REVIEW ARTICLE

Prognostic value of Holter monitoring in congestive heart failure

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Abstract

Congestive heart failure (CHF) is an increasingly widespread, costly and deadly disease, frequently named as epidemics of the 21 century. Despite advancement in modern treatment, mortality rate in CHF patients remains high. Therefore, risk stratification in patients with CHF remains one of the major challenges of contemporary cardiology. Electrocardiographic parameters based on ambulatory Holter monitoring have been documented to be independent risk predictors of total mortality and progression of heart failure. Recent years brought an increased interest in evaluation of dynamic Holter-derived ECG markers reflecting changes in heart rate and ventricular repolarization behavior. It is widely accepted that structural changes reflecting myocardial substrate are better identified by means of imaging techniques, Holter monitoring on the other hand provides complementary information on myocardial vulnerability and autonomic nervous system. Therefore, combining the electrocardiographic stratification with assessment of myocardial substrate may provide the complex insight into interplay between factors contributing to death.

The present article reviews the literature data on the prognostic role of various Holter-based ECG parameters, with special emphasis to dynamic ECG risk markers — heart rate variability, heart rate turbulence, repolarization dynamics and variability — in predicting mortality, as well as different modes of death in patients with CHF. (Cardiol J 2008; 15: 313–323)

Key words: congestive heart failure, Holter monitoring, risk stratification, heart rate variability, heart rate turbulence, repolarization dynamics

Introduction

Congestive heart failure (CHF) is an increasingly widespread, costly and deadly disease, frequently named as epidemics of the XXI century. The population of patients with CHF is growing and the clinical spectrum of this group is changing with markedly increasing subgroup of patients with preserved left ventricle ejection fraction (LVEF) [1, 2]. Despite advancement in modern treatment, mortality rate in CHF patients, even those with predominant diastolic dysfunction, remains high [3].

Approximately 50–60% of CHF patients will die within 5 years of diagnosis. The prognosis worsens with advancement of heart failure and the mortality rate in patients in NYHA class IV is as high as 50% per year. The mode of death depends mainly on the NYHA functional class. Patients with less advanced CHF more frequently die suddenly, while those in NYHA class IV are more likely to die of pump failure [4, 5].

Early neurohumoral activation with sympathetic overdrive interplaying with progressive hemodynamic changes constitutes the main feature of

heart failure independently of its etiology [6]. Even though diagnosis of heart failure is based on symptoms with supporting evidence from imaging techniques, the abnormalities in electrocardiographic parameters significantly contribute to overall clinical picture and clinical decisions. Continuous ambulatory Holter ECG monitoring is not considered as a basic diagnostic method in the diagnosis of CHF, however, it may serve as a valuable tool in risk stratification. Several ECG parameters reflecting underlying structural disease, electrical instability or autonomic nervous system imbalance may be evaluated during Holter monitoring. Recent years brought an increased interest in evaluation of dynamic Holter-derived ECG markers reflecting changes in heart rate and ventricular repolarization behavior. The possibility of evaluation of dynamic parameters and the ability of prolonged ECG monitoring in the ambient setting when the patients are involved in their daily activities constitute the main advantages of Holter analysis as compared to standard surface ECG.

Traditional ECG risk predictors: Heart rhythm, heart rate, arrhythmia

Heart rhythm

With no doubt surface 12-leads ECG remains as one of the most useful tests in the diagnosis and prognosis of CHF patients, providing data on the heart rhythm, heart rate, and morphological changes in subsequent ECG curve's components. The presence of atrial fibrillation, sinus tachycardia or wide QRS is related to worse prognosis. Ambulatory ECG monitoring allows for detecting paroxysmal arrhythmias, evaluating heart rate and dynamics of arrhythmia giving insight to electrical activity of the heart during daily activities and during night hours.

