

Clinical profile of patient with cardioembolic stroke

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Abstract

Background: Stroke is a significant global cause of both mortality and morbidity. Cardioembolic stroke comprises 15-30% of all cases of ischemic stroke. Limited clinical studies have been conducted on cardioembolic stroke, particularly in the context of India. The objective of our study was to analyze the demographic, risk factor, and clinical characteristics of patients with cardioembolic stroke in Central India.

Methods: A prospective study was conducted at the Inpatient Department of teaching hospital in Central India collecting necessary information and data from all cases diagnosed as cardioembolic stroke.

Results: 325 patients were diagnosed to have acute Ischemic stroke. Of the 38 patients (11.6%) diagnosed with cardioembolic stroke, 17 (46%) were females. Mean age was 53.5±12.2 years. Occurrence of cardioembolic stroke was seen to be higher (71% vs 28.9%, p value<0.0001) in patients of older age group (46 years or more). A significant proportion of patients of the older age group (37%) had hypertension (p value=0.0048). Coronary artery disease (CAD) was the most prevalent cardiac disorder, observed in 21 patients (55.2%), valvular heart disease in 11 patients (28.9%) and atrial fibrillation in 7 patients (18.4%). Limb weakness (84.2%) and Middle Cerebral Artery (MCA) territory (73.6%) infarct were observed in majority of the patients.

Conclusions: Prevalence of cardioembolic stroke in this region is lower than reported worldwide. While male predominance of cardioembolic stroke was noted, old age and hypertension were the major vascular risk factors identified. CAD was the major source of cardioembolism.

Keywords: Cardiac risk factors, Heart, Stroke

INTRODUCTION

Ischemic stroke is a leading cause of morbidity and mortality, and the identification of its etiology can pose challenges. The Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria is utilized to categorize subtypes of ischemic stroke according to suspected causes into five distinct groups: cardioembolic (CE) stroke, large-artery atherosclerosis, small vessel disease, other known causes, and undetermined causes.[1] According to research, CE strokes, which account for over 25% of all strokes, have been found to be associated with more severe clinical outcomes, heightened disability, and increased mortality rates.[2] All stroke etiologies exhibit a substantial degree of overlap in their risk factor profiles. It is worth noting that the risk of stroke in cardioembolic (CE) stroke caused by atrial flutter (AF) is influenced by systemic risk factors, including those encompassed by the CHA₂DS₂-VASC score.[3] However, it should be noted that certain risk factors have the potential to contribute to the development of both large artery atherosclerosis and small vessel disease. Additionally, it is widely believed that these vascular risk factors play a role in the occurrence of cardioembolic (CE) stroke by contributing to the formation of a left atrial substrate, also known as atrial cardiomyopathy. This condition increases the likelihood of developing blood clots and atrial fibrillation. Identifying these factors in cardioembolic stroke may aid in the stratification of risk and the implementation of preventive strategies.

Stroke is a significant contributor to both morbidity and mortality worldwide. Specifically, cardioembolic stroke is responsible for 14-30% of all cases of cerebral infarctions globally.[4-8]. Cardioembolic stroke exhibits greater severity and recurrence rates compared to non-cardioembolic stroke.

Due to shifting demographic profiles and rising life expectancies, low and middle-income countries are experiencing a growing prevalence of risk factors for cardiac embolism. It is projected that these risk factors will triple by the year 2050.[9]The user's text is too short to rewrite. Embolism from the heart to the brain can occur through three mechanisms: blood stasis and thrombus formation in an enlarged left cardiac chamber, release of material from an abnormal valvular surface, and atrial fibrillation resulting in inadequate contraction and stasis primarily in the left atrial appendage. Rheumatic heart disease and ischemic heart disease are the primary causes of cardioembolic stroke in India, accounting for 29% and 27% respectively. However, globally, atrial fibrillation is the most common risk factor for cardioembolic stroke.[10] Early confirmation of cardioembolic stroke is essential for effective management and can significantly decrease the risk of stroke recurrence. This is due to the fact that cardioembolism leads to more severe strokes and has a higher recurrence rate compared to other types of ischemic stroke.[11] High-risk sources of cardiac embolism include

atrial fibrillation or flutter, rheumatic heart disease (RHD), systolic heart failure, mechanical prosthetic valve, left atrial or ventricular thrombus, recent myocardial infarction (<4 weeks), dilated cardiomyopathy, infective endocarditis, regional left ventricular akinesia, atrial myxoma, and patent foramen ovale with thrombus. This study aimed to investigate the demographic and clinical profiles, prevalence, and risk factors of cardioembolism in the Central Indian population. Limited clinical studies on cardioembolic stroke in India have prompted the need for further research in this area.

