clue medical

# Explanations of terms and definitions

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## ➜ Single-channel ECG for recording application-specific ECG sections

As is already well known, the pump function of the heart arises from an electrical excitation that is normally triggered by the sinus node and runs through the heart's own conduction system to the muscle cells. The changes in electrical potential in the heart, called an electrocardiogram (ECG), can be detected at characteristic places on the surface of the body as discharges and recorded as a time function for a certain period of measurement. Since the analysis of the occurring heart beats (RR intervals) is at the center of the evaluation in the „clue medical" family, and these are the same in each lead, a single-channel ECG is sufficient. The simplest application necessary for telemedical applications can be achieved by using fixed electrodes on the back side of the housing. A second ECG amplifier enables the evaluation of other bipolar leads with adhesive electrodes.

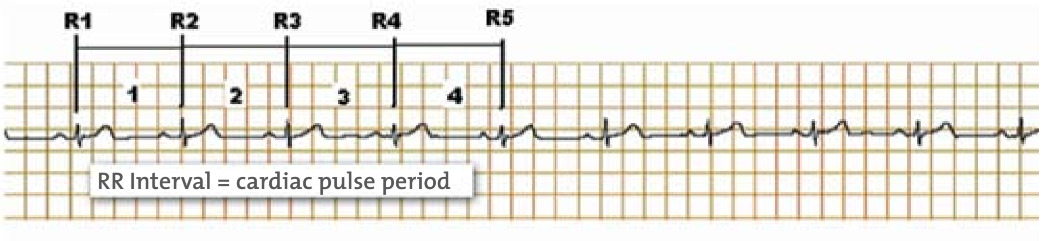


*Fig. :
Time section from
a 1-channel tele-ECG
including marked
RR-intervals as associated
heart periods*

## ➜ Period of measurement

With the aid of signal theory, it can be shown that a minimum period of measurement of 120 seconds is necessary for the quantification of the vegetative components of the cardiovascular system at the time of testing; this is the basic module of the "clue medical" family. Twenty-four hour records are also possible on the basis of this basic module; in this case, only the intervals between heart beats are recorded and transmitted.

## ➜ Autonomic nervous system

The autonomic nervous system, which consists of the sympathetic, parasympathetic and intestinal nervous systems, innervates the smooth muscles of all organs as well as the heart and glands. It regulates the functions of breathing, circulation, digestion, metabolism, glandular secretion, body temperature and reproduction that are so important to life. It cannot be arbitrarily controlled, or can barely be controlled - it is autonomic.
It is one of the two information systems between the individual organs along with the hormone system.

## ➜ Sympathetic nervous system

A component of the autonomic nervous system. It regulates the cardiovascular system, including organ activity, and causes increases in performance, elevates heart rate (pulse), blood pressure and other things, and is also an expression or measurement of stress. The organs controlled by the sympathetic nervous system are the smooth muscle fibers of all organs (vessels, intestines, excretory and sexual organs, hair, pupils), the heart muscle fibers and many glands (sweat glands, salivary glands, digestive glands). The fat cells, liver cells, renal tubuli, lymphatic tissues (e.g. thymus, spleen, lymph nodes) and parts of the immune system are also innervated by the sympathetic nervous system.



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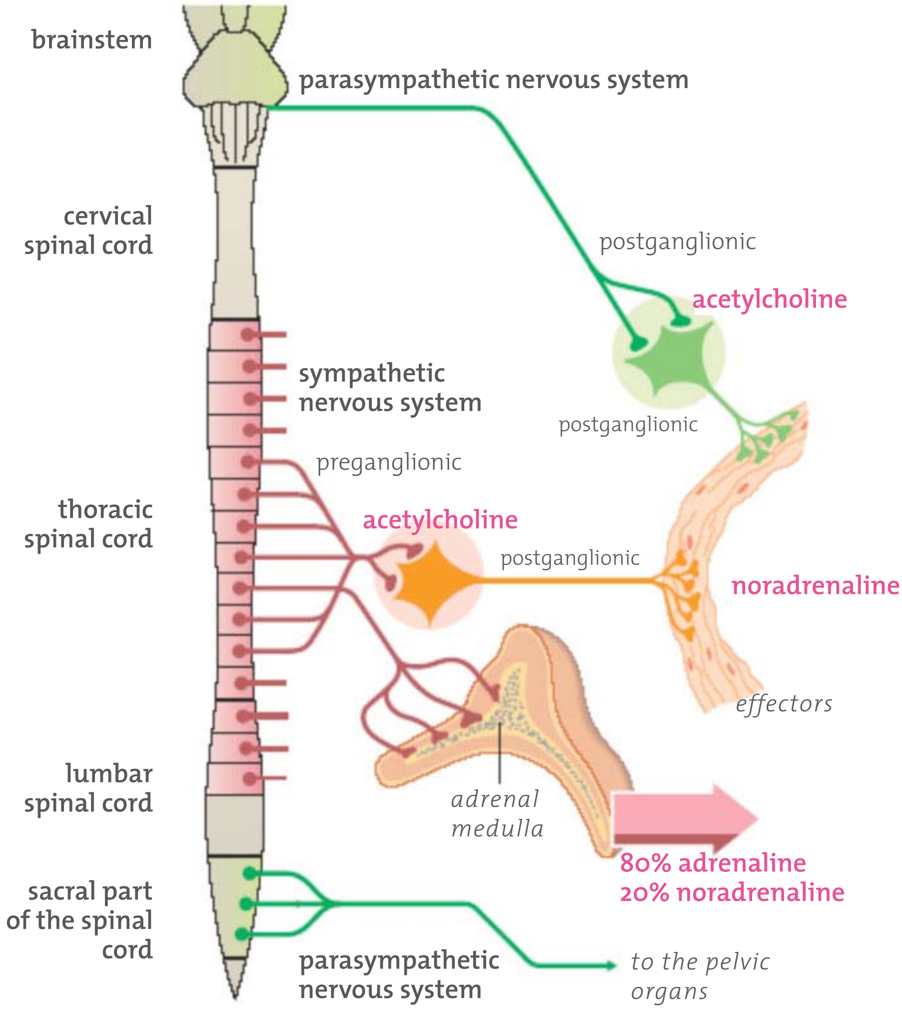
## ➔ Parasympathetic nervous system

Other components of the autonomic nervous system. It is also called the „calming branch of the nervous system“ because it serves metabolism, regeneration and the buildup of the body's own reserves. The parasympathetic nervous system provides for rest, recovery and protection and involuntarily controls most of the internal organs as well as circulation. It reduces the heart rate (pulse) and blood pressure and is strongly influenced by the breathing. The parasympathetic nervous system controls the smooth musculature and the glands of the digestive tract, the organs of elimination, the sexual organs and the lungs. It also innervates the atria of the heart, the tear and salivary glands in the head and the internal eye muscles. On the other hand, it has no direct influence on the sweat glands or the entire vascular system (with a few exceptions such as in the genital organs). As is generally known, herein lies the critical difference from the sympathetic nervous system which innervates all the vessels.

