INTRODUCTION

The use of 24-hour ambulatory electrocardiogram (AECG) monitoring is of importance in the evaluation of patients with suspected frequent (daily) arrhythmic events. Recorders use patient-activated event markers and time markers allowing for a symptom-rhythm correlation. Over the past several years, as stated in the ACC/AHA guidelines, traditional uses of the 24-hour AECG for arrhythmia detection have widened to include, among others, ST segment monitoring for possible ischemia, heart rate trend and heart rate variability analysis post-myocardial infarction (MI) [1]. 24-hour AECG is also excellent for quantifying the burden of atrial and ventricular ectopy. This has become easily available and feasible mainly secondary to the increased use of multichannel and telemetered signals. After the use of a 24-hour AECG, it is also crucial that the recording be reviewed by experienced and competent personnel (physician or technician) to obtain an accurate result.

INDICATIONS FOR PLACING A 24-HOUR AMBULATORY ELECTROCARDIOGRAM MONITOR

The indications for placing a 24-hour AECG monitor vary widely. The established guidelines for the use of a 24-hour ECG are detailed in the American College of Cardiology/American Heart Association Guidelines for Ambulatory Electrocardiography: Executive Summary and Recommendations (1999) [1].

・ Assess symptoms possibly related to rhythm disturbances
・ Assess risk for future cardiac events in patients without symptoms from arrhythmia
・ Assess anti-arrhythmic medication
・ Assess pacemaker and implantable cardioverter defibrillator (ICD) function
・ Assess for ischemia
・ Monitor pediatric patients. It is also crucial that the recording be reviewed by experienced and competent personnel (physician or technician) to obtain an accurate result.

RÉSUMÉ : L’interprétation d’un électrocardiogramme ambulatoire de 24 heures est importante pour l’évaluation des patients susceptés de présenter des épisodes arythmiques. Nous présentons dans cet article des signes cliniques révélateurs lors de l’interprétation de l’ECG 24 h.

Mots-clés : électrocardiogramme de 24 heures, épisodes arythmiques, interprétation

These encompass the indications for placement of a 24-hour AECG to:

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Prognosis and risk stratification for sudden cardiac death (SCD), post-myocardial infarction and congestive heart failure (CHF)

On many occasions, patients present with symptoms that are not immediately explained by an obvious diagnosis. In such cases, 24-hour AECG monitoring may be helpful in determining the reason for their symptoms, specifically if it is of cardiac origin.

Such variables as heart rate variability (HRV) – the measure of change in the length of the R-R interval, under autonomic control – and the presence of ectopy or pauses reflect the balance of the autonomic system and may give a clue to the diagnosis.

Heart rate turbulence (HRT – heart rate response after a premature ventricular contraction) and how it relates to baroreflex function (tested after the injection of phenylephrine) also helps in prognosis. Based on previous studies, reduced baroreceptor function had been linked to increased cardiac filling pressures and worse CHF, due to decreased sensitivity to the vagal tone. It is worth noting that age was found to be a big factor in baroreceptor dysfunction. As per a study performed in Italy, HRT was significantly correlated to baroreflex sensitivity (BRS) [8]. Being a non-invasive test, requiring no drug administration, HRT measurement via 24-hour AECG monitoring can act as a more feasible surrogate for BRS. Therefore, we can conclude that abnormal HRT on 24-hour AECG can be correlated with a worse prognosis in CHF, as is diminished baroreflex function. In another small study by Koyama et al., HRT onset and slope were studied in CHF patients with and without history of ventricular tachycardia versus normal controls. It was shown that turbulence slope was significantly lower and turbulence onset was significantly higher in patients with CHF as compared to controls. HRT slope and onset were not significantly different whether the CHF patient had had ventricular tachycardia or not. Upon subgroup analysis, HRT slope revealed better prognostic value in the prediction of CHF death and hospitalization but not in the prediction of fatal ventricular arrhythmias [9]. The conclusion that HRT slope and onset are prognostic, however, does not seem to apply to patients with hypertrophic cardiomyopathy [10].