Atrial fibrillation (AF) is markedly more prevalent in CHF patients than in general population [7]. In mild to moderate CHF the prevalence of AF is estimated at 10–15% while in patients with more advanced heart failure (in NYHA class IV) AF is present in up to 50% of patients [8]. Heart failure predisposes to AF and on the other hand AF may worsen the prognosis of CHF patients significantly aggravating heart failure symptoms. Several mechanistic links between heart failure and AF include volume-related atrial dilation, increased dispersion of refractoriness in atria, catecholamine-induced atrial fibrosis, and atrial channel remodeling [9]. There are conflicting data as to whether the presence of chronic atrial fibrillation is an independent

predictor for an increased mortality in heart failure [10–19]. AF was found to be an independent predictor of mortality in the Framingham study [10]. In heart failure populations of the Vasodilators in Heart Failure Trial (V-HeFT) [11] and the Prospective Randomized Study of Ibopamine on Mortality and Efficacy (PRIME) [12] studies, AF was not identified as a significant predictor of mortality, whereas analysis of data from the Studies of Left Ventricular Dysfunction (SOLVD) showed that AF was a significant predictor of mortality as well as a predictor of CHF hospitalizations [13]. Data from the Carvedilol or Metoprolol European Trial (COMET) further added to controversy by showing that AF was not predictive of mortality in heart failure patients [14]. On the other hand, new occurrence of AF, especially coinciding with heart failure decompensation was shown to be a marker of worse prognosis [20].

As both rate control and rhythm control strategies are nowadays accepted in management of AF patients, prolonged Holter recording is useful for monitoring appropriate ventricular response rate. Criteria for adequate rate control vary with patient age but usually achieving ventricular rates between 60 and 80 beats per minute at rest and between 90 and 115 beats per minute during moderate exercise is indicated [21]. Tachycardia-related unfavorable impact of AF on CHF has been recognized for years, however the question whether tachycardia itself or heart rate irregularity related to AF are responsible for the worsening of heart failure remains open [22]. On the other hand, data exists indicating that lower, and not higher rates in AF patients, may be associated with worse prognosis [23]. In a subpopulation of 77 patients with advanced heart failure and AF from PRIME II study, lower heart rate (< 80 bpm) was an independent predictor of all-cause mortality during a mean of 3.3 years follow up (HR = 2.9; CI = 1.4–5.8, p = 0.002).

Heart rate

Heart rate is probably the easiest ECG parameter to assess, however the results of different studies evaluating its prognostic value yield conflicting results. Unfavorable tachycardia is a common feature in CHF related to sympathetic overdrive. The adequate control of the heart rate is essential in all, not only AF patients, with heart failure. Prolonged heart rate monitoring is nowadays included in home-monitoring systems in CHF patients, being one of the markers of the need for therapy modification [24]. High resting heart rate is well accepted risk predictor for all-cause mortality, but its relation to cardiac and sudden death remains

controversial. Similarly, no consensus exists on the high risk cut off value of heart rate [25–27]. Last decade brought ongoing interest in evaluation of possible benefits of pharmacological heart rate reduction. Beta blockers have been documented to reduce total mortality as well as sudden death. As documented by metaanalyses, reduction in heart rate achieved with beta blockers use was related to better survival in CHF patients [28, 29]. The higher heart rate reduction was, the higher benefit in context of mortality risk was observed. In the CIBIS Trial the heart rate reduction was the most powerful multivariate predictor of survival [30]. Subsequent CIBIS II trial documented that both baseline heart rate as well as heart rate reduction were independently associated with outcome in CHF patients [31]. It is worth emphasizing that the majority of data from clinical trials indicating unfavorable impact of resting tachycardia on outcome in CHF patients is based on heart rate assessed either during physical examination or from surface ECG. Suprisingly, in respect to CHF patients few data is available on the prognostic value of mean heart rate assessement on Holter monitoring, which should be more reproducible than a single heart measurement during a clinical visit. On the other hand studies based on Holter monitoring showed that not only high resting heart rate but also heart rate range during 24 hours, expressed by simple parameter as delta heart rate, may identify patients at risk of progressive pump failure death [32, 33]. Delta heart rate, defined as a maximum circadian change in heart rate over 24 hours during Holter monitoring was independently related to death due to pump failure in a cohort of 190 patients with CHF in NYHA class II–III (HR = 3.7, CI = 1.7–8.2, p = = 0.0013 for Δ heart rate ≤ 50 bpm [32]. Similarly, in a study of Baker and Koeling based on 355 patients with dilated cardiomyopathy not only mean heart rate but also the heart rate range during Holter monitoring were predictive of mortality (RR = 0.99, p = 0.008 per bpm). Patients with heart rate range equal or less than 76 bpm had significantly worse survival as compared to those with higher values [33].

