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SHORT REPORT

Antiarrhythmic drug loading at home using remote monitoring: a virtual feasibility study during COVID-19 social distancing

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The epidemiological necessity for distancing during the COVID-19 pandemic has resulted in postponement of non-emergent hospitalizations and increase use of telemedicine. The feasibility of virtual antiarrhythmic drug (AAD) loading specifically with digital QTc electrocardiographic monitoring (EM) in conjunction with telemedicine video visits is not well established. We tested the hypothesis that existing digital health technologies and virtual communication platforms could provide EM and support medically guided AAD loading for patients with symptomatic tachyarrhythmia in the ambulatory setting, while reducing physical contact between patient and healthcare system. A prospective pilot, case series was approved by the institutional ethics committee, entailing three subjects with symptomatic arrhythmia during the COVID-19 pandemic who were enrolled for virtual AAD loading at home. Clinicians met with participants twice daily via video visits conducted after QTc analysis (Kardia 6L mobile sensor) and telemetry review (Mobile Cardiac Outpatient Telemetry of silent arrhythmias). Participants received direct instruction to either terminate the study or proceed with the next single dose of AAD. All participants completed contactless loading of five AAD doses, without untoward event. Scheduled video visits allowed dialogue and participant counselling where decision-making was guided by remote review of EM. Participant adherence with transmissions and scheduled visits was 98.3%; a single electrocardiogram was delayed beyond the 2 hours of post-dose schedule. This virtual approach reduced overall expenditures based on retrospective comparison with previous AAD load hospitalizations. We found that a 'virtual hospitalization' for AAD loading with remote EM and twice-daily virtual rounding is feasible using existing digital health technologies.

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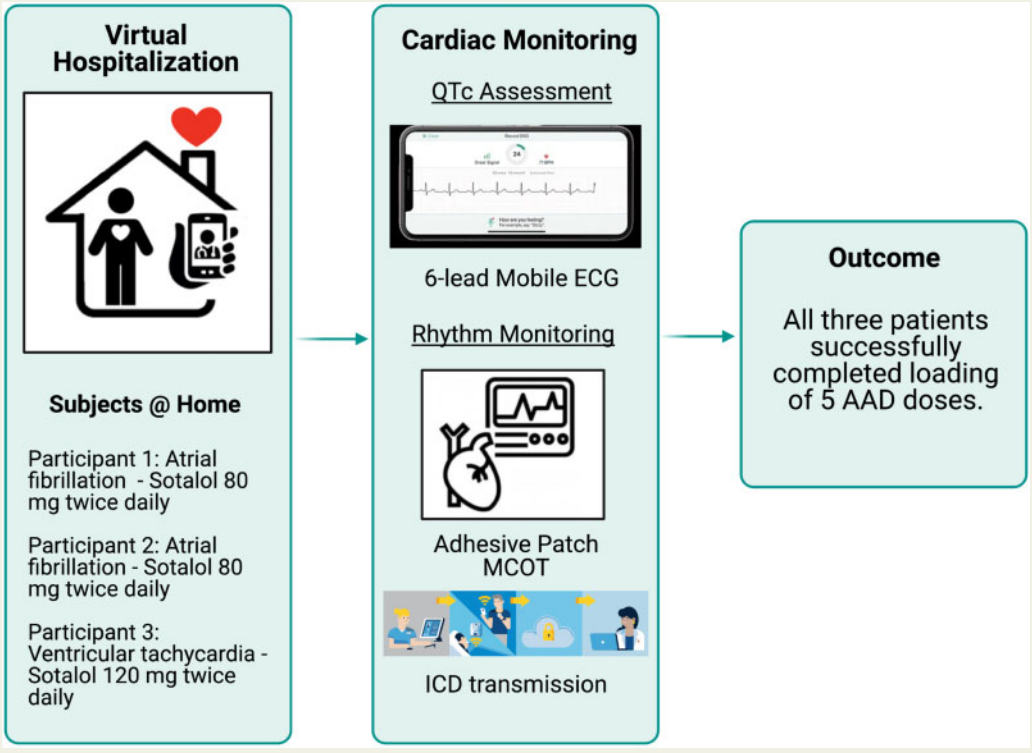
Graphical Abstract