*Fig.:*
***Origin and structure of the peripheral autonomic nervous system.***

*On the left are the origins of the cellular bodies of the preganglionic neurons of the sympathetic nervous system (red) and the parasympathetic nervous system (green) in the brain stem and the different sections of the spinal cord. To the right of this is a schematic illustration of the path of the pre- and postganglionic sympathetic and parasympathetic neurons. The synaptic transfer agents of the two-tier neuronal chains of the peripheral autonomic nervous system in the ganglia and effectors as well as the nature of their postsynaptic receptors are also indicated. The adrenal medulla (bottom middle) consists of converted postganglionic sympathetic cells. Sympathetic activation of these cells (by way of preganglionic cholinergic axons) releases adrenaline (80%) and noradrenaline (20%) from them.*
*[from: G. Grohmann, Jena / Germany: Autonomes Nervensystem und Herz-Kreislauf-Funktion - zur medizinischen Anwendung von kardiovaskulären Kenngrößen, abgeleitet mit „clue medical“ der Telovital GmbH Wien (Autonomic nervous system and cardiovascular function – on the medical application of cardiovascular parameters derived using „clue medical“ from Telovital GmbH Vienna). Communication from Telovital GmbH Vienna 2008]*



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→ Tachogram of the heart period

**If, for each heart action μ within an established measurement period (e.g. 2 minutes** with „clue medical"), the associated heart period TH(μ) (i.e. the respective RR-interval) is determined, and if this is applied as a function of the corresponding heart action, then a „tachogram of the heart period" is obtained as a characteristic cardiovascular function. Such a representation therefore illustrates the fluctuations from heart beat to heart beat and therefore heart rate variability as well.
**Cardiological classification of heart rate as [heart beats per minute]** [according to Wehr M: Praktische Elektrokardiographie und Elektrophysiologie des Herzens.
Ein diagnostischer und therapeutischer Leitfaden für Studenten und Ärzte (Practical electrocardiography and electrophysiology of the heart: A diagnostic and therapeutic guideline for students and physicians). 1st Edition; Fischer Stuttgart, New York 1988]:

- **Normaler Sinusrhythmus: 60 ... 80 min$^{-1}$** [Herzperiodendauer = 750 ... 1000 ms]
- Bradykardie: ≤ 60 min$^{-1}$ [Herzperiodendauer ≥1000 ms]
- Tachykardie: ≥ 100 min$^{-1}$ [Herzperiodendauer ≤600 ms]
- Borderline: 80 ...100 min$^{-1}$ [Herzperiodendauer 600 ... 750 ms]

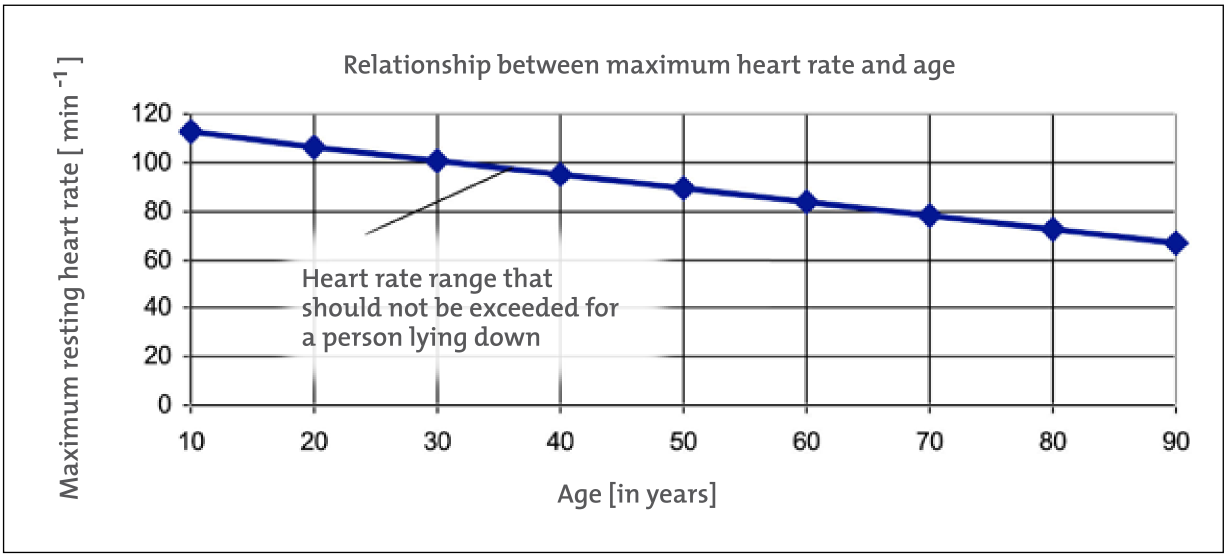


*Fig.: Relationship between the maximum resting heart rate of a person lying down and age [according to Jose, A D: Effect of combined sympathetic and parasympathetic blockade on heart rate and cardiac function in man. Am. J. Cardiol. 18 (1966), 476-478]. This shows that the maximum resting heart rate in the horizontal position normally falls with increasing age.*



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## → Heart rate variability (HRV)

Heart rate variability (HRV) is understood as fluctuations in heart rate from heart beat to heart beat over the established period of measurement. According to this, the heart beat is not normally even; instead, it fluctuates in a characteristic manner. The HRV is a parameter of the autonomic function of the heart as well as a measure of its regulatory capacity.