Ventricular premature beats

Ventricular premature beats (VPB) as well as their complex form like couplets or ventricular tachycardia (VT) runs are frequently observed in patients with CHF. The presence of premature ventricular beats has been documented in up to 85% of patients with severe heart failure [34–36]. Relationship between ventricular arrhythmia and sudden death is not clear, however the majority of trials showed a significant correlation between the presence of nonsustained VT and cardiac death [37–40]. In Captopril-Digoxin Multicenter Study [37] VPB, couplets and nsVT were univariate predictors of total mortality. The presence of at lest 2 episodes of nsVT was related with 3-fold increase in total mortality, and was an independent predictor of sudden death. In V-HeFT II study [38] nsVT and pairs identified patients with increased mortality. GESICA trial [39] documented that nsVT was associated with increased risk for both all-cause mortality, and sudden death. There is also data demonstrating that length, but not the rate, of nsVT increases the risk of major arrhythmic events [41]. Spontaneous sustained ventricular tachycardia is infrequent in Holter recordings, but if present, predicts sudden death [42]. Even though ventricular tachycardia is considered as a marker of arrhythmic events, its role as a risk stratifier for both arrhythmic and non-arrhythmic death may be supported by observation from MADIT II trial where appropriate therapy by an ICD for VT/VF was associated with an increased risk for heart failure and non-sudden death [43].

Holter-derived risk predictors related with autonomic nervous system and repolarization

Heart rate variability (Table 1)

Heart rate variability (HRV) is a measure of the cyclic variation of normal-to-normal RR intervals that reflects cardiac autonomic function and may be considered as a marker of sympathetic and parasympathetic influence on the modulation of heart rate. Therefore, evaluation of HRV has become one of the integral component of autonomic nervous system assessment in different subsets of patients, especially in those with underlying structural heart disorders. Patients with CHF, even those with predominant diastolic dysfunction, have decreased spontaneous heart rate variability [44, 45]. The extent of HRV reduction correlates with the advancement of CHF expressed by measurements of ejection fraction, NYHA class or BNP levels [46].

Decreased HRV has been for years considered as an independent and strong marker of risk for all cause mortality or heart failure death [47], while data on predicting sudden death is conflicting. It is difficult to compare the predictive value of HRV parameters in prognosis of CHF patients, as they have been analyzed by different methods and in different time intervals [48–61]. Early reports on

Table 1. Prognostic value of heart rate variability (HRV) and heart rate turbulence (HRT) in patients with congestive heart failure.

