

A Quantitative Systematic Review of Normal Values for Short-term Heart Rate Variability in Healthy Adults

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Abstract and Introduction

Abstract

Heart rate variability (HRV) is a known risk factor for mortality in both healthy and patient populations. There are currently no normative data for short-term measures of HRV. A thorough review of short-term HRV data published since 1996 was therefore performed. Data from studies published after the 1996 Task Force report (i.e., between January 1997 and September 2008) and reporting short-term measures of HRV obtained in normally healthy individuals were collated and factors underlying discrepant values were identified. Forty-four studies met the pre-set inclusion criteria involving 21,438 participants. Values for short-term HRV measures from the literature were lower than Task Force norms. A degree of homogeneity for common measures of HRV in healthy adults was shown across studies. A number of studies demonstrate large interindividual variations (up to 260,000%), particularly for spectral measures. A number of methodological discrepancies underlined disparate values. These include a systematic failure within the literature (a) to recognize the importance of RR data recognition/editing procedures and (b) to question disparate HRV values observed in normally healthy individuals. A need for large-scale population studies and a review of the Task Force recommendations for short-term HRV that covers the full-age spectrum were identified. Data presented should be used to quantify reference ranges for short-term measures of HRV in healthy adult populations but should be undertaken with reference to methodological factors underlying disparate values. Recommendations for the measurement of HRV require updating to include current technologies.

Introduction

In 1996, the European Society for Cardiology and the North American Society of Pacing and Electrophysiology supported a Task Force which issued a seminal paper: "Heart rate variability: Standards of measurement, physiological interpretation and clinical use" (*Circulation*, 1996; 93, 1043–1065). Reference normal values for short-term measures of heart rate variability (HRV) in healthy adults were published as an appendix to the paper. Some of these values, however, were approximated from studies involving small sample sizes. As a result, these data are considered as "unsuitable for definite clinical conclusions to be drawn from."^[1] The Task Force stressed the need for large prospective population studies to establish normal HRV standards including age and sex subsets. This need was considered greatest for HRV values obtained from short-term recordings.

The interest in HRV as a measurement of autonomic function lies in its clinical importance. A reduced HRV is a powerful and independent predictor of an adverse prognosis in patients with heart disease^[2–4] and in the general population.^[5,6] Despite the important prognostic power of HRV, it is still not a widely used tool in clinical settings. Key issues relating to this fact include the most appropriate analysis method(s), the recommended length of electrocardiogram recordings, and the conditions in which they should be assessed.^[7] Arguably an additional key factor is the lack of agreed normative values for HRV, without which classifying "abnormal" HRV remains difficult. In the majority of other clinically health-related measures (e.g., blood pressure, heart rate, forced vital capacity), established norms are routinely compared to provide an indication of current health status. There is no clear explanation why this is not the case for HRV.

Since 1996, publications assessing and reporting both 24-hour and short-term HRV in healthy and clinical populations have increased. Pinna and colleagues^[8] report an increase in the number of yearly publications from 391 to 584 in the period 2000 to 2006, respectively. Taylor and Studinger^[9] reported an average of 10 articles related to HRV published

weekly during 2005. These "newer" studies provide a potential source of normative data for common HRV measures in healthy populations. Moreover, by comparing values between publications, it may be possible to identify factors contributing to discrepancies in HRV values.

Methods

Search Strategy

The PubMed and Ovid databases were searched using the mesh term "heart rate variability" and: "short""term""short-term" and "five." A second search using 13 terms in conjunction with the previous search terms was then performed. Full text articles were then obtained and their bibliographies searched for further studies not identified electronically. The full set of search strategy terms are illustrated in Figure 1.

