Heart Rate Variability: An Old Metric with New Meaning in the Era of Using mHealth technologies for Health and Exercise Training Guidance. Part Two: Prognosis and Training

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Abstract
It has been demonstrated that heart rate variability (HRV) is predictive of all-cause and cardiovascular mortality using clinical ECG recordings. This is true for rest, exercise and ambulatory HRV clinical ECG device recordings in prospective cohorts. Recently, there has been a rapid increase in the use of mobile health technologies (mHealth) and commercial wearable fitness devices. Most of these devices use ECG or photo-based plethysmography and both are validated for providing accurate heart rate measurements. This offers the opportunity to make risk information from HRV more widely available. The physiology of HRV and the available technology by which it can be assessed has been summarised in Part 1 of this review. In Part 2 the association between HRV and risk stratification is addressed by reviewing the current evidence from data acquired by resting ECG, exercise ECG and medical ambulatory devices. This is followed by a discussion of the use of HRV to guide the training of athletes and as a part of fitness programmes.

Keywords
Heart rate variability, exercise, athletic training, mobile health technologies, prognosis, athletic performance

Disclosure: David Hadley and Victor Froelicher are partial owners and developers of ECG analysis software Cardiac Insight. There is no mention of their products in this review. Nikhil Singh, Kegan James Moneghetti, Jeffrey Christie and Daniel Plews have no conflicts of interest to declare.

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DOI: https://doi.org/10.15420/aer.2018.30.2

Estimation of Prognosis Using HRV
The association of heart rate variability (HRV) and prognosis, both for all-cause and cardiovascular (CV) mortality, has been studied using ECG at rest, with exercise and in the ambulatory setting. A meta-analysis by Hillebrand and colleagues found that, using both resting and ambulatory ECG monitoring, lower HRV is associated with a 32–45 % increased risk of first CV event in patients without known CV disease.1 Additionally, elevated HRV demonstrates a protective effect, with an increase in standard deviation of the normalised NN interval (SDNN) of 1 % resulting in an approximate 1 % reduction of fatal or non-fatal CV disease event.

Resting ECG for HRV Prognosis
The Zutphen study assessed HRV obtained from resting ECGs in 878 men aged 50–65 years, referred as the middle-aged cohort, who were followed up 15 years later.2 Participants from the original cohort method of analysing 900 patients without CAD and using successive R-R intervals (RMSSD), and percentage of R-R intervals that differ by 50 ms (pNN50).3 Demographic-adjusted survival analysis showed increased RR of all-cause death and incident coronary artery disease in the lowest tertile compared with intermediate and highest tertiles for all variables. RR of mortality for SDNN in the lowest tertile compared with intermediate and highest tertiles (<30 ms) was 2.10 compared with the intermediate group.

Yoo and colleagues compared HRV with the Framingham Risk Score to determine if HRV values could serve as an acceptable substitute for a CHD risk assessment.4 The study involved 85 adults using resting ECG measurements in the seated position taken after 20 minutes of rest.

The Rotterdam study enrolled 5,272 patients aged 55 years (mean = 69 ± 9) and acquired 10-second rest 12-lead ECGs.5 SDNN values were put into quartiles with the 25th, 50th, and 75th percentiles corresponding to values of 9.6 ms, 15.2 ms, and 25.9 ms, respectively. The investigators found that patients in the lowest quartile had an 80 % increase (HR 1.80, 95 % CI [1.0–3.2]) for cardiac mortality compared with patients in the third quartile after adjustments for age and sex. Patients in the highest quartile had the most pronounced adjusted risk for cardiac mortality (HR 2.3, 1.3–4.0), suggesting that low or high SDNN can be associated with mortality in an older population.

The Atherosclerosis Risk In Communities (ARIC) study used a case-cohort method of analysing 900 patients without CAD and using 2-minute ECGs, SDNN, root mean square of the differences in successive R-R intervals (RMSSD), and percentage of R-R intervals that differ by 50 ms (pNN50).3 Demographic-adjusted survival analysis showed increased RR of all-cause death and incident coronary artery disease in the lowest tertile compared with intermediate and highest tertiles for all variables. RR of mortality for SDNN in the lowest tertile (<30 ms) was 2.10 compared with the intermediate group.

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Table 1: Nomenclature for Common Heart Rate Variability Measurements

| Abbreviation | Units        | Description                      |
|--------------|--------------|----------------------------------|
| SDNN         | ms           | Standard deviation of NN intervals|
| SDRR         | ms           | Standard deviation of RR intervals|
| pNN50        | %            | Percentage of successive RR intervals that differ by more than 50 ms |
| RMSSD        | ms           | Root mean square of successive RR interval differences |
| HF           | ms/Hz/nu     | High-frequency power             |
| LF           | ms/Hz/nu     | Low-frequency power              |

Patients with Framingham risk > 10% were found to have significantly depressed SDNN, RMSSD, and in high-frequency (HF) values. These signals, however, appeared to be isolated to men and there was no statistically significant relationship between Framingham risk score and HRV among women in this small cohort.

These findings extend to cohorts with established CV disease. Studying only patients with dilated cardiomyopathy, La Rovere and colleagues found reductions in HRV to be predictive of sudden death. A resting ECG of 8 minutes’ duration was obtained with spontaneous respiration, as well as a controlled breathing period. Patients with dilated cardiomyopathy were found to have reductions in low frequency (LF) power with spontaneous (30 ms² versus 45 ms², p=0.01) and controlled-breathing (28 ms² versus 41 ms², p=0.02). Reduced LF power during controlled breathing was found to be predictive of sudden death during a 3-year follow-up period (RR 2.8, 95% CI [1.2–6.8]), independent of left ventricular dimensions.