Author	No. of patients	Studied population	Follow-up (av.)	Results
HRV				
Nolan et al. [49]	443	UK Heart Study CHF, class I–III NYHA; mean LVEF 41%	482 days	Annual mortality of 51.4% for SDNN < 50 ms; SDNN < 50 ms — RR = 9.4 (4.1–20.6) for total mortality and RR = 2.54 (1.50–4.30) for heart failure death; not predictive for sudden death
Ponikowski et al. [50]	102	CHF, NYHA class II–IV; mean LVEF 26%; 76% ischemic etiology	584 days	SDNN, SDANN and LF predictive for mortality 1 year mortality 22% in pts with SDNN < 100 ms
Boveda et al. [51] Galinier et al. [52]	190	CHF, NYHA class II–IV; mean LVEF 28%, 45% ischemic etiology	22 months	SDNN < 67 predictive for all-cause mortality (RR = 2.5, CI = 1.5–4.2) InLF < 3.3 predictive for sudden death (RR = 2.8, CI = 1.2–8.6)
Bilchick et al. [53]	127	CHF-STAT Study II–III NYHA class; mean LVEF 26%; 75% ischemic etiology	34 months	SDNN < 65.3 predictive for all-cause mortality (RR = 3.72) and borderline significant (p = 0.08) for sudden death (RR = 2.40)
Fauchier et al. [61]	116	Idiopathic dilated cardiomyopathy; mean LVEF 34%	53 months	SDNN < 100 ms predictive for sudden death
La Rovere et al. [55]	202	CHF mild to moderate; mean LVEF 24%	3 years	Controlled breathing LF < 13 ms^2 predictive for sudden death
Hadase et al. [56]	54	CHF; mean LVEF 40% in survivors	19.8 months	VLFln < 6 predictive for all cause mortality
HRT				
Grimm et al. [67]	242	Marburg Study Dilated idiopathic cardiomyopathy; mean LVEF 30%	41 months	TO as predictor of transplant free survival. TO and TS — only univariate predictors of major arrhythmic events
Koyama et al. [66]	50	CHF; mean EF 39%, 32% ischemic etiology	26 months	Abnormal TS (≤ 3 ms/RR) predictive for death and hospitalizations for heart failure (HR = 10.2, CI = 3.2–37.5)
Kawasaki et al. [70]	104	Hypertrophic cardiomyopathy	27 months	HRT failed to predict death and arrhythmic events
Moore et al. [68]	358	UK Heart Study CHF, class I–III NYHA; mean LVEF 41%	5 years	Abnormal TS (≤ 2.5 ms/RR) predicts heart failure decompensation
Klingenheben et al. [74]	114	Frankfurt Dilated Cardiomyopathy database; mean LVEF 28%	22 months	HRT not predictive for arrhythmic events
Cygankiewicz et al. [73]	607	MUSIC Trial CHF, NYHA class II–III; mean LVEF 37%, 50% ischemic etiology	44 months	Abnormal TS (≤ 2.5 ms/RR) and HRT2 predictive for all-cause mortality, sudden death and heart failure death (for HRT2 HR = 2.52; 2.25 and 4.11, respectively for modes of death)

CHF — congestive heart failure; NYHA — New York Heart Association; LVEF — left ventricle ejection fraction, SDNN — standard deviation of NN, SDANN — standard deviation of averaged NN intervals, LF — low frequency, RR — relative risk, CI — confidence interval, VLF — very low frequency, TO — turbulence onset, TS — turbulence slope, EF — ejection fraction, HR — hazard ratio, HRT — heart rate turbulence

predictive value of HRV showed that reduced HRV parameters were related with 20-fold increased risk of death in patients awaiting heart transplantation [48]. Standard deviation of NN intervals (SDNN) is the best known, best validated and easiest HRV parameter, however different cut-offs were proposed as predictive. In the UK-Heart Study SDNN below 50 ms was associated with death due to progressive heart failure, but failed to predict sudden death [49]. The other studies indicated SDNN below 100 ms [50], 67 ms [51], or 65.3 ms [53] as predictors of mortality in CHF patients. There is a constant trend in all the published studies toward high prognostic value of depressed HRV in predicting heart failure death and all-cause mortality.

Even more controversies exist in terms of frequency domain components. The findings of these studies are difficult to compare mainly due to different methodological approaches. Decreased LF and VLF component are the most frequently reported HRV spectral measures related with mortality in CHF patients [55, 56]. In a study by La Rovere et al. [55] low frequency power measured from short term recordings during controlled breathing was found to be a powerful predictor of sudden death in 202 patients with moderate to severe CHF [55]. Different components of spectral analysis were documented to be related to different types of death. In a group of 330 CHF patients in NYHA class I–III decreased night-time VLF was related to progressive heart failure, while decreased night-time LF values were associated with sudden death [57]. Non-linear measures of heart rate variability were also reported as markers of mortality in CHF patients [58, 59]. Recently published study by Maestri et al. [60] aimed to compare several nonlinear HRV methods, in predicting mortality in patients with CHF. The authors of this study demonstrated that despite differences in prognostic values, assessment of nonlinear indices provides important prognostic information on top of clinical data.

