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# Swiss Stroke Society position paper on atrial fibrillation monitoring and management after ischaemic stroke: a shift from understanding the index stroke to preventing the next one

**Thomas Meinel[a], Markus Arnold[b], Laurent Roten[c], Philipp Krisai[de], Marie-Luise Mono[f], Catherine Gebhard[c], Leo Bonati[gh], Timo Kahles[i], Urs Fischer[j], Marcel Arnold[a], Mira Katan[bj], on behalf of the Swiss Stroke Organisation**

[a] Stroke Research Centre Bern, Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Bern, Switzerland
[b] Department for Neurology, University Hospital Zurich, Zurich, Switzerland
[c] Department of Cardiology, Inselspital, Bern University Hospital, and University of Bern, Bern, Switzerland
[d] Cardiology Division, Department of Medicine, University Hospital Basel, Basel, Switzerland
[e] Cardiovascular Research Institute Basel, Basel, Switzerland
[f] Stroke Unit, Stadtspital Triemli, Zurich, Switzerland
[g] Department of Neurology, University Hospital Basel, Basel, Switzerland
[h] Department of Research, Reha Rheinfelden, Rheinfelden, Switzerland
[i] Department of Neurology and Stroke Centre, Cantonal Hospital of Aarau, Aarau, Switzerland
[j] Department of Neurology and Stroke Centre, University Hospital Basel and University of Basel, Basel, Switzerland

## Summary

This position paper on the detection of atrial fibrillation after ischaemic stroke is a statement of the "Heart and Brain" committee of the Swiss Stroke Society. This position paper summarises present knowledge on the detection of atrial fibrillation after ischaemic stroke or transient ischaemic attack. An interdisciplinary standard for monitoring on the stroke unit and after discharge is proposed respecting recent developments and Swiss particularities. The main evolution in the field is that the role of atrial fibrillation screening after stroke or transient ischaemic attack has shifted from understanding the index stroke to preventing the next stroke; it therefore should also be performed in patients with certain other stroke aetiologies, e.g. symptomatic carotid artery stenosis. The duration of atrial fibrillation monitoring should be based on an individualised risk assessment incorporating clinical characteristics as well as cardiac and laboratory biomarkers. Given the paucity of randomised controlled data on this topic, this position paper intends to give practical advice to healthcare professionals involved in stroke care in Switzerland based on a consensus between experts in the field.

Thomas Meinel, MD, PhD
Inselspital
Bern University Hospital
Freiburgstrasse 10
CH-3010 Bern
thomas.meinel[at]insel.ch

**ABBREVIATIONS**

**MR-proANP:** mid-regional pro-atrial natriuretic peptide
**NT-proBNP:** N-terminal pro-B-type natriuretic peptide
**TIA:** transient ischaemic attack

## Introduction

Ischaemic stroke is a major cause of disability and mortality worldwide [1]. Atrial fibrillation is the most common cardiac arrhythmia, affecting up to 2% of the European population [2]. Up to a quarter of ischaemic strokes can be attributed to atrial fibrillation, and atrial fibrillation increases the risk of ischaemic stroke significantly [3]. Besides the 25% of ischaemic stroke caused by atrial fibrillation, an increasing number of patients with ischaemic stroke have atrial fibrillation (whether causally related or not) [4]. Incidence and prevalence of atrial fibrillation vary by sex [5], age, race/ethnicity, geographical region and intensity of screening. Accordingly, the incidence of atrial fibrillation is higher in men than in women, higher in Western European countries than in Eastern European countries [6] and increases rapidly with age: at the age of 80 years, over 10% of the population are affected by atrial fibrillation with atrial fibrillation starting at an older age in women [7, 8]. Atrial fibrillation-associated strokes are particularly severe [9], have a high recurrence risk [10–12] and a worse prognosis than ischaemic strokes of other aetiologies [13].

In patients with stroke and no other clear aetiology, the benefit of atrial fibrillation monitoring and detection is obvious, because oral anticoagulation reduces recurrent stroke in atrial fibrillation patients with a relative risk reduction of up to 60–70% [14]. However, recent data shows that the incidence of atrial fibrillation does not differ between cryptogenic stroke patients [15] and stroke caused by large-artery or small-vessel disease [16] – presumably because shared cardiovascular risk factors cause both arteriosclerotic disease as well as atrial fibrillation. Hence, another relevant percentage of patients with ischaemic stroke

have atrial fibrillation – without atrial fibrillation necessarily being the cause of the index ischaemic stroke – and atrial fibrillation screening and treatment may also benefit these patients because it may prevent future stroke of cardioembolic origin. Effective anticoagulation in the event of an ischaemic stroke in patients with atrial fibrillation is associated with a reduced stroke severity and better outcome compared to patients without effective anticoagulation [17, 18].

However, atrial fibrillation can be difficult to detect, as it is often asymptomatic and sporadic [6]. Various monitoring strategies are available to detect subclinical atrial fibrillation, including in-hospital and outpatient monitoring with the use of external and implantable recorders as well as wearables and app-based technology [6, 19]. This guideline aims to provide recommendations on screening for atrial fibrillation in patients with ischaemic stroke or transient ischaemic attack (TIA) in order to enable effective secondary prevention through anticoagulation and novel treatment strategies.

### Epidemiology in Switzerland

Around 1–2% of the population is affected by atrial fibrillation – the most common cardiac arrhythmia – translating to around 150,000 individuals in Switzerland [20]. Atrial fibrillation cases will likely double in the upcoming decades [21]. Every year, about 16,000 strokes occur in Switzerland, with around 4000 of them attributable to atrial fibrillation [22]. Half of this latter group has known atrial fibrillation (and often inadequate treatment – especially in women [23]), whereas the other half is newly diagnosed with atrial fibrillation after stroke [24]. The absolute number of strokes is higher in women than in men in Switzerland while the relative proportion of stroke events per age group is lower in women [22].

### Embolic stroke of undetermined source

Due to the better safety profile of direct oral anticoagulants (DOAC), it had been hoped that atrial fibrillation screening would no longer be necessary and that all patients with an embolic ischaemic stroke pattern and without any other obvious stroke cause would benefit from DOAC treatment. However, the trials failed to show a benefit of DOAC therapy *ex juvantibus* [25]. Certain hypothesis-generating embolic stroke of undetermined source subgroups (impaired renal function [25], patients aged >75 years [26] and left ventricular dysfunction [27], or dilated left atrium[28]) could benefit from empirical DOAC therapy. However, the ARCADIA trial did not show a benefit of apixaban over antiplatelet therapy [29] even in those patients with the highest quartile of left atrial myopathy [30]. Further adequately powered randomised trials addressing these subpopulations are needed. In the meantime, an embolic stroke of undetermined source without detected atrial fibrillation is currently insufficient to initiate DOAC treatment.

### Purpose of the position paper

The purpose of this position paper was primarily to translate the most recent and rapidly evolving evidence on this topic into country-specific recommendations reflecting peculiarities and conditions of the Swiss healthcare system. We aimed to provide concise yet comprehensive practical advice for atrial fibrillation screening after ischaemic stroke or TIA. Secondly, we aimed to cover knowledge gaps and blind spots of recommendations of the available international guidelines. The position paper is intended to provide guidance to physicians involved in the care of stroke patients. In line with the nature of a position paper, the labelling of evidence levels has been omitted, as it mainly represents the expert opinions based on lower evidence levels and clinical experience. Therefore, it is not intended to replace any international guidelines but rather complement them.

### Search strategy, consensus and composition of the module working group

The recommendations presented are evidence-based and supported by a literature review. For this purpose, the members of the working group reviewed international guidelines on atrial fibrillation monitoring after stroke, including those by the European Stroke Organisation (ESO), the European Society of Cardiology, the American Heart Association/American Stroke Association, as well as the certification criteria of international stroke societies. Additionally, original articles not yet incorporated in the international guidelines were included. Recommendations were reviewed and discussed among the full committee to ensure diverse perspectives. In case of discrepancy, recommendations were voted on to reach consensus. The references provided are representative and not exhaustive.

The writing group for this position paper was appointed by the Swiss Stroke Society and included three stroke neurologists (MK, MA, TRM) and two cardiac electrophysiologists (PK, LR).

