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ORIGINAL ARTICLE

Evaluation of ECG Repolarization Parameters in a Worker Cohort Working the Night Shift

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Abstract

Objectives: **Night Shift work is an increasingly common working order that affects human well-being and it is little known about its arrhythmic role in the cardiovascular system. We aimed to investigate the effect of working at night shifts on P-wave dispersion (Pd), QT and QTc dispersions (QTd, QTcd resp) on surface electrocardiography.**

Methods: **We included 286 foundry workers who work at night shift and 100 foundry workers who work on day time only. The night shift workers were divided into three subgroups according to the length of time they worked at night shift. Surface electrocardiography and blood tests were applied for all participants.**

Results: **Pd, QTd and QTcd values increased in the night shift workers compared to the day time workers ($p < 0.05$). In subgroup analysis; the night shift workers for more than 15 years had a significantly higher Pd, QTd and QTcd compared to others ($p < 0.001$). Correlation analysis revealed significant positive correlations with working duration and Pd ($r = 0.578$, $p < 0.001$) and QTcd ($r = 0.417$, $p < 0.001$). In the linear regression analysis, working duration at night shift was significantly associated with Pd and QTcd values, independent from other associated clinical risk parameters.**

Conclusions: **This study makes one of the first attempts to assess changes in ECG parameters reflecting tendency to rhythm disturbances, in night shift workers. Our results further underline the importance of covering a comprehensive evaluation of ECG in periodical health check-ups in night shift workers to evaluate the risk of both atrial and ventricular arrhythmias.**

Keywords: Shift work, Night work, Shift worker, P-wave dispersion, QTc dispersion

1. Introduction

Shift work is an increasingly common working order in today's economy which constitutes approximately 21% of the workforce in Europe [1]. Shift work that is organized outside of regular, fixed working hours during the day, can be disposed as two or three teams for 24 hours, night shifts only or long shifts (e.g. 24 hours and 48 hours) alternately or fixed schedules. However, as a part of shift working system, working at night has many negative effects on human physiology by causing sleep disorders, fatigue, some nutritional and psychosocial issues. Cardiovascular system is also negatively affected in night shift workers. A metanalysis of 320,002 participants found that shift workers are at increased risk for ischemic heart disease and each year spent on shift work was associated with a 0.9% increase in the risk [2]. The diurnal variation of blood pressure in the night shift workers was changed from a dipper to a non-dipper pattern which increased the risk of hypertension among the night-shift workers [3]. Moreover, working longer and more frequent at night shifts have been postulated as a jeopardy of atrial fibrillation (AF) [4].

Electrocardiography (ECG) is an easily accessible, inexpensive and non-invasive cardiovascular system screening and diagnostic test. P wave dispersion (Pd), QT wave dispersion (QTd) and corrected QT dispersion (QTcd) are the measurements which

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are obtained from ECG, demonstrating the regional heterogeneity of atrial and ventricular repolarization respectively. Increased values of these parameters have been considered to be predictive for left atrium enlargement, left ventricular hypertrophy, diastolic dysfunction, heart failure, hypertension ventricular arrhythmias and most evidently for AF [5–7]. In addition to those, high values of Pd and QTd are associated with increased risks of all-cause and cardiovascular mortality. Although there is increasing evidence in the literature showing the negative effects of night shift work on health, especially on the cardiovascular system, the clinical parameters have not been evaluated sufficiently.

In this study, we aimed to examine the Pd, QTcd and QTd in ECGs of the night shift workers to assess whether working at night is associated with increased susceptibility of arrhythmias.

Nomenclature

AF	Atrial fibrillation
ALT	Alanine aminotransferase
AST	serum aspartate aminotransferase
BMI	Body mass index
DBP	Diastolic blood pressure
ECG	Electrocardiography
GFR	glomerular filtration rate
hs-CRP	High sensitive C reactive protein
HDL	High density lipoprotein
LDL	Low density lipoprotein
Pd	P wave dispersion
Pmax	P maximum
Pmin	P minimum
SBP	Systolic blood pressure
QTc max	QTc maximum
QTc min	QTc minimum
Qtd	QT dispersion
Qtcd	QTc dispersion
WBC	Whole blood cell count

2. Methods

This retrospective study was conducted in our hospital which is located nearby an organized industrial zone, in 2021. Ethics committee approval was obtained and the study complies with the Declaration of Helsinki.

2.1. Study population

A total of 824 shift workers who applied to our cardiology outpatient clinic for routine periodical health control from a metal foundry industry were included.

Initially, the employees were divided into two main groups; the group of the night shift workers included those who worked at least 8 night shifts (between 23:00 p.m. to 07:00 a.m.) per month for more than one year (n = 598), and the group of daytime workers who worked during daylight hours (between 08:00 a.m. to 07:00 p.m.) solely (n = 226).

