

Elevated Blood Pressure, Decreased Heart Rate Variability and Incomplete Blood Pressure Recovery after a 12-hour Night Shift Work

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Abstract: Elevated Blood Pressure, Decreased Heart Rate Variability and Incomplete Blood Pressure Recovery after a 12-hour Night Shift Work: Ta-Chen Su, et al. Department of Internal Medicine, National Taiwan University Hospital, Taiwan—Shift work has been associated with increased risk of cardiovascular disease. This study was designed to determine the hemodynamic effects of 12-hour (12-h) shifts, and changes in blood pressure (BP) and heart rate variability (HRV) during 36 h rest time following 12-h shifts. Fifteen male shift workers with a mean age of 32.9 yr were recruited from a semiconductor factory. Ambulatory BP (AmBP) monitoring was performed for a total of 48 h for each participant. Six workers were monitored for 48 h by Holter electrocardiogram on both the day and night shifts. Paired self-comparison was used to estimate the difference between two hourly measurements of 12-h BP, HR, and HRV using the same timetable intra-individually. We also applied mixed models to estimate the effects of 12-h shifts on the delayed recovery of BP and heart rate (HR) in six workers who completed 96-h AmBP monitoring, including a 48-h night shift-rest period and another day shift period. Results showed that 12-h night shift work gave a persistently elevated systolic and diastolic BP (SBP and DBP) and HR, and decreased HRV compared to 12-h day shift work with the corresponding resting time. In addition, there was delayed SBP and DBP recovery on the first 12-h rest time in night shift workers, which was further

demonstrated on the second 12-h rest time after adjustment for possible confounders through mixed models. In conclusion, 12-h night shift work may elevate BP and HR and decrease HRV. It is also associated with delayed BP recovery.
(*J Occup Health* 2008; 50: 380–386)

Key words: Blood pressure, Heart rate variability, 12-hour night shift work, Delayed recovery

Shift work has been associated with increased risk of cardiovascular disease (CVD)¹⁻³. Working shifts impacts on the cardiovascular (CV) system of workers. These are measurable impacts which are supported by a number of epidemiologic studies^{1,2}. Yet empirical data as to their pathophysiology are quite limited. A recent review of the data shows that shift workers have a 40% increased risk of CVD³, but the mechanisms involved in different types of shift work, especially 12-h night shift work, on the delayed recovery of blood pressure (BP) remain unclear². A study in the United State showed extended work shifts increased the risk of motor vehicle accidents among hospital interns⁴. Other concerns were also reported by the U.S. National Institute of Occupational Safety and Health (NIOSH) regarding the impact of overtime shift work⁵.

The 24-h ambulatory BP (AmBP) is an accurate reflection of dynamic BP changes during work and rest, day and night, and is probably a good predictor of long-term damage to cardiovascular health risks, such as clinical CVD and carotid atherosclerosis^{6,7}. AmBP is also widely used in studies on the health effects of night shift workers^{8,9}. Heart rate variability (HRV) has also been implicated in the risk of cardiac events¹⁰, and worksite studies have shown that decreased HRV is linked