METHODS

This study was a prospective observational study conducted Department of Cardiology and Neurology at Sri Aurobindo Medical College and Mohak Superspeciality Hospital-Indore. Duration 12 Months January 2022 to December 2022. The Institutional Ethics Committee approved the study protocol, and permission from the hospital superintendent was obtained before the initiation of the study.

That included patients diagnosed with cardioembolic stroke. Stroke is characterized by a sudden onset of localized neurological impairment, which is confirmed through brain imaging techniques such as computed tomography (CT) or magnetic resonance imaging (MRI). A neurologist confirmed the presence of a cardioembolic stroke by assessing the patient's clinical presentation, neuroimaging profile, and evidence of a high-risk cardiac source through Echocardiography and Electrocardiogram. Additionally, the possibility of a large-artery plaque was ruled out. All patients with confirmed diagnosis of cardioembolism were recruited consecutively after obtaining consent from the patients themselves or their relatives. A proforma was used to assess demographic and clinical profiles, as well as vascular risk factors and risk factors for cardioembolism. The collected details were meticulously analyzed and documented by a certified neurologist.

The study included patients aged 18 years and older who had been diagnosed with cardioembolic stroke and had completed their workup. Participants who did not provide consent, as well as children and pregnant women, were excluded from the study. A structured proforma was used to collect reliable variables including demographic details, vascular risk factors, co-morbid illnesses, associated cardiac illnesses, clinical features, and echocardiographic findings. The patient's demographic characteristics, such as age, sex, and length of hospitalization, were recorded. Data on the medical history of diabetes mellitus, hypertension, heart disease, prior stroke, migraine, thyroid disorder, and any other relevant medical conditions were gathered. The study incorporated laboratory parameters, including fasting lipid profile and glycosylated hemoglobin. The study also considered the individual's habitual history of smoking, alcohol use, or tobacco chewing. Information on the location of the stroke, whether it was cortical or subcortical, and the occurrence of haemorrhagic conversion of the infarct was gathered. The necessity of triple therapy, which includes both dual antiplatelet therapy and oral anticoagulant, as compared to using only an anticoagulant, was also validated.

RESULTS

Among the cohort of 651 individuals with acute Ischemic stroke, a total of 76 patients (11.6%) were identified as having experienced a cardioembolic stroke within the preceding five-year period. The initial characteristics of the study participants. The average age of individuals diagnosed with cardioembolic stroke was 53.5 ± 12.2 years, with a range of 30 to 81 years. Among the patient population, 41 individuals (53.9%) were male, while 35 individuals (46%) were female. The male to female ratio observed in the study was 1.17:1. Among the patients, 22 individuals (28.9%) experienced an early occurrence of stroke, defined as stroke occurring at or before the age of 45. On the other hand, 54 patients (71%) experienced stroke at an older age. The study observed a higher incidence of cardioembolic stroke in patients belonging to the older age group (46 years or above), and this correlation was found to be statistically significant (p value < 0.0001). There were no statistically significant differences observed in the age of onset of cardioembolic stroke between male participants (mean age = 53 ± 12 years) and female participants (mean age = 54.2 ± 12.5 years). Among patients with cardioembolism, hypertension was identified as the most prevalent vascular risk factor, accounting for 57.8% of cases (Table 1).

Table 1: Baseline characteristics of patients with cardio-embolic stroke.

Variables	N (%)
Male	41 (53.9)
Age group (years)	
≤45	22 (28.9)
>45	54 (71)
Smoking	26 (34.2)
Alcohol use	23 (30.2)
Diabetes mellitus	31 (40.7)
Hypertension	44 (57.8)
Prior stroke	5 (6.5)

Thyroid disease	4(5.2)
Hyperlipidemia	28 (36.8)

The present inquiry pertains to the identification and examination of risk factors associated with cardioembolic stroke. The prevailing cardiac disorder linked to cardioembolism in the current investigation was coronary artery disease (CAD). Approximately 42 patients, accounting for 55.2% of the total, were diagnosed with coronary artery disease (CAD), while valvular heart disease was observed in 22 patients, representing 28.9% of the sample (Table 2).

