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Assessing Heart Rate Variability from Real-World Holter Reports

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Abstract. **Real world clinical Holter reports are often difficult to interpret from a heart rate variability (HRV) perspective. In many cases HRV software is absent. Step-by-step HRV assessment from clinical Holter reports includes: making sure that there is enough usable data, assessing maximum and minimum heart rates, assessing circadian HRV from hourly average heart rates, and assessing HRV from the histogram of R-R intervals and from the plot of R-R intervals or heart rate vs. time. If HRV data are available, time domain HRV is easiest to understand and less sensitive to scanning errors. SDNN (the standard deviation of all N-N intervals in ms) and SDANN (the standard deviation of the 5-min average of N-N intervals in ms) are easily interpreted. SDNN < 70 ms post-MI is a cut point for increased mortality risk. Two times ln SDANN is a good surrogate for ln ultra low frequency power and can be compared with published cut points. SDNNIDX (the average of the standard deviations of N-N intervals for each 5-min in ms) < 30 ms is associated with increased risk in patients with congestive heart failure. RMSSD (the root mean square of successive N-N interval difference in ms) < 17.5 ms has also been associated with increased risk post-myocardial infarction. Frequency domain HRV values are often not comparable to published data. However, graphical power spectral plots can provide additional information about whether the HRV pattern is normal and can also identify some patients with obstructive sleep apnea.**

Key Words. **heart rate variability, risk stratification, ambulatory ECG monitoring**

Readers of this volume must have realized that there is usually a gap between heart rate variability (HRV) data available to those who have made the contributions reported here, and the data available to them from their own clinical Holter laboratories. In an ideal world, clinical Holters would be carefully scanned, with meticulous attention to accurate labeling of each beat and interval, and HRV would be calculated with validated software that would provide both accurate values and excellent graphics. The reality, however, is that Holter technicians may be poorly trained, poorly paid and under pressure to process a large number of Holter recordings each day. Furthermore, the accurate and uniform detection of the onset of each QRS may not be relevant to the clinical lab. Finally, HRV software may be nonexistent or not validated and produce results (e.g., ultra low frequency power based on 10-minute intervals rather than 24-hours) that are not comparable to published values. Despite these limitations, as will be seen, information about HRV can usually be gleaned from almost any Holter report.

Are the Data Really There?

Holter recordings can have significant amounts of missing data, due to poor hook ups or other problems. Most Holter reports list the number of analyzable minutes in each hour of the recording. At a *bare* minimum, at least half of the data should be there, both during the day and during the night. Also, most Holter reports list the number of beats analyzed. A good rule of thumb is that a recording has about 100,000 beats. Significantly fewer beats deserves investigation. Multiplying the average heart rate by 60 minutes per hour and then 24 hours per day permits computation of the expected number of beats. Also, if more than 20% of the detected beats are ectopic, because the interval before and after each ectopic beat is usually eliminated from the analysis, numerical estimates of HRV will not be accurate.

Estimating HRV When There is No HRV Software

Even when there is no HRV software on the clinical scanner, a qualitative estimate of HRV (i.e., whether it is low, moderately depressed, relatively normal or high) can generally be made from the information and graphical plots that are usually available.

1. *The average, maximum and minimum heart rates*. Usually there is an automatically-generated strip for the maximum and minimum heart rates, so the reader can easily tell

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if these values at least exist on the recording. However, if there is a significant range between the maximum and minimum heart rates, e.g., below 60 bpm at night and above 110 bpm during the day, it is evidence for (but not proof of) reasonable HRV. If there is not a significant range of heart rates, especially if the patient has a high average HR, HRV will most likely be depressed. Again, if there is a lot of missing data, this needs to be interpreted with caution.