**Special heart rate variability measures:**
a) self-adjusting average quadratic heart period deviation during the measuring time $T_{measure}$ [basic module for „clue medical" = 120 s] for M measurements, which is called the „**standard deviation**" sTH in statistics and signal processing and corresponds to the **„absolute heart rate variability" SDNN** with the dimension „second" or [ms]:

$$\text{SDNN [ms]} = s_{TH} \text{ [ms]} = \sqrt{\frac{1}{M-1}\sum_{\mu=1}^{M}[T_H(\mu) - \overline{T_H}]^2}$$

In this equation, $\overline{T_H}$ represents the average heart period occurring during a measuring time $T_{measure}$. The corresponding reciprocal value is the average heart rate

$$\overline{f_H}\,[Hz\ bzw.\ \min^{-1}] = \frac{1}{\overline{T_H}}$$

b) If the absolute heart rate variability SDNN is based on the average heart period $\overline{T_H}$ of the established measurement time, then a non-dimensional measurement is obtained, which is usually indicated as a **„relative heart rate variability" CV** in percent:

$$\text{CV [\%]} = \frac{s_{TH}\text{ [ms]}}{\overline{T_H}\text{ [ms]}}\ 100\text{ [\%]}$$



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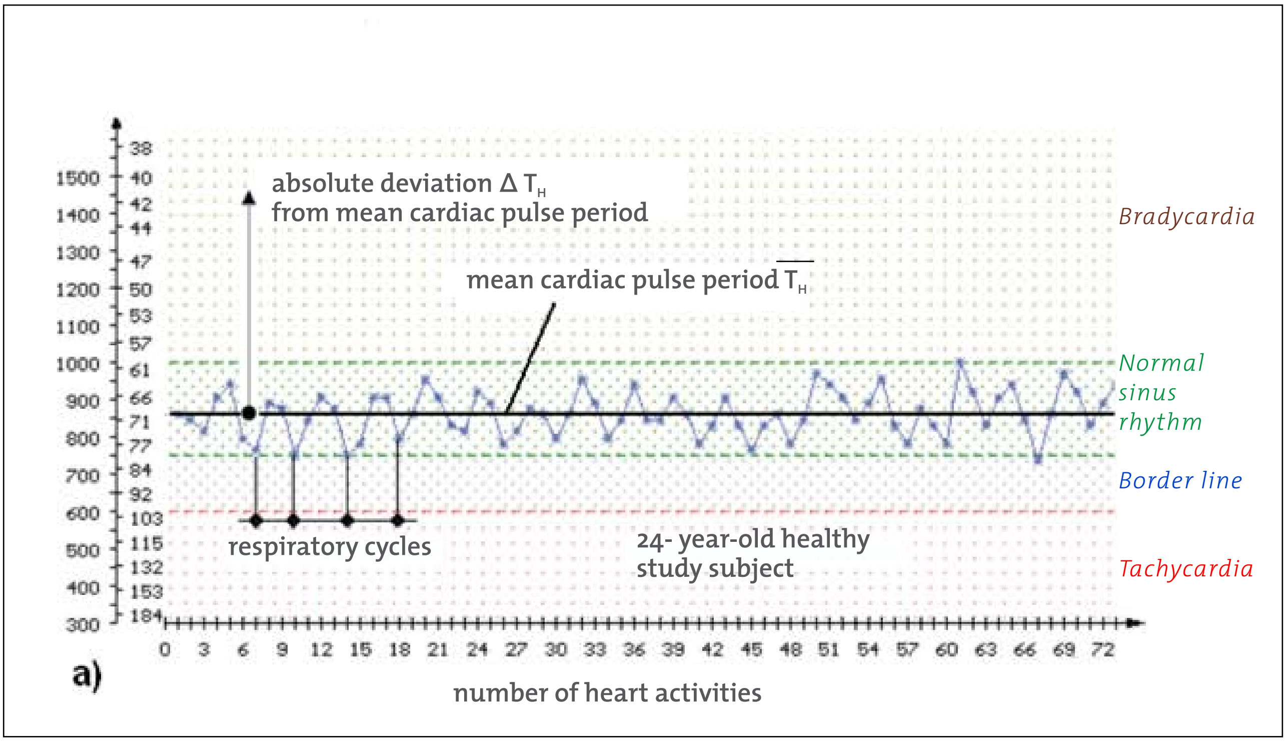


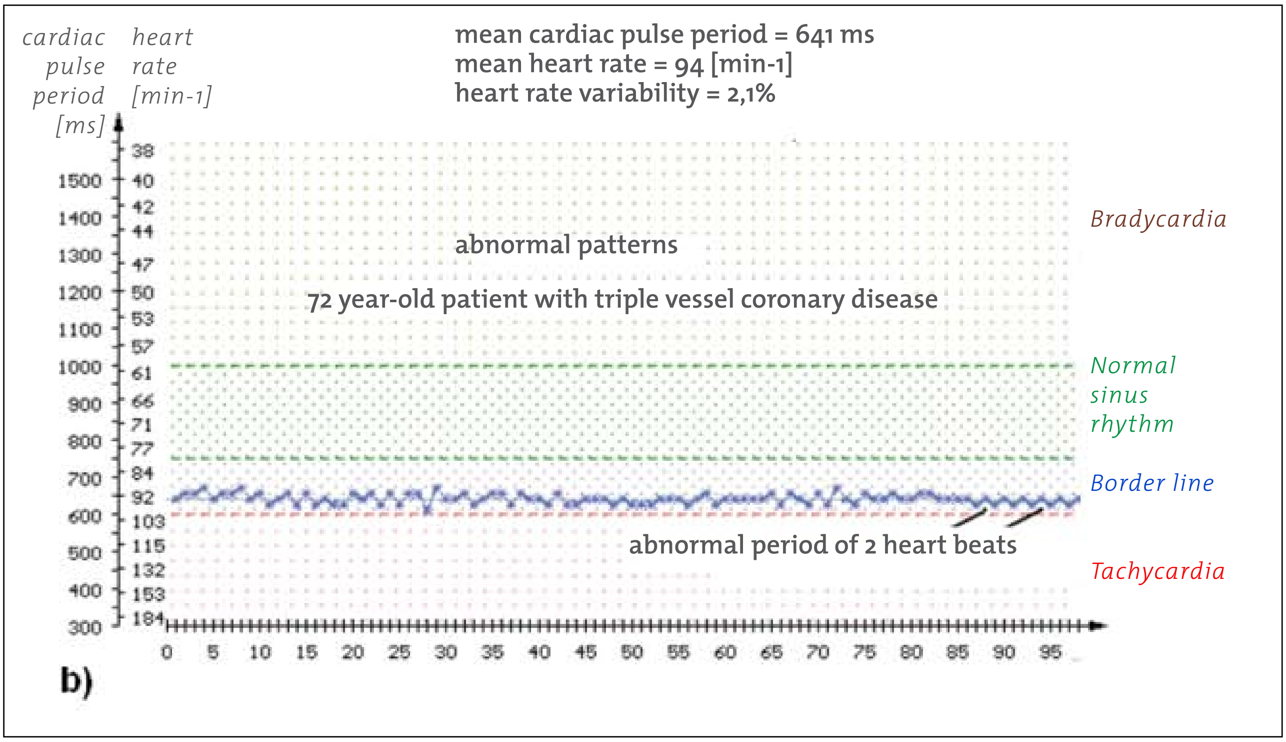
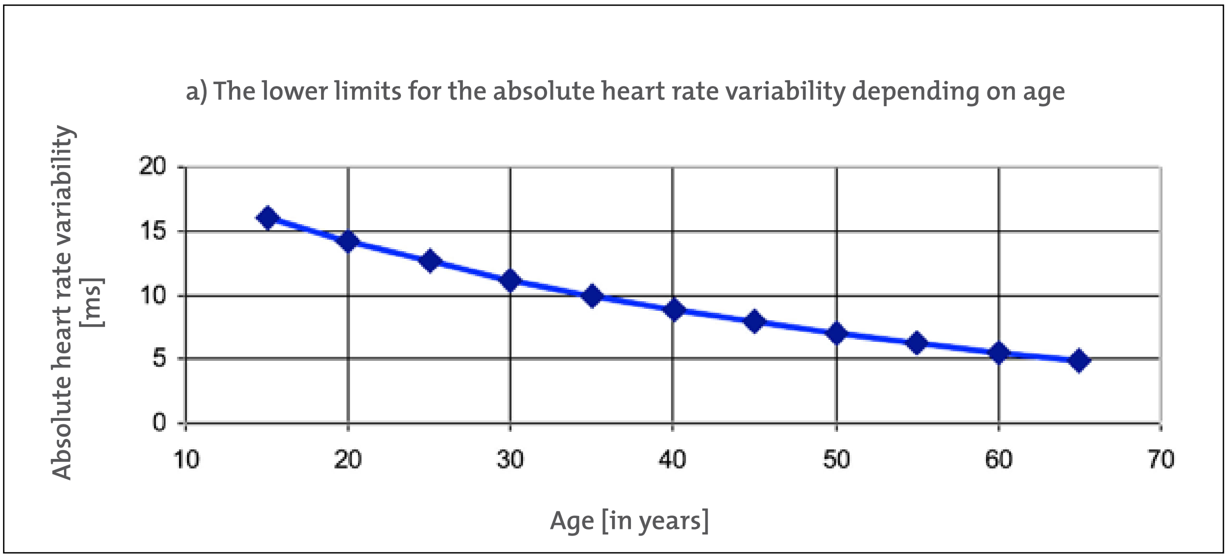




