

Short Communication

Embollic Stroke of Undetermined Source in Iranian Population: A Subgroup Analysis from TOSSI Study

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Keywords

- Embolic Stroke of Undetermined Source
- Incidence
- Recurrence
- Mortality
- Rate

Abstract

Reported frequency of embolic stroke of undetermined source (ESUS) ranged from 7-33%. An estimated annual stroke recurrence risk in these patients is 2.3–6.8 % and, mortality rate is 5.2%. There is no documented data about ESUS frequency and the recurrence rate in Asia. Present study aimed to demonstrate, the incidence and recurrence rate of ESUS. We analyzed the ESUS subgroup data from TOSSI study and follow them after 1 year by telephone call. All thromboembolic event including ischemic stroke, transient ischemic attack, myocardial infarction, pulmonary thromboemboli and deep vein thrombosis and all deaths was recorded. The rate of ESUS was 42.77%, higher than even reported data. ESUS recurred in 12.12% of patients during 1 year follow up. The annual mortality rate was 8.45%. In Conclusion, incidence, recurrence and mortality rate of ESUS in Iran is higher than international reported rates.

ABBREVIATIONS

ESUS: Embolic Stroke of Undetermined Source

INTRODUCTION

The clinical construct of “embolic stroke of undetermined source” (ESUS) was introduced to identify patients with non-lacunar cryptogenic ischemic strokes in whom embolism was the likely stroke mechanism, first in 2014 [1,2]. In such patients some potential embolic source (PES) can be found such as atrial cardiopathy, occult paroxysmal atrial fibrillation (AF), aortic atheromatous disease, substenotic carotid plaque, left ventricle disease, cardiac valvular disease, paradoxical embolism, cancer and other hypercoagulopathy state [3]. Reported frequency of ESUS ranged from 7% in UK to 33% in Argentina and mean of 17%. An estimated annual stroke recurrence risk in these patients is 2.3–6.8 % and, annually mortality rate is 5.2% [4].

There is no documented data about ESUS frequency and recurrence rate in Asia. The latest study from Qatar and Saudi Arabia reported ESUS frequency 30.88 % and 20% [5,6]. This study aimed to document ESUS incidence, recurrence and mortality rate.

MATERIALS AND METHODS

In TOSSI study from 166 patients underwent intravenous thrombolytic therapy, 71 (42.77%) classified as ESUS. We analyzed these ESUS subgroup data from TOSSI study and follow

them after 1 year by telephone call. All thromboembolic event including ischemic stroke, transient ischemic attack, myocardial infarction, pulmonary thromboemboli and deep vein thrombosis and all deaths was recorded. Descriptive statistics for baseline demographic, clinical were performed. For continuous variables, median and interquartile range values were calculated. For categorical variables, percentage proportions were calculated. Annual rates presented by percent per year.

The TOSSI study protocol was approved by the ethical board committee of Mazandaran University of Medical Sciences, Sari, Iran (code:IR.MAZUMS.REC.1398.718). This trial has been registered in ClinicalTrials.gov (NCT04309357). Trial protocol can be found at www.clinicaltrials.gov.

RESULTS AND DISCUSSION

The median age of patients with ESUS was about 8 years younger (67 vs 75) and primary NIHSS score was 4 point lower (8 vs 12) than others. Prior antiplatelet use and previous stroke or TIA was slightly higher in ESUS patients in comparison with other stroke subtypes. Also, 9.85% of ESUS patients had history of hypothyroidism vs 3.15 % in others. But Symptomatic hemorrhage, fatal hemorrhage and in-hospital mortality in ESUS patients was significantly lower than other stroke subtypes (Table 1). Fourteen (19.71%) patients had no PES, 32(45.07%) 1, 19(26.76%) 2 and 6(8.45%) 3 PES. During 1 year follow up Lost to follow up occurred in 5 patients; 8/66(12.12%) patient

Table 1: Patients' characteristics and clinical data.