Resting HRV measurements have been used to link enhanced sympathetic autonomic nervous system (SANS) activity with myocardial destabilisation and arrhythmogenic potential. HRV, however, serves as an indirect measurement of SANS, given its action on baroreceptors and the sinoatrial node. Periodic repolarisation dynamics (PRD), which can be obtained by focusing on low-frequency patterns of resting 3D ECGs, may serve as a more direct measurement. Factors that lead to heterogeneous sympathetic activation, such as previous MI, diabetes, and inherited channelopathies, are all associated with greater PRD at rest. Previous studies have shown resting PRD to predict post-MI mortality independent of established risk factors such as left ventricular ejection fraction, the Global Registry of Acute Coronary Events (GRACE) score, increased QT-variability index, and reduced HRV. These findings extend to cohorts with established CV disease. Studying patients from the original Framingham study, Tsuji et al found an increased risk of all-cause mortality in patients with depressed HRV. Using 2-hour ambulatory ECG monitoring, the investigators considered 736 patients from the original Framingham study. They found that, with adjustment for age, sex, and clinical risk factors, patients 1 SD below the mean for SD of NN intervals (SDNN), LF, very LF (LFV), HF, and total power all had increased risks of all-cause mortality over 4 years. SDNN was the only time-domain factor with elevated risk after adjustment (HR 1.38, 95% CI [1.13–1.70], p=0.019). Decreased values of LF were associated with highest adjusted risk (1.70, 95% CI [1.37–2.09], p=0.001) of all HRV parameters. Additionally, a study combining patients from the original Framingham study and the Framingham Offspring Study (n=2,501, average age 53 years), demonstrated that with 2-hour ambulatory ECG monitoring, patients with lower SDNN had significantly higher rates of heart disease (12.40 versus 2.06).

A long-term prospective study by Kikuya reported results from ambulatory BP data obtained from 1,542 subjects (mean 62 years, 40% male) in Japan. BP and HR measurements were taken every 30 minutes using an ambulatory cuff-oscillometric device, as the patients went about their normal day and night routines. Patients were divided by SDNN into three groups (mean - SD, mean + SD, mean + SD) for analysis. A significant inverse linear relationship was noted for daytime HRV and cardiovascular death (p=0.008) during the mean follow-up period of 8.5 years, even after adjustment for use of beta blockers. The lowest HRV tertile was found to have HR of 3.64 (p=0.02). Changes in night-time HRV did not show a similar risk of CV death. The Autonomic Tone and Reflexes After MI (ATRAMI) study considered the prognostic value of SDNN in 1,284 patients with recent MI. Patients with MI within the previous 28 days were enrolled in the study and followed with ambulatory Holter monitoring for SDNN analysis. Baroreflex sensitivity was also assessed by measuring rate-pressure response to infusion of phenylephrine. Multivariate analysis showed that patients with SDNN <70 ms or baroreflex sensitivity <3 ms/mmHg showed increased risk of cardiac mortality. In patients with depression of both parameters, 2-year mortality was 17% compared with 2% in patients where the parameters had remained stable. Klieger et al. demonstrated similar post-MI results with a RR of mortality of 5.3 in post-MI patients with SDNN <50 ms in those that had >100 ms. The Gruppo Italiano per lo Studio della Sopravvivenza nell’Infarto Miocardico (GISSI-2) study analysed the usefulness of HRV in patients who had a recent MI that had been treated with fibrinolytic therapy. Of 567 patients, 7.8% died of cardiovascular causes during 1,000 days of follow-up. HRV parameters exhibited elevated RR for SDNN (RR 3.0), RMSSD (RR 2.8) and NNS0 (RR 3.5).

While often used to predict mortality, a review by Reed et al looked at HRV as a predictor of ventricular tachyarrhythmias (VTAs). Vybrial et al showed no consistent changes in HRV indices in 24 patients who wore Holter monitors and developed ventricular fibrillation. Huijker et al, however, found significant reductions in HR and HRV indices (SDANN, HF, LF) in post-MI patients who developed ventricular tachycardia compared with those without arrhythmic events. These changes occurred in the 1-hour period preceding VTA, and the degree of reduction was more pronounced in patients with sustained arrhythmias. Shusterman et al demonstrated that the presence of a change in HRV alone, within a 2-hour period before arrhythmic events, could predict the development of VTAs.
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**Table 2: Mortality Risk Associated with Various Heart Rate Variability Measurements Using Ambulatory ECG**

| Study Name              | Number of Patients | Monitoring Method       | HRV Parameters          | Conclusions                                                                 |
|-------------------------|--------------------|-------------------------|-------------------------|-----------------------------------------------------------------------------|
| Zutphen study           | 878 (middle-aged cohort) 885 (elderly cohort) | Resting ECG, 15–30 sec | SDNN                    | SDNN <20 ms associated with increased risk of CHD (RR 2.1, 95 % CI [1.1–4.1]) and all-cause mortality (RR 2.1, 95 % CI [1.4–3.0]) respectively |
| Rotterdam study         | 5,272              | Resting ECG, 10 sec     | SDNN                    | SDNN in lowest and highest quartiles had increased risk of cardiac mortality: HR 1.8 (95 % CI [1.0–2.3]) and 2.3 (95 % CI [1.3–4.0]) respectively |
| ARIC study              | 900                | Resting ECG, 2 min      | SDNN, rMSSD, SSSD, pNN50 | Increased risk of all-cause mortality for patients in the lowest tertile of all parameters (RR 1.47–1.91) |
| Yoo et al. 2011†        | 85                 | Resting ECG             | SDNN, rMSSD, VLF, LF, HF, LF/HF, TP | SDNN (28ms versus 36ms, p=0.037), rMSSD (28ms versus 29ms, p=0.007), and LF/HF (4.7ms versus 5.5ms, p=0.008) are depressed in patients with FRS >10 % |
| La Rovere et al. 2003†  | 444                | Resting ECG, 8 min      | SDNN, LF and HF         | Increased risk of sudden death with reduced LFP (RR 2.8, 95 % CI [1.2–6.8], p=0.02) |

FRS = Framingham risk score; HF = high frequency power; HRV = heart rate variability; LF = low frequency power; LF/HF = low frequency to high frequency power ratio; ln HF = natural log of the high-frequency measurement; pNN50 = percentage of RR intervals that differ by 50ms; rMSSD = root mean square of the differences between successive intervals; SDANN = standard deviation of median 5-minute A-A intervals; SDAN = standard deviation of all R-R intervals; TP = total power; VLF = very low frequency power.

