Review Article

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Minimal or No Touch Electrocardiography Recording and Remote Heart Rhythm Monitoring during COVID-19 Pandemic Era

Alexander Edo Tondas[1,2], Rolando Agustian[2], Moza Guyanto[2]

Abstract

At the end of year 2019, the world faced an outbreak of a highly virulent novel Coronavirus disease (COVID-19), which changed the way physicians, including cardiologists, do their routine clinical practice. As distance limitation and efficient use of personal protective devices must be employed to prevent the pandemic spreading, even simple electrocardiogram (ECG) taking that involves directly placing electrode leads on a patient's body may become riskier. This review will discuss the possibility of minimal or no touch EKG using the latest wireless technologies, beneficial in monitoring COVID-19 patients for cardiovascular problems or patients who seek cardiac care, but with posing risk of concomitant COVID-19.

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Keyword: COVID-19, SARS-CoV-2, physical distancing, electrocardiogram, heart rhythm monitoring

[1] Biomedicine Doctoral Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2] Cardiology & Vascular Medicine Department, Mohammad Hoesin General Hospital, Palembang, Indonesia

Koresponden:
Alexander Edo Tondas MD,
Cardiology & Vascular Medicine Department, Mohammad Hoesin General Hospital, Palembang, Indonesia
E-mail: edotondas@fk.unsri.ac.id

Introduction

Coronavirus is a large group of viruses that cause mild to severe respiratory tract disease. There are at least two types of coronavirus that are previously known to cause severe complaints such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The virus related to coronavirus disease 2019 (COVID-19) is SARS-CoV-2, a new entity firstly identified in the city of Wuhan, China on December 2019 and since then the pandemic has escalated on a global scale rapidly, with increasing mortality rate. Based on scientific evidence, COVID-19 can primarily be transmitted from human to human through close contact and respiratory droplets.[1] Currently, no airborne transmission was reported from an analysis of 75,465 patients in China.[2]

The people most at risk of contracting this disease are people who are in close contact with COVID-19 patients, including those who treat COVID-19 patients.[3] Recommendations for preventing the spread

of infection are through regular hand washing, applying the ethics of coughing and sneezing, and avoiding direct contact. Minimizing direct contact is currently applied through physical distancing policies. The physical distancing policy recommended by the Centers for Disease Control and Prevention (CDC) includes limiting a minimum distance of 2 meters from other people and avoiding crowds or groups, which is the range of potential droplet release by a patient or people at risk by coughing, talking or sneezing.[4] Distance limitation has proven effective in reducing COVID-19 transmission rates, as evidenced by the declining of new COVID-19 patient curve model after the policy of distancing was carried out.[5] A study from Harvard, estimated from a computer modeling that recurrent wintertime outbreaks of SARS-CoV-2 will probably occur after the initial wave, and prolonged or intermittent physical distancing should be maintained possibly as late as the year 2022 to hasten the acquisition of herd immunity towards this disease.[6] Therefore, a radical change in how we approach patients in medicine, especially in cardiology should be anticipated.

Currently there is limited data on the spesific ECG changes associated with SARS-CoV-2. He et al. obtained a series of ECG variations in COVID-19 patients, such as McGinn-White sign (S1Q3T3), AV block, ST elevation change, ventricular tachycardia, sinus tachycardia, to right bundle branch block. Furthermore, some patients with COVID-19 may present features similar to myocarditis[7] or come with emergencies such acute coronary syndromes (ACS), requiring immediate electrocardiogram (ECG) taking. Likewise, some medications under investigation for COVID-19 treatment may have cardiovascular complications.[8] In these scenarios, minimal or no-touch technique in ECG acquisition maybe beneficial to minimize direct exposure to SARS-CoV-2.

