

Silent Strike: Stroke in Context of Endocarditis – Brain Imaging as a Catalyst for Diagnosis

IULIA-COSMINA STOICAN¹, DORIN DRAGOȘ^{2,3}, ATENA PAPAGHEORGHE⁴, SUZANA MARIA GUBERNA^{3,5},
SORIN TUTA^{1,3}, MARIA MIRABELA MANEA^{1,3}

¹Neurology Department, National Institute of Neurology and Neurovascular Diseases, Bucharest, Romania

²Internal Medicine Department, University Emergency Hospital, Bucharest, Romania

³“Carol Davila” University of Medicine and Pharmacy, Bucharest Romania

⁴Neurosurgery Department, University Emergency Hospital, Bucharest, Romania

⁵Cardiology Department, Prof. Dr. Bagdasar-Arseni, Emergency Clinical Hospital, Bucharest, Romania

Abstract

Introduction: Endocarditis is a pathology which is rarely encountered in clinical practice that presents itself in various manners, thus posing a great challenge for the clinician in the process of formulating a timely diagnosis, especially given its potentially lethal evolution. The diagnosis of infective endocarditis is based on Modified Duke Criteria. A wide array of complications may accompany endocarditis, including septic or thrombotic emboli to various territories – those occluding branches of cerebral arteries result in ischemic strokes, which may be demonstrated by brain imaging and the symptoms which may range from mild mental status alteration to deep coma.

Objective: Assessment of brain imaging as a diagnostic tool for bacterial endocarditis.

Materials and methods: This is a nested case-control study, in which 84 patients with ischemic stroke were enrolled, half of them having endocarditis related stroke (cases), and the other half stroke due to cardioembolism from other sources or to large-artery atherosclerosis (controls).

Results: Brain imaging revealed statistically significant differences between the two cohorts, endocarditis related stroke being more strongly associated with multiple territories involvement, multiple lesions coexistence, watershed lesions, and a greater extent of ischemia all these may serve as valuable diagnostic clues. Among these findings, the presence of multiple lesions has been the most sensitive tool ($Sn = 0.786$, $Sp = 0.857$, $LR+ = 5.497$, $LR- = 0.25$), while the involvement of multiple arterial territories had the highest specificity and positive likelihood ratio for endocarditis-related stroke ($Sn = 0.738$, $Sp = 0.929$, $LR+ = 10.394$, $LR- = 0.282$). A larger ischemic lesion as quantified by pc-ASPECTS score (more than by the ASPECTS score) also increases the likelihood of endocarditis as the cause of ischemic stroke, with an AUROC of 0.7361 (95% CI 0.629-0.843).

Conclusions: Early brain imaging could play a crucial role in endocarditis, helping the clinician to suspect this diagnosis. Further studies are needed to understand the role of early brain imaging when Modified Duke Criteria fail to establish the diagnosis.

Keywords: brain imaging; ischemic stroke; ischemia; Modified Duke Criteria; endocarditis.

Abbreviation list:

ASPECTS – Alberta stroke Programme early computed tomography score

CT – computed tomography

ESR – erythrocyte sedimentation rate

IQR – interquartile range

MRI – magnetic resonance imaging

pc-ASPECTS – posterior circulation Alberta stroke Programme early computed tomography score

What is new? What is important?

Given the high mortality associated with endocarditis-related ischemic stroke, it is imperative to reassess the current modus operandi used in diagnosing the etiology of ischemic stroke. Brain imaging may be a useful tool for speeding up the diagnosis of endocarditis (which may be suspected based on the predilection for multiple lesions and extensive multi-territorial cerebral ischemia), the delayed diagnosis of which may result in postponed or improper treatment.

INTRODUCTION

Endocarditis is an inflammatory disorder affecting the innermost layer of the heart which usually involves valvular endocardium but may involve other regions of the endocardium as well. Its etiology can be either bacterial, resulting in infective endocarditis, or non-bacterial, also known as non-bacterial thrombotic endocarditis, the latter being commonly associated with malignancies. A daunting aspect of this disease is the polymorphic spectrum of complications, including neurovascular events, primarily ischemic stroke and cerebral abscess. Ischemic stroke is a consequence of reduced or arrested blood flow to a brain region, resulting in metabolic dysregulation, generated by various pathophysiological mechanisms [1–3].