Afterwards, the night shift group was divided into 3 subgroups according to their cumulative working years at night shifts; those who have 5 or less working years in total (group1, n = 223), those who have worked between 6 and 15 years (group2, n = 195) and those who have worked more than 15 years (group3, n = 180). After applied exclusion criteria; 16 patients from daytime worker group, 1 patients from group1, 3 patients from group2 and 4 patients from group3 were excluded. Then, using 2:1 stratified random sampling method 105 patients in daytime worker group, 111 in patients in group1, 96 in patients in group2 and 88 in patients in group3 were assessed for ECG analyzing. In the final step, 14 patients whose ECGs were not suitable for evaluation, were also excluded. Hereby, a total of 386 subjects included in the study (Fig. 1).

Age, smoking status, body mass index (BMI), complete blood count, biochemistry parameters and ECGs of the subjects, all of whom were healthy male employees, were obtained from hospital records, e-Nabõz (the national health registry system) and working durations and other chronic diseases were recorded from the factory database by permission of the general manager and the occupational physician of the factory. BMI was calculated by dividing the body weight to the square of the height (kg/m^2).

The exclusion criteria of the study were as follows: presence of known structural heart disease, rhythm disorders including atrial flutter or fibrillation, frequent ventricular preexcitation, atrioventricular conduction abnormalities, any known acute or chronic inflammatory diseases, liver, kidney and/or thyroid dysfunction, electrolyte imbalance, familial hyperlipidemia, diabetes mellitus, morbid obesity, pulmonary, gastrointestinal, immunological, oncological, psychiatric and collagen vascular diseases and patient with unclear P wave and QT interval in the ECGs [8,9].

2.2. ECG evaluation

In the study, 12-lead ECGs with 25 mm/sec speed and 1-mV/cm, electrocardiographic investigation acquired in the morning, in a silent room after 10 minutes resting position. Scanned ECG sheets were stored digitally as computer images We draw two vertical lines on the images; a line for the onset of the wave first appears and another vertical line for

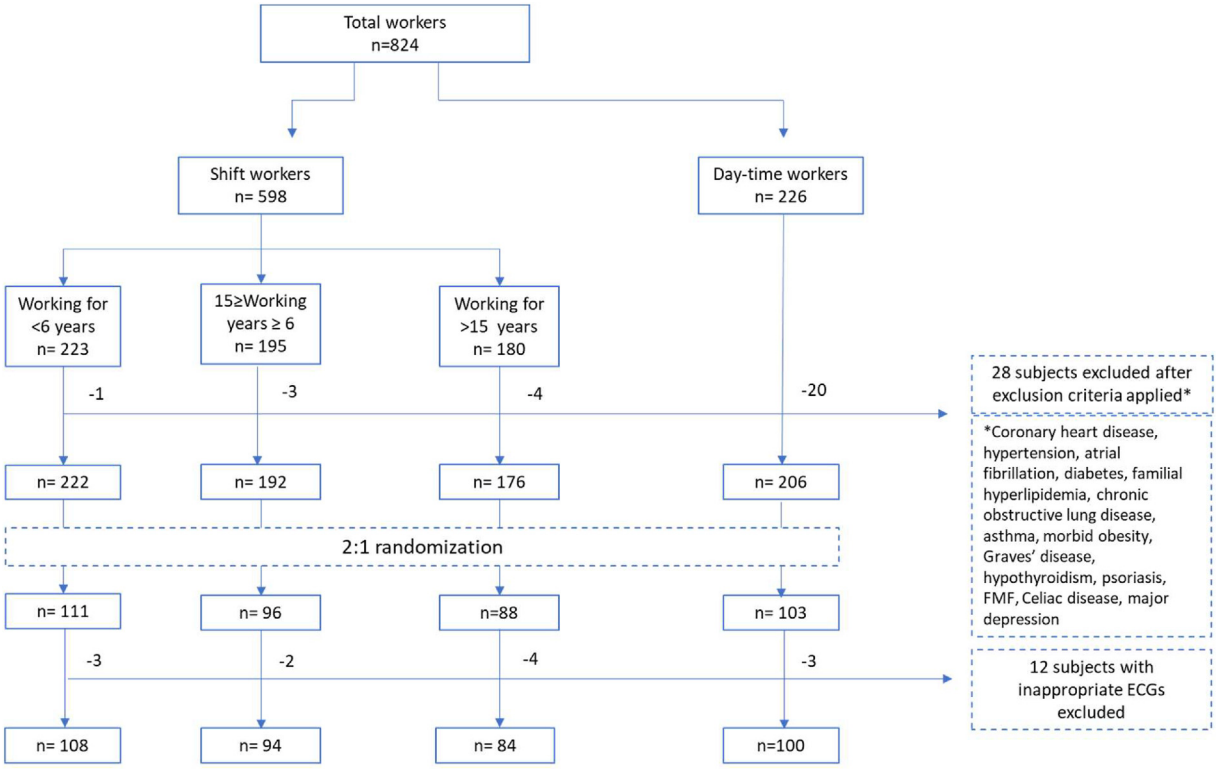

Fig. 1. Flow chart of Study population.

