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PERSPECTIVE

Self-palpation for detection of paroxysmal atrial fibrillation: Much noise with little signal

Kazem Rahimi^{1,2}*, Paulus Kirchhof^{3,4,5,6}

1 Deep Medicine, Big Data Insitute, Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom, 2 NIHR Oxford Biomedical Research Centre, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, 3 Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, United Kingdom, 4 Department of Cardiology, University Heart and Vascular Center Hamburg, Hamburg, Germany, 5 SWBH and UHB NHS Trusts, Birmingham, United Kingdom, 6 AFNET, Münster, Germany

* kazem.rahimi@cardiov.ox.ac.uk

Patients with atrial fibrillation (AF) are at substantially increased risk of various adverse cardiovascular events, such as stroke, myocardial infarction, heart failure, and vascular dementia [1]. Given that such risks can be partially mitigated through preventive measures, it is important to understand how to better identify people affected by AF and how better identification might change treatment decisions or outcomes.

The cardinal feature of AF is the presence of an irregular pulse. Advocating for pulse palpation might, then, seem a simple and ubiquitously available solution for detecting undiagnosed AF. Indeed, previous research has shown that such a simple screening method, when adopted by trained health professionals, is as good as systematic screening with the use of ECG [2]. Hence, systematic pulse palpation is recommended during routine clinical encounters of atrisk patients [3,4]. However, although such screening will detect chronic forms of AF when patients are seen by health professionals, it neither detects intermittent, paroxysmal AF nor facilitates the diagnosis of AF in populations not assessed by health professionals. These "holes in the current screening net" might be plugged by regular self-pulse palpations by laypersons.

In this context, Faris Ghazal and colleagues compared self-pulse palpation to simultaneously recorded ECGs in an important study reported in *PLOS Medicine* [5]. They recruited around 1,000 individuals aged 65 years and over from 4 primary care centres in Sweden. All participants were trained on how to monitor irregular pulse rhythms 3 times a day over a 2-week period. Importantly, they were also given a handheld ECG device and were advised to record their heart rhythm simultaneously with self-palpation. This resulted in 53,782 simultaneous pulse palpations and ECG recordings (51 recordings per individual). Intermittent ECG recordings were confirmed to be effective in detecting 27 patients with AF (2.7%, 95% CI 1.8– 3.9). Only a small minority of recordings (42 patients) required verification with a heart rhythm patch that was worn over 5 days (with AF being verified in just 4 of these patients, i.e., 10%). All but 2 individuals had paroxysmal AF, illustrating the power of patient-operated ECG devices.

But how well did self-palpation perform? In short, not very well. Only 15 of the 27 individuals with newly diagnosed AF reported at least 1 episode of irregular pulse during the screening period. This translates to a sensitivity of 56% (95% CI 35%–75%) for diagnosis of AF by self-palpation at the individual level or 25% (95% CI 20%–30%) at the level of episodes of self-palpation. More importantly, the positive predictive value of self-palpation was disappointingly low (7%, 95% CI 5%–10%). This means that for each correctly detected irregular pulse, there

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were about 13 false alerts. This relationship did not change when the cumulative detection rate for each participant was considered: for each correctly diagnosed participant with AF, there were 12 participants who felt an abnormal rhythm on at least 1 occasion that could not be verified in simultaneous ECG recordings. This stable error rate suggests that the positive predictive value of self-palpation could not be increased by simply changing the duration or frequency of the screening period. Consequently, the adoption of lay self-palpation would likely lead to a substantially increased downstream demand for verification of false alarms, which will render an apparently low-cost strategy unsuitable for resource-constrained health systems. Furthermore, in routine clinical practice, the training of patients in self-palpation might not be of comparable quality as in Ghazal and colleagues' study, and given that verification of heart rhythm is likely to be asynchronous to self-palpation episodes, a subsequent lack of clinical confirmation of a paroxysmal abnormal rhythm might create substantial anxiety among patients. Thus, this study provides clear evidence against a policy of routine self-palpation for detection of paroxysmal AF.

