REVIEW PAPER

International Journal of Occupational Medicine and Environmental Health 2020;33(4)
https://doi.org/10.13075/ijomeh.1896.01560

MEASURING THE EFFECTS OF NIGHT-SHIFT WORK ON CARDIAC AUTONOMIC MODULATION: AN APPRAISAL OF HEART RATE VARIABILITY METRICS

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Abstract
Night-shift workers may develop poor cardiovascular health. Studies about heart rate variability (HRV) metrics could identify risk factors in this population and be used to examine the effectiveness of interventions for optimizing the health of night-shift workers. The purpose of this review was to examine the use of HRV methodologies in studies about night-shift work. Overall, 34 articles met the selection criteria and underwent a methodological critique. The main conclusion across these studies was that night-shift work could increase the sympathetic influences on the variability between heartbeats. In many cases, however, important methodological details were omitted (e.g., the number and duration of electrocardiogram recordings, sampling rates, R–R segment duration, wavelet transform methods). Recommendations include adding measures of disease outcomes, using ≥250 Hz sampling rates and 600-s R–R segments, and measuring sleep and circadian rhythms. With these approaches, researchers can design investigations that identify therapeutic targets for improving the health of night-shift workers. Int J Occup Med Environ Health. 2020;33(4)

Key words:
sleep, circadian rhythm, heart rate variability, sympathetic nervous system, night shift, parasympathetic nervous system

INTRODUCTION

Working at night – and sleeping during the day – may contribute to poor cardiovascular health. Approximately 30% of the workforce in industrialized countries works night shifts [1], but the health effects of this schedule remain poorly understood. The earliest reports about work schedules as a cardiovascular disease risk factor were based on longitudinal studies of men working in European factories [2–4]; a later series of publications examined cardiovascular outcomes in women enrolled in the U.S. Nurses' Health Study [5,6]. Although data from some of these cohorts did not conclusively demonstrate a relationship between night-shift work and cardiovascular diseases [2,3], there was a consensus that certain workers could be vulnerable, especially when night-shift work continued for many years [5,6].

In a study of factory workers in Sweden, the incidence of ischemic heart disease was significantly higher if night-shift work was conducted for 11–15 years; the risk profile increased further after working night shifts for 16–20 years [4]. In American nurses, ≥6 years of night-shift work was found to increase the risk for developing coronary heart disease [5], while nurses who reported ≥15 years of rotating night-shift work had an elevated incidence of stroke [6]. Findings from

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Received: October 7, 2019. Accepted: April 8, 2020.
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these early longitudinal studies provided a limited understanding of disease mechanisms – the investigations did not include direct measurements of cardiovascular and neurobiological function.

A 1994 paper by Hadjiolova et al. [7] marked an important shift away from interpreting morbidity/mortality statistics to measuring electrocardiogram (ECG) patterns in night-shift workers. Hadjiolova et al. calculated hourly mean heart rates to compare day- and night-shift workers, and their findings demonstrated that circadian patterns in these mean heart rates were different in men vs. women when working at night [7]. Following their publication, ECG recordings were added to many cross-sectional studies about night-shift work, and researchers calculated heart rate variability (HRV) metrics.

Today, prevailing hypotheses suggest that autonomic homeostasis could be affected by atypical work/sleep schedules and that night-shift schedules may lead to reduced variability in the timing between heartbeats. Data from patients with cardiovascular disease risk factors indicate that alterations in the autonomic modulation of the heart rate could predict which patients will develop ischemic and hypertensive disease [8,9]. For example, in patients with risk factors for coronary artery disease (N = 1043), Goldenburg et al. [8] found that low HRV was associated with myocardial ischemia detected by exercise stress echocardiography or myocardial perfusion imaging. In a larger cohort (N = 11 061) with a 9-year follow-up period, Schroeder et al. [9] found low HRV to predict hypertension. These studies about the potential predictive value of HRV did not, however, address occupational risk factors.

Generally, HRV metrics provide information about the neural mechanisms regulating the heart rate. Electrical activity of the sinoatrial node sets the timing for heartbeat intervals; conduction of the electrical stimulus through the ventricles is identified by upward deflections, R waves, in the ECG tracing. A healthy cardiovascular system demonstrates fluctuations in the intervals between heartbeats, rather than maintaining fixed intervals, in response to physical and psychological stimuli [10]. Sympathetic efferent nerves from the medulla innervate the sinoatrial node, transmitting signals to accelerate the heart rate. Parasympathetic signals, transmitted via vagus nerve branches innervating the sinoatrial and atrioventricular nodes, slow down the conduction of the electrical impulses. These opposing neural influences regulate the intervals between consecutive heartbeats [11].

To measure the sympathetic and parasympathetic nervous system (SNS and PNS, respectively) influences on HRV, segments of the ECG tracing that are free from artifact or arrhythmia are used to calculate R–R intervals (RRIs [normal-to-normal R waves may also be called N–N intervals]). The R–R (or N–N) interval series reflects a sequence of irregular intervals, which can be decomposed to reveal the frequency content of the signal; the bands are then classified as:

- very high frequency (VHF),
- high frequency (HF),
- low frequency (LF),
- very low frequency (VLF),
- ultra low frequency (ULF).

