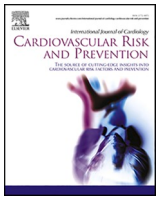
International Journal of Cardiology Cardiovascular Risk and Prevention 19 (2023) 200219

Contents lists available at ScienceDirect

International Journal of Cardiology Cardiovascular Risk and Prevention

journal homepage: www.journals.elsevier.com/international-journal-of-cardiology-cardiovascular-risk-and-prevention



Sex difference in cardiac performance in individuals with irregular shift work

Mi Zhou [a], Junqing Zhang [a], Jinyi Zhao [a], Mingjiao Liao [a], Siming Wang [a], Da xu [a], Bingyan Zhao [a], Chuan Yang [a], Guoqing Hou [b], Jing Tan [a], Jun Liu [c], Wenjun Zhang [a,**], Lixue Yin [d,*]

[a] Department of Ultrasound in Medicine, Sichuan Provincial People's Hospital Wenjiang Hospital, Chengdu, China
[b] Department of Cardiology, Sichuan Provincial People's Hospital Wenjiang Hospital, China
[c] Department of Ultrasound in Medicine, Sichuan Provincial People's Hospital, China
[d] Cardiovascular Ultrasound and Non-Invasive Cardiology Department, Sichuan Provincial People's Hospital, Chengdu, China

ARTICLE INFO

Handling Editor: D Levy

Keywords:
Shift work
Night shift
Left ventricular function
Global longitudinal strain
Gender difference

ABSTRACT

Background: sex differences existed in animal behavioral adaption and activity rhythms when exposed to chronic disruption of the circadian rhythm. Whether these differences extend to cardiac performance has not been fully investigated by cardiac imaging technology.

Methods: One hundred and thirty patients enrolled in this study. Patients were divided into the day shift (DS) group and the irregular shift (IRS) group based on whether involved in the night shift and the frequency of the night shift. Comparisons of clinical data and cardiac imaging parameters were performed to identify the sex difference in cardiac function in the participants with day shift work or irregular shifts.

Results: The absolute value of GLS was significantly lower in male IRS group than in male DS group. In females, no significant difference was tested in left ventricular function between the two groups. In male participants, Weekly work hours (WWH) was positively correlated with HR ($r = 0.51$, $p = 0.02$) and QTc duration ($r = 0.68$, $p < 0.00$), and weakly negatively correlated with the GLS ($r = -0.38$, $p = 0.05$). Amongst patients, there was a 2.67-fold higher relative risk (RR) for impaired GLS in males than in females, with a 95 % confidence interval (CI) of 1.20–5.61. Moreover, there was an increased risk in the male IRS group compared to the female IRS group to develop impaired GLS (RR:3.14, 95 % CI 1.20–7.84).

Conclusions: The present study suggests that chronic circadian disruption brings cardiac dysfunction in people with night-shift work. Gender differences exist in the impact of circadian rhythmicity on cardiac function and may help to guide the work schedule and breaks in shift workers and bring forward prevention strategies in response to chronic circadian disruption.

1. Introduction

Individuals with frequent night-shift or long working hours suffer from sleep disorders and nutritional imbalance and therefore have an increased probability of cardiometabolic syndrome, injury, and infection which were caused by altered circadian rhythms and impairment of immune response and function [1–5]. Recently, a study from the University of Pennsylvania reported that female mice showed stronger behavioral adaption and activity rhythms than male mice when exposed to chronic disruption of circadian rhythm; this phenomenon is sustained in humans which females tend to have a lower incidence of metabolic syndrome than male, which were demonstrated from the UK biobank data [6].

Sex differences in circadian regulation and the sleep-waking system are modulated by biological clocks, steroid hormones, and clock gene expression [7–9]. Estrogenic signaling pathway has substantial activating effects on the temporal structuring and expression of daily and circadian behavior due to ESR1 and ESR2 activation [10,11]. Estrogen signaling disruption has been associated with psychological, neurological, cardiovascular, and metabolic diseases [12–14]. Whether these sex

* Corresponding author.
** Corresponding author.
E-mail addresses: 529270049@qq.com (W. Zhang), yinlixue_cardiac@163.com (L. Yin).

https://doi.org/10.1016/j.ijcrp.2023.200219
Received 7 August 2023; Received in revised form 10 September 2023; Accepted 2 October 2023
Available online 7 October 2023

differences extend to the cardiac performance due to the disruption of the sleep-wake cycle and circadian rhythmicity has not been fully investigated by quantitatively evaluated by cardiac imaging technology. The aims of the present study were two, 1) to investigate the difference in cardiac function between individuals with day shift and night shift and 2) to explore if any sexual difference in cardiac performance in individuals who are exposed to chronic night shift work.

2. Materials and methods

2.1. Study population

This prospective single-center study enrolled participants who presented to the Sichuan Provincial People's Hospital Wenjiang Hospital for health check between December 2022 and February 2023. The study protocol was approved by the institutional review boards of the hospital. Clinical and demographic data were collected from the electronic patient records. Weekly work hours (WWH) were computed for all participants. All patients underwent standard 12-lead electrocardiogram (ECG), transthoracic echocardiography (TTE), and blood tests for cardiac enzymes. The inclusion criteria were age $\geq$18 years and willingness to participate in the study. The exclusion criteria were known coronary artery disease, congenital heart disease, hyperthyroidism, inability to finish all the tests, poor image quality for echocardiography and speckle tracking analysis, and unwillingness to provide written informed consent. Participants were divided into the day shift (DS) group and the irregular shift (IRS) group. DS group was defined as participants involved in day work only or rare night shift (<1 time/week). IRS group was described as 2 times or more night shift rotations per week besides the day shift work.

