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Prevalence of atrial fibrillation in ischemic stroke and associated risk factors: A hospital-based study in Indonesia

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Abstract:

CONTEXT: The prevalence of ischemic stroke increases each year. One such important factor is the presence of atrial fibrillation (AF), but data regarding this are scarce in Indonesia.

AIMS: This study aimed to understand the prevalence of AF in ischemic stroke and its associated risk factors.

SETTINGS AND DESIGN: A cross-sectional study was conducted from January 2021 to 2023 in Fatima Hospital, through medical records.

SUBJECTS AND METHODS: Subjects were ischemic stroke patients aged ≥18 years. Additional data included demographic characteristics, congestive heart failure (CHF), hypertension, diabetes mellitus, stroke history, vascular disease, AF, dyslipidemia, Glasgow Coma Scale, and anticoagulant usage.

STATISTICAL ANALYSIS USED: Data were analyzed using Chi-square, Fisher, Student's *t*-test, Mann–Whitney, and logistic regression.

RESULTS: Out of 148 subjects, AF was detected in 16 (10.8%). Among these, 14 (87.5%) had a CHA2DS2-VASc score of ≥2 and were given anticoagulant therapy. A higher proportion of subjects aged over 75 years was observed in the AF group (31.2% vs. 3.8%; $P < 0.001$). A similar pattern was seen with CHF and dyslipidemia (CHF: 56.3% vs. 8.3%; $P < 0.000$; dyslipidemia: 93.7% vs. 58.3%; $P < 0.005$). CHF and dyslipidemia increased the risk of AF by 27-fold ($P = 0.001$, odds ratio [OR]: 27.400) and 21-fold ($P = 0.013$, OR: 21.812), respectively.

CONCLUSIONS: These findings underscore the importance of vigilant screening for AF in ischemic stroke, particularly in patients with CHF and dyslipidemia, to guide appropriate anticoagulation therapy and reduce the risk of recurrent stroke. This study was limited by its single-center design and small sample size. A larger, multicenter study is recommended.

Keywords:

Atrial fibrillation, ischemic stroke, prevalence, risk factor

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Introduction

The hallmark of a stroke is the abrupt onset of clinical symptoms, which appear as focal or widespread neurological impairments. These symptoms can be severe, lasting more than 24 h, or even fatal, with no discernible cause other than vascular issues.[1] The annual incidence of stroke is on the rise. A report by the World Stroke Organization indicated that in 2022, there were 150 incidences of stroke per 100,000 people.[2] This rising pattern is also visible in Indonesia, increasing from 7% in 2013 to 10.7% in 2018.[3] Ischemic stroke,

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constituting 71% of all stroke occurrences globally, stands as one of the most prevalent types of stroke.[4] Risk factors for ischemic stroke include modifiable and nonmodifiable factors. Among the numerous modifiable risk factors, atrial fibrillation (AF) emerges as one of paramount significance. Studies confirm that AF substantially heightens the likelihood of experiencing an ischemic stroke by 4–5 times.[5]

Typical cardiac rhythm anomalies such as AF arise from irregular electrical impulses within the heart, precipitating fibrillation in the atria which induces tachyarrhythmia.[6] The worldwide prevalence of AF cases is 1% and increases to 9% in people aged over 75 years.[7] Attributed to its irregular cardiac rhythms, AF bears a heightened propensity for the formation of blood clots or thrombi. These thrombi have the potential to occlude blood vessels, culminating in the occurrence of ischemic stroke.[8]

Numerous global studies have explored the association between ischemic stroke and AF, revealing that individuals affected by both conditions typically experience poorer prognoses. However, there has been ongoing debate regarding the prevalence of AF in cases of ischemic stroke. Discrepancies in lifestyle choices, epidemiological profiles among nations, and variations in research methodologies contribute to the challenge of accurately estimating AF frequencies in the general population. In line with Indian investigations, AF manifests in 25% of ischemic stroke occurrences, particularly affecting women with enlarged atria and individuals over 60 years old.[9] Meanwhile, research in Spain indicates that AF emerges as a subsequent diagnosis in up to 28% of ischemic stroke cases.[10] In addition, an Egyptian study unveiled that 26% of patients treated for ischemic stroke had no prior diagnosis of AF, yet 44% exhibited AF upon electrocardiographic assessment.[11]

Nevertheless, comprehensive data regarding the prevalence of AF among ischemic stroke patients in Indonesia remain scarce. A study conducted in the country revealed that stroke patients diagnosed with AF necessitated prolonged treatment, exhibited increased disability levels, and generally experienced inferior outcomes compared to stroke patients without AF.[12]

The lack of research in Indonesia has spurred the initiation of this study, which seeks to ascertain the prevalence of AF among individuals affected by ischemic stroke in a specific region of Indonesia. In addition, the study aims to identify the risk factors that render ischemic stroke patients more predisposed to developing AF.