**Table 3: Mortality Risk Associated with Various Heart Rate Variability Measurements Using Resting ECG**

| Study Name              | Number of Patients | Monitoring Method       | HRV Parameters          | Conclusions                                                                 |
|-------------------------|--------------------|-------------------------|-------------------------|-----------------------------------------------------------------------------|
| Tsuji et al. 1994‡      | 736                | 2-hour ambulatory ECG   | LFP, LFF, HFP, LF/HF, TP, SDNN, rMSSD, pNN50+ | All HRV parameters except LFP/HF associated with increased risk of cardiac events (p=0.016–0.0496); adjusted HR for lnSDNN <1 SD from mean 1.45 (95 % CI [1.13–1.85], p=0.003) |
| Tsuji et al. 1996†      | 2,501              | 2-hour ambulatory ECG   | LFP, LFF, HFP, LF/HF, TP, SDNN, rMSSD, pNN50+ | All HRV parameters except LFP/HF associated with increased risk of cardiac events (p=0.016–0.0496); adjusted HR for lnSDNN <1 SD from mean 1.45 (95 % CI [1.13–1.85], p=0.003) |
| Kikuya et al. 2000‡     | 1,542              | Ambulatory blood pressure monitor | SDNN                     | Patients in lowest tertile have increased risk of all-cause mortality (HR 3.70, p=0.003) |
| La Rovere et al. 1998‡  | 1,284              | 24-hour Holter monitor  | SDNN                    | SDNN <70 ms had increased risk of CV-related death (RR 5.3, 95 % CI [2.49–11.4], p=0.0001) compared with >105 ms |
| Klierger et al. 1987‡   | 808                | 24-hour Holter monitor  | SDNN                     | SDNN <50ms had increased risk of all-cause mortality compared with >100 ms (34 % versus 9 %, p <0.0001, RR 5.3) |
| Zuanetti et al. 1996‡   | 567                | 24-hour Holter monitor  | SDNN, rMSSD, NNN50+     | Risk of all-cause mortality elevated for NNN50+ <200, SDNN <70 ms, or rMSSD <17.5 ms (HR 2.8–3.5) |
| Adamson et al. 2004‡    | 288                | CRT-P                   | SDAAM                   | Elevated risk of all-cause mortality for SDAAM < 50 ms (HR 3.20, p=0.02) |
| Sherazi et al. 2015‡    | 719                | CRT-D                   | SDAAM                   | SDNN <93ms associated with increased all-cause mortality (HR 2.10, 95 % CI [1.14–3.87], p=0.017) |
| Nolan et al. 1998‡      | 433                | UK-Heart trial          | SDAAM                   | SDNN <93ms has all-cause mortality RR 1.62 (95 % CI [1.16–2.44]) |

CRTP = cardiac resynchronisation therapy-defibrillator; CRT-P = cardiac resynchronisation therapy pacemaker; HF = high frequency power; HRV = heart rate variability; LF = low frequency power; LF/HF = low frequency to high frequency power ratio; ln HF = natural log of the high-frequency measurement; pNN50 = percentage of RR intervals that differ by 50ms; rMSSD = root mean square of the differences between successive R-R intervals; SD = standard deviation; SDAAM = SD of 5 min median A-A intervals; SDNN = SD of 5 min R-R intervals; SDAAD = standard deviation of NN intervals; SDNNk = mean SD of all R-R intervals; TP = total power; VLF = very low frequency power.

Focusing on patients with an ejection fraction lower than 35 %, New York Heart Association (NYHA) functional class III or IV, and QRS duration >130 ms, Adamson and colleagues sought to assess the feasibility of implantable cardiac resynchronisation devices for prognostic purposes in an ambulatory setting. Using atrial intervals, HRV was defined as the standard deviation of median 5-minute a-a intervals over each 24-hour period (SDAAM). They found that the patients with the lowest SDAAM (<50 ms) had the highest all-cause mortality (HR 3.2, p=0.02) and CV-related death (HR 4.4, p=0.01) compared with higher SDAAM values over a 12-month follow-up period. Additionally, absolute SDAAM values were lower in the inpatients who were included in the study.

The Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronisation Therapy (MADIT-CRT) trial followed patients with ejection fraction lower than 30 %, QRS duration >130 ms, and non-ischaemic heart failure with NYHA functional class I or II, randomising them to either cardiac resynchronisation therapy (CRT-D) or ICD alone. In a retrospective analysis of these patients, Sharazi et al found that...
| Study                  | Number of Participants, Sex and Fitness Level | Exercise | HRV Measurement Timing | HRV Analysis Method | HRV Recording Method | Main Findings                                                                 |
|-----------------------|---------------------------------------------|----------|------------------------|---------------------|----------------------|-------------------------------------------------------------------------------|
| Uusitalo et al. 1998  | 9 F, endurance trained athletes             | Individualised training programme, progressively increased training load for 6−9 weeks; 4−6 weeks of recovery training | Before and after 4 weeks, after 6−9 weeks of training; after 4−6 weeks of recovery training | TD, FD              | 5-min supine (0.2 Hz respiration rate)                                       | Overtrained athletes trend of lowered HRV for four weeks of overload and raised HRV after recovery period; non-overtrained athletes had raised HRV for duration of the training period. |
| Uusitalo et al. 2000  | 9 F, well-trained                           | 6−9 weeks | Before and after 4 weeks and after 9 weeks | TD, FD              | 25-min supine, 5 min standing                                           | Lower HRV after heavy training supine rest/over-training. Lower HRV after standing. |
| Hedelin et al. 2000   | 6 M, 3 F elite canoeists                     | 6 days of overload training (50 % raised training load) | Before and after the 6-day training camp | FD                  | Supine and 70° vertical tilt (0.2 Hz respiration rate), duration not reported | No change in HRV                                                            |
| Hedelin et al. 2000   | 1 junior skier                               | Monitored during training period | Pre, post and recovery | FD                  | Supine and head tilt (12 breaths/min respiration rate)                   | Raised HRV during OT; lowered HRV during recovery. |
| Bosquet et al. 2003   | 9 M, well-trained endurance athletes         | 4 weeks of overload training (100 % more than usual) + 2 week recovery | Baseline, after 4 and 6 weeks | FD                  | 5 h nocturnal period (spontaneous respiration)                           | No change in HRV; lower performance, higher fatigue, reduced Lctₓ⁻ₓ. |
| Mount et al. 2004     | 7 with overtraining syndrome, 8 controls; 8 endurance trained | Diagnosed as having overtraining syndrome | After a diagnosis of overtraining syndrome | FD                  | Electrocardiographic 20 min supine, 10 min tilted 60°                     | Lowered HRV when suffering from OT syndrome. |
| Baumert et al. 2006   | 5 M, 5 F endurance trained athletes          | 2-week overload training | 1 week before training, after 1 week of training and after four days of recovery after training | TD, FD              | Supine (no specific details given)                                        | Lowered HRV following overload period, raised HRV following recovery period. |
| Hyynen et al. 2006    | 6 M, 6 F, 6 F, 6 F, 6 F, 6 F, 6 F, 6 F, 6 F | Post-training period | 3−6 weeks after overtraining diagnosis | TD, FD              | During sleep and 5 min supine rest upon waking                           | No change in HRV during sleep, overtrained had a lower HRV upon waking.       |
| Hyynen et al. 2008    | 6 M, 6 F, 6 F, 6 F, 6 F, 6 F, 6 F, 6 F, 6 F | Post-training period | 3−6 weeks after overtraining diagnosis | TD, FD              | Supine, orthostatic and relaxation                                      | Overtrained had a lower HRV orthostatic, HRV supine and relaxation. |
| Plews et al. 2012     | 1 F NFOR 1 M control                         | 77-day period; 23-hour training (4 3) per week | Morning resting every day; values averaged over 1-week | TD                  | Morning resting, 5 min supine                                           | Lowered HRV in overtrained group. |
| Dupuy et al. 2013     | 11 M endurance athletes                      | 3 week, 2 week overload, 1 week taper | Pre/post 2 week overload, post 1 week taper | TD, FD              | Nocturnal HRV over 4 hours and during SWS                               | Lowered HRV during SWS, no change to HRV in 4-hour recording during FOR.    |
| Plews, et al. 2013    | 3 M Olympic gold medalists FOR                | 62-day period prior Olympic Gold medal trials | Every day, values averaged over 1 week | TD                  | Morning resting 5 min supine                                            | Raised HRV during FOR. |
| Le Meur et al. 2013   | 21 M triathletes                             | 3-week overload period to FOR | Every-day; values averaged over 1 week | TD                  | Morning resting Supine 8 min, standing                                  | Raised HRV during FOR supine and standing 7 min. |
| Schmitt et al. 2013   | 47 elite nordic skiers. 27 M, 30 F           | Over 4 year period during fatigued and non-fatigued state | Before training on various occasions | FD                  | Resting 8 min supine, 7 min standing                                    | Lowered HRV when fatigued. |
| Tian et al. 2013      | 34 F wrestlers                               | During 11 international competitions during 2007, 2010, 2011 | Resting values weekly | TD, FD              | Supine HRV using Omega Wave standardised procedure                       | Large changes in HRV associated with both FOR and NFOR.                      |
| Bellinger et al. 2016 | 15 M runners/ triathletes                    | 1 week light, 2 weeks heavy, 10-day taper | Morning resting every day; values averaged over 1 week | TD                  | Morning resting Supine, standing                                      | Raised HRV standing. No change to HRV supine during FOR.                    |
| Bellinger et al. 2017 | 12 M cyclists                                | 1 week light, 2 week heavy, 10-day taper | Morning resting every day | TD                  | Morning resting, 3 min standing                                        | Raised HRV during FOR. |
| Flatt et al. 2017     | 10 F swimmers                               | 5 weeks, 1 week baseline, 2-week overload, 2-week taper | Morning resting every day | TD                  | Morning resting, 1 min sitting                                         | Lowered HRV during overload (FOR).                                          |
| Coates et al. 2018    | 28 endurance trained                         | 1 week light, 3-week overload, 1 week recovery | Beginning of each training phase | TD                  | Supine 5 min spontaneous breathing                                     | No change to HRV during FOR.                                                |

F = female; FD = frequency domain; FOR = functionally overreaching; HRV = heart rate variability; Lctₓ⁻ₓ = peak blood lactate concentration following an incremental exercise test; M = male; NFOR = non functionally overreached; OT = overtraining; SWS = slow wave sleep; TD = time domain.
patients in the lowest tertile of SDNN (≤93 ms) had higher rates of
death or heart failure (24 % versus 17 %, p=0.004).22 Similar outcomes
were shown using frequency domain measures such as VLF (28 %
versus 14 %, p<0.001). The overall results agreed with the UK Heart
Failure Evaluation and Assessment of Risk Trial (UK-Heart) trial, which
showed increased risk of death in patients with heart failure and
depressed SDNN values.23 In their sub-study analysis, the MADIT-CRT
investigators concluded that ambulatory HRV analysis in heart failure
patients may identify patients who would most benefit from CRT; low
HRV showed no benefit with CRT-D versus ICD alone, while patients
with preserved HRV treated with CRT-D had a lower risk of death. It
appears that not only can HRV be used to assess the risk of death and
hospitalisation in patients with heart failure, but it may also be used to
determine candidates for CRT-D therapy.

Exercise HRV and Prognosis
In the first study of exercise, HRV and prognosis, Dewey and
colleagues performed time and frequency-domain HRV analysis on
R-R interval data taken from 1,335 subjects (95 % male; mean age
58 years) during the first and last 2 minutes of treadmill testing and
the first 2 minutes of recovery.24 Cox survival analysis was performed
for the 53 cardiovascular and 133 all-cause deaths that accrued during
the 5-year mean follow-up. After adjusting for potential confounders,
greater root mean square successive difference in R-R interval during
peak exercise and recovery, greater HF power and percentage of HF
power, lower percentage of LF power, and lower ratio of LF to HF
during recovery were significantly associated with increased risks for
all-cause and CV death. Of all time-domain variables considered, the
log of the root mean square successive difference during recovery
was the strongest predictor of CV mortality (adjusted HR 5.0, 95 % CI
[1.5–17.0] for the top quintile compared with the lowest quintile). Log
HF power during recovery was the strongest predictor of CV mortality
in the frequency domain (adjusted HR 5.9, 95 % CI [1.3–25.8], for the
top quintile compared with the lowest quintile). They concluded that
exercise-induced HRV variables during and after clinical exercise
testing strongly predict both CV and all-cause mortality independent
of clinical factors and exercise responses in a clinical population.

