

[REVIEW ARTICLE]

Current Use and Future Needs of Noninvasive Ambulatory Electrocardiogram Monitoring

Takanori Ikeda

Abstract:

Remarkable progress has been seen in monitoring systems using noninvasive ambulatory electrocardiograms (ECGs). In the Holter ECG system, 12-channel formats have been utilized as diagnostic tools, particularly for the detection of transient or silent myocardial ischemia and dynamic electrical disorders. In patients diagnosed with cryptogenic stroke, despite negative results on standard ECG tests, continuous ambulatory ECG monitoring for up to 30 days has been shown to increase the detection rate of transient atrial fibrillation. At present, a waterproof Holter ECG system is available. Recently, continuous late potential measurements using the time domain method and frequency domain T-wave alternans using the spectral analysis method for 24 hours have been applied to the Holter ECG and developed as novel risk stratification markers. Wearable ECG monitors that are built into belts, vests, wristbands, adhesive patches, and mobile smartphones have been used as fitness products for athletes and healthcare products for the general population. In the future, such devices may be used as remote monitoring tools for the detection of arrhythmias.

Key words: ambulatory ECG, Holter ECG, wearable ECG, remote monitoring, risk stratification

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Introduction

Ambulatory electrocardiogram (ECG) monitors are often used to detect, document, and characterize abnormal electrical activity during daily activities. (1) It should be emphasized that ambulatory ECG monitoring is noninvasive, easy to use, relatively inexpensive, and readily available compared to other medical devices. The latest progress in ambulatory ECG is remarkable. What was considered impossible just 10 years ago has now become possible. At present, Holter ECG recordings can be performed with 12-channel formats while taking a bath and can be used for up to 4 weeks of single-channel recording. Furthermore, specific markers analyzed using ambulatory ECG recordings have been used to predict future arrhythmic events.

Recently, remote monitoring using continuous wearable recorders and mobile smartphones became available for application to general healthcare, but in the future, these devices may be able to be used to detect arrhythmias in symptomatic patients. Thus, modern ambulatory ECG monitors have numerous characteristics and advantages in daily clinical practice.

In this review article, the current use and future needs with respect to noninvasive ambulatory ECG monitoring and techniques are introduced and discussed.

Application as a diagnostic tool for cardiac disorders

A conventional Holter ECG is generally used to diagnose and assess potential arrhythmias or conduction disturbances, but it is difficult to use as a diagnostic tool for cardiac disorders because the most common systems have only 2-3 channels. However, recently, the Holter system that has 12 channels was developed and used as a diagnostic tool (2). This system may be able particularly useful for diagnosing transient or silent myocardial ischemia and dynamic electrical disorders that occur occasionally and for a brief duration, such as Brugada syndrome. In fact, it has been reported that continuous or ambulatory 12-lead ECG monitoring has potential utility in the diagnosis of asymptomatic myocardial ischemia, identifying the location of ischemia or

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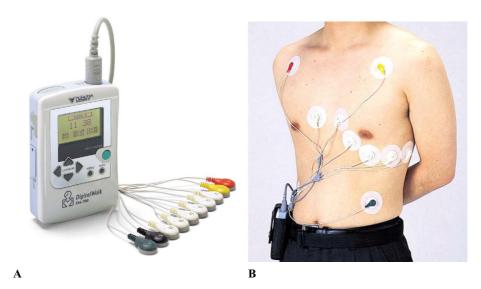


Figure 1. A: Holter 12-lead ECG recorder (FM-700[®]). B: Representative mounting of electrodes. A and B, ©2020 Fukuda Denshi, Tokyo, Japan. All rights reserved. Used with the permission of Fukuda Denshi.



Figure 2. Waterproof Holter ECG recorder (FM-960[®]). ©2020 Fukuda Denshi, Tokyo, Japan. All rights reserved. Used with the permission of Fukuda Denshi.

culprit coronary artery after peripheral vascular surgery (3), and for the detection of a typical ECG pattern of patients in whom Brugada syndrome is suspected (4, 5).

The novel Holter 12-lead ECG system makes use of 10 electrodes (Fig. 1), similar to the standard 12-lead ECG systems, and permits recording periods of up to 48 hours. A double-blinded study demonstrated that Holter 12-lead ECG recordings are not significantly different from those of a standard 12-lead ECG regarding measurements of ECG parameters but are more variable (6). In the future, Holter 12-lead ECG monitoring systems will be used in the evaluation of interventional therapeutic procedures and the effects of cardiovascular medicines. In addition, such monitoring might be useful for localizing the origin of ventricular tach-yarrhythmias.