There are disputes about the origin and clinical utility of the VHF oscillations (in the range of 0.4–0.9 Hz [12]). Corresponding with respiratory-cycle heart rate variations, HF oscillations (in the range of 0.15–0.4 Hz) are commonly used to estimate PNS regulation of the heart rate. In turn, LF oscillations (in the range of 0.04–0.15 Hz) have been attributed to SNS and PNS influences on the heart rate, and to baroreflex activity [13,14], while VLF (0.003–0.04 Hz) and ULF (<0.003 Hz) reflect influences on HRV such as circadian rhythms, core body temperature fluctuations, and metabolic and endocrine factors. Due to the long time period of the VLF and ULF signals, ECG recordings lasting ≥24 h are required to accurately quantify these frequency bands [13].

The spectral area (power) of each frequency is determined by applying a variety of possible methods, such as the fast Fourier transform (FFT), used to convert the RRI series from the time domain into the frequency domain (revealing sinusoidal signals with different frequencies [15]).

Time-domain HRV metrics also provide information about SNS and PNS influences on the heart rate. The standard deviation of normal-to-normal RRIs (SDNN) reflects the activities of both SNS and PNS [10]. Of note is the fact that SDNN values of <50 m/s have been associated with a greater risk for cardiovascular morbidity and mortality [16]. Another measure, the root mean square of successive differences (RMSSD), is calculated by determining each successive time difference between heartbeats (in m/s), calculating the average squared results, and then determining the root of the total. The RMSSD provides an index of vagal cardiac control; RMSSD values correlate with respiratory modulation of the heart rate via the vagus nerve [13]. Investigators also determine the number of normal sinus intervals that differ by >50 m/s from the preceding interval (NN50). This value is often reported as a percentage (pNN50), and is found to correlate with both HF power and PNS activity [13].

Currently, there is no consensus about the relationships among work schedules, cardiovascular function, and long-term outcomes. While HRV studies might provide some important insights into the associated neural mechanisms, there is a lack of information about interpreting HRV measures in occupational health studies. Considering the need to understand the risk factors unique to the night-shift population, the purpose of this review was to examine the use of HRV methodologies in studies about night-shift work.

METHODS

A literature search was conducted using the recommended Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA [17]), as illustrated in Figure 1.

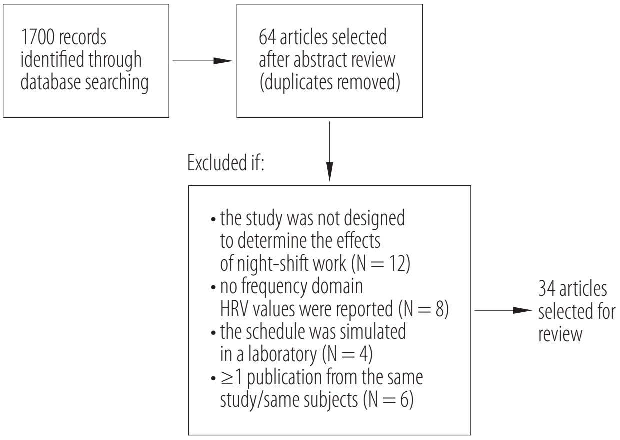

Figure 1. PRISMA flowchart for the selection of articles for the review paper on the use of HRV methodologies in studies about night-shift work

Publications in English were searched for in NCBI PubMed, Google Scholar, and the Cochrane Library, using the terms “heart rate,” “heart rate variability,” and “night shift.” To be eligible for the review, studies were required to have subjects with work schedules that included the clock hours of 0:00–6:00. Studies were excluded if their aims were not relevant to examining the effects of night-shift work on HRV (e.g., focused on exposure to workplace hazards, workplace accidents, or workers’ fatigue/job strain) or if night-shift schedules were simulated in a laboratory setting.

To be eligible for the review, the study was required to include frequency-domain HRV metrics. If an author stated that HRV metrics were measured but failed to report any values in the text, tables, or figures, then the study was excluded. In cases where the same subjects’ data were summarized in different papers, only one of the publications (the one with the most detailed HRV methods and results) was selected for the review. When authors intentionally omitted methodological details because the methods were reported in previous publications, the papers cited for the methods were obtained and used to evaluate their approach.

RESULTS

Thirty-four studies met the review criteria. As shown in Table 1, sample sizes ranged 6–665 subjects. Investigators recruited samples that were exclusively male or female for 20 of the studies [18–37]. Across the studies, women represented approximately 47% of the subjects. Rotating schedules were common in law enforcement agencies, factories, and healthcare facilities [19–23,25,26,28,29,31,32,35,38,39]. Firefighters, emergency medical technicians, and physicians were the only occupations involving 24-h work periods; depending on their responsibilities, these schedules allowed for rest breaks when subjects could sleep [27,30,33,34,40–44]. Night-shift start times and durations were variable across occupations. The average duration of night-shift work, excluding the extended duty schedules of physicians and first responders, was 11±3 h, and the schedules typically required 3±2 consecutive days of working at night.