Subjects and Methods

Study design

We implemented an observational cross-sectional study design. The inclusion criteria consisted of subjects aged over 18 years, and having been diagnosed with ischemic stroke; confirmed through history, clinical examination by a neurologist, and supported by concurrent radiological findings on a computed tomography scan. Established diagnoses of ischemic stroke were then inserted into the medical record database based on International Classification of Disease (ICD-10) coding. The exclusion criteria included hemorrhagic stroke and transient ischemic attack (TIA). Subjects who met both the inclusion and exclusion criteria were included as research subjects.

Data collection

Data collection was carried out through medical records from January 2021 to 2023 at Fatima Hospital, West Kalimantan. Samples were taken using the consecutive sampling method. A total of 155 patients were screened as having ischemic stroke following the allocated period of the study based on ICD-10 coding. Seven were proven to be of nonvascular origin and hence were excluded. The remaining 148 subjects all had electrocardiograms (ECGs) recorded and were taken as samples [Figure 1]. Independent variables included gender, age, CHA2DS2-VASc score, congestive heart failure (CHF), hypertension (HTN), diabetes mellitus (DM), history of stroke/TIA, vascular disease, dyslipidemia, Glasgow Coma Scale (GCS) score at admission, and use of oral anticoagulant drugs (OAC), namely Vitamin K antagonists. The diagnoses of CHF, DM, and dyslipidemia were taken through ICD-10 coding of the medical record database previously established by an internist. The dependent variable was the prevalence of AF. AF was established through history taking, clinical examination by an internist, and supported by stereotypical findings on an ECG. We calculated a minimal sample size of 147 subjects using the sample size for proportion in the survey type of studies formula.

Data analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Categorical data were depicted in proportions (n%). A normality test on numerical data was first carried out using the Kolmogorov–Smirnov test. Normally distributed data ($P \geq 0.05$) were presented in the form of mean and standard deviation, whereas abnormally distributed data ($P < 0.05$) were presented in the form of median and range. An initial bivariate analysis was undertaken to identify statistically significant factors correlated with AF among patients

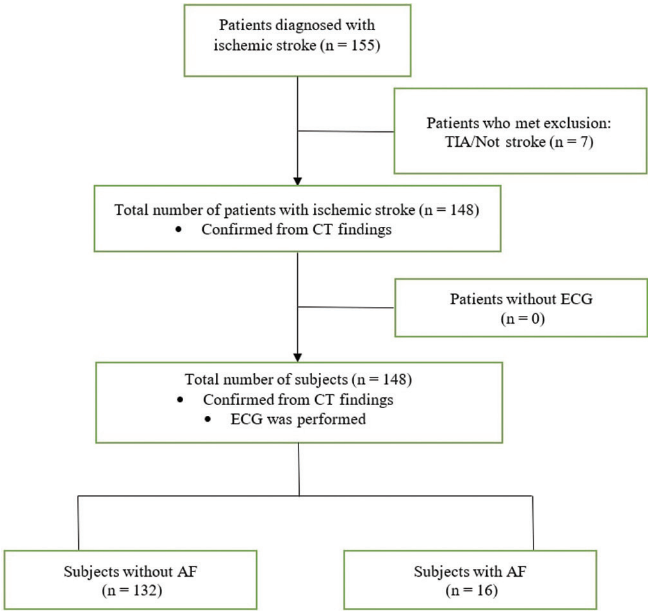

Figure 1: Algorithm of sample selection and diagnosis

diagnosed with ischemic stroke. The Chi-square test was utilized for categorical variables, with the Fisher test chosen as an alternative should test requirements fail. Numerical-categorical variables underwent analysis using the Student's-*t*-test. In instances where the assumptions for the Student's-*t*-test were not satisfied, the Mann–Whitney test was employed as an alternative. Variables that exhibited statistical significance during the bivariate analysis were subjected to further examination through multivariate analysis employing logistic regression. All assumptions for logistic regression were satisfied before running the model.