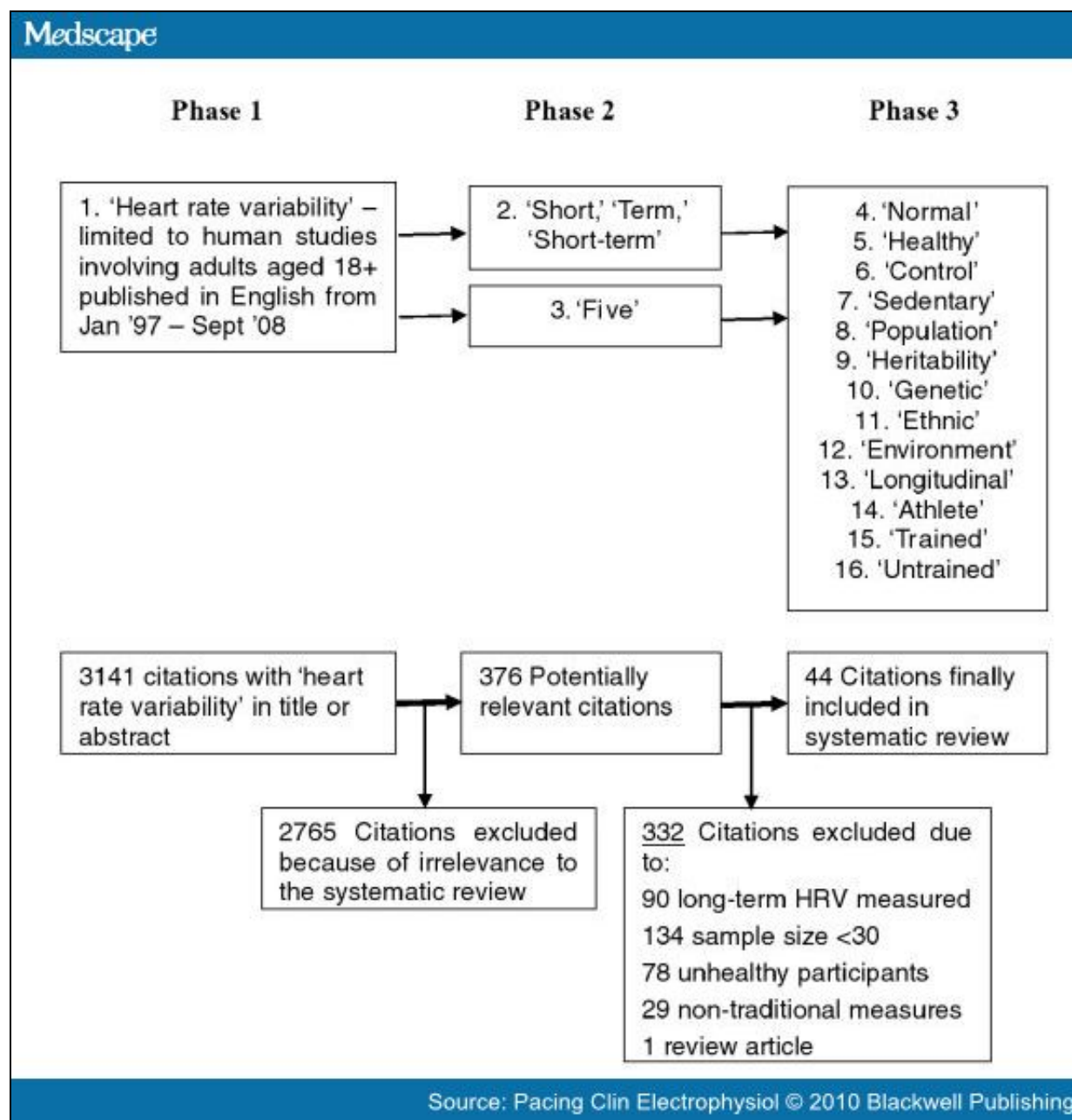


Figure 1.

Schematic of search "strings" added to the PubMed and Ovid databases for retrieval of citations assessing short-term

measures of HRV in healthy adults. Also indicated are the inclusion and exclusion processes.

Selection Criteria and Review Process

Only English language publications involving healthy adults of at least 18 years were included. As this study was only interested in short-term HRV, publications reporting 24-hour measures of HRV were excluded. A sample size greater than 50 was originally an inclusion criterion but was later lowered to 30. The requirement for all publications to present the mean RR interval was also an original criterion later revoked. These two actions were performed as only 22 papers were eligible for inclusion when the original criteria were applied. Publications were rejected if they presented HRV values other than in Task Force-recommended formats (i.e., absolute, log-transformed, or back-transformed units).

Data Analysis and Synthesis

The nature of the data (i.e., analysis of group means) does not support inferential analysis. Descriptive statistics are presented including: mean, standard deviation (SD), median, and range. Measures such as the coefficient of variation ($CV = SD/mean \times 100$) provide an index of the dispersion of mean values between studies. To identify factors underlying between-study differences, values for measures equating to greater than 1.5 SD from the mean publication value were considered discrepant. A value of 1.5 SD was chosen to provide a more conservative reference range for consideration of discrepant values. Assessment of possible factors underlying discrepant values was then made on a study-by-study and measure-by-measure basis. Percentage differences were used to assess between-group differences based on sex, spectral decomposition technique, and the use of paced versus free breathing protocols.

Data are presented for time and frequency measures of HRV most commonly reported within the literature. Measures of HRV often demonstrate skewed distributions and are reported as natural logarithms. Absolute and log-transformed units are presented for the following measures:

1. Standard deviation of normal-to-normal (NN) intervals (SDNN);
2. Root mean square of successive differences between NN intervals (rMSSD);
3. Proportion of successive NN intervals greater than 50 ms (pNN50%);
4. Very low-frequency spectral power (VLF); and
5. Total spectral power (TP), low-frequency power (LF), and high-frequency power (HF) in both ms^2 and normalized units and the ratio of LF power to HF power (LF:HF).

Measures of TP and VLF from short RR recordings are physiologically ambiguous and for this reason their use is not recommended by the Task Force.^[1] The Task Force also prefers the use of rMSSD to pNN50 due to its mathematical robustness. Data from studies reporting TP, VLF, and pNN50 were included in the initial review stages but were not entered into the final analysis of means. These measures were included to allow the reviewer a complete assessment of the discrepancy between studies in adherence to the Task Force recommendations.