### Atrial fibrillation definitions

We followed the European Society of Cardiology definition of atrial fibrillation, namely an episode of atrial fibrillation on a standard 12-lead ECG recording or a single-lead ECG tracing of >30 seconds' duration with no discernible repeating P waves and irregular RR intervals (when atrioventricular conduction is not impaired) [6]. For implantable cardiac monitors, a minimum duration of 6 minutes is required for the diagnosis of subclinical atrial fibrillation. For the diagnosis of clinical atrial fibrillation (whether symptomatic or asymptomatic), a documentation of atrial fibrillation on a 12-lead ECG or on a rhythm strip of ≥30 seconds' duration is necessary. Wearables using automated algorithms to assess heart beat variability, e.g. via photoplethysmography, are currently insufficient to make a final diagnosis of atrial fibrillation without ECG proof. However, the diagnosis can be made if at least a single-lead ECG recording of sufficient quality showing atrial fibrillation is available and is reviewed according to the criteria mentioned above by an expert in ECG interpretation.

### Wearable single-lead devices and novel detection devices

The development of mobile health technologies for atrial fibrillation detection is progressing rapidly, with hundreds of apps and more than 400 wearable activity monitors cur-

rently available [6]. These devices mostly analyse beat-to-beat variability and are useful as a first, coarse screening step. If these devices recognise pulse irregularities of sufficient duration, atrial fibrillation may be the cause. However, pulse irregularities may also have other causes, like frequent premature atrial or ventricular complexes, or simply represent recording artefacts. Whereas wearable single-lead devices that use photoplethysmography do not allow to diagnose atrial fibrillation, devices that record a single-lead ECG of sufficient quality (such as some smartwatches and other wearable single-lead devices) can be used for atrial fibrillation diagnosis. To make the atrial fibrillation diagnosis, the same criteria apply as mentioned above for the diagnosis of clinical atrial fibrillation. Namely, at least a single-lead ECG tracing of >30 seconds' duration with no discernible repeating P waves and irregular RR intervals has to be documented, or a standard 12-lead ECG showing atrial fibrillation. These single-lead ECG tracings potentially showing atrial fibrillation should always be reviewed by a physician with sufficient experience in rhythm analysis to confirm the diagnosis of atrial fibrillation, as these ECG tracings can be very tricky to assess. In case of doubt or if the quality of the rhythm strip is insufficient for a definite diagnosis, atrial fibrillation diagnosis should be rejected.

One drawback of these devices is that they are currently mainly used by the younger generations and their use is less popular among the elderly stroke population. Nevertheless, wearable single-lead devices may provide an alternative and an accessible way of atrial fibrillation screening.

## Key concepts

### Beyond aetiology

Aetiological stroke work-up, as traditionally practiced, aimed to identify the underlying cause of an index stroke in order to tailor secondary prevention strategies specific to that cause. In the context of an ageing patient population with generally higher vascular risk, multiple potential underlying causes of stroke often coexist, with variable attributable risk over time. Focusing solely on identifying the most likely stroke mechanism for an event and assigning a mutually exclusive stroke aetiology does not necessarily determine potential future stroke mechanisms and offer the best protection. In the STROKE-AF trial [16], atrial fibrillation screening by implantable cardiac monitors had a similar diagnostic yield in patients with stroke attributable to large-artery disease or small-vessel disease as compared to the original trials done in cryptogenic stroke populations [15]. Thus, atrial fibrillation screening seems equally important in ischaemic stroke cases where mechanisms other than atrial fibrillation are likely involved to effectively prevent future events. Another argument for performing rhythm monitoring regardless of stroke aetiology stems from the randomised MonDAFIS study [31], where an additional Holter ECG for up to seven days as compared to standard of care was linked to a lower all-cause mortality, potentially driven by detection of other relevant abnormal ECG findings and adequate (non)pharmacological management [32].

We therefore recommend basing decisions on the duration of atrial fibrillation screening on the individual patient risk of incident atrial fibrillation regardless of the presumed index stroke aetiology. Specifically, this could mean that patients with a symptomatic carotid stenosis with high individual risk for atrial fibrillation might qualify for prolonged cardiac monitoring.

### Structured rhythm rounds

For those patients, where telemetry is performed in the hospital, a structured rhythm round as part of stroke unit care might improve the atrial fibrillation detection rate [33]. This includes screening the 24-hour heart rate spectrum for drops or increases >20 beats per minute in heart rate with consecutive evaluation of the corresponding ECG strips. Second, changes in the amplitude of heart rate variation can be identified and similarly evaluated. Third, all tachycardia >120 beats per minute or bradycardia <40 beats per minute events are evaluated. Fourth, automatically detected episodes of arrhythmia (tachy-/bradycardia, flat line, ventricular arrhythmia) can be verified. Fifth, the 24-hour "beat-to-beat" registration overview can be screened for irregularities in RR intervals and atrial fibrillation episodes. An automated analysis may be helpful in this context, but requires a manual and expert physician validation of the ECG findings [34, 35]. If the first monitoring is done using ambulatory Holter ECG, the same high-quality and standardised evaluation of the ECG should be ensured.

### Atrial fibrillation burden

The term "atrial fibrillation burden" in relation to continuous device-based monitoring refers to either the longest observed atrial fibrillation episode or the percentage of time spent in atrial fibrillation [36]. Atrial fibrillation burden can only be reported reliably with continuous long-term monitoring. As a basic principle, the longer the duration of monitoring for atrial fibrillation, the higher the yield of atrial fibrillation screening [31, 37–39]. Most importantly, with shorter monitoring, atrial fibrillation is mainly detected in patients with a high atrial fibrillation burden. This also impacts the risk of recurrence, which was 5-fold higher if atrial fibrillation was detected by standard ECG as opposed to a 14-day Holter ECG [40]. Vice versa, a long monitoring duration increases the likelihood of diagnosing atrial fibrillation in patients with a low or very low atrial fibrillation burden [36].

If atrial fibrillation is diagnosed with intermittent Holter monitoring, it can be assumed that the atrial fibrillation burden is relatively high, and oral anticoagulation is clearly indicated. For long-term continuous monitoring with implantable cardiac monitors, the cut-off of atrial fibrillation burden at which anticoagulation should be initiated remains controversial.

In *primary prevention*, evidence suggests that atrial fibrillation episodes lasting more than 24 hours carry a relevant increase in the risk of stroke and warrant anticoagulation treatment [41]. Similarly, the LOOP study randomising individuals with stroke risk factors to atrial fibrillation screening by implantable cardiac monitors versus standard of care concluded that despite higher atrial fibrillation de-

tection rates, not all screen-detected atrial fibrillation merits anticoagulation since anticoagulation initiation did not significantly reduce the risk of stroke or systemic arterial embolism [42]. This is in line with the fact that the STROKESTOP study found that screening for atrial fibrillation with a 14-day Holter ECG showed a small absolute risk reduction of about 1% over a follow-up of 7 years [43], presumably because only atrial fibrillation with a higher burden was picked up by the shorter monitoring duration as compared to the LOOP trial.

The recently published, event-driven NOAH AFNET 6 trial randomised patients who had at least one additional risk factor for stroke and device-detected atrial high-rate episodes of ≥6 minutes duration to edoxaban versus placebo or aspirin if indicated. The median $CHA_2DS_2$-VASc score was 4 and 10% of patients had previous stroke or TIA. The incidence of stroke was low at about 1% per patient-year in both groups but the composite safety event, including death and major bleeding, occurred more frequently in the edoxaban group [44]. A subanalysis of patients with atrial high-rate episodes >24 hours duration did not find an interaction between episode duration and anticoagulation therapy [45].

In the ARTESIA trial, patients with subclinical atrial fibrillation lasting 6 minutes to 24 hours detected only by long-term continuous monitoring with pacemakers or defibrillators were randomised to anticoagulation with apixaban or aspirin treatment. The mean $CHA_2DS_2$-VASc score was 3.9 and 9% of patients had previous stroke, TIA or systemic embolism. The rate of stroke or systemic embolism was low in both groups and reduced from 1.21% per patient-year in the aspirin group to 0.78% in the apixaban group with more severe strokes occurring in the aspirin group [46]. However, major bleeding increased from 0.94% per patient-year in the aspirin group to 1.71% in the apixaban group. This was mainly driven by an increase in gastrointestinal bleeding whereas fatal or intracranial bleeding was not different among groups. Of note, atrial fibrillation episodes of >24 hours duration occurred in 24% of patients a mean of 18 months after inclusion, and mandated study termination in these patients. Another 34% of patients discontinued trial medication prematurely.