Keywords Telemedicine • Antiarrhythmic loading • Arrhythmia • Digital health

Introduction

Guideline-directed management of symptomatic tachyarrhythmia includes strategic rhythm control. Outpatient initiation of the antiarrhythmic drug (AAD) Sotalol is permitted on an individualized basis,[1,2] though clinicians often pursue Sotalol loading and dose escalation with hospitalization to enable electrocardiographic monitoring (EM) for QT interval prolongation or ventricular arrhythmias. The epidemiological necessity for distancing during the COVID-19 pandemic has resulted in postponement of non-emergent hospitalizations, as well as increase use of telemedicine by healthcare systems to care for its patients.[3] While trans-telephonic electrocardiogram (ECG) has been used in the past to help monitor effectiveness of AAD, the feasibility of a 'virtual hospitalization' for AAD loading specifically with remote QTc monitoring in conjunction with telemedicine video visits has not been well established. We tested the hypothesis that existing digital health technologies and virtual communication platforms could provide EM and support medically guided AAD loading for patients with symptomatic tachyarrhythmia in the ambulatory setting.

Methods

We completed a prospective pilot study approved by the institutional ethics committee, entailing three subjects during the COVID-19 pandemic who were enrolled for virtual AAD loading at home following informed consent. We included individuals with symptomatic, paroxysmal atrial or ventricular arrhythmias and indication for rhythm control based on guidelines.[1] An existing implantable cardioverter-defibrillator (ICD) was mandatory for protection against drug-induced arrhythmia. Electrocardiograms generated with a Kardia 6L mobile sensor (AliveCor, Mountain View, CA, USA) were used for QT interval monitoring and an interpretable baseline was necessary prior to the initial AAD dose; the longest manual measurement from any of six leads was used to guide decision-making. Remote transmission from existing ICD (Carelink portal, Medtronic, Dublin, Ireland) and adhesive patch Mobile Cardiac Outpatient Telemetry (MCOT; Zio AT, iRhythm portal, San Francisco, CA, USA) were used to monitor arrhythmias. Electrocardiographic monitoring transmissions were reviewed at baseline and twice daily at specified times (*Figure 1*). Clinicians met with participants virtually twice daily via telemedicine video visits conducted after telemetry review and QTc analysis; participants received direct instruction to either terminate the study or proceed with the next single dose of AAD. The study was

