variables. The primary outcome was any high risk CSE identified on TEE but not TTE. Secondary outcomes included a composite of non-PFO CSE and each individual source of cardiac embolism on TEE, as well as specific management changes at any time point following TEE and only attributed to TEE findings (or lack of findings). Prespecified management changes included PFO closure, escalation to dual antithrombotic therapy, or use of therapeutic anticoagulation. Logistic regression was used to estimate the association between clinical and radiographic findings with the presence of a high-risk CSE, with adjustment for all variables significant to p</=0.1. Logistic regression was also used to estimate the odds of being recommended for a TEE versus not, with adjustment for all

variables significant to $p \leq 0.1$. Time to management change in patients with CSE on TEE was evaluated using Kaplan-Meier survival curves, with comparisons made between PFO and non-PFO CSE using a log-rank test of equality. No adjustments were made due to low event rates.

All tests were performed at the two-sided level with an alpha of 0.05, using STATA v15.0 (College Station, TX). Missing data were minimal and not imputed. All analyses were considered exploratory, therefore no adjustments were made for multiple comparisons. P-values were provided for convenience and should be interpreted with caution. This study was approved by the local institutional review board.

Results

Of the 2,404 consecutive adult patients with acute ischemic stroke evaluated during the study period, 263 met inclusion criteria (Fig. 1, Table 1) and were followed for a median of 12.8 months (IQR 3.5–28.9 months) after admission for stroke. Among included patients, 133 (51%) were ordered for a TEE due to concern for an occult CSE. Generally, younger patients and patients with fewer vascular risk factors were recommended for a TEE (Supplementary Table 1). After adjustment for all predictors of TEE being ordered ($p \leq 0.1$), only younger age (aOR 0.96 per year, 95%CI 0.93–0.99, p = 0.010) and stroke affecting multiple vascular territories (aOR 1.84, 95%CI 1.01–3.36, p = 0.046) were independently associated with a TEE order.

Table 1
Demographic Data.

	All included patients (n = 263)
Age, median (IQR)	53 (46–57)
Female sex, no. (%)	103 (39)
Race, no. (%)	
White	123/227 (55)
Black	83/227 (37)
Asian	6/227 (3)
Other	14/227 (6)
Hispanic, no. (%)	43/239 (18)
Primary insurance provider, no. (%)	
None	34/261 (13)
Medicaid	91/261 (35)
Medicare	45/261 (17)
Private/Other	91/261 (35)
Medical history, no. (%)	
Hypertension	182 (69)
Tobacco use	94/260 (36)
Diabetes mellitus	99 (38)
Dyslipidemia	102 (39)
Coronary artery disease	34 (13)
Congestive heart failure	19 (7)
Prior stroke	49 (19)
Peripheral artery disease	5 (2)
Baseline NIHSS, median (IQR)	5 (2–10)
LVO, no. (%)	36 (14)
Ejection fraction, median % (IQR)	55 (55–60)
Ejection fraction < 40%, no. (%)	26 (10)

	All included patients (n = 263)
HCT or MRI findings, no. (%)	
Cortical infarction	167 (64)
Infratentorial infarction	94 (36)
Infarction in > 1 vascular territory	63 (24)

TEE findings

A TEE was ultimately performed in 108 patients (81% of those with orders), the majority of which were performed during the hospitalization for stroke (Table 2). A high-risk CSE was identified in 36 patients (33%), the majority of which were PFOs (n = 29; Table 2). All patients with an ASA had an associated PFO, while 2 of 5 patients with excess atrial mobility had an associated PFO. Four patients had high-risk valvular lesions (all involving the aortic valve), including 1 patient with marantic endocarditis (Fig. 2), 1 patient with a degenerated/ruptured leaflet, 1 with heavy calcification, and 1 with significant Lambl's excrescence. Three patients had aortic arch plaque > 4mm in thickness with or without ulceration, and 1 patient had a left atrial appendage thrombus (without AF). One-hundred eight patients (41%) underwent outpatient cardiac event monitoring, 56 of whom had also undergone TEE. Abnormalities on outpatient event monitoring were captured in 11 patients (8 with AF, 1 sinus bradycardia, 1 atrial bigeminy, 1 2nd degree AV block). Of the 8 patients who were found to have paroxysmal atrial fibrillation, only 1 had a CSE on TEE, which was a PFO. Detailed results for event monitoring and left atrial morphology are being reported separately.