Current practice for the diagnosis of infective endocarditis is based on the use of the Modified Duke Criteria [4]. Research has been conducted to explore the potential of brain imaging to enhance the pre-existing methods of diagnosing endocarditis in the context of ischemic stroke. This is due to the growing necessity to ensure timely and effective treatment for this condition [5,6]. This study aims to compare the clinical and imaging aspects of stroke caused by endocarditis with stroke induced by a different etiology (another source of cardioembolism or large-artery atherosclerosis) and to assess the usefulness of brain imaging as a tool for diagnosing endocarditis when Modified Duke Criteria are not met.

MATERIALS AND METHODS

We conducted a nested case-control study in which we enrolled 42 patients admitted to the Neurology Department of the National Institute of Neurology and Neurovascular Diseases Bucharest over the course of 99 months (September 2014 – December 2022). The inclusion of the patients in the study group was based on coexisting diagnoses of endocarditis and ischemic stroke. Modified Duke Criteria were employed for diagnosing infective endocarditis [4]. Subsequently, we assembled an equally sized control group similar to the study group in terms of demographics and cardiovascular risk factors and including endocarditis-free patients with ischemic stroke due to cardioembolism (originating from sources other than valvular vegetations) or to large-artery atherosclerosis.

The following parameters were evaluated for both cohorts: demographics, risk factors, laboratory results, brain imaging (MRI + CT), and outcome.

Regarding patients' outcome (evaluated at discharge), three categories were employed: improved (patients discharged in a better condition than at admission), worsened (patients transferred to other departments or hospitals due to various serious complications), and deceased.

Descriptive statistics included the calculation of the median (Q1, Q3) as the continuous numerical variables had an asymmetric distribution. Hemorrhagic transformation was classified according to the ECASS II system [9].

Shapiro-Wilk test was used to assess the normality of data distribution. Mann-Whitney test with continuity correction was used to compare continuous (numerical) variables.

Fisher's exact test was employed to compare categorical parameters; the dependent categorical variable was endocarditis (either present or absent); the independent categorical variables were: age, gender, arterial hypertension, type 2 diabetes, dyslipidemia, chronic kidney disease, chronic heart failure, history of myocardial infarction, concomitant neoplasm, hemorrhagic transformation, presence of multiple ischemic lesions, involvement of multiple arterial territories, presence of watershed lesions, associated bleeding, deceased – for all these the two possible values being yes/present and no/absent.

When multiple comparisons were performed, the significance level (commonly set at 0.05) was lowered according to Bonferroni correction: the corrected significance level was 0.05 divided by the number of comparisons. All the statistical calculations were performed using the R language and environment for statistical computing and graphics (version 4.2.3.); the employed packages were dplyr, tidyverse, ggplot2, ggpubr, mosaic, mediation. For calculating sensitivity (Sn), specificity (Sp), positive likelihood ratio (LR+), negative likelihood ratio (LR-) with confidence intervals, we used the diagnostic test calculator from <https://ebm-tools.knowledgetranslation.net/calculator/diagnostic/>.

To calculate the area under the receiver operating characteristic curve (AUROC) and the corresponding 95% confidence interval we have employed the ROC Calculator from <https://www.statkingdom.com/roc-calculator.html> and the 95% confidence interval calculator from <https://riskcalc.org/ci/>, respectively.

RESULTS

Out of the 42 patients in the endocarditis group, the definite diagnosis of endocarditis was established in 21 cases (50%), while in the remaining 21 (50%), the diagnosis was deemed possible, based on the Modified Duke Criteria.

From 11511 patients admitted during the same period with stroke not related to endocarditis, we chose another 42 patients as controls, matched with the cases by age, sex, cardiovascular diseases/

risk factors (arterial hypertension, type 2 diabetes, dyslipidemia, chronic kidney disease, chronic heart failure, history of myocardial infarction), and concomitant neoplasm (see Table 1).

There was a statistically significant difference between the two groups when assessing the baseline laboratory parameters, with higher values in the endocarditis group for ESR ($p=0.009$) and neutrophil count ($p<0.001$), and lower values for hemoglobin level ($p<0.001$) as shown in table 2.

