Efficacy of Smartphone Based Monitoring for Early Detection of AF

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Wonju College of Medicine
Expected or hypothetical potential advantages of detecting AF in an asymptomatic stage

- Prevention of *thromboembolic events and stroke* by institution of oral anticoagulation in patients at risk
- Prevention of subsequent onset of *symptoms*
- Prevention and/or *reversal of electrical/mechanical atrial remodeling*
- Prevention and/or reversal of *tachycardiomyopathy* at atrial and ventricular level
- Prevention and/or reversal of *AF-related hemodynamic derangements*
- Prevention of *AF-related morbidity and reduction of AF-related hospitalizations*
- Reduction of *AF-related mortality*
Screening tools

CLINICAL SCREENING

ECG SCREENING > SINGLE LEAD

- Single-lead ECG monitor
- Holter monitor
- Watch-cam recorder

> MULTI-LEAD

- Multi-lead ECG monitor

> NEW TOOLS

- Photoplethysmographic app
- Smartphone + casing electrode
- Smartphone handheld ECG

IMPLANTED DEVICES

- Pacemaker
- Implantable cardioverter defibrillator
- Implantable loop recorder
- Telemetry
Detection of atrial fibrillation: meta analysis
**Smartphone : ECG tracing**

**Alivecor KardiaMobile**
- $99.00
- Works with most smartphones & tablets (Android & iOS)
- FDA 510k approval in 2012
- Bipolar lead I
- Real time and is also stored, being instantly transmitted by the phone

**KardiaBand**
- The only EKG solution for Apple Watch® Series 1-3
- Accurate and instant analysis for detecting atrial fibrillation (AF) and normal sinus rhythm in an EKG
Smartphone: Photoplethysmography

Oscillometric analysis

Samsung simband smartwatch
Smart Phone (Alivecor) ECG

A

B

C

D
Accuracy of smart phone ECG

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Absolute Mean Difference and Pearson Correlation Between Smartphone and 12-Lead ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Heart Rate (bpm)</td>
</tr>
<tr>
<td></td>
<td>Absolute Mean Difference ± SD</td>
</tr>
<tr>
<td>Division I athletes (n = 95)</td>
<td>5 ± 5</td>
</tr>
<tr>
<td>Healthy young adults (n = 120)</td>
<td>5 ± 4</td>
</tr>
<tr>
<td>Cardiology clinic patients (n = 120)</td>
<td>6 ± 11</td>
</tr>
<tr>
<td>Study population (n = 335)</td>
<td>5 ± 7</td>
</tr>
</tbody>
</table>

bpm = beats per minute; msec = milliseconds; SD = standard deviation.

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Sensitivity and Specificity of Smartphone ECG for Atrial Fibrillation/Flutter, AV Block, and QRS Delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG Abnormality</td>
<td>Group (n)</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>Athletes (123)</td>
</tr>
<tr>
<td></td>
<td>HYA (128)</td>
</tr>
<tr>
<td></td>
<td>Patients (130)</td>
</tr>
<tr>
<td></td>
<td>Total (381)</td>
</tr>
<tr>
<td>AV block</td>
<td>Athletes (123)</td>
</tr>
<tr>
<td></td>
<td>HYA (128)</td>
</tr>
<tr>
<td></td>
<td>Patients (130)</td>
</tr>
<tr>
<td></td>
<td>Total (381)</td>
</tr>
<tr>
<td>QRS delay</td>
<td>Athletes (123)</td>
</tr>
<tr>
<td></td>
<td>HYA (128)</td>
</tr>
<tr>
<td></td>
<td>Patients (130)</td>
</tr>
<tr>
<td></td>
<td>Total (381)</td>
</tr>
</tbody>
</table>

athletes = elite athletes; HYA = healthy young adults; patients = cardiology clinic patients.
ATRIAL FIBRILLATION AND SMARTPHONE EVENT MONITORS

1. Internet-enabled mobile ECG (iECG)
2. Photoplethysmographic pulse wave signals (PPG)
Internet-enabled mobile ECG (iECG)
Smartwatch Algorithm for Automated Detection of Atrial Fibrillation

Kardia Band (KB) (AliveCor, Mountain View, California)

Study participants:
Consecutive patients with a diagnosis of AF who presented for scheduled elective cardioversion

Comparison
Pre-CV ECG and KB recording, Post-CV ECG and KB recording

KB algorithm

Rhythm irregularity
P wave absence

Possible AF

50<HR<100 bpm
normal

HR <50 or >100 bpm
Unclassified

Automated Atrial Fibrillation Detection Algorithm Using Novel Smartwatch Technology

The smartwatch strap with an electrode sensor that records heart rhythm

Patient places thumb on the sensor to record rhythm

The application utilizes an algorithm to differentiate sinus rhythm (SR) from atrial fibrillation (AF), or would label the recording as unclassified if it does not meet certain criteria

