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Indexes of cardiac autonomic profile detected with short term Holter ECG in health care shift workers: a cross sectional study

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Summary

Background: *The assessment of early effect of shift work-related circadian rhythms desynchronization and work-related stress in health care workers has gained a primary role among the duties of the occupational physician.* **Objectives:** *Aim of our study was to assess the cardiac autonomic modulation through quantification of sinus rhythm variability, as an index of the adaptability to shift work of the cardiovascular system in healthcare shift workers.* **Methods:** *We measured Heart Rate Variability (HRV) by short-term (60 minutes) Holter Electrocardiography (ECG) during the regular duties in the respective department of 42 healthcare workers (31 nurses and 11 physicians) of an Italian Hospital (12 male and 30 females, aged 24-58 years), working on 3 shifts with a forward fast rotation with rest at the end of the night shift (7 am - 2 pm; 2 pm - 10 pm; 10 pm - 7 am) or in a fixed daytime shift (8 am - 2 pm). Measurements were all performed between 9 am and 12 am for fixed day workers and between 9 am and 12 pm or between 10 pm and 1 am for shift workers. The following HRV parameters were compared between the subgroups of shift workers and daytime workers: mean heart rate (HR), standard deviation of all normal RR (NN) intervals (SDNN), standard deviation of the averages of NN intervals in all 5-minute segments of a recording (SDaNN) and the triangular index (the integral of the density distribution divided by the maximum of the density distribution). We used parametric tests for independent series to compare HRV parameters by subgroups within the study subjects. We also tested correlation between the variables of interest and the association between HRV and shift work modality, along with other covariates, by means of a multiple linear regression analysis.* **Results:** *We found significantly lower values of SDaNN in shift workers compared with workers engaged solely on day shifts (50.80 ms vs 66.71 ms; p=0,014). The mean heart rate did not show any significant difference between day workers and shift workers (85.78 bmp vs 85.53 bpm respectively). Multivariate analysis showed a significant association between SDNN and female gender and age, while no significant associations were found between HRV and shift work.* **Discussion:** *The autonomic control of the heart rhythm could be disrupted by desynchronization of the biological rhythm secondary to the organization of shift work and night work. Shift work is an important factor of social and biological distress, influencing the adaptability of the cardiovascular system to stimuli and demands of work organization.*

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Riassunto

***«Indici di profilo autonomico cardiaco valutati attraverso Holter ECG di breve durata in operatori sanitari esposti a lavoro a turni: studio trasversale»*. Introduzione:** *Gli operatori sanitari rappresentano una categoria di lavoratori tradizionalmente esposta a lavoro a turni, che può causare una desincronizzazione del ritmo circadiano endogeno che caratterizza le principali variabili biologiche, ed essere concausa nell'insorgenza di patologie e disturbi a carico dell'apparato cardiovascolare. In questo contesto, assume sempre maggiore importanza la valutazione di indici precoci di effetto sull'apparato cardiovascolare.* **Obiettivi:** *L'obiettivo dello studio è stato di valutare la variabilità della frequenza cardiaca (HRV) quale indice di regolazione autonomica cardiaca in funzione dell'esposizione a differenti turni di lavoro lungo le 24 ore, in un campione di operatori sanitari.* **Metodi:** *L'HRV è stata misurata attraverso una registrazione Holter ECG di breve durata (60 minuti) in un campione di 42 operatori sanitari (31 infermieri e 11 medici), durante lo svolgimento delle normali attività di reparto. Gli operatori sanitari coinvolti operavano con due diverse modalità di turnazione: un sottogruppo era impiegato su 3 turni lavorativi (turnisti: 07 - 14; 14 - 22; 22 - 07) con rotazione rapida in fase e riposo alla fine del terzo turno; l'altro sottogruppo svolgeva l'attività in un unico turno lavorativo diurno (diurni: 08 - 14). I seguenti parametri HRV sono stati confrontati tra i due sottogruppi di lavoratori turnisti e diurni attraverso test statistici parametrici: frequenza cardiaca media (HR), deviazione standard dei normali intervalli RR (SDNN), deviazione standard degli intervalli NN medi in segmenti temporali di 5 minuti (SDaNN), indice triangolare (integrale della distribuzione di densità diviso per il massimo della distribuzione di densità). È stata inoltre condotta un'analisi di correlazione tra le variabili e un'analisi multivariata attraverso una regressione lineare multipla, per verificare l'associazione tra parametri che descrivono la variabilità spontanea della frequenza cardiaca, il tipo di turno e alcune delle caratteristiche della popolazione studiata.* **Risultati:** *I valori di SDaNN erano significativamente più bassi nel gruppo dei turnisti rispetto ai lavoratori diurni (50.80 ms vs 66.71 ms), mentre la frequenza cardiaca media non ha mostrato differenze nei due gruppi. L'analisi multivariata ha invece evidenziato un'associazione significativa tra SDNN, età e il genere femminile, ma non con la modalità di turnazione.* **Discussione:** *Nel presene studio è stata evidenziata una riduzione di uno degli indicatori di variabilità dell'intervallo RR nei lavoratori turnisti rispetto ai lavoratori diurni. Questo risultato potrebbe essere espressione di un'alterazione del ritmo circadiano endogeno verosimilmente prodotto dal lavoro a turni. Ulteriori indagini sono necessarie per confermare questa osservazione.*

