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ORIGINAL ARTICLE

Ultra-short-term heart rate variability using a photoplethysmography-based smartphone application: a TeleCheck-AF subanalysis

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Aims Autonomic nervous system activation plays an important role in the pathophysiology of atrial fibrillation (AF). It can be determined using heart rate variability (HRV). We aimed to evaluate the feasibility of using photoplethysmography (PPG) recordings for the assessment of the ultra-short-term HRV.

Methods and results TeleCheck-AF is a structured mobile health approach, comprising the on-demand use of a PPG-based smartphone application prior to a scheduled teleconsultation to ensure comprehensive remote AF management. Participants with at least one PPG recording in sinus rhythm were included to assess resting heart rate, root mean square of successive differences (RMSSD), patient compliance and data consistency. In total, 855 patients [39.4% women] with 13 465 recordings were included. Patient compliance was 95.2% (IQR 76.2–114.3%). Median heart rate per patient was 66.5 (IQR 60.0–74.0) b.p.m., median RMSSD per patient was 40 (IQR 33–50) ms and median recording consistency was ±5.2 (IQR 3.8–7.0) b.p.m. and ±14.8 (IQR 9.3–21.1) ms, respectively. RMSSD was lower in men than women, in patients with CHA_2D_2-VA-Score 0, with a

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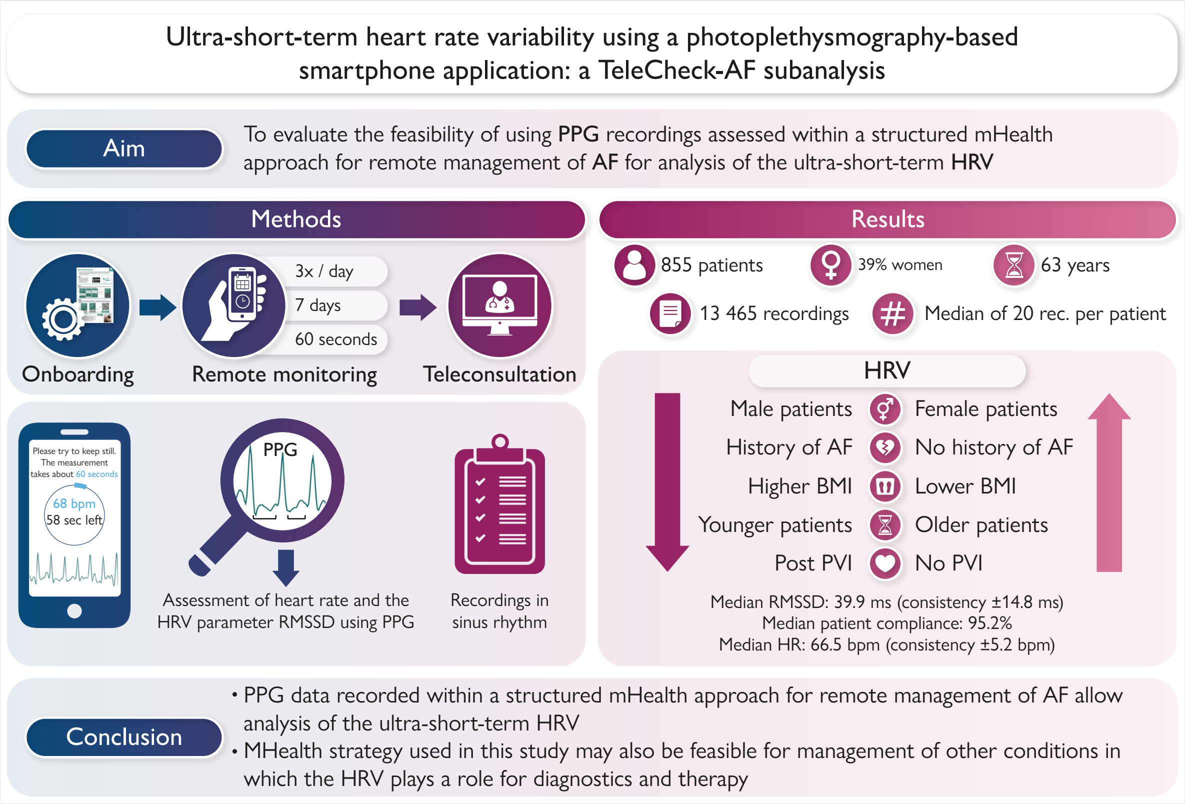
Conclusion history of AF, and following ablation of AF. Older age and lower body mass index were associated with higher RMSSD. The ultra-short-term HRV can be determined in 1-min PPG recordings with high user compliance and high inter-recording consistency within a structured mobile health AF management approach. The strategy used in this study may also be feasible for the management of other conditions in which the HRV plays a role for diagnostics and therapy.

Graphical Abstract



Keywords Remote monitoring • Digital devices • Photoplethysmography • Heart rate variability • Atrial fibrillation • Telemonitoring

Background and objectives

Heart rate variability (HRV) displays the current function of the autonomic nervous system. Assessment is not only non-invasive and low in cost but can also be beneficial for the management of various diseases.[1] One example is patients with atrial fibrillation (AF), as the cardiac autonomic nervous system plays an important role in the pathophysiology of AF.[2] Moreover, various therapeutic approaches for heart rate (HR) and/or rhythm control used in patients with AF are known to also affect the autonomic nervous function.[3,4]

However, as the HRV is mostly assessed using 24-h Holter monitoring, usage has yet to be limited.[1] Previous studies have demonstrated the feasibility of deriving the HRV from shorter electrocardiogram (ECG) recordings, such as 5-min recordings (referred to as short-term HRV) or recordings of <5 min (referred to as ultra-short-term HRV).[5,6] Parameters assessing the time domain of the HRV include the standard deviation of the NN interval (SDNN), the pNN50 (percentage of absolute differences in successive NN values > 50 ms), as well as the root mean square of successive differences (RMSSD).[7] Since the SDNN depends on the length of the recording and no correlation has been demonstrated for the SDNN or pNN50 between 5-min recordings and shorter durations (1 min or 10 s), while RMSSD, shows a good correlation for these timeframes, the RMSSD is the recommended parameter for assessing the ultra-short-term HRV in such short recordings.[7,8]

Several studies have evaluated the use of shorter HRV recordings with durations of <5 min.[6,8–11] Such a short recording duration may not only be advantageous for integration into daily clinical practice but may also be more applicable with digital devices capable of providing these data.