*fig.: Time section of 1 minute of a tachogram of the heart period (RR-intervals) and their reciprocal value of heart rate, including the definition of the heart period deviation ΔTH:*

*a) 24-year-old normal subject: A respiratory sinus arrhythmia is clearly illustrated with the breathing periods. A pronounced heart rate variability is can also be seen.*

*b) 72-year-old female patient with 3-vessel coronary heart disease: In addition to the high average heart rate of 94 min-1, the heart rate variability is obviously low. No respiratory sinus arrhythmia can be seen. At the end of the 60 second tachogram, the heart periods alternate periodically with the abnormal periods of 2 heart beats.*



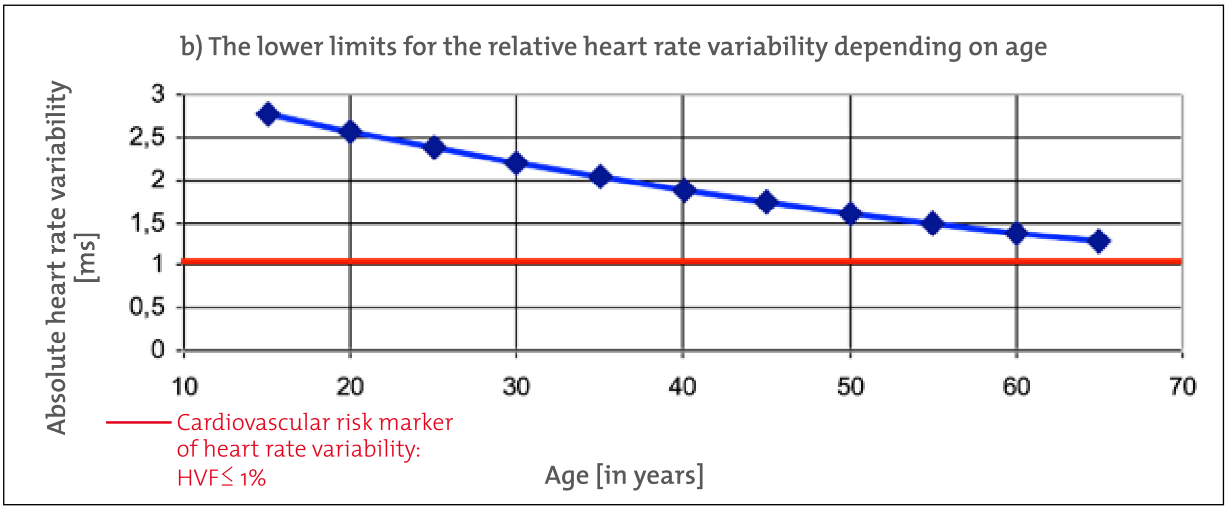




*Fig.:*
*Lower limits for absolute [a)] and [b)] relative heart rate variability in relation to age as 2.5% percentiles [according to Agelink MW et al: D (2001) Standardized tests of heart rate variability: normal ranges obtained from 309 healthy humans, and effects of age, gender, and heart rate. Clinical Autonomic Research 11: 99-108 (2001)]. The values are to be evaluated so that only 2.5% of the examined subjects had a smaller value measured than did the respective age group as a whole. This can therefore be considered the lower limit for both normal and abnormal HRV findings. In general, the diagrams above show that heart rate variability decreases with increasing age.*

*Agelink cites the following examples in this regard:*
*Example 1: A resting SDNN of 32.5 ms („normal" > 8.9 ms) is measured in a 42-year-old subject.*
*Interpretation: normal.*
*Example 2: Also in a 42-year-old subject, a resting SDNN of 7.5 ms is measured („normal" > 8.9 ms).*
*Interpretation: abnormal.*
*Example 3: A resting SDNN of 7.5 ms („normal" > 4.9 ms) is measured in a 65-year-old subject.*
*Interpretation: normal.*

*Agelink points out, however, that a multitude of individual conditions (smoking, stress, infections, etc.) may influence the testing results. In the case of abnormal results, therefore, a physician should be contacted as soon as possible. On the other hand, of course, a „normal" heart rate variability is not a guarantee of health and should not replace a doctor's examination when there are existing health problems. Communication from Telovital GmbH Vienna 2008]*



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*Agelink MW et al:* D (2001) Standardized tests of heart rate variability: normal ranges obtained from 309 healthy humans, and effects of age, gender, and heart rate. Clinical Autonomic Research 11: 99-108 (2001):

**a) How does heart rate variability (HRV) react to heavy physical load (such as an hour of athletic activity)?**

The HRV reacts in a highly sensitive manner to very different loads, especially to physical exertion. It decreases as the pulse rises („sympathicotonic condition"). Then it remains low until the body has largely recovered. This can last up to 24 hours (depending on the workload performed). If the HRV has still not normalized after this amount of time, this may indicate a „state of overtraining". In this case, affected persons usually feel tired and their condition worsens with additional training. Regular HRV measurements are therefore appropriate for recognizing a „state of overtraining" relatively quickly and countering it with sufficient rest or adjustment of the training load.