Introduction

Shift work, particularly night shift work, can adversely affect workers' health and well-being (4, 8, 9, 24, 26). Detrimental effects such as an increase of arterial blood pressure, increasing risk of cardiovascular diseases and sleep disturbance (28), as well as cardiovascular abnormalities were found in shift workers (13, 23, 25). In order to determine the impact of shift work on the cardiac autonomic control, non-invasive methods to explore the heart function can be applied, such as the detection of the Q-T interval prolongation (13, 20-22) and of Heart Rate Variability (HRV) (5, 12, 14, 31-33), with routine electrocardiography. HRV is an indicator of heart rate fluctuation around the average heart rate and its continuous monitoring is practical, easy and repeatable (30). Several studies have found a detrimental effect of shift work on affecting HRV parameters, analyzed in the time domain and in the frequency domain (10, 23, 25). Relevant changes in cardiac autonomic tone, as detected by HRV measurements, were found in 24h shift workers exposed to sleep deprivation (25). An autonomic dysregulation was also found among night shift nurses when measuring HRV coherence ratios in the sleep period (6).

To assess HRV, some different methods have been used, including long-term Holter ECG registration lasting 24 hours or very short monitoring ECG such as 300 RR interval (13). Short term HRV can be considered a reliable predictor of cardiac death in chronic heart failure patients (19). In particular, a reduction in HRV parameters represents a negative factor, associated with an increased risk of sudden cardiac death in patients with chronic heart failure, independently of many other variables (19). Aim of this study was to investigate HRV parameters as an indicator of autonomic cardiac function among subjects employed in different work shifts, by using a short term Holter ECG monitoring.

Methods

From June 2011 to July 2014, we enrolled forty-two health care workers (12 male and 30 females) aged between 24 and 58 years (mean age 38 years, SD 9.5), employed by an Italian Hospital. Eleven subjects were medical doctors and thirty were nurses. Fifteen subjects worked in a fixed daytime shift (daytime workers: hours 08-14), while twenty-seven were employed in a forward fast rotating schedule (shift workers: hours 7 am - 2 pm; 2 pm - 10 pm; 10 pm - 7 am). All workers were recruited based on their own particular tasks at the time of the last health surveillance check. Enrolled workers were all free from cardiovascular diseases, and no one of them were excluded from the study. For each subject under examination a questionnaire was administered before the start of the test, investigating the following parameters: age, height, weight, occupation, smoking habit, previous illnesses, ongoing medication, type of work shift. Clinical features of the examined population are reported in table 1. Besides, activities carried out during the Holter ECG recording and the respective time of starting and ending were registered.

Each subject underwent a short-term (60 minutes) Holter electrocardiography (ECG) recordings while performing their regular tasks during their work shift. For the subgroup of daytime workers, the recording took place in a range of time between 9:00 and 12:00 AM, while for the shift workers subgroup, recordings were performed between 9:00 and 12:00 AM for the morning shift and between 10:00 PM and 01:00 AM for the night shift. No recordings were performed during the evening shift. A total of 31 recordings in the morning period (15 daytime workers and 16 for shift workers) and 11 recordings in the night period (all shift workers) were performed.

For all tasks, the Holter registrations took place while health personnel attended to typical tasks of their job, such as patients assistance, drug delivery, venipunctures and updating medical charts. No acute stress conditions or heavy workload occurred during ECG registrations. The following HRV parameters were measured during each test performed: mean heart rate, maximum and minimum heart

Table 1 - Clinical features of the study population and different subgroups.