Additional subgroup analysis was conducted, dividing the participants into two groups based on the age at which they experienced the onset of stroke. The first group consisted of individuals aged 45 years or younger, while the second group included those aged 46 years or older. There was a statistically significant difference in the prevalence of hypertension between the older age group (46 years or more) and the younger group, with a higher proportion of patients in the older age group exhibiting hypertension (p-value=0.0048). In comparison to the younger population experiencing early onset of cardioembolic stroke, the older age group exhibited a greater prevalence of coronary artery disease (CAD) at a rate of 61.1% and cardiomyopathy at a rate of 22.2%. However, the observed difference did not reach statistical significance. The prevalence of valvular heart disease (40.9%) and left ventricle apical clot (22.7%) was observed to be significantly higher in the younger age group compared to the older age group, as indicated in Table 4.

Table 2: Cardiac disorders observed in study group.

Cardiological abnormalities	N (%)
Coronary artery disease	42 (55.2)
Valvular heart disease	22 (28.9)
Cardiomyopathy	14 (18.4)
Arrhythmia	15 (19.7)

The study revealed that within the population of individuals diagnosed with coronary artery disease (CAD), the primary cause of cardioembolism was identified as left ventricular (LV) dysfunction characterized by a low ejection fraction, specifically less than 55%. In the study population, a total of 22 patients, accounting for 52.3% of the sample, exhibited left ventricular dysfunction characterized by a low ejection fraction. The minimum recorded ejection fraction among these patients was 28.6%, as indicated in Table 3. Chronic Rheumatic Heart Disease (CRHD) and atrial fibrillation have been identified as potential etiologies for high source cardiac embolism, as indicated in Table 3. Cardioembolic stroke was attributed to 21% of cases, with CRHD being the leading cause, while atrial fibrillation accounted for 18.4% of cases.

Table 3: Specific cardiac disorder observed in study population.

Variables	Number (n=76) (%)
Atrial fibrillation (AF)	14 (18.4)
Valvular AF	9 (64.2)
Non-valvular AF	5 (35.7)
Junctional rhythm	1 (1.3)
Chronic Rheumatic Heart disease (CRHD)	16 (21)
Prosthetic valve replacement done	10 (62.5)
No valve replacement	6 (37.5)
Recent Myocardial Infarction (MI)	12 (15.7)
Anteroseptal MI	6 (50)
Inferior wall MI	3 (25)
Anterolateral MI	3 (25)
Dilated cardiomyopathy	12 (15.7)
Alcoholic	6 (50)
Ischemic	4 (33.3)
Combined	2 (16.6)
Restricted cardiomyopathy	2 (2.6)
Non Rheumatic valvular disease	6 (7.8)
Ischemic	4 (66.6)
Sclerotic valvular disease	2 (33.3)
Left ventricle apical clot	9 (11.8)
Left ventricular dysfunction and low ejection fraction (<55%)	22 (28.9)

The clinical characteristics

The prevailing clinical manifestation observed in the majority of cases was limb weakness, specifically characterized by focal deficit. Hemiparesis was observed in 61.8% of the patients, hemiplegia in 22.3%, and aphasia in 11.8% of the patients. The average duration of hospitalization was found to be 11±6 days. A significant proportion of the patients (50%) exhibited a Modified Rankin Score of 4 upon admission.

The current investigation revealed that there was a predominance of cardioembolic infarction in the anterior circulation. The results of neuroimaging indicated the presence of a Middle cerebral artery infarct (MCA) in 56 individuals, accounting for 73.6% of the total sample. Additionally, multiple artery infarcts were observed in 6 patients, representing 7.8% of the sample. Out of the individuals who experienced MCA territory infarcts, it was observed that a total of 32 patients (57.1%) had incurred a non-dominant right MCA territory infarct. The majority of patients exhibited multiple infarcts in the middle cerebral artery (MCA), while a minority presented with single large infarcts in the striatocapsular and capsuloganglionic regions. The patient presented with multiple instances of arterial infarction, which encompassed combined involvement of the anterior circulation, specifically the middle cerebral artery (MCA) and the anterior cerebral artery (ACA). Additionally, there were cases of combined anterior and posterior circulation infarctions, involving the MCA, posterior cerebral artery (PCA), and infarctions in the cerebellum. A total of 8 patients, accounting for 10.5% of the sample, experienced baseline haemorrhagic transformation. The overwhelming majority of cardioembolic strokes in this study were found to have lesions in a cortical territory, as evidenced by 59 patients, accounting for 77.6% of the total sample (Table 5).

