Heart Rate Variability

FAQ

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# TABLE OF CONTENT

1. **Background: Physiology** ........................................................................................................... 3  
   a) What is Heart Rate Variability (HRV)? .................................................................................. 3  
2. **Methodology** .......................................................................................................................... 4  
   a) What do you need to obtain HRV? ......................................................................................... 4  
   b) How is HRV determined? ....................................................................................................... 5  
   c) What are the most frequently used parameters? ................................................................. 6  
3. **Clinical Aspects** ......................................................................................................................... 8  
   a) What are the important HRV findings? ............................................................................... 8  
   b) What are the important HRV findings in diseases? ........................................................... 10  
   c) What Does HRV teach about arrhythmias? ......................................................................... 12  
   d) What are the existing treatments influencing the autonomic nervous system? ............. 14  
4. **Applications** ............................................................................................................................. 15  
   a) What does “footprint“ mean? .............................................................................................. 15  
   b) How is the HRV footprint plot build up? ............................................................................ 16  
   c) Which kind of information can be retrieved? ...................................................................... 18  
5. **References** ................................................................................................................................... 21
1. Background: Physiology

a) What is Heart Rate Variability (HRV)?

Cardiovascular variables such as:
- heart rate
- arterial blood pressure
- stroke volume

all fluctuate on a beat-to-beat basis. These variations are induced by signals from the nervous system to the cardiovascular regulation. Simply put: parasympathetic (vagal) activity will lower heart rate and sympathetic activity will raise heart rate. It is a continuous balance between the activity of both antagonist systems that regulates heart rate (and other cardiovascular variables) around a mean value.

Schematic working model:

![Figure 1: Schematic Model](image-url)
2. Methodology

a) *What do you need to obtain HRV?*

**First step: ECG Registration**
The first step in obtaining HRV parameters is the recording of an ECG tracing. The duration of a recording can extend from a minimum of 10 min. to a maximum of 24 hours in Holter recordings. These signals are analog/digital converted for computer processing. In order to have a good time resolution a sampling rate of at least 200 Hz is necessary, giving a time resolution of 5 ms.

**Second step: Peak Detection**
The recognition of the QRS complex and peak detection (lower part of the figure)¹.

**Third step: RR calculations**
The distance (time) between consecutive peaks is determined: \( RR_1, RR_2, RR_3, \ldots \). Only sinus beats have to be analysed². A single premature beat causes an abrupt increase followed by a decrease in heart rate and has an impact on the HRV analyses.

Some devices only detect the QRS peaks and save the RR distances, without storing the ECG

![Figure 2: What do you need to measure HRV](image-url)
b) How is HRV determined?³

The time series of RR intervals obtained from the ECG are collected in the RR
interval tachogram.
The HRV evaluation may be performed in the Time Domain or in the Frequency
Domain⁴.

Time Domain Method:
The measurement in Time Domain determines the heart rate at any point of time
or the RR interval of the normal intrinsic complexes. The RR-histogram gives the
distribution of the RR intervals. From this figure mean value and standard
deviation of RR intervals over a time period can be obtained.

Frequency Domain Method:
The analysis in the Frequency Domain shows the power spectral density as
calculated by Fourier analyses and expressed by amplitude (ms²/Hz) versus
frequency (Hz). By definition, spectral analysis decomposes any stationary time
dependent signal into its sinusoidal components.

Two frequency components⁵ have been found: low frequency (LF): 0.04-0.15 Hz
and high frequency (HF): 0.16-0.4 Hz. The HF-components have been linked to
parasympathetic (vagal) activity and the LF more integrated to: mixed
sympathetic-parasympathetic activity and baroreflex control.
Especially for analysis in the frequency domain, only sinus beats have to be
analysed⁶. A single premature beat causes an abrupt increase followed by a
decrease in heart rate. The frequency content of the impulse-like artefact is a
broad: it adds power in the high frequency zone.

Figure 3: HRV can be measured with Time Domain or Frequency Domain Method

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c) What are the most frequently used parameters?