Received Apr 27, 2007; Accepted May 27, 2008

Published online in J-STAGE Jul 25, 2008

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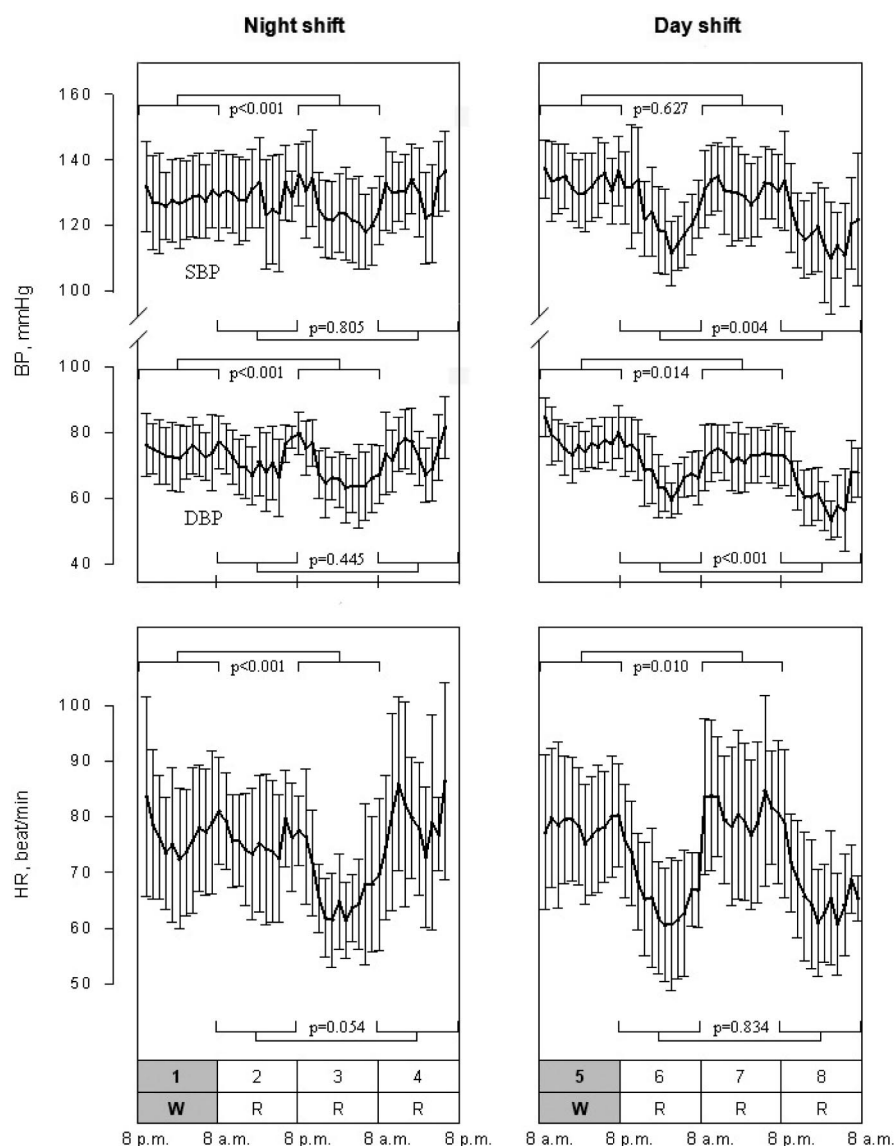


Fig. 1. Average values and 95% confidence intervals of eleven workers in a continuous 48-h monitoring of BP and HR during and after night or day shift work. Period 1 (shaded area) was the night shift work for 12 h, and periods 2–4 were the off-duty resting times of 36 h. Period 5 (shaded area) was day shift work for 12 h, and periods 6–8 were off-duty resting times of 36 h. *p* value: the difference of BP and HR between two 12-h durations.

to shift work^{8, 11}). This study was conducted to explore the potential CV effects of 12-h shifts by monitoring 24-h Holter electrocardiography (ECG) and AmBP.

Methods

Subjects

Fifteen healthy male shift workers from a semiconductor factory were recruited for this study. Eleven workers each completed either the day shift or the night shift 48-h AmBP studies. Among them, 6 were randomly selected and invited to complete a 96-h

monitoring, including 48-h night and 48-h day shift periods, during which they also carried a Holter ECG monitor for 48 h in both the day and night shifts at the same time as AmBP was performed. The 48-h shift work periods consisted of shift work for 12 h and off-duty resting of 36 h. The schematic overview of hemodynamic monitoring is shown in Fig. 1. The ethics committee of the National Taiwan University College of Public Health approved this study before its commencement.

