PERSPECTIVE

Wearables, Smartphones and Novel Anticoagulants: We Will Treat More Atrial Fibrillation, but Will Patients Be Better Off?

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The widespread adoption of medical practices without a firm evidence base is common and the current growing enthusiasm for atrial fibrillation screening offers a real-time example of this phenomenon. Although no randomized trials supporting the utility of screening for atrial fibrillation exist, proponents suggest that such screening should be considered. Atrial fibrillation is a common condition that is often asymptomatic. It is also a condition associated with serious morbidity, primarily resulting from stroke. We practice at a time in which the ability to detect atrial fibrillation is becoming easier and treatments are becoming less onerous. Screening for atrial fibrillation may be beneficial but there is also a reasonable likelihood that its harms will outweigh its benefits. In this article we make the case that adopting this practice prior to data from randomized controlled trial would be a mistake. If screening for atrial fibrillation is adopted without such a robust evidence base we may well later discover that this course of action was wrong.

KEY WORDS: atrial fibrillation; medical decision making; medical reversal; anticoagulation.

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A randomized trial that supports the utility of screening for atrial fibrillation does not exist. Proponents of screening note, however, that the prerequisites have been met: the diagnosis is common, there is effective treatment, there is a latent phase, there are several accepted tests, and the natural history is known.¹ Moreover, screening is becoming easier with each passing year. Not only do many Americans now carry a smartphone with numerous apps capable of measuring their own pulse but in 2014 the US FDA approved the AliveCor detection app, an app which can diagnose atrial fibrillation at home.² The NIH's Mobilizing Research program will most likely increase the number similar technologies. In addition, over 36 million Americans presently use externally worn sensors to monitor their heart rate and this number is expected to grow.³

The combination of increased access to monitoring and the aging of the population will mean that the number of diagnosed cases of atrial fibrillation will rise, from 2.7 million Americans today to nearly double that in the next few decades.³ Adding the availability of novel anticoagulants to this environment, free from the hassles of monitoring, it is likely that the medical profession will soon practice a more aggressive anticoagulation treatment strategy: anticoagulating many people whose atrial fibrillation is asymptomatic, is diagnosed at home, is infrequently present, and who would have previously remained undiagnosed.

As such, the stage is set to watch the adoption of a new medical screening practice in real time, one with a plausible rationale but without clear randomized trial evidence that it improves outcomes. While it is intuitive, and certainly possible, that finding and treating more atrial fibrillation will improve outcomes by decreasing stroke rates, we do not know that treating patients caught in a wider net will be beneficial. In the coming years, we may discover that we were correct in our adoption (the increased diagnosis and treatment of atrial fibrillation benefits our patients) or our course of action was wrong (the diagnosis increases the use of novel drugs, with their attendant risks, and does not substantively decrease the rate of stroke or death). Will widespread opportunistic screening be validated, or will it become another medical reversal?⁴

The enthusiasm to look harder for cases of atrial fibrillation arises from data and the availability of treatment. In 2014, we learned that patients hospitalized with cryptogenic stroke and no diagnosed atrial fibrillation have a 9.9 % prevalence of atrial fibrillation detected by 30-day event monitors following discharge. This compares to a rate of only 2.5 % in a control group who were only monitored for 24 h (absolute difference, 7.4 percentage points; 95 % CI, 3.4 to 11.3; $P < 0.001$).⁵ The authors of this study suggest that their results, combined with evidence that asymptomatic atrial fibrillation increases the risk of stroke,⁶ amounts to “strong evidence supporting adoption of a more intensive approach to the detection of atrial fibrillation in patients with unexplained stroke or TIA.” Recently, a Viewpoint in JAMA took the argument one step further arguing for screening for atrial fibrillation.¹

Screening for atrial fibrillation, whether in patients who have had a stroke or not, seems reasonable, but it is not supported by evidence. Although a rate of undetected atrial

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fibrillation of 9.9 % is high, we do not know the rate of atrial fibrillation among matched patients recently discharged after hospitalization for non-stroke illnesses. In addition, recent studies have suggested that decreased arrhythmia burden is associated with decreased risk of stroke.⁷ Patients diagnosed with atrial fibrillation on long-term monitoring likely have a lower arrhythmia burden than those diagnosed while in the hospital. Lastly, we know from older data that warfarin provides no benefit over aspirin for stroke patients who are not diagnosed with atrial fibrillation while in the hospital.⁸ Certainly a subset of these patients had undetected atrial fibrillation. Thus, the benefit of anticoagulation likely depends on both the burden and the prevalence of atrial fibrillation.

The studies that support our current approach to patients with atrial fibrillation could be a course in evidence-based medicine: few therapies are grounded in as many landmark studies. The benefit of anticoagulation in patients with non-valvular atrial fibrillation was first defined in the early 1990s.⁹ These data were later refined through the development of clinical decision rules to tailor the intensity of anticoagulation to an individual patient.¹⁰ In 2002, a landmark trial demonstrated that rate control was at least as effective as rhythm control.¹¹ This study reversed the common practice of routinely prescribing rhythm control in patients with atrial fibrillation, a practice not based on strong evidence. Most recently, multiple randomized controlled trials have demonstrated that novel oral anticoagulants are at least as safe and effective as warfarin for stroke prevention in patients with atrial fibrillation.^{12–14}

The benefit of treating atrial fibrillation that is found after a more aggressive search for the arrhythmia will probably be lower than we are accustomed to, and this benefit may not be well predicted by our current clinical decision tools. The risks and costs of anticoagulation will be the same. Patients in whom asymptomatic atrial fibrillation is detected through screening, and who fall below the current risk estimate that warrants anticoagulation, would experience no benefit from the screening. Although they would not be exposed to risk from anticoagulation, they would be labeled with a previously undiagnosed illness. The balance of risk and benefits should be defined by large randomized controlled trials, but there appears little professional interest in launching these trials. Certainly, few are likely to be sponsored by makers of novel anticoagulants.

Even in our era of evidence-based medicine, much of what we do is not based on evidence. Many practices are difficult to study, predate the era of randomized controlled trials, and some have been accepted (and approved) based on less than reliable evidence combined with a perceived need to adopt the treatment quickly. A new but common trend is the broadening of diagnostic categories based on advances in technology and extrapolating the results of early studies (in more severe disease states) to less severe conditions. This is true for

pulmonary embolism, where we increasingly find smaller clots of unclear significance,¹⁵ reductions in the ejection fraction diagnosed on cardiac MRI, and the presence of coronary artery disease made by more sophisticated stress tests. In all these cases, while it is possible that expanding treatment may be of benefit, it is not certain it will be. The use of carefully constructed randomized trials is critical. In their absence, we should not be surprised if some newly adopted medical practices turn out to be later reversed. The stars have aligned to search for and treat more atrial fibrillation; however, it remains uncertain whether or not our patients will be better off.

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