**b) Is the HRV subject to daily fluctuations?**

Yes. A difference between day and night rhythms is especially apparent, with the influence of the sympathetic nervous system dominating during the day and that of the parasympathetic nervous system during the night. The HRV also fluctuates according to the stage of sleep, which has motivated some sleep researcher to classify sleep stages according to the HRV. Hormones also appear to be able to trigger fluctuations in the HRV over the course of a day.

**c) How can disturbing influences (agitation, expectation) as evidenced by blood pressure measurements (high blood pressure in response to a doctor's examination, for instance) be avoided?**

„White coat" effects can be avoided by leaving the person to be examined alone for a few minutes. The recording works without a physician or other specialist needing to be present. If the person being examined still cannot relax, distraction tactics can be suggested (a few friendly words or even a short therapeutic discussion, 3 knee-bends, relaxing music, a slide show ...)

**e) What medications can influence the HRV?**

It is primarily the anticholinergic drugs that reduce the HRV (thus, antidepressants, for example). There is not yet a complete list.



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## → FFT spectrum

From the calculated tachogram of the heart period, a function in the time domain, an equivalent representation in the frequency range can be derived through a mathematical operation - called the FFT spectrum or „(performance) spectrum of the heart rate variability“ in the technical literature. This spectrum consists of characteristic frequency ranges used as a basis in the „clue medical“ family:
**„Low Frequency“ frequency range (LF) 0.04 to 0.15 Hz:** A predominantly sympathetic cardiovascular activity can be attributed to this range, and therefore also psychological and physical stress.
**„High Frequency“ frequency range (LF) 0.15 to 0.4 Hz:** Typical of this range is parasympathetic (vagal) activity, and therefore breathing-synchronous heart rate fluctuations of the respiratory sinus arrhythmia.
**„Very High Frequency“ frequency range (VHF) 0.4 to 0.5 Hz:** This range, lying outside the activity of the autonomic components of the cardiovascular system, can be considered a cardiac risk marker.

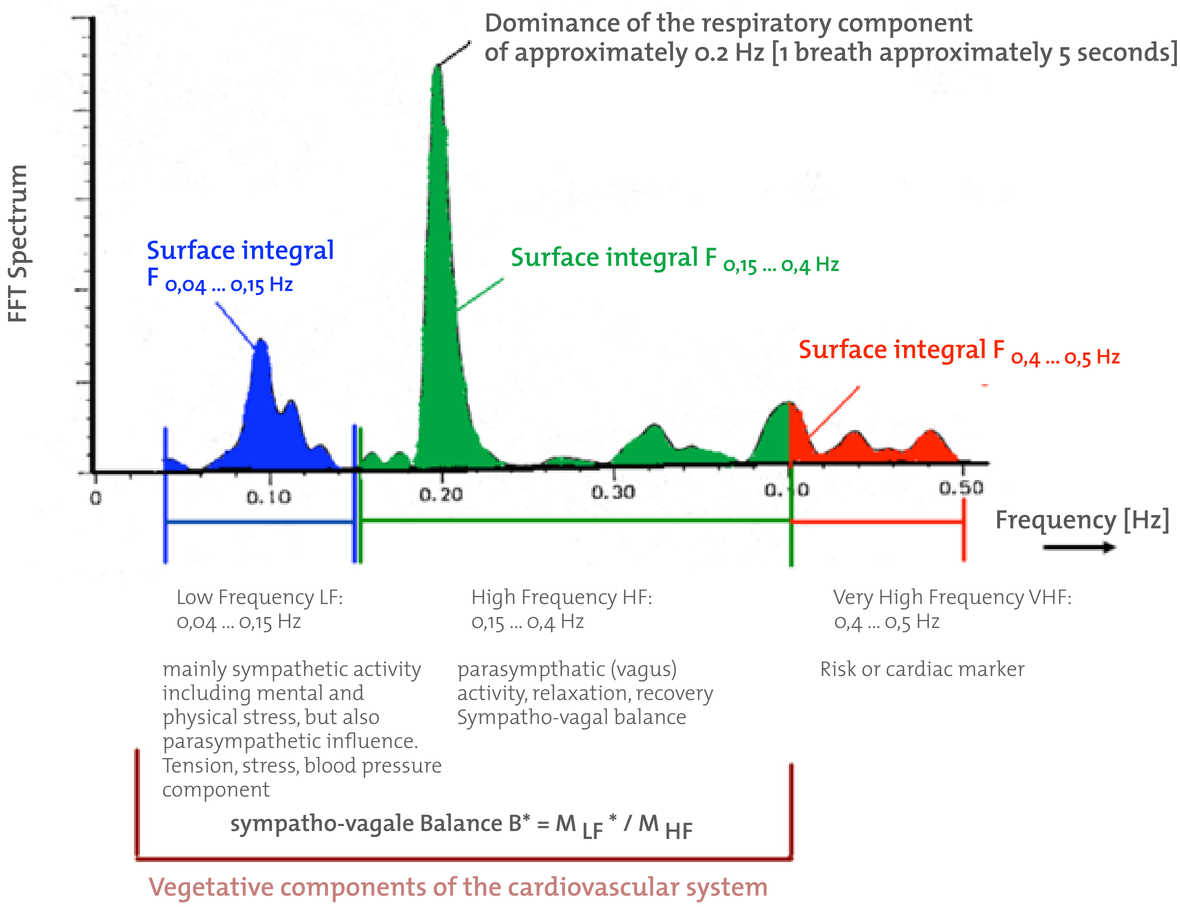


*Fig.: FFT spectrum derived from the tachogram of the heart periods of a healthy 20-year-old subject, including the frequency range characteristics LF, HF and VHF*



