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ARTICLE

Health effects of seasonal variation in cardiovascular hemodynamics among workers in forest environments

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Abstract

Seasonal variation in cardiovascular functions (CVFs) associated with climatic changes is an important emerging public health issue. The objectives of this study were to demonstrate seasonal variation in CVFs by comparing intra-individual differences between winter and summer among people working in a forest environment and to discuss the possible mechanisms accounting for the health effects of seasonal variation in cardiovascular hemodynamics. A total of 72 staff members of the Experimental Forest of National Taiwan University were recruited for continuous health monitoring during two seasons to investigate the intra-individual seasonal variation in CVFs, complete blood counts, and biochemical examinations. CVFs were assessed by measuring the arterial pressure waveform by a cuff sphygmomanometer using an oscillometric blood pressure device, and aortic stiffness was measured by brachial-ankle pulse wave velocity (baPWV). The results showed that cholesterol levels, white and red blood cell counts, and platelet counts were higher in winter than in summer. Subjects showed not only higher vascular stress, as indicated by higher levels of brachial systolic and diastolic blood pressure (SBP and DBP), central end-SBP and DBP, systemic vascular resistance (SVR), and baPWV, but also lower cardiac activities, including lower levels of heart rate, left ventricular contractility, and cardiac output in winter than in summer. The central and brachial BP, cardiac output, SVR, and baPWV were significantly associated with temperature changes in seasonal variation after controlling related confounding factors. This study provides evidence of higher vascular stress and susceptibility to atherothrombosis during winter compared with summer.

Keywords seasonal variation · cardiovascular function · hypertension · health effect · winter

Introduction

Cardiovascular diseases are among the leading causes of morbidity and mortality worldwide, and their rates of increase have become a major focus of epidemiological and experimental studies [1]. An estimated 17.3 million people, representing ~30% of the total global deaths, died from cardiovascular diseases in 2008 [2]. The increasing risk of cardiovascular diseases is dependent not only on diabetes, hypertension, hypercholesterolemia, smoking habits, and genetics but also on dietary habits, work factors, and psychosocial factors [3–8]. However, climate change and seasonal variation (i.e., heat waves and cold spells) as cardiovascular risk factors have not been thoroughly investigated [9]. In particular, changes in temperature have been linked with cardiovascular diseases [10]. Furthermore, the type of natural environment that can be beneficial to human health is an emergent issue. Many studies have demonstrated that a forest environment may benefit health

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by reducing blood pressure (BP), pulse rate, and cholesterol level, decreasing sympathetic activity and enhancing parasympathetic activity, boosting immune functions (levels of natural killer-cell activity), attenuating subclinical atherosclerosis, and influencing cardiovascular and metabolic parameters in humans [11, 12].

Seasonal variation in cardiovascular disease-related mortality has been demonstrated to be associated with temperature changes [13]. The adverse effects of exposure to extreme ambient temperatures under heat waves and cold spells constitute a significant public health issue [14]. In particular, elderly people are more susceptible to cardiovascular morbidity and mortality when exposed to temperature changes [10]. Studies have reported higher mortality and morbidity in winter than in other seasons of the year [15, 16]. Seasonal variations in wind speed, temperature, and reduced physical activity during the winter months were found to be significantly associated with an increased risk of deep venous thrombosis [17, 18]. The seasonal increase in pulmonary embolism episodes has been related to changes in peripheral vasoconstriction, levels of coagulation factors, and reduced activity [19, 20]. A large home-based BP monitoring study in Japan, the HOMED-BP study, reported significant seasonal variation in BP, particularly in winter compared with summer [21]. Lower temperature and higher ambient air pollution in winter were found to be significantly associated with an increased risk of cardiovascular diseases. However, it is difficult to demonstrate which of the two has more significant association with increased risk of cardiovascular events in winter in a metropolis city, such as Taipei. Studies on changes in cardiovascular functions (CVFs) and the possible mechanism associated with these changes in different seasons are still limited.

The objectives of this study were to demonstrate seasonal variation in CVFs by comparing intra-individual differences between winter and summer among people working in a forest environment and to discuss the possible mechanisms accounting for the health effects of seasonal variation in cardiovascular hemodynamics during winter.

