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A New Diagnosis of Nonvalvular Atrial Fibrillation in Ischemic Stroke Patients Admitted to Stroke Unit: a Conceptual Replication Study

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ABSTRACT

Ischemic stroke constitutes a significant morbidity and mortality source, with atrial fibrillation (AF) identified as a leading contributory factor. Particularly, nonvalvular AF presents diagnostic challenges due to its intermittent and often asymptomatic nature. Understanding the prevalence and detection patterns of AF associated with stroke is paramount for efficacious therapeutic interventions. In an observational study conducted at the Neurological Institute of Thailand's stroke unit, 549 acute ischemic stroke patients underwent ECG monitoring. The data revealed a 15.5% incidence of AF, bifurcated into 8.0% previously diagnosed and 7.5% newly diagnosed cases. Of the latter, 41.7% were detected through continuous ECG monitoring, with a detection time spanning from 18 minutes to 17 days during admission, emphasizing a median detection interval of approximately 2.29 days. Given the findings, we advocate for an extended continuous ECG monitoring duration of 2-3 days in specialized stroke units, aligning with previous research and augmenting precision in secondary stroke prevention modalities.

Keywords: Atrial fibrillation; Continuous ECG monitoring; Ischemic stroke; Stroke unit

1. Introduction

Ischemic stroke primarily contributes to mortality and morbidity, leading to a significant disease burden [1]. According to the Thai Epidemiologic Stroke Study [2], the stroke prevalence rate in Thailand stands at 1.88. Atrial fibrillation (AF) is a prevalent supraventricular tachyarrhythmia with a

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lifetime risk of 25% [3]. It is defined by its rapid and irregular atrial activation, which results in ineffective atrial contractions [4]. Significantly, cardio embolism, predominantly associated with AF, is the predominant etiology of stroke in elderly populations and is associated with more severe clinical manifestations and poorer prognoses [5]. Additionally, AF is associated with an increased rate of hemorrhagic transformation post-intravenous thrombolytic therapy in acute ischemic stroke, further exacerbating outcomes [6]. The AF subtype that does not present with significant mitral stenosis or mechanical heart valves is classified as nonvalvular AF [7]. The manifestations of AF can vary; it is termed paroxysmal if it resolves within 7 days, persistent if it extends beyond 7 days, and long-standing persistent if it persists for more than 12 months [8]. Effective anticoagulation therapy can mitigate the risk of ischemic strokes induced by AF. Approximately 20%-30% of individuals with ischemic stroke and transient ischemic attack (TIA) have a prior AF diagnosis [9]. However, for those without a preceding arrhythmia identification, as many as 24% may be diagnosed with AF upon comprehensive cardiac monitoring [10].

The intermittent and often asymptomatic presentation of nonvalvular atrial fibrillation (NVAF) complicates its diagnosis. The risk associated with paroxysmal AF parallels persistent AF, indicating that unrecognized paroxysmal AF might account for a substantial proportion of ischemic strokes [11]. Consequently, improving the detection of post-stroke NVAF is imperative [12]. Atrial fibrillation cases can be categorized into known AF before the stroke and atrial fibrillation detected after the stroke (AFDAS). The aggregate detection rate of AF stands at approximately 11.5% [13]. Utilizing a standard 12-lead electrocardiogram (ECG) post-stroke or transient ischemic attack (TIA), the incidence of newly identified AF ranges between 2% and 5%. When employing a 24-hour Holter monitor, this detection rate is between 2% and 6% [14].

In a clinical context, a stroke unit is a dedicated department within a medical facility specifically oriented toward managing stroke patients. This unit encompasses a multidisciplinary team with specialized training in stroke care [15]. Continuous training programs and acquiring a Stroke Competence Certificate reinforce their expertise. The Committee for Standard Stroke Center Certification (SSCC) oversees the certification of stroke units in Thailand [16].

The American Stroke Association and Thai clinical guidelines advocate a minimum of 24-hour ECG monitoring in ischemic stroke patients within a stroke unit to detect underlying AF [17, 18]. Yet, optimal strategies regarding the timing and duration of monitoring for acute ischemic stroke or TIA nonvalvular AF remain ambiguous [19, 20]. Our conceptual replication research aimed to determine the incidence of newly detected AF and ascertain the most effective ECG monitoring period for its identification in patients with acute ischemic stroke.

2. Materials and Methods

2.1 Study approval and design

This observational research was sanctioned by the Neurological Institute of Thailand's ethics committee (Approval No.: 59068). The study period extended from July 2019 to May 2020, during which ECG monitoring was carried out on patients with acute ischemic stroke admitted to the Neurological Institute of Thailand's (NIT) stroke unit.