The app informs the patient if AF is detected; the results are transmitted to the patient's physician

<table>
<thead>
<tr>
<th>Method for interpreting the recording:</th>
<th>% of patients with interpretable results</th>
<th>Accuracy of AF diagnosis compared to 12 lead electrocardiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>App algorithm only</td>
<td>66%</td>
<td>93% sensitivity; 84% specificity</td>
</tr>
<tr>
<td>Physician only</td>
<td>87%</td>
<td>99% sensitivity; 83% specificity</td>
</tr>
<tr>
<td>Recordings labeled as “unclassified“ by the app algorithm when reviewed by physician</td>
<td>100%</td>
<td>100% sensitivity; 80% specificity</td>
</tr>
</tbody>
</table>

Limitation of iECG

- the high proportion of nonusable recordings
- the need for active involvement of the patient,
- a feature that does not allow for “continuous” rhythm screening.
Photoplethysmographic pulse wave signals (PPG)
Photoplethysmography

- As a reference signal,
  - a heart rate monitor chest belt (Wahoo TICKR, Model SHRM1G, Wahoo Fitness, 90 West Wieuca Rd NE #110, Atlanta, GA)

WATCH AF Trial

Reference
Cardiologists’ iECG diagnoses

Comparison
the PPG algorithm
the automated iECG interpretation,

PPG
Gear fit 2
study version of the Heartbeats application
(Preventicus GmbH, Jena, Germany).

iECG
AliveCor

PPG
Wavelet wrist band
iPad mini

Diagnostic accuracy of PPG algorithm

Correctly classified cases by the 1 min PPG algorithm

Cardiologists’ diagnosis

SR (n=271)
- PPG - SR: 98%
- PPG - AF: 2%
- n=5

AF (n=237)
- PPG - SR: 94%
- PPG - AF: 6%
- n=15

## Diagnostic accuracy of PPG algorithm

<table>
<thead>
<tr>
<th></th>
<th>1-min PPG (n=508)</th>
<th>iECG (n=549)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>93.7 (89.8–96.4)</td>
<td>99.5 (97.5 - 99.9)</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>98.2 (95.8–99.4)</td>
<td>97.4 (94.7 - 98.9)</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>97.8 (94.9–99.3)</td>
<td>97.6 (95.0 - 99.0)</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>94.7 (91.4–97.0)</td>
<td>99.2 (97.3 - 99.9)</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>96.1 (94.0–97.5)</td>
<td>98 (96.9 - 99.2)</td>
</tr>
<tr>
<td>LR+</td>
<td>52.1 (23.5–160.7)</td>
<td>38.2 (3.9 -90.8)</td>
</tr>
<tr>
<td>LR-</td>
<td>0.064 (0.011–0.036)</td>
<td>0.007 (0.03 - 0.001)</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>142 (21.8)</td>
<td>101 (15.5)</td>
</tr>
<tr>
<td>CCR(%)</td>
<td>74.8</td>
<td>83.1</td>
</tr>
</tbody>
</table>

CCR; corrected classified rate, LR+; positive likelihood ratio

DETECT AF PRO

Reference: iECG (AliveCorVR, Mountain View, CA, USA)

Heartbeats algorithm (Version 20171120, PreventicusVR, Jena, Germany)

DETECT AF PRO

672 Subjects assessed for eligibility

18 Subjects excluded
   5 Double acquisitions
   5 Missing PPG files
   3 Missing iECG files
   1 Age < 18 years
   4 Missing informed consent

654 Subjects were included

62 Subjects excluded
   43 Insufficient quality of PPGs
   17 Insufficient quality of iECGs
   1 Insufficient quality of PPG AND iECG
   1 Spontaneous conversion of heart rhythm

592 Subjects for final analysis

248 AF
344 SR

September 2016 and October 2017
University Hospital Basel, Switzerland,
University Medicine Greifswald, Germany

# Accuracy

<table>
<thead>
<tr>
<th></th>
<th>Heartbeats algorithm</th>
<th></th>
<th></th>
<th>Kardia algorithm</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-min</td>
<td>3-min</td>
<td>5-min</td>
<td>1-min</td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>89.9 (85.5–93.4)</td>
<td>91.3  (86.5–94.7)</td>
<td>91.5  (85.9–95.4)</td>
<td>99.6  (97.9–100)</td>
<td></td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>99.1 (97.5–99.8)</td>
<td>98.7  (96.7–99.6)</td>
<td>99.6  (97.8–100)</td>
<td>97.8  (95.3–99.2)</td>
<td></td>
</tr>
<tr>
<td>No diagnosis (%)</td>
<td>6.7</td>
<td>13</td>
<td>32.2</td>
<td>18.8</td>
<td></td>
</tr>
<tr>
<td>CCR(%)</td>
<td>88.8</td>
<td>77.6</td>
<td>60.9</td>
<td>82.2</td>
<td></td>
</tr>
</tbody>
</table>