2.2. ECG and transthoracic echocardiographic measurements

The standard 12-lead digital ECG (iMAC 12, Zoncare, Hubei, China) was performed with the patient at rest. The degree of the ECG axis, PR interval, QT interval, and QTc interval were automatically recorded and evaluated by one experienced cardiologist who was blinded to the study design. Conventional transthoracic echocardiography (Vivid I, GE Medical Systems, Tirat Carmel, Israel, 1.5–3.6 MHz, phased array transducer) was performed according to the clinical guidelines of the American Society of Echocardiography (ASE). The left ventricular ejection fraction (LVEF) was evaluated using Simpson's biplane method. Diastolic function was assessed by the *trans*-mitral early (E) and late (A) inflow velocity, E/A ratio, and the early (e') and late (a') diastolic velocities of the septal mitral annulus measured using Doppler echocardiography.

2.3. Two-dimensional speckle tracking echocardiography (2D-STE)

The STE analysis was performed on an offline workstation (Echo PAC PC version 203, GE Healthcare). A standard border was automatically created to encompass the endocardium to the epicardium once the region of interest in the left ventricle's endocardium was manually confirmed. For each view, the left ventricular myocardium was automatically divided into six typical segments. The absolute value of LV global longitudinal strain (GLS) was calculated by the average peak longitudinal strain of apical 4-, 2-, and 3-chamber views. Peak strain dispersion (PSD) was automatically acquired after the completion of strain analysis of the three apical chamber views. All strain values were presented as percentages (%).

3. Statistical analysis

All continuous variables (CV) tested whether satisfied with normal distribution by the Kolmogorov-Smirnov method. CV with normal distribution was reported as Mean $\pm$ Standard deviation (SD), otherwise expressed as median or interquartile range. Categorical variables were presented as numbers of participants and percentages. The differences in CV between the day shift group and the irregular shift group were analyzed using the independent *t*-test or Mann-Whitney *U* test, if applicable. The difference in categorical variables between groups was analyzed by the Chi-square test. The correlation coefficient between weekly working hours and other cardiac parameters was calculated by Pearson or Spearman methods. The intra-observer reproducibility or inter-observer reproducibility was analyzed by paired *t*-test or Bland-Altman analysis, respectively. P-values <0.05 (two-sided) were considered statistically significant in all test hypotheses. All the analyses were performed using SPSS 26.0 software (IBM SPSS Statistics 26.0, USA).

4. Results

4.1. Clinical characteristics of the study groups

A total of 255 patients who came for a health check at Sichuan Provincial People's Hospital Wenjiang Hospital were enrolled in this study. 73 of whom were excluded due to known significant cardiovascular disease. One hundred and thirty patients enrolled in the final analysis after excluding 42 patients without complete data and 10 patients with poor echocardiographic image quality. Patients were divided into the DS group and IRS group based on whether involved in the night shift and the frequency of the night shift. The flow chart for data collecting and analysis is depicted in Fig. 1.

The mean age of the 130 patients was 34.49 $\pm$ 7.45 years, and 26 patients (20 %) were male. Seventy-two patients were divided in the DS group and 58 patients were divided in the IRS group. Five patients (3.8 %) had hypertension, 1 patient (0.8 %) had a history of diabetes mellitus, and 7 patients (5.4 %) had hyperlipidemia. Patients with a history of significant cardiovascular disease, including coronary artery disease, valvular disease, heart failure, arrhythmias, and vascular disease were not included in the study. The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) were 120.30 $\pm$ 15.52 and 75.55 $\pm$ 11.58 mm of mercury (mmHg) respectively. There were no significant differences in body mass index (BMI), comorbidities, and cardiac enzymes between the DS group and the IRS group. The comparison of clinical characteristics between the DS group and the IRS group was described in Table 1.

4.2. Cardiac imaging parameters

Table 2 shows the comparison of cardiac imaging between the DS group and the IRS group. Heartbeats (HR), degree of the cardiac axis, QRS duration, PR interval, and QT duration did not significantly differ between the DS group and IRS group. However, QTc duration was longer in the IRS group compared to the DS group. The diastolic function evaluated by the E, E/A ratio, e', a', and e'/a' ratio was different between the two groups, however, E/e' ratio was the same between the DS group and IRS group. Although left ventricular systolic function assessed by LVEF was the same between groups, the absolute value of GLS was significantly lower in the IRS group than in the DS group.

A comparison of clinical data and cardiac imaging parameters in male between the DS group and IRS group are given in Table 3. In male patients, QTc duration was longer in the IRS group compared to the DS group, and no notable difference was examined in clinical data and other ECG parameters between the two groups. Additionally, the difference in E, E/A ratio, and GLS was sustained in male patients between the DS group and IRS group. In addition, only 2 male patients in the IRS group worked three shifts per week, as opposed to the other 12 male patients who worked two shifts per week. Subgroup analysis indicated that the E/A ratio was decreased in males with 3 shifts (0.84 $\pm$ 0.09) compared to the male patients with 2 shifts (1.29 $\pm$ 0.28), however, E/e' ratio, LVEF, and GLS were the same between the two groups.