Table 1

Baseline characteristics of the two groups analyzed with Fisher's exact test

Characteristic	Odds ratio (95% confidence interval)	(a,b,c,d)
Male gender	0.91 (0.35-2.33)	(20, 22, 21, 21)
Arterial hypertension	0.91 (0.35-2.33)	(20, 22, 21, 21)
Type 2 diabetes	1 (0.34-2.97)	(31, 11, 31, 11)
Dyslipidemia	0.41 (0.15-1.08)	(20, 22, 29, 13)
Chronic kidney disease	1.57 (0.34-8.24)	(38, 4, 36, 6)
Chronic heart failure	2.11 (0.7-6.7)	(34, 8, 28, 14)
History of myocardial infarction	0.3 (0.03-1.84)	(36, 6, 40, 2)
Concomitant neoplasm	2.09 (0.28-24.34)	(40, 2, 38, 4)

a = control group, characteristic absent, b = control group, characteristic present, c = study group, characteristic absent, d = study group, characteristic present

Table 2

Baseline laboratory parameters for the two groups;

Laboratory parameter	Study group Median value, (Q1-Q3)	Control group Median value, (Q1-Q3)	p-value
Serum creatinine level (mg/dL)	0.885 (0.71-1.165)	0.925 (0.7625-1.11)	0.71
Hemoglobin level (g/dL)	12.5 (10.03-13.55)	14 (12.3-14.875)	0.0064
Neutrophil count (*1000/uL)	9 (7-12.3)	6.78 (4.95-8.61)	0.00095
White blood cells count (*1000/uL)	11 (8.95-15)	9.26 (7.55-12.1775)	0.028
Platelet count (*1000/uL)	217 (153.65-260.75)	249.5 (195.25-291)	0.026
Erythrocyte sedimentation rate (mm/h)	37.5 (19.25-75.75)	20 (9.75-37.75)	0.009

Q1 = first quartile, Q3 = third quartile, p-value was calculated by means of Mann-Whitney test. As 6 comparisons were performed, the significance threshold for p-value was lowered to $0.05/6 \approx 0.01$. The statistically significant results are highlighted by bold typing

Table 3

The diagnostic performance of imaging findings on brain CT

Brain CT characteristic	Sn	Sp	LR+	LR-
Hemorrhagic transformation	0.19	0.905	2	0.895
Multiple lesions	0.786	0.857	5.497	0.25
Multiple arterial territories	0.738	0.929	10.394	0.282
Watershed lesions	0.429	0.857	3	0.666

Sn = sensitivity, Sp = specificity, LR+ = positive likelihood ratio, LR- = negative likelihood ratio

As regards the findings on cerebral imaging, there was a statistically significant difference in lesion patterns between the two groups, with multiple injuries ($p < 0.001$), multi-territorial (including both posterior and anterior circulation) involvement ($p < 0.001$), and watershed lesions ($p = 0.0072$) being more common in endocarditis group. In terms of hemorrhagic transformations, there was no statistically significant difference between the two groups ($p = 0.35$). Associated cerebral hemorrhage (intraparenchymal or subarachnoid) occurred only in the endocarditis group (in 4 patients). The diagnostic performance of these findings is illustrated in Table 3.

Multiple lesions were proven to be the most sensitive tool among these findings, with $Sn = 0.786$, $Sp = 0.857$, $LR+ = 5.497$, $LR- = 0.25$. On the other hand, the involvement of multiple arterial territories had the highest specificity and positive likelihood ratio for endocarditis-related stroke ($Sn = 0.738$, $Sp = 0.929$, $LR+ = 10.394$, $LR- = 0.282$). Watershed lesions and hemorrhagic transformation

have also shown high specificity, but with lower sensitivity and high negative likelihood ratio ($Sn = 0.429$, $Sp = 0.857$, $LR+ = 3$, $LR- = 0.66$ for watershed lesions, $Sn = 0.109$, $Sp = 0.905$, $LR+ = 2$, $LR- = 0.895$, for hemorrhagic transformation).