Despite the strong association found in the study by Dewey et al.,
other investigators, such as Nieminen et al., have argued that these
findings may be predominantly driven by heart rate alone.25,26 As
HRV is associated with HR physiologically (autonomic system) and
mathematically (R-R interval), further consideration of this relationship
is required to integrate these variables in risk stratification. Pradhanap
and colleagues explored this by assessing the effect of HR correction
on pre- and post-exercise HRV.27 They selected 1,288 patients from
the Finnish Cardiovascular Study cohort. Inclusion criteria included
completing a maximum effort exercise test and good quality HRV
measurement for at least 2 minutes during rest, immediately before
exercise and during post-exercise recovery. All participants were
followed for cardiac and non-cardiac mortality for a mean time
of 54 months. The investigators concluded that exercise-induced
HRV parameters (RMSSD, VLF power, LF power, p<0.001 pre- and
post-exercise) strongly predict cardiac mortality with similar but
weaker association found for non-cardiac mortality. Consistent with
contemporary data presented by Sacha et al., they showed that when
predicting both cardiac and non-cardiac mortality, weakening HRV
dependence on HR at rest improved prognostic capacity.28 Future
studies are required to quantify the clinical significance of HRV
recorded during exercise with a different HR and respiratory rate.

Rest and Exercise HRV for Training
The use of HRV as a tool to track and monitor the status of athletes
has gained much interest over recent years.29 The desire to be the best
often pushes the athlete to the fine line between the maximisation of
effective training (achieved by duration, frequency and intensity) and
ineffective training (e.g. maladaptation, non-functional overreaching
and overtraining).30 Given the fact that adaptive responses to a training
load or stimulus are individual,31-34 it is understandable that the ability
to independently assess positive or negative training adaptation would
be advantageous to athletes, sport scientists and coaches alike.

HRV and Training Maladaptation
The hypothesis behind the early detection of non-functional
overreaching (NFOR) or overtraining (OT) and fatigue is the possibility
of assuring adequate recovery through specified rest between training.
By allowing recovery based on the constantly changing dynamic of the athlete and the amount of further training needed, the
recovery optimises future performance. The performance begins to
decline if the recovery is not adequate, resulting in a continuum from
functional overreaching (F-OR), NFOR, OT and, eventually, overtraining
syndrome (OTS).32

In athletes, changes in the patterns of their autonomic nervous system (ANS) reflected by altered HRV may serve as useful objective
parameters for managing their physical fatigue. Information regarding
the extent to which the body recovers after training may provide useful
data to avoid NFOR, OT and OTS. Many studies have examined HRV
and overtraining have revealed ambivalent findings, with increases,
decreases, and no change in HRV reported (Table 4).35-38 In one case
study, a junior skier with reported OT had a substantially increased
HRV and the values subsequently decreases once the athlete had
undergone a recovery period.39 Conversely, Mourot et al.40 showed
that overtraining was associated with decreased HRV. Seven athletes
had endurance training and had been clinically diagnosed with OTS.
However, given the continuum from F-OR to OTS, and the difficulty in
deciphering between stages, these differences observed may be due to
inconsistencies in the accurate diagnosis of the fatigue stage.39,40
This may be one of the reasons why more recent studies have
focused on F-OR rather than NFOR and OT, which can be quantified
by decreases and subsequent increases in performance (after a taper
period).39,40,41 Accordingly, these data demonstrate the importance of
understanding where each athlete sits on this continuum of fatigue
(F-OR→NFOR→OT→OTS). Such knowledge is critical for the accurate
interpretation of HRV results to regulate athlete training.

Plews et al. showed substantial reductions in HRV in an NFOR elite
triathlete before a competitive race.42 It was suggested that the
equivocal findings in HRV studies considering NFOR, OT or OTS, may
also be due to problems with recording methodologies. As day-to-day
HRV values are too variable, the authors demonstrated that when
HRV were averaged over a 1-week period, they consistently showed
substantially lower HRV values because of NFOR. Such findings have
been subsequently supported by other research studies.43,44

HRV and Training Adaptation
Endurance training elicits marked changes in cardiorespiratory
function in both sedentary and active individuals, concomitant to
changes in cardiac vagal activity, as evidenced by reduced resting and
exercise HR.45 As such, the individualised nature of changes in HRV is
fundamental to its use as a marker of training adaptation.46
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Table 5: Longitudinal and Cross-Sectional Studies Related to the Effects of Long-Term Exercise Training on Vagal-Related HRV and Performance/Fitness