the offset of the wave (for P wave or QT interval separately). After these two points are determined with vertical lines, the wave duration were gauged utilizing manual calliper [10]. P wave duration was evaluated in all 12 leads. P wave was designated as the time from the first atrial deflection from isoelectric line to rejoin of atrial wave to the baseline. P maximum (Pmax) was determined the widest measurable P wave duration whereas P minimum (Pmin) was the narrowest one among all of 12 leads. Pd was obtained subtracting minimum P measurement from maximum P wave measurement (Pd= Pmax-Pmin) [11]. QT interval duration was evaluated in all 12 leads as well. QT interval was delineated as the period between the origination of the Q wave and termination of the T wave. To eliminate the impact of heart rate on QT, QT interval was corrected following Bazett's formula (QTc = QT/$\sqrt{}$RR). In patients with U waves, QT was measured to the lowest point of the curve between the T and U waves. QTc maximum (QTc max) and QTc minimum (QTc min) were defined as the longest and the shortest measurable QT interval durations, respectively. QTd was calculated as differences between maximum and minimum QT duration (QTd = QT max- QT min) and QTcd was calculated as differences between maximum and minimum QTc duration (QTcd = QTc max- QTc min) [12]. Inter-observer coefficients of variations were measured to examine the reproducibility.

2.3. Statistical analyses

All statistical analyses were conducted by SPSS statistical software Version 21.0. (Statistical Package for the Social Sciences, Chicago, IL). Among descriptive variables, normally distributed and continuous variables were reported as mean ± standard deviation, non-normally distributed variables were reported as median (minimum-maximum) values. Shapiro Wilk test and probability plots were utilized to appraise the distribution of variables normally or not. Student's t-test was used to analyze the differences in the means and the Mann-Whitney test was used to analyze median values. One Way ANOVA was used in multiple comparisons in cases where the data were distributed normally and TUKEY HSD test was applied in order to determine difference between the variables. Kruskal Wallis test was used in multiple comparisons in cases where the data were not normally distributed and Tamhane test was applied in order to determine difference between the variables. Pearson correlation test was applied for correlation analysis. Simple and multiple linear regression analyses were conducted with Pd, QTd and QTcd as

Table 1. Baseline demographic, clinic, laboratory and ECG characteristics of shift workers and control.

	Daytime Worker (n = 100)	Night Worker (n = 286)	P Value
Working Duration (years)	11.56 ± 8.97	10.78 ± 8.21	0.472[a]
Age (years)	39.32 ± 8.79	37.23 ± 8.89	0.043[a]
BMI (kg/m^2)	26.86 ± 2.63	26.84 ± 3.60	0.953[a]
Smoking (n,%)	47 (47)	149 (48,7)	0.417[c]
Heart Rate (min)	80.11 ± 14.50	80.67 ± 14.39	0.738[a]
SBP (mmHg)	125.67 ± 9.57	127.47 ± 8.95	0.088[a]
DBP (mmHg)	78.08 ± 5.88	79.50 ± 5.97	0.040[a]
Hemoglobin (gr/dL)	15.42 (11.37–18.02)	15.50 (10.70–18.40)	0.370[b]
Hematocrit (%)	46.05 (32.4–53.2)	45.9 (33.4–54.3)	0.506[b]
WBC (103/μL)	6.7 (2.5–13)	7.86 (3.96–16.27)	<0.001[b]
Platelet (103/μL)	241 (112–438)	256 (106–539)	0.064[b]
hs-CRP (mg/L)	0.25 (0.01–2.8)	0.77 (0.01–2.96)	<0.001[b]
Glucose (mg/dL)	98.09 ± 12.30	91.40 ± 15.46	<0.001[a]
Creatinine (mg/dL)	0.94 ± 0.11	0.94 ± 0.13	0.881[a]
GFR (mL/min/1.73 m2)	112.26 ± 19.28	101.42 ± 16.22	<0.001[a]
Total Cholesterol (mg/dL)	200.12 ± 37.83	208.04 ± 35.05	0.058[a]
HDL (mg/dL)	43.36 ± 8.4	41.28 ± 7.60	0.023[a]
LDL (mg/dL)	125.19 ± 31.33	133.08 ± 29.65	0.025[a]
Triglyceride (mg/dL)	157.87 ± 31.76	168.37 ± 49.71	0.049[a]
ALT (IU/L)	21 (15–60)	21.9 (5–135.8)	0.898[b]
AST (IU/L)	22 (16–35)	20.4 (12–98)	<0.001[b]
P maximum (ms)	95.44 ± 5.37	98.71 ± 9.46	<0.001[a]
P minimum (ms)	57.30 ± 5.54	59.12 ± 7.60	0.029[a]
P dispersion (ms)	38.16 ± 3.54	39.59 ± 3.91	0.001[a]
QT maximum (ms)	403.97 ± 20.86	404.66 ± 23.50	0.796[a]
QT minimum (ms)	371.51 ± 20.35	369.47 ± 21.77	0.412[a]
QTdispersion (ms)	32.46 ± 7.714	35.19 ± 8.940	0.007[a]
QTc maximum (ms)	461.59 ± 33.67	463.03 ± 28.30	0.678[a]
QTc minimum (ms)	424.51 ± 31.86	422.73 ± 25.82	0.579[a]
QTc dispersion (ms)	37.08 ± 8.87	40.32 ± 10.27	0.005[a]