Although beat-to-beat intervals to determine the HRV are traditionally derived from ECG recordings, photoplethysmography (PPG)-based monitoring using hand-held devices such as smartphones or smartwatches is easily accessible and widely used in more and more patients with AF. Current PPG algorithms can detect pulse-peaks of PPG waveforms for accurate HR and rhythm determination.[12–16] Less studies have focused on the feasibility and recording-recording consistency of using PPG-derived pulse-peak intervals for the determination of HRV in patients within a structured mobile health (mHealth) approach. One of these mHealth-based strategies is the TeleCheck-AF project, which incorporates PPG-based monitoring of HR and rhythm monitoring using a CE-marked app-based on-demand infrastructure combined with teleconsultation to optimize remote management of AF.[17,18]

This study aimed to evaluate the feasibility of using PPG recordings collected within the structured mHealth approach TeleCheck-AF for the analysis of the ultra-short-term HRV.

Methods

TeleCheck-AF project

The TeleCheck-AF project was an international multicentre project developed during the COVID-19 pandemic implementing an on-demand app-based infrastructure for remote management of AF. Details and first results have been previously described.[19–24] In brief, this integrated infrastructure included app-based on-demand HR and rhythm monitoring followed by a teleconsultation to ensure comprehensive AF management using a PPG-based smartphone application (FibriCheck®, Qompium NV, Hasselt, Belgium). Patients were instructed to measure HR and heart rhythm at least three times per day and in case of symptoms for seven consecutive days prior to teleconsultation, with each measure lasting 60 s. Patient data were collected using a standardized electronic case report form distributed to all participating centres involved in the retrospective per-patient analysis of the TeleCheck-AF cohort. Information on baseline clinical characteristics, including demographics and medical history, was extracted from patients' electronic health records at the initiation of app-based HR and rhythm monitoring. Retrospective data collection from the participating TeleCheck-AF centres was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committees of the participating centres.

Patient population

Patients ≥ 18 years scheduled for teleconsultation in one of the 41 participating centres were managed within the TeleCheck-AF project between April 2020 and July 2021. Ten of the participating centres included at least 25 patients and were included in this analysis: (1) Maastricht University Medical Center +, Maastricht, the Netherlands; (2) Hannover Heart Rhythm Center, Hannover, Germany; (3) Ziekenhuis Oost-Limburg, Leuven, Belgium; (4) Medical University of Graz, Graz, Austria; (5) University Hospital Cologne, Cologne, Germany; (6) Radboud University Medical Center, Nijmegen, the Netherlands; (7) Rijnstate Hospital, Arnhem, the Netherlands; (8) Medical University of Warsaw, Warsaw, Poland; (9) Liverpool Heart and Chest Hospital, Liverpool, United Kingdom; (10) King George Hospital, Ilford, United Kingdom.

Data collection

Patients with at least one PPG recording in sinus rhythm (SR) were included and all recordings in SR were analyzed (*Figure 1*).

HR and HRV determination

HR and ultra-short-term HRV were automatically assessed for every 1-min recording in SR and with sufficient quality. Categorisation of the signal quality as sufficient or insufficient, as well as rhythm evaluation of the recording were performed automatically as described elsewhere.[25] Recordings evaluated as sufficient quality were then used to calculate the HR and ultra-short-term HRV.[26] HRV was quantified as the RMSSD of the recorded beat-to-beat intervals.[26] To ensure adequate calculation of RMSSD,[1,7,27] beat-to-beat intervals of ectopic beats within a recording were excluded prior to assessment as these should not be considered for the computation of the RMSSD according to the current HRV guidelines.[7] In more detail, beats were detected automatically by identifying the inter beat intervals that showed more than a relative 30% difference as compared to the previously assumed normal inter beat interval. Such beats were then removed before automatic evaluation of the RMSSD.

Patient adherence was defined as number of performed measurements per number of expected measurements[28] including all types of measurements (e.g. SR, low quality, AF) over the prescription period (three attempts per day for 7 days; $n = 21$) and was calculated in percent per patient. Recording consistency (standard deviation over all recordings within each patient) was calculated for HR and HRV. Different subgroups were analyzed for differences in HR and HRV.

Statistical analysis

Normal distribution was tested by applying the Shapiro–Wilk test. Categorical variables are presented as numbers (%). Continuous data are presented as median and interquartile range (IQR). As data did not follow a normal distribution, the non-parametric Mann–Whitney *U* test was used for between-group comparisons. Correlation analysis was done using Spearman test and spearman correlation coefficient (rs).

Data merging was performed using Python (NumPy, version 1.19.5, Python Software Foundation, version 3.8.6). Statistical analysis was performed using SPSS (Version 29, IBM, Armonk, NY, USA). P-values < 0.05 were considered statistically significant.

Results

Patient characteristics

In total, 855 patients (39.4% women) were included in the analysis. Median age was 63 (IQR 56–70) years. Baseline characteristics are shown in *Table 1*.

Most patients had a history of AF (86.4%), and most of these patients also had a history of AF ablation (59.4%). Detailed arrhythmia-related patient characteristics are shown in *Table 2*.

Patient adherence

The total number of recordings in SR included in the analysis was 13 465. Median number of all recordings per patient was 20 (IQR 16–24) in total and 16 (IQR 11–20) in SR. Median patient adherence was 95.2% (IQR 76.2–114.3%), and the adherence was high among all age groups (*Figure 2*). Only patients aged <30 years were shown to exhibit a median adherence below 90% [median adherence 85.7% (IQR 54.8–95.2%; $n = 17$)]. Women had a better adherence than men [women: 100% (IQR 81.0–123.8%); men: 95.2% (IQR 71.4–109.5%); $P < 0.001$].