A meta-analysis of the NOAH AFNET 6 trial and ARTESIA trial confirmed that oral anticoagulation with edoxaban or apixaban reduces the risk of stroke in patients with device-detected atrial fibrillation but increases the risk of major bleeding (i.e. mainly gastrointestinal bleeding) [47]. Subanalyses on patients with previous stroke or TIA have not yet been published. Of note, in both trials most devices were pacemakers, defibrillators and cardiac resynchronisation devices and only a very small proportion were implantable cardiac monitors.

In *secondary prevention*, and in particular after an ischaemic stroke, the cut-off to justify the initiation of DOAC therapy is an ongoing debate and might be shorter than for primary prevention. Given the fact that there is an interaction of the $CHA_2DS_2$-VASc score and the risk of stroke in atrial fibrillation patients, the threshold for initiating anticoagulation should incorporate the cardiovascular risk profile as reflected by the $CHA_2DS_2$-VASc score, the longest detected atrial fibrillation episode, as well as individual patient factors and preferences (table 1) [48]. For example, CT-based models like the $S_2$TOP-BLEED+ score [49] or MRI-based models like the MICON score [50] can help estimate ischaemic and haemorrhagic risks after ischaemic stroke depending on different antithrombotics. If only shorter episodes are recorded, atrial fibrillation monitoring should be continued as the atrial fibrillation burden may evolve and oral anticoagulation treatment become necessary in the future.

**Table 1:**
Suggested atrial fibrillation duration registered on *implantable cardiac monitors* that should trigger the evaluation of anticoagulation therapy by a qualified physician.

| Setting | CHADS-VASc score | Suggested atrial fibrillation duration by implantable cardiac monitor reasonable to trigger initiation of anticoagulation | Notes |
|---|---|---|---|
| Primary prevention | 0–2 | 24 hours | |
| | 3 or higher | 6 min – 24 hours | Anticoagulation can be considered in patients *with high* ischaemic risk and *low bleeding risk* [47, 51] |
| | | >24 hours | |
| Secondary prevention | 0–1 | | Not possible after an ischaemic stroke or transient ischaemic attack |
| | 2 | 1 – 6 hours | |
| | 3 or higher | Minimum 6 minutes | |

This table does not apply to atrial fibrillation diagnosed by 12-lead-ECG, inpatient or outpatient telemetry. In this setting, any episode ≥30 seconds' duration is sufficient for the evaluation of initiation of anticoagulation.

The decision to initiate anticoagulation should take into account a thorough assessment of patient factors and preferences as well as individualised assessment of ischaemic and bleeding risk [6].

In TIA patients, the probability of a vascular event should be taken into account; note that TIA was defined in the derivation study of the $CHA_2DS_2$-VASc score as a focal neurological deficit lasting <24 hours and probably included patients who would be classified as minor stroke based on contemporary brain imaging with MRI.

In addition to the initiation of anticoagulation, all aspects of the holistic ABC care bundle should be optimised after atrial fibrillation diagnosis. In addition, rhythm control interventions should be considered and discussed in patients with atrial fibrillation diagnosed within the last 12 months.

A meta-analysis of the NOAH AFNET 6 trial and ARTESIA trial confirmed that direct oral anticoagulant (DOAC) therapy reduces the risk of stroke in patients with device-detected atrial fibrillation but increases the risk of major bleeding [47]. Importantly, in both trials most devices were pacemakers, defibrillators and cardiac resynchronisation devices and only a very small proportion were implantable cardiac monitors. Hence, the minimal duration on an implantable cardiac monitor that warrants anticoagulation is less certain, given the fact that most patients in those trials had a previous cardiac condition.

## Key clinical variables and biomarkers for individual risk stratification

Based on pathophysiological considerations, various factors have been proposed to either increase the yield of atrial fibrillation detection rates during prolonged monitoring or to identify atrial fibrillation cases associated with a higher risk of stroke recurrence. These include clinical variables, blood-based biomarkers, ECG and echocardiography parameters as well as brain-imaging characteristics. Most of the current supporting evidence was derived either from cryptogenic stroke or embolic stroke of undetermined source cohorts and less from the whole ischaemic stroke population.

### Clinical variables

The most prominent predictors for the detection of atrial fibrillation following a stroke are older age and more severe stroke [52]. Furthermore, established cardiovascular risk factors such as hypertension are known to be associated with an increased risk of atrial fibrillation detection. We suggest incorporating evidence for clinical manifest heart failure with or without reduced ejection fraction and arteriosclerotic disease (peripheral or coronary heart disease) [52].

### ECG markers

For clinical practice we suggest a cut-off of >500 supraventricular extrasystoles over 24 hours or any atrial runs ≥20 beats per minute as a reasonable marker to classify high-risk patients [53–55].

In addition, P-terminal force in lead V1 (PTFV1), the product of the amplitude and duration of a terminal negative deflection of a biphasic P-wave in lead V1 >4000 μV × ms and an ECG marker of left atrium abnormality, might also advocate for prolonged heart rhythm monitoring [56].

### Cardiac imaging

The presence of spontaneous echo contrast or direct evidence of thrombi in the atrium can be indicative of underlying atrial fibrillation [57]. Moreover, valvular abnormalities, particularly rheumatic mitral valve stenosis or severe mitral and tricuspid valve insufficiency, are recognised as risk factors for atrial fibrillation development [57]. In addition to these factors, left atrial enlargement is a promising biomarker for stratifying patients at high and low risk for atrial fibrillation [58, 59]. A left atrial volume index incorporating body size might be an even more reliable marker than left atrial diameter alone and further measurements of left atrial function have been linked to higher risk of atrial fibrillation detection [60–62]. Whereas most of the evidence is available by markers assessed by echocardiography, those biomarkers are theoretically also available on cardioaortic CT and MRI, however the cut-offs are less established with those novel imaging options.

### Brain imaging

From a theoretical perspective, it remains plausible that specific lesion patterns observed on MRI – such as evidence of large wedge-shaped territorial infarcts, chronic cortical and cerebellar infarcts or cortical infarction in multiple vascular territories – may indicate a higher likelihood of atrial fibrillation detection [63]. However, the evidence in this regard remains conflicting. For instance, a subanalysis of the CRYSTAL-AF study found no significant association between acute lesion size, location or number of lesions and the detection of subclinical atrial fibrillation [64]. Conversely, a recent subanalysis of the MonDAFIS study showed multiple lesions and an extensive spatial distribution of lesions as factors associated with a higher rate of atrial fibrillation detection [65]. Also, chronic cortical lesions were associated with atrial fibrillation [66]. Furthermore, it is important to note that atrial fibrillation can be detected in a substantial proportion of lacunar strokes [16, 67]. Consequently, we do not recommend identifying low-risk patients solely based on imaging patterns.

### Blood-based biomarkers

Among several blood-based biomarkers, the natriuretic peptides, i.e. atrial and brain-derived natriuretic peptide and especially their cleaved by-product MR-proANP along with NT-proBNP, are the most robust and studied biomarkers for atrial fibrillation risk assessment after stroke. Whereas the proposed cut-offs vary slightly (especially for NT-proBNP), we suggest that MR-proANP levels below 92 pmol/l [68] or NT-proBNP levels below 200 pg/ml [69, 70], can be utilised to classify patients into a low-risk group while MR-proANP levels above 200 pmol/l [68, 71–73] or NT-proBNP levels above 400 ng/l [19, 74] can be utilised to define high-risk patients. It is recommended to obtain either of these biomarkers in the acute setting; however only for MR-proANP have the cut-offs been validated in all stroke subtypes within the first five days of symptom onset. Since the biomarkers may be influenced by renal function, body mass index, age and sex [75], the suggested values should be interpreted as guidance and not as absolute cut-offs – further studies in this direction are needed.

### Atrial fibrillation detection risk scores

Several risk scores to predict newly detected atrial fibrillation after stroke have been developed, but methodological weaknesses as well as restriction to specific stroke subpopulations are problematic. Moreover, the performance of risk scores in discriminating correctly was variable and the clinical utility remains uncertain [76].

The suggested biomarkers for risk stratification and thresholds are summarised in figure 1. Given the limited evidence to justify the superiority of any single marker, we propose a simplified algorithm aimed at stratifying patients into low, moderate and high risk for atrial fibrillation.