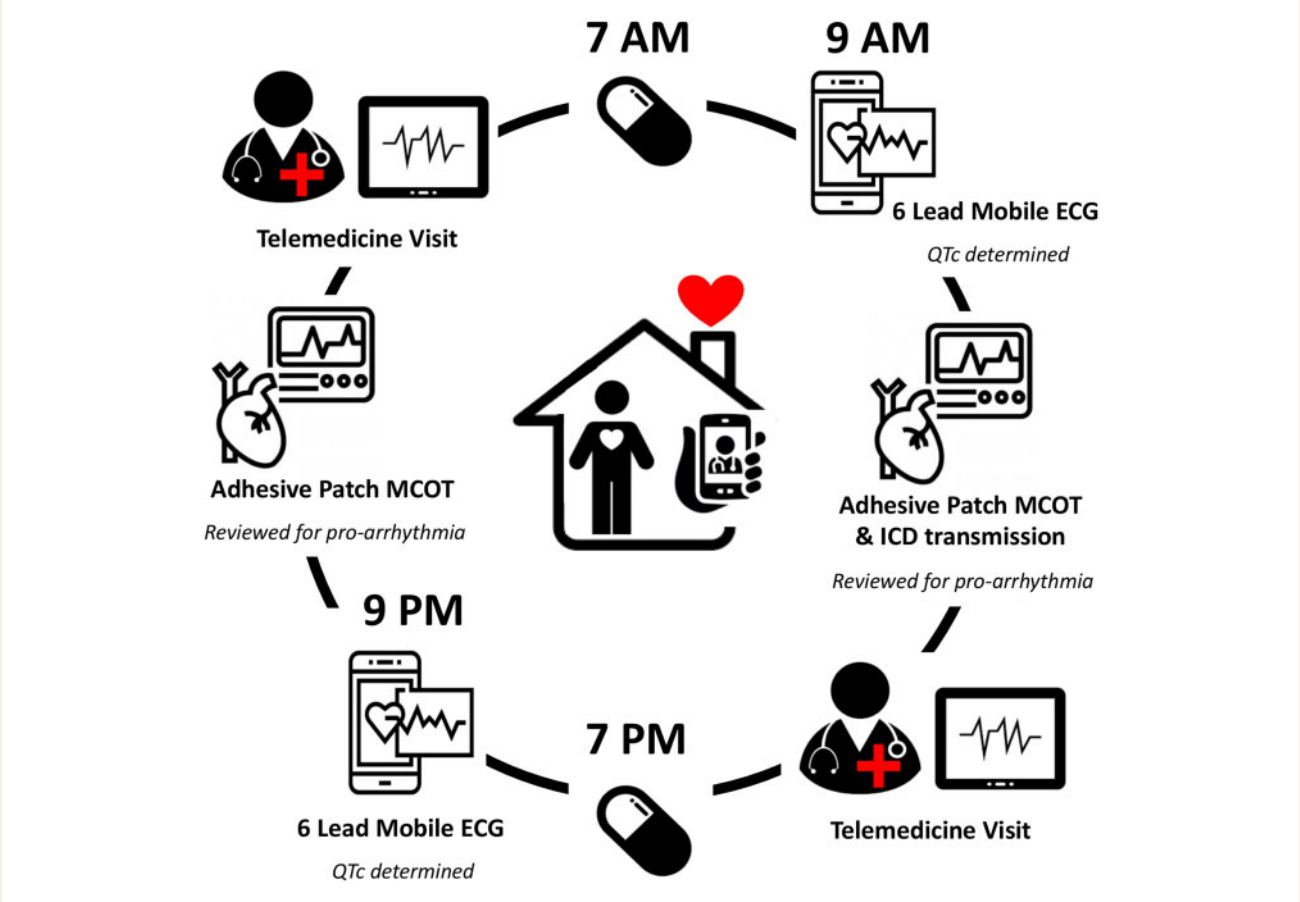


Figure 1 Virtual hospitalization for antiarrhythmic drug loading. Scheduled telemedicine visits and remote electrocardiographic monitoring allowed clinicians to virtually counsel participants at home through a five-dose antiarrhythmic drug load to prevent recurrence of symptomatic arrhythmia. ECG, electrocardiogram; ICD, implantable cardioverter-defibrillator; MCOT, mobile cardiac outpatient telemetry; QTc, corrected QT interval.

completed when a participant had taken five doses of AAD or if manifestations of pro-arrhythmia were identified on EM. Upon completion, encounters were reviewed for overall costs and participants were asked to complete a questionnaire surveying comfort using the Kardia 6L device, motivation for participation, and open-ended feedback regarding the delivery of telemedicine care and overall experience during the study.

Results

Following a single outpatient phlebotomy and 12-lead ECG, the remainder of the study was completed remotely and in the absence of in-person encounters. Participant #1 (35-year-old woman, hypertrophic cardiomyopathy, ejection fraction 35%, and symptomatic, paroxysmal atrial fibrillation) completed loading of Sotalol 80 mg every 12 hours. Participant #2 (40-year-old male with alpha-actinin-2 deletion, history of ventricular fibrillation, sinus bradycardia, and symptomatic, paroxysmal atrial fibrillation) completed loading of Sotalol 80 mg every 12 hours. Participant #3 (60-year-old male with hypertrophic cardiomyopathy and symptomatic ventricular tachycardia episodes refractory to Sotalol 80 mg twice daily) completed dose escalation to Sotalol 120 mg every 12 hours.

Per participant, there were: six Kardia ECGs, three ICD interrogations, five MCOT reviews, and six telemedicine visits. Participant compliance and adherence with scheduled transmissions and visits was 98.3%; a single ECG was delayed beyond the 2 hour post-dose timetable prior to the implementation of reminder notifications. 94.4% (17/18) of Kardia transmissions were interpretable for QT analysis (all sinus) without significant artefact; a single uninterpretable ECG (motion artefact) required an additional phone call to advise repeat transmission. All participants completed contactless loading of five AAD doses without development of QTc prolongation or arrhythmia. Virtual AAD loading added personnel requirements (to instruct participants through the protocol, co-ordinate EM, review EM), telemedicine visits, and product costs for the Kardia 6L ($149) sensor and MCOT ($695 out-of-pocket price), but it eliminated inpatient costs (facility fees, pharmacy service, nursing costs, environmental services, and technical fees).