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BMI: Body mass index, DBP: Diastolic blood pressure, GFR: glomerular filtration rate, HDL: High density lipoprotein, hs-CRP: high sensitive C reactive protein, LDL: Low density lipoprotein, SBP: Systolic blood pressure, WBC: White blood cell count.

[a] Mean ± SD in cases where the data were distributed normally, analyzed by student's *t*-test.

[b] median (minimum-maximum) values were presented in cases where the data were not normally distributed, analyzed by Mann-Whitney *U* test.

[c] analyzed by qi-square test.

dependent variables P value < 0.05 was considered as statistically significant and a 95% confidence interval was adopted.

3. Results

Baseline demographic, clinic, laboratory and ECG characteristics of shift workers and daytime workers were illustrated in Table 1. There was no distinction between two groups in terms of heart rate, BMI, smoking status, hemoglobin, hematocrit, platelet counts, high sensitive C reactive protein (hs-CRP), serum creatinine, alanine aminotransferase (ALT), QTmax, QT min, QTc max and QTcmin values (NS). Whole blood count (WBC), Pmax, Pmin, Pd, QTd and QTcd values were significantly higher in the night shift workers as compared to daytime workers (p < 0,05). Furthermore, glomerular filtration rate (GFR), serum aspartate aminotransferase (AST) and glucose levels of the shift workers were lower than daytime workers (p < 0.05). We also observed significant differences in serum lipid levels between two groups. The interobserver agreement for measurements of Pd, QTd and QTcd was near excellent with intraclass correlation coefficients of 0.935, 0.910 and 0.910 respectively (p < 0.01).

In the subgroup analysis, there were statistically significant differences among four groups according to working duration, age, BMI, smoking, WBC, hs-CRP, creatinine, GFR, glucose, HDL and triglyceride levels and Pmax, Pmin, Pd, QTmax, QTd, QTcmax and QTcd values (p < 0.05). Baseline demographic, clinic, laboratory and ECG characteristics are demonstrated for four groups in Table 2.

Correlation analysis revealed a significant positive correlation between working duration and Pd (r = 0.578, p < 0.001) and moderate positive correlations between working duration and QTd

Table 2. Baseline demographic, clinic, laboratory and ECG characteristics according to four groups.