Results

Database searches retrieved a total of 3,141 citations (Fig. 1). Shortlisted citations were retrieved and checked at the title/abstract level excluding 2,765 papers. Complete articles for the remaining 376 studies were checked for compliance to inclusion/exclusion criteria. Reasons for exclusion included measurement of longer-term HRV (e.g., 24 hours), a sample size <30 , assessment of nonhealthy participants, failure to present values for, or to measure, traditional time- and/or frequency-domain HRV, or the paper was a review article. Therefore, only 44 (12%) eligible trials were identified. The total sample size from these 44 papers was 21,438 participants.

Data from the present study are presented as follows:

- Table SI—Participant demographics and details of the methodologies employed for all publications that met the inclusion criteria;
- Table SII—Values for the HRV measures corresponding to each study in Table SI;
- —Summary data including the overall mean, SD, CV, and range in values for each of the HRV measures in Table SII;

Table I. Summary of Data from Table SII: Cross Study Overall Mean and Range in Values for Approved Task Force Measures of Short-Term HRV

HRV Measure	Absolute Values						Log-Transformed Values					
	No. of Studies	Mean	SD	CV (%)	Median	Range	No. of Studies	Mean	SD	CV (%)	Median	Range
mRR (ms)	30	926	90	10	933	785–1,160	n/a	n/a	n/a	n/a	n/a	n/a
SDNN (ms)	27	50	16	32	51	32–93	4	3.82	0.23	6	3.71	3.57–4.07
rMSSD (ms)	15	42	15	37	42	19–75	4	3.49	0.26	7	3.26	3.26–3.41
LF (ms ²)	35	519	291	56	458	193–1,009	18	5.01	1.76	35	5.02	2.05–7.31
LFnu	29	52	10	19	54	30–65	n/a	n/a	n/a	n/a	n/a	n/a
HF (ms ²)	36	657	777	118	385	82–3,630	18	4.76	1.78	37	4.96	0.08–6.95
HFnu	30	40	10	25	38	16–60	n/a	n/a	n/a	n/a	n/a	n/a
LF:HF	25	2.8	2.6	93	2.1	1.1–11.6	7	0.69	0.73	106	0.58	–0.16–1.98

n/a = nonapplicable; SD = standard deviation; CV = coefficient of variation (SD/mean × 100); mRR = mean RR interval; SDNN = standard deviation of normal-to-normal intervals; rMSSD = root mean square of successive differences; LF = low-frequency spectral power; HF = high-frequency spectral power; LF:HF = ratio of low-frequency power to high-frequency power; nu = normalized units; ln = natural logarithm.

- —Summates data in Table SII based on sex;

Table II. Comparison of Absolute and Log-Transformed HRV Values from Included Publications According to Sex

HRV Measure	Mean Absolute Values from All Studies According to Sex*					Mean Log-Transformed Values from All Studies According to Sex				
	No. of Studies		Measure Value		Difference (%)	No. of Studies		Measure Value		Difference (%)
	M	F	M	F		M	F	M	F	
mRR (ms)	9	7	922	885	8	No data [§]		No data	No data	

SDNN (ms)	3	4	40 [†]	36 [†]	9	▪	No data	No data	No data	▪
rMSSD (ms)	2	1	21 [†]	19 [†]	11	▪	No data	No data	No data	▪
LF (ms ²)	9	8	356	414	14	8	4	5.04	4.19	20
LFnu	6	9	53	46	17	▪	No data	No data	No data	▪
HF (ms ²)	10	8	475	516	8	8	4	4.86	4.10	18
HFnu	7	7	39	38	3	▪	No data	No data	No data	▪
LF:HF	3	6	2.3	1.2	91	2	1	0.36 [‡]	0.15 [‡]	140

*Data are means regardless of spectral method; [†]Data from AR studies only; [‡]Data from FFT studies only.

§Refers to the fact that no comparable data between males and females were available from any of the included studies; mRR = mean RR interval; SDNN = standard deviation of normal-to-normal intervals; rMSSD = root mean square of successive differences; LF = low-frequency spectral power; HF = high-frequency spectral power; LF:HF = ratio of low-frequency power to high-frequency power; nu = normalized units.

- —Summates data in Table SII based on breathing protocol and spectral method;

Table III. Comparison of Absolute HRV Values from Included Publications According to Breathing Protocol and Spectral Decomposition Methods

HRV Measure	Mean Absolute Values According to Free or Paced Breathing Pattern*					Mean Absolute Values According to Spectral Decomposition Method [†]				
	No. of Studies		Measure Value		Difference (%)	No. of Studies		Measure Value		Difference (%)
	NB	PB	NB	PB		AR	FFT	AR	FFT	
mRR (ms)	20	6	928	948	2	12	14	881	943	7
SDNN (ms)	20	5	49	59	17	11	14	42	59	29
rMSSD (ms)	8	4	43	55	22	5	10	26	44	40
LF (ms ²)	26	15	500	440	12	17	13	484	441	10
LFnu	25	3	51	58	12	13	13	55	47	18
HF (ms ²)	27	16	434	963	54	17	14	348	647	45
HFnu	27	2	39	43	9	13	16	36	40	10
LF:HF	21	6	2.72	2.76	0.01	12	12	2.9	1.7	71

*Values are means from all studies using free breathing (NB) and paced breathing (PB) protocols without accounting for sex or spectral decomposition method; [†]Data are means from all AR or FFT studies without accounting for sex. mRR = mean RR interval; SDNN = standard deviation of normal-to-normal intervals; rMSSD

= root mean square of successive differences; LF = low-frequency spectral power; HF = high-frequency spectral power; LF:HF = ratio of low-frequency power to high-frequency power; nu = normalized units.