Relief from 'avoiding contact' with the healthcare system during the pandemic 'while continuing to receive care' was the strongest motivator for participation. Initially, participants described less than maximal (≤7/10) perceived ease using the Kardia 6L, however, by the completion of the study each reported the highest level of comfort operating

Table 1 Comparison: QTc analysed by Kardia 6L device and 12-lead electrocardiogram

	Pre-Sotalol loading			Post-Sotalol loading		
	Pre 12L ECG (ms)	Pre *Kardia* 6L (ms)	Δ (ms)	Post 12L ECG (ms)	Post *Kardia* 6L (ms)	Δ (ms)
Participant 1	420	423	+3	439	430	-9
Participant 2	419	417	-2	415	421	+6
Participant 3	422	430	+8	459	451	-8

The Kardia 6L device was used to generate digital 2 hour post-dose electrograms permitting remote QTc monitoring during virtual hospitalization for AAD loading; initial and final Kardia ECGs were compared with 12-lead ECGs, performed pre- and post-study completion, with agreement (within 10 ms).
6L, 6-lead; 12L, 12-lead; AAD, antiarrhythmic drug; ECG, electrocardiogram; ms, milliseconds; QTc, corrected QT interval

the mobile sensor and transmitting ECGs. All three participants ranked overall satisfaction with their care at the highest rating (10/10), driven by 'convenience', 'effective communication', and symptom relief. Beyond COVID-19 concerns, participant #1 offered a major perceived benefit of avoiding separation from her child, and participant #2, avoiding missing essential work. If a future AAD load was recommended, unanimously all participants favoured virtual loading.

Discussion

We demonstrate a potential contactless care pathway to virtually direct the loading of AAD for patients with symptomatic atrial and ventricular arrhythmia and existing ICD, applying (i) serial digital QTc, (ii) remote patch telemetry, and (iii) telemedicine visits. Scheduled visits by video allowed dialogue and participant counselling, akin to inpatient rounding, where decision-making was guided by remote review of EM, including examination of baseline and 2 hour post-dose ECGs. The Kardia 6L device received FDA clearance for QT interpretation through demonstrated accuracy compared with 12-lead ECG[4,5] and was utilized in our study to remotely monitor for QTc prolongation while administering Sotalol at home. Although select MCOT devices have received similar approval from the FDA, we used the Zio AT monitor strictly as telemetry. Initial and final Kardia 6L ECGs were compared for QT analysis to 12-lead ECGs performed pre- and post-study completion, respectively, *Table 1*; measurements in our study were consistent with previous reports establishing agreement between 12-lead ECG and Kardia 6L.

This virtual approach appears to reduce overall expenditures based on retrospective comparison with previous AAD load hospitalizations[6,7] (Supplementary material online, *Table S1*), though economic benefit should be validated in a larger study. It ought to be highlighted, amongst only three participants the adherence to the EM transmission schedule was near but not perfect, and use of automated reminder notifications may be beneficial to both patients and clinicians[8]; also, motion artefact can limit manual analysis of the Kardia 6L ECG which may be corrected by trans-telephonic instruction and repeat transmission. This pilot study, burgeoned from epidemiological necessity for distancing during the COVID-19 pandemic, is a proof-of-concept for expansion of telemedicine including remote AAD loading and ultimately highlights the potential for a larger trial to (i) better assess the safety of virtual AAD loading and (ii) to investigate an expanded role for wearable defibrillators.

In conclusion, we found that a 'virtual hospitalization' for AAD loading with remote EM and twice-daily virtual rounding is feasible using existing digital health technologies.

Supplementary material

Supplementary material is available at *European Heart Journal – Digital Health* online.

Conflict of interest: Dr M.V.P. is a consultant for Apple, Inc., AltaThera, and Boehringer; and receives research grants from Apple Inc. and the National Heart Lung Blood Institute. All others involved have no conflicting relationships to the contents of this paper to disclose.

Data availability

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

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