Impact of CHA2DS2-VASc score on smartphone-based screening for atrial fibrillation: A pre-specified subgroup analysis of the eBRAVE-AF trial

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Background: The eBRAVE-AF trial showed that digital smart-device based screening for atrial fibrillation (AF) more than doubled the detection rate of treatment-relevant AF when compared to usual care.

Purpose: In this pre-specified subgroup analysis, we investigated the effect of CHA2DS2-VASc score on compliance, efficacy of digital screening, and the interaction of CHA2DS2-VASc score and AF-triggered major adverse cardiovascular complications (MACCE).

Methods: 5,551 individuals, free of AF were randomized to digital screening (n=2,860) or usual care (n=2,691). For digital screening, participants used a certified app to screen for irregularities in their pulse waves by means of photoplethysmography (PPG). Abnormal findings were confirmed by a 14-day Holter-ECG. The primary endpoint was newly diagnosed AF treated with oral anticoagulation (OAC) within 6 months. After 6 months, participants crossed over to a second study phase with reverse assignment. For this analysis we combined the two phases using multilevel clustered Cox-regression analysis. CHA2DS2-VASc score was dichotomized at a cut-off of ≤3.

Results: The median CHA2DS2-VASc score was 3 ± 1, the median age was 65 ± 11 years, 31% participants were females. Participants performed a median of 53 ± 62 PPG-measurements with no significant difference in participants with CHA2DS2-VASc score ≤3 (52 ± 61) and CHA2DS2-VASc score >3 (54 ± 65, p=0.269). During a median follow-up time of 12 months 102 participants reached the primary endpoint (including 2 endpoints in the cross-over window). A CHA2DS2-VASc score >3 (n=1,205; 33 events) compared to CHA2DS2-VASc score ≤3 (n=4,346; 69 events) was a significant predictor for reaching the primary endpoint (HR 1.78; 95% CI 1.18-2.70; p=0.006). Digital screening significantly increased the detection rate of AF requiring OAC in participants with CHA2DS2-VASc score >3 (HR 2.11; 95% CI 1.00-4.42; p=0.049; Fig 1A) and CHA2DS2-VASc score ≤3 (HR 2.43; 95% CI 1.43-4.13; p=0.001; Fig 1B). There was no interaction (p=0.758) between CHA2DS2-VASc score and the efficacy of digital screening. The rate of MACCE in participants with CHA2DS2-VASc score >3 (5.2%; 95% CI 3.8-6.6%) and CHA2DS2-VASc score ≤3 (4.6%; 95% CI 4.0-5.3%) was not significantly different (HR 1.14; 95% CI 0.76-1.71; p=0.539). However, only in participants with CHA2DS2-VASc score ≤3 MACCE were associated with previously diagnosed AF (HR 9.77; 95% CI 5.08-18.79; p<0.001 vs. 1.43; 95% CI 0.28-7.37; p=0.618 in participants with CHA2DS2-VASc score >3; p-interaction=0.034).

Conclusion: In a large-scale clinical trial, comparing digital screening to usual care for detecting AF requiring OAC a CHA2DS2-VASc score >3 did not influence compliance but was associated with higher risk for developing AF requiring OAC. CHA2DS2-VASc score >3 was not associated with higher rate of MACCE. However, only in participants with CHA2DS2-VASc score ≤3, these MACCE were triggered by previously diagnosed AF.
**Fig. 1:** Detection of atrial fibrillation requiring oral anticoagulation in participants with a CHA\(_2\)DS\(_2\)-VASc score > 3 (A) and CHA\(_2\)DS\(_2\)-VASc score ≤ 3 (B) stratified by screening method (red: digital screening; blue: usual care; HR: hazard ratio)