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Reference values of heart rate variability from 10-second resting electrocardiograms: the Lifelines Cohort Study

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Introduction

Heart rate variability (HRV), the variation in time intervals between consecutive heart beats, is commonly used to index the functionality of the cardiac autonomic nervous system in healthy individuals and patients suffering from various cardiovascular and non-cardiovascular disorders.[1] However, there are currently no population-based HRV reference values for men and women separately covering a wide age range, with the notable exception of the recent work of van den Berg and colleagues who described this for 10-second (ultra-short) electrocardiogram recordings.[2] While highly valued, in their study HRV data were derived from multiple cohorts using different electrocardiogram recording techniques, and a sample-dependent, exponential correction formula was used to correct for the influence of mean heart rate on HRV. We therefore aim to estimate HRV reference values derived from 10-second electrocardiogram, both uncorrected and generically corrected for heart rate,[3] from a single population sample with a wide age range.

Methods

Data from a large population-based study in the north of The Netherlands aiming to investigate risk factors for multifactorial diseases[4] (Lifelines Cohort Study and Biobank) were used. From 10-second resting electrocardiogram recordings, inter-beat intervals (IBIs, in ms) were obtained from 153,793 participants. Participants with cardiovascular disease, hypertension, type 2 diabetes, obesity and the use of anti-depressants, beta-blockers and vagal modulating agents were excluded ($n = 64,433$) as were electrocardiogram recordings with excessive noise and ectopic (non-sinus node) beats ($n = 4586$). HRV values were estimated from the remaining 84,772 participants (59.5% women; mean age 40.8 (range 13–91) years). Details on HRV calculation have been published elsewhere.[5] In short, the root mean square of successive differences (RMSSD, in ms) between IBIs were calculated as HRV index. In addition, taking into account the effect of mean IBI, corrected RMSSD (cRMSSD) was calculated.[3] We categorised participants into 12 5-year age bins. Centile curves, as a function of age, were estimated using the Box–Cox T-distribution of the gamlss function in R. Comparable with the recent paper by van den Berg et al.,[2] we chose to report the 2nd and 98th percentiles as lower and upper limits, respectively. The study was approved by the medical ethical committee of the University Medical Center Groningen. All participants were fully informed and gave consent prior to participation.

Results and discussion

The mean of IBI, median, 2nd and 98th percentiles of RMSSD and cRMSSD per age bin, for women and men separately, are given (Table 1). Men had higher IBIs at all ages. For women the highest median RMSSD of 66.5 ms was observed in the youngest age category (13–14 years) and lowest value of 16.1 ms in the oldest age category (75 + years). This was comparable for men with values of 67.4 and 14.9 ms, respectively. Figure 1 illustrates the centile curves as a function of age. In both sexes, the 25th percentile, median and 75th percentile of RMSSD steadily became lower from a young age until age

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Table 1. Reference values of RMSSD and cRMSSD per age bin for women and men separately.