As shown in Table 2, half of the studies were cross-sectional and obtained data from 1 ECG recording [21,22,25–28,31,32,34,40,45,46]. Depending on the aims of the study, the duration of a single ECG monitoring session ranged 3 min – 96 h. Other investigators required subjects to undergo ECG recordings at multiple time points (lasting 5 min – 24 h) with a range of 1–28 days between the recordings [18–20,23,24,29,30,35,38,41–44,47,48]. One study repeated ECG monitoring after 1 year to determine the effects of a new scheduling policy [36]. As shown in Table 3, most studies included both frequency- and time-domain HRV measures.

Many different approaches to spectral analysis were found across the studies. The RRI segment lengths, window methods, and wavelet transformation approaches varied across the studies (Table 2). The shortest segments used for the RRI series were 64, 100, or 120 s [18,22,35,45], but segment lengths were typically 300 [24,26,33,34,38,40,42,47,49] or 600 s [32,39,41,43,46]. Spectral windows were applied in a few studies to remove discontinuities in the signal. Window functions were used to taper the sinusoidal shape of the signal and served a variety of purposes, such as reducing signal noise, improving time resolution, and enhancing the accuracy of signal amplitude. Most studies did not report the use of windowing techniques, but others identified the use of Hamming [18,38] and Hann [19,23,45] windows. In 1 study, the ends of the data series were padded with zeros to taper the signal to 0 before the power spectrum was computed by FFT [49].

Notably, FFT was the most commonly reported approach for deconstructing the RRI series to determine HF and LF power [18,23,34,35,39,40,43,47,49]; 7 studies specifically referred to using Welch's method, which involves a discrete Fourier transform to calculate periodograms that are averaged to reduce variance in the individual power measurements [19,21,26,30,33,36,45]. The parametric AR method was applied in 5 studies [20,22,29,44,51]. Discrete wavelet transform [38], Lomb-Scargle periodogram [24], and coarse-graining spectral analysis [32] were also used to transform the RRI series to reveal the power spectra. None of the publications included a justification for selecting a specific analytic method, and the approach to reporting LF and HF power was not consistent across the reviewed studies. Following the recommendations of the HRV Task Force [50], several studies reported both absolute values (m/s^2) and normalized values (n.u., calculated by dividing LF or HF power by total power and multiplying by 100) [19,20,23,47]. It was also common to square-root [19,42] or log [19,21,22,24,26,28,35,38,39,47,49] transform the LF and HF values, an approach that improves the likelihood of achieving normally distributed data.

The majority of the studies concluded that SNS influences (using the LF component of HRV) on the heart rate modulation were elevated in night-shift workers (Table 4) [18,21,22,25–27,30,33–36,38–40,43–45,49,51]. However, comparisons across the studies were challenging because there were many differences in occupational norms and

Table 1. Demographic characteristics and work schedules in the review on the use of heart rate variability (HRV) methodologies in studies about night-shift work, based on 34 studies

Reference	Participants				Work			
	n	age [years]	females [%]	occupation	schedule type	start time (clock time)	duration [h]	consecutive night shifts [n]
Adams et al. [45]	12	M±SD: 34±4	33	physicians	n.r.	0:00	9	n.r.
Amirian et al. [40]	29	range: 30–40	45	physicians	on-call	15:30	17	n.r.
Boudreau et al. [38]	15	M±SD: 30±5	53	police officers	rotating	23:00	8	7
Chung et al. [18]	20	M±SD: 27±3	100	nurses	fixed	23:30	8	3–4
Dutheil et al. [44]	17	M±SD: 39±7	63	physicians	on-call	18:30 or 8:30	10–24	1
Freitas et al. [19]	12	M±SD: 39±7	0	security guards	rotating	22:00	8	n.r.
Furlan et al. [20]	22	M±SD: 39±3	0	factory workers	rotating	22:00	8	5
Ha et al. [35]	134	range: 25–44	0	factory workers	rotating	n.r.	n.r.	n.r.
Harbeck et al. [41]	20	range: 26–42	55	physicians	on-call	n.r.	n.r.	n.r.
Hulsegge et al. [46]	665	range: 18–68	44	multiple occupations	varied	varied	n.r.	n.r.
Ishii et al. [22]	47	range: 22–59	100	nurses	rotating	0:30 or 16:30	8.5	1–2
Ito et al. [23]	10	M±SD: 33±3	100	nurses	rotating	21:40	12	n.r.
Järvelin-Pasanen et al. [36]	48	range: 20–59	100	nurses	rotating	21:00	10	n.r.
Karhula et al. [24]	95	range: 31–59	100	nurses	varied	21:00	10	n.r.
Kunikullaya et al. [47]	36	M±SD: 26±4	30	telephone support	fixed	22:00	8	7
Langelotz et al. [60]	8	Me: 32	13	physicians	on-call	n.r.	24	n.r.
Lee et al. [25]	162	M±SD: 32±6	0	factory workers	rotating	19:30	12	5
Lee et al. [33]	12	M±SD: 38±8	0	physicians	extended	8:00	24	1
Lo et al. [26]	16	range: 25–35	100	nurses	rotating	0:00	8	4
Lyytikäinen et al. [27]	14	M±SD: 34±9	0	firefighters	extended	8:00	24	1
Malmberg et al. [39]	19	range: 26–55	43	physicians	extended	16:00	16	1
Mitani et al. [34]	9	range: 28–52	0	emergency medical technicians	extended	9:00	24	1
Monteze et al. [28]	431	Me: 34	0	factory workers	rotating	19:00	6	4
Munakata et al. [29]	18	M±SD: 29±2	100	nurses	rotating	21:30	11	2
Neufeld et al. [30]	14	M±SD: 27±7	100	emergency medical technicians	extended	n.r.	24	1

Table 1. Demographic characteristics and work schedules in the review on the use of heart rate variability (HRV) methodologies in studies about night-shift work, based on 34 studies – cont.