In female patients, E and A were decreased in the IRS group,

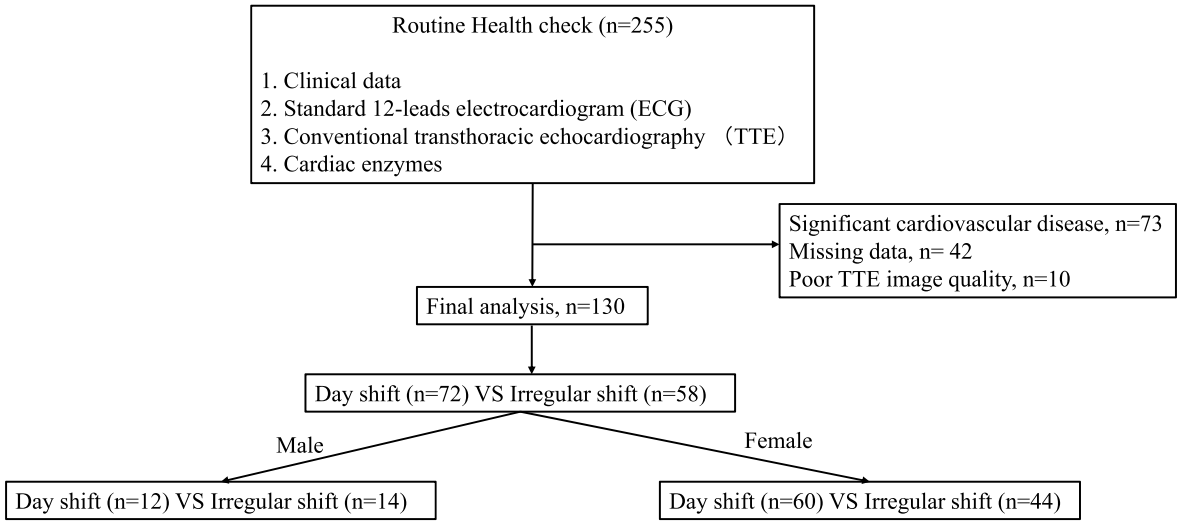


Fig. 1. Flowchart of the study enrollments.

Table 1
Comparisons of clinical data between day shift and irregular shift workers recovered from COVID-19.

Parameters	Total (n = 130)	Day shift (n = 72)	Irregular shift (n = 58)	P value
Age, years	34.49 ± 7.45	34.56 ± 8.23	34.41 ± 6.41	0.30
Male sex (n, %)	26 (20)	12 (16.7)	14 (24.1)	0.38
BMI (kg/m^2)	22.22 ± 2.40	22.26 ± 2.45	22.18 ± 2.36	0.14
Weekly work hours	44.22 ± 4.65	41.93 ± 3.74	47.03 ± 4.13	<0.00
SBP, mmHg	120.30 ± 15.52	120.70 ± 15.60	119.81 ± 15.55	0.53
DBP, mmHg	75.55 ± 11.58	76.23 ± 11.61	74.70 ± 11.58	0.53
Comorbidities				
HT, n (%)	5 (3.8)	3 (4.2)	2(3.4)	0.99
DM, n (%)	1 (0.8)	0 (0)	1(1.7)	–
Hyperlipidemia, n (%)	7 (5.4)	3 (4.2)	4 (6.9)	0.70
CK-MB, IU/L	11.00 (8.58, 14.45)	11.00 (8.55, 15.50)	11.30 (8.35, 12.80)	0.51
TNI, ng/ml	0.009 (0.007, 0.01)	0.009 (0.007, 0.01)	0.01 (0.007, 0.02)	0.08

BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; HT = hypertension; DM = diabetes mellitus; CK-MB= Creatine kinase-MB; TNI = troponin I.

however, no significant difference was tested in the E/A ratio, e'/a' ratio, and E/e' ratio between the two groups. In the IRS group, 10 patients worked with 3 shifts per week and 34 patients worked with 2 shifts per week. No significant difference in cardiac imaging parameters was observed in the subgroup analysis. Detailed comparison in female patients is presented in Table 4.

4.3. WWH and other cardiac imaging parameters

In male participants, WWH was positively correlated with HR (r = 0.51, p = 0.02) and QTc duration (r = 0.68, p < 0.00) (see Table 5). In addition, the absolute value of GLS was weakly negatively correlated with the WWH (r = -0.38, p = 0.05). In comparison, no correlation was found between WWH and any cardiac imaging parameters in female participants.

4.4. Sex difference in the impaired GLS

Amongst patients, there was a 2.67-fold higher relative risk (RR) for impaired GLS in males than in females, with a 95 % confidence interval (CI) of 1.20–5.61. Furthermore, there was an increased risk in male patients in the IRS group compared to the female patients in the IRS group to develop impaired GLS (RR:3.14, 95 % CI 1.20–7.84). Analysis of RR for impaired GLS between males and females, males with irregular shift work, and females with irregular shift work are depicted in Fig. 2. In addition to the impaired GLS, 2 patients (3.4 %) in the IRS group received cardiac medication due to combined of moderate pericardial effusion or T wave abnormality which was indicated by serial ECG.

Table 2
Cardiac imaging screening in individuals with day shift or irregular shift.

Parameters	Total (n = 130)	Day shift (n = 72)	Irregular shift (n = 58)	P value
Electrocardiogram				
HR beats/minute	80.29 ± 10.14	80.75 ± 10.16	79.70 ± 10.20	0.42
Degree of the axis, °	46.19 ± 35.90	45.24 ± 35.33	47.38 ± 36.87	0.61
QRS duration, ms	65.08 ± 37.46	65.81 ± 36.25	64.17 ± 39.21	0.36
PR interval, ms	108.30 ± 61.93	110.06 ± 60.14	106.12 ± 64.55	0.41
QT duration, ms	271.14 ± 153.67	275.40 ± 149.67	265.84 ± 159.65	0.46
QTc duration, ms	409.17 ± 16.19	408.13 ± 18.70	410.53 ± 12.27	0.04
Echocardiography				
E, cm/s	0.84 ± 0.20	0.89 ± 0.19	0.77 ± 0.18	<0.00
EDT, ms	183.97 ± 62.93	183.68 ± 68.13	184.33 ± 56.40	0.17
A, cm/s	0.59 ± 0.16	0.62 ± 0.17	0.55 ± 0.15	0.72
E/A ratio	1.52 ± 0.55	1.54 ± 0.50	1.50 ± 0.60	0.04
e', cm/s	0.10 (0.09, 0.12)	0.11 (0.09, 0.12)	0.10 (0.08, 0.11)	0.008
a', cm/s	0.08 (0.08, 0.10)	0.07 (0.06, 0.10)	0.08 (0.06, 0.11)	0.11
e'/a' ratio	1.40 (1.14, 1.81)	1.40 (1.14, 1.81)	1.25 (0.80, 1.62)	0.02
E/e ratio	8.53 (6.90, 10.07)	8.52 (6.90, 10.07)	8.14 (6.57, 9.04)	0.27
LVEF, %	64.38 ± 4.70	64.94 ± 4.42	63.67 ± 4.96	0.75
GLS	20.17 ± 2.28	20.64 ± 2.10	19.58 ± 2.36	<0.00
PSD, ms	41.78 ± 9.72	41.84 ± 7.81	41.71 ± 11.74	0.97

HR = heart beats; E = *trans*-mitral early inflow velocity; A = *trans*-mitral late inflow velocity; e' = the early diastolic velocities of the septal mitral annulus; a' = the late diastolic velocities of the septal mitral annulus; LVEF = left ventricular ejection fraction; GLS = global longitudinal strain; PSD = peak strain dispersion.

