Journal of Electrocardiology 55 (2019) 87–90

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

Clinical stage of acquired immunodeficiency syndrome in HIV-positive patients impacts the quality of the touch ECG recordings

Mikolaj Kaminski [a], Piotr Prymas [a], Anna Konobrodzka [a], Piotr Filberek [a], Greta Sibrecht [a], Wojciech Sierocki [a], Zofia Osinska [a], Andrzej Wykretowicz, MD, PhD [a], Suave Lobodzinski, MD, PhD [b], Przemyslaw Guzik, MD, PhD [a,*]

[a] Department of Cardiology-Intensive Therapy, Poznan University of Medical Sciences, 49 Przybyszewskiego, 60-355 Poznan, Poland
[b] California State University, Department of Electrical and Biomedical Engineering, 1250 Bellflower Blvd, Long Beach, CA 90840, United States of America

ARTICLE INFO

Keywords:
Acquired immunodeficiency syndrome
ECG quality
Human immunodeficiency virus
Mobile health
Touch ECG

ABSTRACT

Introduction: HIV patients are at higher risk for cardiovascular disease and cardiac arrhythmias which can be recorded by a handheld single lead ECG device. Quality of ECG depends on the skin condition, which worsens with the progression of HIV infection.
Objective: To study the quality of the ECG signal acquired by a mobile ECG device in patients with different clinical stages of human immunodeficiency virus (HIV) infection.
Patients and methods: We studied the quality of 30-second single lead ECGs obtained by a handheld ECG device (Kardia; AliveCor Inc., San Francisco, USA) in 263 Kenyan adults (203 women) in various stages of HIV. The recordings were made during routine check-ups at the outpatient clinics. ECG quality was categorized as readable (not interfering with clinical interpretation) or unreadable (impossible clinical interpretation). The progression of the HIV infection was estimated using the World Health Organization AIDS Clinical Staging (WACS) scale, ranging from stage 1 (asymptomatic generalized lymphadenopathy) to stage 4 (wasting syndrome and Kaposi sarcoma).
Results: The median age of patients was 46 (39–53) years. ECG was readable in 201 patients (76.4%) and unreadable in 62 (23.6%). The WACS score > 1 was associated with 3.95 odds ratio (95% confidence interval 2.14–7.29; $p < 0.0001$) for the acquiring an unreadable ECG (univariate logistic regression adjusted to age, sex, body mass index and time since HIV).
Conclusions: ECG quality recorded by a touch ECG device worsens with advancing HIV infection. For this reason, the accuracy of arrhythmia diagnosis by mobile ECG appears to be limited in HIV patients.

Introduction

Human immunodeficiency virus (HIV) causes the acquired immunodeficiency syndrome (AIDS), a progressively destructive process complicated by malnutrition, waste, development of other infectious and neoplastic diseases, and shorter life duration [1,2]. HIV patients have typical, not related to AIDS, risk factors for the cardiovascular (CV) disease (e.g., diabetes, obesity or smoking) [3]. However, the presence of AIDS or its pharmacological treatment adds new CV risk factors such as proatherogenic dyslipidemia, chronic inflammation or increased activity of the renin-angiotensin-aldosterone system [4]. Consequently, hypertension, premature ischemic heart disease or atrial fibrillation (AF) are frequent in HIV patients.

The AF risk increases with the HIV load and AIDS duration [4]. To avoid clinical complication of untreated AF (e.g., ischemic stroke), HIV patients should regularly have their ECG checked. Still, the acquisition of standard 12 lead ECG is unavailable for many patients living in places with limited resources healthcare system. For them, using a mobile ECG device seems a practical solution [5].