Clinical trial registry

Clinical trial registry was not applicable in this particular study for no intervention was done regarding subjects.

Results

A total of 148 subjects were collected from January 2021 to 2023. The average age of the subjects was 57.4 (±10.8) years, with the majority being male (54.1% vs. 45.9%). When admitted to the emergency room, the subjects' median GCS score was 15 (6–15). A total of 20 (13.5%) subjects had CHF, and 129 (87.2%) had a history of HTN. There were 60 (40.5%) subjects who had DM, and 60 subjects also had a history of ischemic stroke. History of vascular disease and dyslipidemia were found in 40 (27%) and 92 (62.2%) subjects, respectively. A mere 16 (10.8%) subjects were diagnosed with AF. Among those, 14 (87.5%) had a CHA2DS2-VASc score ≥2, and all of them received OACs. The median CHA2DS2-VASc score among subjects with AF was 3 [Table 1].

Table 1: Demography and clinical characteristics

Variable	*n*=148
Age (years), mean±SD	57.44±10.81
CHF	
Yes	20 (13.5)
No	128 (86.5)
GCS on admission, median (minimum–maximum)	15 (6–15)
HTN	
Yes	129 (87.2)
No	19 (12.8)
Age ≥75 years	
Yes	10 (6.8)
No	138 (93.2)
DM	
Yes	60 (40.5)
No	88 (59.5)
History of ischemic stroke	
Yes	60 (40.5)
No	88 (59.5)
Vascular disease	
Yes	40 (27)
No	148 (73)
Age 69–74 years	
Yes	35 (23.6)
No	113 (76.4)
Female	
Yes	68 (45.9)
No	80 (54.1)
Dyslipidemia	
Yes	92 (62.2)
No	56 (37.8)
AF	
Yes	16 (10.8)
No	132 (89.2)
AF with CHA2DS2-VASc ≥2	
Yes	14 (87.5)
No	2 (12.5)
AF receiving anti-coagulants	
Yes	14 (87.5)
No	2 (12.5)
CHA2DS2-VASc score, median (minimum–maximum)	3 (0–7)

SD: Standard deviation, GCS: Glasgow Coma Scale, AF: Atrial fibrillation, CHF: Congestive heart failure, HTN: Hypertension, DM: Diabetes mellitus

The average age of the AF group was higher than the non-AF group, although not to a significant effect. Gender differences were unremarkable, with slightly more males in the non-AF group. The GCS score at admission had the same median between the two groups, but the minimum GCS in the AF group was lower compared to the non-AF group ($P = 0.003$). In the AF group, the proportion of subjects who were >75 years old (31.2% vs. 3.8%; $P < 0.001$) or had CHF (56.3% vs. 8.3%; $P < 0.000$), was higher compared with the non-AF group. A similar discovery was perceived in subjects who had vascular disease (50% vs. 24.2%; $P < 0.038$) and dyslipidemia (93.7% vs. 58.3%; $P < 0.005$). However, other components of the CHA2DS2-VASc score such

Table 2: Bivariate analysis of factors associated with atrial fibrillation

Variable	AF (*n*=16), *n* (%)	Non-AF (*n*=132), *n* (%)	*P*
Age (years), mean±SD*	60.5±12	57.07±10.65	0.232
GCS on admission, median (minimum–maximum)†	15 (6–15)	15 (7–15)	0.003
CHA2DS2-VASc score, median, minimum–maximum)†	5 (0–7)	3 (0–7)	0.004
Age ≥75 years§			
Yes	5 (31.2)	5 (3.8)	0.001
No	11 (68.8)	127 (96.2)	
CHFǀ			
Yes	9 (56.3)	11 (8.3)	0.000
No	7 (43.8)	121 (91.7)	
HTN§			
Yes	13 (81.3)	116 (87.9)	0.435
No	3 (18.8)	16 (12.1)	
DMǀ			
Yes	6 (37.5)	54 (40.9)	0.793
No	10 (62.5)	78 (59.1)	
History of ischemic strokeǀ			
Yes	8 (50)	58 (43.9)	0.645
No	8 (50)	74 (56.1)	
Vascular diseaseǀ			
Yes	8 (50)	32 (24.2)	0.038
No	8 (50)	100 (75.8)	
Femaleǀ			
Yes	8 (50)	60 (45.5)	0.730
No	8 (50)	72 (54.5)	
Dyslipidemia§			
Yes	15 (93.7)	77 (58.3)	0.005
No	1 (6.3)	55 (41.7)	
Age 65–74 yearsǀ			
Yes	7 (43.8)	28 (21.2)	0.061
No	9 (56.3)	104 (78.8)	