The work schedule of the workers was a cycle of 12-h day or night shifts for 3 continuous days with rest for

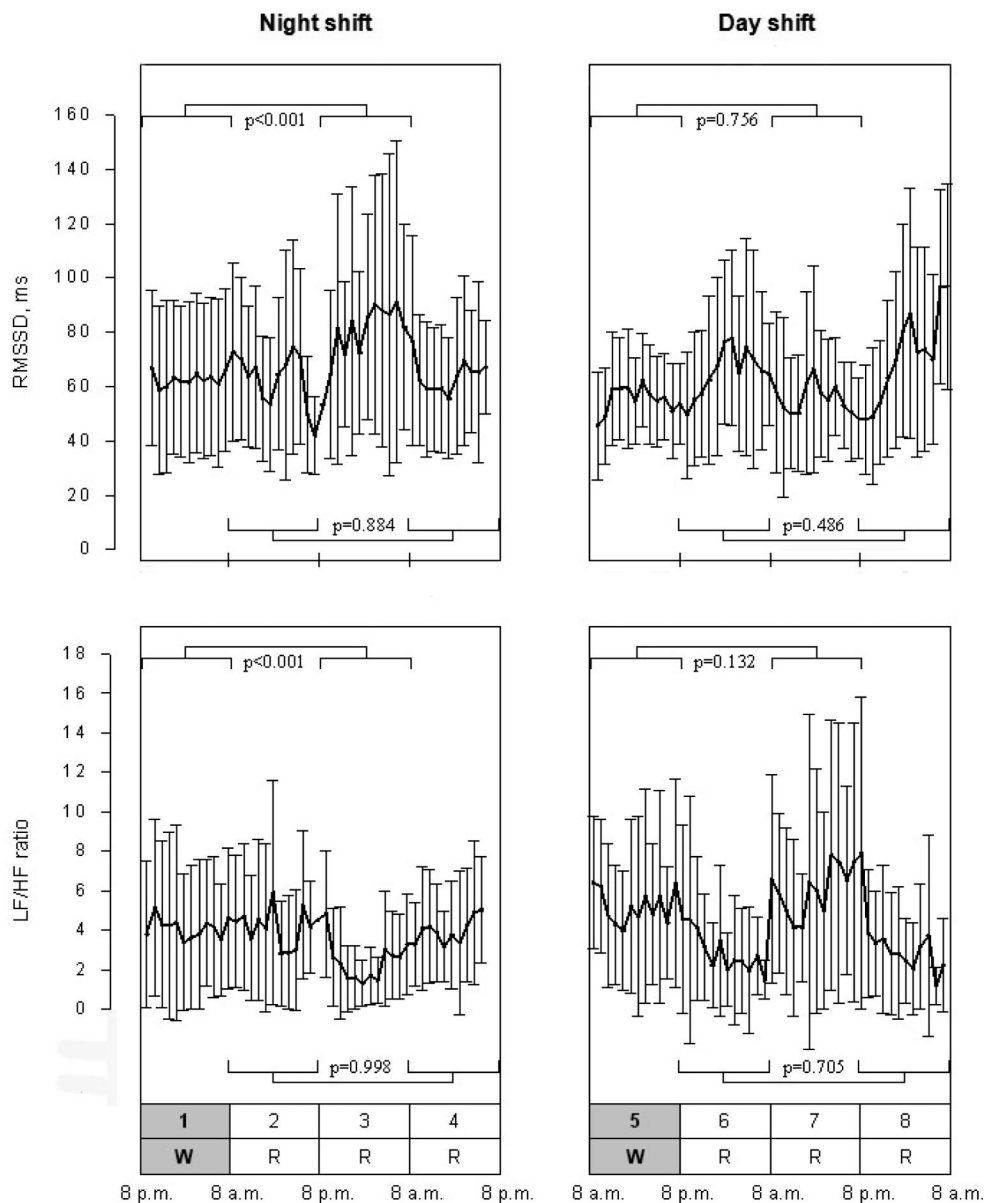


Fig. 2. Average values and 95% confidence intervals of 48-h continuous monitoring of time domain (RMSSD) and frequency domain (LF/HF ratio) of heart rate variability during and after night or day shift work in six workers. *p* value: the difference of BP and HR between two 12-h durations.

two continuous days before the next working day, and this cycle continued for 1 month. After obtaining informed consent, the workers were recruited on the last working day of the shift cycle in order to monitor continuously the following 48 h. Except for the day shift, all of the workers were instructed to perform regular static physical activities during the monitoring time and to sleep in the nighttime. After the night shift, they also were suggested to go to sleep. Vigorous physical activities were prohibited during the continuous AmBP or ECG monitorings.