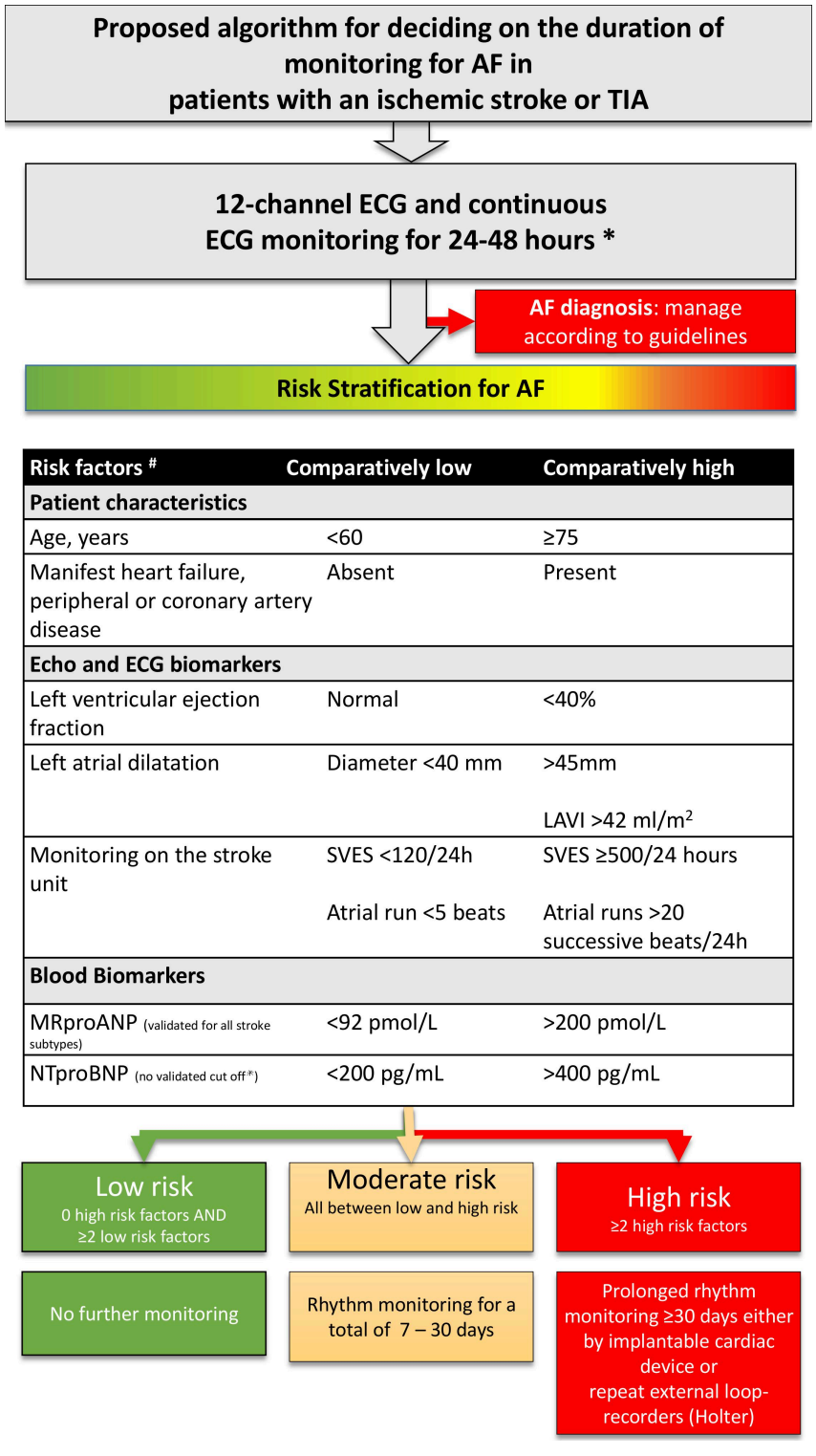
## Flow chart

In this flow chart, we propose a pragmatic algorithm for atrial fibrillation monitoring after ischaemic stroke or TIA. The individual components of the decision algorithm (low or high pre-test probability for detecting atrial fibrillation) are based on observational studies. The biomarkers are collinear and the proposed decision-making process as a whole has not yet been validated. Ongoing studies will clarify whether intensified rhythm monitoring in patients

with recent ischaemic stroke leads to a decrease in recurrent thromboembolism (e.g. NCT04371055).

In accordance with the recommendations of professional societies [6, 19, 77–80], all patients with ischaemic stroke should receive a standard 12-lead ECG on admission, followed by continuous ECG monitoring for a minimum of 48 hours (preferably ECG monitoring on the stroke unit, alternatively by ambulatory Holter ECG). In patients with a clear different aetiology and no shared cardiovascular risk factors (e.g. cervical artery dissection), it is reasonable

**Figure 1:** Algorithm for determining the duration of ECG monitoring after ischaemic stroke or transient ischaemic attack based on a risk stratification for atrial fibrillation (AF) and applicable to all aetiologies of the index event. * In patients with a clear different aetiology and no shared cardiovascular risk factors (e.g. cervical artery dissection), it is reasonable to deviate from the recommended minimum. The 48h ECG monitoring is preferably done on the stroke unit, alternatively by ambulatory Holter ECG. # The available biomarkers should be used without the need to obtain all biomarkers. LAVI: left atrial volume index; MR-proANP: mid-regional pro-atrial natriuretic peptide; NT-proBNP: N-terminal pro-B-type natriuretic peptide; SVES: supraventricular extrasystole; TIA: transient ischaemic attack.




| Risk factors # | Comparatively low | Comparatively high |
|---|---|---|
| **Patient characteristics** | | |
| Age, years | <60 | ≥75 |
| Manifest heart failure, peripheral or coronary artery disease | Absent | Present |
| **Echo and ECG biomarkers** | | |
| Left ventricular ejection fraction | Normal | <40% |
| Left atrial dilatation | Diameter <40 mm | >45mm<br>LAVI >42 ml/m$^2$ |
| Monitoring on the stroke unit | SVES <120/24h<br>Atrial run <5 beats | SVES ≥500/24 hours<br>Atrial runs >20 successive beats/24h |
| **Blood Biomarkers** | | |
| MRproANP (validated for all stroke subtypes) | <92 pmol/L | >200 pmol/L |
| NTproBNP (no validated cut off*) | <200 pg/mL | >400 pg/mL |

to deviate from the recommended minimum. An analysis software for continuous ECG analysis can optimise detection rates of atrial fibrillation on the stroke unit and should be used if possible. We recommend extended rhythm monitoring up to 30 days and long-term monitoring according to the individual risk stratification, provided that the patient is suitable for anticoagulation. The sequential approach is recommended given the fact that atrial fibrillation will be picked up by a standard 12-lead ECG on admission in about 8%, by stroke unit monitoring in about 4%, by short external continuous monitoring (Holter ECG) in about 8% and by prolonged external loop recorders in another 4% of patients [39]. Hence, costly and invasive testing can be avoided if the first tests already confirm the diagnosis of atrial fibrillation. As opposed to the ESO guideline on atrial fibrillation screening after stroke or TIA, we strongly recommend the use of biomarkers for selection of patients for prolonged monitoring (see guidance in figure 1). The ESO recommendation to avoid the use of biomarkers for excluding patients from prolonged monitoring and the suggestion to use implantable devices instead of non-implantable devices is in our opinion inappropriate for Switzerland given the availability, costs, logistic and patient barriers of invasive ECG monitoring.

Monitoring should be carried out as soon as possible after the stroke, as atrial fibrillation recurrence is highest early after an ischaemic stroke. We do not recommend using prolonged monitoring if risk stratification indicates a low risk for atrial fibrillation.

## Expert recommendations for current knowledge gaps

We suggest making no distinction for atrial fibrillation monitoring between patients with confirmed ischaemic stroke, patients with a clear-cut TIA and patients with a non-consensus TIA if relevant differential diagnoses of a TIA do not seem likely. This is due to the fact that also non-consensus TIAs bear a high risk of recurrence of major cardiovascular events including stroke [81].

The recommendations given apply regardless of the biological sex, since so far no relevant differences for atrial fibrillation monitoring and benefit of anticoagulation have been reported. However, many referenced studies either did not explore sex differences or had insufficient representation of women. Additionally, there is a notable absence of data concerning the influence of sociocultural gender on atrial fibrillation monitoring.

From a pathophysiological perspective, it might be reasonable not to differentiate between patients with manifest ischaemic stroke and patients with incidentally discovered post-ischaemic brain lesions with regards to atrial fibrillation monitoring, if no other more likely aetiology of the lesion (prior cardioaortic intervention, neuroinflammatory disease, etc.) is present. However, evidence for this approach is lacking and studies ongoing (NCT04449523).

