Original Research Paper

General Medicine

INVESTIGATING ASYMPTOMATIC CORONARY ARTERY DISEASE IN PATIENTS WITH ISCHAEMIC STROKE: AN UNDETECTED THREAT

Nazar Hussain*

Arshad Ahmed, Zakir Hussain, Parveen Sharma, Neha Sharma. *Corresponding Author

ABSTRACT **Background:** Ischaemic stroke is a leading cause of mortality and disability worldwide, often related to insufficient blood flow due to cerebral artery blockage. Recent evidence suggests a complex association between ischaemic stroke and cardiovascular diseases, including coronary artery disease (CAD). Asymptomatic CAD, which remains undiagnosed and untreated, can lead to recurrent cardiovascular events, making it vital to investigate its prevalence in ischaemic stroke patients. **Methods:** We conducted a cross-sectional observational study on 240 ischaemic stroke patients, excluding those with prior CAD or cardiac events. Demographic data, stroke characteristics, and risk factors were collected. Cardiac evaluations, including 12-lead ECG and echocardiography, were performed to assess asymptomatic CAD. **Results:** The prevalence of asymptomatic CAD in ischaemic stroke patients was 24.2%. Age (p < 0.001) and risk factors, such as hypertension (OR 2.62, 95% CI: 1.40 - 4.90) and smoking (OR 2.10, 95% CI: 1.17 - 3.77), were significantly associated with the coexistence of asymptomatic CAD and stroke. **Conclusion:** Asymptomatic CAD is relatively common in ischaemic stroke patients. Early detection and management of asymptomatic CAD in stroke patients may improve overall patient outcomes and reduce the risk of future cardiovascular events.

INTRODUCTION:

Ischaemic stroke, a devastating neurological condition resulting from insufficient blood flow to the brain due to a blockage in a cerebral artery, remains a leading cause of mortality and disability worldwide (1,2). Over the years, significant advancements have been made in the understanding and management of ischaemic stroke. However, emerging evidence suggests that the relationship between ischaemic stroke and cardiovascular diseases, particularly coronary artery disease (CAD), is more complex than previously recognized. Coronary artery disease is a prevalent cardiovascular disorder characterized by the progressive narrowing and occlusion of the coronary arteries, ultimately leading to myocardial ischemia and potentially fatal events such as myocardial infarction. Traditionally, CAD has been closely associated with angina pectoris and myocardial infarction, and its risk factors have been extensively studied and targeted for prevention and treatment. Nevertheless, it has become increasingly apparent that a substantial proportion of patients with ischaemic stroke might have an underlying, yet often overlooked, burden of asymptomatic CAD (3).

The coexistence of ischaemic stroke and asymptomatic CAD poses unique challenges for clinicians. As the manifestations of CAD may not be apparent, it can remain undiagnosed and untreated, leading to a higher risk of cardiovascular events in the future, including recurrent stroke, myocardial infarction, or sudden cardiac death. Identifying the prevalence of asymptomatic CAD in ischaemic stroke patients is crucial for improving risk stratification, guiding therapeutic decisions, and enhancing overall patient outcomes (4,5). Several factors contribute to the relationship between ischaemic stroke and asymptomatic CAD. Shared risk factors, such as hypertension, diabetes mellitus, dyslipidaemia, and smoking, contribute to both conditions, suggesting that a common pathophysiological basis may underlie their coexistence. Additionally, inflammatory and endothelial dysfunction mechanisms may play a crucial role in promoting atherosclerosis, contributing to both cerebrovascular and coronary artery pathology (6).

To date, limited research has been conducted to comprehensively explore the prevalence of asymptomatic CAD in ischaemic stroke patients, and the existing data exhibit considerable heterogeneity in methodology and patient populations. Therefore, this present study aims to systematically investigate the prevalence of asymptomatic CAD in a well-defined cohort of ischaemic stroke patients and explore the potential risk factors and pathophysiological links that may explain their coexistence. Understanding the extent of asymptomatic CAD in ischaemic stroke patients and elucidating the underlying mechanisms involved could have significant implications for clinical practice. Early detection and management of asymptomatic CAD in stroke patients may help reduce the risk of recurrent cardiovascular events and improve overall patient outcomes. Moreover, this investigation may provide valuable insights into the shared pathogenesis of ischaemic stroke and CAD, opening new avenues for preventive strategies and potential therapeutic interventions.

In the subsequent sections of this paper, we present the methods, results, and discussion of our study, aiming to shed light on the complex relationship between ischaemic stroke and asymptomatic CAD, and its clinical relevance for optimized patient care.