Prognostic role of HRV in prediction of sudden death remains controversial, however the majority of studies demonstrated no prognostic significance of HRV in predicting sudden cardiac death (SCD). Only a study of Fauchier et al. [61] showed that reduced SDNN < 100 ms was independent risk predictor of sudden death and arrhythmic events in patients with dilated cardiomyopathy. The paucity of clear evidence for the association between depressed HRV parameters and SCD might be due to the difficulty in categorizing the sudden or arrhythmic nature of death, but also could be due to lack of strong evidence for this association. The auto-nomic nervous system operates differently in various patients depending not only on the disease but also on the advancement of the disease process. Heart rate variability parameters successfully predict CHF worsening and total mortality in CHF patients indicating that autonomic dysfunction is a part of the overall clinical picture in such patients, but these parameters seem to have little or no prognostic significance for predicting SCD in such patients.

Heart rate turbulence (Table 1)

Heart rate turbulence (HRT), defined as a biphasic reaction of sinus node in response to a premature ventricular beat, consisting of an early acceleration and subsequent deceleration of heart rate, was introduced into electrocardiology in 1999, and since then has been proved as a powerful predictor of mortality in postinfarction patients [62–65]. Blunted HRT reaction has been observed in various subgroups of patients with cardiomyopathies and heart failure independently on the underlying etiology [66–69]. Only patients with hypertrophic cardiomyopathy did not differ in terms of HRT values from control subjects [70]. It has been suggested that HRT, considered as vagally-dependent effective measure of baroreflex sensitivity [71, 72] related to the advancement of heart failure, might be used as a marker of congestive heart failure staging [69, 72].

Data on the predictive value of HRT in patients with cardiomyopathies and/or heart failure remain limited. The majority of data related abnormal HRT with progression of disease [66–68, 73]. In the Marburg Study [67] turbulence onset was found a significant predictor of transplant free survivals in 242 patients with idiopathic cardiomyopathy. In a study of Koyama [66] including 50 patients with heart failure (both of ischemic and idiopathic etiology) abnormal turbulence slope defined as > 3 ms/RR was predictive for progression of heart failure including deaths and hospitalizations due to CHF worsening. These observations were confirmed by data from UK Heart Study in patients with mild to moderate heart failure where abnormal turbulence slope was found to be an independent risk predictor of death due to decompensated heart failure [68]. Studies including patients with nonischemic cardiomyopathy failed to demonstrate the usefulness of HRT in predicting arrhythmic events [67, 70, 74]. Our group as the first documented that abnormal HRT, especially turbulence slope predicts not only total mortality and heart failure progression, but also sudden death in 607 CHF patients in NYHA class II–III of both ischemic and non-ischemic etiology, from

MUSIC Trial. Abnormal heart rate turbulence was found in our study to be predictive for mortality, regardless of the classification of mode of death. However, consistent with postulated mechanisms of HRT relating this phenomenon to abnormal baroreflex sensitivity and autonomic imbalance, abnormal HRT showed a trend toward a stronger association with heart failure death than with sudden death. Similarly to previous reports, turbulence slope was a significant risk stratifier for all modes of death, while turbulence onset was predictive only for total mortality and heart failure death (Fig. 1) [73].

Repolarization dynamics (Table 2)

Static measures of QT duration and QT dispersion have been for years considered as risk factors in patients with CHF, however their predictive value was usually overwhelmed by clinical covariates [75–79]. Several different methods have been described to evaluate dynamicity of repolarization [80–82]. Our group reported increased number of peaks of prolonged QTc interval, e.g. the proportion of QTc intervals above the prespecified threshold (QTc > 500 ms) as a marker of life-threatening arrhythmias in postinfarction patients [81]. Similarly to coronary patients increased percentage of QT peaks was found in patients with dilated cardiomyopathy as compared to healthy subjects [83]. In recent years, QT/RR slope analyzed from long term Holter recordings has become the most popular method to evaluate QT adaptation to changing heart
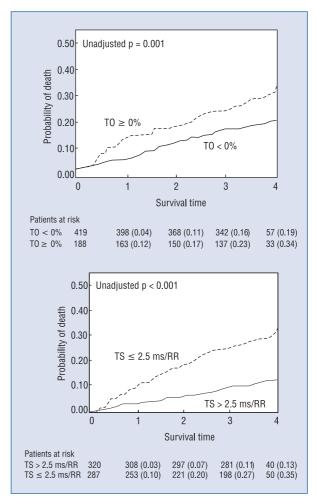

Figure 1. Cumulative probability of death according to abnormal values of turbulence onset (TO) and turbulence slope (TS) in the MUSIC Study.