Methods

Study design and population

This study design aimed to determine the health effects of seasonal variation in CVFs among staff members working in a forest environment for more than 1 year. Among 160 forest staff members (FSM) of the Experimental Forest of National Taiwan University (NTU), 100 volunteers were invited to participate in this study, excluding those with clinical diabetes, documented cardiovascular diseases, and age exceeding 61 years. Prior to the test, all participants provided written informed consent for health monitoring during winter and summer. They underwent a series of detailed examinations and questionnaire surveys approved by the 37th meeting (30 January 2013) of the Research Ethics Committee of the NTU Hospital and conducted during winter (6–17 January 2014) and summer (6–21 June 2014) in Nantou County, Taiwan. The eventual analysis included 72 FSM for this study.

Site descriptions and temperature observation of the forest environment

The Experimental Forest at Xitou covers ~2,349 ha and is mainly composed of natural hardwood forest and some plantations, predominantly conifers. The annual rainfall was 2590 mm between 1941 and 2010, where 80% of the rainfall occurred between May and September. The mean relative humidity and temperature from 2011 to 2015 were 88% and 17 °C, respectively, according to the Xitou monitoring station of the Central Weather Bureau.

Ambient air temperature and relative humidity instruments (Metone 083 C, Met One Inc., Oregon, USA) for forest environmental monitoring were set in the Xitou Experimental Forest. Temperature and relative humidity measurements were recorded daily for every minute during the study period.

Baseline examination

Blood samples were obtained via the ante-cubital vein of each participant after overnight fasting for 10–14 h. The low- and high-density lipoprotein cholesterol (LDL-C and HDL-C), plasma glucose, and serum cholesterol and triglyceride levels were measured using an autoanalyzer (Toshiba, TBA-200FR; Toshiba, Tokyo, Japan). Biochemical examination for each participant was performed according to standard lab protocols/methods.

Brachial-ankle pulse wave velocity

BP was measured twice (left and right hands) after at least 5 min of rest in a sitting position in a quiet classroom of the Tourist Center of Xitou Experimental Forest. The BP used in the analyses was the average of two measurements. The brachial-ankle pulse wave velocity (baPWV) was measured using a noninvasive vascular screening device (Colin VP-1000; Colin Co., Ltd., Komaki, Japan) in the morning after the participants received oral glucose tolerance test (OGTT). This device recorded the baPWV, electrocardiogram, and arterial BP simultaneously from all four limbs (at both left and right brachia and ankles) and calculated the ankle-brachial index. Subjects were examined in the supine position. Electrodes were placed on both wrists to obtain an electrocardiogram. The cuffs were connected to a sensor that measured the volume pulse form and an oscillometric pressure sensor that measured the BP. The time interval between the wave front of the brachial waveform and the ankle waveform was defined as the pulse transit time between the brachia and the ankle (ΔTba). The distance between the arm and ankle was estimated automatically according to the subject's height. The distance from the heart to the brachia (Db) was measured using the following equation: Db = 0.2195 × height of the patient (cm) −2.0734. The distance from the heart to the ankle (Da) was measured using the following equation: Da = 0.8129 × height of the patient (cm) + 12.328. The baPWV was calculated using the following equation: baPWV = (Da–Db)/ΔTba. The validity and reproducibility of baPWV measurements have been reported earlier [22, 23].

Cardiac and vascular function assessments

The arterial pressure waveform was recorded by a cuff sphygmomanometer using an oscillometric BP device (DynaPulse 200 M, Pulse Metric Inc., San Diego, CA) [24]. The arterial pressure waveform was measured from left and right hands after at least 5 min of rest in a sitting position in a quiet classroom. The data were electronically transmitted from the collection site to a central analysis center. BP was determined by changes in pressure waveform according to Bernoulli flow effects. Central end-SBP and end-DBP (cSBP and cDBP), vascular compliance and peripheral resistance of the brachial artery were derived by incorporating the arterial pressure signals from a standard cuff sphygmomanometer using a physical model. This method has been validated against invasive and noninvasive measurements [25]. Brachial artery compliance (BAC) was calculated at mean arterial pressure by theoretical design. Brachial artery distensibility and resistance (BAD and BAR) were derived from the modified formula of BAC, which were associated with cardiovascular risk factors among healthy young adults in the Bogalusa heart study [26, 27].

The above method has also been employed to derive other hemodynamic parameters, including cardiac hemodynamics, such as the maximum rate of left ventricular pressure rise (LV dP/dt max), stroke volume (SV), cardiac output (CO), and cardiac index (CI), and its application has also been proved in our recent study [28, 29].