| Study                        | Number of Participants, Sex and Fitness Level | Exercise                                                                 | HRV Measurement | HRV Recording Method | Main Findings                                                                 |
|------------------------------|-----------------------------------------------|---------------------------------------------------------------------------|------------------|----------------------|-------------------------------------------------------------------------------|
| Hedelin et al. 2000          | 8 M, 9 F elite junior cross-country skiers and canoeists | 7 months of training during competitive season                             | Before and after 7-month training period | FD                   | 5 min supine (spontaneous respiration), 1 min supine (0.2 Hz respiration rate), 5 min 70° vertical tilt | No change to HRV after training; higher pre-training HRV related to raised VO2 max. |
| Yamamoto et al. 2001         | 7 M healthy students                          | 40 min cycling training at 80% VO2 peak four times a week (matched with raised fitness) | Pre-exercise, 10 min; 20 min post-exercise. Baseline, after 4, 7, 28 and 42 days of training | TD, FD                | 5 min seated (0.25 Hz respiration rate)                                     | Raised HRV = raised VO2 max. |
| Iellamo et al. 2002          | 7 M elite junior rowers                       | 9 months of progressively raised training load (from detrained to maximal training state) | Baseline, after 3 and 6 months (75% training load), after 9 months (100% training load) | FD                   | 10 min supine (spontaneous respiration)                                    | Lowered HRV = higher rowing performance |
| Pichot et al. 2002           | 6 M sedentary middle-aged adults              | 2 months of intensive training plus 1 month of overload                   | Baseline, 2 x during weeks 3, 5, 7, and 8 (intensive), 1 x during week 9 (transition), 2 x during week 10−14 (overload), 1 x during week 21 (post detraining) | TD, FD                | 24 hour “Holter” recording, 4-hour nocturnal period analysed (spontaneous respiration) | Raised HRV = raised VO2 max. |
| Porter et al. 2001           | 8 M elite runners                             | 3 weeks of moderate and 12 weeks of intensive training                   | End of each training phase                          | TD, FD                | 4 min 16 sec, tilt test                                                    | Higher HRV = no change to VO2 max. |
| Carter et al. 2003           | 12 M, 12 F                                   | 12 weeks (2 x 4 weeks of training, 2 week taper)                         | Beginning and end of training programme             | TD, FD                | Resting 10 min supine                                                      | Higher HRV = higher 2-mile running performance |
| Garet et al. 2004            | 4 M, 3 F swimmers                             | 3 weeks of intensive training, 2 week taper                              | Nocturnal HRV the night before competition and in the rest week, + 2 times per week in weeks 1–5 | TD, FD                | 6 hours night sleep                                                        | Higher HRV = higher swimming performance |
| Mourot et al. 2004           | 8 M sedentary adults                          | Control subjects performed 3 x 45 min sessions per week for 6 weeks     | Pre- and post-training intervention for control subjects | TD, NL                | 10 min supine, standing, steady-state exercise, seated (spontaneous respiration) | Higher HRV = higher VO2 max. |
| Atlaoui et al. 2007          | 9 M, 4 F elite swimmers                      | 4 weeks of overload, 3 weeks of taper                                    | After 27 weeks of normal training (pre-overload), after overload, after taper | TD, FD                | 5 min supine on waking (spontaneous respiration)                          | No change to HRV after training; Raised HRV = raised swimming performance |
| Manzi et al. 2009            | 8 M recreational endurance athletes          | 6 months of individualised training culminating with a marathon          | Pre-training (detrained state), after 8, 16, and 24 weeks of training | FD                   | 10 min supine (spontaneous respiration recorded rate of 0.26–0.27 Hz)      | Lowered HRV = raised marathon performance |
| Buchheit et al. 2010*        | 14 M moderately trained runners              | 9-week training programme                                                | Resting waking values measured daily, after exercise measured every 2 weeks | TD                   | 5 min supine on waking, and 3 min standing after a 5 min submaximal exercise test (both spontaneous respiration) | Raised HRV = improved 10 km running performance and MAS (responders to training) |
| Buchheit et al. 2011*        | 15 M soccer players                          | 11 days of training in heat                                               | Recorded during warm-up on days 3, 4, 5, 9, 10 and 11 | TD                   | Last 3 min of resting 5 min post-exercise                                  | Raised HRV = raised yo-yo intermittent recovery test |
| Buchheit et al. 2011*        | 55 M soccer players                          | Within 2 months of the start of the competitive season                   | Before incremental test                              | Resting 10 min        | Lowered HRV = associated raised VO2 max.                                   | |
| Buchheit et al. 2012*        | 46 M age 15.1 ± 1.5 years                    | Three consecutive tests (October, January and May)                        | Post-submaximal run in the afternoon (3 pm)        | TD                   | Resting 5 min after exercise                                                | Raised HRV = raised estimate maximal cardiiorespiratory function |
| Grant et al. 2013*           | 145 healthy 18–22 years                      | Cross-sectional                                                          | Before VO2 max testing                               | TD, FD, Poincare plot and HR | 10 min recording in the morning before midday HR accounted for 17 % of the variation in VO2 max. HR only added an additional 3.1 % | |
The changes in HRV in response to endurance training programmes have been extensively studied (Table 5). In people who have been sedentary or who have trained recreationally, endurance training for 2, 6 and 9 weeks has been shown to induce parallel increases in aerobic fitness and HRV.\(^{45,46,47}\) For example, previously sedentary men completed 9 weeks of intensive endurance training followed by 4 weeks of overload training and had large increases in maximal aerobic capacity (+20 %) and vagal-related HRV (+67 %).\(^{48}\) While this is the response typically seen in sedentary and recreationally trained people after a period of endurance training, the response in people who have an extensive training history can be decidedly different. In these athletes, the HRV response to training is inconsistent, with longitudinal studies showing no change in fitness (VO\(_2\) max uptake) despite increases in HRV, and cross-sectional studies showing lower HRV in association with superior fitness.\(^{49,50}\) In elite distance runners training for 18 weeks (6 weeks moderately intensive and 12 weeks intensive) culminating in a half marathon or marathon, there was no change in VO\(_2\) max, but a 45 % increase in HRV.\(^{51}\) Conversely, in 55 young male soccer players, lower HRV was associated with higher VO\(_2\) max and maximum aerobic speed.\(^{52}\)

Plews et al. used data from elite rowers at the Olympics.\(^{53}\) They showed a consistent HRV trend before peak performance, with substantial increases in HRV (above baseline) before a decline to baseline values as the competition approached (during a taper period). Such trends have since been validated in experimental studies by both Le Meur et al. and Bellenger et al. with athletes functionally adapting to training (F-OR).\(^{54,55}\) Le Meur et al. showed that triathletes who responded positively to 3 weeks of overload training had substantial increases in RMSSD (96 % chance of an HRV increase) followed by reductions to baseline after a 1-week taper. Those classified in the F-OR had large increases in running performance over an incremental running test (effect size 1.17 \(\pm\) 0.22). Similarly, Bellenger et al showed HRV increases in triathletes (effect size = 0.62 \(\pm\) 0.26) after a 2-week heavy training period. These increases were reduced after a 10-day taper which coincided with improved 5 km running time trial performance (effect size -0.34 \(\pm\) 0.08). Importantly, in both these studies, there were observed reductions in performance after the training overload period, when HRV was substantial higher. Accordingly, in such cases, increases in HRV are indicative of coping with intensified training (i.e. F-OR), not increases in performance. Improved performance was only observed after the taper period when HRV had reduced back towards baseline levels.