Continuous AmBP measurements

Forty-eight-hour BP monitoring was recorded with the cuff sphygmomanometer of an oscillometric BP device using Dynapulse 5000 (Pulse Metric Inc. San Diego, CA, U.S.A.). This method has been validated against invasive measurements¹²⁾, and was used in our previous study of 24-h BP monitoring⁷⁾. Daytime monitoring was set during the 7 a.m.–10 p.m. period, with consecutive measurements every 15 min, while nighttime BP was measured during the 10 p.m.–7 a.m. period every 30 min.

Heart rate variability measurements

During day or night shift work, 48-h continuous ambulatory ECG monitoring was performed for six participants using a 3-channel ambulatory ECG recorder (Pacerecorder, Model 461A) with a sampling rate of 250 Hz (4 msec.). Each channel was scanned on a Del Mar 563 Holter Analysis System (Del Mar Avionics, Irvine, CA, USA). The QRS complexes were automatically classified and manually verified as normal sinus rhythm, atrial or ventricular premature beats, or noise by comparison with adjacent QRS morphology. The R-R intervals were deduced from the adjacent normal sinus beats (i.e., N-N intervals) and their interval time series were then transferred to a personal computer and post-processed by a program written in the Matlab language (version 5.2, The Mathworks Inc., Natick, MA, USA). Missing intervals of the raw R-R data were interpolated by the cubic spline method and re-sampled at 4 Hz by the Ron-Berger method.

Time and frequency domain parameters

For the entire study population, time domain measurements, including mean N-N intervals, standard deviation of N-N intervals (SDNN), and root-mean-square successive differences (RMSSD), were calculated every 5 min. The power spectrum densities were estimated by Welch's averaged periodogram method¹³⁾, while the low frequency (LF) power (0.04–0.15 Hz) and high frequency (HF) power (0.15–0.4 Hz) were derived for each 5-min segment. The LF to HF ratio was used as an index of sympathovagal balance status.

Statistical analysis

To improve statistical efficiency, paired self-comparisons of cardiovascular parameters were used per hour. We summarized the blood pressure monitoring and HRV as average hourly measurements for comparison between resting time and working time intra-individually. For each participant, the mean difference between the two sets of hourly measurements was estimated by comparing the effects of 12-h night or day shift work on BP, HR, and HRV with the corresponding resting time using the same hour-to-hour timetable intra-individually. We also adopted a design of self-comparison to control the potential confounding effects of biological rhythm for a specific person. For example, the hemodynamic data of 8–9 a.m. during the work shift were compared with the corresponding data of 8–9 a.m. 24 h later. Similarly, BP measured during 9–10 p.m. was compared with BP during 9–10 p.m. 24 h later. The results are summarized in Figs. 1 and 2. Accordingly, there are 12 paired comparisons of hemodynamic parameters or HRV in each time period.

Because blood pressure continuously changes within a person and repeated measurements were made during

BP monitoring, we could not treat such measurements as fully independent of the person. In other words, there were auto-correlations for every BP measurement within a person and such measurements were treated as a “random effect” within that person. All of the major determinants of BP were included in the statistical model in a multiple regression analysis, and they were called “fixed effects”. The “mixed regression model” was a multiple linear regression model that primarily dealt with repeated measurements for individuals and contained both fixed and random effects¹⁴⁾.

To control potential confounders of BP and HR, mixed regression models were constructed for six workers who completed 96-h AmBP monitorings to assess the effects of 12-h work shift on hemodynamic parameters. In this model, we treated age, BMI, duration of shift work, smoking and drinking habits, day (vs. night), work (vs. rest), and interaction between day (vs. night) and work (vs. rest) as covariates. The 12-h means of hour-to-hour comparisons were entered separately in the mixed model as dependent variables. Because the LF and HF power had a skewed distribution in this study, we performed logarithm transformations on LF, HF, and LF/HF ratio.