CCR: corrected classified rate, LR +; positive likelihood ratio
AF screening with PPG

Local newspaper in Layman’s press

Qompium N.V. (Hasselt, Belgium)

Each measurement is automatically analysed by the algorithm. Measurements indicative of an irregular rhythm are reviewed by medical technicians under supervision of cardiologists.
AF screening with PPG

12,046 unique PPG measurements

9,733 PPG measurements of insufficient quality for analysis

110,713 PPG measurements with enough quality for analysis

98,586 classified as normal regular heart rhythm by the algorithm

No further action (89%)

1,212 classified as possible irregular heart rhythm by the algorithm

9,722 classified as premature and/or missed beats by the algorithm

Final diagnosis after confirmatory offline analysis of the raw PPG signal:
- Normal regular rhythm (n=4,812)
- Frequent and irregular ectopic beats (n=4,450)
- Bigeminy (n=107)
- Trigeminy (n=40)
- Atrial fibrillation (n=26)
- Atrial flutter (n=3)
- Bradycardia episode (n=3)
- Tachycardia episode (n=3)
- Noise (n=278)

2,405 classified as possible atrial fibrillation by the algorithm

Final diagnosis after confirmatory offline analysis of the raw PPG signal:
- Normal regular rhythm (n=895)
- Frequent and irregular ectopic beats (n=808)
- Trigeminy (n=4)
- Atrial fibrillation (n=569)
- Atrial flutter (n=10)
- Tachycardia episode (n=1)
- Noise (n=118)
AF screening with PPG

**Table 1** Characteristics of the screened population ($n = 12,328$)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No AF diagnosis</th>
<th>AF diagnosis</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$N$</td>
<td>12,192</td>
<td>136 (1.1%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>49 ± 14</td>
<td>62 ± 11</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Male gender</td>
<td>7,084 (58%)</td>
<td>100 (74%)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>174 ± 9</td>
<td>177 ± 9</td>
<td>0.129</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>79 ± 16</td>
<td>88 ± 16</td>
<td>0.002</td>
</tr>
<tr>
<td>Body mass index (kg/m$^2$)</td>
<td>26 ± 4</td>
<td>28 ± 4</td>
<td>0.004</td>
</tr>
</tbody>
</table>
AF screening with PPG

Frequency of smartphone-based photo-plethysmography measurements of insufficient quality for analysis during the study period.

Patient-reported outcomes
- One hundred screening-positive subjects consented to provide this information
- 40 patients: no Hx of AF and Dx confirmed on ECG
- 60 patients: known AF and 28% received an adjustment of their current care strategy

Cumulative diagnostic yield (curve) and prevalence (arrow) for atrial fibrillation during the 7-day screening period.
Apple Heart Study

Overall Goal
To evaluate the ability of the irregular pulse notification algorithm to identify Afib and guide subsequent clinical evaluation

- Notification burden
- Subsequent Afib diagnosis
- Algorithm performance
- Safety
- Pragmatic and generalizable
- Scalable study procedures
Apple Heart Study
Apple Heart Study

- Eligible for ePatch
- No AF/other arrhythmia on ePatch report
  - Recommend participant to proceed with usual care
- Second video visit with Study Doctor
- AF/other arrhythmia on ePatch report
  - Recommend participant to contact their healthcare provider
- 90-Day Questionnaire and End of Study Questionnaire
Apple Heart Study

Primary Endpoints
- Afib > 30 seconds on ECG patch in ≥ 65 years
- Simultaneous Afib on ECG Patch and individual tachogram

Secondary Endpoints
- Simultaneous Afib on ECG Patch w/ notification
- Self-reported contact w/ health care provider

Notification
- Irregular Rhythm Identified
- Connect to Telehealth Doctor
- Mail ECG Patch
- Discuss Heart Results
Apple heart study

Overall Cohort
Total Population 419,297

Notification
Pulse Notification 2,161 (0.5%)
First Study Visit 945 (44%)
At SVI: 291 (31%)
- Emergent symptoms: 20
- Prior Afib or flutter: 174
- Current Anticoagulant use: 90
- Other reasons: 33

ECG Patch
ECG Patch Shipped 658 (70%)

EOS Survey 90-Day Survey
Completed 90-day Survey 1,376 / 2,161 (64%)

No Notification (PN)
417,136 (99.5%)

ECG Patch Returned & Analyzed 450 (68%)

Completed EOS Survey 929 / 2,161 (43%)