Ischemia extent (evaluated using ASPECTS and pc-ASPECTS scores [7,8]) was larger in the endocarditis group, with larger infarctions both in the posterior circulation ($p < 0.001$), and the anterior circulation ($p = 0.011$), with both models having a predictive power, but with a higher AUROC for pc-ASPECTS, as shown in Figure 1.

Concerning the outcome, there were no fatalities in the control group, all patients being improved at discharge; by contrast, in the endocarditis group there were 16 deaths, while other 14 patients needed to be transferred due to their worsened condition (Table 4). The median in-hospital survival time in the endocarditis group was 12 days.

Table 4

Clinical outcomes of the two groups (p value = 4×10^{-13} – as calculated by Fisher's exact test)

Clinical outcome	Study group (42 patients)	Control group (42 patients)
Improved	12	42
Worsened	14	0
Deceased	16	0

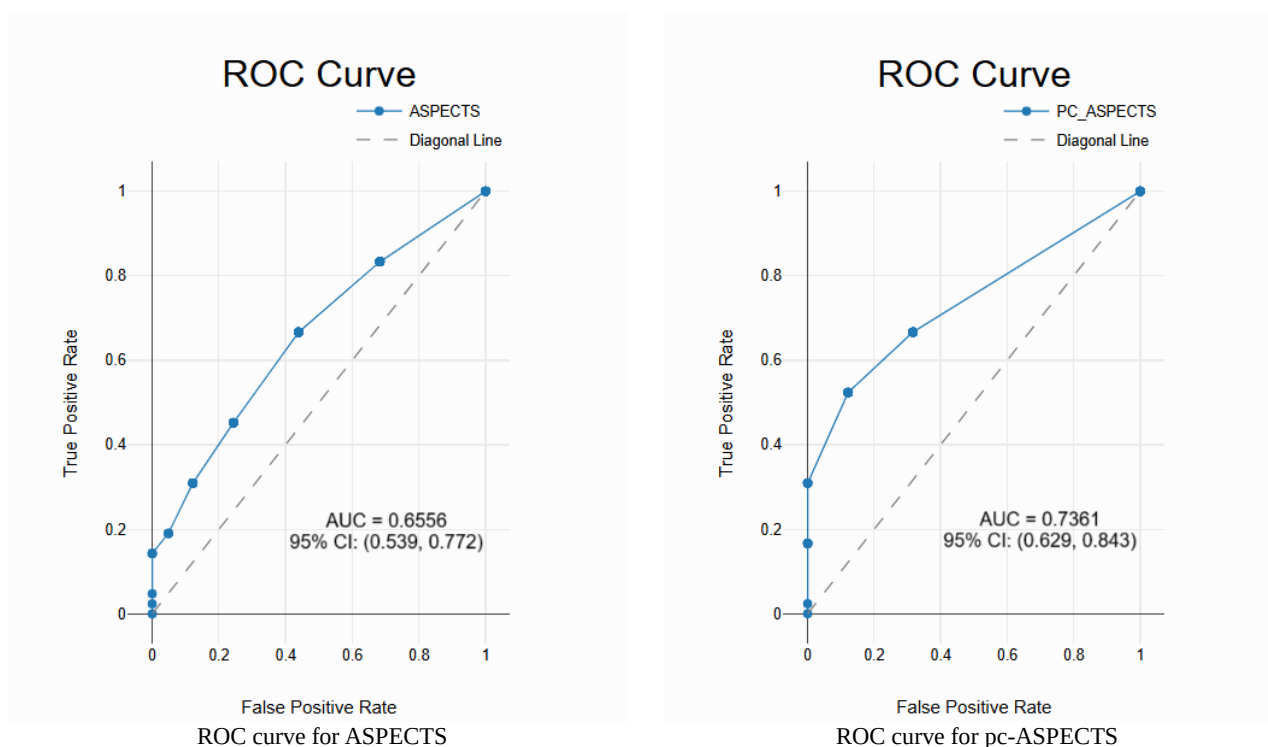


Figure 1. The area under the receiver operating characteristic curve (AUROC) was used to evaluate the performance of ASPECTS and pc-ASPECTS in predicting endocarditis-related stroke.