*Independent *t*-test, †Mann–Whitney, ǀChi-square, §Fisher's exact test. SD: Standard deviation, GCS: Glasgow Coma Scale, CHF: Congestive heart failure, HTN: Hypertension, DM: Diabetes mellitus, AF: Atrial fibrillation

Table 3: Bivariate analysis of Glasgow Coma Scale on admission with CHA2DS2-VASc Score

Variable	CHA2DS2-VASc ≥2 (*n*=14)	CHA2DS2-VASc <2 (*n*=2)	*P*
GCS on admission, median (minimum–maximum)*	15 (6–15)	13.5 (12–15)	0.861

*Mann–Whitney. GCS: Glasgow Coma Scale

as HTN, DM, history of ischemic stroke, and female gender did not have a significant influence [Table 2]. In addition, the GCS score at admission was associated with the incidence of AF but was not associated with the CHA2DS2-VASc score [Table 3].

Subjects with a higher GCS at admission had a higher risk of AF ($P = 0.022$, odds ratio [OR]: 1.440 [1.055–1.966]). Moreover, subjects with a history of CHF were 27 times more likely to develop AF ($P = 0.001$, OR: 27,400 [4160–180,456]), and subjects with dyslipidemia were 21 times more likely to develop AF ($P = 0.013$, OR: 21,812 [1899–250,552]).

Discussion

Prevalence, demographics, and subject characteristics

In this study, the observed prevalence of AF stood at 10.8%. Comparable rates were noted in African research, where AF prevalence was documented at 11%.[13] Notably, several other studies have reported higher incidence figures. For instance, a study spanning from 2004 to 2013 in South Korea documented an AF prevalence of 16.3% among ischemic stroke cases. Similarly, investigations conducted in the United States (US) from 2004 to 2018 and in Sweden from 2005 to 2010 reported AF prevalence rates of 18.4% and 33.4%, respectively.[14-16] Conversely, findings from India yielded a slightly lower AF prevalence rate of 8%.[17] While the prevalence of AF in this study is only slightly different from other Southeast Asian countries, it is meaningfully lower than the rates reported in Western populations [Table 4]. This discrepancy may be influenced by ethnic differences, as research has shown that East Asians, including Southeast Asians, have a lower genetic

Table 4: Logistic regression of factors associated with atrial fibrillation

Variable	*B*	Wald	*P*	OR (95% CI)
GCS on admission	0.365	5.284	0.022	1.440 (1.055–1.966)
CHF	3.311	11.850	0.001	27.400 (4.160–180.456)
Age >75 years	2.318	3.457	0.063	10.160 (0.882–117.041)
Vascular disease	−1.064	1.275	0.259	0.345 (0.054–2.188)
Dyslipidemia	3.082	6.125	0.013	21.812 (1.899–250.552)
Constant	−7.348	8.190	0.004	0.001

OR: Odds ratio, 95% CI: Confidence interval, GCS: Glasgow Coma Scale, CHF: Congestive heart failure

predisposition to AF, likely due to variations in genetic loci associated with AF risk.[18]

The mean age of individuals afflicted with ischemic stroke was 57.4 years (±10.8). This finding aligns with investigations conducted in India by Shaikh *et al.*, where the mean age was reported at 53.8 years (±8.34), and by Bhana *et al.*, where the mean age stood at 56.7 years (±11.2).[17,19] In contrast, studies conducted in Europe and Western nations typically report a higher mean age, attributable to the longer life expectancy in developed regions compared to developing ones. This could be another reason why the prevalence in this study was lower than those in Western countries. In our study, AF prevalence was significantly higher in patients aged over 75 years, a demographic that might be underrepresented in Indonesia's general stroke population, considering the life expectancy in Indonesia lies at 69.4 years for males and 73.5 years for females.[20]

While many subjects in our study presented with recognizable risk factors for ischemic stroke such as a history of HTN, dyslipidemia, DM, and prior stroke, only a minority exhibited CHF (13.5%) or vascular disease (27%). These proportions closely mirror findings by Bhana *et al.*, who reported CHF prevalence at 19.3%, and by Mayet *et al.*, where vascular disease was documented in only 9% of ischemic stroke cases.[13,17]