Results

The basic characteristics of the 15 shift workers were: age of 32.9 ± 4.8 yr, body mass index (BMI) 25.1 ± 2.8 Kg/m², and cholesterol level 199.3 ± 24.3 mg/dl on the average. The average duration of shift work was 3.3 yr and 60% were smokers. Their physical activities did not change during the entire study period.

Among the 11 workers on the night or day shift, significant cardiovascular effects were found and associated with night shift work were found for systolic and diastolic BP (SBP and DBP), HR, and HRV (Table 1, Figs. 1 and 2). However, the corresponding effects of the day shift were much smaller, with no significant effects for SBP and HRV. In addition, delayed recoveries of SBP and DBP after the night shift were demonstrated (Table 1). SBP and DBP of time period 3 were higher than those of time period 8, but there was no significant corresponding effect in day shift workers, time period 7 vs. 4. As shown in Figure 2, compared with BP in the first 12-h rest period, BP of the third 12-h rest period decreased in day shift workers. These results indicate that night shift work exerted greater cardiovascular effects. In contrast, in the first 12-h rest period, workers were supposed to be taking a rest or sleeping after a 12-h night shift (verified by diaries that they went to sleep before 12 a.m.). However, their average BP was still as high as their BP on the corresponding time on the following day, which indicated an incomplete BP recovery. The delayed recovery in HRV was not significant in either shift.

The mixed models (Table 2) showed a higher SBP,

Table 1. Comparison of blood pressure, heart rate, and heart rate variability between shift work and rest

	Work (Time 1)	Rest (Time 3)	Paired difference		Rest (Time 3)	Rest (Time 8)	Paired difference	
	Mean \pm SE	Mean \pm SE	Mean \pm SE	<i>p</i>	Mean \pm SE	Mean \pm SE	Mean \pm SE	<i>p</i>
Night shift								
BP ($n_1=11$, $n_2=127$)								
SBP, mmHg	129.0 \pm 1.0	122.4 \pm 1.0	-6.6 \pm 1.2	<0.001	123.9 \pm 1.3	121.0 \pm 1.7	-2.9 \pm 1.4	0.041
DBP, mmHg	74.5 \pm 0.7	66.6 \pm 0.8	-7.9 \pm 1.0	<0.001	69.5 \pm 1.1	62.5 \pm 1.1	-7.0 \pm 1.2	<0.001
HR, beat/min	75.0 \pm 1.0	66.5 \pm 0.9	-8.6 \pm 1.0	<0.001	66.8 \pm 1.1	68.1 \pm 1.1	1.2 \pm 1.1	0.275
HRV ($n_1=6$, $n_2=70$)								
RMSSD, ms	58.8 \pm 2.3	84.1 \pm 4.1	25.3 \pm 3.3	<0.001				
SDNN, ms	12.1 \pm 0.6	20.5 \pm 1.3	8.4 \pm 1.1	<0.001				
Log (LF)	6.8 \pm 0.7	7.2 \pm 0.8	0.5 \pm 0.7	<0.001				
Log (HF)	5.5 \pm 1.0	6.8 \pm 1.0	1.3 \pm 1.0	<0.001				
Log (LF/HF ratio)	1.4 \pm 0.6	0.7 \pm 0.7	-0.8 \pm 0.7	<0.001				
	Work (Time 5)	Time (Time 7)	Paired difference	<i>p</i>	Rest (Time 4)	Rest (Time 7)	Paired difference	<i>p</i>
Day shift								
BP ($n_1=11$, $n_2=117$)								
SBP, mmHg	132.4 \pm 0.8	131.9 \pm 1.0	-0.5 \pm 1.1	0.627	131.0 \pm 1.5	130.7 \pm 1.7	-0.2 \pm 2.2	0.915
DBP, mmHg	76.1 \pm 0.6	74.0 \pm 0.7	-2.1 \pm 0.9	0.014	74.2 \pm 1.3	73.4 \pm 1.0	-0.8 \pm 1.3	0.539
HR, beat/min	78.3 \pm 1.0	81.3 \pm 1.3	3.0 \pm 1.1	0.010	76.0 \pm 1.4	79.2 \pm 1.5	3.2 \pm 1.6	0.057
HRV ($n_1=6$, $n_2=66$)								
RMSSD, ms	55.5 \pm 1.6	56.3 \pm 2.7	0.8 \pm 2.5	0.756				
SDNN, ms	12.4 \pm 0.8	12.1 \pm 1.1	-0.3 \pm 0.7	0.671				
Log (LF)	6.8 \pm 0.5	6.6 \pm 0.6	-0.2 \pm 0.5	0.007				
Log (HF)	5.5 \pm 0.9	5.4 \pm 1.3	-0.1 \pm 0.9	0.330				
Log (LF/HF ratio)	1.5 \pm 0.7	1.4 \pm 1.0	-0.1 \pm 0.6	0.301				

