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Current Review of Atrial Fibrillation Detected After Stroke

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Abstract. Patients with atrial fibrillation (AF) have a greater probability of a stroke event than patients without AF. As a result of developments in cardiac monitoring, the diagnosis of AF during an ischemic stroke or transient ischemic attack has improved these years. More cases of AF detected after stroke (AFDAS) are reported, which has implications for future risk of recurrent stroke and prevention. This article provides the current review of AFDAS's monitoring and brief management.

Keyword: Atrial fibrillation, atrial fibrillation detected after stroke, ischemic stroke, monitoring

Abstrak. *Pasien dengan fibrilasi atrium (AF) memiliki kemungkinan lebih besar untuk mengalami kejadian stroke dibandingkan pasien tanpa AF. Dengan kemajuan dalam metode pemantauan jantung, diagnosis AF pasca stroke iskemia atau serangan iskemik transien telah meningkat beberapa tahun terakhir. Semakin banyak kasus AF yang didiagnosis setelah stroke (AFDAS) dilaporkan, yang memiliki implikasi pada risiko stroke berulang dan terapi pencegahan di masa depan. Artikel ini bertujuan untuk memberikan tinjauan terkini tentang pemantauan dan manajemen singkat dari AFDAS.*

Kata Kunci: fibrilasi atrium, fibrilasi atrium yang terdeteksi pasca stroke, stroke iskemia, pemantauan

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1. Introduction

The global report in 2019 stated that there were 12.2 million stroke incidences across the globe which caused about 6.55 million deaths. Ischemic stroke represents 62.4 % of all stroke incidents [1]. Atrial fibrillation (AF) is a known risk factor in acute ischemic stroke and a reliable mortality

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predictor following the first stroke. The stroke risk increased five-fold by atrial fibrillation. Previous studies stated that acute ischemic stroke (AIS) and transient ischemic attack (TIA) are the initial manifestation in 2 to 5% of AF cases which are identified around the time of the first AF diagnosis leading to worse prognosis [2], [3].

Recent developments in the technologies used to monitor patients have led to significant scientific discoveries on strokes and AF. One-quarter of stroke patients who underwent post-stroke monitoring are eventually diagnosed with AF. Acute ischemic stroke has been reported to increase the risk of AF. The incidence of AF diagnosis is eight times higher in patients with AIS than without [4]. The previously unknown – newly diagnosed AF is crucial for the preventive management associated with recurrent stroke and mortality risks [5], [6]. Atrial fibrillation, particularly paroxysmal, can be asymptomatic and challenging to identify. Unfortunately, it is reported that this asymptomatic AF carries the same risk of stroke and mortality as symptomatic AF [7]. Therefore, this article will discuss the relevance of monitoring atrial fibrillation following an ischemic stroke as secondary prevention.

2. Terminology of post-stroke atrial fibrillation

Atrial fibrillation is a supraventricular tachyarrhythmia characterized by inadequate atrial contraction due to disorganized atrial electrical activity. It is described electrocardiographically by "irregular R-R intervals, the absence of recurrent P waves, and irregular atrial activation". The traditional classification of AF is based on the episode's presentation, duration, and spontaneous termination of the episode. The European Society of Cardiology (ESC) published the most recent guideline in 2020 and defined paroxysmal AF as atrial fibrillation that resolves within 7 days of onset, either spontaneously or with intervention. In contrast, persistent AF persists longer than seven days and includes episodes resolving in cardioversion (both pharmacological and electrical cardioversion) [5].

Experts have recommended new terminologies to classify AF following acute ischemic stroke. Newly-diagnosed AF in stroke/TIA patients can generally be classified as (1) known atrial fibrillation (KAF) or (2) AF detected after stroke (AFDAS). AFDAS is an umbrella term for any pattern of atrial fibrillation (whether it is paroxysmal, persistent, or permanent) identified by any cardiac rhythm monitoring method following an ischemic stroke or TIA. AFDAS involves pre-existing but undiagnosed atrial fibrillation in addition to new cases of atrial fibrillation that developed around or immediately after the stroke event [8]–[10].