2. *Hourly average heart rates*. Hourly average heart rates are usually available on Holter reports. Look for a clear circadian rhythm, i.e., a distinctly higher heart rate during the daytime and lower nighttime average heart rates. If this is absent, the patient has low HRV. Occasionally, a patient has a monotonic increase or decrease in HR throughout the recording which can result in normal-seeming HRV numbers in an abnormal situation.
3. *The Histogram of R-R or N-N intervals*. The shape of the histogram of N-N (normal-to-normal) or R-R intervals clearly indicates whether HRV is normal, low or very low. Such histograms are usually available. Keep in mind that the Holter scanner often has many options for what is included in the report, and if what you need is not there, it may be possible to get the report format changed. Ectopic beats, or intervals with missing beats are likely to be found in the tails of the histogram, while the central part contains most of the N-N intervals. Narrower histograms are associated with decreased HRV. Figure 1 shows examples of N-N interval histograms for patients with normal, moderately depressed and severely depressed and totally abnormal HRV. One histogram-based index of HRV (HRV triangular index), which was developed for use independent of scanning quality, could be roughly estimated from the R-R or N-N histogram [1]. HRV triangular index is the total number of N-N beats (possibly available from the Holter report) divided by the number of beats in the modal frequency (i.e., the group of beats with the highest peak in the histogram). The number of beats in the modal frequency can be

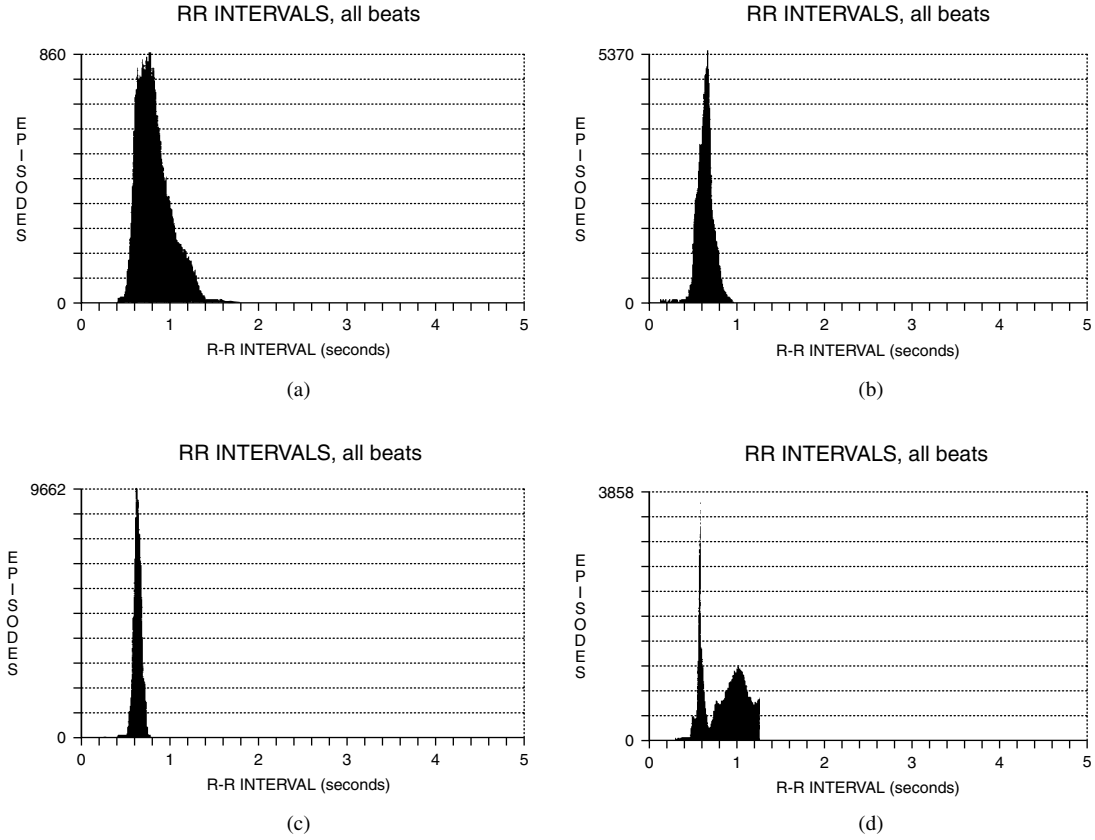

Fig. 1. *Examples of R-R histograms from (a) a normal subject, (b) a cardiac patient with decreased HRV, (c) a cardiac patient with very low HRV and (d) a patient with an extremely abnormal R-R interval distribution and a large number of ventricular ectopic beats.*