n_1 , means number of participants; n_2 , means effective hourly measurements during two 12-h monitorings; RMSSD, root-mean-square successive differences; SDNN, standard deviation of N-N intervals; HF, high frequency power; LF, low frequency power. Paired difference was the difference of measurements according to hour-to-hour comparison between shift work and rest at the same timetable intra-individually.

DBP, and HR in work (vs. rest), day (vs. night), and their interaction. Incomplete SBP and DBP recoveries were found in time period 3 of night shift workers (compared to time period 8), but not in time period 7 of day shift workers, after adjustment for confounding factors.

Discussion

The major findings of this study indicate that 12-h night shifts have significant CV effects in terms of BP, HR, and HRV. The consistent findings of delayed recovery of SBP and DBP on the first and second 12-h rest periods of night shift workers also corroborate these CV effects. In addition, the findings are the same in both simple comparison and in multivariate analysis.

To our knowledge, this study is one of the few studies⁷⁾ that has used a mixed regression model to correlate multiple BP measurements, with repeated measurements as its

determinant (Table 2). Previous studies have often taken the average value of repeated BP measurements^{8,9,11)}. The rationale of using the mixed model is the assumption that repeated measurements have a random effect, which corresponds more to the multiple measurements of BP at a fixed CV characteristic for each subject. Statistically, it is generally more efficient than simply taking the mean and can improve the detection power despite a limited number of study subjects.

We also used hour-to-hour (time-to-time) paired comparisons for each time period (work vs. rest time 2, or rest time 1 vs. rest time 3), thereby realizing 12 pairs of comparisons of hemodynamic variables for each subject. This new method may be more appropriate for comparison and may increase the power of detection for time-dependent and physiological diurnal variations of BP and HR.

Table 2. Estimates of regression coefficients resulting from mixed models for the effects of 12-h shift work on blood pressure and heart rate

Effects	Systolic BP		Diastolic BP		HR	
	Est. \pm SE	<i>p</i>	Est. \pm SE	<i>p</i>	Est. \pm SE	<i>p</i>
Intercept	141.11 \pm 35.27	<0.001	104.89 \pm 18.13	<0.001	94.03 \pm 35.88	0.009
Age, yr	-0.33 \pm 0.56	0.555	-0.39 \pm 0.29	0.182	-0.39 \pm 0.57	0.489
BMI, kg/m ²	-0.16 \pm 0.88	0.856	-0.69 \pm 0.45	0.123	-0.02 \pm 0.89	0.981
Shift duration, yr	-0.17 \pm 0.65	0.788	-0.15 \pm 0.34	0.652	0.01 \pm 0.66	0.983
Smoking, current	-4.74 \pm 4.16	0.255	-3.93 \pm 2.13	0.066	-7.31 \pm 4.24	0.085
Drinking, current	-4.16 \pm 4.96	0.402	0.50 \pm 2.56	0.847	-0.54 \pm 5.04	0.915
Work time (day vs. night)	5.70 \pm 1.40	<0.001	3.42 \pm 1.10	0.002	8.01 \pm 1.25	<0.001
Work status (work vs. rest)	5.36 \pm 1.33	<0.001	6.31 \pm 1.04	<0.001	9.70 \pm 1.19	<0.001
Interaction (work time and status)	-1.98 \pm 1.92	0.304	-1.56 \pm 1.51	0.302	-4.65 \pm 1.72	0.007
Time period 3 vs. Time period 8 *	4.15 \pm 1.47	0.005	5.63 \pm 1.15	<.001	0.51 \pm 1.32	0.699
Time period 4 vs. Time period 7*	-1.7 \pm 1.58	0.281	0.02 \pm 1.24	0.987	-2.04 \pm 1.42	0.151
AIC	7285.7		6818.1		7081.0	