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## → Spectral measurements

By determining the respective integral square measures for the frequency ranges 0.04 ... 0.15 Hz and 0.15 ... 0.4 Hz for a derived FFT spectrum and dividing by the respective normal values, non-dimensional „spectral measurements“ M, in percent, can be introduced:
**$M_{LF}$*** [%]... weighted measurement for sympathetic activity, stress and load
**$M_{HF}$*** [%]... Measurement for parasympathetic activity, relaxation and recovery
**$M_{LF}$*** represents the measurement MLF multiplied by the square of the average heart rate, which corresponds to the standardized square measures above. The result of this is that higher heart rates greatly increase this weighted measurement MLF, while frequencies lower than the normal heart rate value of about fH = 70 min-1 significantly reduce it. This agrees completely with the physiological behavior since higher heart rates activate the sympathetic nervous system while frequencies below the normal value activate the parasympathetic nervous system.
Likewise, an integral measure for the VHF frequency range of 0.4 to 0.5 Hz can be determined and compared to a normal value. If the measured value exceeds this „target value“, it should be considered a **marker of cardiac risk.**

## → Weighted balance

We know from physiology that the sympathetic nervous system is predominantly mapped in the LF range of the FFT spectrum derived from the heart period tachogram, but that this range may also include vagal (parasympathetic) portions. As a result, a balance calculated on the square ratio of the LF and HF range can only be analyzed under certain conditions. Taken as a basis, the measurements $M_{LF}$* above, as a weighted measurement, and MHF lead to the **weighted balance $B^* = M_{LF}^* / M_{HF}$.**

## → Cardiovascular stress

Stress affects the autonomic nervous system by increasing sympathetic activity and inhibiting the vagal nerve. Based on this, the measurement MLF*, derived from the FFT spectrum, represents a measurement of sympathetic activity, stress and load, while the measurement MHF is an expression of parasympathetic activity, relaxation and recovery. Since the weighted balance B is derived as a quotient from both measurements MLF* and MHF, an increase in B can be taken as an increase in sympathetic activity, stress and load. If, on the other hand, the weighted balance is reduced, a reduction of these sympathetic components, or an increase in parasympathetic activity, relaxation and recovery can be assumed. In this sense, MLF* and B represent quantitative measurement of cardiovascular stress.



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25-year-old normal person:

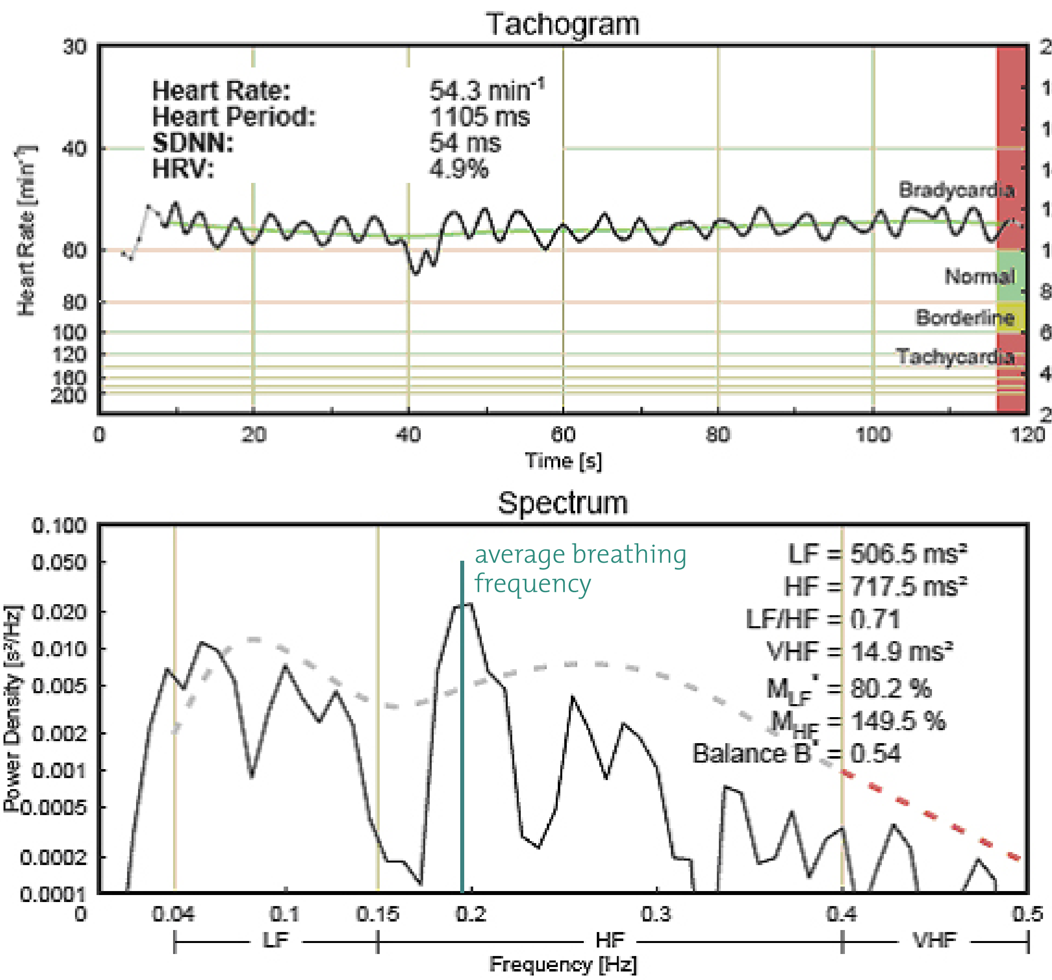


*Fig.: Cardiovascular state (tachogram of the heart periods, FFT spectrum with spectral measurements and weighted balance) in a normal 25-year-old while lying down.*
*All measurements and calculated characteristic values indicate normal behavior.*
*An average breathing frequency of about 0.2 Hz can be derived from the maximum of the FFT amplitude in the HF frequency range.*
*The VHF square measure of 14.9 ms2 lies within the calculated normal range so that there is no risk marker.*
*[Note: - - - - derived average course of „normal“ FFT (average age 25 ± 5 years of age)]*

*[This „clue medical“ measurement was derived under the supervision of Prof. Dr. D. Schmidtbleicher at the Institute for Sports Science of the Johann-Wolfgang-Goethe University in Frankfurt]*



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**54-year-old patient with acute coronary syndrome:**

