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Editorial

Screening for atrial fibrillation: Need for an integrated, structured approach☆

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Atrial fibrillation (AF) is a very common disease, particularly in the elderly, and the number of affected patients has been predicted to increase in the next decades [1,2]. The existence of a link between AF and ischemic stroke is now well established, with AF being present in around 30% of patients reporting an ischemic stroke, as well as with stroke being the first clinical manifestation of previously unknown AF in over 25% of AF-related strokes [3].

AF is frequently asymptomatic [4], is usually observed in complex clinical profiles, and accounts for severe outcomes in terms of stroke and mortality, irrespective of the absence of symptoms [5,6]. The observation that ischemic stroke may occur in a significant number of patients with unknown, unrecognized, untreated or undertreated AF (i.e. untreated with oral anticoagulants for stroke prevention) supports the idea that it is necessary to plan screening strategies in order to identify AF patients whose substantial thromboembolic risk [7,8] should be treated with oral anticoagulation drugs whose efficacy in preventing stroke is well known [2,9,10].

Different approaches have been proposed for AF screening [7]:

- systematic screening, i.e. the methodological screening of all subjects;
- community screening, i.e. the methodological screening of all subjects living in a specific geographical area;
- screening targeted to high risk populations, i.e. the methodological screening of all subjects presenting specific clinical characteristics;
- opportunistic screening, i.e. screening of some subjects taking advantage of opportunities and circumstances such as patients aged > 65 years who undergo a medical check by the general practitioner.

In the AF screening process, diagnosis is usually the result of a process that includes: positivity to a specific test (pulse palpation, automated blood pressure monitors, single-lead or multi-lead ECG devices, pulse photoplethysmographic devices or sensors used in applications for smartphones, wrist bands and watches), followed by a clinical evaluation and confirmed by a 12-lead ECG [7]. In general, there are substantial differences between AF screening and other screening procedures in which the link between the screening test and the pathologic condition is much more indirect.

Regarding the benefits of searching for undetected AF, only limited evidence is available on the clinical usefulness of screening initiatives in terms of stroke prevention [11,12]. In a cohort study that evaluated 5555 asymptomatic patients who had an incidentally detected AF, treatment with oral anticoagulants (warfarin) was associated to a 1.5-year follow-up with a significantly lower occurrence of stroke (1.3% vs. 3.9%), and an overall incidence of stroke in anticoagulated patients similar to control subjects without AF (1.2%). Moreover, the adjusted cumulative mortality in patients with untreated, incidentally-detected ambulatory AF was significantly lower in anticoagulated patients (4.2%) than in untreated patients (7.2%). Even though these data do not stem from a prospective screening programme, they demonstrate the value of targeted searching for AF to reduce the incidence of AF-related stroke and to improve patient outcome [11]. Interesting data on the value of AF screening are also reported by the 5-year follow-up of the STROKESTOP study, in which a population-based screening of subjects aged 75 years was associated to a reduction in the occurrence of ischaemic strokes, even though the results were based on a limited number of subjects and hence could not provide a definitive evidence [12].

Among the most recent international guidelines and their updates on AF diagnosis and management, only few of them provided recommendations about AF screening procedures (Table 1). Although the 2014 National Institute for Health and Care Excellence (NICE) AF guidelines [13] refer to pulse palpation as the only recommended

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Table 1
Current guidelines recommendations about procedures in screening strategies for atrial fibrillation.

Guideline	Year	Screening Method	Screening Approach	Recommendations	Strength of Recommendation	Level of Evidence
NICE [13]	2014	Pulse Palpation	Targeted	Perform pulse palpation in all patients presenting with symptoms/clinical events suggesting the presence of AF	–	–
ESC [14]	2016	Pulse Palpation/ECG	Opportunistic	Opportunistic screening for AF is recommended in patients > 65 years	I	B
			Systematic	Systematic ECG screening may be considered for patients > 75 years or at high risk of stroke	IIb	B
NHFA/CSANZ [15]	2018	Point-of-Care ECG	Opportunistic	Opportunistic screening is recommended in patients ≥ 65 years	Strong	Moderate
KHRS [16]	2018	Pulse Palpation/ECG	Opportunistic	Opportunistic screening for AF is recommended in patients > 65 years	I	B
			Systematic	Systematic ECG screening may be considered for patients > 75 years or at high risk of stroke	IIa	B