2.2 Setting

The Stroke Unit for Acute Cerebrovascular Disease operates under the Neurology Division of the Neurological Institute. Established on August 9, 2006, this unit caters to both male and female patients aged 15 years and above suffering from acute

cerebrovascular diseases. With a focus on adherence to professional standards, this unit provides superior care, ensuring patient safety and optimal hospitalization duration. The unit functions round-the-clock with a capacity of 11 patient beds and holds certification from the SSCC. For ECG monitoring, the IntelliVue MX850 device from Philips was employed.

2.3 Participant selection and data collection

Consecutive patients admitted during the study period, clinically diagnosed with acute ischemic stroke and confirmed via neuroimaging (CT/MRI) on admission, were incorporated into the study. Prior to inclusion, informed consent was obtained from all participants. Collected demographic data encompassed aspects such as age, gender, risk factors, past medications, and existing comorbidities. Furthermore, all patients had been subjected to a 12-lead ECG prior to their admission. During their hospitalization in the stroke unit, continuous ECG monitoring was performed, meticulously recording the detection time and mode for any emergent AF.

2.4 Statistical Analysis

For data analysis, SPSS software version 16.0 was employed. This included assessment of baseline characteristics, detection mode and date, and correlations with risk factors. The employed statistical tests comprised the t-test, Chi-square test, and logistic regression for the computation of odds ratios.

3.Results

From July 2019 to May 2020, a total of 549 patients diagnosed with acute ischemic stroke were admitted to the NIT stroke unit and subsequently included in our research cohort. The median age of these patients was 63.3 years, and 55% were male. The presence of hyperthyroidism was noted in 3.8% of patients, a prior history of AF in 9.3% (however, AF was detected in initial ECG in only 8%), and a history of heart disease in 6.9%. The most prevalent heart diseases were ischemic and valvular heart diseases. In our sample, atrial fibrillation was identified in 15.5% of cases, comprising 8.0% previously diagnosed AF and 7.5% newly diagnosed cases. Baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics of 549 patients.

		%
Age (years)	Range 18-95	Mean 63.3
Sex: male	303	55
History of hyperthyroidism	21	3.8
History of AF	51	9.3
Underlying heart disease	38	6.9
Type of heart disease:		
Ischemic heart disease	14	36.8
Valvular heart disease	15	39.5
other arrythmia	1	2.6
other heart disease	7	18.4
- unknown	1	2.6

Risk factors associated with atrial fibrillation are delineated in Table 2. Significant correlations were found between the presence of AF and variables such as age, prior history of AF, and heart disease. Specifically, every incremental year in age increased the odds of AF by a factor of 1.041. Heart disease was found to significantly amplify the risk of AF detection (OR = 4.706) when compared to patients without any heart conditions. A conspicuous pattern was observed where individuals with previously diagnosed AF commonly had a history of heart disease.

Table 2. Association between patients without atrial fibrillation (AF), all AF, known AF, and first diagnosis of AF.

Patient characteristics	No AF(%)	All AF (%) *p*-value OR, 95%-CI	Known AF (%) *p*-value OR, 95%-CI	First diagnosis AF (%) *p*-value OR, 95%-CI
Patients	465	85 (15.3)	44(8.0)	41
Age	62.25±14.35	69.54±12.96 *p* <0.001* 1.041, 1.022-1.060	70.25±12.86 *P* <0.001* 1.045, 1.019-1.072	68.90±13.326 *P* =0.005 1.036, 1.010-1.062
Male, female	259,206	43, 42 *p* =0.373 1.234, 0777-1.961	24,20 *P* =0.871 1.053, 0.566-1.959	19,22 *P* =0.242 1.463, 0.771-2.776
History of hyperthyroidism	16(3.4)	4 (5.9) *p* =0.349	4(9.1) *P* =0.066	1(2.4) *P* =0.731

		1.750, 0.624-4.912	2.800, 0.893-8.776	0.700, 0.090-5.416
History of AF	6 (1.3)	46 (54.1) p <0.001** 90.034, 36.190-223.986	44(100) P <0.001*** 1.185E, 0.000	2(4.9) P =0.078 3.915, 0.764-20.046
Underlying heart diseases	22 (4.8)	16 (18.8) P <0.001** 4.627, 2.316-9.245	13(29.5) P <0.001*** 8.386, 3.850-18.189	3(7.3) P =0.473 1.575, 0.451-5.504
Type of heart disease				
Valvular heart disease	5(22.7)	P=0.046** 10 (62.5)	P =0.025** 9(69.2)	P =0.781 1(33.3)
Ischemic heart disease	11(50.0)	3 (18.8)	1(7.7)	2(66.7)
Other arrythmia	1(4.5)	0(0)	0(0)	0(0)
Other heart disease	5(22.7)	2(12.5)	2(15.4)	0(0)
Unknown	0(0)	1(6.3)	1(7.7)	0(0)

*= t-test, **= Pearson Chai-Square, ***= Fisher's Exact test, ****=Mann-Whitney test.