- Summates data from studies displaying interindividual range in a number of HRV measures.

Table IV. Publications Presenting Interindividual Variation in Approved Task Force Short-Term Measures of HRV

Author and Date	Number of Participants	mRR (ms)	SDNN (ms)	rMSSD (ms)	LF (ms ²)	LFnu	HF (ms ²)	HFnu	LF:HF
Agelink et al. ¹³ (1998)	69	NR	NR	6.9–99.4	NR	NR	NR	NR	0.29–11.00
Fagard et al. ¹¹ (1998)	587	NR	NR	NR	4–6,397* 1–6,924*	NR	4–10,751* 2–7,513*	NR	NR
Sinnreich et al. ¹⁶ (1998)	293	NR	3.39–4.05 ln [†]	2.88–3.57 ln [†]	4.63–6.24 ln [†]	NR	4.07–5.49 ln [†]	NR	NR
Pikkujämsä et al. ²³ (2001)	392	573–1,402	13–168	NR	35–5,941	11–98	10–7,231 2.30–8.89 ln	3–72	0.24–17.10
Sucharita et al. ²⁵ (2002)	93	NR	NR	NR	NR	NR	13–6,830	19–93	NR
Rajendra Acharya ¹⁰ et al. (2004) (<i>mean lower and upper values from three age groups</i>)	125	NR	41–67	53.6–70.4	NR	NR	NR	NR	1.6–1.9
Kurosawa et al. ⁴⁵ (2007)	66	NR	NR	NR	86–1,874‡	NR	98–3,938‡	NR	NR

*Value is geometric; †Values are 25th–75th percentile; ‡Values are 5 and 95 percentiles; NR = not reported; mRR = mean RR interval; SDNN = standard deviation of normal-to-normal intervals; rMSSD = root mean square of successive differences; LF = low-frequency spectral power; HF = high-frequency spectral power; LF:HF = ratio of low-frequency power to high-frequency power; nu = normalized units; ln = natural logarithm.

Data from Rajendra Acharya et al.^[10] listed in Table SI are not included in Table SII. This study only presented the range in values for measures of HRV without providing a mean value. These data are included in .

Table IV. Publications Presenting Interindividual Variation in Approved Task Force Short-Term Measures of HRV

Author and Date	Number of Participants	mRR (ms)	SDNN (ms)	rMSSD (ms)	LF (ms ²)	LFnu	HF (ms ²)	HFnu	LF:HF
Agelink et al. ¹³ (1998)	69	NR	NR	6.9–99.4	NR	NR	NR	NR	0.29–11.00

Fagard et al. ¹¹ (1998)	587	NR	NR	NR	4–6,397* 1–6,924*	NR	4–10,751* 2–7,513*	NR	NR
Sinnreich et al. ¹⁶ (1998)	293	NR	3.39–4.05 ln [†]	2.88–3.57 ln [†]	4.63–6.24 ln [†]	NR	4.07–5.49 ln [†]	NR	NR
Pikkujämsä et al. ²³ (2001)	392	573–1,402	13–168	NR	35–5,941	11–98	10–7,231 2.30–8.89 ln	3–72	0.24–17.10
Sucharita et al. ²⁵ (2002)	93	NR	NR	NR	NR	NR	13–6,830	19–93	NR
Rajendra Acharya ¹⁰ et al. (2004) (mean lower and upper values from three age groups)	125	NR	41–67	53.6–70.4	NR	NR	NR	NR	1.6–1.9
Kurosawa et al. ⁴⁵ (2007)	66	NR	NR	NR	86–1,874 [‡]	NR	98–3,938 [‡]	NR	NR

*Value is geometric; [†]Values are 25th–75th percentile; [‡]Values are 5 and 95 percentiles; NR = not reported; mRR = mean RR interval; SDNN = standard deviation of normal-to-normal intervals; rMSSD = root mean square of successive differences; LF = low-frequency spectral power; HF = high-frequency spectral power; LF:HF = ratio of low-frequency power to high-frequency power; nu = normalized units; ln = natural logarithm.

Analysis of Short-term HRV Data from the Literature

Descriptive statistics for data from all the included studies are presented in . There was a large range in values between studies. Compared with frequency-domain measures, time-domain measures of HRV demonstrated less variation between studies. For measures reported in absolute units, the largest variation was observed for HF (CV = 118%) with a range in values across studies of 3,548 ms². Mean RR interval demonstrated the smallest variation (CV = 10%; range = 375 ms). In log-transformed units, HF again demonstrated the largest variation between studies (CV = 37%, range = 6.87 ln units). The SDNN demonstrated the smallest variation (CV = 6%, range 0.50 ln units).