Resting HR

Median resting HR was 66.5 (IQR 60.0–74.0) b.p.m. Median recording consistency within the prescription period was ± 5.2 (IQR 3.8–7.0) b.p.m. Women had a significantly higher HR than men. Patients with a history of AF were shown to have a significantly lower HR than patients without a history of AF. HR was significantly higher in patients with history of AF ablation than in patients without AF ablation. Patients prescribed with beta-blocker (BB) and/or antiarrhythmic drugs (AADs) were shown to have a lower HR in comparison to patients not prescribed with BB and/or AADs. Moreover, patients with higher thromboembolic risk (defined as CHA_2DS_2-VA-score ≥2 points) were shown to have a lower HR compared with patients with low thromboembolic risk (defined as CHA_2DS_2-VA-score = 0 points). Details are depicted in *Figure 3*.

Older age was significantly associated with lower HR ($P < 0.001$; rs = −0.186). No association was found between HR and body mass index (BMI) ($P = 0.290$, rs = 0.037).

Ultra-short-term HRV

Median RMSSD was 39.9 (IQR 33.0–50.1) ms. Median recording consistency within the prescription period was ±14.8 (IQR 9.3–21.1) ms.

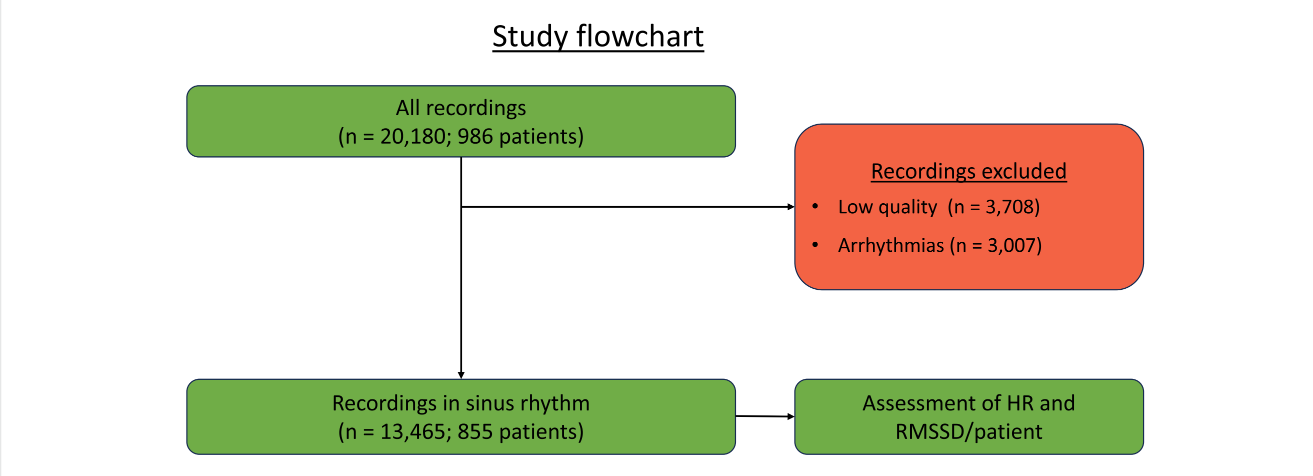


Figure 1 Study flowchart for the analysis of recordings. HR, heart rate; RMSSD, root mean square differences.

Table 1 Baseline characteristics

Parameter	Patients included ($n = 855$)
Female (*n*, %)	337 (39.4)
Age (years) (median, IQR)	63 (56–70)
Heart failure (*n*, %)	92 (10.8)
Coronary artery disease (*n*, %)	109 (12.7)
Hypertension (*n*, %)	403 (47.1)
Diabetes mellitus (*n*, %)	69 (8.1)
Chronic obstructive pulmonary disease (*n*, %)	39 (4.6)
Chronic kidney disease (*n*, %)	38 (4.4)
Body mass index (kg/m^2) (median, IQR)	26.8 (24.4–29.7)

IQR, interquartile range.

Table 2 Arrhythmia-related patient characteristics

Parameter	Patients included ($n = 855$)
History of AF (*n*, %)	739 (86.4)
History of Aflut (*n*, %)	190 (22.2)
History of AT (*n*, %)	59 (6.9)
History of SVT (*n*, %)	91 (10.6)
History of cardioversion (*n*, %)	294 (34.4)
History of AF ablation (*n*, %)	508 (59.4)
o Cryo-PVI	230 (45.3)
o RF-PVI	257 (50.6)
o Hybrid ablation or minimal invasive surgery	13 (2.6)
o Redo PVI	28 (5.6)
Medication (*n*, %)	
●Oral anticoagulation	628 (73.5)
●Beta-blocker	464 (54.3)
●Antiarrhythmic drugs	308 (36)
Thromboembolic risk (*n*, %)	
●CHA_2DS_2-VA-Score = 0	222 (26.0)
●CHA_2DS_2-VA-Score = 1	232 (27.1)
●CHA_2DS_2-VA-Score ≥ 2	367 (42.9)
●Unknown	34 (4.0)

AF, atrial fibrillation; Aflut, atrial flutter; AT, atrial tachycardia; SVT, supraventricular tachycardia; Cryo-PVI, cryoballoon pulmonary vein isolation; RF-PVI, radiofrequency pulmonary vein isolation.

Women had a significantly higher HRV than men. Patients with a history of AF had a significantly lower HRV than patients without a history of AF. No differences were found regarding the use of BB and/or AADs. Results remained consistent in only those patients with a history of AF. Patients with higher thromboembolic risk (defined as CHA_2DS_2-VA-score ≥ 2) were shown to have a higher HRV compared with patients with low thromboembolic risk (defined as CHA_2DS_2-VA-score = 0). Furthermore, patients with a history of AF ablation were shown to have a lower HRV than patients with a history of AF and no such procedure. Details are depicted in *Figure 4*.

In patients with history of AF, contrary to previous studies, older age correlated with higher HRV ($P < 0.001$; rs = 0.183). A higher BMI was associated with a lower HRV ($P = 0.015$; rs = −0.92).

Discussion

The aim of this study was to evaluate the feasibility of using PPG recordings assessed within a structured mHealth strategy for analysis of the ultra-short-term HRV.