On the other hand, this study confirmed prior reports that patient-operated intermittent ECG recordings with handheld devices are effective for diagnosing paroxysmal AF [6,7]. Such devices may soon be replaced by emerging consumer applications, implantable devices, or various predictive algorithms that will enable detection of ever more subtle episodes of AF at lower unit costs [8–10]. These could facilitate the detection of the rare paroxysms of AF presently found in 15%–30% of elderly patients when continuous, long-term monitoring is applied [11,12].

However, the question of the consequence of more accurate and comprehensive AF detection and how to manage patients once atrial arrhythmias have been correctly identified is more complicated than might be assumed from the scope of this study. To assess these implications, we not only need to have confidence in the performance of the diagnostic tool but also need information on whether the treatment of subclinical, screening-detected forms of AF is beneficial for patients. Even putting the cost, inconvenience, and potential harm of any treatment aside, the extrapolation of benefits of treatments established among those identified through clinical encounters to those diagnosed through screening is prone to error, in part because of methodological challenges such as lead time and overdiagnosis bias. Such challenges are now well known to the oncology community, in which efforts to diagnose slow-progressing cancers early have not improved outcomes materially and, in some instances, caused avoidable harm [13]. In this vein, the conventional wisdom, which considers AF as a binary phenomenon that should be managed in the same way irrespective of how it was diagnosed and in whom, seems no longer tenable [12,14,15]. Fortunately, several controlled trials evaluating patients with potentially milder forms of AF are underway, for instance, testing anticoagulation therapy in patients with rare episodes of AF detected by implanted device [16,17] or in patients with AF detected by lay screening [18]. Such studies will likely provide reliable information on the impact of wider screening strategies for AF detection and treatment.

However, until such evidence becomes available, those who seek to detect even shorter spells of irregular heart rhythm will have to face the ambiguity of the meaning of the diagnosis and the uncertainty of its consequences. Notwithstanding, patients and consumers should be advised that we do have greater certainty on how to measure and modify cardiovascular risk despite the uncertainties surrounding the detection of short spells of AF outside clinical settings.