Cardiovascular Implications in Therapeutic Options for COVID-19

To date, there has been no truly globally agreed-upon therapy as standard therapy for COVID-19. However, there have been several drugs proposed as alternative therapies in COVID-19 patients. Hydroxychloroquine has been included in the COVID-19 management guidelines issue and led by the Indonesian Lung Doctors Association, in addition to other additional therapies such as azithromycin, vitamin C, oseltamivir, etc. The recommended use of hydroxychloroquine is 400 mg / 24 hours for 5 days.[9] Chloroquine and its derivatives allegedly have the ability to inhibit the replication of several intracellular microorganisms including coronaviruses in vitro. Chloroquine and hydroxychloroquine have a similar mechanism of action, that is increasing endosomal pH and interfering with the SARS-CoV-2 cellular receptor glycosylation process, and ultimately inhibit the infection ability of the virus itself.[10] Chloroquine also contains the enzyme quinone reductase-2, which is involved in sialic acid biosynthesis (acidic monosaccharides of cell transmembrane proteins required for ligand recognition), that allows chloroquine to be used as a broad-spectrum antiviral agent.[11] Some experimental studies show chloroquine and its derivatives can inhibit the process of viral receptor glycolization on cellular surfaces, including ACE-2 receptors, so that it cannot bind to these ACE-2 receptors expressed in lung, heart, kidney, and intestine.[12]

However, hydroxychloroquine has significant cardiovascular side effects, that is prolongation of the QT interval, related to abnormal repolarization process of the ventricular myocardium.[9] The normal corrected QT interval using Bezett's formula in women is around 470 ms and 450 ms in men. QT interval prolongation causes concern because of it's relationship with the occurrence of sudden cardiac death, especially fatal torsade de pointes, a polymorphic ventricular arrhythmia.[13] The mechanism of hydroxychloroquine in inducing prolongation of the QT interval is not fully understood. Capel et al. In their 2015 study showed that hydroxychloroquine has an inhibitory effect on hyperpolarization-activated ion channels (also known as "funny current" channels, If) along with delayed rectifier potassium currents. (IKr) and L-type calcium ion currents (ICal). The inhibitory effect of hydroxychloroquine on pacemaker cells is known to cause a delay in depolarization speed and a decrease in heart rate.[14] The use of hydroxychloroquine, especially when administered concomitantly with other QT prolonging drugs such as azithromycin, requires close ECG monitoring. Some medical centers suggested recommendations for this vulnerable group of patients: (1) to perform a basic ECG recording, (2) to withhold drug administration in patients with baseline QT prolongation (eg, QTc ≥500 ms) or with known congenital long QT syndrome, (3) to monitor