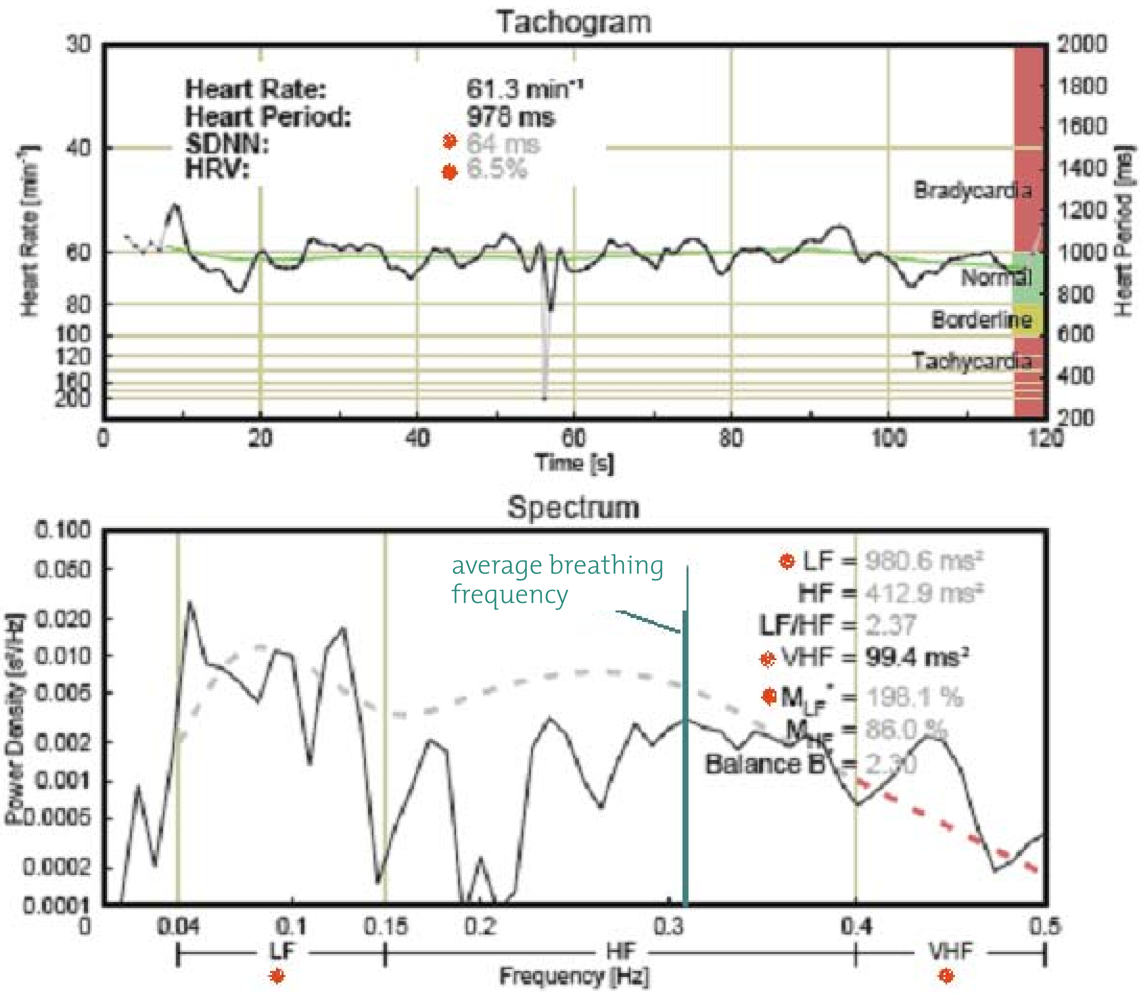


*Fig.: Heart period tachogram and associated FFT spectrum, including spectral measurements, characteristic values and integral spectral VHF value in a 54-year-old patient with acute coronary syndrome. In addition to the increased VHF spectrum value, the LF value and the derived measurement $M_{LF}$* as well as balance B* are also at the upper limit of normal. This means we must assume a high level of cardiovascular sympathetic activity and therefore reduced microcirculation in the heart as well as cardiovascular stress, even if the heart rate is completely normal at 61.3 min$^{-1}$.*

*Likewise, a heart rate variability of 64 ms, or 6.5%, appears abnormally high in a 54-year-old coronary patient, in spite of tend elimination.*
*The average breathing frequency of about 0.31 Hz (average breathing period ≡ 3.2 s) is also elevated.*
*Note: Abnormal values are marked in red.*
*[This „clue medical“ measurement was derived under the supervision of Prof. Dr. med. J. Kastner, Medical University of Vienna, University Clinic for Internal Medicine II, Cardiology Section]*



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**48-year-old patient with myocarditis due to streptococcal pneumonia and dilatative cardiomyopathy (heart transplant in 1995):**

