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Original Article

Neurologic Complications in Infective Endocarditis: Data from the Iranian Registry of Infective Endocarditis

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Summary

Introduction: Neurological complications (NCs) in patients with infective endocarditis (IE) are life-threatening and can be avoided or managed properly if diagnosed early. We aimed to determine the incidence and risk factors of NC in a large group of patients with IE.

Methods: Patients with definite or possible IE diagnosed based on the Duke criteria were included from 2006 to 2019. Data were derived from the single-center Iranian Registry of Infective Endocarditis (IRIE) retrospectively. NCs may be diagnosed on admission or during hospitalization till discharge. NCs were classified into the following categories: embolic cerebral events, hemorrhagic stroke, brain abscess, and mycotic aneurysms.

Findings: In this study, 456 (65.9%) patients had definite and 236 (34.1%) had possible IE. Moreover, 16.5% of the patients had a history of stroke or transient ischemic attack (TIA), and 57.2% of the patients had a vegetation size>1 cm. The most common predisposing factors of IE were congenital heart disease (33.9%) and prosthetic valve (25.5%), respectively. The most frequently isolated microorganism in the blood cultures was *Staphylococcus aureus* (11.8%), followed by *Streptococcus viridans* (9.3%). The most common NCs were cerebral embolic events (91 patients, 19%) and cerebral mycotic aneurysms (31 patients). The most frequently used mechanical valve in patients with NCs is the mitral valve, followed by the aortic valve. Fifteen patients (16.1%) with NCs had in-hospital mortality.

Conclusion: Our findings reveal that NCs are common, so it is highly recommended to perform a neurological consultation in all left-sided endocarditis cases and initiate antibiotic therapy, despite not knowing the exact microorganism on the first day.

Keywords: Neurologic complications, Infective endocarditis, Registry, Left-sided endocarditis

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Introduction

The incidence of infective endocarditis (IE) has been increasing because of an increasing number of persons who inject drugs (PWID) (intravenous substance) and the increasing use of prosthetic cardiac valves. The incidence of neurological complications (NCs) of IE is 25%-35%, but varies with the infecting organism. Such complications are associated with a significantly higher mortality rate.[1] NCs can involve various cerebrovascular and infectious events and are especially common in patients with mitral valve abnormalities.[2] Cerebral mycotic aneurysms are recognized complications of IE and may result in intracranial hemorrhage.[3] Intracranial hemorrhage is also caused by septic arteritis. Embolization of infected material causes cerebral microabscesses and meningitis, as well as stroke or transient ischemic attack (TIA), which is more common in the middle cerebral artery.[4]

Neurologic complications are frequent in IE patients who require ICU admission. However, correct and on-time diagnosis of IE and following medical versus surgical approach requires a multidisciplinary approach.[5] International multicenter studies are providing new, important findings based on the experience of tertiary centers.[6,7] Between 2006 and 2019, all adult patients with a possible or definite diagnosis of IE based on the modified Duke criteria were enrolled in the Iranian Registry of Infective Endocarditis (IRIE) by an expert team.[8] IRIE aimed to improve the management of IE through a better understanding of the demographic, clinical, therapeutic, and prognostic features of the disease among the Iranian population.

Local data regarding the IE causative microorganism, patient predisposing factors, and surgical and neurologic complications are assessed over time by this registry. The purpose of this study is to investigate the prevalence of enological complications and related factors in patients with IE in a tertiary center where a remarkable number of patients with IE are enrolled in IRIE.

Methods

Participants

This retrospective observational study included adult patients consecutively diagnosed with possible or definite IE based on the modified Duke criteria between 2006 and 2019 who were enrolled in the IRIE, which is a prospective single-center observational registry held in Rajaie Cardiovascular Medical and Research Center as a tertiary center with a high number of patients with IE who were referred to this center. This study was approved by the local ethical committee according to the Declaration of Helsinki. All patients underwent clinical examination, electrocardiogram, echocardiography, microbiology, and biochemistry lab tests. Multislice computed tomography (CT) or magnetic resonance imaging (MRI) to find any types of cardiac and extra-cardiac complications was performed for patients based on the physician's opinion. NCs were categorized into two time points: on admission and during hospitalization. The collected variables were demographic data; history of IE and other cardiac or non-cardiac disease; predisposing IE factors; type of endocarditis (native or prosthetic); vegetation, abscess, fistula, severe regurgitation or stenosis as well as systolic and diastolic function on echocardiography; infecting microorganism; antibiotic therapy (type, dose, date of initiation and termination); indication for surgery and surgical data (if performed); mortality; and date, type, and extent of NCs. Inclusion criteria were patients aged > 18 years with a diagnosis of definite or possible IE per the Modified Duke Criteria. Exclusion criteria were the presence of an alternative diagnosis explaining the findings, symptom resolution following less than four days of antibiotic therapy, or failure to meet the criteria for possible IE. Both transthoracic and transesophageal echocardiography were performed in all patients.