DISCUSSIONS

This study aimed to identify the role of brain imaging in the context of endocarditis related stroke. Given the lack of specificity of the wide array of neurological symptoms engendered by endocarditis induced ischemic stroke [11,12], one may not suspect at first the underlying condition. The Modified Duke Criteria alone cannot ensure a definitive diagnosis in all cases [6], thus prompting clinicians to develop further methods [13,14] to uncover this pathology. This was also visible in our study, where only half of the patients from the study group met the criteria for the definite diagnosis. Consequently, in recent years, there has been increasingly more research focusing on the use of brain imaging in such cases [13–17].

Laboratory results usually point to systemic involvement, as highlighted by our study too, consistent with previous literature [2]: elevated neutrophil count and ESR and decreased hemoglobin level on admission were more common in endocarditis associated stroke.

Early cerebral imaging, whether it is CT or MRI, has proven to be of great usefulness in the context of ischemic stroke, particularly when it occurs as a complication of endocarditis. Our study suggests that some patterns of injury (including the involvement of multiple territories, the coexistence of multiple lesions, and a greater extent of the ischemia-afflicted cerebral territory) plead for endocarditis as the source of the cerebral ischemia-generating emboli. Our study also pointed out an association between watershed ischemia and endocarditis, in agreement with previous studies [18], despite the control group having a significant prevalence of major artery atherosclerosis, which could result in hemodynamically significant stenoses known to be associated with watershed lesions. We also attempted to assess the impact of susceptibility weighted imaging MRI (as was done in some recent studies [10]), but unfortunately our study was limited by the reduced access to such technology. Further studies comparing only cardioembolic ischemia with endocarditis-related ischemia, consistently evaluated by MRI with sequences that have a high sensitivity for vascular events may help advance our knowledge.

Better results in terms of management and outcome of patients suffering from endocarditis-related stroke may be achieved if the Modified Duke Criteria and cerebral imaging are employed timely [5] in cases of stroke patients presenting with fever and altered lab results, until blood

culture results arrive, as empirical antibiotic therapy might be ineffective and insufficient [19]. The relative reluctance to perform thrombolysis (endocarditis being regarded as a contraindication, albeit long-debated) and endovascular treatment in the context of endocarditis [9,20,21] did not interfere with our results, as none of the patients in the study group underwent thrombolytic therapy or mechanical thrombectomy, although etiology was unknown at presentation.

The mortality rate was much higher in the study group, however the real survival rate may be significantly lower, as we were unable to further monitor the patients after being transferred to other departments (e.g. Infectious Diseases department).

While our study has managed to prove its hypothesis, it is imperative to acknowledge its limitations, such as its retrospective character, the long time span over which data was collected, during which the standard of diagnosis and care changed, the small size of our study cohort, the monodisciplinary character of our unit, resulting in limited access to various investigation methods [22] (such as transesophageal echocardiography), the scarcity of MRI examinations, and the need to transfer many of our patients to other units (which prevented follow-up imaging of the ischemic lesions and hemorrhagic transformations, as well as outcome and lab results monitoring). However, CT scan, although one of the simplest and most accessible cerebral imaging methods, has proven to be reliable in uncovering key elements suggesting endocarditis as the etiology of ischemic stroke.

CONCLUSIONS

To this day, endocarditis remains a dreaded clinical entity with a challenging diagnosis process, despite the recent revision of the Duke Criteria. Nonetheless, both clinical and laboratory findings are useful in suggesting the diagnosis, as our study has proven.

This study found that early brain imaging is a valuable and reliable instrument that aids the clinician in raising the suspicion of endocarditis in patients presenting with stroke and no apparent underlying condition. Considering the wide array of possible cerebral imaging techniques, further studies with larger and more homogenous samples are required to determine if extensive brain imaging investigations are warranted as cost-effective tools able to provide useful clues for diagnosis and treatment.

Introducere: Endocardita este o patologie întâlnită mai puțin frecvent în practica medicală, care se prezintă în forme variate, reprezentând astfel o provocare pentru clinician în procesul de formulare a unui diagnostic precoce, mai ales având în vedere evoluția potențial fatală. Diagnosticul se bazează pe criteriile Duke modificate pentru a confirma existența endocarditei infecțioase. O gamă largă de complicații poate fi asociată endocarditei, printre care cele septice sau embolice în diverse teritorii – dintre acestea, ocluzia în teritoriile vasculare cerebrale va duce la accident vascular ischemic, ce poate fi sugerat de imagistica cerebrală și de simptome ce variază de la ușoară alterare a stării de conștiință până la comă profundă.