	ESUS med/ n(IQR/%)	Other Stroke Subtypes med/ n(IQR/%)
Age	67(59-75)	75(62-80)
Male	39(54.92)	52(54.73)
NIHSS score	8(6-12)	12(10-16)
Previous stroke or TIA	19(26.70)	23(24.21)
Prior antiplatelet use	29(40.84)	36(37.89)
Hypothyroiditis	7(9.85)	3(3.15)
Diabetes mellitus	25(35.21)	28(29.47)
Hypertension	48(67.60)	64(67.36)
Hyperlipidemia	15(21.12)	25(26.31)
Coronary artery disease	24(33.80)	41(43.15)
Current smoking	9(12.67)	12(12.63)
Mild to moderate valvular heart disease	10(6.2)	20(21.05)
Substenotic carotid plaque	30(18.07)	23(24.21)
All type hemorrhage	8(11.26)	21(22.1)
Symptomatic intracerebral hemorrhage	2(2.81)	13(13.68)
Fatal hemorrhage	0	5(5.26)
In-hospital mortality	1(1.40)	24(25.26)
Annual mortality	6(8.45)	35(36.84)
Recurrence rate	8(12.12)	N/A
Sample size	71	95

had another stroke and 1 had myocardial infarction. Deep vein thrombosis, pulmonary thrombo-emboli or other systemic embolism not reported. Fifty three (80.3%) were under treatment with ASA, 10(15.15%) ASA and clopidogrel, 2(0.3%) clopidogrel and 1(1.15%) rivaroxaban. All 8 patients with recurrent stroke were receiving ASA alone. The most risk factor among patients with recurrence was hypertension (5/8) following substenotic carotid plaque (4/8), 1 had no risk factor. Annual mortality rate was 8.45% vs 36.84% in others.

When we compare our result with international studies, there is no significant difference between patients clinical phenotype and risk factors [2, 5-7], unless history of hypothyroidism. Although, thyroid hormone affects virtually every anatomic and physiologic component of the cardiovascular system [8]; we don't know this finding is accidental or there is a causative relationship.

More important observation is higher incidence, recurrence and mortality rate of ESUS in our study. One limitation of our

study was incomplete evaluations and small sample size. Patients underwent brain CT scan, transthoracic echocardiography, carotid dopplersonography, at least 24 hours cardiac monitoring; but not all patients assessed by magnetic resonance arteriography (MRA) and transoesophageal echocardiography. It is possible that, those patients in whom carotid dopplersonography showed substenotic carotid plaques had stenotic plaque if assessed by MRA or CT angiography.

CONCLUSION

In conclusion, it seems ESUS incidence and recurrence rate in Iran is high. However, for confirmation more multi-centric studies with greater sample size in Iran and other countries in Asia are recommended.

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REFERENCES

- Hart RG, Diener HC, Coutts SB, Easton JD, Granger CB, O'Donnell MJ, et al. Embolic strokes of undetermined source: the case for a new clinical construct. *Lancet Neurol*. 2014; 13: 429-38.
- Ntaios G, Perlepe K, Lambrou D, Sirimarco G, Strambo D, Eskandari A, et al. Prevalence and Overlap of Potential Embolic Sources in Patients With Embolic Stroke of Undetermined Source. *J Am Heart Assoc*. 2019; 8: e012858.
- Diener H, Bernstein R, Hart R. Secondary Stroke Prevention in Cryptogenic Stroke and Embolic Stroke of Undetermined Source (ESUS). *Curr Neurol Neurosci Rep*. 2017; 17: 64.
- Hart RG, Catanese L, Perera KS, Ntaios G, Connolly SJ. Embolic Stroke of Undetermined Source: A Systematic Review and Clinical Update. *Stroke*. 2017; 48: 867-872.
- Perkins JD, Akhtar N, George P, Salam A, Bandey H, Babu B, et al. Prevalence, Characteristics and Risk Factors for Embolic Stroke of Undetermined Source in West and South Asia and North African Population Residing in Qatar. *J Stroke Cerebrovasc Dis*. 2020; 29: 104666.
- Al Khathaami AM, Al Bdah B, Alnosair A, Alrebdi R, Alwayili S, Alhamzah S, et al. Embolic Stroke of Undetermined Source in Saudi Arabia: Prevalence, Patient Characteristics, and Outcomes. *J Stroke Cerebrovasc Dis*. 2019; 28: 104390.
- Piffer S, Bignamini V, Rozzanigo U, Poletti P, Merler S, Gremes E, et al. Different Clinical Phenotypes of Embolic Stroke of Undetermined Source: A Subgroup Analysis of 86 Patients. *J Stroke Cerebrovasc Dis*. 2018; 27: 3578-3586.
- Grais, Ira Martin, James R. Sowers. Thyroid and the heart. *Am J Med*. 2014; 127: 691-698.

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