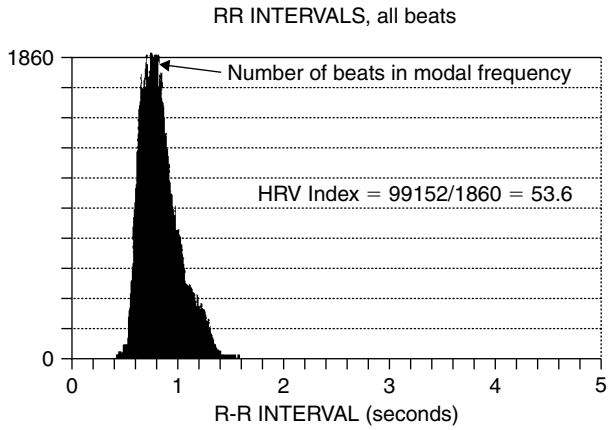

Fig. 2. *Calculation of the HRV triangular index.*

estimated from the y-axis of the histogram plot, assuming some sort of scale is provided. Figure 2 illustrates this calculation. HRV triangular index <15 can be considered severely depressed and HRV triangular index <20 can be considered moderately depressed [1].

4. *Plots of HR vs. time.* Many Holter scanners provide a plot of HR or N-N intervals vs. time and may include the highest and lowest values for each 5 minute interval. This too provides a visual picture of HRV. Figure 3 provides sample plots for a normal subject, one with moderately depressed HRV, one with very low HRV and one with atrial fibrillation. A clear circadian rhythm and a reasonable range of heart rates at every point suggest normal HRV. Atrial fibrillation is associated with a very broad range of heart rates. The plot of heart rate ranges should relatively uniform across time, although it is common for it to widen at night. Several epochs of increased HR range dispersed thru the day are likely to represent an abnormal rhythm.

HRV from Scanners with HRV Software

1. *Time Domain Indices of HRV*. Most Holter scanners provide values for SDNN, SDANN, SDNNIDX (also known as SD or as ASDNN), pNN50 and rMSSD. These are likely to be

