Screening for Atrial Fibrillation—More Data Still Needed

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In 2018, the US Preventive Services Task Force (USPSTF) published an evidence report and scientific review of electrocardiographic (ECG) screening for atrial fibrillation (AF). Based on this review, the task force concluded that there was inadequate evidence to assess whether screening with ECG identifies asymptomatic adults 65 years or older with previously undiagnosed AF more effectively than usual care. The task force noted that no trials had shown a benefit of screening for AF with ECG on clinical outcomes. The final statement of the task force was that there was insufficient evidence regarding the balance of benefits and harms of such screening (I statement). The USPSTF did not change its I statement.

In this issue of JAMA, the USPSTF has updated its evaluation of this topic, which included an expanded review to include other screening tests in addition to ECG, and reached the same conclusion, despite the availability of recent clinical trials. In the recent Recommendation Statement, “The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for AF (I statement).” This decision differs from the 2020 European Society of Cardiology (ESC) guideline, which endorsed opportunistic screening for AF by pulse palpation or ECG rhythm strip in patients 65 years or older (class I recommendation) and advised to consider systematic ECG screening to detect AF in people 75 years or older, or those at high risk for stroke (class IIa). What is new since 2018, why are the newest data considered insufficient by the USPSTF to recommend either to screen or not to screen, and why did the ESC reach a different recommendation than the USPSTF?

New since 2018 are only 2 completed large clinical trials that involved randomization of study participants to screening compared with no screening and also included assessment of important clinical outcomes. The STROKESTOP study, published in 2021, involved more than 28,000 people invited to participate. Of the 14,387 invited to perform intermittent ECG twice daily for 14 days of screening, only 7,165 actually participated. After a mean follow-up of 6.9 years, significantly fewer primary combined end point events, including ischemic or hemorrhagic stroke, systemic embolism, bleeding leading to hospitalization, and all-cause mortality, occurred in the intervention group (4456/13,979 [31.9%]) than in the control group (4616/13,996 [33.0%]); absolute difference, 1.1%; hazard ratio, 0.96 [95% CI, 0.92-1.0]; P = 0.045). The authors concluded that they had demonstrated a small benefit of the screening. As described in the USPSTF Evidence Review, the study was judged to be only fair quality because of lack of masking of the intervention and lack of central outcomes determination.

The second study, the randomized LOOP study, was a trial to assess the role of implantable loop recorders in patients aged 70 to 90 years without known AF, with at least 1 additional stroke risk factor (hypertension, diabetes, previous stroke, or heart failure) for AF ascertainment and clinical outcomes. The study involved 1501 patients randomized to implanted loop recorder and 4503 patients randomized to usual care (1:3). Mean age was 74.7 years. AF of at least 6 minutes’ duration was detected in 31.8% of the loop recorder group and in 12.2% of the usual care group (any duration of AF in this group) during a median follow-up of 64.5 months. The protocol called for initiation of anticoagulation in the loop group for any episode of AF lasting more than 6 minutes. The authors interpreted the results to have shown that loop recorder screening resulted in a large increase in AF detection and anticoagulation initiation but no significant reduction in the risk of stroke or systemic arterial embolism. The authors suggested that the findings might imply that not all episodes of AF should result in use of anticoagulation, since short episodes of AF may not increase the risk of stroke. This study was not included in the 2021 USPSTF report because it did not meet inclusion criteria for the Evidence Review.

The other new evidence since the 2018 USPSTF report addressed other questions besides key question 1 of the Evidence Review commissioned by the task force (“Does screening for AF with selected tests improve health outcomes [ie, reduce all-cause mortality, reduce morbidity or mortality from stroke, or improve quality of life] in asymptomatic older adults?”). As such, based on this additional evidence, the USPSTF did not change its I statement.

The ESC addressed the question of AF screening extensively in its 2020 guideline on diagnosis and management of atrial fibrillation. The guideline states clearly that randomized trial data to confirm the major outcomes benefits from screening for AF and inform the choice of optimal screening are “scarce.” As in the USPSTF report, the ESC noted that a number of studies have shown that, compared with usual care, AF can be detected in more asymptomatic people by using deliberate methods in the clinic or using several implantable and wearable technologies, and by intermittent self-screening methods such as an external ECG handheld device, similar to the approach in STROKESTOP. Risks of such screenings were noted in the ESC report and include...
anxiety generated by abnormal findings, misinterpretation of the ECG results that could result in overdiagnosis and overtreatment, and the possibility of unnecessary downstream testing. Despite the lack of outcomes data from clinical trials, the ESC committee concluded that AF screening as noted above was justified because of the likely benefit of early detection and treatment in selected older individuals.

What are the next steps in trying to resolve whether screening for AF in asymptomatic individuals is justifiable based on well-studied benefits and harms? One important point raised by the LOOP trial is whether there is a threshold for AF duration that is most strongly associated with stroke risk and therefore most likely to benefit from anticoagulation. In the LOOP trial, AF of 6 minutes’ duration was chosen, and this was supported by a meta-analysis that involved 7 studies of 15,353 patients that reported stroke risk in subclinical AF. The LOOP study authors questioned whether this short duration of AF may have led to many low-risk patients being diagnosed and treated. Specifically, in a study of 21,768 nonanticoagulated patients with cardiovascular implanted devices, stroke risk crossed a threshold of greater than 1% per year in a population with mean age 68.6 (SD, 12.7) years at AF duration 23.5 hours or longer when CHA2DS2-VASc score was 2, and at longer than 6 minutes when CHA2DS2-VASc score was 3 or 4.

Future trials may need to consider enrolling only higher-risk patients and identifying those with AF of longer duration. As with many clinical trials, estimated event rates used in study design often do not match the actual results, so very large trial sizes are needed. Additionally, trials need to recognize the need for longer monitoring periods (preferably continuous), and perhaps novel wearables will allow long-term monitoring, with accurate interpretation of the ECG and long-term adherence. As the USPSTF and a recent report from a National Heart, Lung, and Blood Institute Workshop noted, many questions about screening for atrial fibrillation remain unanswered.

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ARTICLE INFORMATION

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REFERENCES