The main results of this analysis demonstrate that (1) PPG data recorded within an mHealth telemedicine infrastructure allow analysis of the ultra-short-term HRV and (2) high patient adherence and high inter-recording consistency. Therefore, using PPG recordings assessed within a digital health framework for analysis of the ultra-short-term HRV is feasible.

Median adherence in this analysis was good with 95.2% (IQR 76.2–114.3%). In line with findings of another sub-analysis of the

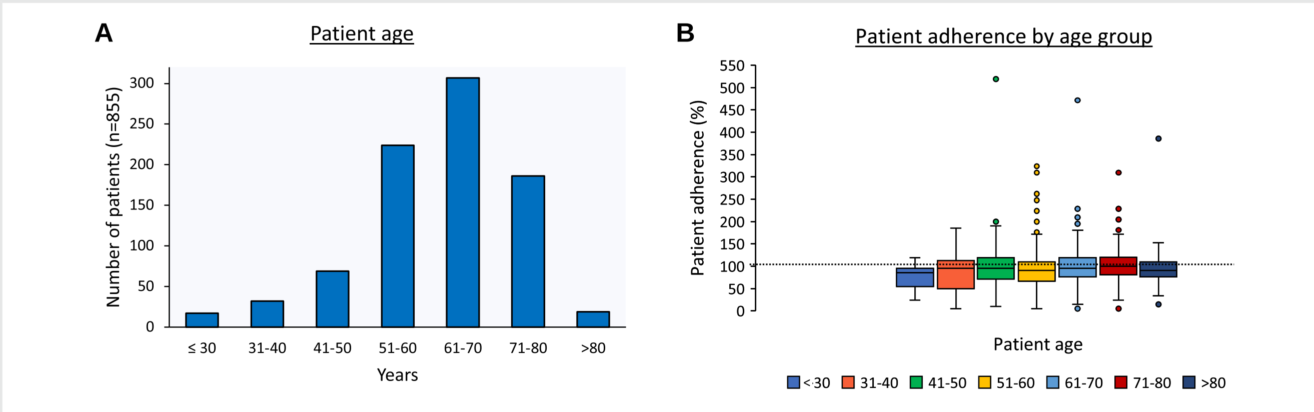


Figure 2 Patient age depicted in groups (*A*) and patient adherence by age group (*B*).

TeleCheck-AF study, older age was associated with higher adherence.[28] Notably, patients < 30 years in this analysis were the only group with a median adherence below 90%.

In this sub-analysis of the multicentered TeleCheck-AF project, HR as well as ultra-short-term HRV were assessed.

In a previous analysis, HR assessment using a PPG-based smartphone application in patients with a history of AF has been shown to be accurate in 93.8% of recordings with a tendency for underestimation of the HR in AF, especially during tachycardic episodes.[29] Median HR in this analysis was 66.5 (IQR 60.0–74.0) and, thus, in normal range with high inter-recording consistency [±5.2 (IQR 3.8–7.0) b.p.m.] and in line with other studies evaluating the inter- and intraindividual variability in daily resting HR.[30] As in previous analyses, women were shown to have a higher HR than men,[30] older patients had a lower HR than younger patients,[31] and patients prescribed with beta-blockers or AADs had a lower HR than others.[32]

Thus, as results of the evaluation of the HR are in line with previous analyses, data used in this analysis are sufficient for further analysis of the ultra-short-term HRV.

Short-term HRV

Previous studies have evaluated the feasibility and reliability of PPG-based HRV assessment using handheld devices.[5,6,33,34] However, evaluation of these aspects has mostly been performed in healthy individuals and athletes.[5,6,33,34] Data regarding patients with cardiac diseases are scarce.[35]

Median RMSSD in this cohort was 39.9 ms (IQR 33.0–50.1) ms with high median inter-recording consistency ± 14.8 (IQR 9.3–21.1) ms. This RMSSD is lower than the mean RMSSD stated in a previous analysis assessing the RMSSD using PPG-based recordings (69 ± 37 ms).[6] However, assessment of the RMSSD in the other analysis was performed in healthy individuals using the app for evaluating the HRV after sport activities[6]—therefore not displaying the patient cohort examined in this study. Another analysis evaluating the HRV derived PPG-data recorded using a smartwatch in patients after ST-elevation myocardial infarction and ischaemic stroke showed a short-term HRV of 30.3 (IQR 24.1–41.7) ms and, thus, in line with the lower ultra-short-term HRV assessed in this analysis.[35]

Therefore, a lower RMSSD in the cohort displayed in this analysis is expected and consistent with previous studies, likely resulting from altered parasympathetic and sympathetic characteristics in patients with pre-existing cardiac conditions.

As found in previous studies[36,37] women had a higher HRV than men indicating a higher vagal tone in female patients.

Notably, in contrast to previous studies, older patients in this analysis were shown to have a higher RMSSD than younger patients. This finding contradicts existing literature, in which a decrease in RMSSD with increasing age is well documented,[6,38] reflecting the known reduction in autonomic function with increasing age.[39] A potential explanation for this difference may be that, unlike in many previous studies where younger patients were normally healthy individuals, younger patients in this cohort were not healthy but had relevant comorbidities. These comorbidities may have not only led to development of AF but also caused relevant impairment of the autonomic nervous system leading to a relevant shift in the difference of the RMSSD for age in this analysis.

Participants with a history of AF in this analysis were shown to have a lower RMSSD than patients without a history of AF. Moreover, patients after ablation for AF were shown to have a lower RMSSD than patients with a history of AF without such a procedure.

Previous studies have shown that pulmonary vein isolation using thermal ablation energy such as radiofrequency or cryoballoon ablation results in relevant changes of the HRV as confirmed in our analysis.[40] These changes are independent of the thermal source used[40] and correlate with short- and long-term ablation success[41] . Thus, further studies may be required to determine if the approach analyzed in this study is feasible to ensure AF ablation success.

The use of beta-blockers is associated with an increase in the vagal modulated RMSSD displaying the improvement in parasympathetic tone.[42] Current data evaluating the effect of AADs on the short-term HRV are scarce. In this analysis, no difference in RMSSD was seen for patients with beta-blockers and/or AADs compared with patients without one of these medications. However, as mentioned previously, most patients prescribed with beta-blockers in this patient cohort suffered from AF. Therefore, a potential increase in the short-term HRV due to the use of beta-blockers may have interfered with a lower HRV in patients with a history of AF, also shown in this study.