Table 2
TEE data and findings.

	All included patients (n = 263)
TEE ordered, no. (%)	133 (51)
TEE performed, no. (%)	108/133 (81)
TEE performed during hospitalization, no. (%)	105/123 (86)
TEE performed after discharge	3/10 (30)
Time from admission to TEE, median days (IQR)	
All patients	3 (2–5) (n = 108)
Inpatient TEEs	3 (2–5) (n = 105)
Outpatient TEEs	12 (12–125) (n = 3)
High-risk CSE on TEE*, no. (%)	36/108 (33)
PFO	29/108 (27)
ASA	5/108 (5)
PFO + ASA	5/108 (5)
Intracardiac thrombus	1/108 (1)
Valvular abnormality*	4/108 (4)
Intracardiac tumor	0/108 (0)
Aortic arch plaque > 4mm and/or ulcerated	3/108 (3)
ROPE score, median (IQR)	5 (4–6) (n = 108)

Predictors of high-risk CSE on TEE

There was no association between higher Risk of Paradoxical Embolism (ROPE) score [14] and a high-risk CSE on TEE (Table 3) or with a PFO (OR 1.22, 95%CI 0.94–1.58, p = 0.14). In unadjusted regression, high-risk CSE was significantly associated with lower National Institutes of Health Stroke Scale (β= -0.02, 95%CI -0.03- -0.004, p = 0.01), lack of proximal intracranial occlusion (OR 0.13, 95%CI 0.02–1.03, p = 0.054), and no prior tobacco use (OR 4.10, 95%CI 1.52–11.08, p = 0.005), while there was a trend toward a relationship with a history of no dyslipidemia (OR 0.49, 95%CI 0.21–1.15, p = 0.10). After entering each of these variables into a multivariable model, tobacco use (aOR 0.16, 95%CI 0.05–0.49, p = 0.005) and history of dyslipidemia (aOR 0.27, 95%CI 0.10–0.73, p = 0.009) were strongly and inversely associated with a high-risk CSE on TEE, while lower NIHSS trended toward an association with high-risk CSE (aOR 0.92 per point, 95%CI 0.83–1.01, p = 0.094; Table 3).

Table 3
Independent predictors of high-risk CSE.

	No high-risk CSE on TEE (n = 72)	High-risk CSE* on TEE (n = 36)	p-value	Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
Age, median (IQR)	51 (43–56)	50 (44–57)	0.97	-0.001* (-0.01-0.01)	0.92		
Female sex, no. (%)	29 (40)	15 (42)	0.89	1.06 (0.47–2.39)	0.89		
White race, no. (%)	33/63 (52)	20/31 (65)	0.27	1.65 (0.68–4.01)	0.27		
Hispanic, no. (%)	13/63 (21)	6/35 (17)	0.68	0.80 (0.27–2.32)	0.68		
Medical history, no. (%)							
Hypertension	49 (68)	21 (58)	0.32	0.66 (0.29–1.50)	0.32		
Prior tobacco use	32/71 (45)	6/36 (17)	< 0.01	0.24 (0.09–0.66)	< 0.01	0.16 (0.05–0.49)	< 0.01
Diabetes mellitus	25 (35)	11 (31)	0.67	0.83 (0.35–1.95)	0.67		
Dyslipidemia	34 (47)	11 (31)	0.15	0.49 (0.21–1.15)	0.1	0.27 (0.10–0.73)	< 0.01
Coronary artery disease	8 (11)	5 (14)	0.68	1.29 (0.39–4.27)	0.68		
Congestive heart failure	6 (8)	1 (3)	0.42	0.31 (0.04–2.72)	0.29		
Prior stroke	9 (13)	7 (20)	0.34	1.69 (0.57–4.98)	0.34		
Peripheral artery disease	1 (1)	1 (3)	1	2.03 (0.12–33.40)	0.62		