Use in identifying the cause of cryptogenic stroke

Recently, ambulatory ECG monitoring has been used to identify individuals with undiagnosed atrial fibrillation (AF) who may benefit from treatment to reduce their risk of serious adverse events. It is well known that AF is a main cause of ischemic stroke (cerebral embolism). The results of patients diagnosed with cryptogenic stroke or embolic stroke of undetermined source (ESUS) sometimes appear normal on standard ECG tests, including 24- to 48-hour Holter ECG monitoring. When continuous ambulatory ECG monitoring for a longer time is applied, the detection rate of transient (paroxysmal) AF is increased. In fact, it has been reported that ambulatory ECG monitoring (a dry-electrode belt monitor worn around the chest) with a 30-day recording period significantly improved the detection of AF in patients with ESUS (7). Recently, the mSToPS trial has revealed that the use of immediate home-based ECG monitoring (selfapplied wearable patch ECG recorder) improved the detection rate of paroxysmal AF in individuals with risk factors for AF (8). In these patients, oral anticoagulation therapy is strongly recommended to prevent ischemic stroke caused by AF.

However, as shown in recent studies (9, 10), long-term ECG monitoring with an insertable cardiac monitor can achieve increased detection rates of undiagnosed AF.

Application while taking a bath or shower

Generally, patients are unable to take a bath or shower during ambulatory ECG recording. We previously reported that the majority of cardiac arrests occurred in patients' residences, and about half of the events had occurred in the bathroom (11). This is even more prominent in elderly patients. Recently, a small waterproof Holter ECG monitor was developed and used in clinical practice (Fig. 2). This al-

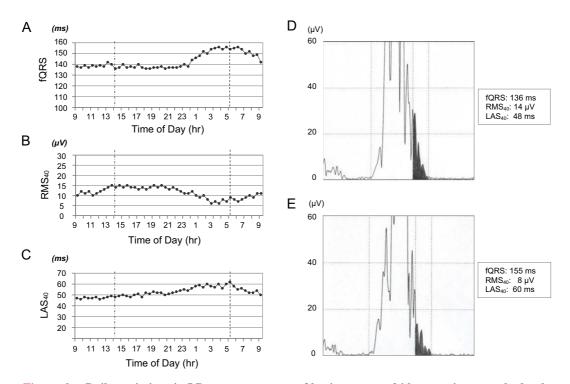


Figure 3. Daily variations in LP parameters every 30 minutes over 24 hours using a newly developed Holter ECG-based signal-averaging system (SCM-6600[®]; Fukuda Denshi, Tokyo, Japan). A: Trend graph of filtered QRS duration, B: trend graph of root mean square voltage of the terminal 40 ms of the filtered QRS complex, C: trend graph of duration of low-amplitude signals (<40 μ V) in the terminal, filtered QRS complex, D: negative LP determination at a time of 14: 10, Day 1, and E: positive LP determination at a time of 5: 10, Day 2.

lowed patients the freedom to go about their daily routine, including bathing or showering, without interrupting daily cardiac monitoring. The use of waterproof ambulatory ECG systems should be considered if the patients have any symptoms in the bathroom. These devices would also be useful for risk management in competitive swimmers.

Application in risk stratification for serious cardiac events

Ambulatory (Holter) ECG may play a role in the assessment of the prognosis and risk stratification of various cardiac disorders. It is well known that heart rate variability (HRV), heart rate turbulence (HRT), and QT variability/dynamics evaluated using Holter ECG monitoring are risk stratification markers for cardiac mortality or arrhythmic events. In addition to these conventional markers, ventricular late potentials (LPs) and T-wave alternans (TWA) have also been measured using Holter ECG monitoring and used for risk stratification for serious cardiac events. These relatively new indices are introduced below.

LPs by signal-averaged ECGs using Holter ECG recordings

Ventricular LPs detected by signal-averaged ECGs (SAECGs), which reflect a conduction delay, have been widely utilized to detect high-risk individuals among patients with cardiac disorders, such as myocardial infarction

(MI), Brugada syndrome (12), and arrhythmogenic right ventricular cardiomyopathy (ARVC) (13). Recently, it has become possible to monitor LP continuously for 24 hours using a newly developed SAECG system that is applied to ambulatory (Holter) ECG, now commercially available (14). LPs are analyzed automatically every 30 minutes over 24 hours using data from a digital Holter ECG recorder and are presented on a trend graph covering 24 hours (Fig. 3). Three parameters were assessed using a computer algorithm: the filtered QRS duration, the root mean square voltage of the terminal 40 ms of the filtered QRS complex, and the duration of low-amplitude signals (<40 µV) in the terminal, filtered ORS complex. Using this system, LP parameters are demonstrated with daily and dynamic variations in patients with Brugada syndrome but not in those with ARVC (15). Further prospective studies may be conducted to evaluate whether LP assessed over 24 hours is useful in risk stratification for arrhythmic events or sudden cardiac death (SCD) in some cardiac disorders, including Brugada syndrome, ARVC, and MI.