Clinical implementation

Data from this analysis show that assessment of the ultra-short-term HRV using PPG-based handheld devices in this mHealth telemedicine setting is feasible with high patient adherence and inter-recording consistency. Therefore, it may be helpful to further optimize the management of patients with AF. This on-demand mHealth approach is a useful tool allowing not only comprehensive management for AF but also structured assessment of ultra-short-term HRV. The approach is aligned with the principles of integrated care and has the potential to improve health outcomes, optimize care processes and enhance patient engagement.

Integration of such an approach into routine care could be beneficial for patients with a history of AF to monitor therapy effectiveness e.g. after initiation of new medications or post-ablation.

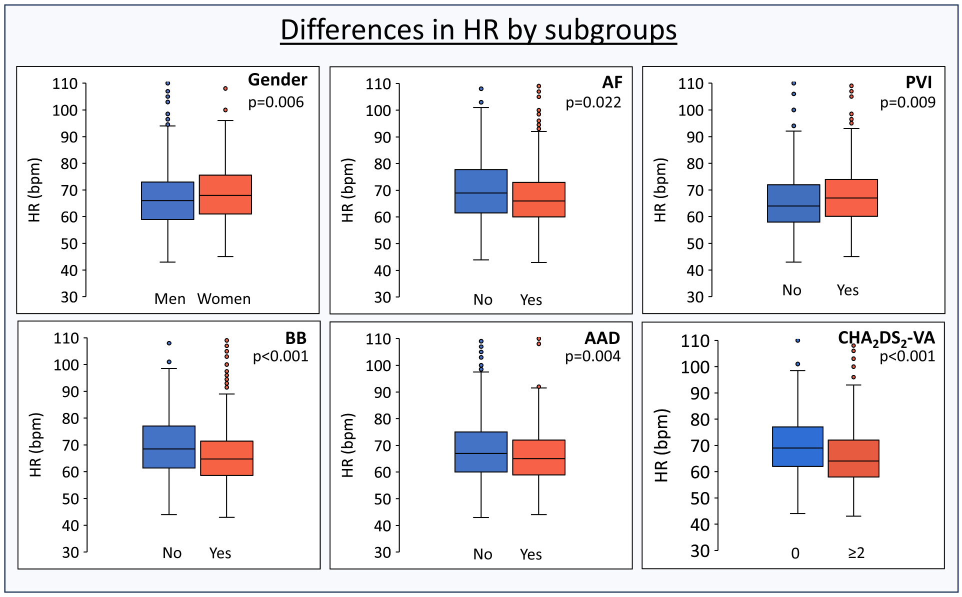


Figure 3 Differences in HR by subgroups. AAD, antiarrhythmic drugs; AF, patients with history of atrial fibrillation; BB, beta-blocker; PVI, pulmonary vein isolation.

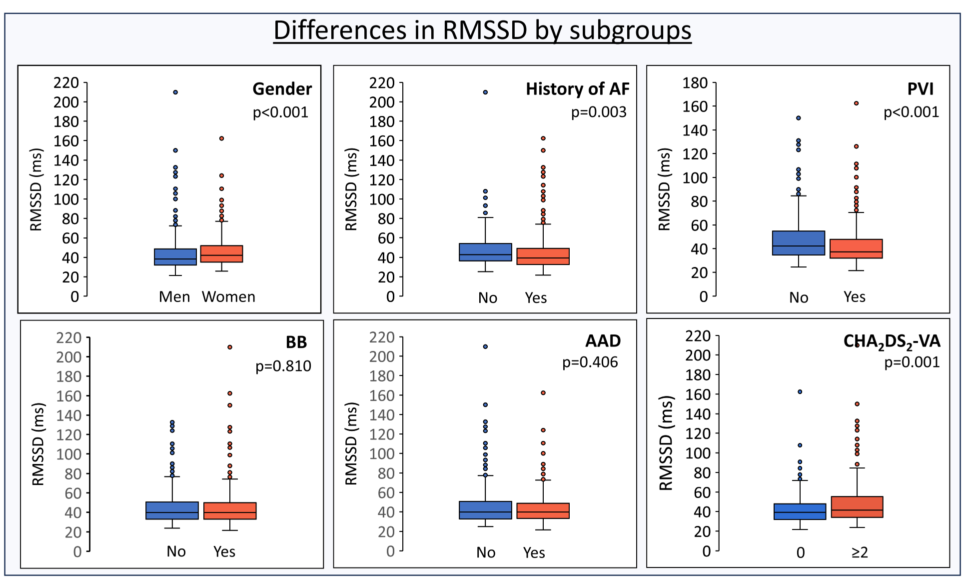


Figure 4 Differences in RMSSD by subgroups. AAD, antiarrhythmic drugs; AF, atrial fibrillation; BB, beta-blocker; PVI, pulmonary vein isolation; RMSSD, root mean square differences.

Moreover, implementation of this method into routine care could enhance self-management of patients, optimize follow-up workflows and provide detailed knowledge about treatment responses about the HRV.

Nevertheless, several practical considerations must be considered before implementation into daily clinical practice. Patient digital literacy plays an important role and should be addressed prior to clinical integration. Physicians should, on the one hand, identify patients with limited digital literacy. However, this aspect is not always age-dependent, as older patients with adequate clinical literacy have been shown to demonstrate good compliance with mHealth approaches, as shown previously.

In addition to the patient's literacy, it is equally important that physicians themselves have sufficient digital literacy, as this is crucial not only for understanding but for adequately interpreting digital health data. Therefore, education and training are of relevance—not only for patients but also for physicians—to maximize the potential benefits of such an mHealth approach.

Another important aspect includes cost and time-related factors, such as costs for device acquisition, the need for adequate data management infrastructure to minimize time needed as well as adequate software integration into existing electronic health record systems. However, these costs could be beneficial by providing long-term benefits like improved patient outcomes and more efficient resource utilisation. Finally, integration into existing clinical workflows is crucial to minimize the additional time burden of physicians. This would require interoperability with existing clinical systems, user-friendly dashboards for clinicians and, most importantly, (semi-)automated data analysis to reduce the workload for the responding physician.