Definition of NCs

NCs may be diagnosed on admission or during hospitalization till discharge or after surgery if it is performed. NCs were classified into the following categories: embolic cerebral events (TIA, stroke), hemorrhagic stroke, brain abscess, and mycotic aneurysm.

The diagnosis of embolic and hemorrhagic complications was based on clinical findings and CT imaging or MRI data. The diagnosis of TIA depends on the quality and quantity of information available and the time of assessment. The main criteria used are focal neurologic signs or symptoms referable to known cerebral arterial distributions without direct measurement of blood flow or cerebral infarction on imaging of the brain.[9] Stroke presents clinically as neurologic deficits of sudden onset, diagnosed by CT in about two-thirds of cases in which ischemic changes are evident and major (multiple cerebral embolisms or a single embolism affecting ≥ 30% of a brain lobe) or diagnosed by MRI in minor ischemic stroke (embolism affecting < 30% of 1 brain lobe). Identification of the occluded intracranial vessel and evaluation of the extracranial carotid, extracranial vertebral, aortic arch, and proximal great vessels is required for management of both TIA or minor stroke and major ischemic stroke.[10] Hemorrhagic complications included primary intracerebral hemorrhage, hemorrhagic infarction, intracranial aneurysm, and subarachnoid hemorrhage diagnosed by CT angiography or/and MRI. The diagnosis of mycotic aneurysm was always supported by cerebral arteriography, and brain abscesses were diagnosed by CT.[11]

Statistical Analysis

Statistical analyses were performed with SPSS software version 22 for Windows (SPSS Inc., Chicago, Illinois). Data were expressed as mean ± standard deviation (SD) for interval and count (%) for categorical variables. All variables were tested for normal distribution with the Kolmogorov-Smirnov test. Categorical values were compared by the chi-square test or Fisher's exact test. To compare the mean variables between two groups, an independent t-test or Mann-Whitney U test was used. Continuous variables were compared using the two-tailed Wilcoxon test. Repeated measures ANOVA followed by a Bonferroni post-test was used to assess parametric distributions. For non-parametric distributions Friedman test was applied. P values < 0.05 were considered statistically significant.

Results

The study population consisted of 693 patients with IE, including 466 (67.2%) males and 227 (32.8%) females, at a mean age ± SD of 45 ± 16 years. Based on the modified Duke criteria, 456 (65.9%) patients had definite and 236 (34.1%) had possible IE. Moreover, there are 106 patients with definite NC and 29 patients with possible NC. The demographic, echocardiographic findings, history of disease, and predisposing factors of IE in all patients are summarized in Table 1. In this study, 16.5% of the patients had a history of stroke or TIA, and 57.2% of the patients had a vegetation size > 1 cm. The most common predisposing factors of IE were congenital heart disease (33.9%) and prosthetic valve (25.5%), respectively. The most frequently isolated microorganism in the blood cultures was *Staphylococcus aureus* (11.8%), followed by *Streptococcus viridians* (9.3%). In the first examination, upon arrival at the hospital, 91 patients had cerebral embolic events, and 2 patients had subarachnoid hemorrhage (SAH) (Table 2). In-hospital complications are shown in Table 2.

The most common NCs at discharge examination were cerebral embolic events (43 patients) and cerebral mycotic aneurysms (31 patients). Moreover, 26(36.1%) patients with NCs had positive blood cultures. There was no significant relationship between positive blood culture and NCs (P: 0.95). There was no significant relationship

Table 1. Demographic characteristics and history of disease in all patients

Characteristics	Total
Gender	
Male	466 (67.2)
Female	227 (32.8)
Age (year)	45.1 ± 16.9
Echocardiographic findings	
Vegetation	592 (85.4)
Vegetation > 1 cm	366 (57.2)
Abscess	56 (8.0)
Perforation	66 (9.5)
History of disease	
Previous stroke/TIA	115 (16.5)
Previous pulmonary embolism	10 (1.44)
Arterial hypertension	202 (29.14)
Previous hemorrhagic events	12 (1.73)
Diabetes mellitus	125 (18.03)
Predisposing factors of IE	
Congenital heart disease	235 (33.9)
Prosthetic valve	177 (25.5)
Intravenous drug user	79 (11.4)
Device-related IE	52 (7.5)
Previous infective endocarditis	60 (6.5)

Abbreviations: TIA: transient ischemic attack; IE: infective endocarditis. Continuous data are presented as mean ± standard deviation; categorical data are presented as n (%).