Table 3
Comparison of cardiac performance between males with day shift or irregular shift.

Parameters	Total (n = 26)	Day shift (n = 12)	Irregular shift (n = 14)	P value
Age, years	34.73 ± 8.65	32.75 ± 9.71	36.43 ± 7.58	0.29
SBP, mmHg	132.42 ± 13.52	130.45 ± 9.19	134.08 ± 16.53	0.53
DBP, mmHg	85.58 ± 10.44	84.09 ± 10.37	86.85 ± 10.75	0.53
BMI (kg/m^2)	24.05 ± 2.38	24.79 ± 2.59	23.41 ± 2.06	0.14
CK-MB, IU/L	13.11 ± 6.16	13.62 ± 6.24	12.64 ± 6.31	0.70
TNI, ng/ml	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.96
Electrocardiogram				
HR, beats/ minute	80.68 ± 10.12	78.91 ± 8.96	82.45 ± 11.30	0.42
QRS duration, ms	45.96 ± 38.06	83.92 ± 27.33	71.35 ± 38.92	0.36
PR interval, ms	127.58 ± 56.45	137.58 ± 44.34	119.00 ± 65.52	0.41
QT duration, ms	293.58 ± 128.90	314.25 ± 100.94	275.86 ± 150.32	0.46
QTc duration, ms	400.36 ± 20.48	391.36 ± 20.30	409.36 ± 17.03	0.04
Echocardiography				
E, cm/s	0.74 ± 0.16	0.83 ± 0.16	0.66 ± 0.12	<0.00
EDT,ms	192.73 ± 56.24	176.33 ± 58.44	206.79 ± 52.28	0.17
A, cm/s	0.61 ± 0.15	0.62 ± 0.18	0.60 ± 0.13	0.72
E/A ratio	1.26 ± 0.36	1.41 ± 0.38	1.14 ± 0.29	0.04
e', cm/s	0.10 (0.08, 0.12)	0.11 (0.08, 0.12)	0.09 (0.07, 0.11)	0.21
a', cm/s	0.10 ± 0.02 (0.08, 0.11)	0.10 (0.08, 0.11)	0.10 (0.09, 0.10)	0.63
e'/a' ratio	1.06 (0.79, 1.38)	1.17 (0.83, 1.48)	0.97 (0.76, 1.23)	0.17
E/e ratio	7.75 ± 2.28	8.10 ± 2.38	7.45 ± 2.23	0.48
LVEF, %	63.73 ± 5.69	63.33 ± 3.77	64.07 ± 7.06	0.75
GLS	18.39 ± 2.08	19.50 ± 1.09	17.45 ± 2.29	<0.00
PSD, ms	45.66 ± 10.57	45.77 ± 9.88	45.58 ± 11.50	0.97

BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; HT = hypertension; DM = diabetes mellitus; CK-MB= Creatine kinase-MB; TNI = troponin I; E = *trans*-mitral early inflow velocity; A = *trans*-mitral late inflow velocity; e' = the early diastolic velocities of the septal mitral annulus; a' = the late diastolic velocities of the septal mitral annulus; LVEF = left ventricular ejection fraction; GLS = global longitudinal strain; PSD = peak strain dispersion.

Table 4
Comparison of cardiac performance between females with day shift or irregular shift.

Parameters	Total (n = 104)	Day shift (n = 60)	Irregular shift (n = 44)	P value
Age, years	34.43 ± 7.16	34.70 ± 8.04	34.07 ± 5.83	0.66
SBP, mmHg	117.24 ± 14.51	118.38 ± 15.69	115.68 ± 12.75	0.37
DBP, mmHg	73.01 ± 10.45	74.25 ± 11.08	71.30 ± 9.40	0.18
BMI (kg/m^2)	21.77 ± 2.20	21.70 ± 2.10	21.85 ± 2.35	0.74
CK-MB, IU/L	10.80 (8.45, 13.80)	11.86 (8.55, 14.95)	10.54 (7.15, 12.38)	0.38
TNI, ng/ml	0.009 (0.07, 0.01)	0.009 (0.007, 0.01)	0.01 (0.007, 0.02)	0.11
Electrocardiogram				
HR, beats/ minute	80.18 ± 10.21	81.20 ± 10.47	78.75 ± 9.81	0.30
QRS duration, ms	62.06 ± 37.83	62.18 ± 36.91	61.89 ± 39.47	0.97
PR interval, ms	103.48 ± 62.56	104.55 ± 61.65	102.02 ± 64.45	0.84
QT duration, ms	265.53 ± 159.32	267.63 ± 157.13	262.66 ± 164.05	0.88
QTc duration, ms	411.69 ± 13.90	412.22 ± 15.99	410.94 ± 10.47	0.69
Echocardiography				
E, cm/s	0.86 ± 0.20	0.91 ± 0.19	0.80 ± 0.19	<0.00
EDT,ms	181.78 ± 64.56	184.25 ± 69.72	178.41 ± 57.40	0.65
A, cm/s	0.58 ± 0.17	0.62 ± 0.17	0.54 ± 0.15	<0.00
E/A ratio	1.59 ± 0.57	1.58 ± 0.52	1.61 ± 0.64	0.79
e', cm/s	0.11 (0.09, 0.12)	0.11 (0.09, 0.12)	0.10 (0.09, 0.11)	0.09
a', cm/s	0.07 (0.06, 0.10)	0.07 (0.06, 0.08)	0.08 (0.06, 0.11)	0.10
e'/a' ratio	1.42 (1.11, 1.85)	1.62 (1.21, 2.00)	1.39 (0.90, 1.83)	0.07
E/e ratio	8.50 ± 2.31	8.66 ± 2.29	8.14 ± 2.49	0.27
LVEF, %	64.54 ± 4.43	65.18 ± 4.44	63.66 ± 4.32	0.08
GLS	20.61 ± 2.11	20.90 ± 2.16	20.21 ± 2.00	0.10
PSD, ms	40.81 ± 9.30	40.94 ± 7.15	40.64 ± 11.71	0.88

BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; HT = hypertension; DM = diabetes mellitus; CK-MB= Creatine kinase-MB; TNI = troponin I; E = *trans*-mitral early inflow velocity; A = *trans*-mitral late inflow velocity; e' = the early diastolic velocities of the septal mitral annulus; a' = the late diastolic velocities of the septal mitral annulus; LVEF = left ventricular ejection fraction; GLS = global longitudinal strain; PSD = peak strain dispersion.

4.5. Reproducibility

The inter-observer variability and the intra-observer variability of the echocardiographic measurements for this study were assessed by comparing the variation between two sonographers and the same sonographer respectively. The results of inter-observer variability and intra-observer variability was depicted in Fig. 3.

5. Discussion

The present study demonstrates that sexual differences conserved in cardiac performance in shift workers who suffered chronic circadian disruption. Patients in the irregular shift group displayed longer QTc duration and impaired diastolic function which was assessed by the decreasing of E/A ratio, e', e'/a' ratio, and the increasing of a'. Moreover, the left ventricular global function evaluated by LVEF was reduced in the irregular shift group than in the day shift group. Further study findings exhibited the sexual difference in the impairment of cardiac performance in shift workers were summarized as follows: (i) Male participants with irregular shift work demonstrated longer QTc duration and impaired E, E/A ratio, and GLS than the males with day shift work. (ii) There was no significant difference in left ventricular systolic and diastolic function between females with irregular shift and day shift work. (iii) In male patients, weekly work hours were positively correlated with HR and QTc duration, and weakly negatively correlated with GLS. (iv) Male participants (RR:2.67, 95 %: 1.20–5.61), especially males in the irregular shift group (RR:3.14, 95 % CI 1.20–7.84), showed a higher risk of developing impaired GLS than females.

In the present study, we show that only males in the irregular shift group demonstrate a longer QTc duration, and a positive correlation was observed between weekly work hours and heart rate or QTc duration. And thus, we tentatively put forward that gender difference may exist in cardiac impairment among irregular shift workers for the first time. Previous studies have suggested that disruption of the circadian cycle brings cardiometabolic disorders and obesity in people with night-shift rotation than those with permanent day-shift work [1,15–18]. Sleep deprivation or poor sleep quality was associated with negative effects on cardiac repolarization, characterized by prolonged QT interval, QTc interval, and arrhythmias [19–21]. Previous experimental study revealed that female mice presented with better resilience to left anterior descending coronary artery ligation as compared to males [22]. Recently, a hybrid study compounded animal experiments and clinical data, revealed that changes in transcriptomic rhythmicity and increased

Table 5
Correlation between WWH and other parameters.

	Coefficient	P value
Male		
HR	0.51	0.02*
QT duration	-0.22	0.29
QTc duration	0.68	<0.00*
E	-0.33	0.10
A	-0.14	0.47
E/A ratio	-0.18	0.37
LVEF	-0.11	0.58
GLS	-0.38	0.05
Female		
HR	0.00	0.99
QT duration	-0.17	0.09
QTc duration	0.05	0.67
E	-0.11	0.29
A	-0.16	0.11
E/A ratio	0.10	0.33
LVEF	-0.01	0.93
GLS	-0.07	0.51

WWH = weekly work hours; HR = heart beats; E = *trans*-mitral early inflow velocity; A = *trans*-mitral late inflow velocity; LVEF = left ventricular ejection fraction; GLS = global longitudinal strain.

systolic blood pressure due to irregular circadian rhythms were observed in male mice but were prevented in females [6]. Coincidentally, another study reported that reduced heart rate variability was observed in males with night shift rotation but not women [23]. This is probably the consequence of the protective effect of estrogen in response to circadian cycle changes and cardiometabolic disease [6,24].

The present study shows an impairment of left ventricular diastolic function and global longitudinal strain which were observed only in males with irregular shift work compared to those with day shift work. Partially consistent with findings that have investigated the effects of acute and short-term sleep deprivation (24-h shift) on cardiac function, displayed with decreased myocardial deformation in the left and right ventricle and left atrium as well as increased E/e'ratio [25–27]. In contrast, another study revealed that a 24-h shift with short-term sleep deprivation has significantly increased the blood pressure and circumferential strain, and longitudinal strain assessed by cardiac magnetic resonance [28]. In light of the findings for sleep deprivation on cardiac function being controversial, further study with a large sample is warranted to identify the impact of short-term, and long-term circadian disturbance in cardiac deformation and explore the distinction in myocardial performance between males and females who are exposed to the chronic circadian disruption.

Although gender differences in cardiac impairment due to chronic circadian disruption which revealed by the present study, there are also limitations. First, the sample size of the study is small and only 20 % of participants are male. Second, all participants enrolled were from the same company that provided health care services, our findings stem from those highly selected participants may not generalize to other people with different types of shift work. Last, further study with a larger sample could identify the impact of short-term or long-term circadian disturbance and gender difference on cardiac deformation.