Early rhythm control for patients with a diagnosis of atrial fibrillation in the past 12 months has proven beneficial for lowering the risk of cardiovascular outcomes as compared to usual care. Patients with atrial fibrillation and (recent) stroke were underrepresented in the pivotal early rhythm control trial [82]. However, subgroup analysis suggested an even bigger benefit of rhythm control in patients with prior stroke [83]. Another study from Korea confirmed the feasibility and potential efficacy of rhythm control in stroke patients [84].

Thus, we suggest to consider early rhythm control interventions in patients with atrial fibrillation diagnosed after stroke. Such a strategy might include initiation of oral antiarrhythmics on the stroke unit. Interdisciplinary discussion with cardiology regarding an evaluation of pulmonary vein isolation >3 months after the stroke would be advisable.

In patients with an intermediate likelihood of patent foramen ovale (PFO)-related stroke in whom percutaneous PFO closure is considered, at least a 7-day Holter ECG should be done before closure to exclude paroxysmal atrial fibrillation. If atrial fibrillation is detected in these patients, we recommend initiating long-term anticoagulation, and to reassess the indication for PFO closure with a patient-specific decision on whether to proceed with the intervention. There is uncertainty regarding the benefit of PFO closure on top of anticoagulation treatment since only one trial (CLOSE) compared PFO closure to anticoagulation [85].

There is an ongoing debate on whether atrial fibrillation detected after stroke has a differential risk for recurrent events as compared to atrial fibrillation known before stroke [24, 86, 87]. There is also evidence suggesting that certain stroke locations (e.g. insular cortex lesions) can trigger atrial fibrillation through neurogenic mechanisms [88]. We currently do not recommend differentiating between the two entities regarding the decision to initiate anticoagulation until higher-quality evidence concerning these subgroups is available.

## Key take-home messages

- The *role of atrial fibrillation screening has expanded from understanding the index stroke to preventing the next stroke*. This might be equally important for stroke mechanisms other than cardioembolism in patients with a cardiovascular risk profile (e.g. lacunar stroke or symptomatic carotid stenosis).
- The decision on the optimal atrial fibrillation screening strategy and *duration of ECG monitoring should be based on individual risk classification*. We recommend utilising demographic/clinical features and available *biomarkers to classify patients into low-, moderate- and high-risk atrial fibrillation categories* (figure 1).
- While *patients with ischaemic stroke or transient ischaemic attack (TIA) should receive 24–48 hours of continuous ECG monitoring* (either on the Stroke Unit or by telemetry monitoring thereafter), *prolonged cardiac monitoring* including implantable cardiac monitors *should be considered in patients with high risk of atrial fibrillation* (regardless of aetiology)**.**
- The yield and accuracy of *ambulatory atrial fibrillation diagnosis depends on the device and duration* of monitoring; in general, it increases from wearable single-lead devices to external loop-recorders (ELR) to implantable cardiac monitors.
- *In case of atrial fibrillation diagnosis through continuous monitoring* by an implantable cardiac monitor, *the burden of atrial fibrillation should be incorporated in*

*an individual risk-benefit decision on initiation of direct oral anticoagulation weighing the individual ischaemic and bleeding risk* using established risk models.

– *Atrial fibrillation diagnosed by single-lead recording, e.g. from wearable single-lead monitors, needs to be verified* by a physician with sufficient experience in rhythm analysis to confirm the diagnosis of atrial fibrillation. In case of doubt or if the quality of the rhythm strip is insufficient for a definite diagnosis, the atrial fibrillation diagnosis should be rejected.

– In patients with an *intermediate likelihood of patent foramen ovale related stroke in whom percutaneous PFO closure is considered, at least a 7-day Holter ECG should be done before closure* to exclude paroxysmal atrial fibrillation.

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**References**

1. Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, et al.; GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol. 2021 Oct;20(10):795–820. http://dx.doi.org/10.1016/S1474-4422(21)00252-0.
2. Al-Khayatt BM, Salciccioli JD, Marshall DC, Krahn AD, Shalhoub J, Sikkel MB. Paradoxical impact of socioeconomic factors on outcome of atrial fibrillation in Europe: trends in incidence and mortality from atrial fibrillation. Eur Heart J. 2021 Feb;42(8):847–57. http://dx.doi.org/10.1093/eurheartj/ehaa1077.
3. Yaghi S, Kamel H. Stratifying stroke risk in atrial fibrillation beyond clinical risk scores. Stroke. 2017 Oct;48(10):2665–70. http://dx.doi.org/10.1161/STROKEAHA.117.017084.
4. Yiin GS, Li L, Bejot Y, Rothwell PM. Time Trends in Atrial Fibrillation-Associated Stroke and Premorbid Anticoagulation: Population-Based Study and Systematic Review. Stroke. 2019 Jan;50(1):21–7. http://dx.doi.org/10.1161/STROKEAHA.118.022249.
5. Volgman AS, Benjamin EJ, Curtis AB, Fang MC, Lindley KJ, Naccarelli GV, et al.; American College of Cardiology Committee on Cardiovascular Disease in Women. Women and atrial fibrillation. J Cardiovasc Electrophysiol. 2021 Oct;32(10):2793–807. http://dx.doi.org/10.1111/jce.14838.
6. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al.; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021 Feb;42(5):373–498. http://dx.doi.org/10.1093/eurheartj/ehaa612.
7. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA. 2001 May;285(18):2370–5. http://dx.doi.org/10.1001/jama.285.18.2370.
8. Linde C, Bongiorni MG, Birgersdotter-Green U, Curtis AB, Deisenhofer I, Furokawa T, et al. Sex differences in cardiac arrhythmia: A consensus document of the european heart rhythm association, endorsed by the heart rhythm society and Asia pacific heart rhythm society. Europace. 2018;20(10):1565-1565ao. http://dx.doi.org/10.1093/europace/euy067.
9. Lin HJ, Wolf PA, Kelly-Hayes M, Beiser AS, Kase CS, Benjamin EJ, et al. Stroke severity in atrial fibrillation. The Framingham Study. Stroke. 1996 Oct;27(10):1760–4. http://dx.doi.org/10.1161/01.STR.27.10.1760.
10. Hart RG, Eikelboom JW. Reducing the risk of recurrent stroke in patients with AF. Lancet Neurol. 2012 Jun;11(6):479–81. http://dx.doi.org/10.1016/S1474-4422(12)70096-0.
11. Seiffge DJ, Werring DJ, Paciaroni M, Dawson J, Warach S, Milling TJ, et al. Timing of anticoagulation after recent ischaemic stroke in patients with atrial fibrillation. Lancet Neurol. 2019 Jan;18(1):117–26. http://dx.doi.org/10.1016/S1474-4422(18)30356-9.
12. Seiffge DJ, De Marchis GM, Koga M, Paciaroni M, Wilson D, Cappellari M, et al.; RAF, RAF-DOAC, CROMIS-2, SAMURAI, NOACISP, Erlangen, and Verona registry collaborators. Ischemic Stroke despite Oral Anticoagulant Therapy in Patients with Atrial Fibrillation. Ann Neurol. 2020 Feb;87(5):677–87. http://dx.doi.org/10.1002/ana.25700.
13. Steger C, Pratter A, Martinek-Bregel M, Avanzini M, Valentin A, Slany J, et al. Stroke patients with atrial fibrillation have a worse prognosis than patients without: data from the Austrian Stroke registry. Eur Heart J. 2004 Oct;25(19):1734–40. http://dx.doi.org/10.1016/j.ehj.2004.06.030.
14. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med. 2007 Jun;146(12):857–67. http://dx.doi.org/10.7326/0003-4819-146-12-200706190-00007.
15. Sanna T, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al.; CRYSTAL AF Investigators. Cryptogenic stroke and underlying atrial fibrillation. N Engl J Med. 2014 Jun;370(26):2478–86. http://dx.doi.org/10.1056/NEJMoa1313600.
16. Bernstein RA, Kamel H, Granger CB, Piccini JP, Sethi PP, Katz JM, et al.; STROKE-AF Investigators. Effect of long-term continuous cardiac monitoring vs usual care on detection of atrial fibrillation in patients with stroke attributed to large- or small-vessel disease: the stroke-af randomized clinical trial. JAMA -. JAMA. 2021 Jun;325(21):2169–77. http://dx.doi.org/10.1001/jama.2021.6470.
17. Meinel TR, Branca M, De Marchis GM, Nedeltchev K, Kahles T, Bonati L, et al.; Investigators of the Swiss Stroke Registry. Prior Anticoagulation in Patients with Ischemic Stroke and Atrial Fibrillation. Ann Neurol. 2021 Jan;89(1):42–53. http://dx.doi.org/10.1002/ana.25917.
18. Xian Y, O'Brien EC, Liang L, Xu H, Schwamm LH, Fonarow GC, et al. Association of preceding antithrombotic treatment with acute ischemic stroke severity and in-hospital outcomes among patients with atrial fibrillation. JAMA -. JAMA. 2017 Mar;317(10):1057–67. http://dx.doi.org/10.1001/jama.2017.1371.
19. Schnabel RB, Haeusler KG, Healey JS, Freedman B, Boriani G, Brachmann J, et al. Searching for Atrial Fibrillation Poststroke: A White Paper of the AF-SCREEN International Collaboration. Circulation. 2019 Nov;140(22):1834–50. http://dx.doi.org/10.1161/CIRCULATIONAHA.119.040267.
20. Samim D, Choffat D, Vollenweider P, Waeber G, Marques-Vidal P, Méan M. Prevalence of atrial fibrillation : the Swiss population-based CoLaus|PsyCoLaus study. Herz. 2023 Feb;48(1):48–54. http://dx.doi.org/10.1007/s00059-021-05090-7.
21. Di Carlo A, Bellino L, Consoli D, Mori F, Zaninelli A, Baldereschi M, et al.; National Research Program: Progetto FAI. La Fibrillazione Atriale in Italia. Prevalence of atrial fibrillation in the Italian elderly population and projections from 2020 to 2060 for Italy and the European Union: the FAI Project. Europace. 2019 Oct;21(10):1468–75. http://dx.doi.org/10.1093/europace/euz141.