	No high-risk CSE on TEE (n = 72)	High-risk CSE* on TEE (n = 36)	p-value	Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
Baseline NIHSS, median (IQR)	5 (2–12)	3 (1–6)	0.01	-0.02* (-0.03--0.004)	0.01	0.92 (0.83–1.01)	0.09
LVO, no. (%)	13 (18)	1 (3)	0.03	0.13 (0.02–1.03)	0.05	0.20 (0.02–2.02)	0.17
Ejection fraction < 40%, no. (%)	7 (10)	2 (6)	0.72	0.55 (0.11–2.77)	0.47		
HCT or MRI findings, no. (%)							
Cortical infarction	45 (63)	24 (67)	0.67	1.20 (0.52–2.78)	0.67		
Infratentorial infarction	27 (38)	12 (33)	0.67	0.83 (0.36–1.93)	0.67		
Infarction in > 1 vascular territory	20 (28)	11 (31)	0.76	1.14 (0.48–2.75)	0.76		
ROPE score, median (IQR)	6 (4–7)	6 (5–7)	0.25	1.16 (0.91–1.48)	0.23		

Management changes following TEE

TEE led to a significant change in the secondary stroke prevention strategies for 14 patients with a high-risk CSE and 6 patients without an identifiable CSE (Fig. 1). Of the 14 patients with management changes following identification of a high-risk CSE, 12 had a PFO–6 of whom underwent closure, 4 were anticoagulated (2 of whom also had a lower extremity deep vein thrombosis), and 2 were switched from single to dual antiplatelet therapy. The 2 additional patients with management changes had valvular lesions; 1 was anticoagulated and 1 was switched from single to dual antiplatelet therapy. Time to any management change was significantly more delayed in patients who underwent PFO closure versus any other change in management (unadjusted p = 0.001 by log-rank, Fig. 3). All PFO closures took place in the year 2017 or subsequent years, after publication of trials demonstrating superiority of closure [15–17]. Of the 6 patients with PFO who were treated with escalation of antithrombotic therapy (Fig. 1), 3 were given this recommendation after the publication of successful PFO closure trials in 2017 after a risk/benefit discussion of treatment options with either the patient's primary cardiologist or neurologist. The most

common reason for deferral of PFO closure in 23 patients with a PFO was loss to follow-up (n = 6), anticoagulation pursued in lieu of closure (n = 4), and PFO considered too small (n = 4; Supplementary Table 4). None of the antithrombotic adjustments reported here were recommended on the basis of findings from outpatient cardiac event monitoring.

Discussion

In this single-center observational cohort study of young-to-middle aged stroke patients with mechanisms that could not be attributed to AF, large vessel stenosis, or small vessel disease, the addition of a TEE to a comprehensive stroke evaluation resulted in a high probability of identifying an occult, high-risk CSE and subsequent change in management. One in three patients in this cohort who underwent TEE were found to have cardiac abnormalities which could have led to changes in secondary stroke prevention. Interestingly, only 6 of 29 patients with a PFO underwent PFO closure, despite the fact that half of the included patients in this cohort were admitted following publication of seminal PFO closure trials [15–17] demonstrating superiority of this intervention to medical management. More than half of patients who did not undergo PFO closure either failed to follow-up in outpatient clinic–which is a common concern with the population in our region–were thought to have a PFO too small to intervene upon, or were empirically anticoagulated based on a risk-benefit discussion with the patient's neurologist and/or cardiologist.

The majority of non-lacunar strokes are embolic in nature and in this young cohort of stroke patients, cardiac and arterial sources are the most likely origin of embolus [1], therefore structural cardiac imaging must be obtained. Compared to TTE, TEE has been shown to have higher sensitivity for characterizing aortic arch plaque thickness and mobility, visualization of the left atrial appendage, detecting infectious, marantic, or neoplastic valvular lesions, and identifying the presence and size of a PFO with associated high-risk features (e.g., atrial septal aneurysm) [8]. The diagnostic utility of TEE was further confirmed in our study by identifying a CSE in 33% of patients without a known stroke mechanism. Of those patients, most had a PFO. Unsurprisingly, in this saturated sample of young patients with frequent cortical strokes, few vascular risk factors, and no other traditional stroke mechanism on etiologic workup, the average Risk of Paradoxical Embolism (ROPE) score was high–indicating a high attributable risk of stroke to a potential PFO if identified. As the ROPE score essentially serves as an inverse indicator of comorbid vascular disease, it is intuitive that the ROPE score could be repurposed to predict the presence and attributable risk of stroke to many types of high-risk CSEs (other than PFO).