There is an increasing number of studies showing the clinical utility of mobile ECG technologies, including handheld devices. Kardia (AliveCor Inc., San Francisco, USA) is an example of the handheld touch ECG device capable of recording a single lead ECG and transmitting it to a smartphone. In contrast to the standard 12 lead ECG recorders that use patient cables and adhesive electrodes, Kardia requires minimal training and may be readily used anytime and anywhere, both by medical professionals, patients themselves and by their family members. This device received the Food and Drug Administration clearance for the diagnosis of AF and has been used in many clinical studies [5–11]. It is possible to acquire multiple non-standard ECG leads with Kardia by holding one metal sensor in the right hand and

* Corresponding author at: Department of Cardiology-Intensive Therapy, Poznan University of Medical Sciences, 49 Przybyszewskiego, 60-355 Poznan, Poland.
E-mail address: pguzik@ptkardio.pl (P. Guzik).

https://doi.org/10.1016/j.jelectrocard.2019.05.011
0022-0736/

touching different body locations with another sensor [10]. Due to a poor skin-sensor interface, the quality of the ECG signal is sometimes far from optimal and may negatively impact proper ECG interpretation. The quality of the ECG depends on many factors like sensor pads cleanness, air humidity and temperature and, most importantly, skin conductive properties which frequently change in the course of HIV infection due to xerodermic state and dermatoses [12].

In this study, we investigated the quality of the ECG signal acquired by a touch ECG device (Kardia) in patients with different clinical stages of established HIV infection at two outpatient clinics in Kenya.

Material and methods

Study design

In this prospective study, 30-second ECGs were recorded by Kardia in 263 adult HIV positive patients at the outpatient clinics of the Mission Hospitals in Muthale and Mutomo in Kitui County, Kenya during routine check-ups. No exclusion criteria were applied. The ECGs were collected between August and September of 2016. The local Bioethical Committee at the Strathmore University in Nairobi, Kenya approved the study (permission reference number SU-IRB 0073/16), and each participant gave informed consent. All study data were anonymized.

Clinical staging of established HIV infection

To assess the progression of the HIV infection, the World Health Organization recommends using the AIDS Clinical Staging (WACS) [1] scale, which is a four-stage system designed specifically for the developing countries with limited access to CD4+ cell counters. The WACS assessment starts from the asymptomatic HIV positive patients with generalized lymphadenopathy (stage 1), through the presence of unexplained moderate to severe weight loss, mild to severe bacterial, viral and fungal infections (stages 2 and 3), and ending with the development of HIV-wasting syndrome and Kaposi sarcoma (stage 4). The clinical staging of HIV patients enrolled in this study was regularly assessed by the medical professionals working in both outpatient clinics.

Recording of ECG

All ECGs were collected by trained medical students who voluntarily participated in the program "Treating with a mission" (leczymyzmisja.pl/en/) under the auspices of the Poznan University of Medical Sciences, Poznan, Poland.

All ECGs (standard lead I) were acquired from patients sitting upright on a chair. Each patient was holding the Kardia's sensors in the fingers of the right and left hands (attempt 1). The ECG signal was transferred to an iOS or Android smartphone for instant visual inspection and assessment of the ECG quality. For completely unreadable ECGs, two additional attempts were made. With a patient still holding one of the Kardia's sensors in the right hand, the second sensor touched the chest area corresponding to V1 location (attempt 2), and if this approach failed, then the region corresponding to V5 location (attempt 3). If all three attempts failed no other recording was acquired. During each attempt, Kardia's sensors touched the finger and chest areas with no visible pathological skin changes. Each recorded ECG was presented to a patient, a medical professional taking care of the patient on the site, and stored in the smartphone's internal memory for further detailed analysis by a cardiologist.

Data analysis

Kardia allows saving the recorded ECG as a pdf file and this format substantially limits the detailed measurement of the signal and noise amplitudes. In consequence, the ECG quality was analyzed only visually and, based on this approach, divided into two categories – readable and unreadable (Table 1). The readable category (score 0) contained ECG with at least good quality or some technical artifacts which, however, did not interfere with the clinical interpretation. The unreadable recording (score 1) contained ECG with excessive noise and artifacts making its interpretation either uncertain or utterly impossible.

Only ECGs with a readable signal underwent further evaluation for the following findings: different types of supraventricular (premature narrow-QRS preceded or not by a visible P wave) and ventricular arrhythmias (premature wide-QRS unpreceded by any P wave), including AF, atrioventricular conduction abnormalities, and the visually determined ECG signal quality.

Statistical analysis

Continuous data are shown as median and the 25th, and 75th percentiles. The comparisons of continuous data between the groups of readable vs. unreadable ECGs were made using the Mann-Whitney *U* test. The dichotomized data are shown as numbers and percentages. The logistic regression analysis (unadjusted or adjusted to the patient's essential clinical characteristics) quantified the odds ratio (OR) with 95% confidence interval (CI) for the presence of the unreadable ECG in different clinical stages of HIV infection. Statistical data analysis was performed using MedCalc Statistical Software version 18.10 (MedCalc Software bvba, Ostend, Belgium). Results of statistical comparisons were considered statistically significant if p-value < 0.05.