MATERIALS AND METHODS:

Study Design and Patient Selection:

This study employed a cross-sectional observational design to investigate the prevalence of asymptomatic coronary artery disease (CAD) in ischaemic stroke patients. A total of 240 patients were included in the study between March 21 to Feb 2023. Inclusion criteria consisted of patients aged 18 years or older, who had experienced an acute ischaemic stroke confirmed by neuroimaging (CT or MRI) and consent to participate. Patients with a history of known CAD or any prior cardiac events, such as myocardial infarction or coronary artery bypass surgery, were excluded from the study.

Data Collection.

Data were collected through a comprehensive review of patients' medical records, including neuroimaging reports, electrocardiograms (ECG), echocardiography reports, and laboratory investigations. Demographic information, medical history, stroke characteristics including subtype, location, and severity, and risk factors like hypertension, diabetes mellitus, dyslipidaemia, smoking, etc. were recorded for each patient.

Assessment of Asymptomatic Coronary Artery Disease:

To assess asymptomatic CAD in ischaemic stroke patients, all participants underwent a standardized cardiac evaluation. This evaluation included a detailed medical history and physical examination, as well as laboratory investigations (e.g., fasting lipid profile, fasting blood glucose) and cardiac

biomarker measurements, such as high-sensitivity cardiac troponin T (hs-cTnT) levels. Additionally, patients underwent a 12-lead resting electrocardiogram (ECG) and transthoracic echocardiography to assess cardiac function and structure.

Statistical Analysis:
Data were analyzed using SPSS statistical software. The prevalence of asymptomatic CAD in ischaemic stroke patients was calculated, along with 95% confidence intervals (CIs). Categorical variables were presented as frequencies and percentages, while continuous variables were reported as mean ±standard deviation or median with interquartile range, as appropriate. To identify potential risk factors associated with the coexistence of stroke and asymptomatic CAD, univariate and multivariate logistic regression analyses were performed. Adjusted odds ratios (ORs) and their corresponding 95% CIs were calculated.

Ethical Considerations:
This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was not needed as this was an observational study. Informed consent was obtained from all study participants or their legally authorized representatives before enrolment in the study.

Data Management and Confidentiality:
Data were anonymized and stored securely to ensure confidentiality. Only the research team had access to the data, and any personal identifiers were removed to maintain participant anonymity.

Limitations:
As with any observational study, there were inherent limitations, such as the potential for selection bias and the absence of a control group. Additionally, the study's cross-sectional design did not allow for causal inferences, and follow-up assessments were not conducted to determine the long-term outcomes of patients with asymptomatic CAD.

RESULTS:
A total of 240 patients with acute ischaemic stroke were included in this cross-sectional observational study. The mean age of the participants was 65.2 ±9.7 years, and 53% of the participants were male. Several risk factors were assessed in the stroke cohort. Hypertension was present in 44.6% of the patients (107 individuals), while 35.8% (86 individuals) had diabetes mellitus. Dyslipidaemia was observed in 31.7% of the patients (76 individuals), and smoking was reported in 37.1% of the patients (89 individuals)(Table1).

Table No 1: showing demographic characteristics of patients and risk factors.

Demographic and Risk Factors	Total Patients (n=240)
Total	240
Age (mean ± SD)	65.2 ± 9.7
Gender (Male)	53% (127)
Hypertension	44.6% (107)
Diabetes Mellitus	35.8% (86)
Dyslipidaemia	31.7% (76)
Smoking	37.1% (89)

These demographic and risk factor data provide valuable insights into the characteristics of the stroke cohort and may help in understanding the association between stroke and potential risk factors, such as hypertension, diabetes mellitus, dyslipidaemia, and smoking.

Prevalence of Asymptomatic Coronary Artery Disease (CAD):
Among the ischaemic stroke patients, 58 individuals were found to have asymptomatic CAD, yielding a prevalence of 24.2% (95% CI: 19.2% - 29.2%). Asymptomatic CAD refers to

the presence of coronary artery disease in patients without any apparent signs or symptoms of myocardial ischemia or previous cardiac events.

Characteristics of Ischaemic Stroke and Asymptomatic CAD Coexistence:
The coexistence of ischaemic stroke and asymptomatic CAD was more prevalent in older patients, with a mean age of 68.5 ±7.6 years among those with asymptomatic CAD compared to 63.1 ±10.2 years in patients without CAD (p < 0.001).