As the HRV is not only relevant in patients with a history of AF but in various other conditions, implementation of a structured digital health framework may also be beneficial in other cohorts. This may include patients with heart failure. It is known that the HRV is markedly reduced in these patients and an increase in HRV is associated with improvement of the LVEF.[43,44] Therefore, the HRV can be used as an independent predictor for LVEF improvement and, hence, as an early indicator of response to treatment.[44] In patients with chronic heart failure, a reduced short-term HRV has been shown to be a strong predictor for sudden cardiac death.[45] Authors conclude that the HRV may be beneficial to identify patients who would benefit from an implantable cardioverter defibrillator.[45]

However, evaluation of the HRV is not only limited to cardiac diseases but is of relevance in many other disciplines. To name some examples, low HRV was e.g. associated with different psychiatric conditions such as schizophrenia, depression and anxiety.[46–48] In patients who suffered from a stroke, a reduced HV was affiliated with the severity of stroke, as well as with complications and mortality.[49] In patients with neurologic disorders, a reduced HRV was associated with cognitive impairment in patients with dementia. Moreover, in patients with epilepsy, an increase in HRV was seen shortly before the beginning of a seizure[48] and HRV helped to identify patients in pre-ictal states.[48,50]

Further studies are needed to assess the use of the mHealth-based method used in this study in these other patient cohorts.

Implications for future research may include evaluation of the long-term use of such an approach to predict clinical outcomes and therapy success. Moreover, patient centred outcome such as quality of life and treatment adherence should be addressed in future studies to assess and enhance patient satisfaction together with clinical relevance for PPG-based HRV assessment in daily clinical practice. Finally, this structured mHealth approach needs to be assessed in broader patient cohorts, including those with other cardiovascular diseases, comorbidities and non-cardiac conditions.

Limitations

This study has several limitations. The TeleCheck-AF project included patients who were willing and able to use the mHealth tool provided. Therefore, the infrastructure analyzed in this study may only be useful for a selected number of patients. Moreover, as digital literacy might be more common in younger than in older patients, more younger patients than normally present in studies analyzing patients for remote monitoring of AF may have been included in this analysis. As a result, data may not be generalisable for all patients eligible for remote AF management. Nevertheless, previous data have shown that older age is a predictor for optimal adherence and motivation in patients analyzed during TeleCheck-AF.[28]

Patient adherence in this study was high. Nonetheless, as these were only selected measurements three times a day and in case of symptoms, there is a relevant gap of data that may have led to results not displaying the real-world data.

Although several studies have evaluated the use of ultra-short-term HRV recordings, most of them were conducted using ECG recordings. Data validating ultra-short-term HRV recordings using PPG are sparse. Therefore, the results should be interpreted with caution.

Finally, analysis revealed a relevant number of outliers. To ensure adequate calculation and to limit outliers, RR intervals of ectopic beats within a recording were excluded prior to assessment. However, outliers still existed and could have influenced the results.

Conclusions

PPG data recorded within a structured mHealth approach for remote management of AF allow analysis of the ultra-short-term HRV. Next to patients using this mHealth approach for remote management of AF, a structured digital health framework for assessment of the ultra-short-term HRV may also be feasible for management of other health conditions in which the ultra-short-term HRV plays an important role for diagnostics and therapy.

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Author contributions

H.A.K.H. designed the study, collected the data, conducted the analysis, and drafted the manuscript. M.M., D.S., J.M.H., H.G., D.S., A.S., M.H., D.V., T.D.C., S.E., M.N., E.S., R.M.J.v.d.V., D.G., S.-M.C., P.L., R.P., C.H.F., A.S., K.B., J.M.-L., M.G., A.N.L.H., and N.A.H.A.P. were involved in the development of the TeleCheck-AF strategy, collected the data, and contributed to the writing process of the manuscript. D.D. and D.L. contributed equally in designing the study, supervising this project, conducting the analyses, and revising the manuscript. All authors made substantial contributions to the manuscript, revised it critically for important intellectual content, approved the final version, and are accountable for all aspects of the work.

Conflict of interest: H.A.K.H. received modest lecture honorary and/or advisory fee from AstraZeneca, Abbott, Cardiomatics, Medtronic, Zoll and a travel and fellowship grant from Boston Scientific and Abbott. D.D. received modest lecture honorary, travel grants and/or a fellowship grant from Abbott, Astra Zeneca, Biotronik, Boehringer Ingelheim, Boston Scientific, Daiichi Sankyo, Medtronic, Microport, Pfizer, Sanofi, Zoll and serves as an editorial board member for EHJ-DH. D.L. serves as an editorial board member for EHJ-DH. S.E. and T.D.C. are employed by Qompium. J.M.H. received modest lecture honorary and/or advisory fee from Biotronik and serves as an editorial board member for EHJ-DH. D.S. reveived modest lecture honorary and research grant from Abbott, Biosense Webster and Boston-Scientific. M.M. received speaker fees/honoraria from Abbott, Bayer Healthcare, Biosense Webster, Biotronik, Amomed, AOP Orphan, Boston Scientific, Daiichi Sankyo, BMS/Pfizer and research grants from Biosense Webster, Abbott. The rest of the authors declare no conflict of interest.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

References

1. Matusik PS, Matusik PT, Stein PK. Heart rate variability and heart rate patterns measured from wearable and implanted devices in screening for atrial fibrillation: potential clinical and population-wide applications. *Eur Heart J* 2022;**44**:ehac546.