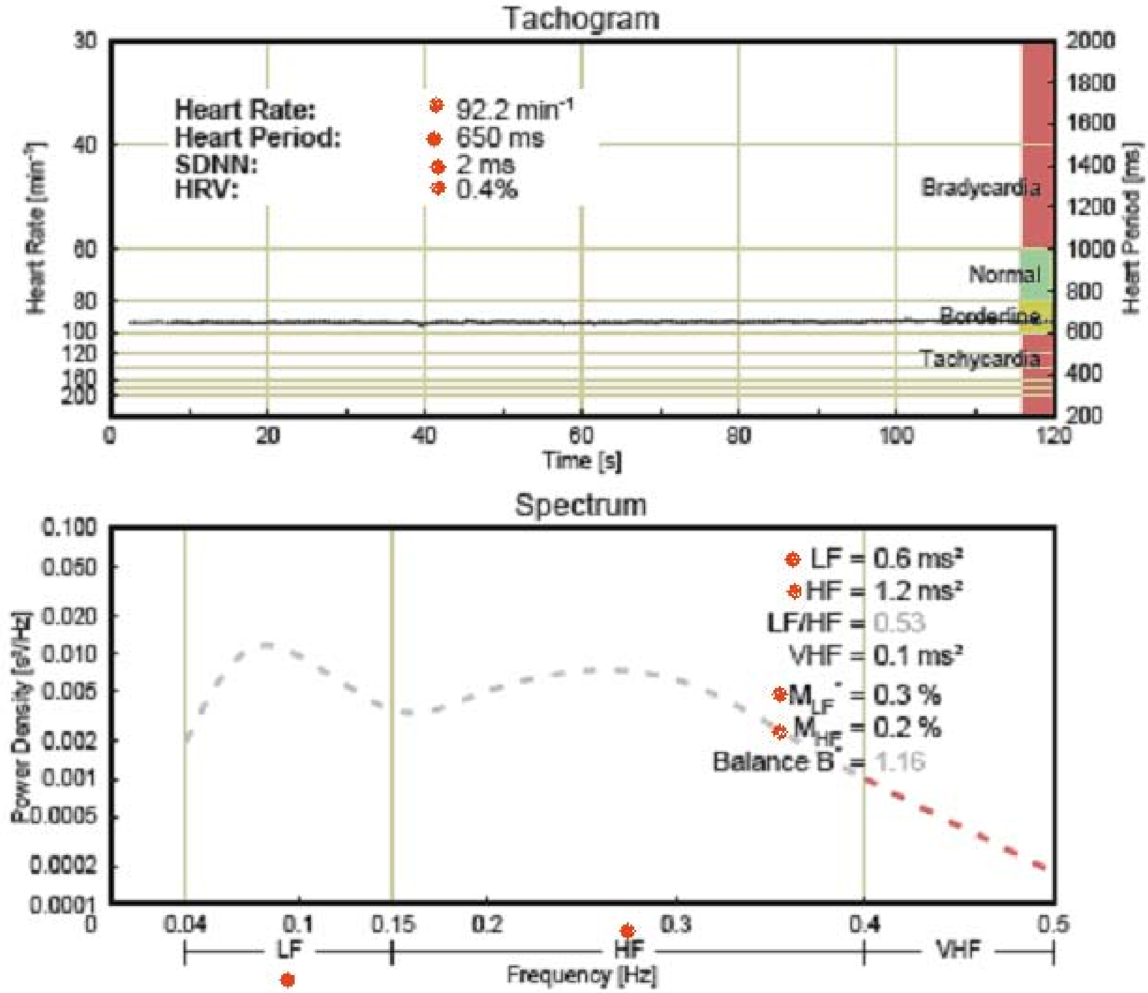


*Fig.: Heart period tachogram and associated FFT spectrum, including spectral measurements and characteristic values in a 48-year-old patient with myocarditis due to streptococcal pneumonia and dilatative cardiomyopathy (heart transplant in 1995) [RRsys = 107 mmHg, RRdiast = 64 mmHg].*
*There is practically no influence of the autonomic components on the cardiovascular function, the corresponding measurements are insignificantly small, and balance B* cannot be defined here.*

*The heart rate variability is nearly zero and the heart rate is almost tachycardic. Note: Abnormal values are marked in red.*
*[This „clue medical“ measurement was derived under the supervision of Prof. Dr. med. J. Kastner, Medical University of Vienna, University Clinic for Internal Medicine II, Cardiology Section]*



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## → Average values of cardiovascular parameters derived from a group of 98 test subjects with healthy cardiovascular systems with an average age of 25 ± 5 years with „clue medical"

The following average values for cardiovascular parameters were derived from two measurements each in a group of 98 test subjects with healthy cardiovascular systems [average age 25 ± 5 years] at the Institute for Sports Science of the Johann-Wolfgang-Goethe University in Frankfurt under the supervision of Prof. Dr. D. Schmidtbleicher as „normal values" for such a group. These were used as the basis of orientation for physicians using „clue medical".

| Abbreviation | Name of the parameter | Value range |
|---|---|---|
| $\overline{f_H}$ | mean heart rate | 51 ... **61,3** ... 77 [min-1] |
| SDNN | absolute heart rate variability | 26 .. **53** ...106 ms |
| CV | Variation coefficient = relative heart rate variablity | 2.9 ... **5.5** ... 10.3 % |
| LF | LF-surface | 90 ... **420** ... 2000 ms2 |
| HF | HF-surface | 95 ... **525** ... 2900 ms2 |
| VHF | VHF-surface | 2 ... **17.4** ...80 ms2 |
| $M_{LF}$ * | spectral measured value MLF weighted with the square of the mean heart rate | 23 ... **100** ... 450 % |
| $M_{HF}$ | spectral measured unit for the HF frequency range | 18 ... **100** ... 550 % |
| B* | weighted balance | 0.2 ... **1** ... 5 |
| LF/HF | „simple" balance as the ratio of LF- to HF-surface | 0.19 ... **0.81** ... 3.4 |

*Table: „Orienting normal ranges" of cardiovascular parameters, derived from 98 test subjects with healthy cardiovascular systems [average age 25 ± 5 years]*



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→ **Comments on normal cardiovascular values:**

Due to the existence of non-linearities in the cardiovascular system, the principle of „normal values or ranges“ is questioned since, in such a case, normal values or ranges must always be considered in reference to a „working point“. The sports scientist A. Horn [Horn, A: Diagnostik der Herzfrequenzvariabilität in der Sportmedizin - Rahmenbedingungen und methodische Grundlagen (Diagnosis of heart rate variability in sports medicine – basic conditions and methodical foundations). Diss., Faculty of Sports Science, Ruhr University of Bochum 2003] also investigates this problem, among others, in her dissertation and comes to the conclusion that „It is questionable whether normal values can be defined“. Because of the occurrence of these non-linearities, we must come to the conclusion that the determination of „normal cardiovascular parameters“ is also practically impossible. The determination of cardiovascular parameters always assumes a linearization. It is possible, however, along with the indication of „orienting normal ranges“ and with reference to the average age (see table above), to determine „minimal“ **values („lower limits for heart rate variability“**, see page 6) while still remembering that such a system may be unstable.

To supplement and expand this orientation, there are also so-called „functional tests“ of a non-invasive type known to medicine that can be conducted in order to characterize the behavior of the non-linear cardiovascular system more comprehensively. According to Reichel [Reichel, G.: Apparative Diagnostik peripherer vegetativer Funktionsstörungen (Instrument-based diagnosis of peripheral autonomic functional disturbances). psycho 19 (1993) Nr. 5, 319-325], following acoustic, optical, electrical or respiratory and other types of excitation of the sympathetic nervous system, or after reactionary vasoconstriction resulting from irritation from cold, the sudorimotor fibers of the peripheral nerves are excited, so that both peripheral and cardiovascular microcirculation are normally reduced in these cases. Cardiovascular microcirculation can be indirectly ascertained with „clue medical“ by evaluating the heart period tachogram and FFT spectrum.
Another simple functional test is the internationally used and standardized cardiovascular „**Ewing test**“, which can be ideally performed using „clue medical“:

- **Derivation of the resting ECG in the horizontal position (recording time of 2 minutes)**
- **Derivation of the ECG in the active standing position (recording time of 2 minutes)**

The behavior of the circulatory system can be characterized and quantified at the same time by recording the change in heart rate as a transitional process and therefore the corresponding characteristic values and measurements.
[see the document „**Cardiac function diagnostics for the autonomic nervous system using the tele-analyzer „clue medical**““]



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