Results

The median age of all patients was 46 (39–53) years, 203 were women (77%). There were 181 (68.8%) of asymptomatic HIV positive patients in WACS = 1, and 82 (31.2%) symptomatic patients with WACS > 1. For all patients, the median time since HIV diagnosis was 7 (5–9) years, WACS score 1 (1–2), body mass index 21.1 (19.1–24.3) kg/m^2 and heart rate 76 (68–86) beats/min.

The ECGs were readable in 201 patients (76.4%) and unreadable in 62 (23.6%), including 58 (22.1%) individuals with an uncertain interpretation and 4 (1.5%) subjects with the worst quality making the ECG interpretation impossible. Except for the clinical staging of HIV infection, there were no other significant clinical differences between patients with readable and unreadable ECG (Table 2). ECG examples from patients from each WACS group are shown in the Supplementary material as Fig. 1.

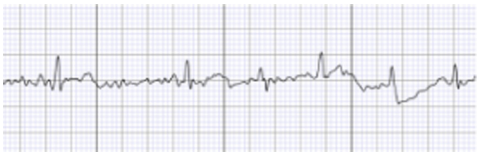
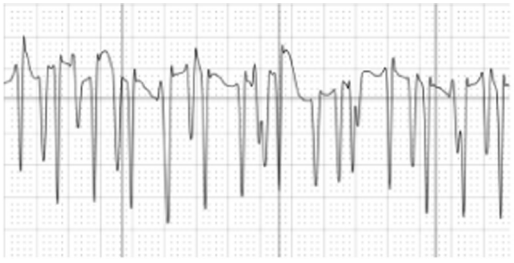
Seventeen (8.5%) out of 201 patients with a readable ECG presented resting tachycardia whereas 19 (9.5%) bradycardia. Single supraventricular and ventricular premature beats were found in 2 (1%) and 10 (5%) patients, respectively, and the second-degree atrioventricular block (Mobitz 2 type) in 1 patient (0.5%). No other arrhythmias, including AF, were found in the studied group.

The number of patients with unreadable ECGs was as follows: 27 (14.9%) out of 181 in the WACS 1 grade, 9 (40.9%) out of 22 in the WACS 2 grade, 21 (42.0%) out of 50 in the WACS 3, and 5 (50.0%) out of 10 in the WACS 4.

The univariate logistic regression showed that an increase of the WACS score by 1 was associated with a significantly higher risk for acquiring an unreadable ECG by Kardia device both in the analysis unadjusted (OR: 1.96; 95% CI: 1.46–2.62; $p < 0.0001$) and adjusted (OR: 1.87; 95% CI 1.38–2.53; $p < 0.0001$) to patient's' age, sex, body mass index and time since HIV diagnosis.

Since there was a significant difference in the rate of an unreadable ECG between subjects with the WACS equal 1 and WACS over 1, we repeated logistic regression analysis. Compared with patients with WACS = 1, those with WACS > 1 had a four-fold higher risk of getting an unreadable ECG by Kardia in the unadjusted (OR: 4.25; 95% CI: 2.33–7.73; $p < 0.0001$) and adjusted (OR: 3.95; 95% CI 2.14–7.29; $p < 0.0001$) analysis.

Table 1
The quality score of ECG recorded by Kardia according to the number of artifacts and the feasibility of clinical interpretation.

Quality score	Signal artifacts	ECG example
0	None or some but not interfering with the clinical interpretation	
1	Many with uncertain interpretation	
1	Not recognizable ECG, impossible clinical interpretation	

Discussion

In this study, we have found that a 30-second ECG acquired by a touch ECG device may be, on average, unreadable in >20% of HIV patients. This rate increases to 40–50% with the progression of clinical staging of HIV infection, regardless of patients' age, gender, duration of HIV infection and body mass index. We were surprised to find out, that it is four-fold more probable to record an unreadable ECG by Kardia in patients with the more advanced stage of HIV infection, i.e., WACS over 1.