Table 2. Neurological complications

	On admission	In-hospital complication
Cerebral embolic events	91 (13.13)	43 (6.20)
Cerebral mycotic aneurysm	0 (0)	31 (4.47)
Subarachnoid hemorrhage (SAH)	2 (0.28)	5 (0.72)
Brain abscess	0 (0)	23 (3.31)

Data are presented as n (%).

between the type of microorganism and NCs ($P > 0.05$) (Table 3). Although this difference is not statistically significant, NCs in patients with prosthetic valves were higher than in patients with native valves (20% in patients with prosthetic valves vs. 12.4% in patients with native valves, $P = 0.47$). The type of mechanical valves in patients with NCs is shown in Table 4. The most frequently used mechanical valve in patients with NCs is the mitral valve, followed by the aortic valve. There is no significant relationship between the type of mechanical valve and NCs (Table 4). Fifteen patients (16.1%) with NCs had in-hospital mortality that was not statistically significant compared to 87 patients (17.2%) who died without NCs.

Discussion

This study and the results of the present study may help to identify IE patients who are at increased risk of NCs.

Table 3. Association between microorganism and neurological complications

	With neurological complications	Without neurological complications	*P* value
Positive blood cultures	26 (36.1)	222 (35.7)	0.95
Staphylococcus aureus	10 (13.9)	53(8.5)	0.13
Staphylococcus coagulase negative	4 (5.6)	34 (5.5)	0.97
Streptococcus viridans	5 (6.9)	37 (6)	0.74
Enterococcus	3 (4.2)	57 (9.2)	0.15
Streptococcus bovis	2 (2.8)	7 (1.1)	0.24
Pseudomonas	2 (7.7)	24 (3.9)	0.64
Brucella	0 (0)	5 (0.8)	0.44
Fungal infection (*Candida, Aspergillus*)	0 (0)	8 (1.3)	0.33
Klebsiella	0 (0)	7 (1.1)	0.36

Data are presented as n (%). Categorical variables were compared using the chi-square test or Fisher's exact test.

The outcome in these populations appears to depend on the type of event, with moderate-severe ischemic stroke and brain hemorrhage being associated with a significant excess in mortality. Most patients in our study were male, and the most infected valve was the mitral valve, and the most common microorganism was *S. aureus*. The most prevalent predisposing factor was congenital heart disease (33.9%), followed by prosthetic valve (25.5%). The total prevalence of NCs in the current study was 13.4% (93/693 patients), with embolic events being the most common complication, with a prevalence of 19%.

Clinical presentation of patients with NCs is variable and includes stroke, TIA, intracerebral or subarachnoid hemorrhage, brain abscess, meningitis, and toxic encephalopathy.[12] In this study, the most common NCs at discharge examination were cerebral embolic events and cerebral mycotic aneurysm, followed by brain abscess and subarachnoid hemorrhage (SAH). Although intracardiac vegetations can cause life-threatening embolic events, timely diagnosis with noninvasive imaging—such as echocardiography to determine their size and location—allows for prompt intervention that can prevent these complications. The overall risk of peripheral embolism is 20-50%, and once antibiotic therapy is started, this risk decreases to 6-21%.[13] The brain and the spleen are the most frequent sites of embolization in left-sided IE, while pulmonary embolism is frequent in native right-sided and pacemaker lead IE.[14]

The size of the vegetation is one of the most powerful predictors of embolic events, especially vegetation size of more than 30 mm.[15] In our study, 80% of patients with IE had vegetation, and about 60% of them had a vegetation size of more than 1 cm. Vegetation on the anterior leaflet of the mitral valve may embolize more often,[14] in line with our study. While García-Cabrera et al studied 1,345 patients with left-sided endocarditis, they reported all

Table 4. The relationship between type of mechanical valve and neurological complications

	Mitral valve	Pulmonary valve	Aortic valve	Tricuspid valve	*P* value
Patients with neurological complications	18 (31)	0 (0)	18 (16.1)	0 (0)	0.33

Data are presented as n (%). Comparisons between valve types were performed using the chi-square test.

results regarding microorganism, NCs, embolic events, age, and sex, which were similar to our findings, except that the most infected valve was the aortic valve in their study (88% mitral vs 94% aortic valve).[1]

It is advisable to revise anticoagulant therapy in episodes associated with a high risk of neurological events, such as cases caused by *S. aureus*, mitral valve involvement, and large vegetation, especially in patients with any signs or symptoms of neurological deficits. In these cases, before anticoagulant therapy, we should do 4-vessel brain angiography to recognize if there is any vessel abnormality. In larger vegetation size, we should consider early surgical intervention. Based on our findings, the risk of postoperative bleeding appears to be low in cases with small ischemic strokes when surgery is performed immediately and in moderate-severe episodes when the intervention takes place after 2 weeks. The main limitations are its single-center design, which reduces generalizability; its retrospective design, which may cause bias; and the lack of a standardized neuroimaging protocol for all patients, likely resulting in underdiagnosis of NCs. Furthermore, the relatively low rate of microorganism identification and the absence of comprehensive multivariate statistical analysis limit the ability to specify independent risk factors or make pathogen-specific conclusions.