Also unsurprising was the overall low proportion of patients with proximal large vessel occlusion. Despite the high number of patients with cortical infarcts, most strokes were only mild-to-moderate in severity with only 1 in 7 patients having a proximal LVO. These data are consistent with previously published literature indicating that emboli from these high-risk CSEs (largely PFOs) may be physiologically distinct from emboli due to AF or cervicocephalic atherosclerotic disease. According to several observational studies involving cryptogenic or cardioembolic stroke populations, patients with PFO have generally

milder presenting deficits and less frequent intracranial occlusions when compared to patients without PFO, or with other sources of cardiac embolism (e.g., AF) [18–20].

The vast majority of patients in our study had a TEE performed during the hospitalization for the index event, with a change in medical management occurring much sooner compared to PFO closure in patients with high-risk CSE. This is not surprising since secondary stroke prevention strategies in PFO management mitigate long-term risk of a small magnitude over several years (3–6 years) [15–17], with preliminary PFO closure trials failing to demonstrate efficacy after short-term follow-up (2–4 years) [21–22]. In contrast to the low annualized risk of recurrent stroke with PFO (~ 1%/yr), the risk of recurrent stroke is far greater in patients with valvular lesions [23] and aortic arch plaque (2–4%/yr) [13]. Therefore, earlier and more aggressive medical management may be indicated. Additionally, almost half of our patients were evaluated in the era prior to the publication of successful PFO closure trials in 2017 [15–17]. Therefore, the proportion of patients with management changes following TEE is likely an underestimation of potential beneficiaries with this intervention. Furthermore, inclusion of patients before 2019 likely explained why 6 patients with normal TEE findings were empirically anticoagulated for cryptogenic stroke. All but one of these patients were anticoagulated prior to publication of two randomized clinical trials which failed to demonstrate superiority of anticoagulation with rivaroxaban [2] or dabigatran [3] over aspirin in ESUS.

Prior to our study, there has been limited data evaluating the impact of TEE on clinical management following cryptogenic stroke. One retrospective cohort study of 263 patients with cryptogenic stroke reported that TEE identified a potential etiology of stroke in approximately 42% of patients–similar to the 33% who underwent TEE in this cohort–however only 1 patient (0.4%) had a management change [24]. This contrasts with our experience in which a tenfold higher proportion of patients had a management change following TEE. Larger cohorts representing more diverse populations and institutional experiences are called upon to validate these findings.

Limitations

This study represents the observational experience of a single, tertiary-care referral center over a 5-year period and is limited by its small sample size, retrospective nature, and loss to follow-up. Our Comprehensive Stroke Center is located in an underserved community with many patients of low socioeconomic status and this could discourage providers from ordering outpatient TEEs due to the concern for a low likelihood of follow up in outpatient clinic. However, we observed no significant impact between insurance status and recommendation for TEE in this population (Supplementary Table 1). The only independent predictors of TEE being clinically recommended in this cohort were younger age and presence of infarcts spanning multiple vascular territories.

Although TEE facilitated the recognition of high-risk CSE in a large proportion of patients without an identifiable cause of stroke, this study was underpowered to determine whether such information led to actionable changes that would reduce the risk of secondary events. Recurrent events in this population,

stratified by assessment with and findings from outpatient cardiac event monitoring and structural cardiac abnormalities (e.g., left atrial diameter), are being reported in detail separately. That said, larger, multicenter randomized clinical trials and meta-analyses have demonstrated that PFO closure [15–17], anticoagulation [25], and dual antithrombotic therapy with high-intensity statin [13], are superior to conventional medical management for secondary stroke prevention in at-risk patients.

It is important to recognize that TEE is not a procedure without risk [26], and that transcranial doppler with agitated saline has a similar sensitivity and specificity to TEE for detecting a right-to-left shunt [27]. However, based on data from this saturated cohort of young patients without a known cause of stroke–and therefore a high suspicion of occult CSE, TEE led to the recognition of high-risk CSEs other than PFO in 6% of tested patients (n = 7/108) who had otherwise unremarkable TTEs. Therefore, we would argue that TCD with agitated saline could be useful as a safe screening tool for right-to-left shunt, but a normal TCD/saline study should not obviate the need (or advantage) of TEE.

