

CLINICAL APPLICATIONS OF HEART RATE VARIABILITY

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ABSTRACT

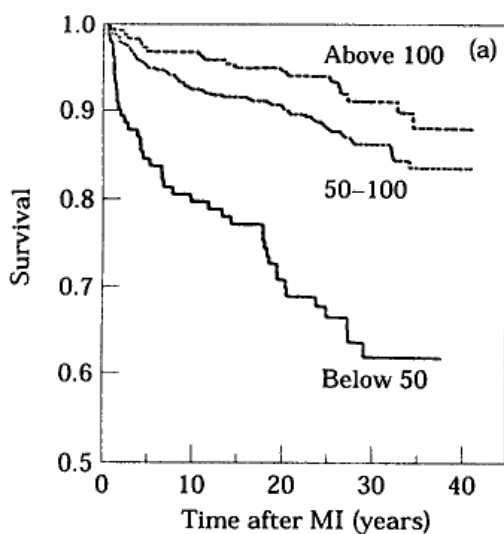
Although HRV has been the subject of many clinical studies targeting a wide range of cardiac and non-cardiac diseases and clinical conditions, consensus on the practical application of HRV in medicine has been achieved in only two clinical scenarios. A decrease in HRV can be used as a predictor of risk after acute myocardial infarction and as an early sign of the development of diabetic neuropathy.

Keywords: heart rate variability, heart attack, HRV

Risk assessment after acute myocardial infarction

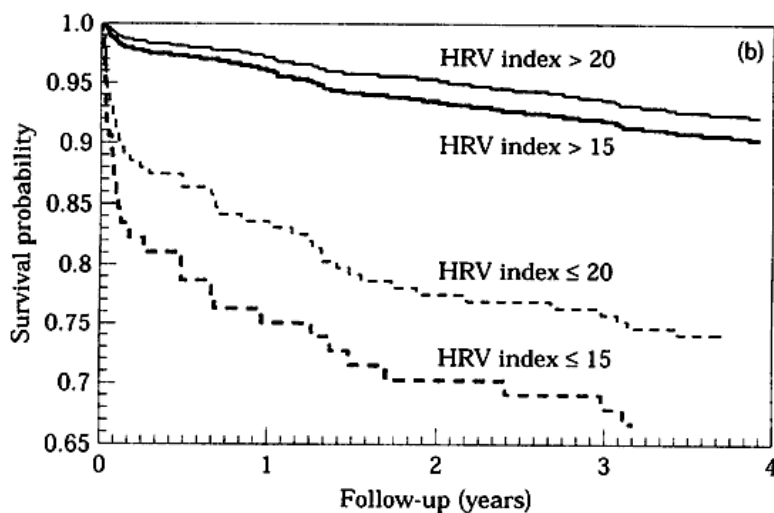
The fact that in patients after acute myocardial infarction, the absence of respiratory sinus arrhythmia is associated with an increase in in-hospital mortality was the first in a number of observations that demonstrated the prognostic value of HRV assessment for identifying patients at risk.

Reduced HRV is a significant predictor of mortality and arrhythmic complications (eg, symptomatic sustained ventricular tachycardia) in patients with acute MI. The predictive value of HRV is independent of other factors used to stratify post-MI risk, such as decreased left ventricular ejection fraction, increased ectopic ventricular activity, and the presence of late ventricular potentials. In order to predict overall mortality, the value of HRV is comparable to the value of the left ventricular ejection fraction, but exceeds it in relation to the prediction of arrhythmias (sudden cardiac death and ventricular tachycardia). This allows one to speculate that HRV is a more significant predictor of arrhythmic mortality than non-arrhythmia mortality. However, there were no clear differences between HRV in patients who died suddenly and not suddenly after an acute MI. However, this can be explained by the peculiarities of the definition of sudden cardiac death, which includes not only death from cardiac arrhythmias, but also fatal reinfarctions and other acute cardiovascular disorders.



Rice. 1. Cumulative survival rate of patients after myocardial infarction.

Graph (a) shows survival stratified according to the 24-hour SDNN score into three groups at 50 and 100 ms levels. (Reproduced with permission [16]). Graph (b) shows similar curves stratified according to the 24-hour triangular HRV index at levels 15 and 20 (data from St. George's Post-infarction Research Survey Program)



The value of conventional time and frequency response analysis has been extensively explored in several independent prospective studies, but due to the use of optimized breakpoints defining normal and reduced HRV, these studies may slightly overestimate the predictive value of HRV. Despite this, due to the sufficient volume of the studied populations, the confidence intervals of such boundary values are rather narrow. Thus, the analysis criteria for 24-hour HRV, namely $SDNN < 50$ ms and a triangular HRV index < 15 for severely reduced HRV, or $SDNN < 100$ ms and a triangular index < 20 for moderately reduced HRV, can be widely applied.

It is not known whether different measures of HRV (eg, determination of short-term and long-term components) can be combined in a multivariate analysis to improve post-MI risk stratification. There is, however, a consensus that the combination of other measures with HRV appears to be redundant.

Pathophysiological aspects

To date, it has not been established whether reduced HRV is part of the mechanism responsible for the increase in postinfarction mortality, or whether it is simply a marker of poor prognosis. Evidence suggests that reduced HRV is not simply a reflection of increased sympathetic or decreased vagal tone due to decreased ventricular contractility, but also characterizes decreased vagal activity, which is closely related to the pathogenesis of ventricular arrhythmias and sudden cardiac death.