Parameters	All sample n. 42		Fixed Day time workers n. 15	Shift workers (All shifts) n. 27
	Range	Mean (sd)	Mean (sd)	Mean (sd)
Age (years)	24-58	38.24 (9.52)	33.60 (7.48)	40.81 (9.67)
BMI (kg/m^2)	18.2-33.9	23.8 (4.33)	24.38 (5.20)	23.48 (3.83)
	N (%)		N (%)	N (%)
Gender				
- male	12 (28.6)		5 (33.3)	7 (25.9)
- female	30 (71.4)		10 (66.7)	20 (74.1)
Smoking habit				
- never + former smokers	33 (78.6)		14 (93.3)	19 (70.4)
- current smokers	9 (21.4)		1 (6.7)	8 (29.6)

BMI=Body Mass Index

rate, SDNN considered as standard deviation of all normal RR (NN) intervals, (ectopic heart beats have been automatically removed if they differed more than 25% from the previous RR interval), SDaNN intended as the standard deviation of the average NN intervals calculated over short periods of 5 minutes, the Triangular index as the integral of the density distribution (that is, the number of all NN intervals) divided by the maximum of the density distribution (30).

SDNN represents the gold standard for the stratification of cardiac risk when measured over a 24h interval time (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996)(30). It can provide information about the autonomic control of cardiac rhythm, considering both long-term and short-term recordings (27). Similarly, SDaNN provides the same information about the autonomic control of cardiac rhythm.

On the other hand, the Triangular index represents a useful tool to discriminate between normal heart rhythms and arrhythmias when considering a long-term recording of 24h (27). However, a 5-min epoch is conventionally used to represent this metric (15).

Measures of central tendency (mean and median) and dispersion (standard deviation) were calculated for all HRV indexes.

The study meets the ethical standards of the journal. The participation in the study was totally voluntary.

Statistics

Comparisons of the HRV parameters between the two categories of shift workers and fixed daytime workers were performed using parametric tests (ANOVA), after confirming the normal distribution of parameters by means of the Kolmogorov - Smirnov test and the visual inspection of the shape distribution. To test the correlation between HRV parameters, and other variables of interest, a Pearson correlation test between parametric variables (HRV parameters, BMI and age) and a Spearman correlation test between HRV and categorical variables (type of work shift - if fixed- daytime workers or shift workers employed in three shifts- time recording, smoking habit, gender) were performed. Lastly, a multivariate analysis was performed to test the association between HRV parameters (as dependent variables) and the shift work modality, along with some personal features such as age, BMI, gender and smoking habit (as independent variables). In detail, a multivariate linear regression model was performed separately for the overall sample and in the subgroups of shift workers and day workers.

Results

Values of central tendency and dispersion for investigated parameters in the overall study population and separately for shift workers, fixed- daytime workers, daytime recordings and night time recordings are reported in table 2.

Comparing HRV parameters between subgroup of shift workers and fixed- daytime workers, including recording performed in all shifts (morning and night shifts), the SDaNN shows a mean value significantly lower in shift workers when compared with fixed daytime workers (mean SDaNN 50.80 msec; sd 16.38 for shift workers vs 66.7; sd 23.83 for fixed-daytime workers; $p=0.01$). SDNN, triangular index and mean HR did not show any significant difference between subgroups of shift workers and fixed daytime workers (table 2). Among the shift workers subgroup, comparisons between daytime recordings and night time recordings did not showed any significant difference (table 2).

The correlation test showed that SDaNN had a significant negative correlation with the shift work ($rho=0.32$; $p<0,05$) and the mean heart rate, and a high positive correlation with SDNN ($rho=0.75$; $p<0.01$) and a moderate correlation with triangular index ($rho=0.566$, $p<0.01$), while SDNN and triangular index did not show any correlation with shift work (table 3).

In the overall study population, the multivariate analysis did not show any significant detrimental effect of shift work on predicting HRV parameters, while female gender tended to decrease only SDNN (table 4). Selecting the subgroup of shift workers and considering the SDNN as dependent variable, the linear regression showed a significant detrimen-

Table 2 - Values of central tendency and dispersion of investigated variables

Parameters	All sample (n. 42)		Fixed Day time workers n. 15	Shift workers All shifts n. 27	Shift workers Morning shift recordings n.16	Shift workers Night shift recordings n. 11	ANOVA* Shift workers Vs Fixed Day workers	ANOVA Morning shift rec. Vs Night shift rec.
	Range	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	p	p
Mean HR (bpm)	58-103	85.69 (10.59)	85.53 (11.42)	85.78 (10.33)	85.50 (12.63)	86.18 (6.14)	0.943	0.870
SDNN (msec)	52.92-158.39	85.88 (20.65)	91.57 (21.75)	82.72 (19.71)	84.79 (23.59)	79.70 (12.63)	0.186	0.520
Triangular index	9-49	20.21 6.90	21.67 (6.31)	19.41 (7.20)	20.25 (8.59)	18.18 (4.6)	0.316	0.474
SDaNN (msec)	25.92-123.31	56.48 20.58	66.71 (23.83)	50.80 (16.38)	51.45 (17.47)	49.87 (15.45)	0.014	0.811