			Mean IBI (ms)	RMSSD (ms)			cRMSSD (%)		
Age bins (years)	Sex	*N*	Mean (SD)	Mean (SD)	Median (2nd, 98th percentile)	*P* value[a]	Mean (SD)	Median (2nd, 98th percentile)	*P* value[a]
13–14	Women	275	862.2 (134.6)	77.7 (51.3)	66.5 (17.4; 232.2)	0.865	8.8 (5.3)	7.6 (2.4; 26.6)	0.865
	Men	278	896.9 (128.2)	80.3 (53.6)	67.4 (12.8; 213.0)		8.7 (5.3)	7.5 (1.7; 22.0)	
15–19	Women	1787	890.7 (146.8)	73.8 (50.5)	60.7 (12.4; 225.9)	0.526	8.0 (4.9)	6.9 (1.7; 22.8)	0.001
	Men	1089	948.4 (163.9)	70.8 (48.8)	59.9 (9.8; 213.2)		7.3 (4.7)	6.3 (1.3; 20.9)	
20–24	Women	3478	886.7 (144.7)	64.7 (47.3)	52.1 (11.3; 205.5)	≤0.001	7.0 (4.5)	5.9 (1.6; 20.6)	≤0.001
	Men	1653	941.7 (159.6)	57.3 (40.1)	47.6 (9.6; 174.0)		5.9 (3.7)	5.0 (1.4; 17.1)	
25–29	Women	5262	902.8 (144.9)	58.0 (40.0)	47.5 (11.5; 180.7)	≤0.001	6.2 (3.7)	5.3 (1.6; 17.4)	≤0.001
	Men	3454	951.9 (162.7)	52.1 (38.8)	42.3 (10.1; 172.7)		5.3 (3.5)	4.4 (1.3; 16.5)	
30–34	Women	5307	917.2 (138.9)	51.6 (35.4)	42.3 (11.5; 161.0)	≤0.001	5.4 (3.3)	4.7 (1.5; 15.4)	≤0.001
	Men	4058	959.9 (158.7)	45.4 (32.4)	36.9 (10.2; 140.8)		4.6 (2.9)	3.9 (1.3; 13.2)	
35–39	Women	6437	921.6 (137.0)	46.0 (31.9)	37.9 (10.8; 141.9)	≤0.001	4.8 (2.9)	4.1 (1.4; 13.9)	≤0.001
	Men	4456	957.0 (155.3)	39.9 (28.1)	32.8 (8.6; 123.8)		4.0 (2.5)	3.5 (1.1; 11.4)	
40–44	Women	8315	922.8 (138.7)	41.0 (28.6)	33.9 (9.7; 123.7)	≤0.001	4.3 (2.7)	3.7 (1.2; 12.0)	≤0.001
	Men	5507	959.5 (155.2)	35.2 (24.7)	29.0 (8.1; 105.5)		3.5 (2.2)	3.0 (1.0; 10.3)	
45–49	Women	8643	916.6 (137.4)	35.6 (25.5)	29.2 (8.3; 109.5)	≤0.001	3.7 (2.4)	3.2 (1.1; 10.8)	≤0.001
	Men	5947	962.5 (157.7)	31.6 (22.9)	26.0 (7.1; 95.5)		3.2 (2.1)	2.7 (0.9; 9.3)	
50–54	Women	4907	916.9 (135.8)	31.8 (22.0)	26.6 (7.5; 96.3)	≤0.001	3.3 (2.1)	2.9 (1.0; 9.5)	≤0.001
	Men	3396	960.1 (150.1)	28.7 (20.2)	23.7 (6.7; 87.5)		2.9 (1.8)	2.5 (0.9; 8.5)	
55–59	Women	2422	909.0 (132.1)	27.2 (19.4)	22.5 (6.7; 83.6)	0.003	2.9 (1.9)	2.5 (0.9; 8.5)	≤0.001
	Men	1650	961.6 (150.0)	26.2 (21.9)	21.0 (5.5; 89.5)		2.6 (2.0)	2.2 (0.7; 8.4)	
60–64	Women	1968	898.0 (131.1)	25.2 (20.0)	20.5 (5.5; 79.3)	0.025	2.7 (2.0)	2.3 (0.7; 8.5)	≤0.001
	Men	1342	957.9 (150.1)	24.8 (25.0)	19.1 (4.8; 86.6)		2.5 (2.4)	2.0 (0.6; 9.1)	
65–69	Women	1036	888.9 (127.7)	22.9 (20.6)	17.8 (5.0; 83.0)	0.632	2.5 (2.2)	2.0 (0.6; 8.8)	0.008
	Men	834	945.9 (145.7)	24.4 (24.9)	17.7 (4.87; 110.5)		2.5 (2.5)	1.9 (0.6; 11.4)	
70–74	Women	403	890.2 (121.2)	25.2 (31.3)	18.3 (5.0; 115.8)	0.024	2.7 (3.2)	2.0 (0.6; 12.9)	≤0.001
	Men	355	936.3 (139.3)	27.2 (37.6)	16.0 (4.7; 161.9)		2.8 (3.8)	1.6 (0.5; 16.6)	
75+	Women	172	860.5 (131.9)	24.0 (25.0)	16.1 (3.5; 106.2)	0.295	2.7 (2.8)	1.9 (0.5; 14.4)	0.053
	Men	140	931.2 (128.7)	25.4 (31.8)	14.9 (3.7; 130.3)		2.7 (3.3)	1.6 (0.5; 17.4)	

Values are given as mean (SD) and as median (2nd and 98th percentiles).
IBI: inter-beat interval; RMSSD: root mean square of successive differences; cRMSSD: corrected root mean square of successive differences.
[a]Differences in RMSSD median values between women and men.

60 years, and then remained stable. There is also a sharp drop of the 98th percentile from the younger to the older age bins until age 60 years, after which it shows a rise resulting in a wider range of RMSSD values in individuals from age 60 years onwards. The lower normal limit is, however, remarkably stable throughout the lifespan of both sexes. Women aged 20–45 years had on average 5.02 ms significantly higher median RMSSD values than men, and the difference was smaller (2.53 ms) in the age bin 45–59 years but was still significant. There were no sex differences in RMSSD values in the age bins below age 20 years and above age 60 years. Similar results were found for cRMSSD, including the pattern of centile curves as a function of age. With the notable exception for the median sex differences in cRMSSD which were more pronounced and applicable in a wider age range (15–75 years).