Reference	Participants				Work			
	n	age [years]	females [%]	occupation	schedule type	start time (clock time)	duration [h]	consecutive night shifts [n]
Oriyama et al. [31]	15	M±SD: 24±2	100	nurses	rotating	0:00 or 0:30	9	n.r.
Su et al. [21]	6	M±SD: 33±5	0	factory workers	rotating	n.r.	12	3
Takeyama et al. [37]	12	range: 30–60	0	firefighters	extended	8:45	24	0
Thurman et al. [42]	22	M±SD: 41±10	77	physicians	on-call	18:00	14–24	n.r.
Tobaldini et al. [51]	15	M±SD: 27±2	33	physicians	extended	7:00	26	n.r.
Van Amelsvoort et al. [49]	65	M±SD: 33±8	18	multiple occupations	rotating	varied	varied	varied
Wang et al. [43]	8	range: 27–30	63	physicians	on-call	15:00	16	1
Wong et al. [48]	14	41	33	paramedics	rotating	8:00	12	2
Yoshizaki et al. [32]	13	range: 25–53	100	nurses	rotating	18:00	15	1

n.r. – not reported.
Sample size is the number of subjects who worked between 0:00–6:00 and provided data for heart rate variability metrics. Age may include control subjects in addition to night-shift subjects. The percentage of women may also include women in a control group.

Table 2. Methods for electrocardiogram (ECG) monitoring and spectral analysis in the review on the use of heart rate variability (HRV) methodologies in studies about night-shift work, based on 34 studies

Reference	ECG monitoring				RRIs and spectral analyses					Data presentation – normalizations and transformations
	start time	ECG length	n per subject	days between	samples per s	segment duration	window/ padding	overlap [%]	wavelet transform	
Adams et al. [45]	15:00	24 h	1	n.a.	n.r.	120 s [61]*	Hann [61]*	50 [61]*	Welch's	none
Amirian et al. [40]	8:00	48 h	1	n.a.	n.r.	300 s	n.r.	n.r.	FFT	none
Boudreau et al. [38]	23:00, 8:00	8 h	2	7	250 [62]	300 s [62]*	Hamming	n.r.	DWT	none
Chung et al. [18]	n.r.	n.r.	2	3	256	64 s	Hamming	50	FFT	log
Dutheil et al. [44]	8:30	24 h	3	n.r.	n.r.	512 RRIs	n.r.	n.r.	AR [63]*	log
Freitas et al. [19]	16:00	24 h	2	7	200	512 RRIs	Hann	50	Welch's	norm, log, SR
Furlan et al. [20]	n.r.	24 h	3	7	300	n.r.	none	none	AR [64]*	norm
Ha et al. [35]	n.r.	5 min	3	4–5	n.r.	180 s	n.r.	n.r.	FFT	log

Harbeck et al. [41]	8:00	10 min	2	14–28	n.r.	600 s	n.r.	n.r.	n.r.	norm
Hulsegge et al. [46]	n.r.	96 h	1	n.a.	n.r.	600 s**	n.r.	none	n.r.	norm
Ishii et al. [22]	17:00	<2 h	1	n.a.	n.r.	100 s	n.r.	n.r.	AR	log
Ito et al. [23]	8:30	24 h	2	14	125	512 RRIs	Hann	n.r.	FFT	norm
Järvelin-Pas et al. [36]	varied	24 h	2	~365	n.r.	256 RRIs	n.r.	50	Welch's	norm
Karhula et al. [24]	n.r.	24 h	3	n.r.	n.r.	300 s	n.r.	50	LSP	log
Kunikullaya et al. [47]	22:00, 4:00	5 min	2	7	n.r.	300 s	n.r.	n.r.	FFT	norm, log
Langelotz et al. [60]	n.r.	n.r.	10	n.r.	n.r.	600 s	n.r.	n.r.	n.r.	none
Lee et al. [25]	19:30	24 h	1	n.a.	n.r.	n.r.	n.r.	n.r.	n.r.	none
Lee et al. [33]	n.r.	24 h	3	n.r.	n.r.	300 s	n.r.	n.r.	Welch's	norm
Lo et al. [26]	n.r.	48 h	1	n.a.	1000	300 s	n.r.	n.r.	Welch's	log
Lyytikäinen et al. [27]	8:00	96 h	1	n.a.	1000	n.r.	n.r.	n.r.	STFT	none
Malmberg et al. [39]	8:00, 16:00	12–24 h	3	<1	125	600 s	n.r.	n.r.	FFT	log, norm
Mitani et al. [34]	n.r.	24 h	3	n.r.	n.r.	300 s	n.r.	n.r.	FFT	none
Monteze et al. [28]	n.r.	3 min	1	n.a.	1000	n.r.	n.r.	n.r.	n.r.	log
Munakata et al. [29]	n.r.	n.r.	2	1–2	n.r.	512 RRIs	n.r.	n.r.	AR	none
Neufeld et al. [30]	23:00	8 h	7	<1	250	256 RRIs	n.r.	50	Welch's	none
Oriyama et al. [31]	n.r.	n.r.	1	n.a.	250	n.r.	n.r.	n.r.	n.r.	none
Su et al. [21]	n.r.	96 h	1	n.a.	250	n.r.	n.r.	n.r.	Welch's	log
Takeyama et al. [37]	n.r.	24 h or 186 h	1	n.a.	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.
Thurman et al. [42]	n.r.	24 h	4	n.r.	n.r.	300 s	n.r.	n.r.	n.r.	SR
Tobaldini et al. [51]	9:00	n.r.	2	<1	n.r.	n.r.	n.r.	n.r.	AR	norm
Van Amelsvoort et al. [49]	n.r.	24 h	2	varied	n.r.	300 s	0 padding [65]*	n.r.	FFT [65]*	log
Wang et al. [43]	8:00	5 h	3	n.r.	n.r.	600 s	n.r.	n.r.	FFT	none
Wong et al. [48]	6:00	12 h	2	<1	n.r.	n.r.	n.r.	n.r.	n.r.	none
Yoshizaki et al. [32]	15:00	24 h	1	n.a.	250	600 s	n.r.	n.r.	CGSA	none