**Time Domain Parameters:**

**SDNN (or SDRR), (ms):** Standard deviation of the normal to normal (NN) interval over the recorded time interval. Theoretically, the heart rate variance which is equal to \((SDNN)^2\) is identical to the total power (ms\(^2\)) as determined from Frequency analyses (surface under the curve of the PSD) It represents global HRV. SDNN depends on the length of the analyzed recording. A longer recording of the same person gives a higher SDNN value.

In practice, it is inappropriate to compare SDNN measure obtained from recordings of different durations. SDNN calculated from a 24h holter recording represents the circadian variations.

**SDANN (ms):** Standard deviation of the 5-minute mean NN interval over the entire recording. As SDANN values are obtained from successive short 5-minute periods, they estimate changes in heart rate caused by cycles longer than 5 minutes. It represents long-term variations, but it provides no information about short-term variability. In practice, it’s appropriate to compare SDANN values obtained from different durations.

**rMSSD (ms):** The square root of the mean squared successive differences between adjacent RR intervals over the entire recording. It correlates more with the parasympathetic (vagal) activity (high frequency power).

**pNN50 (%):** The percentage of successive interval differences greater than 50 ms computed over the entire recording. It also reflects the parasympathetic (vagal) activity (high frequency power).
**Frequency Domain Parameters:**

**Total power (ms²):** The variance of all NN intervals represents the global activity of the autonomic nervous system.

**LF (ms²):** Power in the LF range 0.04 – 0.15 Hz represents a mixed influence of sympathetic, parasympathetic and baroreflex activity.

**HF (ms²):** Power in the HF range 0.015 – 0.4 Hz represents the parasympathetic activity, respiratory mediated.

**LF/HF:** Represents to some extent sympathovagal balance.

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**Figure 4 : Power Spectral Density (PSD)**

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3. Clinical Aspects

a) What are the important HRV findings?

Circadian variations: During daytime more LF (mostly sympathetic) activity is found and during nighttime more HF (parasympathetic vagal) is found.

Gender variations: A difference in male/female HRV parameters was found.

Ageing: Both males and females show a decrease in HRV parameters with age. Females show a dominant HF power compared to males until the age of 45-50. This behavior is possibly favoring an autonomic cardio protective effect in young and middle aged women.
Physiological: Several studies suggested a link between anxiety, hostility, depression post-myocardial infarction and reduced HRV. In a recent study it was shown that men reporting higher levels of phobic anxiety had lower HRV and hence had increased risk of sudden cardiac death. In another study all HRV parameters (with the exception of HF-component) remained significantly lower in patients with depression than in patients without depression.

Physical training: Numerous studies reported an increased HF-component and a decreased LF on the power spectrum of HRV in physically trained subjects. The fact that physical training has a distinct impact on HRV in healthy subjects implies that exercising may be of value in cardiac rehabilitation.

Smoking: The influence of smoking decreases the HF-component (decrease in parasympathetic modulation) and increase in the LF-component.

Alcohol: The influence of alcohol decreases HRV.

Caffeine: The influence of caffeine increases in HRV.

Other: The impact on HRV of other factors such as recreational drugs, air pollution, development biology, sudden infants dead syndrome, influence of gravity is under investigation.
b) What are the important HRV findings in diseases?

**Myocardial infarction:** Kleiger et al, reported a strong correlation between the SDNN and all cause mortality after MI. This initial study was followed by several studies that have confirmed these results for spectral indices, where LF was the most useful in risk stratification post-MI and the concept was also reinforced for cardiac mortality. HRV is independent of clinical and demographic factors.

**Sudden cardiac death and ventricular arrhythmias:** There is compelling evidence linking sudden cardiac death and ventricular arrhythmias to the autonomic nervous system: increased sympathetic activity appears to be proarrhythmic, whereas β-blocker therapy and enhanced parasympathetic activity counteract this arrhythmogenic insult. The combination of low values of autonomic markers and reduced left ventricular ejection fraction (EF) may thus help to identify a group of post-MI patients at high risk of cardiac death.