Conclusion

One in five patients with acute stroke experience ESUS despite a complete workup with non-invasive imaging. However, randomized clinical trials have shown no advantage of therapeutic anticoagulation over aspirin for secondary stroke prevention [2, 3]. This is largely due to the heterogeneity of patients with ESUS and multitudinous mechanisms at play (e.g., PFO, non-stenotic carotid plaque, aortic arch atheroma, paroxysmal AF). The lack of equipoise for a “universal” secondary prevention strategy emphasizes the importance of an advanced diagnostic assessment in these patients to identify the source of embolism and provide targeted treatment. In our cohort, we found a significant advantage of TEE when added to TTE for identifying a high-risk CSE. Furthermore, these findings led to management changes for a significant number of imaged patients. Our results encourage the regular use of TEEs in young, cryptogenic stroke patients, especially in the inpatient setting, since TEE can identify a CSE that leads to immediate antithrombotic therapy change prior to discharge in a small proportion of patients at high risk for recurrent events. Whether the addition of TEE to the standard stroke diagnostic battery results in a meaningful reduction in recurrent strokes can only be determined in larger studies, or with pooling of these data with the published literature.

Declarations

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Availability of data and material (data transparency): All data and materials support the authors published claims and comply with field standard.

Code availability (software application or custom code): All software application and custom code support the authors published claims and comply with field standard.