AR – autoregressive algorithm; CGSA – coarse graining spectral analysis; DWT – discrete wavelet transform; ECG – electrocardiogram; FFT – fast Fourier transform; LSP – Lomb-Scargle periodogram; Log – logarithmic transformation; norm – normalized (calculated by dividing power of the frequency by total power × 100); RRIs – R–R intervals; SR – square-root transformation; STFT – short-time Fourier transform.

n.a. – not applicable, n.r. – not reported

* This is the reference. The paper from column 1 did not include this information but instead the authors cited an earlier paper about their method (the reference is given in square brackets).

** This denotes that in this study the investigators restricted analyses to the three 5-min intervals when the heart rate was at the lowest levels.

Table 3. Variables calculated to reflect autonomic modulation of the heart rate in the review on the use of heart rate variability (HRV) methodologies in studies about night-shift work, based on 34 studies

Reference	Measure	
	frequency-domain	time-domain
Adams et al. [45]	VHF, HF, LF, VLF, LF:HF ratio	RRI, SDNN
Amirian et al. [40]	HF, LF, LF:HF ratio	none
Boudreau et al. [38]	HF, LF, LF:HF ratio	none
Chung et al. [18]	HF, LF, LF:HF ratio	RRI
Dutheil et al. [44]	HF, LF, LF:HF ratio	SDNN, RMSSD
Freitas et al. [19]	HF, LF, VLF, LF:HF ratio	RRI, SDNN, pNN50
Furlan et al. [20]	HF, LF, LF:HF ratio	RRI, SDNN
Ha et al. [35]	HF, LF	none
Harbeck et al. [41]	HF, LF, LF:HF ratio, total power	none
Hulsegge et al. [46]	HF, LF, VLF, LF:HF ratio	SDNN, RMSSD
Ishii et al. [22]	HF, LF, LF:HF ratio	CVRR
Ito et al. [23]	HF, LF, LF:HF ratio, total power	RRI
Järvelin-Pasanen et al. [36]	HF, LF, LF:HF ratio	RRI, SDNN, RMSSD
Karhula et al. [24]	HF, LF, LF:HF-ratio	RMSSD
Kunikullaya et al. [47]	HF, LF, LF:HF ratio	RRI
Langelotz et al. [60]	HF, LF, LF:HF ratio	RRI, SDNN, RMSSD, pNN50
Lee et al. [25]	HF, LF, LF:HF ratio, total power	RRI, SDNN, RMSSD, pNN50
Lee et al. [33]	HF, LF	RRI, SDNN, NN50, pNN50
Lo et al. [26]	HF, LF, LF:HF ratio	none
Lyytikäinen et al. [27]	HF, LF, VLF, LF:HF ratio, total power	SDNN, RMSSD
Malmberg et al. [39]	HF, LF, VLF, LF:HF ratio, total power	none
Mitani et al. [34]	HF, LF, LF:HF ratio	none
Monteze et al. [28]	HF, LF, LF:HF ratio	RMSSD
Munakata et al. [29]	HF, LF, LF:HF ratio	RRI, SDNN
Neufeld et al. [30]	HF, LF	RRI, SDNN
Oriyama et al. [31]	HF, LF, LF:HF ratio	none

Su et al. [21]	HF, LF, LF:HF ratio	RRI, SDNN, RMSSD
Takeyama et al. [37]	HF, LF, LF:HF ratio	none
Thurman et al. [42]	HF, LF, LF:HF ratio	RRI, SDNN, RMSSD, pNN50
Tobaldini et al. [51]	HF, LF, VLF, total power	None
Van Amelsvoort et al. [49]	HF, LF	SDNN
Wang et al. [43]	HF, LF, LF:HF ratio	SDNN, RMSSD
Wong et al. [48]	HF	RMSSD, pNN50
Yoshizaki et al. [32]	HF, LF, LF:HF ratio	RRI, SDNN

CVRR – coefficient of variance of R–R intervals; HF – high frequency; LF – low frequency; NN50 – number of normal sinus intervals differing by >50 ms from the preceding interval; pNN50 – percentage of normal sinus intervals differing by >50 ms from the preceding interval; RMSSD – root mean square of successive differences in normal sinus intervals; RRI – R–R interval (mean value); SDNN – standard deviation of normal-to-normal R-R intervals; VHF – very high frequency; VLF – very low frequency.