**Hypertension:** A reduction in HRV was found and even more of blood pressure variability.

**Diabetes mellitus:** There is a gradual decline in spectral power in the high and low frequencies with progression of the diabetic autonomic neuropathy.

**Heart failure:** Depressed HRV can be used as a marker of the extent of disease progression. Patients with CHF demonstrated autonomic dysfunction similar to that seen in MI patients, with a withdrawal of parasympathetic tone together with chronic activation of the adrenergic system and impaired arterial baroreflex sensitivity. A worsening NYHA functional class is correlated with a significant progressive decrease in time and frequency domains. Among the spectral components HF power decreased by almost 5 times and LF decreased by 3 times from NYHA class I to class II, with less decrease in higher functional class. This finding suggests that HRV analysis
could be used to detect CHF patients, the severity of the disease and evaluate response to therapeutic interventions. Although these well outlined results are still open to discussion.

Patients with a SDANN values lower then 55 msec had a 20 fold increased risk of Death\textsuperscript{42}. Therefore HRV measurements could give an indication as to the urgency of transplantation.

**Heart transplantation.**\textsuperscript{40,41,42,43} In general a reduced RR variability was consistently observed showing an almost flat Power Spectrum. Furthermore HRV was unable to detect rejection of the donor heart. HRV can be used to assess the risk of death in candidates for transplant.

*Figure 7 : 24 hours holter.*
c) **What Does HRV teach about arrhythmias?**

LF/HF balance: increased sympathetic activity (LF) may facilitate the 3 major mechanisms involved in the genesis of malignant arrhythmias, i.e. enhanced automaticity, triggered automaticity and reentry. Enhanced parasympathetic (vagal) tone (HF-component) on the other hand, will produce an increase in the ventricular fibrillation threshold and thus provides an antifibrillatory effect.

Several studies observed abrupt changes in HRV preceding an episode of atrial fibrillation, nonsustained or sustained ventricular tachycardia. These studies are either anecdotal (registration by coincidence and only few recordings) or else limited due to the R-R interval registration capabilities. The new generation of Implantable devices such as Renewal (Guidant) have integrated capabilities to measure HRV. This will give new possibilities to understand better the changes in HRV before the onset of arrhythmias. Probably also joint time-frequency techniques and methods from non-linear dynamics would have to be used to study these transition phenomena.

![Figure 8: ECG findings 1 hour and immediately before arrhythmia onset for patients with AF after CABG and either low (A) or high (B) RR interval pattern. Measured cardiac cycle length (milliseconds) for each RR interval is shown. Beat-to-beat variations in cycle length (sinus alternans) are noted in patients with high RR interval pattern. N indicates sinus beats; S, supraventricular ectopic beats. (Reprinted with permission)](image-url)
Figure 9: Left, Illustrative signals of 1024 R-R intervals as retrieved from ICDs. Short-long sequences are single ectopic beats. Right, HR spectra computed from these 2 signals. Top, Control conditions. HF peak (top right) represents respiratory sinus arrhythmia seen as fluctuations of high amplitude in R-R signal (top left). Bottom, recording before VTA onset. Sudden decrease at end of R-R signal illustrates VTA onset. Note reduced amplitude of both respiratory sinus arrhythmia and LF fluctuations (bottom left), which manifest as decreased power in overall spectrum (bottom right) compared with control conditions (top right). (Reprinted with permission)
d) What are the existing treatments influencing the autonomic nervous system?

Many treatments or therapeutic interventions have been shown to influence the control of the heart by the autonomic nervous system.

**Beta-blockers:** The most constant effect of Beta-blockers is a decrease in heart rate and an increase in HRV. This effect may play a role in protecting the myocardium and preventing ventricular arrhythmias during transient increases in sympathetic activity.

**ACE inhibitors:** Some conflicting results have been reported: an increase in parasympathetic (vagal) tone is expected, but not in other studies.

**Digitalis:** There is the same interrogation as with ACE inhibitors. In a study digoxin was associated with a significant increase in HRV, while enalapril had remarkably no effect on HRV.