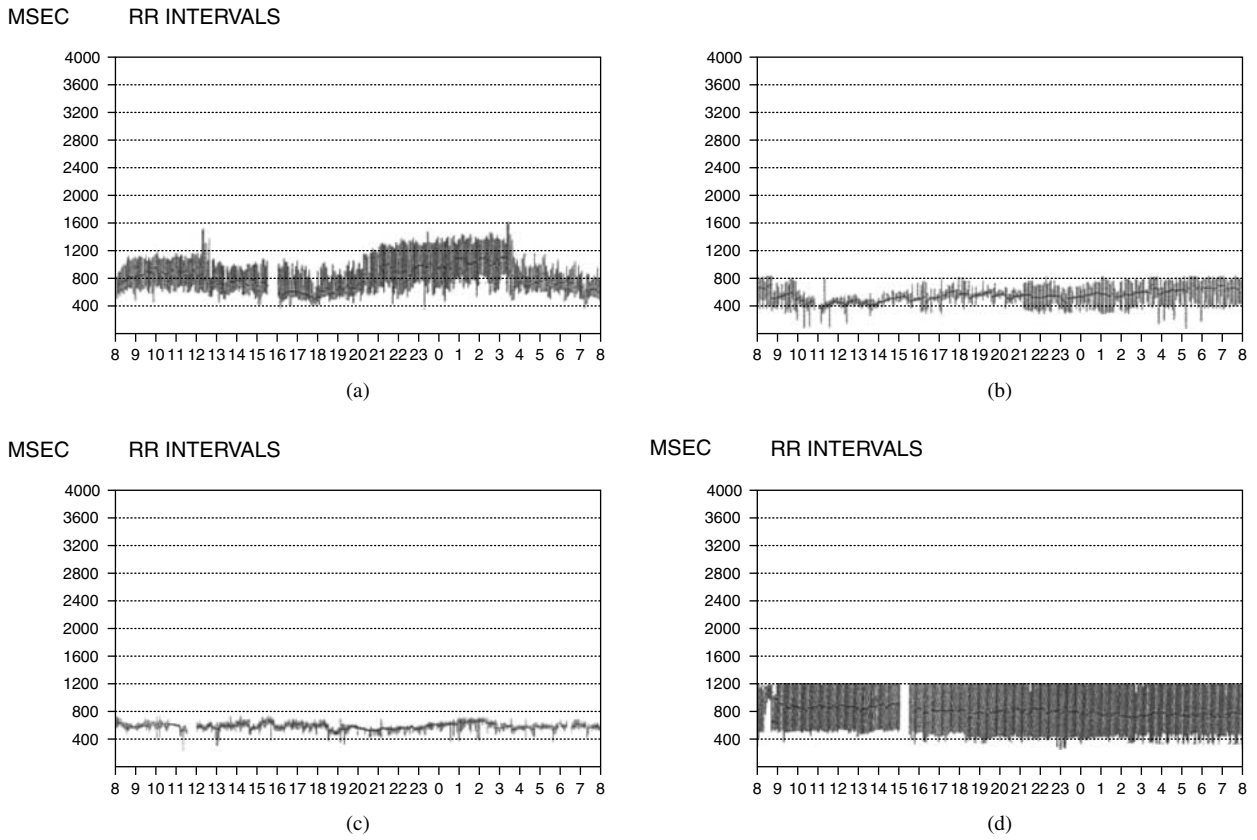

Fig. 3. *Plots of R-R intervals for every 5-min for (a) a normal subject, (b) a cardiac patient with decreased HRV, (c) a cardiac patient with extremely low HRV and (d) a patient with atrial fibrillation. Patients (a), (b) and (c) are identical to those in Figure 1.*

reasonably accurate and comparable to published values. However, it is possible that HRV, as reported on the Holter report, could underestimate true HRV. Some Holter programs have preset limits for maximum and minimum ratios between each beat and the average of those before it (e.g., 0.80–1.20). These preset limits can be changed on a case-by-case basis by the Holter technician but may not be. Where there is significant respiratory sinus arrhythmia, the true ratio is often far higher. The preset ratios may be indicated on the HRV report.

SDNN (the standard deviation of all N-N intervals in ms) is the best known, best validated and easiest to use of the HRV indices. SDNN is relatively insensitive to all but the most egregious scanning errors. In ATRAMI, the most recent study of HRV and outcome, SDNN > 70 ms was associated with a relative risk of 3.2 for mortality during follow up [2]. Identical results were found the GISSI-2 study [3]. What must be kept in mind, however, is that most of the data on HRV and risk stratification were obtained shortly post-MI when risk of mortality is highest. HRV tends to increase during recovery from MI. There are no data for the predictive value of SDNN at other times post-MI. Furthermore, HRV is depressed in patients who are diabetic. These patients are already at high risk of an adverse outcome and there is no evidence that HRV adds to risk stratification in that population. HRV is useful, however, as a screening tool for autonomic neuropathy among diabetics [1]. Another group with decreased HRV is patients with recent (<6 months) CABG surgery [4]. This is a population with a relatively good prognosis in which HRV is meaningless for risk stratification. SDNN, however, is a fairly good negative risk stratifier. Higher values for SDNN almost certainly identify patients at lower risk for mortality. For example, SDNN > 100 ms was associated with a very low risk of mortality in the MPIP (the first study of HRV post-MI) [5].