	Control (n = 100)	Group1 6 >Working years (n = 108)	Group 2 15≥Working years≥6 (n = 94)	Group 3 Working years >15 (n = 84)	P Value
Working Duration (years)	11.56 ± 8.97	2.58 ± 1.31	10.89 ± 2.75	21.20 ± 4.88	<0.001[a]
Age (years)	39.32 ± 8.79	29.44 ± 6.417	38.00 ± 4.77	46.37 ± 5.37	<0.001[a]
BMI (kg/m^2)	26.86 ± 2.63	25.33 ± 3.49	27.32 ± 3.61	28.23 ± 2.99	<0.001[a]
Smoking (n,%)	47 (47)	61 (56)	55 (58)	33 (39)	0.034[c]
Heart Rate (min)	80.11 ± 14.50	78.80 ± 14.51	81.40 ± 14.13	82.26 ± 14.42	0.136[a]
SBP (mmHg)	125.67 ± 9.57	127.57 ± 8.76	126.71 ± 9.18	128.21 ± 8.98	0.249[a]
DBP (mmHg)	78.08 ± 5.88	79.38 ± 6.05	78.77 ± 5.80	80.48 ± 5.98	0.047[a]
Hemoglobin (gr/dL)	15.42 (11.37–18.02)	15.50 (10.70–18.40)	15.50 (11.8–17.5)	15.40 (12.1–18.4)	0.582[b]
Hematocrit (%)	46.05 (32.4–53.2)	46.0 (33.4–53.0)	45.9 (36.2–52.4)	45.7 (39.9–54.30)	0.501[b]
WBC (103/μL)	6.7 (2.5–13)	7.78 (4.20–14.67)	8.24 (3.95–16.27)	7.73 (4.80–14.75)	<0.001[b]
Platelet (103/μL)	241 (112–438)	247.5 (106–525)	258.5 (153–539)	259 (140–417)	0.052[b]
hs-CRP (mg/L)	0.25 (0.01–2.80)	0.50 (0.03–2.25)	1.1 (0.01–2.96)	1.6 (0.01–2.92)	<0.001[b]
Glucose (mg/dL)	98.09 ± 12.29	89.64 ± 15.03	92.93 ± 14.69	91.94 ± 16.73	0.001[a]
Creatinine (mg/dL)	0.94 ± 0.11	0.91 ± 0.15	0.95 ± 0.11	0.98 ± 0.11	0.002[a]
GFR (mL/min/1.73 m2)	112.26 ± 19.28	109.74 ± 17.55	100.43 ± 13.01	91.85 ± 11.53	<0.001[a]
Total Cholesterol (mg/dL)	200.12 ± 37.83	207.51 ± 37.01	208.40 ± 33.09	208.33 ± 34.99	0.304[a]
HDL (mg/dL)	43.36 ± 8.40	42.50 ± 7.91	41.05 ± 7.14	39.98 ± 7.54	0.017[a]
LDL (mg/dL)	125.19 ± 31.33	133.10 ± 31.30	131.96 ± 29.40	134.32 ± 28.01	0.150[a]
Triglyceride (mg/dL)	157.87 ± 31.76	159.55 ± 40.94	176.94 ± 38.67	170.14 ± 66.79	0.010[a]
ALT (IU/L)	21 (15–60)	21.45 (5–116)	21.5 (9.5–135.8)	23.8 (12–70.2)	0.455[b]
AST (IU/L)	22 (16–35)	20.05 (13–65)	20.1 (12–89.1)	20.7 (13.9–98)	0.688[b]
P maximum (ms)	95.44 ± 5.377	92.60 ± 5.463	96.79 ± 6.579	108.70 ± 8.189	<0.001[a]
P minimum (ms)	57.30 ± 5.54	55.32 ± 6.039	58.32 ± 6.439	64.89 ± 7.219	<0.001[a]
P dispersion (ms)	38.16 ± 3.54	37.28 ± 2.86	38.47 ± 2.56	43.81 ± 2.87	<0.001[a]
QT maximum (ms)	403.97 ± 20.86	398.08 ± 22.57	408.79 ± 22.70	408.49 ± 23.92	0.002[a]
QT minimum (ms)	371.51 ± 20.35	367.40 ± 21.24	373.04 ± 20.35	368.12 ± 23.67	0.200[a]
QT dispersion (ms)	32.46 ± 7.71	30.69 ± 7.05	35.74 ± 8.98	40.37 ± 8.11	<0.001[a]
QTc maximum (ms)	461.59 ± 33.67	456.25 ± 26.85	460.37 ± 27.37	474.70 ± 27.84	<0.001[a]
QTc minimum (ms)	424.51 ± 31.86	421.12 ± 25.76	420.14 ± 25.08	427.71 ± 26.30	0.234[a]
QTc dispersion (ms)	37.08 ± 8.87	35.17 ± 7.88	40.31 ± 9.90	46.95 ± 9.67	<0.001[a]

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BMI: Body mass index, DBP: Diastolic blood pressure, GFR: glomerular filtration rate, HDL: High density lipoprotein, hs-CRP: high sensitive C reactive protein.
LDL: Low density lipoprotein, SBP: Systolic blood pressure, WBC: White blood cell count.
[a] Mean ± SD in cases where the data were distributed normally, analyzed by student's *t*-test.
[b] median (minimum-maximum) values were presented in cases where the data were not normally distributed, analyzed by Mann-Whitney *U* test.
[c] analyzed by qi-square test.

(r = 0.385, p < 0.001) and with QTcd (r = 0.417, p < 0.001) (Fig. 2).

In the multivariate regression analysis, working duration in night shift was significantly associated with Pd, QTd and QTcd values when adjusted for other risk parameters which were significantly related in univariate regression analyses. (p < 0.001) (Tables 3–5). Working in night shift was significantly associated in univariate analyses for all of the three parameters, while these relationships lost their significance when adjusted for other relevant factors.

4. Discussion

Our study demonstrated that working night shift has an impact on Pd, QTd and QTcd intervals. To our knowledge, this is the first study conducted in a heavy metal industry population to test the association between night shift work and Pd, QTd, and QTcd intervals. Independent from other variables, Pd, QTd and QTcd prolongations were statistically significantly correlated with the number of working years in the shift workers. Pd and QTcd significantly prolonged among the night shift workers especially who worked above 15 years. However, this prolongation was mild among subjects who worked at night shifts for less than 15 years.