Table I. Summary of Data from Table SII: Cross Study Overall Mean and Range in Values for Approved Task Force Measures of Short-Term HRV

HRV Measure	Absolute Values						Log-Transformed Values					
	No. of Studies	Mean	SD	CV (%)	Median	Range	No. of Studies	Mean	SD	CV (%)	Median	Range
mRR (ms)	30	926	90	10	933	785–1,160	n/a	n/a	n/a	n/a	n/a	n/a
SDNN (ms)	27	50	16	32	51	32–93	4	3.82	0.23	6	3.71	3.57–4.07
rMSSD (ms)	15	42	15	37	42	19–75	4	3.49	0.26	7	3.26	3.26–3.41

LF (ms ²)	35	519	291	56	458	193–1,009	18	5.01	1.76	35	5.02	2.05–7.31
LFnu	29	52	10	19	54	30–65	n/a	n/a	n/a	n/a	n/a	n/a
HF (ms ²)	36	657	777	118	385	82–3,630	18	4.76	1.78	37	4.96	0.08–6.95
HFnu	30	40	10	25	38	16–60	n/a	n/a	n/a	n/a	n/a	n/a
LF:HF	25	2.8	2.6	93	2.1	1.1–11.6	7	0.69	0.73	106	0.58	–0.16–1.98

n/a = nonapplicable; SD = standard deviation; CV = coefficient of variation (SD/mean × 100); mRR = mean RR interval; SDNN = standard deviation of normal-to-normal intervals; rMSSD = root mean square of successive differences; LF = low-frequency spectral power; HF = high-frequency spectral power; LF:HF = ratio of low-frequency power to high-frequency power; nu = normalized units; ln = natural logarithm.

Compared with males, females demonstrated slightly lower values (8–11%) for all time-domain measures of HRV expressed in absolute units (). In the frequency domain, males demonstrated lower values for LF (14%) and HF (8%) power. Males showed substantially higher values for LFnu (17%) but HFnu was similar between sexes. Values for LF (20%) and HF (18%) were substantially lower in females when expressed in log units. Females also demonstrated a lower LF:HF ratio regardless of the unit of expression.

Table II. Comparison of Absolute and Log-Transformed HRV Values from Included Publications According to Sex

HRV Measure	Mean Absolute Values from All Studies According to Sex*					Mean Log-Transformed Values from All Studies According to Sex				
	No. of Studies		Measure Value		Difference (%)	No. of Studies		Measure Value		Difference (%)
	M	F	M	F		M	F	M	F	
mRR (ms)	9	7	922	885	8	▪	No data [§]	No data	No data	▪
SDNN (ms)	3	4	40 [†]	36 [†]	9	▪	No data	No data	No data	▪
rMSSD (ms)	2	1	21 [†]	19 [†]	11	▪	No data	No data	No data	▪
LF (ms ²)	9	8	356	414	14	8	4	5.04	4.19	20
LFnu	6	9	53	46	17	▪	No data	No data	No data	▪
HF (ms ²)	10	8	475	516	8	8	4	4.86	4.10	18
HFnu	7	7	39	38	3	▪	No data	No data	No data	▪
LF:HF	3	6	2.3	1.2	91	2	1	0.36 [‡]	0.15 [‡]	140

*Data are means regardless of spectral method; [†]Data from AR studies only; [‡]Data from FFT studies only. [§]Refers to the fact that no comparable data between males and females were available from any of the included studies; mRR = mean RR interval; SDNN = standard deviation of normal-to-normal intervals; rMSSD = root mean square of successive differences; LF = low-frequency spectral power; HF = high-frequency spectral power; LF:HF = ratio of low-frequency power to high-frequency power; nu = normalized units.

When compared with data derived using autoregressive methods, spectral measures of HRV derived using the fast

Fourier transform (FFT) method were markedly different (). Studies utilizing the FFT method demonstrate lower LF power, a higher HF power (absolute and log-transformed units), and, therefore, a higher LF:HF ratio.

Table III. Comparison of Absolute HRV Values from Included Publications According to Breathing Protocol and Spectral Decomposition Methods

HRV Measure	Mean Absolute Values According to Free or Paced Breathing Pattern*					Mean Absolute Values According to Spectral Decomposition Method [†]				
	No. of Studies		Measure Value		Difference (%)	No. of Studies		Measure Value		Difference (%)
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mRR (ms)	20	6	928	948	2	12	14	881	943	7
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rMSSD (ms)	8	4	43	55	22	5	10	26	44	40
LF (ms ²)	26	15	500	440	12	17	13	484	441	10
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There were large discrepancies in values for HRV measures when obtained under paced versus free breathing conditions (). When conducted under paced breathing conditions, values were higher for all measures of HRV except LF power which was higher during free breathing. Finally, a number of studies revealed large interindividual variation for the majority of HRV measures, with values for one measure (HF) differing by as much as 260,000% between individuals within the same study (Fagard et al.;^[11]).

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Pikkujämsä et al. ²³ (2001)	392	573–1,402	13–168	NR	35–5,941	11–98	10–7,231 2.30–8.89 ln	3–72	0.24–17.10
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Discussion

Results of Literature Retrieval for Normal Values of Short-term HRV

From over some 3,100 citations, only 44 reported short-term measures of HRV in healthy adult participants ($n \geq 30$) and were in accordance with Task Force methodological standards/recommendations. The number of studies was limited by the following factors:

- Many studies of HRV assessed longer term 24-hour monitoring;
- Studies were powered for the use of small sample sizes;
- Studies often include clinical populations without the inclusion of a healthy cohort and/or reference to healthy values;
- Adherence to the Task Force methodological recommendations was poor.