Over recent years, the detection of premature ventricular contraction (PVC) on ECG has been correlated with tachycardia-induced cardiomyopathy. Several studies have used 24-hour Holter monitoring to assess the frequency of PVCs per 24 hours, the duration of the QRS in the premature beat and the presence of multiform PVCs or non-sustained runs of ventricular tachycardia. In a study by Del Caprio Munoz et al., patients who had a decreased left ventricular ejection fraction (LVEF) were more likely to have PVCs, non-sustained ventricular tachycardia, longer duration of PVCs and more frequent multiform PVCs, suggesting that these factors may also be contributing to the cardiomyopathy [11]. One study defined tachycardia-induced cardiomyopathy (TICMP) as LVEF of ≤ 50% in the absence of any detectable underlying heart disease and improvement of LVEF ≥ 15% following effective treatment of index ventricular arrhythmia [12]. In this study, they found that patients with TICMP were more likely male and asymptomatic, as confirmed by the observations of Yokokawa et al. [13]. Via a receiver-operator characteristic curve analysis, the best cutoff for PVC burden that separated between patients with TICMP and a preserved LVEF was at 16%. Other predictors of TICMP were persistent PVCs during the day and the presence of repetitive monomorphic ventricular tachycardia. Another study aimed at determining a similar cutoff value for a PVC burden at which patients are more likely to have cardiomyopathy showed the value to be at 24% [14]. In further analysis, they, too, found that PVC burden is independently associated with cardiomyopathy, with a hazard ratio of 1.12.

Other prognostic variables on a 24-hour AECG, besides ectopic beats, include HRV. Although there exists intrinsic electrical activity of the myocardial cell itself, there are other factors that affect heart rate and rhythm, namely the autonomic nervous system. In 24-hour AECG monitoring, HRV actually measures fluctuations in these autonomic inputs. Thus, both persistently low and extremely high levels of sympathetic input will lead to an attenuated HRV, consistent with increased vagal activity or increased sympathetic activity respectively. HRV consists of many components, each of which is affected by different internal and external factors. There are two indices for HRV by which analysis can take place: time domain analysis and frequency domain analysis [15].

Time domain analysis includes SDNN (the standard deviation of all N-N intervals) which is the most validated variable. Shortly post-MI, SDNN of > 70 ms is associated with a 3.2 relative risk of mortality, as confirmed by several studies. SDNN may not be very accurate in prognosis in the setting of diabetes or coronary artery bypass grafting (CABG) but it may help as a “negative risk stratifier.” SDANN (standard deviation of the average N-N intervals) is another variable that has been studied within HRV. Although cut-offs are not very clear, SDANN is also predictive of increased mortality, as per studies done on patients awaiting heart transplant. As Stein explains in her review, both rMSSD (the root mean square of successive N-N interval difference) and pNN50...
(the percent of differences between normal-to-normal intervals > 50 ms) reflect short-term HRV changes. They reflect the response of the heart rate to the vagal tone. In terms of predictive worth, extremely high values of these variables (i.e., pNN50 > 50%) in a cardiac patient suggest atrial fibrillation [16].

As for frequency domain analysis, the variables are distributed according to frequency: high (HF), low (LF), very low (VLF) and ultra-low (ULF). HF changes with respiration and vagal tone. However, it is not entirely accurate in predicting cardiovascular outcomes. LF is dependent on sympathetic tone, whereby it is greatly diminished in CHF patients. Low LF power has been shown to be associated with sudden death and is a similar risk factor to high LVEDD (left ventricular end-diastolic diameter) and increased PVC count. Additionally, when calculated from a short-term ECG, low LF power, a low LF:HF ratio and low LF power during controlled breathing all predicted SCD [17]. Based on a study performed in Australia, it was shown that VLF power is influenced, not only by decreased vagal/increased sympathetic modulation, but also, by thermal regulation [18]. In an interesting study by Battipaglia et al., VLF, as later discussed, is proven to be associated with cardiovascular mortality through its correlation to ICD shocks. The study showed that “several depressed HRV indices were significantly associated with appropriate ICD shocks in the previous 6 months and VLF amplitude was the only variable significantly associated with ICD shocks recorded since ICD implant”. This data suggests that more elaborate HRV analysis may be helpful in assessing the risk of SCD and need for ICD in patients with dilated cardiomyopathy. Finally, ULF is another variable of HRV that is affected by the body’s circadian rhythm [19].

HRV can help in the risk stratification of patients with heart failure. In progressive cardiac failure, as per a study by Guzetti et al., three factors were found significant: depressed HRV power at night (below 0.04 Hz with VLF ≤ 509 ms²), increased pulmonary wedge pressure (PWP ≥ 18 mmHg) and reduced LVEF (≤ 24%). The study showed that the cumulative 3-year mortality rates were: 7% for patients without risk factors, 20% for patients who had only one risk factor, 32% for patients with two, and 44% for patients with three risk factors. On the other hand, and despite no relation to etiology of cardiomyopathy (ischemic versus non-ischemic), Guzetti et al. found abnormal LF and HF powers (at night) and LVEDS (left ventricular end-systolic dimension) to be associated with SCD in a univariate model. Furthermore, nighttime LF power was the only multivariate predictor of sudden death [20].