Taking these data into account, it has been suggested that there is a bell-shaped relationship between vagally related HRV and fitness/performance.\(^{56}\) This, to some extent, may also be due to HRV saturation which is often seen in athletes with extensive training histories and low resting heart rates.\(^{57}\)

### Using HRV to Guide Training

Given the usability of HRV to track training adaptations, it could be used as a tool to guide daily training. Three studies have shown training guided by the daily recordings of HRV to be superior to (increasing fitness and exercise performance) to training based on conventional methods.\(^{58,59,60}\)

Recently, Vesterinen et al. investigated the effectiveness of using HRV to prescribe training on a day-to-day basis.\(^{61}\) Forty recreational endurance runners were divided into the HRV-guided experimental training group (EXP) and traditional pre-defined training (TRAD). After a 4-week preparation training period, the TRAD group trained according to a predefined training programme including two-to-three moderate (MOD) and high-intensity training (HIT) sessions per week during an 8-week intensive training period. The timing of MOD and HIT sessions in EXP was based on HRV measured every morning. RMSSD was used to prescribe training because of its greater reliability than other HRV spectral indices.\(^{62}\) A 7-day rolling average of RMSSD was calculated because it has been proposed to be more sensitive to track changes in the training status compared with single-day values.\(^{63}\) The MOD/HIT session was programmed if HRV was in an individually determined smallest change. Otherwise, low-intensity training was performed. VO\(_2\) max and 3,000 m running performance were measured before and after both training periods. The number of MOD and HIT sessions was significantly lower (p=0.021, effect size 0.98) in the EXP group (13.2 \(\pm\) 6.0 sessions) compared with TRAD (17.7 \(\pm\) 2.5 sessions). No other differences in training were found.
between the groups. The 3,000 m run time improved in EXP (2.1 % T 2.0 %, p=0.004) but not in the TRAD group (1.1 % T 2.7 %, p=0.118) during the intensive training period. A small but clear between-group difference (effect size = 0.42) was found in the change in running over 3,000 m. VO2 max improved in both groups (EXP: 3.7 %, ± 4.6 %, p=0.027; TRAD: 5.0 % ± 5.2 %, p=0.002). They concluded that there was potential in using resting HRV to prescribe endurance training by individualising the timing of vigorous training sessions.

A study from 2018 split 17 well-trained cyclists into two groups. Group one followed a training plan guided by morning resting HRV (HRV-G, n=8), whereas group 2 followed a more traditional approach (TRAD, n=9), following a similar design to Kiviniemi, on days when the 7-day rolling average of RMSSD fell outside the predetermined individual smallest range, the HRV-G training group would carry out low intensity training (Tables 4 and 5). Following a similar design to Kiviniemi, on days when the 7-day rolling average of RMSSD fell outside the predetermined individual smallest range, the HRV-G training group would carry out low intensity training or rest rather than moderate-intensity training or HIT. The TRAD group’s training regimens included scheduled low-intensity, moderate-intensity, HIT and high-intensity interval training. There were no statistical differences in volume or intensity distribution in either group during the experimental period. Although there were no between-group differences, the HRV-G group substantially increased in peak power output (5.1 ± 4.5 %; p=0.024), upper threshold power (13.9 ± 8.8 %; p=0.004) and 40 km time trial performance (7.3 ± 4.5 %; p=0.005). The TRAD group did not improve significantly in any of these performance measures after their training period. This again supports the possible efficacy of HR-VG training being a suitable method to enhance training adaptations in athletes.

Methodological considerations are important when using HRV to monitor training in athletes. However, it is generally accepted that reductions in HRV are associated with negative performance outcomes, and increases associated with a positive response to higher training loads (Tables 4 and 5). However, such changes must be taken within the context of the training phase (i.e heavy training versus taper), and fitness status of the individual. Both supportive and opposing views have been highlighted in a recent HRV and exercise training meta-analysis by Bellenger et al. The aim of this meta-analysis was to interpret how vagally derived indices of HR could be used to inform training decisions. Focusing on HRV only here, they suggested that improved exercise performance was associated with increases in resting RMSSD (effect size = 0.58). However, there was also a small increase in resting RMSSD (effect size = 0.26) associated with decreases in performance. This supports the idea that, although HRV measures can be useful, they should still be used alongside other measures of training tolerance to aid decision-making.

### Clinical Perspective

- Resting, exercise and ambulatory heart rate variability (HRV) measurements are useful for predicting cardiovascular risk.
- The use of mHealth technologies allows acceptable ambulatory detection of HRV compared with traditional ECG methods.
- The data behind using ambulatory HRV to guide or structure athletic training programmes are limited, but there is a possible benefit in using HRV to optimise performance and prevent over-training.

### Conclusions

The past decade has shown that HRV provides valuable prognostic information that can contribute to risk scores and cardiac variables such as echocardiographic measurements and exercise capacity. There is strong evidence to suggest that elevated HRV has a protective effect against CV disease. Conversely, exercise and HRV show the opposite relationship. Greater HRV during recovery from exercise is associated with an increased risk of all-cause and cardiovascular death. However, other investigators have argued that these findings may be predominantly driven by heart rate alone and further research is required in this area. Over more recent years, the area of HRV and athlete monitoring has been investigated. It is now generally accepted that substantial reductions in HRV are associated with negative adaptations to training and HRV increases are associated with positive adaptations, with an inverted U shape being the optimal trend in HRV in athletes before they reach peak performance. Furthermore, studies that have based daily training sessions on morning resting HRV values have had mostly positive outcomes.

In the era of wearable monitoring devices and increased interest in personalised approaches to lifestyle modification, HRV may provide useful information to direct lifestyle change, guide exercise regimens and monitor for over-training. Given the advancement in wearable HRV recording devices, research is needed to understand the complex relationships between physiology and performance and day-to-day trends. Furthermore, future population studies are needed to assess the potential of HRV information acquired through wearable devices which use photo-based plethysmography and ECG technology and validate its value as a prognostic marker.
24. Nieminen T, Kähönen M, Kööbi T, et al. Heart rate variability.

14. Kleiger RE, Miller JP, Bigger JT Jr, Moss AJ. Decreased heart rate variability during overtraining in male endurance athletes.

Circulation 2000;102:1355–60. https://doi.org/10.1161/01.CIR.102.11.1355; PMID: 10948204.

15. Hynynen E, Uusitalo A, Koskelin N, et al. Cardiac autonomic nervous system responses to overload and tapering in collegiate sprint-swimmers.

Ann Noninvasive Electrocardiol 2013;18:281–8. https://doi.org/10.1111/ajen.12055; PMID: 23852425.

16. Buchheit M, Chivot A, Parouty J, et al. Monitoring endurance running performance using cardiac parasympathetic function.

Int J Sports Med 2014;35:961–9. https://doi.org/10.1055/s-0034-1369810; PMID: 25299064.

36. Buchheit M, Chivot A, Parouty J, et al. Monitoring endurance running performance using cardiac parasympathetic function.

Int J Sports Med 2014;35:961–9. https://doi.org/10.1055/s-0034-1369810; PMID: 25299064.