Completed EOS Survey 293,015 (70%)
Apple Heart Study

Initial Irregular Pulse Notifications

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Notified / Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>2,161 / 419,297</td>
<td>0.52</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 65</td>
<td>775 / 24,626</td>
<td>3.2</td>
</tr>
<tr>
<td>55–64</td>
<td>556 / 42,633</td>
<td>1.3</td>
</tr>
<tr>
<td>40–54</td>
<td>488 / 132,696</td>
<td>0.37</td>
</tr>
<tr>
<td>22–39</td>
<td>341 / 219,179</td>
<td>0.16</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>461 / 177,087</td>
<td>0.26</td>
</tr>
<tr>
<td>Male</td>
<td>1,672 / 238,700</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Overall Cohort
~ 8 Months Monitoring
Apple Heart Study

Afib Yield on ECG Patch

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Observed AF / Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>153 / 450</td>
<td>34</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 65</td>
<td>63 / 181</td>
<td>35</td>
</tr>
<tr>
<td>55–64</td>
<td>47 / 114</td>
<td>41</td>
</tr>
<tr>
<td>40–54</td>
<td>34 / 106</td>
<td>32</td>
</tr>
<tr>
<td>22–39</td>
<td>9 / 49</td>
<td>18</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>26 / 102</td>
<td>26</td>
</tr>
<tr>
<td>Male</td>
<td>124 / 335</td>
<td>37</td>
</tr>
</tbody>
</table>

Mean time to hookup: 13 days
Mean wear time: 6.3 days
Apple Heart Study

Positive Predictive Values

<table>
<thead>
<tr>
<th></th>
<th>Aflib on ECG Patch</th>
<th>Positive Tachograms</th>
<th>PPV* (97.5% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>1,489</td>
<td>2,089</td>
<td>0.71 (0.69–0.74)</td>
</tr>
<tr>
<td>Age ≥ 65</td>
<td>548</td>
<td>914</td>
<td>0.60 (0.56 – 0.64)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Aflib on ECG Patch</th>
<th>Positive Notifications</th>
<th>PPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>72</td>
<td>86</td>
<td>0.84 (0.76–0.92)</td>
</tr>
<tr>
<td>Age ≥ 65</td>
<td>25</td>
<td>32</td>
<td>0.78 (0.64 – 0.92)</td>
</tr>
</tbody>
</table>
Apple Heart Study

- Notification: 2,161 (0.5%)
  - 161 (15%) Afib before study enrollment
- 90-Day Survey: 1,376 / 2,161 (64%)
- Contacted Non-Study Provider: 787 / 1,376 (57%)
  - 218 (28%) Start new medication
  - 262 (33%) Referral to specialist
  - 287 (36%) Additional testing
Advantage of PPG

• Method for large-scale Screening
  – very high specificity of the PPG-based automated AF detection algorithm
  – Low rate of unnecessary follow-up examinations
Limitation of PPG

- Signal quality
- Limited battery duration
- Moderate PPV in lower AF prevalence rates
  - Tool could have its strengths in patients with a high pre-test probability for AF

<table>
<thead>
<tr>
<th>AF Prevalence</th>
<th>Test Criterion</th>
<th>5%</th>
<th>10%</th>
<th>14%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PPG</td>
<td>iECG</td>
<td>PPG</td>
<td>iECG</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>72.7 (69.9-75.4)</td>
<td>66.8 (63.8-69.6)</td>
<td>84.9 (82.5-87.0)</td>
<td>80.9 (78.4-83.3)</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>99.7 (99.1-99.9)</td>
<td>100 (99.7-100)</td>
<td>99.3 (98.5-99.7)</td>
<td>99.9 (99.4-100)</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>97.9 (96.8-98.6)</td>
<td>97.5 (96.3-98.3)</td>
<td>97.7 (96.6-98.5)</td>
<td>97.5 (96.4-98.4)</td>
</tr>
</tbody>
</table>
Limitation of PPG

• potential influences of extrasystoles
• reduced PPG pulse wave tissue penetration in subjects with intense skin pigmentation
• worsening of the signal-to-noise ratio in patients with tremor
• PPG based AF detection devices may still be understood as AF screening tools with a need for a confirmatory ECG for suspected AF.

The role of smartphone AF screening

• potentially disruptive to the traditional model of conventional diagnostic devices requiring physician interpretation
  – blurs the definitions of patient vs. consumer

• Accompanying set of challenges
  – Validation of recordings
    • noise correction, limitations of single lead ECG recordings
  – increased onus on the physician for interpretation of large volumes of transmissions (without established reimbursement)
  – data storage and security.
  – in a general population with low disease prevalence, the risk of false positive results may obviously increase
The role of smartphone AF screening

- It has to be highlighted that the regulations for the validation of medical devices do not constantly apply to, nor are regulatory followed, for apps to be used with smartphones, so that a careful approach has to be advised both to customers and physicians.