* Comparisons between fixed day time workers vs shift workers (all shifts)
HR=Heart Rate; Rec.=recordings

Table 3. Pearson's coefficients correlation and Spearman's coefficients correlation (bold)

	Age	BMI	HR	SDNN	T. Index	SDaNN	Smoking habit	Gender	Shift
Age	1	0.45**	-0.27	-0.01	0.02	-0.29	**0.12**	**0.09**	**0.39***
BMI		1	-0.32*	0.09	0.13	-0.04	**-0.11**	**-0.31***	**-0.05**
HR			1	-0.74**	-0.71**	-0.38*	**0.07**	**0.29**	**0.00**
SDNN				1	0.89**	0.75**	**-0.23**	**-0.31***	**-0.25**
T. Index					1	0.57**	**-0.23**	**-0.25**	**-0.22**
SDaNN						1	**-0.27**	**-0.15**	**-0.32***
Smoking habit							1	**0.07**	**0.27**
Female								1	**0.08**
Shift									1

*=p<0.05 **=p<0.01
HR=Heart rate; BMI=Body Mass Index; T.index=Triangular index; Shift=Shift work modality (fixed day workers or shift workers)

tal effect of BMI and female gender on affecting SDNN (adjusted r^2 =0.44; p=0.01; predictors: age, BMI, gender, smoking habit) (table 5 Model 1). The same result was found considering the Triangular index as dependent variable (table 5 Model 3), while for SDaNN this result was not confirmed (table 5 Model 2). In the subgroup of fixed daytime workers, the linear regression model appears to be not significant for the same predictors on affecting HRV parameters (table 6).

Discussion

Considering globally these results appears that shift work might cause a reduction of SDaNN values, which turns out to be significantly lower in shift workers compared with day workers. The HRV indexes may be used to quantify the cardiac autonomic response to different environmental stimuli (34). It has been previously described that a shift work schedule may modify the circadian os-

Table 4 - Multivariate linear regression analysis. Overall study population (n. 32)

	Model 1 Dependent variable: SDNN			Model 2 Dependent variable: SDaNN			Model 3 Dependent variable: T. Index		
Predictors	Crude Beta coefficient	Adjusted Beta coefficient	P value	Crude Beta coefficient	Adjusted Beta coefficient	P value	Crude Beta coefficient	Adjusted Beta coefficient	P value
Age	0.40	0.18	0.35	-0.25	-0.12	0.55	0.12	0.16	0.43
BMI	-0.65	-0.13	0.48	-0.42	-0.09	0.64	-0.11	-0.07	0.73
Female	-17.48	-0.39	0.02	-8.73	-0.19	0.23	-4.83	-0.32	0.06
Smoking habit	-8.89	-0.18	0.25	-7.97	-0.16	0.29	-3.47	-0.21	0.19
Shift work modality	-8.96	-0.21	0.23	-11.98	-0.28	0.11	-2.04	-0.14	0.42

Model 1: r^2=0.21 adjusted r^2=0.09; standard error=19.60; p=0.12
Model 2: r^2=0.28 adjusted r^2=0.12; standard error=19.31; p=0.09
Model 3: r^2=.17 adjusted r^2=.054; standard error=6.72; p=0.22
HR= Heart rate; BMI=Body Mass Index; T. Index= Triangular Index; shift work modality= fixed day workers or shift workers

Table 5 - Multivariate linear regression analysis. Shift work population (n. 27)

	Model 1 Dependent variable: SDNN			Model 2 Dependent variable: SDaNN			Model 3 Dependent variable: T. Index		
Predictors	Crude Beta coefficient	Adjusted Beta coefficient	P value	Crude Beta coefficient	Adjusted Beta coefficient	P value	Crude Beta coefficient	Adjusted Beta coefficient	P value
Age	1.71	0.84	0.01	0.42	0.41	0.11	0.48	0.65	0.01
BMI	-4.54	-0.88	0.01	1.17	-0.61	0.04	-1.44	-0.76	0.01
Female	-22.46	-0.51	0.01	7.67	-0.06	0.77	-8.03	-0.49	0.01
Smoking habit	-11.73	-0.27	0.07	6.41	-0.29	0.12	-4.52	-0.29	0.09

Model 1: r^2= 0.53 adjusted r^2= 0.44; standard error= 14.71; p=0.01
Model 2: r^2= 0.27 adjusted r^2= 0.14; standard error= 15.18; p= 0.12
Model 3: r^2= 0.41 adjusted r^2= 0.31; standard error= 5.99; p= 0.01
BMI=Body Mass Index; T. Index= Triangular Index; shift work modality= fixed day workers or shift workers