50. Iellamo F, Legramante JM, Pigozzi F, et al. Conversion of atrial fibrillation to sinus rhythm with catheter ablation: comparison of long-term follow-up, Append. Appl Physiol Nutr Metab 2013;38:276–91; https://doi.org/10.1111/j.1399-3137.2013.01490.x; PMID: 23842644.

51. Houle LA, Kruidenier LM, Tulppo MP. Individual responses to aerobic exercise: the role of the autonomic nervous system. Neurosci Biobehav Rev 2009;33:1559–69. https://doi.org/10.1016/j.neubiorev.2009.06.009; PMID: 18551435.

52. Mount L, Bouchardt M, Perrey S, et al. Quantitative Polcar pile testing. J Strength Cond Res 2010;24:1153–64. https://doi.org/10.1519/JSC.0b013e3181d2e6d8; PMID: 20761654.

53. Drewy FE, Freeman AV, Engel G, et al. Novel predictor of post-exercise heart rate recovery to assess physical fitness and heart rate variability response to the exercise treadmill test. Ann Med 2007;39:261–70. https://doi.org/10.1080/0003981070152999; PMID: 17581258.

54. Niemann T, Kähönen M, Keltti T, et al. Effect of heart rate control on pre- and post-exercise heart rate variability to predict risk of mortality: an experimental study on the FINCAVAS cohort. Front Physiol 2018;9:208. https://doi.org/10.3389/fphys.2018.00208; PMID: 29285693.

55. Sacha J. Interaction between heart rate and heart rate variability: implications in athletes and patients treated with antiarrhythmic/antianginal treatment. Front Physiol 2016;7:1128. https://doi.org/10.3389/fphys.2016.01128; PMID: 27702393.

56. Sellier S. What is best practice for training intensity and duration in athletes? J Sports Med Phys Fitness 2016;56:276–79. https://doi.org/10.23736/S0022-4707.15.06463-3; PMID: 27440032.

57. Bouchard C, Américo P, Robillard P, et al. Familial aggregation of GwASmax response to exercise training: results from the HERITAGE Family Study. Am J Epidemiol 1997;146:103–8; https://doi.org/10.1093/oxfordjournals.aje.a009733; PMID: 9387236.

58. National Heart, Lung, and Blood Institute: National Institutes of Health. The NHLBI Total Cardiovascular Risk Profile. Circulation 1998;98:150–6. https://doi.org/10.1161/01.CIR.98.1.150; PMID: 9796404.

59. Anderson SR, Wijeysundera DN, Abraham MP. Continuous autonomic assessment in patients with symptomatic heart failure: a comparison between heart rate variability measured by an implanted cardiac resynchronization device. Circulation 2010;121:1902–10. https://doi.org/10.1161/CIRCULATIONAHA.109.939841; PMID: 20424489.

60. Dewey FE, Freeman AV, Engel G, et al. Novel predictor of post-exercise heart rate recovery to assess physical fitness and heart rate variability response to the exercise treadmill test. Ann Med 2007;39:261–70. https://doi.org/10.1080/0003981070152999; PMID: 17581258.

61. Bellenger CR, Luntz CA, Schumacker RT. Use of heart rate variability to assess autonomic function in athletes. J Sports Sci 2001;19:743–51. https://doi.org/10.1080/026404101100840123; PMID: 11408202.

62. Houle LA, Kruidenier LM, Tulppo MP. Individual responses to aerobic exercise: the role of the autonomic nervous system. Neurosci Biobehav Rev 2009;33:1559–69. https://doi.org/10.1016/j.neubiorev.2009.06.009; PMID: 18551435.

63. Mount L, Bouchardt M, Perrey S, et al. Quantitative Polcar pile testing. J Strength Cond Res 2010;24:1153–64. https://doi.org/10.1519/JSC.0b013e3181d2e6d8; PMID: 20761654.

64. Baumert M, Brechtel L, Lock J, et al. Heart rate variability, blood pressure variability, and baroreflex sensitivity in overreached athletes. Med Sci Sports Exerc 2013;45:1642–7. https://doi.org/10.1249/MSS.0b013e318288281a; PMID: 23270162.

65. Hynynen E, Uusitalo A, Koskelin N, et al. Cardiac autonomic nervous system responses to overload and tapering in collegiate sprint-swimmers. Ann Noninvasive Electrocardiol 2013;18:281–8. https://doi.org/10.1111/ajen.12055; PMID: 23852425.

66. Buchheit M, Chivot A, Parouty J, et al. Monitoring endurance running performance using cardiac parasympathetic function.

Int J Sports Med 2014;35:961–9. https://doi.org/10.1055/s-0034-1369810; PMID: 25299064.

67. Vesterinen E, Hääkkinen K, Hynynen E, et al. Heart rate variability in prediction of in vivo cardiac autonomic nervous system function in recreational endurance runners. Scand J Med Sci Sports 2016;26:1164–76. https://doi.org/10.1111/sjms.12657; PMID: 26975418.

68. Tian Y, Zhv H, Zhao JX, et al. Heart rate variability threshold values for early-warning nonfunctional overreaching in elite Chinese gymnasts. J Strength Cond Res 2017;31:2371–8. https://doi.org/10.1519/JSC.0000000000001271; PMID: 27456544.

69. Bouchard C, Risko I, Lacroix T, et al. Heart rate variability, blood pressure variability, and baroreflex sensitivity in overreached athletes. Med Sci Sports Exerc 2013;45:1642–7. https://doi.org/10.1249/MSS.0b013e318288281a; PMID: 23270162.

70. Buchheit M, Chivot A, Parouty J, et al. Monitoring endurance running performance using cardiac parasympathetic function.

Int J Sports Med 2014;35:961–9. https://doi.org/10.1055/s-0034-1369810; PMID: 25299064.

71. Chen CC, Jeukendrup AE. Does overtraining exist? An empirical analysis of the effects of overtraining in distance runners. J Sports Sci 2002;20:1355–63. https://doi.org/10.1080/02640410210145039; PMID: 12147223.

72. Vesterinen E, Hääkkinen K, Hynynen E, et al. Heart rate variability in prediction of in vivo cardiac autonomic nervous system function in recreational endurance runners. Scand J Med Sci Sports 2016;26:1164–76. https://doi.org/10.1111/sjms.12657; PMID: 26975418.