SDANN (the standard deviation of the 5-min average of N-N intervals in ms) is similar to SDNN and is even less affected by scanning errors. Cutpoints for SDANN are less well-studied. However, among patients awaiting heart transplantation, those in whom SDANN was <55 ms had a 20-fold relative risk of mortality compared to those with higher values [6]. For the mathematically inclined, 2*ln SDANN provides a very good surrogate for ln ultra low frequency power (ULF) [7], another excellent predictor of mortality post-MI. ULF cut points for increased mortality post-MI patients have been reported to be 1600 ms^2 ($\ln ULF = 7.38$) for patients shortly after MI [8] and 5000 ms^2 ($\ln ULF = 8.52$) one year post-MI [9].

SDNNIDX (the average of the standard deviations of N-N intervals for each 5-min in ms) has been most useful in risk stratification for CHF patients. In one study, SDNNIDX < 30 ms had a sensitivity of 75% and a specificity of 90% in predicting death in CHF, but this is not a universal finding [10].

Both rMSSD (the root mean square of successive N-N interval difference in ms) and pNN50 (the percent of differences between normal-to-normal intervals >50 ms) reflect short-term HRV changes. They are also the most sensitive to poor scanning. These indices generally reflect vagal modulation of heart rate [11]. Low values are quite common, and higher values (e.g., pNN50 > 5%) in association with low values for SDNN suggest a high degree of non-respiratory sinus arrhythmia rather than a high degree of vagal modulation of HR. Extremely high values (i.e., pNN50 > 50%) in a cardiac patient suggest atrial fibrillation. Also, historically, some researchers choose to filter their HRV data so that beat to beat changes of >20% are automatically excluded. This practice tends to eliminate the high values that might otherwise be seen. Results of GISSI-2 suggest a cutpoint of rMSSD <17.5 ms to identify post-MI patients a higher risk of mortality.

2. *Frequency Domain HRV*. The values provided by the Holter scanner for frequency domain HRV may not be comparable to published values and may therefore be more difficult to interpret than time domain HRV. Furthermore, since there is a time domain surrogate for virtually every frequency domain index of HRV, interpretation of the numbers themselves is not necessary. Graphical representations of frequency domain HRV, either from single 24-hour averaged plots, or, even better, hourly power spectral plots can be extremely useful. Figure 4 shows 1-hour nighttime power spectral plots for patients with normal HRV and a normal power spectral distribution, low HRV and a normal power spectral distribution, high HRV and an abnormal power spectral distribution and low HRV with an abnormal power spectral distribution. Under normal circumstances, even in patients with low HRV, a clear, although perhaps much smaller, peak will be seen in the high frequency (HF) band (Figure 4) during the nighttime hours and possibly during the daytime if the patient takes a nap. Lack of a clear HF peak during the night suggests that HRV is abnormal, respiration is exceeding irregular or possibly that the patient is sleeping very poorly. However, uneven detection of the onset of the beats on a recording can also result in an abnormal-looking power spectral plot. This is unlikely to be the case if the patient has a normal QRS width and morphology. Also, evidence for sleep apnea or other periodic breathing during the night can be obtained from a characteristic nighttime peak in the very low frequency band. An example is shown in Figure 5.