Obiectiv: Evaluarea imagisticii cerebrale ca instrument de diagnostic pentru endocardita infecțioasă.

Materiale și metode: Prezentăm un studiu retrospectiv de cohortă, cu un lot de 84 de pacienți cu diagnosticul de accident vascular cerebral ischemic, dintre care o jumătate are ca și etiologie endocardita, respectiv cealaltă jumătate de pacienți prezintă eveniment ischemic de cauză aterotrombotică sau altă cauză cardioembolică. Au fost comparate cele două cohorte din punct de vedere al tabloului clinic, analizelor de laborator, modificărilor imagistice cerebrale și mortalitate.

Rezultate: Evaluarea prin imagistică cerebrală pentru cele două cohorte a demonstrat diferențe semnificativ statistice, coexistența leziunilor ischemice multiteritoriale, prezența de leziuni multiple și de leziuni de graniță, dar și de dimensiuni mai mari fiind mai frecvent asociate cu endocardita ca mecanism etiologic și putând fi indicii de diagnostic. Dintre acestea, prezența de leziuni multiple s-a dovedit cel mai sensibil instrument ($Sn = 0.786$, $Sp = 0.857$, $LR+ = 5.497$, $LR- = 0.25$), pe când implicarea multiteritorială a prezentat cea mai mare specificitate, cât și rată a probabilității pozitive pentru infarctul cerebral cauzat de endocardită ($Sn = 0.738$, $Sp = 0.929$, $LR+ = 10.394$, $LR- = 0.282$). O leziune ischemică de mai mari dimensiuni gradată conform scorului pc-ASPECTS (mai mult decât în cazul scorului ASPECTS) crește probabilitatea pentru endocardită ca și cauză a infarctului cerebral, cu AUROC de 0.7361 (95% CI 0.629-0.843).

Concluzii: Imagistica cerebrală precoce poate juca un rol crucial în contextul endocarditei, putând servi clinicianului pentru suspiciunea de diagnostic. Studii viitoare sunt necesare pentru a înțelege rolul imagisticii cerebrale precoce când criteriile Duke modificate nu se dovedesc a fi suficiente în stabilirea diagnosticului.

Correspondence to: Dorin DRAGOȘ, Internal Medicine Department, University Emergency Hospital, Bucharest, Romania
E-mail: dorin.dragos@umfcd.ro

Acknowledgements: We sincerely appreciate the contributions of the medical personnel of the National Institute of Neurology and Neurovascular Diseases Bucharest and the patients who participated in this study. We thank Suzana Maria Guberna for her support, as she had a major contribution to the article.

Funding: This study has received no external funding.

Conflicts of interest: The authors declare no conflicts of interest.

Informed Consent Statement: The study was designed in compliance with the ethical guidelines of the 1975 Declaration of Helsinki. Informed consent was obtained.

REFERENCES

1. HABIB G, LANCELLOTTI P, ANTUNES MJ, BONGIORNI MG, CASALTA JP, DEL ZOTTI F, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC) Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J*. 2015;36(44):3075–3128.
2. SPELMAN DENIS. Complications and outcome of infective endocarditis. *UpToDate Waltham, MA*. Published online 2023.
3. SOTERO FD, ROSÁRIO M, FONSECA AC, FERRO JM. Neurological Complications of Infective Endocarditis. *Curr Neurol Neurosci Rep*. 2019;19(5):23.