Of those patients previously diagnosed with AF, all exhibited AF on their admission ECG. In contrast, among the 41 patients who were newly diagnosed, 58.5% had their admission ECG indicative of AF, while the remaining 41.5% were diagnosed through continuous ECG monitoring. For this subset, the duration to AF detection during admission ranged from 18 minutes to 17 days, with a median time of approximately 2.29 days. Regarding the subtypes of AF, 21 out of the 85 diagnosed patients exhibited paroxysmal AF, of which 14 were newly diagnosed with a median detection period of 2.7361 days. This duration was significantly longer than the median for continuous AF, which was approximately 31.5 minutes, with a p-value less than 0.001****.

Subsequent comparative analysis between patients previously diagnosed with AF and the newly diagnosed cohort revealed that the former displayed a more pronounced history of heart disease (p = 0.009, OR = 0.188 with a 95% confidence interval of 0.049-0.720). While the cohort with known AF appeared marginally older (mean age of 70.25 ± 12.86 years) in comparison to the newly diagnosed group (mean age of 68.78 ± 13.181 years), this age difference was not found to be statistically significant (p = 0.557). Additional risk factors, including gender, hyperthyroidism, and specific heart disease classifications, did not exhibit any significant differential trends between the groups.

3.1 Discussion

Identification of AF subsequent to a stroke is pivotal as it elucidates potential etiological considerations, frequently necessitating a transition from antiplatelet to anticoagulant therapies [21]. Approximately 25% of patients with acute ischemic stroke or TIA are diagnosed with AF following extensive monitoring [22]. In our study, AF prevalence in stroke patients was 15.66%, relatively diminished compared to several European and American datasets, potentially reflecting less intensive ECG monitoring practices within Asian populations. An international study encompassing India and Africa, with infrequent ECG monitoring, recorded AF prevalence rates of 8% and 11% among acute stroke patients, respectively [23, 24]. The AF cohort generally presented as older, possibly correlating with the heightened prevalence of AF among individuals above 60 years. Those with pre-established AF diagnosis predominantly had cardiac comorbidities compared to the newly diagnosed AF group, aligning with findings from Friberg et al. [11] Their study delineated associations between ischemic stroke, AF, and various conditions including cardiac diseases, hypertension, diabetes mellitus, and antecedent strokes [10].

TIA or stroke, contemporary guidelines advocate for AF screening utilizing techniques such as 12-lead ECG, Holter monitoring, telemetry, among other devices. However, consensus regarding optimal duration and precise timing of these evaluations remains unestablished. Predominant stroke guidelines propose cardiac surveillance for 24-72 hours for acute ischemic stroke patients within stroke units. A month-long extended rhythm monitoring is deemed rational for cases with undetermined etiology [17, 25]. Despite numerous randomized trials evaluating intensified TIA or stroke monitoring, most demonstrated enhanced AF detection but lacked conclusive evidence for reduction in subsequent TIA, stroke, or systemic

embolism. A limited-scale trial involving 100 subjects revealed that a 7-day event-monitor identified AF in an additional 16% of participants compared to conventional methodologies, though it did not showcase differences in vascular outcomes [26].

In our research, the incidence of newly diagnosed AF mirrored the known AF cohorts at 7.5% and 8.0%, respectively. A significant 41.7% of the new AF cases were detected via continuous ECG monitoring, ranging from 18 minutes to 17 days during admission, with a median detection interval of 2 days, 6 hours, and 50 minutes. This observation surpasses many extant guidelines, including Thai national recommendations advocating a minimum 24-hour ECG during acute ischemic stroke. Predominantly, paroxysmal AF was ascertained during admission through sustained ECG surveillance. Based on our empirical evidence, we endorse continuous ECG monitoring for 2-3 days subsequent to admission in stroke units. Our study's results align with prior research, underscoring a monitoring window of 3-4 days, particularly imperative for detecting novel and especially paroxysmal AF, which is fundamental in tailoring secondary stroke prevention strategies [19, 20].

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Data Availability Statement

The raw data used to support the findings of this study have been deposited in AF AND stroke NIT: https://www.researchgate.net/publication/374053032_AF_AND_stroke_NIT, DOI: 10.13140/RG.2.2.35186.89286

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