Table 4: Comparison between patients of young and older age onset cardioembolic stroke.

Study variables	Older age (46 years and more) n=54 (%)	Young age (≤45 years) n=22	P value
Mean age	59.6±7.9	38.1±5.1	<0.0001
Male	29 (53.7)	12 (54.5)	1
female	25 (46.2)	10 (45.4)	1
Hypertension	37 (68.5)	7 (31.8)	0.0048
Diabetes mellitus	25 (46.2)	6 (27.2)	0.19
Smoking/ tobacco use	20 (37)	6 (27.2)	0.59
Alcohol use	18 (33.3)	5 (22.7)	0.42
CAD	33 (61.1)	9 (40.9)	0.13
Valvular heart disease			
	10 (18.5)	9 (40.9)	0.07
Cardio- myopathy	12 (22.2)	1 (4.5)	0.09
Atrial fibrillation	10 (18.5)	3 (13.6)	0.7
LV apical clot	5 (9.2)	5 (22.7)	0.14

CAD-Coronary artery disease, LV- Left ventricle

Table 5: Neuroimaging profile of patients with cardioembolic stroke.

Radiological variables	Number (%)
MCA territory infarct	56 (73.6)
ACA territory infarct	3 (3.9)
PCA territory infarct	2 (2.6)
Multiple artery infarcts	6 (7.8)
Cerebellar infarcts	4 (5.2)
Cortical infarcts	59 (77.6)
Subcortical infarcts	9 (11.8)
Baseline haemorrhagic transformation	8 (10.5)

MCA- Middle cerebral artery, ACA-Anterior cerebral artery, PCA-Posterior cerebral artery

The initial treatment for the majority of patients consisted of low molecular weight heparin (LMWH), which was subsequently followed by the administration of a bridging oral anticoagulant. The subsequent therapeutic protocol was observed: In this study, oral anticoagulant therapy was administered as the sole treatment in 28 patients, accounting for 36.8% of the total sample. Double antiplatelet therapy was prescribed to 27 patients, representing 35.5% of the sample. A triple treatment regimen, consisting of oral anticoagulant therapy and double antiplatelet therapy, was administered to 11 patients, accounting for 14.4% of the sample. In addition, oral anticoagulant therapy in combination with a single antiplatelet agent (specifically ecosprin 150 mg) was prescribed to 9 patients, representing 11.8% of the sample. Lastly, a single antiplatelet agent was administered to 2 patients, accounting for 2.6% of the sample. A solitary patient received a

more recent form of oral anticoagulant. The selection of treatment protocols for various conditions was determined by evaluating the CHADS2 score, which stands for congestive heart failure, hypertension, age, diabetes mellitus, and stroke, as well as the presence of haemorrhagic manifestations, both intracranial and extracranial.

DISCUSSION

The incidence of cardioembolic stroke in India appears to be lower in comparison to the rates reported in Western countries, with estimates ranging from 10% to 15% in India and 15% to 30% in Western populations.[12-16] In the current investigation, a total of 76 individuals were identified as having experienced cardioembolic stroke out of a larger cohort of 651 cases of ischemic stroke, representing an incidence rate of 11.6%. The prevalence observed in this study aligns with the findings reported in prior studies conducted in India. One potential explanation for the low occurrence rate could be attributed to the limited utilization of transoesophageal echocardiography and Holter monitoring in all instances, which can be attributed to resource constraints. Individuals diagnosed with cardioembolic stroke are particularly vulnerable to both immediate and prolonged instances of recurrence. Hence, timely confirmation and diagnosis of cardioembolic infarction are of utmost significance in the commencement of anticoagulation therapy for an appropriate secondary preventive measure. Oral anticoagulant therapy has been shown to be effective in reducing the incidence of strokes in patients diagnosed with atrial fibrillation (AF), the most prevalent cardioembolic risk factor. Studies have demonstrated that this treatment can prevent up to 70% of strokes in these individuals. The number provided by the user is 20. To date, a universally accepted gold standard or definitive diagnostic criteria for cardioembolic stroke has not been established. The diagnosis primarily relies on the presence of characteristic clinical manifestations, analysis of neuroimaging findings, identification of the source of cardioembolism, and the exclusion of plaque-related large vessel disease.[17,18,19] There is a scarcity of data pertaining to cardioembolic stroke in South Asian nations. Therefore, conducting a comprehensive investigation to evaluate the frequency, vascular risk factors, clinical characteristics, and cardiac etiology of embolism would undoubtedly yield a more profound understanding of the risk of stroke in this specific population subset hailing from South India.