Acknowledging the high cardiovascular morbidity and mortality rates associated with night work, it is important to elaborate on possible mechanisms to take the necessary preventive measures. Pd measurement has been proven to be a sensitive and specific ECG predictor of AF in various clinical settings. Even, measurement of Pd is recommended to anticipate AF for reducing related adverse cardiac

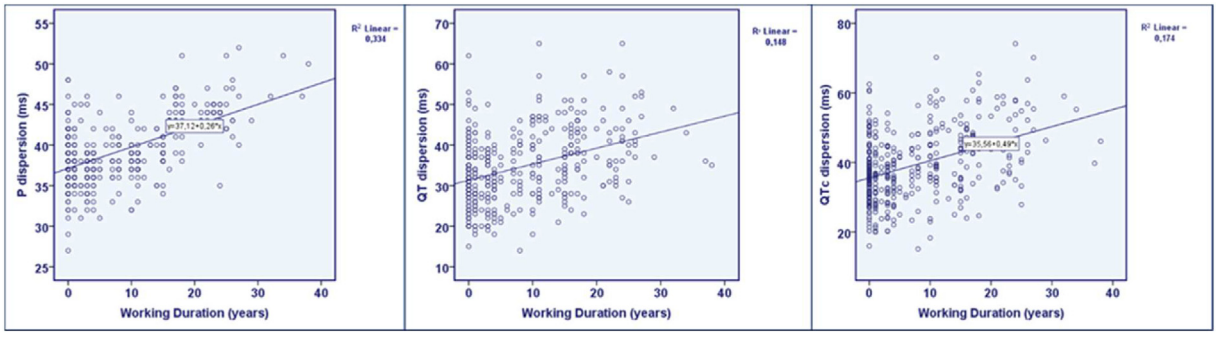

Fig. 2. The scatter plots with correlation coefficients show high correlations between the working duration in shift work with P wave dispersion and mild to moderate correlations between working duration in shift work with QTc dispersion.

Table 3. Univariate and multivariate linear regression analyses for PWD.

	Univariate Regression					Multivariate Regression				
	Beta	Std error	Confidence interval (95%)		P value	Beta	Std error	Confidence interval (95%)		P value
			Lower	Upper				Lower	Upper	
Age	0.235	0.019	0.199	0.272	<0.001	0.115	0.028	0.059	0.171	<0.001
BMI	0.219	0.057	0.107	0.332	<0.001	−0.007	0.048	−0.100	0.087	0.888
Duration	0.263	0.019	0.226	0.300	<0.001	0.222	0.033	0.157	0.286	<0.001
Night or day shift	1.427	0.444	0.555	2.300	0.001	−0.723	0.540	−1.785	0.340	0.182
SBP	0.013	0.022	−0.029	0.056	0.540					
DBP	0.007	0.033	−0.058	0.072	0.840					
WBC	0.076	0.098	−0.117	0.268	0.438					
Platelet	−0.002	0.003	−0.008	0.005	0.626					
Hs-CRP	1.175	0.222	0.738	1.612	<0.001	−0.245	0.207	−0.651	0.161	0.236
Glucose	0.020	0.013	−0.006	0.046	0.135					
GFR	−0.082	0.010	−0.102	−0.061	<0.001	−0.009	0.011	−0.031	0.013	0.426
Tot chol	0.001	0.005	−0.010	0.012	0.873					
HDL	−0.044	0.025	−0.093	0.005	0.080	−0.017	0.020	−0.056	0.021	0.377
LDL	0.004	0.007	−0.009	0.016	0.589					
Triglyceride	0.001	0.004	−0.007	0.010	0.734					
AST	0.011	0.025	−0.038	0.061	0.654					

AST: Aspartate aminotransferase, BMI: Body mass index, DBP: Diastolic blood pressure, GFR: glomerular filtration rate, HDL: High density lipoprotein, hs-CRP: high sensitive C reactive protein, LDL: Low density lipoprotein, SBP: Systolic blood pressure, WBC: White blood cell count.

events [10,11]. Also, a recent meta-analysis has clearly revealed that increased QTd is associated with high risk of ventricular arrhythmic events [13]. In this regard, ECG parameters that we discussed in the present study may be related to future cardiovascular events and contribute to comprehension of high mortality and morbidity rates in this population.

Though factors responsible for elevation in Pd and QTcd values in these individuals have not been clarified completely, irregular food intake, decreased sleep quality and adaptation efforts for tuning the circadian clock have been argued as aggravating aspects for cardiovascular risks and their management for the long-term [14]. Changes in diet and sleeping habits complicate controlling the risk factors such as hyperlipidemia, blood sugar regulation and/or physical inactivity as well.

Insomnia and low quality of sleep are well-known consequences of the shift working system. We considered that sleep disturbances caused by night shifts may have negative effects on Pd and QTcd by impairing endothelial function, acetylcholine-mediated vasodilation and coronary microcirculation as earlier on disclosed [15]. Even though there is not adequate data on results of sleep disturbances to ECG parameters for the long term, acute sleep deprivation has been speculated to increase Pd and QTd in healthy young adults [16,17]. As the results of insomnia; inflammation, sympathetic nerve activation, baroreflex response alteration, cardiac autonomic dysfunction, insulin resistance and improper melatonin secretion trigger the development of a number of cardiovascular diseases risk factors [18,19]. Further to that, sleep disorders that are unpreventable outcome of shift work are associated

Table 4. Univariate and multivariate linear regression analyses for QTD.