In conclusion, we provide population-based RMSSD and cRMSSD reference values using 10-second resting electrocardiogram recordings, from a single cohort with a wide age range. These reference values were derived from a sample at least six times larger than previous studies. These age and sex-specific RMSSD values constitute benchmarks for application in both research and clinical settings in which indications on physiologically plausible ranges are highly valuable.

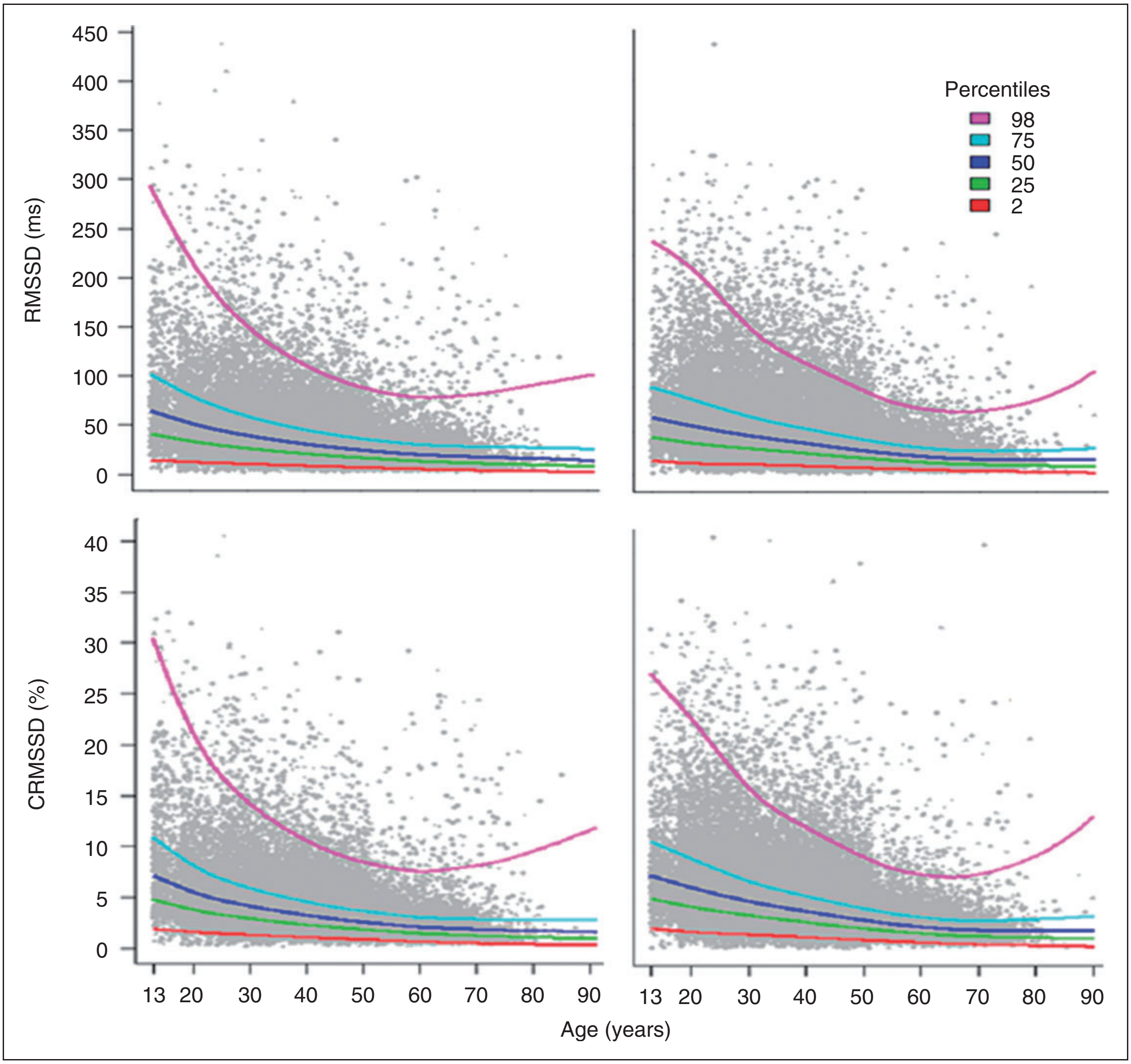

Figure 1. Centile curves of RMSSD (top) and cRMSSD (bottom) as a function of age for men (left) and women (right). RMSSD: root mean square of successive differences; cRMSSD: corrected root mean square of successive differences.

Author contribution

BST, HS and HR contributed to the conception or design of the work. BST, TM, AMR, HS and HR contributed to the acquisition, analysis, or interpretation of data for the work. BST drafted the manuscript. All authors critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work ensuring integrity and accuracy.

Declaration of conflicting interests

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