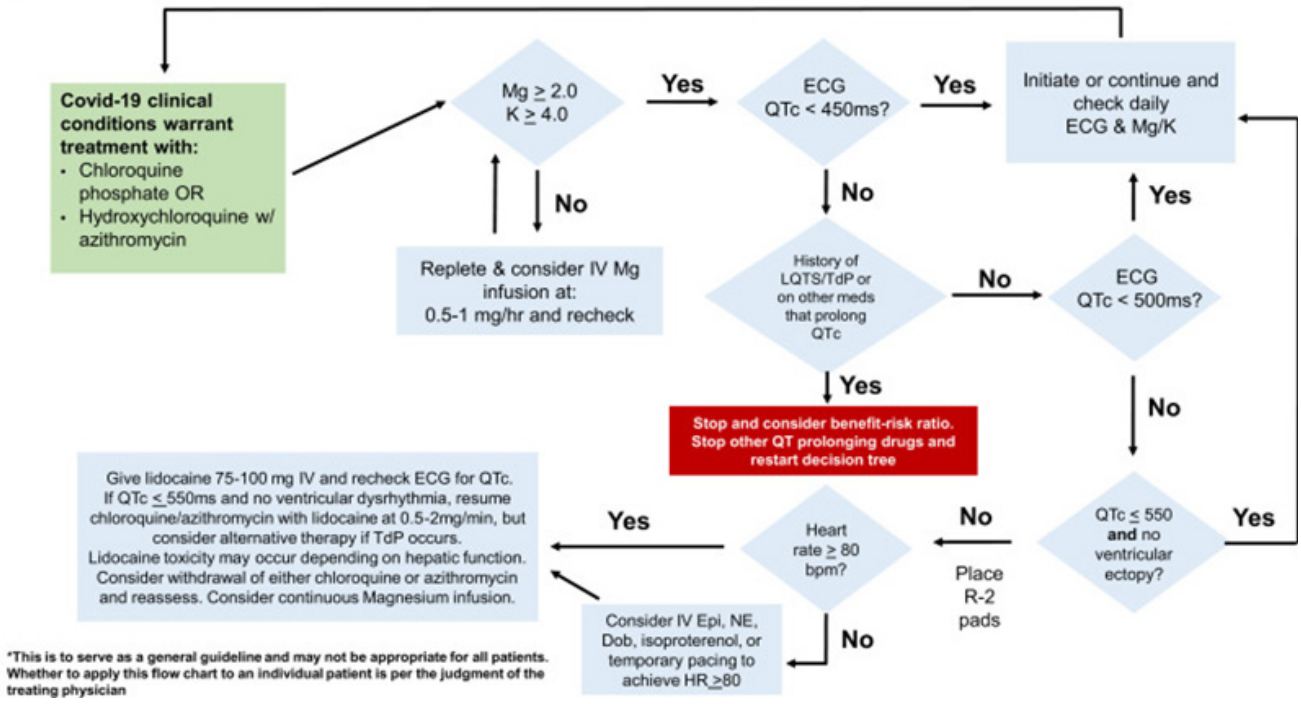


Figure 1. QTc evaluation flowchart in COVID-19 Patients treated with Chloroquine/ Azithromycin.[16] Image used with permission from the respective authors.

heart rhythm and QT intervals, as well as to stop the drug if the QTc is at a value of ≥500 ms, and (4) to prevent other things that can aggravate the condition of QTc prolongation, such as accompanying drugs or electrolyte abnormalities (Figure 1). [15] In cooperative and able patients, wearable and wireless technologies may assist physicians to record and monitor patient's heart rhythm safely and remotely, thus minimizing risky close encounters.

Wearable Technologies for Minimal or No Touch ECG Acquisition

Several ECG recording methods utilize the latest technological developments. The advancement of mobile phone features has played an important role in the process of discovering new ways to record ECGs. Apple Watch is a type of smartwatch released by giant technology company, Apple, which has some of supportive features.[17] Unlike the previous series, the latest 4th generation Apple Watch features a built-in application able to record and display a single lead ECG, thus allowing it to be used independently without having to be paired with an iPhone.[18] The user simply attaches one finger to the digital crown clock and a closed circuit will be formed which will produce an ECG image(Figure 2). [19]

ECG recording technology on the Apple Watch series 4 has also received FDA clearance for early detection of atrial fibrillation (AF) for consumer device. A large study involving approximately 419,000 research subjects, the Apple Heart Study, showed that Apple Watch has a high degree of accuracy in the detection of AF, with diagnostic values that are almost comparable to 12-leads ECG. The Apple watch utilized a light sensor technology, able to measure blood flow at certain intervals using the principle of photoplethysmography, and to detect changes in heart rate regularity. The algorithm will measure intervals between beats, called tachograms, and if there are 5 out of 6 intervals within 48 hours that are outside the normal value, the application will display a notification.[20] In another study conducted by Saghir et al, a 100% rhythm interpretation concordance was found between lead I of Apple 4th series ECG and lead I of 12 leads ECG. The study also found moderate to strong agreement in manual measurement of heart rate and basic intervals between devices represented by Bland-Altman plots, including QTc interval. [21] Based on this finding, it is likely that the Apple Watch may