Statistical analyses

General characteristics, biochemical examination, complete blood counts, baPWV, and CVFs of FSM subjects were compared. The paired *t*-test was employed to detect intra-individual differences of seasonal variation in the same subject. Continuous variables were expressed as the means ± standard deviation, and binary variables were expressed as percentages. All statistical analyses were performed with SAS statistical software (version 9.4, SAS Institute Inc., Cary, NC, USA).

Because there were two measures for each study subject, we used generalized linear mixed-effect models with a random intercept for study subject and a constant correlation for each subject's three measurements to estimate the changes of the cSBP, cDBP, heart rate (HR), CO, systemic vascular resistance (SVR), BAD, and baPWV in different seasons. The covariates considered in the model included age, gender, body weight, smoking habit, alcohol drinking, temperature, nonsedentary work, exercise habit, levels of fasting glucose, and cholesterol, as well as anti-hypertensive medication. Sedentary (vs. nonsedentary) work and exercise habits were included in the analyses in view of their significant influence on cardiovascular hemodynamics.

Results

Table 1 summarizes the general characteristics of the FSM participants. As shown, their mean age was 46.0 ± 10.2 years, and there were more male than female participants (68.5%). Mean waist measurement in winter was 84.6 ± 9.0 cm, which was significantly higher than that in

Table 1 Seasonal variations of general characteristics among staff members working in forest environment ($N = 72$)

Variables	Seasons		*P*-value
	Winter Jan, 2014	Summer Jun, 2014	
Age (years)	46.0 ± 10.19	46.01 ± 1 0.20	—
Male sex (%)	68.5	68.5	—
BMI (kg/m^2)	24.7 ± 3.6	24.3 ± 3.5	0.0317
Waist circumference (cm)	84.6 ± 9.0	82.3 ± 10.0	<0.0001
Temperature (°C)	13.1 ± 0.5	21.5 ± 0.6	<0.0001
Relative humidity (%)	91.4 ± 3.0	91.0 ± 4.2	0.5339
Smoking habit (%)	34.25	28.77	0.4761
Alcohol drinking habit (%)	41.1	31.51	0.2283
Exercise habit (%)	32.88	34.25	0.8609
Hypertension (%)	47.95	24.66	0.0034
Anti-hypertensive medication (%)	19.35	19.35	—
Hypercholesterolemia (%)	34.25	23.29	0.1436

P-value is paired *t*-test of significance between winter and summer

Smoking habit current smoker and ex-smoker, *Alcohol drinking habit* alcohol drinking at least once per week, *Exercise habit* exercise at least three times per week and 30 min each time summer. The prevalence of hypertension (≥140 mmHg in systolic BP or ≥90 mmHg in diastolic BP) in winter was 47.95%, which was higher than that in summer with a statistically significant difference ($p = 0.0034$). The prevalence of hypercholesterolemia (cholesterol level ≥240 mg/dL) was also higher in winter than in summer.

Total cholesterol level among FSM participants in winter was 192.3 ± 41.2 mg/dL, which was significantly higher than that in summer (Table 2). Similarly, LDL-C and HDL-C levels were significantly higher in winter than in summer. Mean Hs-CRP level was 0.24 ± 0.5 mg/dL in winter, which was significantly higher than that in summer. Both white blood cell (WBC) and red blood cell (RBC) counts of participants were significantly higher in winter than in summer. Measurements of BP and baPWV in different seasons are presented in Table 3. As seen, SBP and DBP were significantly higher in winter than in summer. Similarly, the right-, left-, and mean baPWVs among participants were significantly higher in winter than in summer.

Table 2 Seasonal variations of biochemical examination and complete blood counts of staff members living working forest environment ($N = 72$)

Variables	Seasons		*P*-value
	Winter Jan, 2014	Summer Jun, 2014	
Total cholesterol (mg/dL)	192.26 ± 41.2	183.22 ± 30.9	0.0021
Triglycerides (mg/dL)	141.92 ± 112.4	139.60 ± 126.3	0.1371
High-density lipoprotein cholesterol (mg/dL)	54.56 ± 13.0	50.60 ± 10.9	<0.0001
Low-density lipoprotein cholesterol (mg/dL)	117.88 ± 36.7	110.16 ± 27.8	0.0241
High-sensitivity C-reactive protein (mg/dL)	0.24 ± 0.5	0.11 ± 0.2	0.0185
Fasting glucose (mg/dL)	92.41 ± 12.9	86.41 ± 9.8	0.0007
White blood cell (10^3/μL)	6.37 ± 1.6	6.21 ± 1.7	0.0694
Red blood cell (10^6/μL)	5.25 ± 0.6	5.13 ± 0.6	0.0194
Platelet (10^3/μL)	254.07 ± 46.0	248.81 ± 43.9	0.1488

P-value is the paired *t*-test of significance between winter and summer.