Table 6 - Multivariate linear regression analysis. Fixed day work population (n. 15)

	Model 1 Dependent variable: SDNN			Model 2 Dependent variable: SDaNN			Model 3 Dependent variable: T. Index		
Predictors	Crude Beta coefficient	Adjusted Beta coefficient	P value	Crude Beta coefficient	Adjusted Beta coefficient	P value	Crude Beta coefficient	Adjusted Beta coefficient	P value
Age	0.76	-0.40	0.16	-1.38	-0.43	0.13	-0.18	-0.21	0.46
BMI	1.03	0.45	0.10	1.14	0.25	0.34	0.72	0.59	0.04
Female	11.15	-0.39	0.15	-21.77	-0.45	0.10	-4.26	-0.33	0.24
Smoking habit	19.03	0.12	0.61	10.15	0.11	0.64	4.51	0.18	0.45

Model 1: r^2=0.53; adjusted r^2=0.35; standard error= 17.60 p=0.08
Model 2: r^2= 0.54; adjusted r^2= 0.35; standard error= 19.22; p= 0.08
Model 3: r^2= 0.49; adjusted r^2= 0. 29; standard error= 5.33; p= 0.12
BMI=Body Mass Index; T. Index= Triangular Index; shift work modality= fixed day workers or shift workers

cillations of the indexes of cardiac sympathovagal modulation (10). What appears from our data is that the SDaNN has a lower value in shift workers compared with day workers. Our results also show that SDaNN changes among shift workers do not vary by type of shift in which recording took place, whether daytime or night time work shifts. This follows from the fact that the values of SDaNN were not significantly different between night and day records within the same group of shift workers. A decreasing of SDaNN can be interpreted as an effect of changes in the autonomic control of cardiac rhythm (27).

In the subgroup of shift workers, a significant detrimental effect on SDNN was found for BMI and female gender. In this selected population, it appears to be a relevant gender effect, suggesting a more susceptible pattern for female shift workers with higher BMI.

The negative influence of BMI on HRV in the shift workers group can be attributable to continuous changing of mealtimes, high-calorie food intake, junk food, vending machines, very few light/healthy snacks, decreased opportunities for regular physical exercise (1), and also reduced sleep duration and quality (7). Moreover, the influence of gender on the autonomic regulation of cardiac function has been reported in other reports (29, 35). These aspects are significant especially in the health care settings where the female gender represents a high proportion of the work force, exposed to night shift (14).

BMI and age showed significant negative effect on SDNN as similarly reported in a study considering BMI as covariate for HRV dependent variables (2, 16). Despite some studies reported an acute effect of smoking cigarettes on decreasing HRV parameters (18), the results of our study did not show any significant difference between smokers and non-smokers personnel. This result is plausible considering that during work, no one of the subjects smoked cigarettes, therefore an acute effect of smoking cannot be detected in the present study.

This study highlights that shift work can be an important factor in social and biological stress and can be considered as a risk factor for the development of cardiovascular diseases, able to affect the adaptability of the cardiovascular system to stimuli and demands imposed by the work organization. A poor flexibility of the cardiac system, as testified by a lower HRV, would make it more vulnerable to the onset of pathologies or sudden arrhythmia alterations, when considering HRV parameters detected in long-term recorders (3, 11, 17, 19). On the other hand, a short term recorder of HRV parameters can detect early changes in the autonomic cardiac control of the heart rhythm, as suggested by the results of the present study in accordance with previous scientific researches (27).

Some limitations affect this study: first, the cross sectional study design does not allow to make an inference about the causality between shift work and decreasing of HRV parameters. Secondarily, the small study population and the different prevalence rate of male and female subjects could have negatively influenced the results of the study. Further studies should aim to extend the study sample size to better define shift work as a cardiovascular risk factor through HRV recording, and define prevention programs for susceptible individuals. The short term ECG registration is a useful tool in preventive medicine and occupational medicine particularly, because of the good tolerability, repeatability and low cost of this examination. A larger use of HRV monitoring in shift workers could represent a useful method to detected subclinical changes in autonomic nervous system control.

In conclusion, despite such limitations, our experience on a limited sample suggests that HRV is an easy, reliable, repeatable and well-tolerated parameter to monitor cardiac autonomic control among shift workers without interfering with the regular work activity. Lower HRV values represent useful parameters to effectively identify changes in the autonomic regulation of cardiac rhythm, especially in aging working populations exposed to shift work.

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