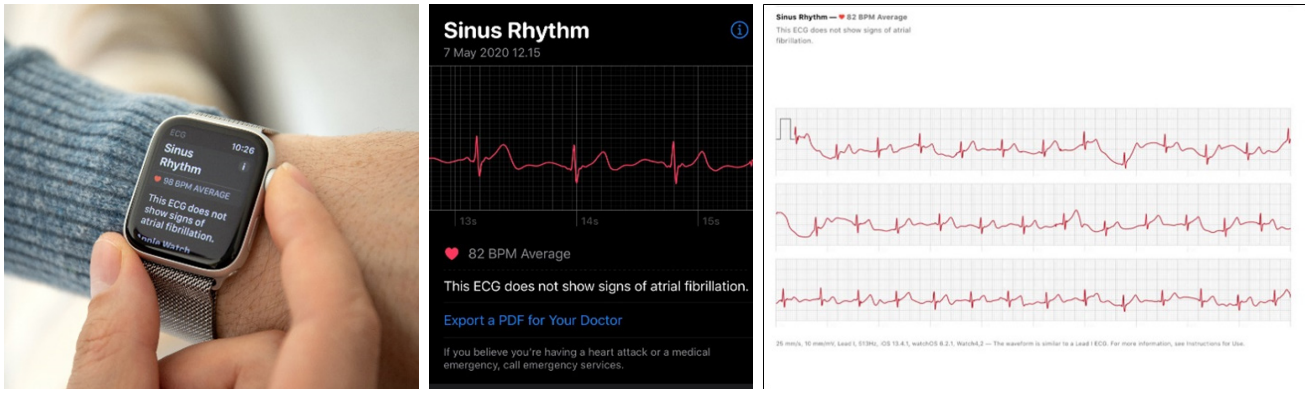
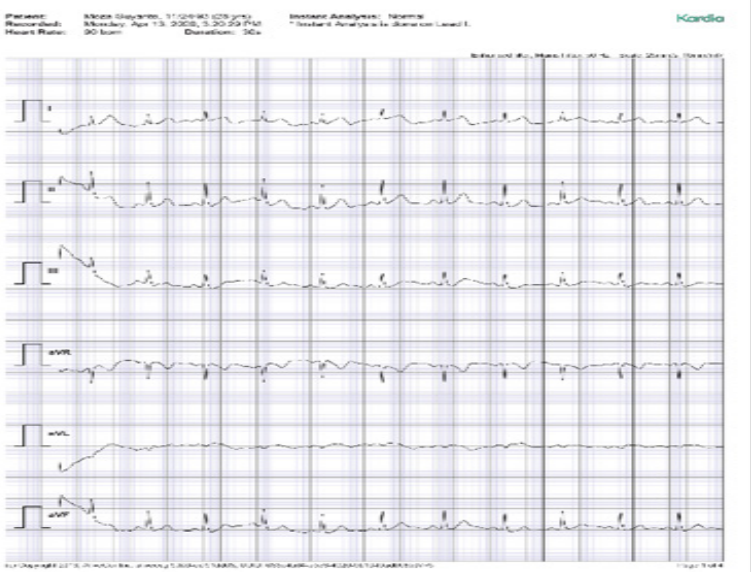


Figure 2. Single-lead ECG taking in Apple Watch Series 4.

Figure 3. Simultaneous 6 leads ECG recording in AliveCor Kardia Mobile 6L by placing the device on the knee or ankle.



have a role in the diagnosis of other heart rhythm disturbance, however, the access to its ECG feature is currently restricted in Asia, including Indonesia . Another challenge in the utility of Apple Watch for routine clinical practice is affordability, especially in developing countries.

Actually, Alivecor is the first company to get FDA clearance for medical-device accessory products, namely KardiaBand, the original ECG recording device attached on early version of the Apple Watch. The recording technique is done by placing a finger on a steel plate located on a smartwatch strap.[22,23] After the discontinuation of KardiaBand following the release of Apple Watch series 4 with its own ECG recording hardware and software, the Kardia Mobile by AliveCor entered the market. Kardia Mobile works with an external case or plate plus a downloadable application to the iOS or Android operating systems on smartphones. The metal sensors on the plate receive the cardiac electric signal which is then converted to an ultrasound FV sound signal (18-24 kHz). Sequently, the application in the smartphone demodulates it into a digital ECG tracing results which can be stored in cloud storage, mobile storage, or directly sent to a particular email.[24,25] Kardia Mobile has the sensitivity and specificity of 98% and 91.4-97% for detecting atrial fibrillation, as stated by Lowres et al and Lau et al in their study. [25–27] The up to date version of Kardia that has been released and received FDA clearance for monitoring QT duration in patients receiving medications that can cause life-threatening QT prolongation is Kardia Mobile 6L, which is able to display six-leads ECG images for 30 seconds on leads I, II, III, aVF, aVR, and aVL. Kardia Mobile 6L has 3 sensors, two of them are similar previous version, while the other one on the bottom of the plate is meant to touch the left knee during recording (Figure 3). [28] With