6. Conclusions

The present study suggests that chronic circadian disruption brings cardiac dysfunction in people with night-shift rotation. These data establish the gender difference existed in the impact of circadian rhythmicity on cardiac function and may help to guide the work schedule and breaks in shift workers and bring forward prevention strategies in response to the chronic effect of circadian disruption.

Authors' contributions

MZ is the principal investigator of the whole study responsible for study conceptualization, study execution, original manuscript drafting,

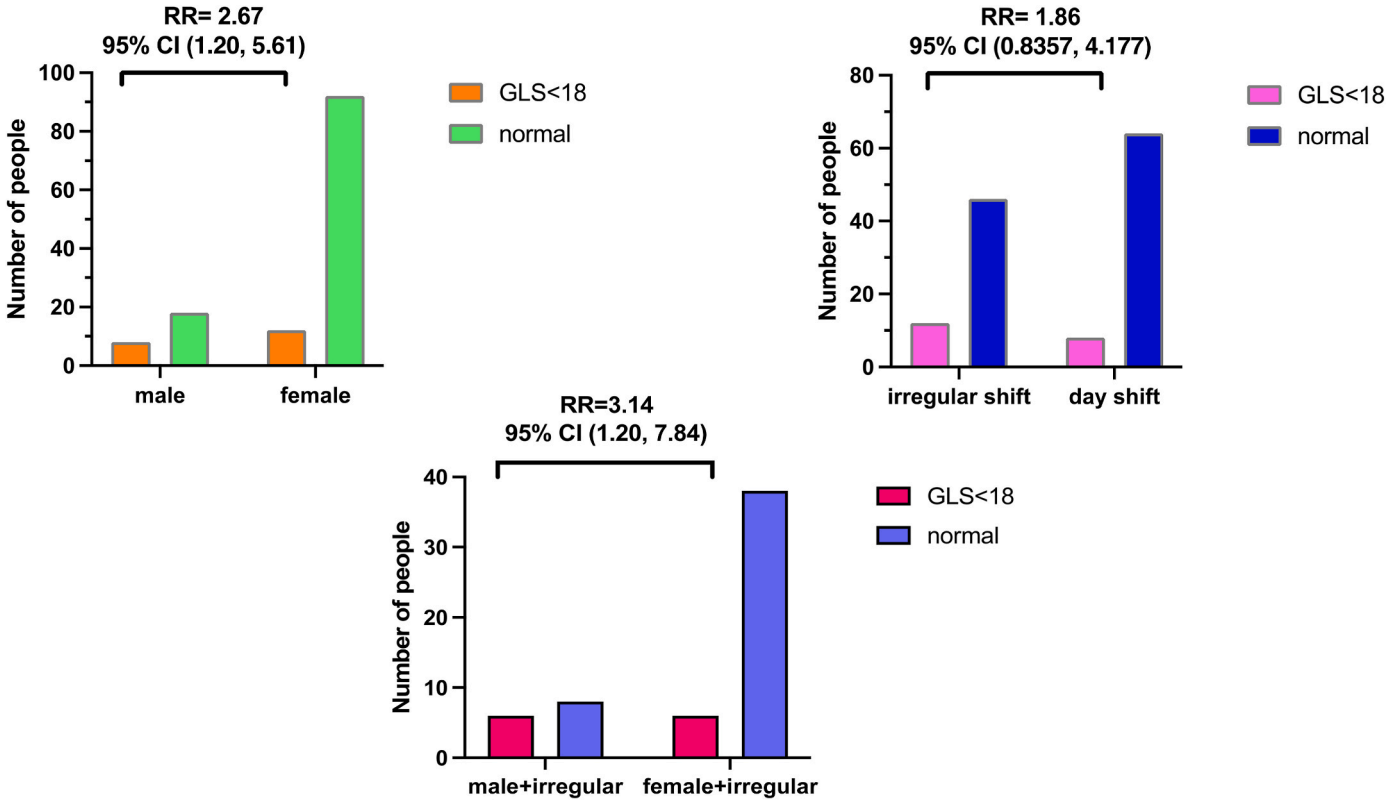


Fig. 2. Analysis of RR for impaired GLS between males and females, males with irregular shift work, and females with irregular shift work.