2. Lande MVD, Rajiv R, Koldenhof T, Arita VA, Nguyen L, Weberndorfer V, *et al.* The role of the autonomous nervous system in atrial fibrillation progression. Data from the RACE V study. *Europace* 2022;**24**:euac053.131.
3. Gerstenfeld EP, Mansour M, Whang W, Venkateswaran R, Harding JD, Ellis CR, *et al.* Autonomic effects of pulsed field vs thermal ablation for treating atrial fibrillation subanalysis of ADVENT. *JACC Clin Electrophysiol* 2024;**10**:1634–1644.
4. Linz D, Elliott AD, Hohl M, Malik V, Schotten U, Dobrev D, *et al.* Role of autonomic nervous system in atrial fibrillation. *Int J Cardiol* 2019;**287**:181–188.
5. Plews DJ, Scott B, Altini M, Wood M, Kilding AE, Laursen PB. Comparison of heart-rate-variability recording with smartphone photoplethysmography, polar H7 chest strap, and electrocardiography. *Int J Sports Physiol Perform* 2017;**12**:1324–1328.
6. Altini M, Plews D. What is behind changes in resting heart rate and heart rate variability? A large-scale analysis of longitudinal measurements acquired in free-living. *Sensors* 2021; **21**:7932.
7. Malik M, Bigger JT, Camm AJ, Kleiger RE, Malliani A, Moss AJ, *et al.* Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Eur Heart J* 1996;**17**:354–381.
8. Nussinovitch U, Elishkevitz KP, Katz K, Nussinovitch M, Segev S, Volovitz B, *et al.* Reliability of ultra-short ECG indices for heart rate variability. *Ann Noninvasive Electrocardiol* 2011;**16**:117–122.
9. Munoz ML, van Roon A, Riese H, Thio C, Oostenbroek E, Westrik I, *et al.* Validity of (ultra-)short recordings for heart rate variability measurements. *PLoS One* 2015;**10**: e0138921.
10. Orini M, van Duijvenboden S, Young WJ, Ramírez J, Jones AR, Hughes AD, *et al.* Long-term association of ultra-short heart rate variability with cardiovascular events. *Sci Rep* 2023;**13**:18966.
11. Maqsood R, Schofield S, Bennett AN, Khattab A, Bull AMJ, Fear NT, *et al.* Validity of ultra-short-term heart rate variability derived from femoral arterial pulse waveform in a British military cohort. *Appl Psychophysiol Biofeedback* 2024;**49**:619–627.
12. Betz K, van der Velden R, Gawalko M, Hermans A, Pluymaekers N, Hillmann HAK, *et al.* Interpretation of photoplethysmography: a step-by-step guide. *Herzschrittmacherther Elektrophysiol* 2021;**32**:406–411.
13. Betz K, Linz D, Duncker D, Hillmann HAK. Charakterisierung der vorhofflimmerlast mittels wearables. *Herzschrittmacherther Elektrophysiol* 2024;**35**:111–117.
14. Svennberg E, Tjong F, Goette A, Akoum N, Biase LD, Bordachar P, *et al.* How to use digital devices to detect and manage arrhythmias: an EHRA practical guide. *Europace* 2022;**24**:979–1005.
15. Svennberg E, Caiani EG, Bruining N, Desteghe L, Han JK, Narayan SM, *et al.* The digital journey: 25 years of digital development in electrophysiology from an Europace perspective. *Europace* 2023;**25**:euad176.
16. van der Velden RMJ, Verhaert DVM, Hermans ANL, Duncker D, Manninger M, Betz K, *et al.* The photoplethysmography dictionary: practical guidance on signal interpretation and clinical scenarios from TeleCheck-AF. *Eur Heart J—Digit Health* 2021;**2**:363–373.
17. Hermans ANL, van der Velden RMJ, Gawalko M, Verhaert DVM, Desteghe L, Duncker D, *et al.* On-demand mobile health infrastructures to allow comprehensive remote atrial fibrillation and risk factor management through teleconsultation. *Clin Cardiol* 2020; **43**:1232–1239.
18. Hermans ANL, Gawalko M, Dohmen L, van der Velden RMJ, Betz K, Duncker D, *et al.* Mobile health solutions for atrial fibrillation detection and management: a systematic review. *Clin Res Cardiol* 2022;**111**:479–491.
19. Gawałko M, Betz K, Hendriks V, Hermans ANL, van der Velden RMJ, Manninger M, *et al.* Changes in healthcare utilisation during implementation of remote atrial fibrillation management: TeleCheck-AF project. *Neth Heart J* 2024;**32**:130–139.
20. Betz K, Haren JV, Duncker D, Manninger M, Lemmink J, Linz D. Network analysis of the social media activities around the #TeleCheckAF project. *Eur Heart J—Digit Health* 2023;**5**:97–100.
21. Manninger M, Hermans ANL, Caracioni AA, Rohrer U, Eberl AS, Vernooy K, *et al.* Photoplethysmography-documented atrial fibrillation in the first week after catheter ablation is associated with lower success rates. *Front Cardiovasc Med* 2023;**10**:1199630.
22. Hermans ANL, Gawałko M, Hillmann HAK, Sohaib A, van der Velden RMJ, Betz K, *et al.* Self-reported Mobile health-based risk factor and CHA2DS2-VASc-score assessment in patients with atrial fibrillation: TeleCheck-AF results. *Front Cardiovasc Med* 2022;**8**: 757587.
23. Gawałko M, Duncker D, Manninger M, van der Velden RMJ, Hermans ANL, Verhaert DVM, *et al.* The European TeleCheck-AF project on remote app-based management of atrial fibrillation during the COVID-19 pandemic: centre and patient experiences. *Europace* 2021;**23**:1003–1015.
24. Pluymaekers NAHA, Hermans ANL, van der Velden RMJ, Gawałko M, den Uijl DW, Buskes S, *et al.* Implementation of an on-demand app-based heart rate and rhythm monitoring infrastructure for the management of atrial fibrillation through teleconsultation: TeleCheck-AF. *Europace* 2021;**23**:345–352.
25. Proesmans T, Mortelmans C, Haelst RV, Verbrugge F, Vandervoort P, Vaes B. Mobile phone–based use of the photoplethysmography technique to detect atrial fibrillation in primary care: diagnostic accuracy study of the FibriCheck app. *JMIR mHealth uHealth* 2019;**7**:e12284.