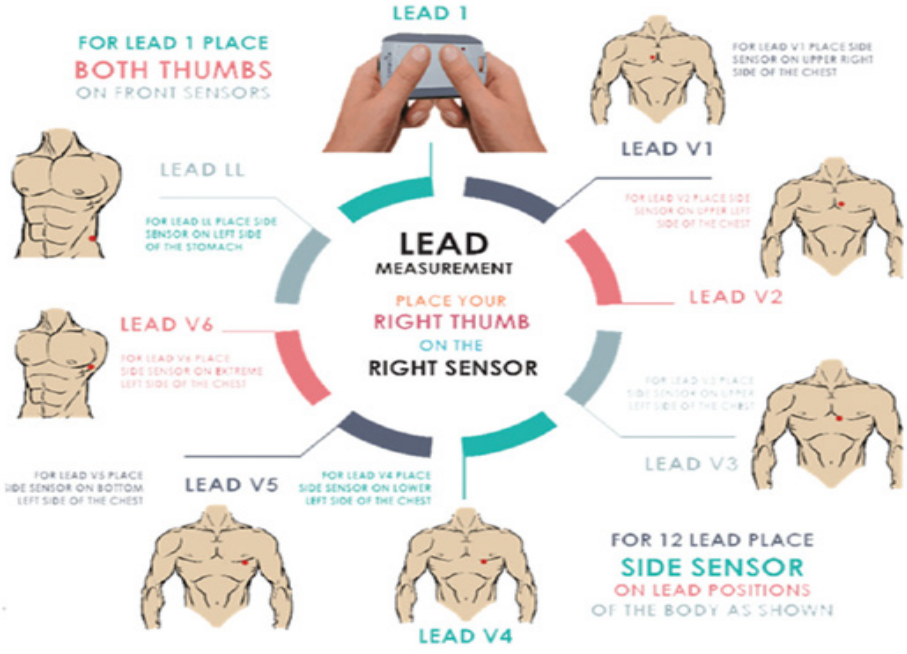


Figure 4. Sanketlife device and steps to take 12-lead ECG recording

a relatively large number of acquired leads compared to other monitoring devices, coupled with a very minimal touch and cableless measurement method, Kardia Mobile 6L can become an attractive alternative as a remote ECG recording tool for COVID-19 patients.

For more consequential cases such as acute coronary syndromes, attempts had been made to modify the AliveCor Heart Monitor in order to acquire 12 leads recording in the ST- LEUIS Study, by attaching two jumper cables to the device and sequentially connect one cable to precordial ECG stickers and another to the left arm (VnL) and the right arm (VnR) as grounding. where a comparison of ST elevation detection was carried out on 12 lead of Alivecor Heart Monitor and conventional 12 lead ECGs. Despite the promising feasibility of using a smartphone to obtain a "12-lead equivalent" ECG recording, the ability for this technology to be utilized autonomously by non-medical personnel still requires further assessment. [29]

Although not FDA approved, Sanketlife is an Indian-manufactured, low cost, pocket-sized, and leadless ECG monitor that can support up to 12 leads. The device is mechanized by SanketLife app running on compatible iOS and Android phones that connect wirelessly via Bluetooth technology to the device. There are two sensors on the front panel of the device for extremity leads and one on the top to be used as the chest lead sensor. The 12 lead ECG can be measured without jelly or any actual electrode, but it must be obtained serially, and not synchronously (Figure 4). The obtained ECG reports can be saved in the cloud for future reference or downloaded and instantly shared with the healthcare professional for immediate clinical advice.[30,31]

Dyundi et al. studied ECG samples obtained using Sanketlife from 1521 random participants and found 15 types of ECG abnormalities from 324 samples (21.3%). This result demonstrated the applicability of the device as a diagnostic test in detecting heart abnormalities from the general population.[32] A comparison study between Sanketlife and standard 12-lead ECG was conducted by Kumar et al with 100 participants. They found that Sanketlife has identified all major ECG abnormalities in high accordance with standard 12-lead ECG with high sensitivity (98.15%) and specificity (100%). It also has high positive predictive value (100%) and negative predictive value (97.36%).[30] Sanketlife has been tested in the general population of India as a quite affordable and practical point-of-care ECG recording method[33]. It have the ability to be used in the outpatient department by physicians, technicians, and even patients with reasonable accuracy, and can prove to be useful in COVID pandemic era.[31] But like every other transient ECG monitoring device, it has difficulty in identifying

time-dependent atrial and ventricular premature beats where continuous 24-hour monitoring is a better method.[30] Specifications of each mobile ECGs are outlined in Table 1.

Ambulatory electrocardiographic (AECG) monitoring is the most widely used method to detect cardiac arrhythmias in the outpatient ambulatory setting at a longer term. The most commonly used AECG is 24-hour Holter monitoring.[34,35] However, conventional 24-hour Holter monitoring often fails to detect the culprit arrhythmia in patients with symptomatic arrhythmia. In the investigation of patients with palpitations, 24-hour Holter monitoring is reported to have a diagnostic yield of 15% to 39%.[34] The Holter is bulky and some patients find it uncomfortable to wear. With advances in technology, miniaturization of such instrumentations is progressing rapidly in concert with the evolution of microelectronic circuits and wireless networking technologies. Patch-based second generation AECG monitoring devices are now available. These patch-based devices have the capability to transmit ECG data wirelessly and can record AECG for longer periods compared to conventional 24-hour Holter.[35,36] In the COVID-19 era, such devices can be a godsend for medical staff to perform minimal touch ECG monitoring, where less cables means less hassle.