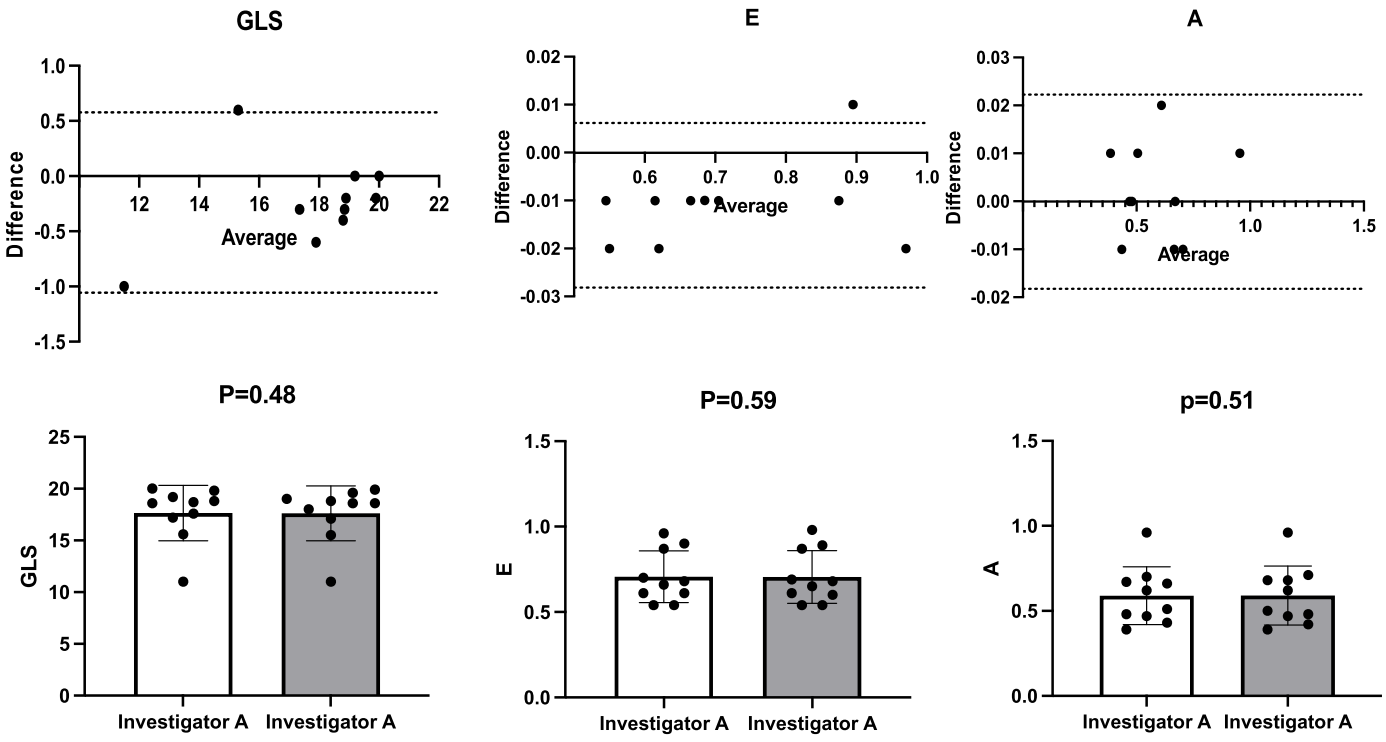


Fig. 3. Findings of inter-observer variability and intra-observer variability.

and study site recruitment. LXY, WJZ, and MZ are major contributors to writing the manuscript. MZ, JQZ, JYZ, MJL, SMW, DX, BYZ, CY, GQH JL, and JT contributed to data collection. All authors read and approved the final manuscript.

Funding

This article was partially funded by Chengdu Municipal Health Commission (2023049).

Acknowledgments

We thank all patients for participating in this study.

References

[1] F.K. Ho, C. Celis-Morales, S.R. Gray, E. Demou, D. Mackay, P. Welsh, S. V. Katikireddi, N. Sattar, J.P. Pell, Association and pathways between shift work and cardiovascular disease: a prospective cohort study of 238 661 participants from UK Biobank, Int. J. Epidemiol. 51 (2022) 579–590, https://doi.org/10.1093/ije/dyab144.

[2] F.R.D. Silva, R.C. Guerreiro, H.A. Andrade, E. Stieler, A. Silva, M.T. de Mello, Does the compromised sleep and circadian disruption of night and shiftworkers make them highly vulnerable to 2019 coronavirus disease (COVID-19)? Chronobiol. Int. 37 (2020) 607–617, https://doi.org/10.1080/07420528.2020.1756841.

[3] S. Rizza, L. Coppeta, S. Grelli, G. Ferrazza, M. Chiocchi, G. Vanni, O.C. Bonomo, A. Bellia, M. Andreoni, A. Magrini, et al., High body mass index and night shift work are associated with COVID-19 in health care workers, J. Endocrinol. Invest. 44 (2021) 1097–1101, https://doi.org/10.1007/s40618-020-01397-0.

[4] B. Loef, D. van Baarle, A.J. van der Beek, E.A.M. Sanders, P. Bruijning-Verhagen, K. I. Proper, Shift work and respiratory infections in health-care workers, Am. J. Epidemiol. 188 (2019) 509–517, https://doi.org/10.1093/aje/kwy258.

[5] J. Ervasti, J. Pentti, S.T. Nyberg, M.J. Shipley, C. Leineweber, J.K. Sørensen, L. Alfredsson, J.B. Bjorner, M. Borritz, H. Burr, et al., Long working hours and risk of 50 health conditions and mortality outcomes: a multicohort study in four European countries, Lancet Reg Health Eur 11 (2021), 100212, https://doi.org/10.1016/j.lanepe.2021.100212.

[6] S.T. Anderson, H. Meng, T.G. Brooks, S.Y. Tang, R. Lordan, A. Sengupta, S. Nayak, A. Mřela, D. Sarantopoulou, N.F. Lahens, et al., Sexual dimorphism in the response to chronic circadian misalignment on a high-fat diet, Sci. Transl. Med. 15 (2023), eabo2022, https://doi.org/10.1126/scitranslmed.abo2022.

[7] N. Santhi, A.S. Lazar, P.J. McCabe, J.C. Lo, J.A. Groeger, D.J. Dijk, Sex differences in the circadian regulation of sleep and waking cognition in humans, Proc. Natl. Acad. Sci. U. S. A. 113 (2016) E2730–E2739, https://doi.org/10.1073/pnas.1521637113.

[8] A.S. Lim, A.J. Myers, L. Yu, A.S. Buchman, J.F. Duffy, P.L. De Jager, D.A. Bennett, Sex difference in daily rhythms of clock gene expression in the aged human cerebral cortex, J. Biol. Rhythm. 28 (2013) 117–129, https://doi.org/10.1177/0748730413478552.

[9] M. Hastings, The brain, circadian rhythms, and clock genes, BMJ 317 (1998) 1704–1707, https://doi.org/10.1136/bmj.317.7174.1704.

[10] M.S. Blattner, M.M. Mahoney, Changes in estrogen receptor signaling alters the timekeeping system in male mice, Behav. Brain Res. 294 (2015) 43–49, https://doi.org/10.1016/j.bbr.2015.07.060.

[11] M.S. Blattner, M.M. Mahoney, Estrogen receptor 1 modulates circadian rhythms in adult female mice, Chronobiol. Int. 31 (2014) 637–644, https://doi.org/10.3109/07420528.2014.885528.