*The time periods of 3 and 4 were the resting time after the night shift, and the time periods of 7 and 8 were the resting time after the day shift. Time periods 8 and 4 were compared as the better resting periods. Please see Fig. 1 for the details. Abbreviations: AIC, Akaike's Information Criterion

During the day shift, the study subjects were under their usual diurnal-nocturnal cycle. Thus, a lack of difference in BP and HRV between working and resting time of the following day is to be expected. When the study subjects worked at night, there was basically no circadian rhythm in BP, HR, and HRV during the night shift, as they were forced to work actively at night and rest the following day. The CV effects are as we anticipated them. In addition to an incomplete BP recovery in the first 12-h rest period, the mixed regression models identified the incomplete SBP and DBP recoveries in the second 12-h rest period after working on a night shift (Table 2). Thus, there are CV effects from the night shift which persisted through the next 24 h.

Boggild and Knutsson proposed that shift work may disturb physiological rhythms and impair control of the circadian rhythm and myocardial performance³⁾. Our study demonstrates significant increases in BP and HR, as well as impaired HRV and autonomic balance in 12-h night shift workers. These are compatible with previous studies of 8-h night shifts^{5, 8, 9, 11)}. In addition, our study extends the findings of delayed recovery of elevated SBP and DBP, which may have potential long-term CV effects after 12-h night shifts.

Acute sleep deprivation is associated with an increased sympathetic activity and decreased parasympathetic modulation¹⁵⁾. In addition, sleep disturbance may also result in sympatho-vagal imbalance^{11, 16)}, and increase premature ventricular complexes in shift workers¹⁷⁾. A recent study of 24-h shift work even found impaired brachial artery endothelial function after night shifts¹⁸⁾. Thus, if long-hour night shifts become a long-term shift

schedule, then some of these workers may become non-dippers⁹⁾. When the time shift is increased to a 12-h shift schedule, the impact of sympatho-vagal imbalance may even be longer, as shown by the delayed recovery in this study.

The limitations of this study include a small sample size and short-term evaluation of CV effects in a cross-sectional design. The measures of short-term changes found in this study may not be suitable for predicting the long-term effects of 12-h shifts. Moreover, we are unable to completely rule out the potential confounding effects of active physical activity during off-shift periods. However, this study had difficulties recruiting workers to participate in the 96-h monitoring with two machines (Holter ECG and AmBP) simultaneously. Thus, we applied the mixed effects model to make the statistical comparisons more efficient, with consistent predictive power as in our previous study⁷⁾. Since we did not detect any significant effect of delayed HRV recovery, which indicates a good accommodation to shift working, the above likelihood of potential confounding effects might be low.

In conclusion, 12-h night shift work has significant short-term CV effects on BP, HR, and HRV. The significant incomplete (or delayed) recoveries of SBP and DBP are evidence of the sustained CV effects, possibly through prolonged sympathetic activation and sympatho-vagal imbalance, of a 12-h night shift. More studies on the CV effects of 12-h work shifts and healthy schedules designed to protect workers in an increasingly global marketplace should be undertaken.

Acknowledgements: This study was supported by grants (NHRI-EX93-9204PP and NHRI-EX97-9721PC) from the National Health Research Institute, Department of Health, Executive Yuan, Taiwan, Republic of China.

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