TWA based on the frequency domain analysis of Holter ECG

TWA is a known risk stratification index for predicting SCD. TWA represents an increased disparity of repolarization in the ventricle on a beat-to-beat basis and may provide a substrate for ventricular fibrillation (16). Initially, micro-

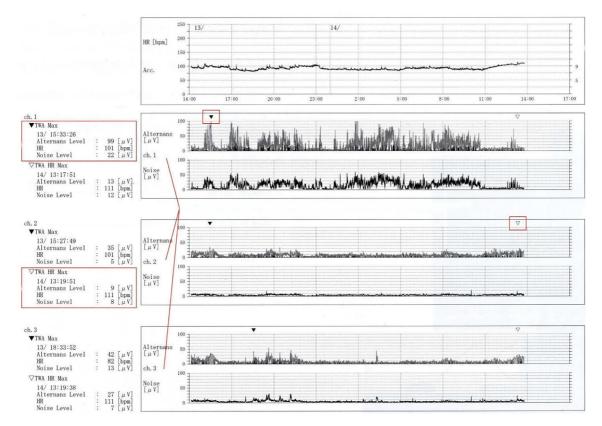


Figure 4. Trend graph of TWA using the spectral analysis method based on the frequency domain TWA analysis of every 128 beats over 24 hours using a newly developed 3-channel Holter ECG system (SCM-6600[®]; Fukuda Denshi, Tokyo, Japan). The upper square indicates the maximum TWA over 24 hours, and the lower square indicates the TWA when the maximum HR was seen.

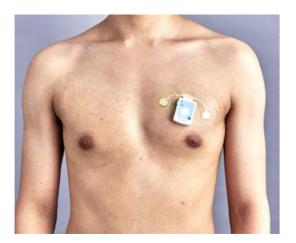


Figure 5. Ambulatory ECG adhesive patch monitor (WR-100[®]). ©2020 Fukuda Denshi, Tokyo, Japan. All rights reserved. Used with the permission of Fukuda Denshi.

volt TWA assessed by the spectral method during an exercise stress test was introduced as a marker to identify patients with an increased risk of arrhythmia events or SCD. The ambulatory (Holter) ECG-based TWA, quantified by the modified moving average method based on the time-domain algorithm, was then introduced as an alternative method of TWA measurement. Some studies support the clinical utility of these markers in risk stratification for arrhythmic events (17). Recently, the spectral analysis method based on the frequency domain TWA analysis of ambulatory ECG was developed as a novel risk stratification marker (Fig. 4). Using this methodology for identifying TWA, some studies have proposed the ability of Holter ECG-based TWA to identify groups at high risk of future ventricular tachyarrhythmias or cardiac mortality (18). Randomized large clinical studies may be conducted in the future to determine the utility of this marker in identifying patients at risk for serious cardiac events compared to other noninvasive ECG markers, such as HRV, HRT, and QT variability/dynamics.

Clinical use of healthcare products

Arrhythmia is the leading cause of SCD not only in patients with organic heart disease but also in the general population. Recently, wearable ECG monitors that are built into belts, vests, wristbands (bracelets), or adhesive patches (Fig. 5) have been marketed as fitness products during exercise for athletes and as healthcare products for the general population. Mobile smartphones are also used to facilitate healthcare in the general population (19). Using an integrated sensor that interfaces with smartphones, it is possible to display and record ECGs (Fig. 6). In addition, devices are used to record ECGs via wearable monitoring devices, such as a wristband that has an external real-time cardiac telemonitoring system with wireless transmission. Recently, a



Figure 6. Personal ECG monitoring using a smartphone for Android or iPhone (Kardia Mobile[®]; AliveCor, Mountain View, USA). Image: KMobile-Demo_Moment.jpg. https:// www.alivecor.com. Accessed June 12, 2020. Used with the permission of AliveCor.



Figure 7. Personal ECG monitoring using a wristbandwatch for Apple Watch (Smart Watch Series 4[®]; Apple, Cupertino, USA). Image: 31847-original.jpg. https://www.wareable. com/apple/page/4. Accessed June12, 2020. Used according to legal-notice statement of Apple.

wristband-watch that enables consumers to record a rhythm strip was launched (Fig. 7). This device may be able to assist in the self-diagnosis of arrhythmias.

Although several products have been specially designed for medical professionals, most are designed to measure the heart or pulse rate rather than rhythm. Users should be aware that ECGs are occasionally not precise and very noisy, particularly during exercise; they are only for reference. In addition, these devices generally have no medical regulatory oversight or approval; therefore, they should not be used for any medical purpose.

However, in the future, the quality of these devices will improve with advances in technology, and they may be applied not only for the management of health conditions with ECG recordings but also for both medical checkups and arrhythmia detection.