Table 4. Qualitative summary of study findings in the review on the use of heart rate variability (HRV) methodologies in studies about night-shift work, based on 34 studies

Topic	Conclusions	Relevant studies
Diurnal and circadian patterns	Investigators tested the hypothesis that rotating/night-shift schedules alter HRV patterns across the day and night. The same subjects were compared as they worked different shifts [19–21,23,25,35,38]; 2 studies included control groups of daytime-only workers [32,47]. The ECG was recorded for ≥24 h [19–21,23,25,32] with the exception of 3 studies using shorter recordings [35,38,47]. To determine subjects' circadian rhythms, 1 study measured fluctuations in salivary melatonin levels [38]. In several studies, 24-h patterns in HF and LF power were evident and corresponded with sleep periods [19–21,23,32]. Sleep-related increases in PNS modulation of the heart rate (increased pNN50 and HF power) occurred even when workers' rest periods were during the daytime [19,20,23,32]. Five studies, however, revealed potentially pathological patterns [21,25,35,38,47]. In factory workers, LF power increased when rotating to the night shift [35], and night factory workers had lower HRV (decreased SDNN and RMSSD) than day-shift employees [21,25]. The LF:HF ratio was elevated in police officers during rest periods but only if the officers' melatonin rhythms had not adapted to working at night [38]. Compared with their day-shift colleagues, night-shift customer service employees demonstrated a trend towards higher LF power and lower HF power, although the comparisons did not reach statistical significance [47].	Freitas et al. [19] Furlan et al. [20] Su et al. [21] Ito et al. [23] Lee et al. [25] Yoshizaki et al. [32] Boudreau et al. [38] Ha et al. [35] Kunikullaya et al. [47]

Table 4. Qualitative summary of study findings in the review on the use of heart rate variability (HRV) methodologies in studies about night-shift work, based on 34 studies – cont.

Topic	Conclusions	Relevant studies
Autonomic parameters off-duty	Subjects were monitored off-duty to test the hypothesis that night-shift workers have elevated sympathetic parameters when resting after work. Most studies were conducted in healthcare workers [18,22,24,26,29,34,45,48]. When night-shift nurses went off-duty, they had higher metrics indicating sympathetic modulation of the heart rate when awake, compared with nurses who worked during the day [22,26]. When nurses were not scheduled to work on consecutive nights – and, therefore, slept at night – their sleep was characterized by higher LF power compared with day-shift nurses [18]. Emergency room physicians demonstrated an elevated LF:HF ratio before and during 8-h night shifts (compared with post-shift values), suggesting that stress in anticipation of work may affect autonomic parameters [45]. Not all studies found signs of elevated sympathetic modulation after night-shift work [24,29,34,46]. Sex differences may exist; Hulsegge et al. reported that in men, but not in women, night-shift work was associated with lower RMSSD, SDNN, and VLF power during sleep [46].	Chung et al. [18] Ishii et al. [22] Karhula et al. [24] Lo et al. [26] Munakata et al. [29] Mitani et al. [34] Adams et al. [45] Hulsegge et al. [46] Wong et al. [48]
Extended duty schedules	The effects of long overnight schedules (16–24 h) were examined in first responders and healthcare providers to determine how extended duty alters HRV. Sleep was permitted when possible on-duty [27,30,33,34,37,39] with the exception of 1 study [51]. For firefighters, on-duty sleep was characterized by lower vagal indices (HF power, SDNN) compared with off-duty sleep [30]. When off-duty, paramedics demonstrated a decline in the LF:HF ratio when asleep vs. awake; however, this pattern was eliminated during a 24-h shift [34]. When naps occurred during the latter hours of firefighters' shifts (clock hours 5:00–7:00), the LF:HF ratio was significantly higher compared with values recorded when firefighters slept earlier in the shift (clock hours 3:00–5:00) [37]. Recovery from an elevated LF:HF ratio was possible in firefighters if they were given 3 days of rest after a 24-h shift [27]. For physicians, increased LF power [33,39,51,60] and reduced HF power [33,39,40,51] were found during night on-call schedules, compared with off-duty or pre-call parameters. In a group of surgeons (residents and specialists), the HF power, SDNN, RMSSD, and pNN50 increased during a 24-h on-call period, which was interpreted as a sign of increasing vagal modulation of the heart rate during extended duty [60]. A different sample, comprised of medical residents, demonstrated lower vagal modulation (HF, RMSSD) in the morning before the 16-h night shift compared with parameters from a daytime work day; the researchers speculated that this response may result from stress in anticipation of the night shift [43]. In emergency room physicians, stress (defined by the number of medical emergencies) was negatively correlated with SDNN [44]. Two studies in on-call physicians did not find night work to have any significant effects on HRV metrics [41,42].	Lyytikäinen et al. [27] Neufeld et al. [30] Lee et al. [33] Mitani et al. [34] Malmberg et al. [39] Amirian et al. [40] Harbeck et al. [41] Thurman et al. [42] Wang et al. [43] Dutheil et al. [44] Langelotz et al. [60] Takeyama et al. [37] Tobaldini et al. [51]