Some of the factors pertaining to the above findings can be more easily explained than others. A preferred use of 24-hour measurements to that of short-term measurements could lie in their greater prognostic power,^[3,52–54] or the additional information such as night:day ratios that can only be determined from 24-hour monitoring. A more plausible explanation lies in the fact that many studies of HRV are retrospective in nature, reporting data from 24-hour Holter monitoring carried out as part of standard cardiac assessment.

The fact that studies utilize only a small sample size may be explained by the nature of the study, limitations in resources, and/or the calculations of statistical power.^[55] Other factors, such as the failure to report the actual values for measures of HRV, were found to occur when studies were interested in change scores^[56] or preferred to present results graphically.^[57]

The failure to report mean RR interval by 54% of the studies is a concern. Because of the reciprocal nature of HR and mean RR interval, studies reporting measures of HRV often choose to report only mean HR^[36,43] or in some cases, neither.^[25,41] This error can be likened to assessing the suspension behavior of a car without acknowledging the car's speed. Such errors also reflect, on the part of both author and publishing editor, failures in understanding of the fundamentals of HRV data and their analysis.

Thirty-six percent of included studies reported TP and VLF which are not recommended from short RR recordings due to their ambiguous physiological meaning under such conditions.^[1] The use of units that differ from standard units (e.g., beats per minute/ $\sqrt{\text{Hz}}$ ^[58]) further limited the number of eligible studies. When such studies are published, they reflect a weakness in adherence to Task Force recommendations. This also demonstrates a lack of coherence between authors and editors as to how and what to present when reporting short-term measures of HRV.

Comparisons Between Literature and Task Force Values

The Task Force does not provide norm values for short-term time-domain measures of HRV and therefore comparisons can only be made between spectral measures. The Task Force figures are as follows: 1,170 ms^2 for LF power, 975 ms^2 for HF power, 54 and 29 for normalized LF and HF, and 1.5–2.0 for the LF:HF ratio. The Task Force LF value is more than 1.5 SD above the mean literature value (519 ms^2). The Task Force HF value is also higher compared with that from the literature (657 ms^2). Task Force and literature-normalized measures of LF and HF power are more homogenous but the Task Force value for LF:HF (1.5–2.0) is considerably lower than the value gained from the literature (2.8).

Reasons for these discrepancies could be due a number of factors including differing characteristics of participants and differences in spectral decomposition methods. The studies from which the norms were obtained were not cited by the Task Force authors so comparisons in terms of participants are not possible. The Task Force report does

provide details as to the frequency bandwidths used for determining LF and HF power distributions. Oscillations in RR intervals occurring at LF were assessed between 0.04 and 0.15 Hz and at HF between 0.15 and 0.4 Hz. Forty-seven percent of the studies presented here report values for LF and HF power obtained at frequency bandwidths differing from those recommended by the Task Force. Some considered oscillations in heart periods at frequencies as low as zero to 0.003 as part of the LF component.^[19,40] Others utilized much lower cutoff values (0.3 Hz) for the HF component.^[21] Discrepancies in LF and HF frequency bands could lead to the inclusion and/or exclusion of oscillations of differing physiological origins and would certainly result in varying values for LF, HF, and/or both. It is both interesting and somewhat telling then that these studies report some of the largest discrepancies for spectral measures of HRV.

From Table SI, it can be seen that the following population-based studies report values for short-term HRV measurements from large samples (~1,000): Rennie et al.,^[6] Kuo et al.,^[18] Dekker et al.,^[20] Liao et al.,^[32] Hemingway et al.,^[36] Britton et al.^[43] On closer examination, a number of these studies were based upon ongoing longitudinal and/or cross-sectional assessments of the same participant populations. While these studies present different sized samples and were testing different hypotheses, there is a potential for significant overlap between their respective samples. This may explain the similarity in values between Dekker et al.^[20] and Liao et al.^[32] and among Rennie et al.,^[6] Hemingway et al.,^[36] and Britton et al.^[43] (Table SII). For these reasons, it could be argued that only three large populations have been assessed since the 1996 Task Force report.^[6,18,43] Moreover, the lowest participant age across these three populations was 40 years. This means that there are currently no published data for short-term HRV measures obtained in a large population including adults aged less than 40. The negative relationship between HRV and age may also explain the relatively low values for HRV measures observed by these studies. The impact these large samples have on the mean publication values presented here is also noteworthy.

Studies Reporting Discrepant Absolute HRV Values

Approximately 85% of studies demonstrated values within 1.5 SD of the mean publications value for one or more short-term HRV measure. Closer scrutiny of the 15% of studies demonstrating values greater than 1.5 SD can help identify conditions leading to disparate values for short-term measures of HRV. Discussion of the following studies demonstrating discrepant values will adopt a measure-by-measure approach: Melanson^[21] (mRR, SDNN, rMSSD, LF, HF), Sandercock et al.^[34] (LF), Evrengul et al.^[40] (SDNN), Mehlsen et al.^[48] (SDNN), Sandercock et al.^[50] (SDNN, rMSSD), Nunan et al.^[51] (LF).