[12] E. Murphy, D.P. Kelly, Estrogen signaling and cardiovascular disease, Circ. Res. 109 (2011) 687–696, https://doi.org/10.1161/CIRCRESAHA.110.236687.

[13] S. Maioli, K. Leander, P. Nilsson, I. Nalvarte, Estrogen receptors and the aging brain, Essays Biochem. 65 (2021) 913–925, https://doi.org/10.1042/ebc20200162.

[14] A.L. Hevener, D.J. Clegg, F. Mauvais-Jarvis, Impaired estrogen receptor action in the pathogenesis of the metabolic syndrome, Mol. Cell. Endocrinol. 418 (Pt 3) (2015) 306–321, https://doi.org/10.1016/j.mce.2015.05.020.

[15] W.J. Cheng, C.S. Liu, K.C. Hu, Y.F. Cheng, K. Karhula, M. Härmä, Night shift work and the risk of metabolic syndrome: findings from an 8-year hospital cohort, PLoS One 16 (2021), e0261349, https://doi.org/10.1371/journal.pone.0261349.

[16] M. Draaijer, K. Scheuermaier, S.T. Lalla-Edward, A.E. Fischer, D.E. Grobbee, F. Venter, A. Vos, Influence of shift work on cardiovascular disease risk in Southern African long-distance truck drivers: a cross-sectional study, BMJ Open 12 (2022), e050645, https://doi.org/10.1136/bmjopen-2021-050645.

[17] M. Skogstad, A. Mamen, L.K. Lunde, B. Ulvestad, D. Matre, H.C.D. Aass, R. Øvstebø, P. Nielsen, K.N. Samuelsen, Ø. Skare, et al., Shift work including night work and long working hours in industrial plants increases the risk of atherosclerosis, Int. J. Environ. Res. Publ. Health 16 (2019), https://doi.org/10.3390/ijerph16030521.

[18] L. Yang, Y. Luo, L. He, J. Yin, T. Li, S. Liu, D. Li, X. Cheng, Y. Bai, Shift work and the risk of cardiometabolic multimorbidity among patients with hypertension: a prospective cohort study of UK biobank, J. Am. Heart Assoc. 11 (2022), e025936, https://doi.org/10.1161/JAHA.122.025936.

[19] M. Cakici, A. Dogan, M. Cetin, A. Suner, A. Caner, M. Polat, H. Kaya, S. Abus, E. Akturk, Negative effects of acute sleep deprivation on left ventricular functions and cardiac repolarization in healthy young adults, Pacing Clin. Electrophysiol. 38 (2015) 713–722, https://doi.org/10.1111/pace.12534.

[20] O. Ozer, B. Ozbala, I. Sari, V. Davutoglu, E. Maden, Y. Baltaci, S. Yavuz, M. Aksoy, Acute sleep deprivation is associated with increased QT dispersion in healthy young adults, Pacing Clin. Electrophysiol. 31 (2008) 979–984, https://doi.org/10.1111/j.1540-8159.2008.01125.x.

[21] S.E.S. Miner, D. Pahal, L. Nichols, A. Darwood, L.E. Nield, Z. Wulffhart, Sleep disruption is associated with increased ventricular ectopy and cardiac arrest in

hospitalized adults, Sleep 39 (2016) 927–935, https://doi.org/10.5665/sleep.5656.
[22] M. Bennardo, F. Alibhai, E. Tsimakouridze, N. Chinnappareddy, P. Podobed, C. Reitz, W.G. Pyle, J. Simpson, T.A. Martino, Day-night dependence of gene expression and inflammatory responses in the remodeling murine heart post-myocardial infarction, Am. J. Physiol. Regul. Integr. Comp. Physiol. 311 (2016) R1243–R1254.
[23] G. Hulsegge, N. Gupta, K.I. Proper, N. van Lobenstein, W. Ijzelenberg, D. M. Hallman, A. Holtermann, A.J. van der Beek, Shift work is associated with reduced heart rate variability among men but not women, Int. J. Cardiol. 258 (2018) 109–114, https://doi.org/10.1016/j.ijcard.2018.01.089.
[24] S.E. Royston, N. Yasui, A.G. Kondilis, S.V. Lord, J.A. Katzenellenbogen, M. M. Mahoney, ESR1 and ESR2 differentially regulate daily and circadian activity rhythms in female mice, Endocrinology 155 (2014) 2613–2623, https://doi.org/10.1210/en.2014-1101.
[25] G. Bingöl, F.A. Demir, E. Özmen, S. Ünlü, Ö. Özden, F. Böyük, H. Tüner, M. Nasifov, V. Çamkıran, İ. Sarı, Acute sleep deprivation: impairment of biventricular function assesed by speckle tracking echocardiography in healthy subjects, Sleep Breath. (2023), https://doi.org/10.1007/s11325-023-02837-w.
[26] G. Açar, M. Akçakoyun, I. Sari, M. Bulut, E. Alizade, B. Özkan, M.V. Yazicioğlu, G. Alici, A. Avci, R. Kargin, et al., Acute sleep deprivation in healthy adults is associated with a reduction in left atrial early diastolic strain rate, Sleep Breath. 17 (2013) 975–983, https://doi.org/10.1007/s11325-012-0786-z.
[27] A. Cincin, I. Sari, M. Sunbul, A. Kepez, M. Oguz, S. Sert, A. Sahin, B. Ozben, K. Tigen, Y. Basaran, Effect of acute sleep deprivation on left atrial mechanics assessed by three-dimensional echocardiography, Sleep Breath. 20 (2016) 227–235, https://doi.org/10.1007/s11325-015-1211-1.
[28] D.L.R. Kuetting, A. Feisst, A.M. Sprinkart, R. Homsi, J. Luetkens, D. Thomas, H. H. Schild, D. Dabir, Effects of a 24-hr-shift-related short-term sleep deprivation on cardiac function: a cardiac magnetic resonance-based study, J. Sleep Res. 28 (2019), e12665, https://doi.org/10.1111/jsr.12665.