Interventions for improving cardiovascular health	The following interventions were hypothesized to reduce the adverse effects of night-shift work on HRV metrics: forward-rotating schedules, bright light therapy, and workplace naps. Two studies indicated that backward-rotating schedules may have the most detrimental effects on HRV and cardiovascular health [36,49]. One year after a hospital implemented a policy designed to improve nurses' schedules (i.e., to reduce backward schedule rotations and the number of consecutive night shifts; as well as to increase flexibility), the researchers found nurses to have lower normalized LF power and higher normalized HF power, compared with the parameters recorded before the policy was implemented [36]. In another study of nurses, taking two 15-min naps during the night-shift was associated with lower LF:HF ratios during work, compared with nurses who could not nap [31]. When bright light therapy was used to adapt police officers to working at night – by shifting the phase of their peak salivary melatonin levels to occur during the daytime – officers' daytime sleep was associated with lower LF:HF ratios compared with non-adapted officers [38]. Although the study by Monteze et al. was not designed to test any interventions, the findings showed that workers' waist circumferences and visceral fat areas correlated negatively with log-transformed HF power and RMSSD, suggesting that dietary interventions may affect PNS modulation of the heart rate in night-shift workers [28].	Monteze et al. [28] Oriyama et al. [31] Boudreau et al. [38] Järvelin-Pasanen et al. [36] Van Amelsvoort et al. [49]

ECG – electrocardiogram; HRV – heart rate variability; PNS – parasympathetic nervous system; SNS – sympathetic nervous system.
Other abbreviations as in Table 3.

research designs. Two important themes emerged in the review: disrupted sleep and circadian rhythms, and job-related stress (Table 4). A variety of methods were used to quantify sleep and circadian rhythms such as sleep diaries and questionnaires [18,25,27,30,31,33,34,38,39,41, 42,46,47,52]; polysomnography recordings [18,38]; and salivary, plasma, or urine biomarker levels (e.g., melatonin, cortisol [29,34,38,41,51,53]). Only a few studies addressed sleep apnea, citing the condition as an exclusion criterion, rather than exploring the role of sleep apnea in cardiovascular responses to night-shift work [33,38,39]. In healthcare providers, work-related cognitive and emotional stress was proposed as a factor contributing to pathological patterns in HRV [36,39,40,43–45], but this theme received less attention in other occupations.

CONCLUSIONS

Many of the reviewed studies indicated that working at night – and sleeping during the day – may lead to cardiac autonomic dysfunction. There were many inconsistent findings across the studies, which could result from studying different schedules and occupations, as well as using different HRV metrics and methods. Recommendations for strengthening future studies are listed in Table 5.

None of the studies provided data defining the relationships between HRV metrics and cardiovascular disease outcomes. In other populations, low HRV (low SDNN and RMSSD) and the HF and LF power bands have been reported as possible predictors of cardiovascular morbidity and mortality [54–56]. In the Atherosclerosis Risk in Communities Study, for example, lower SDNN and RMSSD values were associated with an elevated risk of stroke in subjects with diabetes [54]. After controlling for covariates, women enrolled in the Stockholm Female Coronary Risk Study were found to have a higher 5-year cardiovascular mortality risk when they had low HRV (the SDNN index) 3–6 months after hospitalization for acute coronary syndrome; lower HF, LF, and VLF power also predicted

Table 5. Recommendations for future studies on the use of heart rate variability (HRV) methodologies in studies about night-shift work, based on 34 studies

Recommendation	Rationale
Include multiple time- and frequency- domain parameters and acknowledge the limitations of the LF:HF ratio	to obtain sufficient and reliable data about cardiac autonomic modulation
Conduct longitudinal studies tracking cardiovascular morbidity and mortality outcomes	to determine which HRV metrics predict adverse outcomes and identify specific profiles of night-shift workers with an elevated cardiovascular disease risk
Conduct longer (≥24-h) ECG recordings when possible	to examine circadian rhythms and obtain accurate measures of the SDNN and VLF band
Select appropriate ECG sampling rates for the study (typically ≥250 Hz)	to obtain an adequate precision of the R–R series
Select appropriate RRI segment duration	to obtain an adequate resolution of the spectral information
Report the wavelet transform method and window techniques	to facilitate replicating studies and comparing findings across studies
Include objective measures of sleep, physical activity, and circadian rhythms when feasible; examine sleep apnea syndrome as a contributing factor to HRV and adverse cardiovascular outcomes	to advance knowledge about sleep neurobiology in night-shift workers
Include control groups and repeated measurements of HRV	to enhance the rigor of studies with between-subject and within-subject comparisons

cardiovascular mortality in this cohort [55]. In a study involving repeated HRV measures (4 time points) in patients with end-stage renal disease undergoing hemodialysis, lower normalized LF power and higher normalized HF power were independent predictors of cardiovascular mortality within an 8-year period [56].