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Figures

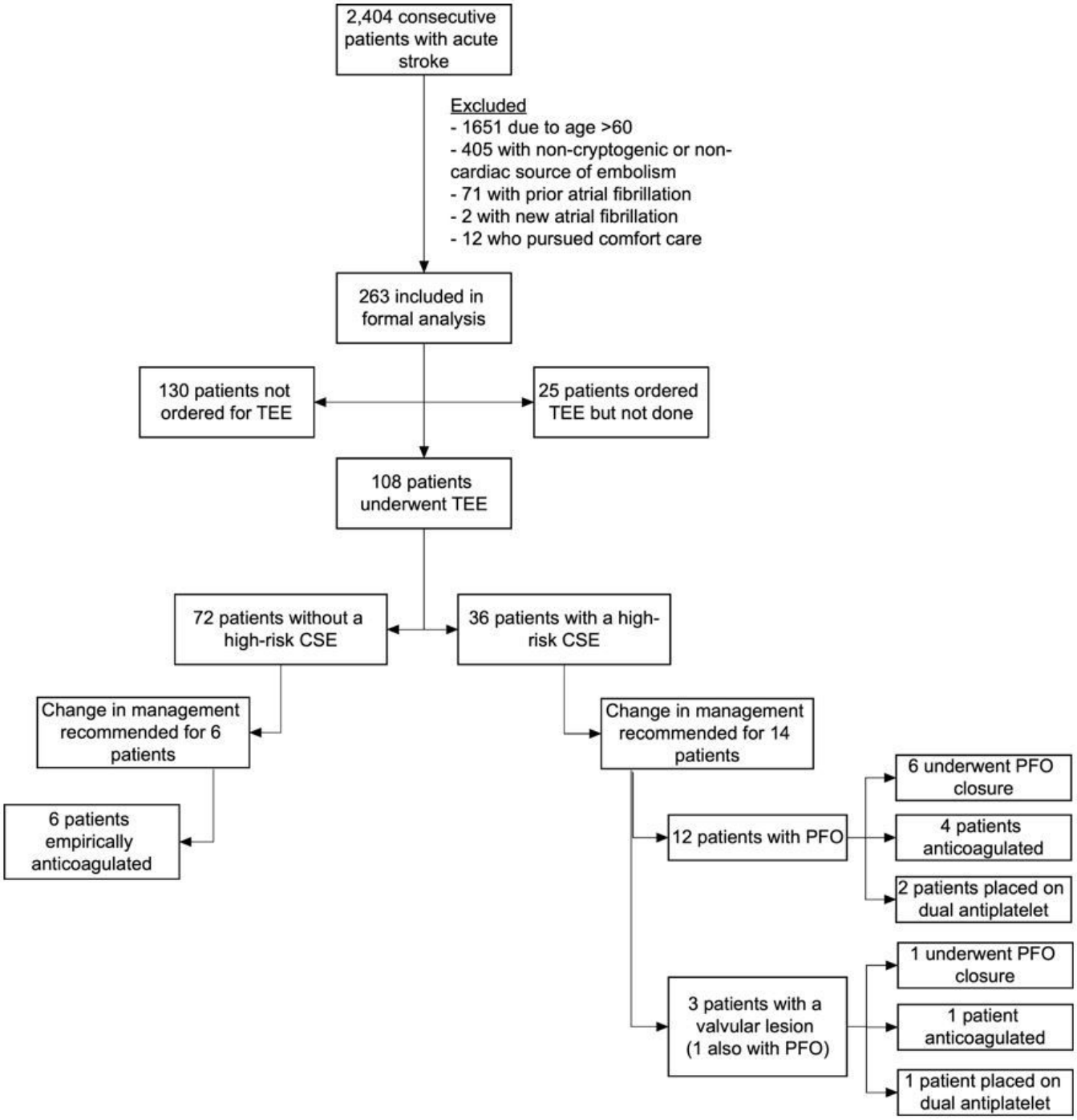

Figure 1

Patient flowchart. TEE denotes transesophageal echocardiography, CSE cardiac source of embolism, and PFO patent foramen ovale.

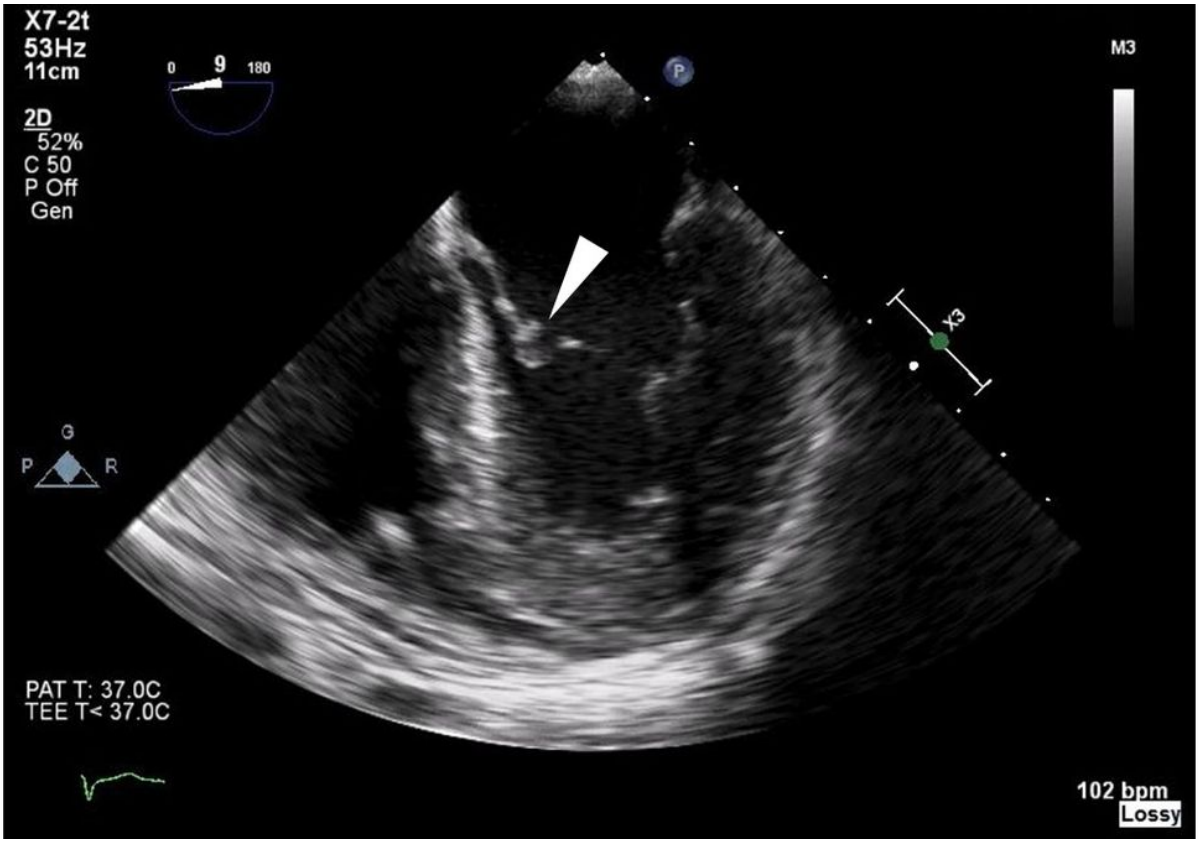

Figure 2

Representative image of an apical four-chamber view demonstrating an 8mm non-mobile echobright density on the ventricular surface of the mitral valve anterior leaflet (arrowhead), indicative of endocarditis