Table 2. Prognostic value of QT dynamicity in patients with congestive heart failure.

Author	No. of patients	Studied population	Follow-up	Results
Pathak et al. [88]	175	CHF, class II–III NYHA, 43% ischemic etiology; mean LVEF 28%	av. 30 months	QT/RR > 0.28 predictive for total mortality (HR = 2.2, CI = 1.24–3.9) and for sudden death (HR = 3.4, CI = 1.43–8.40)
Iacoviello et al. [90]	179	Idiopathic dilated cardiomyopathy; mean LVEF 34%	39 months	QTe/RR > 0.19 predictive for major arrhythmic events HR = 1.38 (1.02–1.85) for 0.05 increase in QT/RR
Watanabe et al. [89]	121	CHF, 84% in NYHA class III–IV, 30% ischemic etiology; mean LVEF 41% in survivors	34 ± 17 months	QT/RR > 0.17 predictive for cardiac death (HR = 4.73, CI = 1.37–18.7) and for sudden death (HR = 11.2, CI = 3.28–21.4)
Cygankiewicz et al. [91]	542	MUSIC Trial CHF, in NYHA class II–III, 49% ischemic etiology; mean LVEF 37%	44 months	Daytime QTe/RR > 0.22 predictive for total and cardiac mortality (HR = 1.58, CI = 1.07–2.32), not predictive for sudden death

CHF — congestive heart failure; NYHA — New York Heart Association; LVEF — left ventricle ejection fraction, HR — hazard ratio, CI — confidence interval, QTe — QTend
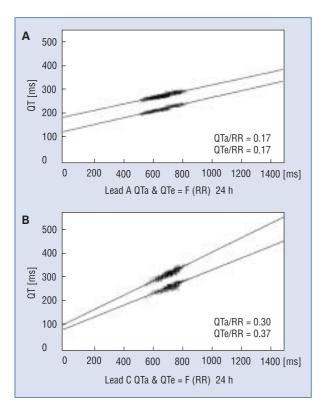
Figure 2. Exemplary QT/RR slopes of a low-risk (**A**) and a high risk (**B**) patient. Steeper slopes are observed in a high risk patient as compared to a low-risk; QTa — QTapex; QTe — QTend.

rate. Steeper slope indicates inappropriate shortening of QT interval at higher heart rate and excessive lenghtening of QT during low heart rate- both mechanisms significantly contributing to the risk of arrhythmic events (Fig. 2). From the pathophysiological point of view steeper QT/RR indicates decreased vagal tone and increased sympathetic activity reflecting the higher vulnerability of myocardium to arrhythmias. At the cellular level sympathetic stimulation prolongs ventricular refractoriness. Therefore, increased QT slope represents increased vulnerability of myocardial substrate to its modulation by autonomic nervous system. Increased QT/RR slopes were observed in patients at risk of cardiac death including postinfarction patients, long QT syndrome patients, and patients with dilated cardiomyopathy [82–87]. Abnormal QT dynamicity was found to predict cardiac events in various populations, mainly in postinfarction patients [82, 84]. Data on prognostic value of QT dynamicity in patients with CHF is limited. In a study by Pathak et al. [88] increased QTe/RR slope assessed over 24 hours was found to be predictive for total mortality and sudden death in a population of 175 patients with chronic heart failure due to ischemic (43%) or idio-