22. Meyer K, Simmet A, Arnold M, Mattle H, Nedeltchev K. Stroke events, and case fatalities in Switzerland based on hospital statistics and cause of death statistics. Swiss Med Wkly. 2009 Feb;139(5-6):65–9.
23. Thompson LE, Maddox TM, Lei L, Grunwald GK, Bradley SM, Peterson PN, et al. Sex differences in the use of oral anticoagulants for atrial fibrillation: A report from the National Cardiovascular Data Registry (NCDR®) PINNACLE registry. J Am Heart Assoc. 2017 Jul;6(7):e005801. http://dx.doi.org/10.1161/JAHA.117.005801.
24. Lyrer F, Zietz A, Seiffge DJ, Koga M, Volbers B, Wilson D, et al.; NOACISP-LONGTERM, Erlangen Registry, CROMIS-2, SAMURAI-NVAF and Verona Registry collaborators. Atrial Fibrillation Detected before or after Stroke: role of Anticoagulation. Ann Neurol. 2023 Jul;94(1):43–54. http://dx.doi.org/10.1002/ana.26654.
25. Hariharan NN, Patel K, Sikder O, Perera KS, Diener HC, Hart RG, et al. Oral anticoagulation versus antiplatelet therapy for secondary stroke prevention in patients with embolic stroke of undetermined source: A systematic review and meta-analysis. Eur Stroke J. 2022 Jun;7(2):92–8. http://dx.doi.org/10.1177/23969873221076971.
26. Diener HC, Sacco RL, Easton JD, Granger CB, Bar M, Bernstein RA, et al. Antithrombotic Treatment of Embolic Stroke of Undetermined Source: RE-SPECT ESUS Elderly and Renally Impaired Subgroups. Stroke. 2020 Jun;51(6):1758–65. http://dx.doi.org/10.1161/STROKEAHA.119.028643.
27. Birnbaum LA, Kamel H, Sheth KN, Sharma R. Left Ventricular Dysfunction Among Patients With Embolic Stroke of Undetermined Source and the Effect of Rivaroxaban vs Aspirin A Subgroup Analysis of the NAVIGATE ESUS Randomized Clinical Trial. 2021;10065:1–7.
28. Healey JS, Gladstone DJ, Swaminathan B, Eckstein J, Mundl H, Epstein AE, et al. Recurrent Stroke With Rivaroxaban Compared With Aspirin According to Predictors of Atrial Fibrillation: Secondary Analysis of the NAVIGATE ESUS Randomized Clinical Trial. JAMA Neurol. 2019 Jul;76(7):764–73. http://dx.doi.org/10.1001/jamaneurol.2019.0617.
29. ESOC 2023 Abstract Book. Eur Stroke J. 2023;8(2 suppl):3–669.
30. World Stroke Congress. WSC23 Late Breaking Abstracts. Int J Stroke. 2023;18(3 suppl):421–58.
31. Haeusler KG, Kirchhof P, Kunze C, Tütüncü S, Fiessler C, Malsch C, et al.; MonDAFIS Investigators. Systematic monitoring for detection of atrial fibrillation in patients with acute ischaemic stroke (MonDAFIS): a randomised, open-label, multicentre study. Lancet Neurol. 2021 Jun;20(6):426–36. http://dx.doi.org/10.1016/S1474-4422(21)00067-3.
32. Olma MC, Tütüncü S, Fiessler C, Kunze C, Krämer M, Steindorf-Sabath L, et al.; MonDAFIS Investigators [Link]. In-Hospital ECG Findings, Changes in Medical Management, and Cardiovascular Outcomes in Patients With Acute Stroke or Transient Ischemic Attack. J Am Heart Assoc. 2023 Jan;12(2):e027149. http://dx.doi.org/10.1161/JAHA.122.027149.
33. Kallmünzer B, Breuer L, Hering C, Raaz-Schrauder D, Kollmar R, Huttner HB, et al. A structured reading algorithm improves telemetric detection of atrial fibrillation after acute ischemic stroke. Stroke. 2012 Apr;43(4):994–9. http://dx.doi.org/10.1161/STROKEAHA.111.642199.
34. Rizos T, Güntner J, Jenetzky E, Marquardt L, Reichardt C, Becker R, et al. Continuous stroke unit electrocardiographic monitoring versus 24-hour Holter electrocardiography for detection of paroxysmal atrial fibrillation after stroke. Stroke. 2012 Oct;43(10):2689–94. http://dx.doi.org/10.1161/STROKEAHA.112.654954.
35. Uphaus T, Grings A, Gröschel S, Müller A, Weber-Krüger M, Wachter R, et al. Automatic detection of paroxysmal atrial fibrillation in patients with ischaemic stroke: better than routine diagnostic workup? Eur J Neurol. 2017 Jul;24(7):990–4. http://dx.doi.org/10.1111/ene.13326.
36. Chen LY, Chung MK, Allen LA, Ezekowitz M, Furie KL, McCabe P, et al.; American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Stroke Council. Atrial Fibrillation Burden: Moving Beyond Atrial Fibrillation as a Binary Entity: A Scientific Statement From the American Heart Association. Circulation. 2018 May;137(20):e623–44. http://dx.doi.org/10.1161/CIR.0000000000000568.
37. Haeusler KG, Tütüncü S, Schnabel RB. Detection of Atrial Fibrillation in Cryptogenic Stroke. Curr Neurol Neurosci Rep. 2018 Aug;18(10):66. http://dx.doi.org/10.1007/s11910-018-0871-1.
38. Wachter R, Gröschel K, Gelbrich G, Hamann GF, Kermer P, Liman J, et al.; Find-AF(randomised) Investigators and Coordinators. Holter-electrocardiogram-monitoring in patients with acute ischaemic stroke (Find-AF$_{RANDOMISED}$): an open-label randomised controlled trial. Lancet Neurol. 2017 Apr;16(4):282–90. http://dx.doi.org/10.1016/S1474-4422(17)30002-9.
39. Sposato LA, Cipriano LE, Saposnik G, Ruíz Vargas E, Riccio PM, Hachinski V. Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. Lancet Neurol. 2015 Apr;14(4):377–87. http://dx.doi.org/10.1016/S1474-4422(15)70027-X.
40. Alvarado-Bolaños A, Ayan D, Khaw AV, Mai LM, Mandzia JL, Bogiatzi C, et al. Differences in Stroke Recurrence Risk Between Atrial Fibrillation Detected on ECG and 14-Day Cardiac Monitoring. Stroke. 2023 Aug;54(8):2022–30. http://dx.doi.org/10.1161/STROKEAHA.123.043672.
41. Van Gelder IC, Healey JS, Crijns HJ, Wang J, Hohnloser SH, Gold MR, et al. Duration of device-detected subclinical atrial fibrillation and occurrence of stroke in ASSERT. Eur Heart J. 2017 May;38(17):1339–44. http://dx.doi.org/10.1093/eurheartj/ehx042.
42. Svendsen JH, Diederichsen SZ, Højberg S, Krieger DW, Graff C, Kronborg C, et al. Implantable loop recorder detection of atrial fibrillation to prevent stroke (The LOOP Study): a randomised controlled trial. Lancet. 2021 Oct;398(10310):1507–16. http://dx.doi.org/10.1016/S0140-6736(21)01698-6.
43. Svennberg E, Friberg L, Frykman V, Al-Khalili F, Engdahl J, Rosenqvist M. Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial. Lancet. 2021 Oct;398(10310):1498–506. http://dx.doi.org/10.1016/S0140-6736(21)01637-8.
44. Kirchhof P, Toennis T, Goette A, Camm AJ, Diener HC, Becher N, et al.; NOAH-AFNET 6 Investigators; NOAH-AFNET6 sites and investigators. Anticoagulation with Edoxaban in Patients with Atrial High-Rate Episodes. N Engl J Med. 2023 Sep;389(13):1167–79. http://dx.doi.org/10.1056/NEJMoa2303062.
45. Becher N, Toennis T, Bertaglia E, Blomström-Lundqvist C, Brandes A, Cabanelas N, et al. Anticoagulation with edoxaban in patients with long atrial high-rate episodes ≥24 h. Eur Heart J. 2024 Mar;45(10):837–49. http://dx.doi.org/10.1093/eurheartj/ehad771.
46. Healey JS, Lopes RD, Granger CB, Alings M, Rivard L, McIntyre WF, et al.; ARTESIA Investigators. Apixaban for Stroke Prevention in Subclinical Atrial Fibrillation. N Engl J Med. 2024 Jan;390(2):107–17. http://dx.doi.org/10.1056/NEJMoa2310234.
47. McIntyre WF, Benz AP, Becher N, Healey JS, Granger CB, Rivard L, et al. Direct Oral Anticoagulants for Stroke Prevention in Patients With Device-Detected Atrial Fibrillation: A Study-Level Meta-Analysis of the NOAH-AFNET 6 and ARTESiA Trials. Circulation. 2024 Mar;149(13):981–8. http://dx.doi.org/10.1161/CIRCULATIONAHA.123.067512.
48. Kaplan RM, Koehler J, Ziegler PD, Sarkar S, Zweibel S, Passman RS. Stroke risk as a function of atrial fibrillation duration and CHA2DS2-VASc score. Circulation. 2019 Nov;140(20):1639–46. http://dx.doi.org/10.1161/CIRCULATIONAHA.119.041303.
49. Hilkens NA, Li L, Rothwell PM, Algra A, Greving JP. Refining prediction of major bleeding on antiplatelet treatment after transient ischaemic attack or ischaemic stroke. Eur Stroke J. 2020 Jun;5(2):130–7. http://dx.doi.org/10.1177/2396987319898064.
50. Best JG, Ambler G, Wilson D, Lee KJ, Lim JS, Shiozawa M, et al.; Microbleeds International Collaborative Network. Development of imaging-based risk scores for prediction of intracranial haemorrhage and ischaemic stroke in patients taking antithrombotic therapy after ischaemic stroke or transient ischaemic attack: a pooled analysis of individual patient data from cohort studies. Lancet Neurol. 2021 Apr;20(4):294–303. http://dx.doi.org/10.1016/S1474-4422(21)00024-7.
51. Rossini R, Peirone A. When to set anticoagulant therapy in asymptomatic AF? looking for a cut-off duration. Eur Hear Journal, Suppl. 2022;24(Si):I143–7.
52. Cameron A, Cheng HK, Lee RP, Doherty D, Hall M, Khashayar P, et al. Biomarkers for Atrial Fibrillation Detection After Stroke: Systematic Review and Meta-analysis. Neurology. 2021 Nov;97(18):e1775–89. http://dx.doi.org/10.1212/WNL.0000000000012769.
53. Binici Z, Intzilakis T, Nielsen OW, Køber L, Sajadieh A. Excessive supraventricular ectopic activity and increased risk of atrial fibrillation and stroke. Circulation. 2010 May;121(17):1904–11. http://dx.doi.org/10.1161/CIRCULATIONAHA.109.874982.
54. Thijs VN, Brachmann J, Morillo CA, Passman RS, Sanna T, Bernstein RA, et al. Predictors for atrial fibrillation detection after cryptogenic stroke: results from CRYSTAL AF. Neurology. 2016 Jan;86(3):261–9. http://dx.doi.org/10.1212/WNL.0000000000002282.
55. Gladstone DJ, Dorian P, Spring M, Panzov V, Mamdani M, Healey JS, et al.; EMBRACE Steering Committee and Investigators. Atrial premature beats predict atrial fibrillation in cryptogenic stroke: results from