HRV assessment for risk stratification after acute myocardial infarction

Traditionally, HRV, used for risk stratification after AMI, is estimated from a 24-hour recording. HRV measured from short ECG recordings also carries prognostic information for risk stratification after AMI, but whether such a method is comparable in significance to 24-hour recording remains unknown [133-135]. HRV, assessed by short electrocardiograms, is reduced in high-risk patients; the prognostic value of reduced HRV increases with the duration of registration. Thus, the use of 24-hour recordings may be recommended for stratification studies after AMI. On the other hand, the analysis of short-term records can be used for primary screening of patients who survived AMI [136]. This assessment has a similar sensitivity,

Spectral analysis of HRV in patients with AMI suggests that VLF and ULF components have a high prognostic value. Since the physiological meaning of these components is unknown and they account for up to 95% of the total power in the analysis of temporal characteristics, the use of individual HRV spectral components for risk stratification after AMI is no more significant than the analysis of those temporal parameters that estimate HRV as a whole.

Dynamics of HRV after acute myocardial infarction

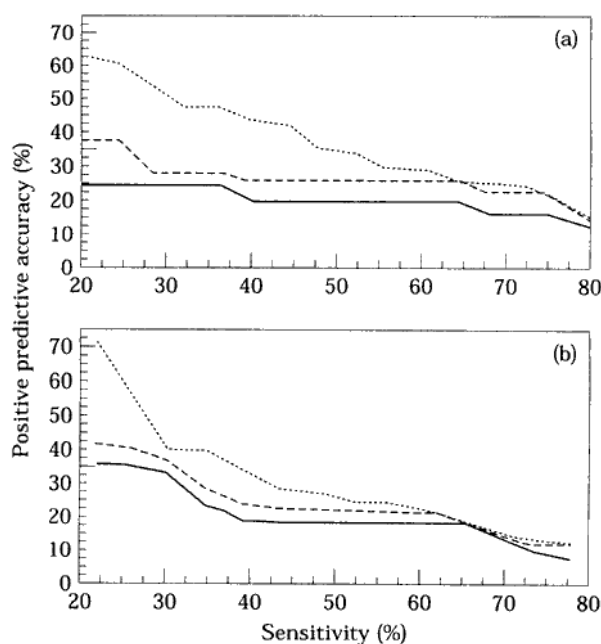
The time period after AMI, during which the HRV decline reaches its highest predictive value, has not been adequately investigated. Despite this, it is generally accepted that HRV should be assessed shortly before discharge from the hospital, i.e. approximately 1 week after the infarction. This recommendation fits well with standard hospital practice regarding the management of post-AMI patients.

HRV declines shortly after an MI and begins to recover within a few weeks. Recovery peaks (but does not return to baseline) 6–12 months after AMI [91, 137]. Assessment of HRV both at the early stage of AMI (after 2-3 days) and before discharge from the hospital (after 1-3 weeks) carries important prognostic information.

HRV assessed later (1 year after AMI) also predicts future mortality [138]. Animal data suggest that the rate of HRV recovery after AMI correlates with risk later on [115].

Using HRV for multivariate risk stratification

The predictive value of HRV by itself is quite modest, but when combined with other methods, it significantly increases its positive predictive accuracy in the clinically important sensitivity range (25-75%) for cardiac death and arrhythmias (Fig. 2).



Rice. 2. Comparison of the positive predictive characteristics of HRV (solid lines) and combinations of HRV with left ventricular ejection fraction (dashed lines) and HRV with left ventricular ejection fraction and number of ectopias on 24-hour records (dotted lines) used to identify the risk of cardiac death in within one year (a) and arrhythmic events within a year (sudden death and/or symptomatic sustained ventricular tachycardia (b) after acute myocardial infarction (data from St. George's Post-infarction Research Survey Program)

Positive predictive accuracy has been reported to increase by combining HRV with mean heart rate, left ventricular ejection fraction, ectopic ventricular activity, high-resolution ECG parameters (eg, presence or absence of late potentials), and clinical examination data [139]. It is not known, however, which of the additional stratification factors are most significant in practice and most appropriate for combination with HRV for multivariate risk stratification.

In order to reach a consensus and develop recommendations on the combination of HRV with other practically significant indicators, it is necessary to conduct systematic multivariate studies on risk stratification after AMI. A number of aspects that are unacceptable for univariate risk stratification need to be studied: it is not known how suitable for multivariate analysis are the boundary indicators that are optimal for

individual risk factors according to the results of univariate studies. It is likely that analysis of various multivariate combinations is needed to optimize predictive accuracy in various sensitivity ranges. Staging strategies should be evaluated to develop optimal diagnostic test sequences used in multivariate stratification.

Summary and recommendations for interpreting the predictive value of reduced HRV after acute myocardial infarction

The following information should be considered when using HRV estimates in clinical trials and/or studies with post-MIA patients.

Reduced HRV is independent of other known risk factors as a predictor of mortality and arrhythmic complications.

There is consensus that HRV should be assessed approximately 1 week after infarction.

Although HRV estimated from short recordings carries some predictive information, 24-hour HRV analysis is a more significant predictor of risk. HRV estimated from short-term recordings can be used for the initial screening of all survivors of AMI.

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