Stage 1 by WACS is characterized by no HIV-related symptoms and no signs on physical examination, except the persistent generalized lymphadenopathy. From the WACS grade, 2 starts an unexplained weight loss from moderate to severe, until the development of the wasting syndrome. It is accompanied by various recurrent or permanent infections, chronic inflammation, and more complex pharmacotherapy. In other words, HIV patients with WACS over 1 are considered as a more advanced stage of the disease [13]. Comparing to healthy people, HIV patients have higher resting energy expenditure and substantial metabolic disarrangements like hyponatremia and hyperkalemia [14–16]. Drying of the skin, known as the xerodermic state [12], is observed in HIV patients with lower CD4 count and as a side effect of applied pharmacotherapy [17–19].

A significant association between skin diseases and the WACS has been reported in HIV patients and skin involvement by infection, and chronic inflammation may be present in up to 90% of them [17,18]. HIV patients present more substantial transepidermal water loss than healthy people [19]. We hypothesize that these factors might alter the skin electrical conductivity and cause an increase in skin-electrode impedance and in-turn a reduction in the ECG quality [20,21].

Limitations of the study.

We decided to make no more than three attempts to record the single lead 30-second ECG by Kardia for practical reasons since the clinics had limited time slots available for check-up examinations. Further, the only visual inspection could be used for the quality assessment of the recorded ECG since the Kardia stores and exports all ECGs only in pdf and no other usable format. However, such simple approach appeared to be effective and practical. Not applying ECG gel or saline solution to the patient's fingers before ECG recording may be another limitation. We have carefully followed Kardia's instructions on how to work with the device: “do not use the sensor on a portion of the body with too much body fat, body hair or dehydrated skin, a successful recording may not be possible”. There is, however, no recommendation that in case of poor signal quality the patient's skin should be moisturized by ionically-active media [22]. Further, the only visual inspection could be used for the quality assessment of the recorded ECG since we had been working with ECGs recorded only in pdf format. However, such a simply approach appeared to be effective and practical. Finally, our study was observational and not explanatory, and altogether the obtained results should be treated as preliminary. Therefore, there may be

Table 2
Comparison of clinical characteristics of patients with a readable and unreadable ECG acquired by the Kardia device.

	Patients with a readable ECG ($N = 201$)		Patients with an unreadable ECG ($N = 62$)		*P* value
	Median	IQR	Median	IQR	
Age [years]	46	39–52	47.5	41–54	*0.17*
Time since HIV diagnosis [years]	7	6–9	7	4–8.5	*0.25*
Body mass index [kg/m^2]	21.4	19.2–24.4	20.4	18.9–24.1	*0.33*
Pulse Rate [beats/min]	76	68–86	79	68–89	*0.32*
WHO AIDS Clinical Stage []	1	1	2	1–3	*<0.0001*

other causes of higher rates of unreadable ECGs by Kardia in HIV patients unknown to the research team.

In summary, the percentage of unreadable ECGs recorded by Kardia ranged from 15 to 50% in HIV patients, depending on the stage of HIV infection. Patients with more advanced HIV have a four-fold higher risk of an unreadable ECG than subjects in the early or benign stage. It appears that handheld devices with dry metal electrodes may not recognize AF and thus underestimate the AF burden in HIV patients. Finally, although not tested in this study, we propose to moisturize the fingers' skin before recording by Kardia. Preliminary results of this study will serve as a starting point to a comprehensive prospective ECG study of the HIV patients.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jelectrocard.2019.05.011.

Funding

This work was supported by an unrestricted Student's Grant of the Student Scientific Society, Poznan University of Medical Sciences, Poznan, Poland [165/2016].

Declaration of Competing Interest

Dr. Suave Lobodzinski is a consultant to Apple Corporation and AliveCor Inc.

No other authors declared any potential conflict of interests.

Acknowledgment

We are grateful to all medical personnel from the outpatient clinics of the Mission Hospitals in Muthale and Mutomo in Kitui County, Kenya who allowed us to perform a basic clinical examination and collect ECGs by Kardia from patients visiting their clinics.