the EMBRACE trial. Stroke. 2015 Apr;46(4):936–41. http://dx.doi.org/10.1161/STROKEAHA.115.008714.
56. Wolder LD, Graff C, Baadsgaard KH, Langgaard ML, Polcwiartek C, Ji-Young Lee C, et al. Electrocardiographic P terminal force in lead V1, its components, and the association with stroke and atrial fibrillation or flutter. Heart Rhythm. 2023 Mar;20(3):354–62. http://dx.doi.org/10.1016/j.hrthm.2022.11.010.
57. Saric M, Armour AC, Arnaout MS, Chaudhry FA, Grimm RA, Kronzon I, et al. Guidelines for the Use of Echocardiography in the Evaluation of a Cardiac Source of Embolism. J Am Soc Echocardiogr. 2016 Jan;29(1):1–42. http://dx.doi.org/10.1016/j.echo.2015.09.011.
58. Perlepe K, Sirimarco G, Strambo D, Eskandari A, Karagkiozi E, Vemmou A, et al. Left atrial diameter thresholds and new incident atrial fibrillation in embolic stroke of undetermined source. Eur J Intern Med. 2020 May;75:30–4. http://dx.doi.org/10.1016/j.ejim.2020.01.002.
59. Schwamm LH, Kamel H, Granger CB, Piccini JP, Katz JM, Sethi PP, et al.; STROKE AF Investigators. Predictors of Atrial Fibrillation in Patients With Stroke Attributed to Large- or Small-Vessel Disease: A Prespecified Secondary Analysis of the STROKE AF Randomized Clinical Trial. JAMA Neurol. 2023 Jan;80(1):99–103. http://dx.doi.org/10.1001/jamaneurol.2022.4038.
60. Baturova MA, Sheldon SH, Carlson J, Brady PA, Lin G, Rabinstein AA, et al. Electrocardiographic and Echocardiographic predictors of paroxysmal atrial fibrillation detected after ischemic stroke. BMC Cardiovasc Disord. 2016 Nov;16(1):209. http://dx.doi.org/10.1186/s12872-016-0384-2.
61. Waldenhjort D, Sobocinski Doliwa P, Alam M, Frykman-Kull V, Engdahl J, Rosenqvist M, et al. Echocardiographic measures of atrial function may predict atrial fibrillation in stroke patients. Scand Cardiovasc J. 2016 Aug;50(4):236–42. http://dx.doi.org/10.1080/14017431.2016.1175657.
62. Stahrenberg R, Edelmann F, Haase B, Lahno R, Seegers J, Weber-Krüger M, et al. Transthoracic echocardiography to rule out paroxysmal atrial fibrillation as a cause of stroke or transient ischemic attack. Stroke. 2011 Dec;42(12):3643–5. http://dx.doi.org/10.1161/STROKEAHA.111.632836.
63. Favilla CG, Ingala E, Jara J, Fessler E, Cucchiara B, Messé SR, et al. Predictors of finding occult atrial fibrillation after cryptogenic stroke. Stroke. 2015 May;46(5):1210–5. http://dx.doi.org/10.1161/STROKEAHA.114.007763.
64. Bernstein RA, Di Lazzaro V, Rymer MM, Passman RS, Brachmann J, Morillo CA, et al. Infarct Topography and Detection of Atrial Fibrillation in Cryptogenic Stroke: results from CRYSTAL AF. Cerebrovasc Dis. 2015;40(1-2):91–6. http://dx.doi.org/10.1159/000437018.
65. Pimentel BC, Ingwersen T, Haeusler KG, Schlemm E, Forkert ND, Rajashekar D, et al. Association of stroke lesion shape with newly detected atrial fibrillation - Results from the MonDAFIS study. Eur Stroke J. 2022 Sep;7(3):230–7. http://dx.doi.org/10.1177/23969873221100895.
66. Vynckier J, Kaesmacher J, Wardlaw JM, Roten L, Beyeler M, Belachew NF, et al. Phenotypes of Chronic Covert Brain Infarction in Patients With First-Ever Ischemic Stroke: A Cohort Study. Stroke. 2022 Feb;53(2):558–68. http://dx.doi.org/10.1161/STROKEAHA.121.034347.
67. Demeestere J, Fieuws S, Lansberg MG, Lemmens R. Detection of Atrial Fibrillation Among Patients With Stroke Due to Large or Small Vessel Disease: A Meta-Analysis. J Am Heart Assoc. 2016 Sep;5(9):e004151. http://dx.doi.org/10.1161/JAHA.116.004151.
68. Schweizer J, Arnold M, König IR, Bicvic A, Westphal LP, Schütz V, et al. Measurement of Midregional Pro-Atrial Natriuretic Peptide to Discover Atrial Fibrillation in Patients With Ischemic Stroke. J Am Coll Cardiol. 2022 Apr;79(14):1369–81. http://dx.doi.org/10.1016/j.jacc.2022.01.042.
69. Wachter R, Lahno R, Haase B, Weber-Krüger M, Seegers J, Edelmann F, et al. Natriuretic peptides for the detection of paroxysmal atrial fibrillation in patients with cerebral ischemia—the Find-AF study. PLoS One. 2012;7(4):e34351. http://dx.doi.org/10.1371/journal.pone.0034351.
70. Fonseca AC, Brito D, Pinho e Melo T, Geraldes R, Canhão P, Caplan LR, et al. N-terminal pro-brain natriuretic peptide shows diagnostic accuracy for detecting atrial fibrillation in cryptogenic stroke patients. Int J Stroke. 2014 Jun;9(4):419–25. http://dx.doi.org/10.1111/ijs.12126.
71. Arnold M, Nakas C, Luft A, Christ-Crain M, Leichtle A, Katan M. Independent Prognostic Value of MRproANP (Midregional Proatrial Natriuretic Peptide) Levels in Patients With Stroke Is Unaltered Over Time. Stroke. 2020 Jun;51(6):1873–5. http://dx.doi.org/10.1161/STROKEAHA.120.029333.
72. De Marchis GM, Schneider J, Weck A, Fluri F, Fladt J, Foerch C, et al. Midregional proatrial natriuretic peptide improves risk stratification after ischemic stroke. Neurology. 2018 Feb;90(6):e455–65. http://dx.doi.org/10.1212/WNL.0000000000004922.