A closer look at the characteristics of the above studies revealed a number of similarities and differences related to study participants, RR interval data recording, artifact identification, and interpolation and spectral decomposition protocols. As these factors can have differing effects depending on the measure, they will be discussed separately for time- and frequency-domain measures, respectively.

Time-domain Measures

The high RR values reported by Melanson^[21] and the high SDNN values reported by both Melanson^[21] and Sandercock et al.^[50] might be explained by their use of young and moderate-to-well trained participants. There is a well-established link between age and HRV, with a decrease in HR for increasing age with younger individuals demonstrating higher values.^[1,16,18,59] SDNN is also a function of the recording length, with longer analyzed recordings producing larger values.^[60] For this reason, the Task Force recommends a standardized duration of 5 minutes for short-term SDNN (and other measures of HRV). These factors most likely explains the larger values observed by Evrengul and colleagues^[40] who determined the SDNN of RR interval data recorded over a 1-hour period. No justification for such a recording length was given by the authors.

Parasympathetic nerve traffic enacts its effects at a much faster (<1 second) rate than sympathetic outflow (>5 seconds); therefore, beat-to-beat changes in RR intervals (rMSSD) are considered a reflection of vagal outflow.^[52,54] Measures of rMSSD are highly variable under conditions of enhanced vagal outflow.^[61] One such condition is paced breathing, particularly in the supine position. In addition, the bradycardia observed for more highly trained individuals is

commonly accompanied by augmented markers of cardiac vagal modulation,^[62,63] although this relationship is not always observed.^[64] The discrepant values for rMSSD reported by Melanson^[21] and Sandercock et al.^[50] are likely to result from the combined effect of young, trained individuals with higher baseline vagal tone and the use of supine and paced breathing protocols.

Frequency-domain Measures

A number of human and animal studies have demonstrated findings of both sympathetic^[65–67] and parasympathetic^[68] origins for LF oscillations and spectral power. An augmented and diminished LF power under parasympathetic blockade has implications for studies where vagal conditions are enhanced, such as during paced breathing conditions.^[68] The higher values observed by Melanson^[21] may be the consequence of a vagally mediated augmentation of LF power resulting from the paced breathing condition.

In healthy normotensive controls, a value of 82 ms² was reported by Piccirillo et al.^[33] Moreover, this value was used to determine "abnormal" HF power in chronic heart failure (CHF) patients. Inclusion of these values in the present study may explain the lower overall mean value for HF power. An important observation is that these values are considerably lower than the Task Force norm value for HF and the mean studies value presented here. As is common throughout the literature, consideration as to the "normality" of the so-called "healthy" values is ignored.

Spectral measures are highly sensitive to technical errors within RR data such as artifacts, misplacement of missing data, poor pre-processing, and nonstationarity. Information regarding error detection methods for 1-hour Holter RR interval data was not provided by Evrengul et al.^[40] and no indication as to the number of errors observed and/or removed was given. The fact that Mehlsen et al.^[48] do not report the performance of any error identification, removal, and/or correction procedures suggest a failure to understand the importance of correct RR interval data in the analysis of its variation. RR intervals were also considered to be "within normal range," yet the authors provide no reference for this so-called "normal" range.

The Task Force^[1] recommendations stress the need for manual editing of RR interval data. Evidence of a strong prognostic value for fully automated measures of HRV^[12] and their accurate and reliable determination compared to traditional methods^[34,51] suggests that the Task Force^[1] recommendations may be outdated. At the very least, they require updating to account for the computational power of current automated RR recording and HRV analysis devices.

Studies Reporting Discrepant Log-transformed HRV Values

Of the studies reporting log-transformed measures of HRV, only one demonstrated discrepant values for HRV measures.^[12] In the study by Ho et al.^[12] data for spectral measures of HRV were obtained in a healthy control group matched for age and sex to a group of patients suffering from CHF. The participants in the control group were 44% female, with a mean age of 72 years and a resting HR of 76 beats/min. There is a well-known age-related decline in HRV that particularly affects measures related to vagal modulations of HR in females.^[18] Data presented elsewhere demonstrate a negative correlation between HR and spectral measures of HRV.^[69] These two factors alone may explain the low values for LF (2.05 ln ms²) and particularly for HF power (0.08 ln ms²) observed by Ho et al.^[12] As with the majority of studies utilizing a control "reference" group, the values presented in the control group are not questioned by the authors as to their normality/abnormality.

Summary of Main Factors Underlining Discrepant Values in Short-term HRV from Healthy Individuals

The measure-by-measure analysis performed for those studies reporting discrepant values revealed a number of underlying factors including:

1. Moderate to high level of participant habitual physical activity;
2. The use of paced breathing protocols, particularly when performed in participants with moderate to high

physical activity levels;

3. Where younger participants are measured, values for HRV are typically higher;
4. Poor reporting and/or performance of RR interval error recognition, removal, and/or correction procedures;
5. The use of differing frequency bandwidths and normalization methods for LF and HF spectral measures;
6. Wide variation in HRV measures between healthy participants of the same study;
7. The misclassification of participants as healthy;
8. A failure of studies to recognize the normality/abnormality of values obtained in healthy participants.