References

[1] WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva: World Health Organization; 2007https://apps.who.int/iris/bitstream/handle/10665/43699/9789241595629_eng.pdf.
[2] 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults, MMWR Recomm Rep 1992;41:1–19.
[3] Seyler L, Lacor P, Allard SD. Current challenges in the treatment of HIV. Pol Arch Intern Med 2018;128:609–16.
[4] Hsu JC, Li Y, Marcus GM, Hsue PY, Scherzer R, Grunfeld C, et al. Atrial fibrillation and atrial flutter in human immunodeficiency virus-infected persons: incidence, risk factors, and association with markers of HIV disease severity. J Am Coll Cardiol 2013;61:2288–95.
[5] Evans GF, Shirk A, Muturi P, Soliman EZ. Feasibility of using Mobile ECG recording technology to detect atrial fibrillation in low-resource settings. Glob Heart 2017;12:285–9.
[6] Lowres N, Neubeck L, Salkeld G, Krass I, McLachlan AJ, Redfern J, et al. Feasibility and cost-effectiveness of stroke prevention through community screening for atrial fibrillation using iPhone ECG in pharmacies. The SEARCH-AF study Thromb Haemost 2014;111:1167–76.
[7] Chan N-Y, Choy C-C. Screening for atrial fibrillation in 13 122 Hong Kong citizens with smartphone electrocardiogram. Heart 2017;103:24–31.
[8] Orchard J, Lowres N, Freedman SB, Ladak L, Lee W, Zwar N, et al. Screening for atrial fibrillation during influenza vaccinations by primary care nurses using a smartphone electrocardiograph (iECG): a feasibility study. Eur J Prev Cardiol 2016;23:13–20.
[9] Soni A, Earon A, Handorf A, Fahey N, Talati K, Bostrom J, et al. High burden of unrecognized atrial fibrillation in rural India: an innovative community-based cross-sectional screening program. JMIR Public Health Surveill 2016;2:e159.
[10] Baquero GA, Banchs JE, Ahmed S, Naccarelli GV, Luck JC. Surface 12 lead electrocardiogram recordings using smartphone technology. J Electrocardiol 2015;48:1–7.
[11] Guzik P, Malik M. ECG by mobile technologies. J Electrocardiol 2016;49:894–901.
[12] Ramos-e-Silva M, de-Moura-Castro Jacques C. Epidermal barrier function and systemic diseases. Clin Dermatol 2012;30:277–9.
[13] Bloomfield GS, Hogan JW, Keter A, Holland TL, Sang E, Kimaiyo S, et al. Blood pressure level impacts risk of death among HIV seropositive adults in Kenya: a retrospective analysis of electronic health records. BMC Infect Dis 2014;14:284.
[14] Kosmiski L. Energy expenditure in HIV infection. Am J Clin Nutr 2011;94:1677S–82S.
[15] Glassock RJ, Cohen AH, Danovitch G, Parsa KP. Human immunodeficiency virus (HIV) infection and the kidney. Ann Intern Med 1990;112:35–49.
[16] Musso CG, Belloso WH, Glassock RJ. Water, electrolytes, and acid-base alterations in human immunodeficiency virus infected patients. World J Nephrol 2016;5:33–42.
[17] Oninla OA. Mucocutaneous manifestations of HIV and the correlation with WHO clinical staging in a tertiary hospital in Nigeria. AIDS Res Treat 2014:1–6.
[18] Hu J, McKoy K, Papier A, Klaus S, Ryan T, Grossman H, et al. Dermatology and HIV/AIDS in Africa. J Global Infect Dis 2011;3:275–80.
[19] Gunathilake R, Schmuth M, Scharschmidt TC, Gruber R, Grabher D, Leslie KS, et al. Epidermal barrier dysfunction in non-atopic HIV: evidence for an “inside-to-outside” pathogenesis. J Invest Dermatol 2010;130:1185–8.
[20] Vargas Luna JL, Krenn M, Cortés Ramírez JA, Mayr W. Dynamic impedance model of the skin-electrode interface for transcutaneous electrical stimulation. PLoS One 2015;10:e0125609.
[21] Lu F, Wang C, Zhao R, Du L, Fang Z, Guo X, et al. Review of stratum corneum impedance measurement in non-invasive penetration application. Biosensors (Basel) 2018;8.
[22] User manual for KardiaTM by AliveCor®. Internet. Available from https://www.alivecor.com/previous-labeling/kardia/08LB12.3.pdf; 2011.