According to our research, it was found that cardioembolic stroke constituted 11.6% of all cases of ischemic strokes. This observation aligns with the prevailing trend observed in hospital-based studies conducted in Hyderabad, a city located in South India, as well as other regions across Asia.[15,16,20,21] Registries originating from Western countries, such as North America, the United Kingdom, and Europe, have documented a comparatively elevated prevalence rate ranging from 15% to 30%.[12-14,22] can be rewritten in a more academic manner The Indo-US Collaborative Stroke Project revealed that India had a higher proportion (24.9%) of cardioembolic stroke cases compared to other countries involved in the study.[23]

Regarding the limitations of our study, it is plausible that certain instances of cardioembolism may have gone unnoticed within our cohort. The utilization of various diagnostic techniques such as continuous electrocardiogram (ECG) recording, Holter monitoring, and transoesophageal echocardiography may have led to the identification of a substantially larger percentage of cardioembolic strokes within the undetermined stroke subgroups.[24] One additional limitation of the study pertained to the relatively low incidence of cardioembolic stroke observed in the population of Hyderabad. Previous research conducted in this particular region indicated a comparable prevalence rate to that observed in other regions. However, it is important to note that racial and ethnic factors exhibit regional variations, which consequently influence the distribution of ischemic stroke subtypes.

Within our cohort, the risk factor profile revealed that hypertension was the primary risk factor linked to cardioembolic stroke. The observed association demonstrated statistical significance (p value < 0.0001) among patients in the older age group as compared to those in the younger age group. Hypertension is widely recognized as the prevailing health condition among individuals, with approximately one in every eight individuals in India experiencing high blood pressure, as reported by the National Family Health Survey. This survey encompassed a substantial sample size of 22.5 million adults residing in 100 districts across India in the year 2017. Cardiac involvement commonly manifests in individuals diagnosed with hypertension. Recent studies have indicated that the use of angiotensin converting enzyme (ACE) inhibitors and angiotensin 1 (AT1) receptor blockers for the treatment of elevated blood pressure may effectively prevent the occurrence of cardiac arrhythmia and significantly reduce the incidence of atrial fibrillation, in comparison to alternative antihypertensive treatments.[25] Therefore, the timely detection and management of hypertension are of utmost importance in the prevention of cardioembolic stroke among individuals in the South Indian population subgroup.

In our cohort, we observed that coronary artery disease (CAD) and valvular heart disease were the primary cardiac sources of embolism. This finding aligns with the report by Kaul *et al.* conducted in South India. A total of 55.2% of the patients included in the study exhibited a medical history of coronary artery disease (CAD) or had recently been diagnosed with CAD. A myocardial infarction of recent occurrence was observed in 15.7% of the patients.[15] Extensive documentation exists regarding the occurrence of stroke within a specific timeframe following acute myocardial infarction, indicating that approximately 2.5% of patients are affected within a period of 2 to 4 weeks subsequent to the