References

- Emdin CA, Anderson SG, Salimi-Khorshidi G, Woodward M, MacMahon S, Dwyer T, et al. Usual blood pressure, atrial fibrillation and vascular risk: Evidence from 4.3 million adults. Int J Epidemiol. 2017; 46 (1): 162–172. https://doi.org/10.1093/ije/dyw053 PMID: 27143136
- Jonas DE, Kahwati LC, Yun JDY, Cook Middleton J, Coker-Schwimmer M, Asher GN. Screening for atrial fibrillation with electrocardiography: Evidence report and systematic review for the US preventive services task force. JAMA. 2018; 320(5):485–498. <u>https://doi.org/10.1001/jama.2018.4190</u> PMID: 30088015
- Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, et al. Screening for atrial fibrillation with electrocardiography: US preventive services task force recommendation statement. JAMA. 2018; 320(5): 478–484. https://doi.org/10.1001/jama.2018.10321 PMID: 30088016
- Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur J Cardio-Thoracic Surg. 2016; 50(5): e1–e88. https://doi.org/10.1093/ejcts/ezw313
- 5. Ghazal, F, Theobald H, Rosenqvist M, Al-Khalili F. Validity of daily self-pulse palpation for atrial fibrillation screening in patients 65 years and older: A cross-sectional study.
- Freedman B, Camm J, Calkins H, Healey JS, Rosenqvist M, Wang J, et al. Screening for Atrial Fibrillation. Circulation; 2017; 135(19): 1851–1867. https://doi.org/10.1161/CIRCULATIONAHA.116.026693 PMID: 28483832
- Svennberg E, Engdahl J, Al-Khalili F, Friberg L, Frykman V, Rosenqvist M. Mass Screening for Untreated Atrial Fibrillation. Circulation; 2015; 131(25): 2176–2184. <u>https://doi.org/10.1161/</u> CIRCULATIONAHA.114.014343 PMID: 25910800
- Yan BP, Lai HSL, Chan CKY, Au ACK, Freedman B, Poh YC, et al. High-throughput, contact-free detection of atrial fibrillation from video with deep learning: a proof-of-concept study. JAMA Cardiol. 2019; 5 (1): 1–7. https://doi.org/10.1001/jamacardio.2019.4004 PMID: 31774461
- Attia ZI, Noseworthy PA, Lopez-Jimenez F, Asirvatham SJ, Deshmukh AJ, Gersh BJ, et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. Lancet. 2019; 394(10201): 861–867. https://doi. org/10.1016/S0140-6736(19)31721-0 PMID: 31378392
- Perez MV, Mahaffey KW, Hedlin H, Rumsfeld JS, Garcia A, Ferris T, et al. Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation. N Engl J Med. 2019; 381: 1909–1917. https://doi.org/10. 1056/NEJMoa1901183 PMID: 31722151
- 11. Healey JS, Alings M, Ha A, Leong-Sit P, Birnie DH, de Graaf JJ, et al. Subclinical Atrial Fibrillation in Older Patients. Circulation. 2017; 136(14): 1276–1283. https://doi.org/10.1161/CIRCULATIONAHA. 117.028845 PMID: 28778946
- 12. Bertaglia E, Blank B, Blomström-Lundqvist C, Brandes A, Cabanelas N, Dan GA, et al. Atrial high-rate episodes: Prevalence, stroke risk, implications for management, and clinical gaps in evidence. Europace. 2019; 21(10): 1459–1467. https://doi.org/10.1093/europace/euz172 PMID: 31377792
- Ilic D, Djulbegovic M, Jung JH, Hwang EC, Zhou Q, Cleves A, et al. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. BMJ. 2018; 362: k3519. https://doi.org/10.1136/bmj.k3519 PMID: 30185521
- Ganesan AN, Chew DP, Hartshorne T, Selvanayagam JB, Aylward PE, Sanders P, et al. The impact of atrial fibrillation type on the risk of thromboembolism, mortality, and bleeding: a systematic review and meta-analysis. Eur Heart J. 2016; 37(20): 1591–1602. <u>https://doi.org/10.1093/eurheartj/ehw007</u> PMID: 26888184
- Rahimi K. Subclinical atrial fibrillation in need of more assertive evidence. Eur Heart J. 2017; 38(17): 1345–1347. https://doi.org/10.1093/eurhearti/ehx122 PMID: 28379323
- Kirchhof P, Blank BF, Calvert M, Camm AJ, Chlouverakis G, Diener H-C, et al. Probing oral anticoagulation in patients with atrial high rate episodes: Rationale and design of the Non–vitamin K antagonist Oral anticoagulants in patients with Atrial High rate episodes (NOAH–AFNET 6) trial. Am Heart J. 2017; 190: 12–18. https://doi.org/10.1016/j.ahj.2017.04.015 PMID: 28760205
- Lopes RD, Alings M, Connolly SJ, Beresh H, Granger CB, Mazuecos JB, et al. Rationale and design of the Apixaban for the Reduction of Thrombo-Embolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation (ARTESiA) trial. Am Heart J. 2017; 189: 137–145. https://doi.org/10.1016/j.ahj.2017. 04.008 PMID: 28625370
- Engdahl J, Svennberg E, Friberg L, Al-Khalili F, Frykman V, Gudmundsdottir KK, et al. Stepwise mass screening for atrial fibrillation using N-terminal pro b-type natriuretic peptide: The STROKESTOP II study design. Europace. 2017; 19(2): 297–302. <u>https://doi.org/10.1093/europace/euw319</u> PMID: 28011798