**Antiarrhythmic therapy:** In a study comparing the effects of amiodarone, flecainide and propafenone on HRV, Zuanetti et al found a decrease in beat-to-beat HRV, as assessed by pNN50, with flecainide and propafenone, whereas there was no change in HRV with amiodarone.

**Ca-channel blockers:** in patients with a recent myocardial infarction, Bekheit et al found no significant effect of nifedipine on LF power. On the contrary, both diltiazem and metoprolol reduced the LF power.

**Nitrates:** activate the sympathetic nervous system.

If after drug therapy there is an activation of the sympathetic nervous system, the treatment will probably not improve survival and may even increase the risk of sudden death. However an increase in parasympathetic tone and/or decrease in sympathetic does not necessarily translate into a beneficial effect of the treatment.
4. Applications

a) What does “footprint“ mean?

The “footprint” value and “footprint” plot are a part of the “HRV monitor”, which is integrated in an Internal Cardioverter Device (ICD) with biventricular pacing capabilities (Contak Renewal, Guidant).

The footprint-plot is a new way to display the beat-to-beat heart rate variability over a period of 24 hours. The footprint-value represents the percentage of the surface used in the daily graphic (HRV footprint plot), which visualize the distribution of the R-R variability versus heart rate.

Figure 10: Footprint value of 67%, this signifies that 67% of the box is covered
b) *How is the HRV footprint plot build up?*

Every 24 hours, a new blank graph starts.

Each RR-interval is visualized by a dot on the footprint plot. the current heart rate on the x-axis and the absolute value of the difference between the RR-interval and the previous one on the y-axis.

Example:
- RR-interval: 1000 ms
- Previous RR-interval: 1050 ms

- On the x-axis (heart rate) at \[
\frac{60 \times 1000}{1000} = 60 \text{ min}^{-1}
\]
- On the Y-axis (RR variability) at 1050 – 1000 = 50 ms

In this manner, all the R-R intervals are visualized. When a dot comes on the same spot as a previous dot, the color will change.
After 24 hours the graphic is complete. The footprint value is equal to percentage of the colored surface of the white box.

Figure 13: Final “footprint” after 24 hours

A new footprint will only be displayed, if:

1. Minimum 67% of the 24 hours collection period contains valid beats.
2. The Contak Renewal pacing parameters are not reprogrammed during the last 24 hours.
c) *Which kind of information can be retrieved?*

The Footprint gives you for the last 24 hours:

**The HRV recent data:**
- Date and Time the 24-hour collection period was completed
- % of Time Used, shows the percentage of the time during the 24-hour collection period in which there were valid intrinsic beats
- Footprint value
- SDANN (ms)

**HRV footprint plot:**
- Mean heart rate (bpm = min-1)
- Min and max heart rate (bpm)

The plot portrays an “at-glance snapshot” of the distribution of variability versus heart rate over a 24-hour period.

**Device settings:**
Current normal HF/brady parameters: Pacing Mode, Lower Rate Limit, Max. Tracking Rate, AV-delay and Pacing Chamber

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As the footprint and footprint plot are a part of the HRV monitor, we can retrieve more information.

The lower part of the HRV-monitor shows a previous stored footprint plot Reference, which helps to visualize the evaluation of the different parameters of the patient.

![HRV improvement on the footprint plot after 1 month of Biventricular Pacing](image)

Carlson G et Al\(^1\), reports a correlation between the $\Delta$ footprint and $\Delta$ peak VO2.

The device stores the daily data (min-, max-, mean heart rate, footprint and SDANN) for a week, and the weekly information for a year.

![HRV Trending](image)
The footprint plot gives additional information on the programmed HF/Brady parameters such as the Lower Rate Limit (LRL).

In Case the LRL is programmed too high, the footprint plot shows a straight cut off at the programmed rate.

In certain cases it is possible to reprogram the LRL lower, to obtain a homogenize footprint plot. This will increase the footprint, which is correlated with peak VO2\textsuperscript{64}.

\textbf{Figure 17: LRL programmed at 50 min\textsuperscript{-1}.}
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