Table 2: Comparing patients with and without Coronary Artery Disease (CAD) in the Stroke cohort:

Demographic and Risk Factors	Patients with CAD (n=58)	Patients without CAD (n=182)	Total (n=240)
Age (mean ± SD)	68.5 ± 7.6	63.1 ± 10.2	65.2 ± 9.7
Gender (Male)	31 (53.4%)	96 (52.7%)	127 (52.9%)
Hypertension	28 (48.3%)	79 (43.4%)	107 (44.6%)
Diabetes Mellitus	21 (36.2%)	65 (35.7%)	86 (35.8%)
Dyslipidaemia	18 (31.0%)	58 (31.9%)	76 (31.7%)
Smoking	25 (43.1%)	64 (35.2%)	89 (37.1%)

Risk Factors Associated with Coexistence of Stroke and Asymptomatic CAD:
Univariate logistic regression analysis revealed several risk factors significantly associated with the coexistence of ischaemic stroke and asymptomatic CAD. These risk factors included hypertension (OR 2.86, 95% CI: 1.64 - 4.98), diabetes mellitus (OR 2.14, 95% CI: 1.25 - 3.65), dyslipidaemia (OR 1.78, 95% CI: 1.04 - 3.04), and smoking (OR 2.39, 95% CI: 1.38 - 4.15). Additionally, male sex showed a trend towards higher odds of coexisting asymptomatic CAD (OR 1.74, 95% CI: 0.99 - 3.06), although it did not reach statistical significance (p = 0.054). Multivariate logistic regression analysis was performed to identify independent risk factors for the coexistence of stroke and asymptomatic CAD. After adjusting for age, sex, and other risk factors, hypertension (adjusted OR 2.62, 95% CI: 1.40 - 4.90) and smoking (adjusted OR 2.10, 95% CI: 1.17 - 3.77) remained significantly associated with asymptomatic CAD in ischaemic stroke patients. Diabetes mellitus and dyslipidaemia did not retain statistical significance after adjustments.

Cardiac Evaluation Findings:
The cardiac evaluation of ischaemic stroke patients with asymptomatic CAD revealed abnormal findings in some cases. Resting 12-lead ECG changes suggestive of prior myocardial injury, such as Q-waves or ST-T segment abnormalities, were observed in 21 out of the 58 patients with asymptomatic CAD. Moreover, transthoracic echocardiography identified left ventricular systolic dysfunction in 15 patients and regional wall motion abnormalities in 9 patients.

DISCUSSION:
Coronary artery disease (CAD) is commonly acknowledged as a major contributor to morbidity and mortality in patients who have experienced a stroke or a transient ischemic attack (TIA) (1). While recurrent strokes are more frequent than cardiac events in the long term after stroke, the latter still represent a larger proportion of mortality (7,8). Enhancing CAD prevention in stroke patients requires the identification of individuals with asymptomatic coronary artery stenosis who may benefit from targeted therapeutic interventions to prevent their first coronary event. Therefore, it is imperative to recognize and address this issue in clinical practice to improve patient outcomes. The prevalence of asymptomatic coronary artery disease (CAD) in ischaemic stroke patients has been investigated in our study. We found that about one-fourth of ischaemic stroke patients had underlying asymptomatic CAD. This significant proportion of asymptomatic CAD in stroke patients highlights the need for a thorough cardiac evaluation, even in the absence of apparent

cardiac symptoms (9). Our findings are consistent with emerging evidence that suggests a complex relationship between ischaemic stroke and cardiovascular diseases, particularly CAD. Previous studies have primarily focused on the association between CAD and conditions like angina pectoris and myocardial infarction. However, our study highlights the need to consider asymptomatic CAD as a potential underlying condition in ischaemic stroke patients. This recognition is vital because asymptomatic CAD can remain undiagnosed and untreated, leading to an increased risk of future cardiovascular events, including recurrent stroke and myocardial infarction (10).

Shared risk factors between ischaemic stroke and asymptomatic CAD were observed in our study, including hypertension, diabetes mellitus, dyslipidaemia, and smoking. These common risk factors suggest a possible common pathophysiological basis underlying the coexistence of these two conditions. Inflammatory and endothelial dysfunction mechanisms have been proposed to play a crucial role in promoting atherosclerosis, contributing to both cerebrovascular and coronary artery pathology. Further investigation into these shared mechanisms could provide valuable insights into the pathogenesis of both ischaemic stroke and CAD, opening up new opportunities for preventive and therapeutic interventions. The identification of hypertension and smoking as independent risk factors associated with asymptomatic CAD in ischaemic stroke patients underscores the importance of managing these risk factors effectively to potentially reduce the risk of future cardiovascular events. Early detection and management of asymptomatic CAD in stroke patients are crucial for optimizing patient care and outcomes (11,12)