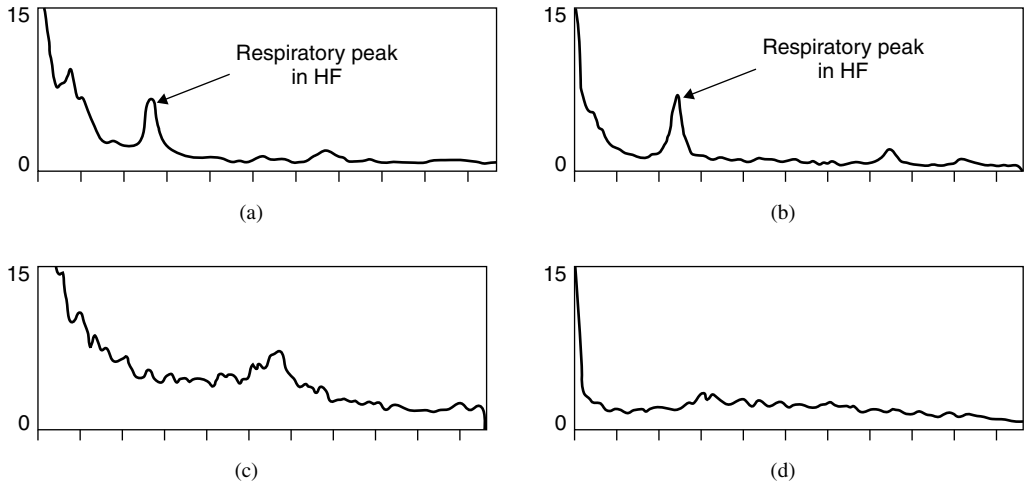

Fig. 4. *Representative nighttime one-hour power spectral plots for (a) a healthy normal subject, (b) a cardiac patient with decreased HRV but preserved vagal modulation of HR, (c) a patient with high HRV and an abnormal power spectral distribution and (d) a patient with decreased HRV and an abnormal power spectral distribution. HRV is measured in ms on the y-axis (0–15 ms), and power spectral frequency on the x-axis (0–1 Hz).*

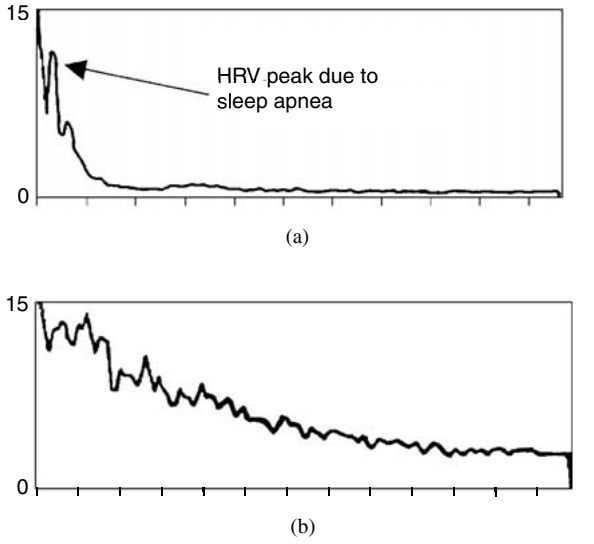

Fig. 5. *(a) Representative nighttime one-hour power spectral plot for a patient with severe sleep apnea. (b) Representative nighttime one-hour power spectral plot for a patient in atrial fibrillation.*

Also, as can also be seen in Figure 5, atrial fibrillation is associated with a completely abnormal power spectral plot.

Conclusion

What then to do with the HRV information obtained from the Holter report? From the strictest, literature-based data, the ideal time to measure HRV for risk stratification is within a week or so post-MI. It must be kept in mind that, even measured at that point, decreased HRV by itself is only a modest predictor of poor outcome. Decreased HRV must be taken as part of the bigger picture of the other risk factors present, e.g., decreased ejection fraction, frequent ventricular ectopy, late potentials, etc. The obvious question when decreased HRV is found is, "Can HRV be increased, and would increased HRV be associated with a better outcome?" This question has not been definitively answered. It is clear that HRV can be increased by various interventions and that many of these, e.g., use of beta-blockers are associated with increased survival [11]. Also, many of the positive lifestyle changes, like smoking cessation, recommended to cardiac patients may increase HRV [12]. Cardiac patients are advised to exercise, and this may also improve autonomic balance [11]. Exercise training has consistently increased HRV in CHF patients in whom baseline HRV is generally low [13,14]. HRV is being explored in the context of optimal risk stratification algorithms for implantation of AICDs. Finally, as previously mentioned, relatively normal HRV, e.g., SDNN > 100 ms in a patient with a recent MI, is a powerful *negative* risk stratifier. That is, patients with preserved HRV, in the absence of other significant risk factors, can be considered lower risk individuals.

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