73. Katan M, Fluri F, Schuetz P, Morgenthaler NG, Zweifel C, Bingisser R, et al. Midregional pro-atrial natriuretic peptide and outcome in patients with acute ischemic stroke. J Am Coll Cardiol. 2010 Sep;56(13):1045–53. http://dx.doi.org/10.1016/j.jacc.2010.02.071.
74. Llombart V, Antolin-Fontes A, Bustamante A, Giralt D, Rost NS, Furie K, et al. B-type natriuretic peptides help in cardioembolic stroke diagnosis: pooled data meta-analysis. Stroke. 2015 May;46(5):1187–95. http://dx.doi.org/10.1161/STROKEAHA.114.008311.
75. Luchner A, Behrens G, Stritzke J, Markus M, Stark K, Peters A, et al. Long-term pattern of brain natriuretic peptide and N-terminal pro brain natriuretic peptide and its determinants in the general population: contribution of age, gender, and cardiac and extra-cardiac factors. Eur J Heart Fail. 2013 Aug;15(8):859–67. http://dx.doi.org/10.1093/eurjhf/hft048.
76. Kishore AK, Hossain MJ, Cameron A, Dawson J, Vail A, Smith CJ. Use of risk scores for predicting new atrial fibrillation after ischemic stroke or transient ischemic attack-A systematic review. Int J Stroke. 2022 Jul;17(6):608–17. http://dx.doi.org/10.1177/17474930211045880.
77. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, et al. Guideline for the prevention of stroke in patients with stroke and transient ischemic attack; A guideline from the American Heart Association/American Stroke Association. Stroke. 2021 Jul;52(7):e364–467. http://dx.doi.org/10.1161/STR.0000000000000375.
78. Schlaganfall-gesellschaft Ö. Positionspapier - Update 2018 Detektion von Vorhofflimmern beim kryptogenen Hirninfarkt. 2018. p. 1–16. Available from: https://www.ögsf.at/wp-content/uploads/2016/11/Positionspapier-2018_OEGSF_neurologisch.pdf
79. Rubiera M, Aires A, Antonenko K, Lémeret S, Nolte CH, Putaala J, et al. European Stroke Organisation (ESO) guideline on screening for subclinical atrial fibrillation after stroke or transient ischaemic attack of undetermined origin. Eur Stroke J. 2022 Sep;7(3):VI. http://dx.doi.org/10.1177/23969873221099478.
80. Häusler KG, Gröschel K, Köhrmann M, Schnabel RB, Anker SD, Brachmann J, et al. Position Paper on Atrial Fibrillation Detection after Ischemic Stroke: Working Group Heart and Brain of the German Cardiac Society (DGK) and the German Stroke Society (DSG). Aktuelle Neurol. 2018;45(2):93–106. Available from: https://www.thieme-connect.de/products/ejournals/pdf/10.1055/s-0043-118476.pdf
81. Tuna MA, Rothwell PM; Oxford Vascular Study. Diagnosis of non-consensus transient ischaemic attacks with focal, negative, and non-progressive symptoms: population-based validation by investigation and prognosis. Lancet. 2021 Mar;397(10277):902–12. http://dx.doi.org/10.1016/S0140-6736(20)31961-9.
82. Kirchhof P, Camm AJ, Goette A, Brandes A, Eckardt L, Elvan A, et al.; EAST-AFNET 4 Trial Investigators. Early Rhythm-Control Therapy in Patients with Atrial Fibrillation. N Engl J Med. 2020 Oct;383(14):1305–16. http://dx.doi.org/10.1056/NEJMoa2019422.
83. Jensen M, Suling A, Metzner A, Schnabel RB, Borof K, Goette A, et al. Early rhythm-control therapy for atrial fibrillation in patients with a history of stroke: a subgroup analysis of the EAST-AFNET 4 trial. Lancet Neurol. 2023 Jan;22(1):45–54. http://dx.doi.org/10.1016/S1474-4422(22)00436-7.
84. Park J, Shim J, Lee JM, Park JK, Heo J, Chang Y, et al.; RAFAS Investigators*. Risks and Benefits of Early Rhythm Control in Patients With Acute Strokes and Atrial Fibrillation: A Multicenter, Prospective, Randomized Study (the RAFAS Trial). J Am Heart Assoc. 2022 Feb;11(3):e023391. http://dx.doi.org/10.1161/JAHA.121.023391.
85. Turc G, Calvet D, Guérin P, Sroussi M, Chatellier G, Mas JL; CLOSE Investigators. Closure, anticoagulation, or antiplatelet therapy for cryptogenic stroke with patent foramen ovale: systematic review of randomized trials, sequential meta-analysis, and new insights from the CLOSE study. J Am Heart Assoc. 2018 Jun;7(12):e008356. http://dx.doi.org/10.1161/JAHA.117.008356.
86. Sposato LA, Chaturvedi S, Hsieh CY, Morillo CA, Kamel H. Atrial Fibrillation Detected After Stroke and Transient Ischemic Attack: A Novel Clinical Concept Challenging Current Views. Stroke. 2022 Mar;53(3):e94–103. http://dx.doi.org/10.1161/STROKEAHA.121.034777.
87. Fridman S, Jimenez-Ruiz A, Vargas-Gonzalez JC, Sposato LA. Differences between Atrial Fibrillation Detected before and after Stroke and TIA: A Systematic Review and Meta-Analysis. Cerebrovasc Dis. 2022;51(2):152–7. http://dx.doi.org/10.1159/000520101.
88. Scheitz JF, Erdur H, Haeusler KG, Audebert HJ, Roser M, Laufs U, et al. Insular cortex lesions, cardiac troponin, and detection of previously unknown atrial fibrillation in acute ischemic stroke: insights from the

troponin elevation in acute ischemic stroke study. Stroke. 2015 May;46(5):1196–201. http://dx.doi.org/10.1161/STROKEAHA.115.008681.