Factors associated with atrial fibrillation

Age is one of the main factors in the occurrence of AF. As age increases, the incidence of AF increases up to 2-fold, especially after the age of 65 years, and reaches 8% at the age of >75 years. The heightened risk of AF is associated with functional and structural changes in the myocardium and vascular system with developing age.[21,22]

Individuals diagnosed with CHF face a 4–6 times greater risk of developing AF. This association is linked to the process of left atrial remodeling, which entails structural and functional alterations. Furthermore, patients with a cardiovascular disease background, particularly a history of myocardial ischemia (MI), exhibit a doubled risk of AF incidence. The prevalence of AF in individuals with a prior MI history varies from 2% to 13%. A study conducted in Sweden highlighted that 15% of ischemic stroke patients diagnosed with AF had a preceding history of MI, underscoring its significance as a substantial risk factor.[16,21,23]

Dyslipidemia is associated with an increased risk of atherosclerosis and coronary heart disease, which in turn increases the risk of AF. Some studies also show that high levels of high-density lipoprotein-C (HDL-C) reduce the risk of AF, whereas high levels of low-density lipoprotein-C (LDL-C) and triglycerides escalate the risk of AF.[24,25] A majority of the subjects in this study suffered from dyslipidemia. One study stated that half of the Indonesian population had a diet consisting of high sugar intake, increased saturated fat, and sodium consumption.[26] Unsurprisingly, this dietary pattern of high sugar and fat is also seen in various other low-middle-income countries (LMICs).

Other components of the CHA2DS2-VASc score did not reveal a significant effect in this study. HTN was prevalent in the majority of patients (87.2%) although it did not reveal a significant association. Research conducted in India in 2017 yielded similar findings ($P = 0.288$).[19] Gender differences did not have a significant effect in this study, with a greater number of male patients (54.1%). Despite the prevalence of AF is higher in men than women, with a male-to-female ratio of 1.11 in 2017, women are recognized to be at a heightened risk of developing AF due to the greater incidence of vascular diseases such as valve disease, HTN, and CHF, as well as pregnancy.[27,28] DM was also found to have no significant effect in this study. Studies conducted in the US showed that DM was not significantly related to AF ($P = 0.43$).[29] Another comparable study stated that DM was not a significant predictor variable for AF without other risk factors in men but was significant in women.[30] Previous history of stroke was not significantly related to AF; this is similar to a cohort study conducted in Taiwan in 2020 with the results that a history of stroke did not have a significant effect on AF in patients both with and without DM.[31]

The CHA2DS2-VASc serves as a valuable tool to calculate the risk of stroke in patients with AF and aids in determining the necessity of OAC therapy. Notably, the components of the CHA2DS2-VASc are thought to be directly linked with the development of AF. Multiple studies have underscored the utility of CHA2DS2-VASc in predicting the presence of AF among individuals with ischemic stroke. Findings have detailed that CHA2DS2-VASc could help predict AF in stroke patients, particularly when supplemented with additional imaging tests.[32] Several other studies show that ischemic stroke patients with AF have higher CHA2DS2-VASc scores than non-AF.[8,16]

Our findings revealed a contrasting association, wherein higher GCS scores were linked to an elevated risk of AF. This discrepancy from previous studies could potentially stem from undocumented underlying conditions among the non-AF group. Ischemic stroke patients experiencing reduced consciousness tend to harbor additional risk factors, including coronary heart disease, heart valve disease, and AF.[33] Numerous studies have shown that both low GCS scores and AF serve as predictors of mortality among individuals with ischemic stroke.[34,35] AF is frequently accompanied by heart failure or coronary heart disease, which can manifest as symptoms like shortness of breath and desaturation. A decrease in oxygen saturation consequent to these conditions may impact the patient's level of consciousness, thereby resulting in a lower GCS score.[36] Furthermore, cardioembolic stroke has also been demonstrated to cause extensive infarction, leading to impaired consciousness.[37]

Subjects who have CHF have a 27-fold risk of developing AF. This is also reflected in a Swedish study where ischemic stroke patients with CHF had 3 times more risk of developing AF, although to a lesser extent.[16] The relationship between AF and CHF is bidirectional. According to the Framingham Heart Study, 57% of patients with CHF may suffer from AF in future, whereas 37% of patients with AF experienced CHF in future.[38] One-way CHF increases the risk of AF is through increased left atrial pressure, acutely or chronically. Increased pressure and atrial distension induce scar tissue formation and fibrosis, ultimately leading to conduction abnormalities, including decreased atrial conduction velocity.[39]