pathic (57%) cardiomyopathy with mean LVEF 27.8%. Of note, the predictive value of QT/RR was higher for prediction of sudden death than of overall mortality. The second study by Watanabe et al. [89] confirmed that QT/RR slope > 0.17 is predictive of total mortality (HR = 4.73, CI = = 1.37–18.7, p = 0.013) and also independently associated with sudden death (HR = 11.2, CI = = 3.28–21.4, p = 0.001) in patients with CHF. Independent prognostic value of QT dynamicity in patients with idiopathic dilated cardiomyopathy was reported by Iacoviello et al. [90] who found that abnormal QT dynamicity was significantly associated with arrhythmic events (VT/VF or SCD) during mean 39-month follow up. At multivariate analysis only the QTe-slope (> 0.19), decreased LVEF and nsVT were independent predictors of poor outcome. The combination of these 3 variables identified the group at the highest risk. It is worth emphasizing that QT/RR allowed for identification of higher risk group among patients with low EF (< 35%). The probability of arrhythmic events in patients with LVEF < 35%, nsVT and increased QT/RR slope was as high as 40%. In our MUSIC Trial in CHF patients with mild to moderate CHF we documented that abnormal QT dynamics expressed as increased daytime QT/RR slopes (> 0.20 for QTa and > > 0.22 for QTe) were independently associated with increased total mortality in multivariate analysis after adjustment for clinical covariates with respective hazard ratios 1.57 and 1.58 p = 0.002. None of the dynamic repolarization parameters was associated with increased risk of SD in the entire population [91].

QT interval being influenced by a variety of factors may change not only in terms of its duration but also morphology. QT variability is an ECG phenomenon consisting of beat-to-beat changes in repolarization duration and morphology appearing without the 2:1 pattern typical for T-wave alternans. These beat-to-beat changes in the T wave amplitude and shape as well as in QT duration, similarly to what is observed in case of QT dynamics, can be analyzed by several novel computerized ECG methods enabling for detection and quantification of subtle, microvolt-level changes, which otherwise remain undetected by the naked eye [92].

There is an increasing interest in the analysis of QT variability in Holter recordings. Berger et al. developed a time-stretching algorithm to quantify changes in repolarization duration and morphology and documented that patients with CHF have increased variability when compared to age-matched healthy subjects [93]. Increased beat-to-beat changes in repolarization duration and morphology

predisposes to electrical instability of the myocardium and may favor initiation and maintenance of reentry arrhythmias. As recently documented by Piccirillo et al. [94], abnormal QT variability can identify high SCD risk group among asymptomatic patients with only mild to moderate left ventricular dysfunction. In a group of 396 patients with congestive heart failure due to ischemic cardiomyopathy with LVEF between 35% and 40% and NYHA class 1, QT variability index greater or equal to the 80th percentile (–0.47) indicated an independent high risk for SCD with hazard ratio of 4.6 (1.5–13.4, p = = 0.006). This finding might suggest that abnormal QT variability may serve as a marker to identify possible candidates to ICD therapy among patients with a moderately depressed LVEF, however this requires further prospective studies.

Conclusions and recommendations

Electrocardiographic parameters based on ambulatory Holter monitoring have been documented to be independent risk predictors of total mortality and progression of heart failure. It seems that modern Holter monitoring may serve also as a valuable tool for investigating factors that may contribute to the mechanism of sudden death. It is widely accepted that structural changes reflecting myocardial substrate are better identified by means of imaging techniques, Holter monitoring on the other hand provides complementary information on myocardial vulnerability and autonomic nervous system. Nevertheless, data regarding its prognostic value in prediction of SCD remains controversial and the positive predictive value of the majority of Holter-based risk stratifiers is low. Therefore, combining of electrocardiographic stratification with assessment of myocardial substrate may provide the complex insight into interplay between factors contributing to death. On the other hand, negative predictive value of Holter risk markers is usually high, therefore it may be used to identify low risk patients.

It is not likely that one specific ECG risk predictor could be found to predict total and sudden death in a heterogeneous population of patients with congestive heart failure. Therefore, it seems that the combination of various ECG risk markers covering different arms of SCD risk triangle may be considered as better approach (Fig. 3).
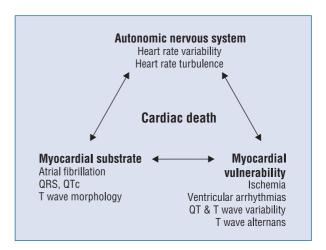
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Figure 3. Factors contributing to cardiac death and corresponding Holter-derived ECG parameters.

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