In the 1970’s, diminished HRV was linked to a poor prognosis post-MI, specifically when it came to in-hospital mortality. Since then, several studies have confirmed that the assessment of HRV in the acute phase following infarction is closely related to the clinical and biochemical indicators of severity [21]. HRV in itself has a predictive value independent of the factors used in post-MI risk stratification, including left ventricular dysfunction and ectopy. When comparing HRV and LVEF, they were found to be equivalent in their correlation to all-cause mortality, but HRV was superior in predicting incidents of arrhythmia (SCD and ventricular tachycardia) [22]. This may correspond to the stronger association of HRV with arrhythmic mortality, as opposed to the non-arhythmic mortality. The predictive value of HRV, in case it is diminished, increases with increasing the length of the recording time. Thus, short ECG recordings are inferior (similar sensitivity but lower specificity) to 24-hour monitoring post-MI in predicting high-risk patients. No specific time post-MI has been shown to be of highest predictive value but there is a general agreement to have a 24-hour AECG placed one week after the index MI [15].

EVALUATION OF THERAPEUTIC INTERVENTIONS

In multiple studies, 24-hour AECG has been used to monitor the efficacy of therapeutic interventions in the setting of arrhythmias. The 24-hour AECG is used after ablation of atrial fibrillation to detect recurrence. Recurrence is determined by a reappearance of atrial fibrillation for > 30 seconds on surface ECG. By using the 24-hour AECG, the burden of atrial fibrillation is determined and the need for repeat interventions is assessed. Typically, after a pulmonary vein isolation procedure, at three-month intervals for up to one year, a 24-hour AECG monitor is placed to identify any recurrence of the atrial arrhythmia. However, due to the intermittent monitoring that it offers, there are gaps of time that may include recurrence of the paroxysmal atrial fibrillation without being picked up. A study done by Hanke et al. compared 24-hour AECG monitoring (every three months post-ablation) to an implantable continuous cardiac monitor. Patients were followed up for a mean of 8.3 months. Most clearly, the difference between both modalities was the amount of time covered by each (2,021 hours and 220,766 hours, respectively). As such, the continuous monitor was able to detect significantly more recurrences than the 24-hour AECG that was only placed at prescheduled times. Upon further analysis, the 24-hour AECG had a failure rate of 34% in detecting atrial fibrillation recurrence. This yields a sensitivity of 0.60 and a negative predictive value of 0.64 for intermittent 24-hour AECG recordings. In line with these findings, the longer the intervals between each 24-hour monitor placement, the lower the sensitivity and negative predictive value. The interpretation of this is dependent on the fact that the daily burden of atrial fibrillation is low, causing the difficulty in detection on intermittent AECG monitoring, even at 3-month intervals. Therefore, it is significant to point out that post-procedural monitoring of cardiac rhythm with continuous monitoring is superior to intermittent 24-hour AECG monitoring at regular intervals and will give more information regarding the need for anticoagulation and further intervention or medical therapy [23].
Additionally, 24-hour AECG monitoring can also be used to follow-up the efficacy of certain cardiac medication. Up to half of the deaths associated with CHF are sudden. Neurohormonal involvement is a cornerstone in this control and, as such, autonomic dysregulation and impaired repolarization reserve play a major role in ventricular arrhythmias. Autonomic dysfunction is characterized by a diminished HRV on 24-hour AECG, as previously discussed, and impaired myocardial repolarization is reflected in an increase in the the interval from the peak of the T wave to the end of the T wave (T-peak to T-end [TPE] interval) or in an interlead variability of the QT interval on ECG, called QT-interval dispersion (QTd). Both parameters, a low HRV and an increased QTd, are used as surrogate markers for arrhythmogenicity and, potentially, mortality [15, 24-28]. Given the above, Akdeniz et al. used 24-hour AECG to assess for changes in QTd and HRV with carvedilol as treatment in CHF [29]. They found that QTd significantly decreased in the carvedilol group as compared with controls. However, HRV parameters did not significantly differ between the two groups, except for SDANN which was statistically significant. From this data, the authors concluded that carvedilol may contribute to less sudden cardiovascular mortality given that it has an effect on myocardial repolarization. The ability to detect and monitor this is through the use of 24-hour AECG recordings. Despite an unclear mechanism by which β-blockade affects QTd, Yildirir et al. reproduced the findings of an improved QTd profile with carvedilol [30]. Via spectral analysis of HRV and baroreflex gain, other studies were also able to confirm the benefit of angiotensin-converting enzyme inhibitors via increasing the HF component of HRV (related to vagal tone) [31] and the benefit of β-adrenergic blockers in CHF, whereby baroreflex gain increases representing an improved baroreceptor function [32].

DECLARATION OF COMPETING INTERESTS: The authors declare that they have no conflict of interest.

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