

## Screening for atrial fibrillation with electrocardiography: the jury is still out

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Atrial fibrillation (AF) is not uncommon in the elderly. In the Framingham Heart Study, the lifetime risk of this arrhythmia from the age of 55 years onwards has recently been estimated to be as high as 37%<sup>1</sup>. This percentage is remarkably higher than the one calculated from the same cohort a decade ago<sup>2</sup>, likely because of a reduction in mortality from competing diseases and intensified medical surveillance, both in general and specifically for AF, as a consequence of increased awareness of this condition.

The most fearsome presentation of AF is systemic embolism and especially ischemic stroke, which becomes particularly threatening at older ages due to higher mortality and probability of long-term sequelae, with functional impairment and ensuing dramatic health care and social costs<sup>3</sup>. The proportion of AF-related strokes among any ischemic stroke is around 10%<sup>4-5</sup> and there is a strong correlation between AF underlying a cerebrovascular event and age or the CHA2DS2-VASc score, which is used to quantify the risk of AF-associated stroke or transient ischemic attack and includes age.

Thus, the elder is prone to AF and its potentially devastating complications. This is a first reason why advocating the search of AF in asymptomatic individuals who are older than a certain threshold age. Second and fundamental, a therapy is available that consistently and noticeably diminishes the risk of cardioembolic cerebral

events secondary to AF, and thus provides a strong rationale to screen apparently unaffected subjects for the arrhythmia. Oral anticoagulation (OAC) are highly effective in preventing AF-related stroke, and the new generation of direct OAC (DOAC) is also characterized by more stable pharmacokinetics and more favorable safety profile as compared with vitamin K antagonists<sup>6</sup>. Moreover, these benefits persist among the old and the very old<sup>7</sup>. To give a measure of the impact of OAC treatment on AF outcomes, in England from 2011 to 2016 a 1% increase in OAC use was associated with a 0.8% decrease in the weekly rate of AF-related stroke, while 4068 more strokes would have occurred in 2015/2016 if the use of OAC had remained at 2009 levels<sup>8</sup>.

Based on these considerations, screening programs for silent AF have been intensively studied.

Any screening strategy must be low-risk and low-cost to be implemented community-wide. Single-time point or repeated electrocardiography (ECG) may meet these requirements and, thereby, has been proposed to screen for unrecognized AF. Technological advances have led to handheld devices with verifiable ECG traces, which combine accuracy and simplicity of use, rendering the prospect of AF screening even more appealing. For instance, participants in the recent REHEARSE-AF study<sup>9</sup> were provided with a monitor attached to a WiFi-enabled iPod to acquire 30-second single-lead ECGs twice weekly or when

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symptomatic over 12 months and transmit the recordings to a secure server. In the STROKESTOP study<sup>10</sup>, ECG were obtained intermittently over two weeks by means of an integrated mobile transmitter, which was activated by placing their thumbs on the device and sent 30-second ECG strip data to a database.

Since the prevalence of AF increases with age, applying these tools to older subjects will make the percentage of cases in which the screening identify AF closer to the total number of positive tests (i.e., the positive predictive value will be higher). Keeping the example of the STROKESTOP study, which recruited 75-76-year-old persons, previously unknown AF was found in 3% of the participants, with 0.5% being diagnosed with AF on the first ECG. By using the same technology with persons in the same age range, but  $\geq 2$  points at the CHADS2 score, AF was discovered in 7.4%<sup>11</sup>. In REHEARSE-AF, a CHADS-VASc score of  $\geq 4$  was the strongest predictor of incident AF<sup>9</sup>. Against this background, there has been enthusiasm for AF screening, both in the scientific community and in the lay literature. However, many questions are still open. Is there any harm of systematic screening for AF with ECG? Does it affect health outcomes, such as all-cause mortality and stroke morbidity and mortality? Which are the benefits and harms of OAC for screen-detected AF? (antiplatelet therapy is not recommended for the prevention of AF-related stroke)<sup>12</sup>. These questions have been addressed by a recent systematic review, carried out to inform the US Preventive Service Task Force and specifically focused on studies that enrolled adults of 65 years of age or older without a history of stroke, transient ischemic attack, coronary heart disease or heart failure<sup>13</sup>. In spite of an extensive work of data extraction and analysis, however, the authors could provide almost no definite answer. In fact, the only firm conclusion they reached is that systematic or opportunistic screening of unselected or explicitly asymptomatic adults with ECG leads to the detection of more cases of AF, as compared with no screening. At sharp odds with the promising results of the studies of AF screening individually considered, the effects of ECG screening cannot be precisely gauged. Importantly, this is the case with the risk/benefit ratio of OAC prompted by detection of unknown AF, but also with other aspects that are often overlooked but are actually extremely relevant in evaluating the feasibility of a screening approach, such as anxiety generated by testing or cost-effectiveness.

Inevitably and laconically, the accompanying recommendation statement by the US Preventive Services Task Force concluded that “the current evidence is insufficient to assess the balance of benefits and harms of screening for atrial fibrillation with ECG”<sup>14</sup>.

The jury is still out.

#### CONFLICT OF INTEREST

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