Conclusion

Our findings demonstrate a high burden of NCs in patients with IEs. To reduce this risk, we recommend prompt initiation of empirical antibiotic therapy upon clinical suspicion of left-sided endocarditis, even before definitive microbiological identification. Considering the complexity of managing patients with NCs—especially those with large vegetations or prosthetic valves—a multidisciplinary team approach involving cardiology, infectious disease, and neurology is essential for optimizing diagnostic evaluation and determining the appropriate timing of interventions.

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Authors' Contribution

Conceptualization: xxxx
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Competing Interests

The authors declare that they have no competing interests.

Ethical Approval

This study was approved by the Rajaie Cardiovascular Medical and Research Center ethical committee according to the Declaration of Helsinki. (IR.RHC.RC.1397.060).

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Intelligence Use Disclosure

The authors used ChatGPT for editing the manuscript. The authors reviewed the text for accuracy and take full responsibility for the final content.

References

1. 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):2272-84. doi: 10.1161/circulationaha.112.000813
2. Sotero FD, Rosário M, Fonseca AC, Ferro JM. Neurological complications of infective endocarditis. Curr Neurol Neurosci Rep. 2019;19(5):23. doi: 10.1007/s11910-019-0935-x
3. Sadeghpour A, Maleki M, Boodagh S, Behjati M, Rezvani L, Ghadrdoost B, et al. Impact of the Iranian Registry of Infective Endocarditis (IRIE) and multidisciplinary team approach on patient management. Acta Cardiol. 2021;76(8):838-41. doi: 10.1080/00015385.2020.1781423
4. Snygg-Martin U, Gustafsson L, Rosengren L, Alsiö A, Ackerholm P, Andersson R, et al. Cerebrovascular complications in patients with left-sided infective endocarditis are common: a prospective study using magnetic resonance imaging and neurochemical brain damage markers. Clin Infect Dis. 2008;47(1):23-30. doi: 10.1086/588663
5. Das AS, McKeown M, Jordan SA, Li K, Regenhardt RW, Feske SK. Neurological complications and clinical outcomes of infective endocarditis. J Stroke Cerebrovasc Dis. 2022;31(8):106626. doi: 10.1016/j.jstrokecerebrovasdis.2022.106626
6. Habib G, Erba PA, Iung B, Donal E, Cosyns B, Laroche C, et al. Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study. Eur Heart J. 2019;40(39):3222-32. doi: 10.1093/eurheartj/ehz620
7. Habib G, Lancellotti P, Erba PA, Sadeghpour A, Meshaal M, Sambola A, et al. The ESC-EORP EURO-ENDO (European Infective Endocarditis) registry. Eur Heart J Qual Care Clin Outcomes. 2019;5(3):202-7. doi: 10.1093/ehjqcco/qcz018
8. Sadeghpour A, Maleki M, Movassaghi M, Rezvani L, Noohi F, Boudagh S, et al. Iranian Registry of Infective Endocarditis (IRIE): time to relook at the guideline, regarding to regional differences. Int J Cardiol Heart Vasc. 2020;26:100433. doi: 10.1016/j.ijcha.2019.100433

9. Coutts SB. Diagnosis and management of transient ischemic attack. Continuum (Minneap Minn). 2017;23(1):82-92. doi: 10.1212/con.0000000000000424
10. Musuka TD, Wilton SB, Traboulsi M, Hill MD. Diagnosis and management of acute ischemic stroke: speed is critical. CMAJ. 2015;187(12):887-93. doi: 10.1503/cmaj.140355
11. Morris NA, Matiello M, Lyons JL, Samuels MA. Neurologic complications in infective endocarditis: identification, management, and impact on cardiac surgery. Neurohospitalist. 2014;4(4):213-22. doi: 10.1177/1941874414537077
12. Thuny F, Avierinos JF, Tribouilloy C, Giorgi R, Casalta JP, Milandre L, et al. Impact of cerebrovascular complications on mortality and neurologic outcome during infective endocarditis: a prospective multicentre study. Eur Heart J. 2007;28(9):1155-61. doi: 10.1093/eurheartj/ehm005
13. Klein I, Iung B, Labreuche J, Hess A, Wolff M, Messika-Zeitoun D, et al. Cerebral microbleeds are frequent in infective endocarditis: a case-control study. Stroke. 2009;40(11):3461-5. doi: 10.1161/strokeaha.109.562546
14. Sonneville R, Mourvillier B, Bouadma L, Wolff M. Management of neurological complications of infective endocarditis in ICU patients. Ann Intensive Care. 2011;1(1):10. doi: 10.1186/2110-5820-1-10
15. Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. Eur Heart J. 2009;30(19):2369-413. doi: 10.1093/eurheartj/ehp285