4. LI JS, SEXTON DJ, MICK N, NETTLES R, FOWLER VG JR, RYAN T, *et al.* Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis.* 2000;30(4):633–638.
5. DUVAL X, IUNG B, KLEIN I, BROCHET E, THABUT G, ARNOULT F, *et al.* Effect of early cerebral magnetic resonance imaging on clinical decisions in infective endocarditis: a prospective study. *Ann Intern Med.* 2010;152(8):497–504, W175.
6. DILLEY JR, CLINCH CR. Blood culture-negative endocarditis presenting as altered mental status. *BMJ Case Reports.* Published online August 23, 2018:bcr-2018-224707.
7. BARBER PA, DEMCHUK AM, ZHANG J, BUCHAN AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. *Lancet.* 2000;355(9216):1670–1674.
8. PUETZ V, SYLAJA PN, COUTTS SB, HILL MD, DZIALOWSKI I, MUELLER P, *et al.* Extent of hypoattenuation on CT angiography source images predicts functional outcome in patients with basilar artery occlusion. *Stroke.* 2008;39(9):2485–2490.
9. FORD G, FREEMANTLE N. ECASS-II: intravenous alteplase in acute ischaemic stroke. European Co-operative Acute Stroke Study-II. *Lancet.* 1999;353(9146):65; author reply 67–68.
10. YONEDA Y, TOKUI K, HANIHARA T, KITAGAKI H, TABUCHI M, MORI E. Diffusion-weighted magnetic resonance imaging: detection of ischemic injury 39 minutes after onset in a stroke patient. *Ann Neurol.* 1999;45(6):794–797.
11. GARCÍA-CABRERA E, FERNÁNDEZ-HIDALGO N, ALMIRANTE B, IVANOVA-GEORGIEVA R, NOUREDDINE M, PLATA A, *et al.* Neurological Complications of Infective Endocarditis: Risk Factors, Outcome, and Impact of Cardiac Surgery: A Multicenter Observational Study. *Circulation.* 2013;127(23):2272–2284.
12. SKINNER CR. Neurological Complications of Endocarditis: Pathophysiologic Mechanisms and Management Issues. In: Chan KL, Embil JM, eds. *Endocarditis.* Springer London; 2006:241–251.
13. KOUIJZER JJP, NOORDERMEER DJ, VAN LEEUWEN WJ, VERKAIK NJ, LATTWEIN KR. Native valve, prosthetic valve, and cardiac device-related infective endocarditis: A review and update on current innovative diagnostic and therapeutic strategies. *Front Cell Dev Biol.* 2022;10:995508.
14. CAHILL TJ, BADDOUR LM, HABIB G, HOEN B, SALAUN E, PETTERSSON GB, *et al.* Challenges in Infective Endocarditis. *Journal of the American College of Cardiology.* 2017;69(3):325–344.
15. CHAMPEY J, PAVESE P, BOUVAIST H, KASTLER A, KRAINIK A, FRANCOIS P. Value of brain MRI in infective endocarditis: a narrative literature review. *Eur J Clin Microbiol Infect Dis.* 2016;35(2):159–168.
16. HESS A, KLEIN I, IUNG B, LAVALLÉE P, ILIC-HABENSUS E, DORNIC Q, *et al.* Brain MRI findings in neurologically asymptomatic patients with infective endocarditis. *AJNR Am J Neuroradiol.* 2013;34(8):1579–1584.
17. VITALI P, SAVOLDI F, SEGATI F, MELAZZINI L, ZANARDO M, FEDELI MP, *et al.* MRI versus CT in the detection of brain lesions in patients with infective endocarditis before or after cardiac surgery. *Neuroradiology.* 2022;64(5):905–913.
18. WANG PE, YAN GZ, TAN BYQ, KEW GS, KUA J, CALIDA MCF, *et al.* Bilateral watershed infarcts in infective endocarditis. *QJM: An International Journal of Medicine.* 2019;112(5):375–376.
19. RAJANI R, KLEIN JL. Infective endocarditis: A contemporary update. *Clin Med.* 2020;20(1):31–35.
20. GRECU N, TIU C, TEREKOASA E, BAJENARU O. Endocarditis and stroke. *Maedica (Bucur).* 2014;9(4):375–381.
21. MAHESHWARI R, CORDATO DJ, WARDMAN D, THOMAS P, BHASKAR SMM. Clinical outcomes following reperfusion therapy in acute ischemic stroke patients with infective endocarditis: a systematic review. *J Cent Nerv Syst Dis.* 2022;14:11795735221081597.
22. HABIB G, BADANO L, TRIBOUILLOY C, *et al.* Recommendations for the practice of echocardiography in infective endocarditis. *European Journal of Echocardiography.* 2010;11(2):202–219.

Received 22nd July 2024