The Zio patch and SEEQ Mobile Cardiac Telemetry (MCT) are two of CE marked, FDA approved, water-resistant, wireless patch-based AECG available.[37] Barret et al. compared the Zio patch with conventional Holter monitor. They found that the Zio patch detected significantly more arrhythmia events than the Holter monitor.[34] Vanegas-Cadavid et al. used SEEQ MCT to monitor 100 participants and showed that extended cardiac monitoring using SEEQ MCT was capable of detecting ECG abnormality in 22% of the patients.[38] Fung et al. compared Zio patch, SEEQ MCT and the standard Holter monitor. The Zio patch, SEEQ MCT, and Holter have data storing capacity of 14 days, 7.5 days (can be extended to 30 days), and 24-72 hours respectively. Both patch-based devices are water-resistant while the standard Holter monitor is not. However, the Holter monitor has multiple ECG channels (3-12) while both patch-based devices have only one ECG channel.[37] Unfortunately, the Zio patch and SEEQ MCT never reached the Indonesian market. In Indonesia, cardiologists are probably more familiar with MyPatch device which offers several patch sizes for adult, pediatrics and neonates alike, or the Spyder device with its Liquid-ECG cloud data storing system. MyPatch device is waterproof while the Spyder device has the option to be removed from its patch during shower and replaced to resume recording afterwards. The comparison of different popular ambulatory ECG devices is described in Table 2.

Conclusion

As the prevalence of COVID-19 increases exponentially, patients presenting with seemingly non-related medical problems may expose health care providers to increased risk of contracting the disease. This mandates for a change in the way cardiologists perform their routine medical practice cardiology, including

Table 1. Comparison of mobile ECG systems

Device	Apple Watch	Kardia Mobile	SanketLife
Manufacturer	Apple Inc. Cupertino, California, USA	AliveCor, Inc. Mountain View, California, USA.	Agatsa Software Pvt Ltd. Noida, Uttar Pradesh, India.
Company Website	https://www.apple.com/	https://www.alivecor.com/	https://www.agatsa.com/
Weight (g)	39.8	18	25
Size (mm)	40 x 34 x 10.7	8.2 x 3.2 x 0.35	7 x 4 x 1
Number of leads	1	6	12
Max Duration of Recording	30 seconds	5 minutes	1 minute
FDA Approval	Yes, for Atrial fibrillation	Yes, for atrial fibrillation & QT interval	No
Functionality in Indonesia	Yes, with restricted ECG function in some Asian countries	Yes, with installation of Kardia App (Android phone)	Yes

Figure 5. (A) MyPatch (B) Spyder

Table 2. Comparison of ambulatory ECG/telemetry systems

Device	Zio Patch	SEEQ MCT	MyPatch	Spyder ECG
Manufacturer	iRhythm Technologies,Inc. San Fransisco, California, USA.	Medtronic,Inc. Minneapolis, Minnesota, USA.	DMS-Service, LLC. Los Angeles, California, USA	WEB Biotechnology Pte Ltd. Singapore.
Company Website	https://www.irhythmtech.com/	https://www.medtronic.com/	https://dms-service.com/	https://spyderecg.web-biotech.com/
Weight (g)	34	50	15	48
Size (mm)	123 x 53 x 10.7	16 x 60 x 15	8.2 x 3.2 x 0.35	60 x 55 x 18
Number of leads	1	1	3	1
Max Duration of Recording	14 days	7.5 days; up to 30 days with deployment of multiple units	14 days	14 days
FDA Approval	Yes	Yes	No.	No.
Functionality in Indonesia	No	No (discontinued by the end of 2018)	Yes,	Yes, (with Cloud based technology)

simple ECG taking to heart rhythm monitoring. Wireless devices and remote technologies may help cardiologists to minimize direct contact between health care personnel and COVID-19 patients as an integral step in limiting its spread and resource utilization.

Acknowledgement

We express our deep respect to all medics and paramedics who are fighting the pandemic in the frontlines and we hope this manuscript may contribute in the new paradigm of medical practice, especially cardiology in response to COVID-19.

Conflict of Interest

None

Publication Agreement

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