infarction event. Cardioembolic stroke in patients with coronary artery disease (CAD) is primarily attributed to several factors, including left ventricular (LV) dysfunction characterized by a low ejection fraction (less than 55%), the presence of a left ventricular aneurysm or thrombus, and the occurrence of associated arrhythmias such as atrial fibrillation.[12,13] Within our study group, it was observed that individuals with coronary artery disease (CAD) predominantly experienced cardioembolism as a result of left ventricular (LV) dysfunction, which was characterized by a low ejection fraction of 52.3%. This underscores the necessity of implementing preventive measures aimed at patients with coronary artery disease (CAD) and ensuring appropriate anticoagulation and medical monitoring for these cohorts. In the present study, it was observed that valvular heart disease accounted for 28.9% of the cardiac risk factors. It is worth noting that a significant proportion of the patients included in the study were diagnosed with chronic rheumatic heart disease (CRHD). A total of 21% of the patient population received a diagnosis of chronic rheumatic heart disease (CRHD), while the remaining patients exhibited valvular involvement as a result of ischemic heart disease and sclerotic valvular disease. Research conducted in India has indicated that cardioembolic stroke in young adults is predominantly caused by CRHD (rheumatic heart disease) and prosthetic valves, accounting for approximately 66% of cases.[26] The current study yielded comparable results, indicating a higher prevalence of valvular heart disease among younger individuals and coronary artery disease among older patients with cardioembolic stroke. This finding stands in stark contrast to the research conducted in developed nations, which indicates that only 2.5% of cardiac risk factors can be attributed to valvular heart disease in cases of cardioembolism.[27] secondary inflammatory reactions, deposition of fibrous tissue, erosions on the luminal surface, and the frequent occurrence of mobile thrombi that extend into the lumen of major arteries such as the aorta and carotids.[28] Cardioembolic strokes can be distinguished from other types of strokes through the identification of atherosclerotic plaque in major blood vessels. This can be achieved by conducting a magnetic resonance angiogram (MRA) or a computed tomography angiogram (CTA) of the brain and neck vessels, which may extend to the aorta. The identification of cardiac abnormalities, whether they are structural or functional, provides indications of the possibility of cardioembolism. This is due to the fact that both types of embolism exhibit similar clinical presentations. Atherosclerotic plaques that develop in the carotid arteries have a significantly higher propensity to embolize to the brain, resulting in the occurrence of stroke or transient ischemic attack (TIA). In our study, the utilization of neck vessel Doppler, MR angiogram of the brain and neck, and 2D Echo played a crucial role in distinguishing between cardioembolic stroke and artery-to-artery embolism.

Arterial embolic stroke is predominantly observed to arise from the left heart as a result of structural or functional abnormalities. Arterial embolism arising from the arterial tree itself is a consequence of atherosclerosis. In the context of artery to artery embolism, the accumulation of cholesterol and other lipids takes place in the intimal-medial layer. Cardiac emboli originating from the cardiac chambers frequently manifest as sizable entities, leading to significant instances of stroke, resulting disability, and mortality. Additionally, there is a high likelihood of both early and late embolic recurrences. Therefore, it is imperative to promptly identify cardioembolic stroke in order to determine the most suitable treatment approach (anticoagulation) and preventive measures.

Nevertheless, it is important to acknowledge that the present study does have certain limitations. Initially, it should be noted that not all patients underwent transoesophageal echocardiography and Holter monitoring. Furthermore, the follow-up period in the study only extended until the point of discharge, thus preventing the establishment of recurrence rates and mortality outcomes at the 90-day mark. Furthermore, it should be noted that due to the hospital-based nature of the study, the findings cannot be extrapolated to the broader general population. However, notwithstanding the limitations, this current investigation represents, to the best of our understanding, the inaugural single-center prospective study conducted over a span of 5 years, with a specific focus on patients diagnosed with cardioembolic stroke originating from South Asia. This study emphasizes that hypertension and coronary artery disease (CAD) are significant contributors to the development of cardioembolism. Therefore, it is imperative to conduct a thorough assessment of each patient in order to identify the risk factors and establish a diagnosis of cardioembolic stroke.

CONCLUSION

The current investigation, conducted using a hospital-based registry in South India, has effectively established a comprehensive database pertaining to cardioembolic stroke within this particular geographic area. The prevalence of cardioembolic stroke in the studied population was observed to be comparable to that of other South Asian countries, yet lower than the reported rates in the Western stroke registry. Cardioembolic stroke exhibited a greater incidence of old age onset and a higher prevalence among males. Hypertension persisted as the primary vascular risk factor, while coronary artery disease (CAD) emerged as the principal cardiac risk factor within the studied population. Understanding these risk factors will be essential in the development and implementation of strategies for effective management of cardioembolic stroke and the establishment of healthcare systems in South India.

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