	Univariate Regression					Multivariate Regression				
	Beta	Std error	Confidence interval (95%)		P value	Beta	Std error	Confidence interval (95%)		P value
			Lower	Upper				Lower	Upper	
Age	0.253	0.048	0.158	0.348	<0.001	0.042	0.075	−0.106	0.189	0.579
BMI	0.167	0.131	−0.092	0.425	0.205					
Duration	0.394	0.048	0.299	0.489	<0.001	0.360	0.086	0.190	0.529	<0.001
Night or day shift	2.732	1.004	0.759	4.706	0.007	−1.835	1.431	−4.649	0.979	0.201
SBP	−0.044	0.049	−0.140	0.051	0.365					
DBP	0.020	0.074	−0.127	0.166	0.790					
WBC	0.082	0.221	−0.352	0.516	0.711					
Platelet	−0.008	0.007	−0.022	0.006	0.259					
Hs-CRP	3.400	0.489	2.439	4.361	<0.001	1.908	0.546	0.833	2.982	0.001
Glucose	−0.017	0.030	−0.076	−0.041	0.562					
GFR	−0.067	0.025	−0.116	−0.018	0.007	0.039	0.029	−0.018	0.097	0.178
Tot chol	0.021	0.012	−0.013	0.045	0.086	−0.004	0.028	−0.59	0.050	0.875
HDL	−0.044	0.057	−0.155	0.068	0.442					
LDL	0.028	0.015	−0.001	0.057	0.056	0.026	0.033	−0.038	0.091	0.1426
Triglyceride	0.010	0.010	−0.009	0.029	0.279					
AST	0.004	0.057	−0.108	0.115	0.946					

AST: Aspartate aminotransferase, BMI: Body mass index, DBP: Diastolic blood pressure, GFR: glomerular filtration rate, HDL: High density lipoprotein, hs-CRP: high sensitive C reactive protein, LDL: Low density lipoprotein, SBP: Systolic blood pressure, WBC: White blood cell count.

Table 5. Univariate and multivariate linear regression analyses for QTDc.

	Univariate Regression					Multivariate Regression				
	Beta	Std error	Confidence interval (95%)		P value	Beta	Std error	Confidence interval (95%)		P value
			Lower	Upper				Lower	Upper	
Age	0.306	0.055	0.198	0.415	<0.001	0.004	0.085	−0.163	0.172	0.960
BMI	0.232	0.151	−0.065	0.529	0.125					
Duration	0.491	0.055	0.383	0.598	<0.001	0.512	0.098	0.320	0.705	<0.001
Night or day shift	3.242	1.154	0.973	5.510	0.005	−3.119	1.626	−60.316	0.077	0.056
SBP	−0.055	0.056	−0.165	0.055	0.325					
DBP	−0.003	0.086	−0.171	0.165	0.973					
WBC	0.306	0.253	−0.192	0.804	0.228					
Platelet	−0.006	0.008	−0.021	0.010	0.479					
Hs-CRP	3.763	0.565	2.653	4.874	<0.001	1.753	0.621	0.532	2.973	0.005
Glucose	−0.012	0.034	−0.079	0.055	0.728					
GFR	−0.089	0.029	−0.145	−0.033	0.002	0.031	0.033	−0.034	0.097	0.345
Tot chol	0.025	0.014	−0.002	0.053	0.073	−0.016	0.031	−0.077	0.046	0.619
HDL	−0.069	0.065	−0.197	0.059	0.289					
LDL	0.036	0.017	0.003	0.069	0.034	0.046	0.037	−0.027	0.120	0.218
Triglyceride	0.010	0.011	−0.012	0.032	0.355					
AST	0.018	0.065	−0.110	0.146	0.787					

AST: Aspartate aminotransferase, BMI: Body mass index, DBP: Diastolic blood pressure, GFR: glomerular filtration rate, HDL: High density lipoprotein, hs-CRP: high sensitive C reactive protein, LDL: Low density lipoprotein, SBP: Systolic blood pressure, WBC: White blood cell count.

with increased cardiovascular morbidity and mortality [20]. Particularly, increased psychological and oxidative stress associated with sleep disorders may be other reasons since there are liable findings reported previously. Working night time has negative impacts on mental health and the studies have shown that the night shift workers have an increased risk of depression and mood disorder [21]. Emotional stress and mental health problems are advocated to predispose arrhythmias or cause symptoms of the rhythm disorders to worsen [22], and besides that two studies illustrated the relationship with mental stress and increased QTd [23] and Pd [21] directly.

Furthermore, irregular sleep periods at different hours changing daily are likely to affect the internal circadian rhythm of the heart in which sleep-wake periods are endogenously regulated. This mechanism modulated by the heart itself ensures adaptation to the environment. When this ability is

deteriorated by induced sympathetic activity after irregular sleeping times, autonomic modulation of the heart is changed and thereby arrhythmias may increase.