Legend: AF = Atrial Fibrillation; CSANZ = Cardiac Society of Australia and New Zealand; ESC = European Society of Cardiology; KHRS = Korean Heart Rhythm Society; NHFA = National Heart Foundation of Australia.

screening activity and recommend to perform it only in those subjects presenting AF symptoms, the increasing evidence that screening enabled to identify a significant number of new AF patients has led to issue recommendations to perform opportunistic screening in subjects ≥65 years old, supported by a high level of evidence [14–16]. Furthermore, the European Society of Cardiology (ESC) and the Korean Heart Rhythm Society (KHRS) guidelines also suggested to consider systematic screening in subjects ≥75 years old, even though with a lower level of evidence [14,15] (Table 1). Several other guidelines (i.e. American College of Cardiology/American Heart Association, American College of Chest Physicians, Canadian Cardiac Society) did not provide specific recommendations on AF screening.

In the present issue of the *European Journal of Internal Medicine,* de Moraes et al. report on the results of an observational cross-sectional study carried out in Brazil based on a centralized reading system of ECG strips, transmitted by a nationwide network of general practitioners, over a 7-year period [17]. Over a total cohort of 676,621 subjects who underwent the 12-leads ECG testing, AF was found in 14,968 (2.2%), with AF subjects being more likely males and older. Hence, on the basis of the collected data, the authors estimated that the Brazilian national AF prevalence was 1.5% for subjects older than 15 years, and a projected increase of half a million patients by 2025, consistent with previous data from other countries [1]. After being diagnosed with AF, a random sample of patients was contacted for a telephone interview through a closed-ended and structured questionnaire. Using the questionnaire, the authors found out that while 53.7% of the patients reported about having been previously diagnosed with AF, up to 34.6% stated that AF was diagnosed on the day of ECG testing. Among those already diagnosed with AF, 88.3% of patients were on treatment or were being referred to a cardiologist (even though 10% were still waiting for consultation) whereas 11.7% had not been referred yet [17]. The fact that this “health need” is underestimated, is shown by the small proportion of AF patients treated with oral anticoagulant drugs: only 22% were treated with vitamin K antagonists (VKAs) vs 68% treated with antiplatelet drugs. As a matter of fact, non-vitamin K antagonist oral anticoagulants (NOACs) were not used despite the reported availability in Brazil. The situation appears to be different in Europe where, despite some geographical differences in the adoption of NOACs, the overall implementation of oral anticoagulation has progressively increased and is currently around 85%, with important implications on long-term outcomes [18–22].

Although the reported study does not represent a prospectively planned AF screening programme, its data suggest the need for an improvement in referral organization, in patient information and in the organization of care for the prescription of oral anticoagulant drugs whenever a new AF is confirmed after a screening assessment. Indeed, an agreed policy for treatment and availability of facilities for both diagnostic pathways and treatment prescription are essential components of screening strategies [23]. A structured organization is also the best way to avoid wasting resources and obtain the most favourable cost-effectiveness [7]. A recent cost-effectiveness analysis based on a model derived from Belgian data [24] showed how a screening initiative followed by structured care based on the guidelines' recommended management with oral anticoagulation prescription was cost-effective not only for subjects ≥65 and ≥ 75 years old, but also in the general population in terms of the reduction of clinical adverse events [25].

The need for an integrated and structured approach to AF screening is also stressed by an analysis of the criticism advanced by the US Preventive Services Task Force [26], which focused on the anxiety that may derive from a positive screening, as well as the potential harms and risks of bleeding that may derive from invasive diagnostic procedures or from the prescription of anticoagulants. Indeed, adequate patient information on the benefits that may derive from screening and on its minimal potential disadvantages should be the basis for promoting a full acceptance and understanding of AF screening initiatives, thus

minimizing anxiety. Further ongoing studies, such as the SAFER study (http://www.isrctn.com/ISRCTN16939438), may help accurately elucidate the benefits of structured AF screening strategies and proper clinical management to reduce stroke risk.

Detection of AF in patients at risk is an important step to improve healthcare. However, the organizational challenges in this field should also consider the parallel need to give an organized clinical response to the rapid growth of mobile health technologies leading to wide availability of apps and sensors for AF detection in smartphones, wearable devices and watches. Checks for a clinical confirmation of AF as well as for appropriate cardiology evaluations and medical advice will be required as an essential component of an appropriate organization targeted to support the diffusion of these technologies.

Declaration of Competing Interest

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