3. AFDAS epidemiology and risk of recurrent stroke

As mentioned previously, despite the fact that AF is a major risk factor for AIS, new AF can also be detected for the first time in patients after AIS without any prior evidence of cardiac arrhythmias. AF following AIS was observed in roughly 5-6% of patients with 72-hour follow-up in several studies [11]–[13], while AFDAS diagnosis can increase to 15 to 20% in studies with more than 7-day monitoring [14]–[16]. The overall rate of post-stroke AF diagnosis during all periods of cardiac monitoring was reported to be 23.7% [5]. It should be emphasized that, in previous studies, Holter was used for monitoring for less than 72 hours, whereas mobile cardiac telemetry or continuous monitoring methods were employed for monitoring for more than 72 hours. The CRYSTAL-AF trial evaluated the use of conventional ECG and implantable cardiac monitors for 12 months and revealed that ICM could detect new AF in 12% of post-stroke patients, whereas conventional ECG only identified 2% of new AF cases [17].

Sposato et al. reported in their retrospective cohort analysis that the ischemic stroke recurrence rate among stroke patients with AFDAS did not differ significantly from sinus rhythm patients. However, only patients with detectable AFDAS in hospital admission were included in this study [9]. One prospective cohort study of stroke patients categorized patients according to cardiac rhythm (ASDAS, KAF, and sinus rhythm) and monitored ischemic stroke recurrence. This study indicated that among 19,604 stroke patients, the probability of ischemic stroke recurrence and mortality in ASDAS patients was comparable to that of KAF (ischemic stroke recurrence was 13.2% vs. 5.7%; the mortality rate of 22.0% vs. 22.1%) and more significant than in patients with normal sinus rhythm. However, some had concerns about the possibility that KAF patients may be misclassified/included in the ASDAS term; therefore, these results should be interpreted cautiously[10].

4. Monitoring

Based on the reported data, the findings of AF in stroke patients are highly dependent on the length of monitoring. Although Holter ECG for 24 hours is currently the recommended minimum monitoring, considerations for longer ECG monitoring for all patients are being explored [18]. In unselected stroke or TIA patients, Holter ECG monitoring for 72-hour was adequate and increased detection of paroxysmal AF from 2.6% in the first 24 hours with 1.8% addition after 72 hours. Continuous monitoring identified paroxysmal AF in almost 93% of ischemic stroke/TIA (follow-up median = 64 hours) cases, while Holter ECG for 24 hours only recognized 34.1%. Therefore, ESC recommended extended continuous rhythm monitoring for at least 72 hours in patients with TIA or ischemic stroke (Class I, level of evidence B) [5].

A number of recommendations have been proposed for patients who require more rigorous monitoring. The STROKE-AF study compared patients with ischemic stroke who had ICM within

ten days of onset to those who received standard therapy. The incidence of atrial fibrillation at six months was 7.9% vs. 0.8% in the ICM group and control group, respectively; this figure increased to 12.1% versus 1.7% at 12 months, respectively [19]. One RCT compared post-stroke patients with normal sinus rhythm and no history of AF who received standard therapy (standard 24 hours of cardiac rhythm monitoring) and patients who received a Holter ECG at day-10, 3- and 6 months after the onset of stroke. This study found 14% of new AF findings in the Holter ECG group, with only 5% identified in the control group at six months [20]

Experts are still debating disagree which patients require extended monitoring. Age, demographics, heart failure, stroke severity, imaging, electrocardiography pattern, or serum biomarkers are suggested to be predictor; however, the definitive clinical approach has not been defined. Advanced age and heart failure are the strongest predictors of AF following ischemic stroke. Longer follow-up primarily depends on the patient's 'AF burden'. Current AF burden definition is the total time of subclinical AF occurrences during a monitoring period (such as 24 hours) [5] AF burden of more than 5.5 hours/day, or > 24-hour episodes, increases the risk of a first stroke diagnosis in patients without prior stroke history. Recent meta-analyses suggested that long-term monitoring of AFDAS patients is categorized into two groups: high- and low-risk of embolism. The AFDAS patients with a higher embolic risk tend to have a higher prevalence of atrial cardiopathy, cardiac comorbidities, and AF burden [21].

5. Management

The CRYSTAL-AF and EMBRACE studies showed that the treatment of the majority of patients with cryptogenic stroke can shift from antiplatelet to oral anticoagulant upon identification of AF. Following the diagnosis of AF, the prevalence of OAC administration increased from 5-10% to over 97% [17], [22]. In a retrospective/prospective cohort analysis, cryptogenic poststroke patients with ICM-diagnosed AF and anticoagulant treatment were compared to those without AF. In this study, 30% of post-cryptogenic stroke patients were found to have AF during monitoring, and 90% received oral anticoagulants. No significant difference was discovered in the recurrent stroke risk between these AF patients on OAC and those without AF. This trial indicated that OACs might reduce AFDAS patients' stroke recurrence risk to the baseline [23]. The finding was similar to another study in which the recurrent stroke and TIA events were reduced in the intervention group (long-term monitoring and OAC treatment in newly AF diagnosed patients) although this study was not powered enough to evaluate this endpoint [20]. As there is still limited evidence for stroke patients, experts' consensus currently agrees to treat significant 30-second AF episodes detected by continuous monitoring with anticoagulant prophylaxis [18].