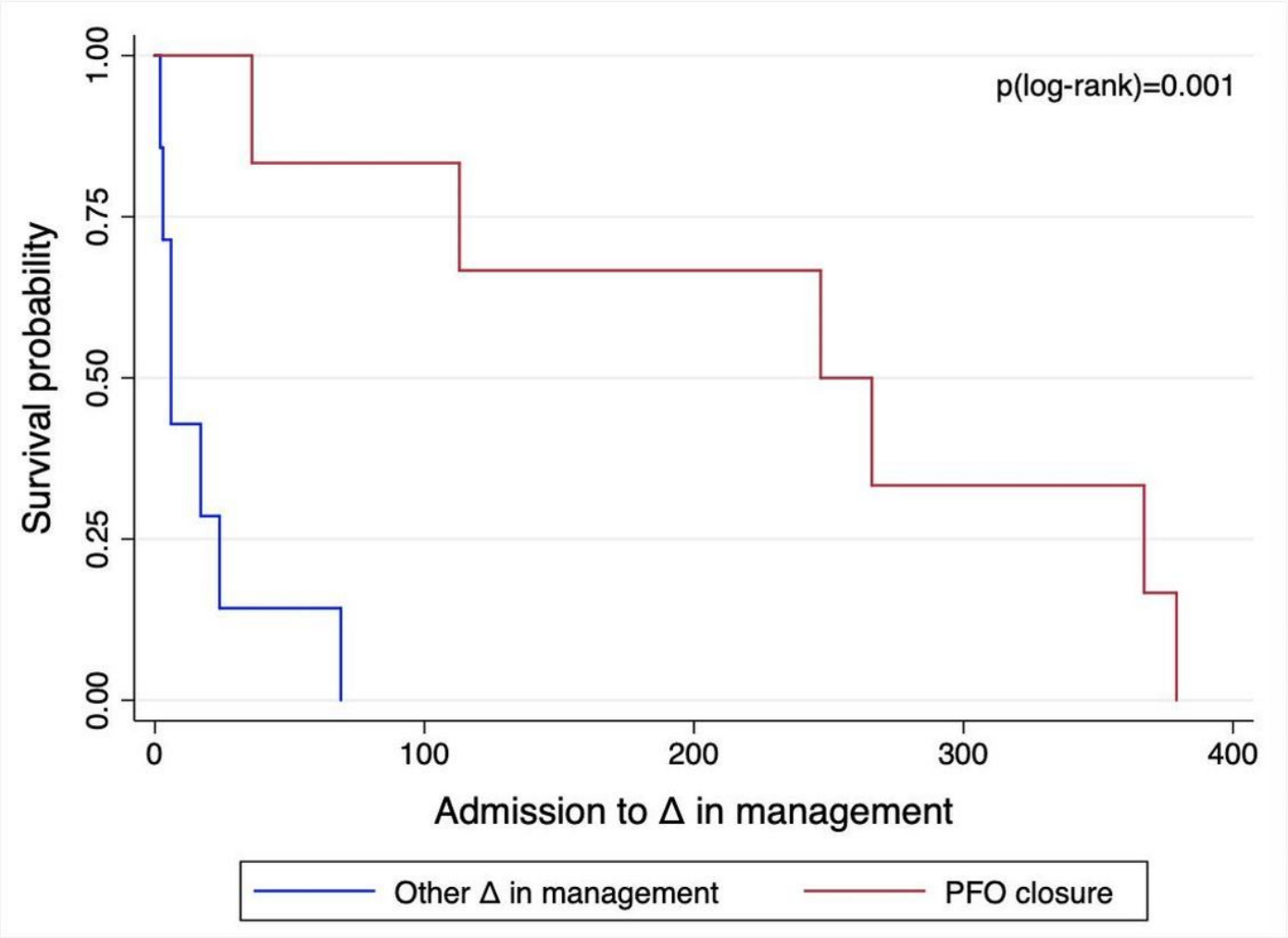

Figure 3

Time to management change in patients with high-risk CSEs. CSE denotes cardiac source of embolism, and PFO patent foramen ovale.

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