Some of the points above (1, 2, 3, and 6) were not unexpected. Of some surprise was the failure to perform error correction procedures by a number of studies and the poor reporting of these procedures by others. The last three summary points are particularly important and highlight the inherent problem of defining a so-called "normal" HRV.

These points are also inter-related in that the failure to question the normality of data when obtained in healthy participants possibly stems from the fact that even in homogenous healthy groups, measures of HRV can display wide interindividual variations (as high as 260,000%, Fagard et al.^[11]).

Table IV. Publications Presenting Interindividual Variation in Approved Task Force Short-Term Measures of HRV

Author and Date	Number of Participants	mRR (ms)	SDNN (ms)	rMSSD (ms)	LF (ms ²)	LFnu	HF (ms ²)	HFnu	LF:HF
Agelink et al. ¹³ (1998)	69	NR	NR	6.9–99.4	NR	NR	NR	NR	0.29–11.00
Fagard et al. ¹¹ (1998)	587	NR	NR	NR	4–6,397* 1–6,924*	NR	4–10,751* 2–7,513*	NR	NR
Sinnreich et al. ¹⁶ (1998)	293	NR	3.39–4.05 ln [†]	2.88–3.57 ln [†]	4.63–6.24 ln [†]	NR	4.07–5.49 ln [†]	NR	NR
Pikkujämsä et al. ²³ (2001)	392	573–1,402	13–168	NR	35–5,941	11–98	10–7,231 2.30–8.89 ln	3–72	0.24–17.10
Sucharita et al. ²⁵ (2002)	93	NR	NR	NR	NR	NR	13–6,830	19–93	NR
Rajendra Acharya ¹⁰ et al. (2004) (mean lower and upper values from three age groups)	125	NR	41–67	53.6–70.4	NR	NR	NR	NR	1.6–1.9
Kurosawa et al. ⁴⁵ (2007)	66	NR	NR	NR	86–1,874 [‡]	NR	98–3,938 [‡]	NR	NR

*Value is geometric; [†]Values are 25th–75th percentile; [‡]Values are 5 and 95 percentiles; NR = not reported; mRR = mean RR interval; SDNN = standard deviation of normal-to-normal intervals; rMSSD = root mean square of successive differences; LF = low-frequency spectral power; HF = high-frequency spectral power; LF:HF = ratio of low-frequency power to high-frequency power; nu = normalized units; ln = natural logarithm.

It is important, however, to recognize other factors could influence discrepancies between studies. Measures of HRV are influenced by diet (caffeine and alcohol intake) and physical and mental stress. Very few of the studies included here include information on these factors and their impact on values presented cannot be determined. When assessing studies reporting so-called normal HRV, readers should employ close scrutiny of the factors outlined above as well as potential other factors (e.g., diet, stress) related to the individual aspects of each study. With consideration of these factors, the data presented in this study may provide users of HRV with reference ranges by which to determine disparate values for common measures of short-term HRV.

Study Limitations

It is possible that some papers meeting the inclusion criteria for the present study would have been missed by the search strategy employed. Arbitrary selection of the selected search terms may have meant that some studies reporting short-term HRV in healthy adults may have been missed. Alternatively, it could be argued that studies missed despite the comprehensive list of search terms may be too ambiguous in terms of the context in which short-term measures of HRV were used.

Study Recommendations

To facilitate between-study comparisons and aid standardization of measurements, studies need to report the outcomes of RR interval data editing procedures. In addition, measures of stationarity or measures taken to address nonstationary signals should be provided. Moreover, editors and reviewers need to adopt greater diligence in ensuring that papers using HRV provide details of data treatment before accepting the paper(s) for publication.

Despite the call for large population-based studies to determine normal HRV standards by the 1996 Task Force paper, there are no studies with participants from the full age spectrum. There is still a need for a population-based study assessing short-term HRV measurements and involving the full age spectrum. A multicenter approach may be the most feasible approach. Such a study would require stringent methodological standards and participant inclusion criteria and awareness of methodological and participant factors known to affect HRV.

There is a need for a revision of current recommendations and standards for the measurement of short-term HRV. These should be made in light of significant developments in the computational power and accuracy of automated RR interval and HRV analysis systems. There is a particular need to stress clarity and transparency by the manufacturers as to the QRS, RR interval, and HRV analysis procedures of new technologies.

Conclusions

Data presented here should be used to quantify reference ranges for short-term measures of HRV in healthy adult populations but should be undertaken with reference to methodological factors underlying disparate values. These include but are not limited to: participant demographic characteristics, including age, sex, and habitual physical activity levels; poor RR interval data editing procedures; poor classification of healthy participants; and a failure to recognize values as disparate. Studies reporting HRV need to recognize the normality of data even when obtained in individuals considered as healthy. The need for large-scale population studies assessing short-term HRV in normally healthy adults still remains. Current recommendations require updating to account for the era of completely automated HRV analysis. Clarification of measurement standards in light of the discrepancies observed between studies is also needed.

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