AF was shown to be 21 times more common in those with dyslipidemia in this investigation. The exact association between AF and dyslipidemia is yet unknown, and there is disagreement over the processes that connect the two conditions. While some investigations suggest a negative correlation between dyslipidemia and AF, others propose the contrary. For instance, studies by Alonso *et al*. and Guan *et al*. have indicated that elevated levels of HDL are associated with a reduced risk of AF development.[25,40] Elevated LDL levels and decreased HDL levels contribute to diminished left ventricular function and the progression to CHF, both recognized risk factors for AF.[41] One meta-analysis conducted by Wang *et al*. discovered that statin therapy was useful for preventing the occurrence of AF, suggesting that lower lipid profiles may be beneficial in preventing AF.[42]

Atrial fibrillation and stroke outcome

The intricate relationship between AF and post-stroke outcomes reveals that AF patients are more likely to experience poor functional outcomes, as reflected by higher modified Rankin Scale scores at 3 months poststroke.[43] The prothrombotic state inherent in AF significantly elevates the risk of recurrent stroke, especially in those with inadequate anticoagulation. Moreover, AF-related hypercoagulability can lead to the formation of microemboli, which may cause silent infarcts, accumulating over time and contributing to cognitive decline and increased long-term disability.[44] Hospital-based cohort studies have shown that initiating OACs early – within 1–4 days after an ischemic stroke, based on stroke severity – can effectively reduce the risk of recurrent stroke or systemic embolism without a significant increase in major bleeding risk.[45]

Clinical implications

Our study provides critical hospital-based data on AF prevalence among ischemic stroke patients in Indonesia, addressing a significant gap in regional healthcare data. The 10.8% prevalence rate underscores the importance of implementing routine AF screening in ischemic stroke patients, even in resource-limited settings, to facilitate timely OAC therapy and prevent recurrent strokes. This approach is crucial for improving patient outcomes in Indonesia and offers valuable insights for similar LMICs facing comparable healthcare challenges. Prioritizing targeted screening and management of CHF and dyslipidemia, particularly through the use of widely accessible statins, presents a practical and cost-effective strategy that could enhance stroke outcomes both nationally and in other LMICs. In addition, a nutrition transition characterized by increased consumption of high-fat and high-sugar diets contributes to the rising prevalence of AF and other noncommunicable diseases in LMICs. Addressing these dietary factors alongside medical management could further improve stroke outcomes and overall cardiovascular health in these regions.

Limitations

Several limitations were present in this study. First, data collected through medical records can cause bias and inaccuracies due to factors such as incomplete documentation, variations in how clinicians record information, and selective reporting which could have potentially influenced our findings. In addition to this, the comorbidities of subjects were not included in data collection, thus causing potential bias regarding the outcome of GCS on admission between the AF and non-AF groups. Regrettably, patient outcomes were also not included due to inadequate data, which hindered analysis of the efficacy of anticoagulant therapy for individuals with AF experiencing ischemic stroke. Furthermore, despite the study spanning 2 years, the analysis did not encompass the annual incidence rate of AF development. Regarding our relatively small sample size of 148 subjects from a single center, a continual multicenter study would be ideal to appropriately represent the overall prevalence of AF in ischemic stroke.

Conclusion

AF is a significant risk factor for ischemic stroke, with a prevalence of 10.8% in the Indonesian stroke patient population. Notably, older age, CHF, and dyslipidemia were strongly associated with an increased risk of AF. These findings underscore the importance of targeted screening and management of AF in ischemic stroke patients, particularly those with CHF and dyslipidemia. Early detection and appropriate anticoagulation therapy could improve outcomes and reduce the likelihood of recurrent strokes.

Author contributions

All authors contributed to concepts, design, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, manuscript preparation, manuscript editing and manuscript review; Guarantor was done by Dr. Theodore Amadeo.

Ethical policy and institutional review board statement

This study conformed to the ethical standards of the Declaration of Helsinki and was approved by the Health Research Ethics and Law Committee of Fatima Hospital, West Kalimantan (No. DK/335/DIR/VI/2023) prior to initiation of the research work, on June 12th, 2023. Written informed consent was received from all study participants.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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