Inflammatory processes have another important determinant both in the etiology and in the progression of arrhythmias. We detected that hs-CRP levels of night shift workers were higher than that of the daytime workers compatible with the Kim et al.'s study which confirmed the relationship between night shift work and augmented levels of inflammatory markers such as interleukin-6, C-reactive protein and tumor necrosis factor [24]. Moreover, Teixeira et al. have obtained supporting finding by attributing their results to both oxidative stress and inflammation which affect endocardial and myocardial cells adversely causing calcium overload and depolarization/repolarization abnormalities ultimately [25]. Consistent with our results, high CRP levels in some specific patient groups have been reported to be associated with increased QTd [26] and Pd [27].

Our results revealed significant increases in a predictor of AF as additional explanation of the high cardiovascular morbidity and mortality related to night work. Prolongation of Pd in the shift workers suggests that this might create a milieu for atrial fibrillation and its adverse events. In a recent large scale observational study, researchers found that working night shifts was associated with a 12% increased risk of AF, compared to daytime workers [4]. The risk was increased for people working night shifts for 10 or more years supposed that they worked average three to eight night shifts in a month [4]. The association between night shift and increase risk of AF has been reported previously, but the relationship between Pd as a predictor of AF with this population has not been investigated before.

Pd was first described by Dilaveris et al., and its predictive ability for AF has been supported by numerous subsequent studies [28]. Pd significantly predicted AF in a 19.8 ± 11.8 months follow-up prospective study examining the pacemaker records of 101 patients. In the same study, Pd values above 40 ms were found to increase the risk of persistent AF by 12.2 times [29]. In a 12-month backward investigation of digitally stored ECG recordings of 8632 individuals, Yoshizawa et al. presented that Pd predicted new-onset AF with a sensitivity of 76.5% and a specificity of 79.4% [30]. Also, there are several studies in patients with implantable cardiac devices that show that longer Pd is associated with new-onset AF, independent from other variables such as age, sex, past medical history and therapy [31,32]. In a prospective study including 251 patients with mean follow up of 66 ± 8 months; Pd and age were found to be independent predictors of progression to persistent AF from paroxysmal AF [33]. Moreover, measurement of Pd has been found to be an effective method in evaluating the efficacy of catheter ablation, AF recurrence and maintenance of sinus rhythm after cardioversion [34,35]. Although, we demonstrated critical increases in Pd values as the AF predictor, it needs to be endorsed by large scale data exhibiting long-term effects of work at night shifts.

In the examining of relationship between shift work and QTc interval, conflicting results have been reported in previous studies [36–38]. In contrast to Murata et al.'s research reporting a significant rise in the mean QTc interval in shift workers, Meloni et al. in their former study, identified no relationship between the QTc interval and shift work. In the following study of Meloni et al., a remarkable increase in the QTc interval was detected in shift workers and they argued that the reason for their different results might be related to the small sample size of their first study. Although it needs to be supported by other studies, our results with a larger number of subjects are consistent with the findings of Murata et al. and the recent work of Meloni et al. Nonetheless, prolonged QTc due to underlying multiple mechanisms which carry distinct arrhythmic potency can give rise to ventricular arrhythmia in regardless of the degree of the elongation of QTc itself [39]. Thus, in addition to determined value of QTc prolongation in arrhythmic predisposition, increased QTd should be considered to provide an additional contribution to predicting the risk of ventricular arrhythmias.

Our study was designed retrospective and observational, thus, we could not analyze the other probable confounding variables such as alcohol consumption, physical activity, psychological stress and diet as components which have impacts on the cardiac autonomous function. However, our entire study population consists of foundry workers and that may be negligible due to similar socio-economical and educational status of the workers. Also, our whole study population consisted of men and we did not assessed gender effect on the issue. However, as we mentioned above shift working order in today's industrialized economy, men stand the major load due to strenuous working conditions. Finally, Healthy worker effect could restrict to generalize our results to the general population in some extent. An individual who continues to work as worker as a result of his well health status, has the ability to improved access to healthcare,

periodical examinations and early treatment opportunities. Those allow the worker maintain his health status when compared to general population. Nevertheless, this phenomenon mainly originates from improper selection of control group. We compared the daytime workers who had the same working order as they work in the same foundry factory. Our study used the same worker population as the reference population. Also, to minimize reduction of the generalizability of the results, we included those working for longer periods of time in the same factory and no comparison was made between those who are recently employed.

5. Conclusions

Our study presented that there were statistically significant increases in P wave dispersion and QT dispersion intervals in the shift workers and affirmed the previous reports with respect to elongations of QTc as consequences of working at night shifts. As predictors of atrial fibrillation and ventricular arrhythmias, increases in P wave and QTc dispersion suggest that cardiac examination including a meticulous ECG evaluation might be applied as a necessary part of periodical follow up of night workers especially working for long years.

Author contribution

Conception and design of Study; Literature review; Acquisition of data; Analysis and interpretation of data; Research investigation and analysis; Data collection; Drafting of manuscript; Revising and editing the manuscript critically for important intellectual contents; Data preparation and presentation; Supervision of the research; Research coordination and management: SBU, KES. Funding for the research: SBU, KES.

Conflict of interest

None.

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