Recent AHA guidelines for stroke management recommend that stroke or TIA patients with identified AF, regardless of the pattern (paroxysmal, persistent, or permanent), receive an anticoagulant regimen to minimize recurrent stroke events. This statement is supported by the fact that AF patients will be categorized as anticoagulant therapy candidates by the stroke risk scoring system in the presence of a prior history of stroke or transient ischemic attack. Patients with a large AIS have an elevated risk of both recurrent ischemic stroke and ICH. The risk of recurrent ischemic stroke was reported at approximately 1% per day in the first two weeks. Meanwhile, the rate of hemorrhagic transformation post-stroke was found to increase by thrombolytics (6 - 21%) compared to the control group (1 - 7%). Oral anticoagulant lowers the likelihood of recurrent ischemic stroke while also raising acute poststroke cerebral hemorrhage risk. Therefore, it is reasonable to delay the use of oral anticoagulants for 14 days after the onset of a stroke in patients with AF and high risk of bleeding [6]. This emphasizes that the decision of oral anticoagulants should be balanced between each individual's ischemic and bleeding risk.

6. Future challenges

The future challenges would probably be defining the most effective method, intensity, and duration of rhythm monitoring after ischemic stroke. Moreover, the methods should be cost-effective and comfortable for patients. For example, widely available Holter ECG causes poor compliance as the device is bulky and sometimes the lead adhesive causes skin irritation. The monitoring device should also be water-resistant to not prevent the patients from doing daily activities. Modern devices such as smartphone photoplethysographic methods could detect irregular heart rhythms using advanced algorithms. Fitness trackers and smartwatches also can monitor the rhythm [18], [24].

A screening strategy to stratify stroke patients with higher risk for AFDAS might be useful, particularly in identifying which patients would benefit from a longer monitoring duration. A systemic review in 2021 evaluated 17 different risk scores, some have been validated, with the scores' performance widely varied, and no score had better performance than another [25]. SAFAS study highlighted the multimodal approach for AFDAS prediction models that included clinical, imaging, and blood biomarkers such as galectin-3, osteoprotegerin, and NT-proBNP [26]. These biomarkers were found to be independently associated with both early (during hospital stay) and delayed (after patients are discharged) AFDAS. Left atrium indexed volume was also found to be more frequent in AFDAS patients. Both early and delayed AFDAS predictive models in the SAFAS study showed moderate predictive values of AFDAS (positive predictive values were 63% and 71%; negative predictive values were 80 and 83%, respectively). Several prior studies had reported some biomarkers that were found to be predictors of AFDAS, including NT-proBNP, Angiotensin-2, Dickkopf-related protein 3, C-reactive protein, and troponin [27],

[28]. These biomarkers would require further studies as they can be predictive to various comorbidities.

The genetic background of arrhythmia has also been studied extensively, and researchers have made a significant breakthrough in understanding it. Among the genes linked with AF, MYH6, MYL4, NPPA, and TTN have the most substantial supporting data [29]. A recent AF genome-wide polygenic score utilized 6.6 million variants in over 500,000 patients and indicated that 6.1% of the general population has a threefold AF risk [30]. A study utilizing 719 SNPs found that 67% of people in the highest quartile were more likely to have AF. Its follow-up study concluded that AF genome-wide polygenic score was related to the incidence of AF more than clinical risk factors, adding more information offered by these variables. Additionally, using 127 variants, another study can identify patients with a two-fold increase in cardioembolic stroke risk, even the additional benefit of these variants has yet to be confirmed [31]. However, most of reported genetic studies results are vaguely defined and hardly used in clinical practice. Future studies on the genetic risk of AF, AFDAS, and therapy outcomes are still needed.

7. Conclusion

In conclusion, AFDAS can be diagnosed without a prior history of the arrhythmia. Recent evidence demonstrates that AFDAS detection following an ischemic stroke event is critical for secondary prevention. To increase the likelihood of identifying a new AF diagnosis, an ischemic stroke patient without a previous AF diagnosis should be followed by a minimum of 72 hours of continuous ECG monitoring. Future studies are required to determine the optimal cardiac monitoring protocol, particularly the methods, duration of cardiac monitoring, and benefit of oral anticoagulants in AFDAS patients.

Conflict of interest

The authors have no conflicts of interest to declare

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