26. Hermans ANL, Isaksen* JL, Gawalko M, Pluymaekers NAHA, van der Velden RMJ, Snippe H, *et al.* Accuracy of continuous photoplethysmography-based 1 min mean heart rate assessment during atrial fibrillation. *Europace* 2023;**25**:835–844.
27. Sassi R, Cerutti S, Lombardi F, Malik M, Huikuri HV, Peng CK, *et al.* Advances in heart rate variability signal analysis: joint position statement by the e-cardiology ESC working group and the European heart rhythm association co-endorsed by the Asia Pacific heart rhythm society. *Europace* 2015;**17**:1341–1353.
28. Gawałko M, Hermans ANL, van der Velden RMJ, Betz K, Verhaert DV, Hillmann HAK, *et al.* Patient motivation and adherence to an on-demand app-based heart rate and rhythm monitoring for atrial fibrillation management: data from the TeleCheck-AF project. *Eur J Cardiovasc Nurs* 2023;**22**:412–424.
29. Gruwez H, Ezzat D, Puyvelde TV, Dhont S, Meekers E, Bruckers L, *et al.* Real-world validation of smartphone-based photoplethysmography for rate and rhythm monitoring in atrial fibrillation. *Europace* 2024;**26**:euae065.
30. Quer G, Gouda P, Galarnyk M, Topol EJ, Steinhubl SR. Inter- and intraindividual variability in daily resting heart rate and its associations with age, sex, sleep, BMI, and time of year: retrospective, longitudinal cohort study of 92,457 adults. *PLoS One* 2020;**15**: e0227709.
31. Santos MAA, Sousa ACS, Reis FP, Santos TR, Lima SO, Barreto-Filho JA. Does the aging process significantly modify the mean heart rate? *Arq Bras Cardiol* 2013;**101**:388–398.
32. Hillmann HAK, Betz K, Linz D, Duncker D. How to: antiarrhythmika in der klinischen anwendung. *Herzschrittmacherther Elektrophysiol* 2023;**34**:82–90.
33. Bellenger CR, Miller DJ, Halson SL, Roach GD, Sargent C. Wrist-based photoplethysmography assessment of heart rate and heart rate variability: validation of WHOOP. *Sensors* 2021;**21**:3571.
34. van Dijk W, Huizink AC, Oosterman M, Lemmers-Jansen ILJ, de Vente W. Validation of photoplethysmography using a Mobile phone application for the assessment of heart rate variability in the context of heart rate variability–biofeedback. *Psychosom Med* 2023;**85**:568–576.
35. Theurl F, Schreinlechner M, Sappler N, Toifl M, Dolejsi T, Hofer F, *et al.* Smartwatch-derived heart rate variability: a head-to-head comparison with the gold standard in cardiovascular disease. *Eur Heart J—Digit Health* 2023;**4**:155–164.
36. Voss A, Schroeder R, Heitmann A, Peters A, Perz S. Short-term heart rate variability—influence of gender and age in healthy subjects. *PLoS One* 2015;**10**:e0118308.
37. Antelmi I, Paula RSD, Shinzato AR, Peres CA, Mansur AJ, Grupi CJ. Influence of age, gender, body mass index, and functional capacity on heart rate variability in a cohort of subjects without heart disease. *Am J Cardiol* 2004;**93**:381–385.
38. Tegegne BS, Man T, van Roon AM, Snieder H, Riese H. Reference values of heart rate variability from 10-second resting electrocardiograms: the lifelines cohort study. *Eur J Prev Cardiol* 2020;**27**:2191–2194.
39. Abhishekh HA, Nisarga P, Kisan R, Meghana A, Chandran S, Raju T, *et al.* Influence of age and gender on autonomic regulation of heart. *J Clin Monit Comput* 2013;**27**:259–264.
40. Andrade JG, Bennett RG, Deyell MW, Bennett MT, Phulka J, Hawkins NM, *et al.* Long-term differences in autonomic alterations after cryoballoon vs radiofrequency atrial fibrillation ablation. *JACC Clin Electrophysiol* 2025;**11**:19–29.
41. Seaborn GEJ, Todd K, Michael KA, Baranchuk A, Abdollah H, Simpson CS, *et al.* Heart rate variability and procedural outcome in catheter ablation for atrial fibrillation. *Ann Noninvasive Electrocardiol* 2014;**19**:23–33.
42. Saleem S, Khandoker AH, Alkhodari M, Hadjileontiadis LJ, Jelinek HF. Investigating the effects of beta-blockers on circadian heart rhythm using heart rate variability in ischemic heart disease with preserved ejection fraction. *Sci Rep* 2023;**13**:5828.
43. Shanks J, Abukar Y, Lever NA, Pachen M, LeGrice IJ, Crossman DJ, *et al.* Reverse remodelling chronic heart failure by reinstating heart rate variability. *Basic Res Cardiol* 2022;**117**:4.
44. Hillmann HAK, Hohmann S, Mueller-Leisse J, Zormpas C, Eiringhaus J, Bauersachs J, *et al.* Feasibility and first results of heart failure monitoring using the wearable cardioverter–defibrillator in newly diagnosed heart failure with reduced ejection fraction. *Sensors* 2021;**21**:7798.
45. Rovere MTL, Pinna GD, Maestri R, Mortara A, Capomolla S, Febo O, *et al.* Short-term heart rate variability strongly predicts sudden cardiac death in chronic heart failure patients. *Circulation* 2003;**107**:565–570.
46. Ramesh A, Nayak T, Beestrum M, Quer G, Pandit JA. Heart rate variability in psychiatric disorders: a systematic review. *Neuropsychiatr Dis Treat* 2023;**19**:2217–2239.
47. Costa T, Hill S, Taylor A, Green A, Black F, Watson S. Autonomic dysregulation in individuals with psychiatric disorders and healthy controls: results from the CAP-MEM observational cohort. *BJPsych Open* 2022;**8**:S48–S49.
48. Arakaki X, Arechavala RJ, Choy EH, Bautista J, Bliss B, Molloy C, *et al.* The connection between heart rate variability (HRV), neurological health, and cognition: a literature review. *Front Neurosci* 2023;**17**:1055445.
49. Yperzeele L, van Hooff RJ, Nagels G, Smedt AD, Keyser JD, Brouns R. Heart rate variability and baroreceptor sensitivity in acute stroke: a systematic review. *Int J Stroke* 2015; **10**:796–800.
50. Billeci L, Marino D, Insana L, Vatti G, Varanini M. Patient-specific seizure prediction based on heart rate variability and recurrence quantification analysis. *PLoS One* 2018; **13**:e0204339.