Many studies omitted important methodological details. Mostly, information was lacking about ECG sampling rates, R–R segment duration, and the methods for calculating the power bands. There have been controversies about the optimal ECG sampling rates required for an adequate precision of the R–R series. Kwon et al. [57] examined different sampling rates by acquiring an ECG at 1000 Hz and then conducting comparisons of the down-sampled recordings at 500, 250, 100, and 50 Hz. Kwon et al. found that the 500 and 250 Hz sampling provided excellent concordance with the frequency-domain metrics calculated from the 1000 Hz sampling rate. As a result, they recommended sampling rates of ≥250 Hz for studies evaluating the LF and HF components of the HRV signal [57].

Sampling rates are particularly important to those researchers who are using portable devices for long-term ECG monitoring because they are limited by battery power and the size of data files. Data from Kwon et al. indicate that researchers should utilize devices that provide ECG sampling rates of at least 250 Hz [57]. Singh et al. [11] recommended using a 4-Hz rate for resampling the RRIs obtained from the ECG so that the intervals are evenly spaced in time before performing spectral analysis. Only 13 of the 34 studies included in the present review reported the ECG sampling rate, yet only 2 of these studies used a sampling rate that was lower than the recommendation from Kwon et al [57].

The duration of R–R segments selected by investigators affects the resolution of the spectral information contained in the signal. Heathers provided recommendations for optimal R–R segment lengths, emphasizing that researchers should ensure that segments contain multiple cycles (at least 10) of the oscillatory information required for frequency-domain measures [14]. Compared with the HF parameter, an accurate estimation of LF oscillations requires longer R–R segments. For example, the resolution of the HF component of a signal (which oscillates at the frequency of respiratory sinus arrhythmia [approximately 0.25 Hz]) can be adequately estimated using a 60-s RRI segment. Heathers recommended that researchers use at least a 300-s RRI segment duration, which allows at least 256 RRIs to be obtained, because this length can be used to accurately determine frequencies as low as 0.03 Hz [14].

Singh et al. [58] analyzed a simulated signal and compared different R–R segment lengths (1024, 512, 256, or 128 samples; the R–R series was resampled at 4 Hz, to transform the signal into an evenly sampled series, with 50% overlapping of segments). On that basis, they concluded that the segments with 256 RRIs produced a smoothed spectral estimate with clearly outlined peaks in the LF and HF bands. The finding is consistent with the recommendation from Heathers that 300 s (which correspond with 256 samples) provide an optimal RRI segment duration for quantifying the LF and HF components of the signal [14,58]. To increase the number of R–R segments available for analyses, researchers can overlap segments by 50%. Singh et al. warns against drawing conclusions from groups of studies using different R–R segment durations [58].

Although there is limited consensus about the optimal methods for transforming the RRI series into the power spectra, and many different approaches are available, it is critical for investigators to report the details of their methodologies (e.g., wavelet transform, overlap, windowing techniques) to aid readers in replicating methods, and also for improving the ability to draw conclusions across studies with similar methods.

Many studies included only a few of the possible HRV metrics; the majority of the reviewed studies examined the LF:HF ratio. It is important to note that the interpretation of the LF:HF ratio is highly controversial. Billman cautioned researchers against assuming that the HF and LF bands reflect purely, and respectively, PNS and SNS activity [59]. The neural information contained in these frequency bands is more complex, despite the fact that many researchers use the LF:HF ratio as a measure of sympatho-vagal balance. Heathers also challenged the widespread use of the LF:HF ratio and argued that the LF and HF fluctuations observed in studies are mediated by both SNS and PNS [14]. Considering these arguments, when investigators report the LF:HF ratio, they should not interpret the value as a quantitative relationship between SNS and PNS influences on heart rate.

Most studies failed to address the role of sleep, including altered circadian rhythms and conditions such as sleep apnea. Sleep disorders in night-shift workers – and the effects on HRV – remain to be fully explored. Three of the reviewed studies tested the effects of interventions (bright light therapy, workplace naps, and schedule modifications promoting flexibility and forward schedule rotations). It is not possible to identify the effects of these interventions on cardiovascular disease risk because none of the studies tracked cardiovascular outcomes >1 year post-intervention [31,36,38]. Because workers with existing cardiovascular disease were generally excluded from HRV research studies, it also remains unknown how night-shift work alters the course of cardiovascular disease in high-risk individuals and whether interventions (e.g., dietary changes, sleep apnea management, work schedule modifications) can effectively reduce cardiovascular morbidity in high-risk workers. Attention to these important questions in the design of future studies can enhance the ability of HRV research to improve the health of night-shift workers.

Clinical significance

Night-shift workers may develop cardiac autonomic dysfunction. It remains unknown how HRV changes correlate with cardiovascular morbidity/mortality in night-shift workers because studies have lacked long-term outcome data. Occupational health research could improve the identification of night-shift related disorders through research examining HRV methods, circadian/sleep-related factors, and long-term cardiovascular outcomes.

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