The author states that he has no Conflict of Interest (COI).

References

- Steinberg JS, Varma N, Cygankiewicz I, et al. 2017 ISHNE-HRS expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry. Heart Rhythm 14: e55-e96, 2017.
- Steijlen ASM, Jansen KMB, Albayrak A, Verschure DO, Van Wijk DF. A novel 12-lead electrocardiographic system for home use: development and usability testing. JMIR Mhealth Uhealth 6: e10126, 2018.
- 3. Ollila A, Virolainen J, Vanhatalo J, et al. Postoperative cardiac ischemia detection by continuous 12-lead electrocardiographic monitoring in vascular surgery patients: a prospective, observational study. J Cardiothorac Vasc Anesth 31: 950-956, 2017.
- Gray B, Kirby A, Kabunga P, et al. Twelve-lead ambulatory electrocardiographic monitoring in Brugada syndrome: potential diagnostic and prognostic implications. Heart Rhythm 14: 866-874, 2017.
- Kakihara J, Takagi M, Hayashi Y, Tatsumi H, Doi A, Yoshiyama M. Utility of 12-lead and signal-averaged Holter electrocardiograms after pilsicainide provocation for risk stratification in Brugada syndrome. Heart Vessels 32: 1151-1159, 2017.
- 6. Wang D, Bakhai A, Arezina R, Täubel J. Comparison of digital 12-lead ECG and digital 12-lead Holter ECG recordings in healthy male subjects: results from a randomized, double-blinded, placebocontrolled clinical trial. Ann Noninvasive Electrocardiol 21: 588-594, 2016.
- Gladstone DJ, Spring M, Dorian P, et al. EMBRACE investigators and coordinators. Atrial fibrillation in patients with cryptogenic stroke. N Engl J Med 370: 2467-2477, 2014.
- **8.** Steinhubl SR, Waalen J, Edwards AM, et al. Effect of a homebased wearable continuous ECG monitoring patch on detection of undiagnosed atrial fibrillation: the mSToPS randomized clinical trial. JAMA **320**: 146-155, 2018.
- Sanna T, Diener HC, Passman RS, et al. CRYSTAL AF investigators. Cryptogenic stroke and underlying atrial fibrillation. N Engl J Med 370: 2478-2486, 2014.
- **10.** Diederichsen SZ, Haugan KJ, Kronborg C, et al. Comprehensive evaluation of rhythm monitoring strategies in screening for atrial fibrillation. Insights from patients at risk monitored long term with an implantable loop recorder. Circulation **141**: 1510-1522, 2020.
- Tsukada T, Ikeda T, Ishiguro H, et al. Circadian variation in outof-hospital cardiac arrests due to cardiac cause in a Japanese patient population. Circ J 74: 1880-1887, 2010.
- **12.** Ikeda T, Sakurada H, Sakabe K, et al. Assessment of noninvasive markers in identifying patients at risk in the Brugada syndrome: insight into risk stratification. J Am Coll Cardiol **37**: 1628-1634, 2001.
- 13. Kamath GS, Zareba W, Delaney J, et al. Value of the signalaveraged electrocardiogram in arrhythmogenic right ventricular cardiomyopathy/dysplasia. Heart Rhythm 8: 256-262, 2011.
- 14. Abe A, Ikeda T, Tsukada T, et al. Circadian variation of late potentials in idiopathic ventricular fibrillation associated with J waves: insights into alternative pathophysiology and risk stratification. Heart Rhythm 7: 675-682, 2010.
- **15.** Abe A, Kobayashi K, Yuzawa H, et al. Comparison of late potentials for 24 h between Brugada syndrome and arrhythmogenic right ventricular cardiomyopathy using a novel signal-averaging system based on Holter ECG. Circ Arrhythm Electrophysiol **5**: 789-795, 2012.
- 16. Verrier RL, Klingenheben T, Malik M, et al. Microvolt T-wave alternans: physiological basis, methods of measurement, and clinical utility consensus guideline by International Society for Holter and Noninvasive Electrocardiology. J Am Coll Cardiol 58: 1309-1324, 2011.

- **17.** Sakaki K, Ikeda T, Miwa Y, et al. Time-domain T-wave alternans measured from Holter electrocardiograms predicts cardiac mortality in patients with left ventricular dysfunction: a prospective study. Heart Rhythm **6**: 332-337, 2009.
- 18. Kawasaki M, Yamada T, Morita T, et al. Risk stratification for ventricular tachyarrhythmias by ambulatory electrocardiogrambased frequency domain T-wave alternans. PACE 38: 1425-1433, 2015.
- **19.** Isakadze N, Martin SS. How useful is the smartwatch ECG? Trends Cardiovasc Med **30**: 442-448.

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