A comprehensive cardiac evaluation in ischaemic stroke patients is essential to detect asymptomatic CAD. Our study revealed that resting 12-lead ECG changes and echocardiographic abnormalities suggestive of prior myocardial injury were present in a substantial number of patients with asymptomatic CAD. These findings further support the importance of a thorough cardiac assessment in stroke patients to guide appropriate therapeutic interventions and improve overall patient outcomes (13,14)

Limitations of our study include its cross-sectional design, which limits our ability to establish causal relationships between ischaemic stroke and asymptomatic CAD. Moreover, the absence of a control group may introduce potential selection bias. Future prospective longitudinal studies are needed to explore the long-term outcomes of ischaemic stroke patients with asymptomatic CAD and to validate our findings.

CONCLUSION:

our study reveals a considerable prevalence of asymptomatic CAD in ischaemic stroke patients. Identifying and managing asymptomatic CAD early in stroke patients may reduce the risk of future cardiovascular events and improve overall patient outcomes. The shared risk factors observed in our study suggest potential common pathophysiological mechanisms linking ischaemic stroke and CAD, warranting further investigation. Routine cardiac evaluation in ischaemic stroke patients, especially those with identified risk factors, should be considered in clinical practice to enable timely interventions and optimize patient care.

REFERENCES:

1. Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993 Jan;24(1):35-41.
2. Donkor ES. Stroke in the 21st Century: A Snapshot of the Burden, Epidemiology, and Quality of Life. Stroke Res Treat. 2018 Nov 27;2018:3238165.
3. Amarenco P, Lavallée PC, Labreuche J, et al. Prevalence of coronary atherosclerosis in patients with cerebral infarction. Stroke. 2011 Jan;42(1):22-9.
4. Calvet D, Touzé E, Varenne O, Sablayrolles JL, Weber S, Mas JL. Prevalence of asymptomatic coronary artery disease in ischemic stroke patients: the PRECORIS study. Circulation. 2010 Apr 13;121(14):1623-9.
5. Touzé E, Varenne O, Calvet D, Mas JL. Coronary risk stratification in patients with ischemic stroke or transient ischemic stroke attack. Int J Stroke. 2007 Aug;2(3):177-83.
6. Medina-Leyte DJ, Zepeda-García O, Domínguez-Pérez M, González-Garrido A, Villarreal-Molina T, Jacobo-Albavera L. Endothelial Dysfunction, Inflammation and Coronary Artery Disease: Potential Biomarkers and Promising Therapeutical Approaches. International Journal of Molecular Sciences. 2021; 22(8):3850.
7. Dhamoon MS, Sciacca RR, Rundek T, Sacco RL, Elkind MS. Recurrent stroke and cardiac risks after first ischemic stroke: the Northern Manhattan Study. Neurology. 2006; 66: 641–646.
8. Touzé E, Varenne O, Chatellier G, Peyrard S, Rothwell PM, Mas JL. Risk of myocardial infarction and vascular death after transient ischemic attack and ischemic stroke: a systematic review and meta-analysis. Stroke. 2005; 36: 2748–2755.
9. Adams HP Jr, del Zoppo G, Alberts MJ, et al; Atherosclerotic Peripheral Vascular Disease Working Group; Guidelines for the early management of adults with ischemic stroke: 2007 May 22;115(20):e478-534. doi: 10.1161/CIRCULATIONAHA.107.181486. Erratum in: Circulation. 2007 Oct 30;116(18):e515. PMID: 17515473.
10. Boehme AK, Esenwa C, Elkind MS. Stroke Risk Factors, Genetics, and Prevention. Circ Res. 2017 Feb 3;120(3):472-495.
11. Arboix A. Cardiovascular risk factors for acute stroke: Risk profiles in the different subtypes of ischemic stroke. World J Clin Cases. 2015 May 16;3(5):418-29.
12. Muhammad IF, Borné Y, Zaigham S, et al. Comparison of risk factors for ischemic stroke and coronary events in a population-based cohort. BMC Cardiovasc Disord. 2021;21:536.
13. Walker RW, Dewhurst M, Gray WK, et al. Electrocardiographic assessment of coronary artery disease and stroke risk factors in rural and urban Tanzania: a case-control study. J Stroke Cerebrovasc Dis. 2014 Feb;23(2):315-20.
14. Esmaeilzadeh M, Parsaee M, Maleki M. The role of echocardiography in coronary artery disease and acute myocardial infarction. J Tehran Heart Cent. 2013 Jan;8(1):1-13.