Brachial SBP and DBP, central cSBP and cDBP, and mean arterial pressure (MAP) among FSM participants were significantly higher in winter than in summer (Table 4). HRs of FSM participants were significantly lower in winter (73.0 ± 11.0 beat/min) than in summer. LV contractility was significantly lower in winter than in summer, with significant differences. Moreover, CO and CI, SV, and SV index (SVI) among participants were significantly lower in winter than in summer. Systemic vascular compliance (SVC) was lower while SVR was significantly higher among participants in winter than in summer. Although BAC and BAD were significantly higher in winter than in summer, BAR was lower in winter than in summer (Table 4).

Table 5 shows the results obtained using mixed linear regression, demonstrating effects of seasonal variations of personal characteristics and temperature on SBP, DBP, cSBP, and cDBP in different seasons. Both SBP and DBP were significantly and positively associated with age, body weight, and fasting glucose level but negatively associated with temperature. The present results indicated average increase in SBP and DBP with changes in age, body weight, and fasting glucose level. In contrast, an average decrease in SBP of 0.90 ± 0.19 mmHg and DBP of 0.84 ± 0.15 mmHg was observed, and similarly in cSBP of 0.74 ± 0.21 mmHg and cDBP of 0.8 0 ± 0.15 mmHg per 1 °C increase in seasonal variation of temperature change after controlling covariates. Moreover, both cSBP and cDBP were consistent with SBP and DBP regarding per seasonal change in age, body weight, and fasting glucose level.

Table 6 shows the effects of seasonal variations of personal characteristics and temperature on HR, CO, SVR, BAD, and baPWV in different seasons obtained using mixed linear regression. Seasonal changes of cardiac function in terms of CO were significantly and positively associated with body weight, temperature, and fasting glucose level. Similarly, seasonal changes of vascular function in terms of SVR were significantly and positively associated with age and male sex but negatively associated with body weight, smoking habit, and temperature (Table 6). In particular, the average decrease in SVR was 9.08 ± 2.17 dynes-sec/cm^5 per kilogram increase in body weight, 108.59 ±

Table 3 Seasonal variations of blood pressure and brachial-ankle pulse wave velocity (baPWV) measured in differrent seasons ($N = 72$)

Variables	Seasons		*P*-value
	Winter Jan, 2014	Summer Jun, 2014	
Systolic blood pressure (mmHg)	122.17 ± 13.6	115.76 ± 11.9	<0.0001
Diastolic blood pressure (mmHg)	75.47 ± 10.1	72.52 ± 9.0	<0.0001
Right baPWV (cm/s)	1490.8 ± 234.6	1435.4 ± 207.8	0.0001
Left baPWV (cm/s)	1472.8 ± 240.1	1414.7 ± 216.0	0.0001
Mean baPWV (cm/s)	1481.8 ± 236.0	1425.1 ± 209.5	<0.0001

P-value is the paired *t*-test of significance between winter and summer.

Table 4 Seasonal variations of cardiac and vascular functions assessed using DynaPulse ($N = 72$)

Variables	Seasons		*P*-value
	Winter Jan, 2014	Summer Jun, 2014	
Systolic blood pressure (mmHg)	120.1 ± 13.6	110.7 ± 12.7	<0.0001
Diastolic blood pressure (mmHg)	78.5 ± 9.9	69.6 ± 9.7	<0.0001
Central end systolic blood pressure (mmHg)	127.0 ± 14.1	119.1 ± 13.2	<0.0001
Central end diastolic blood pressure (mmHg)	74.3 ± 9.5	65.3 ± 9.0	<0.0001
Mean artery pressure (mmHg)	91.2 ± 10.6	82.4 ± 9.9	<0.0001
Pulse pressure (mmHg)	52.7 ± 8.1	53.8 ± 7.6	0.0864
Heart rate (beat/min)	73.0 ± 11.0	75.2 ± 10.4	0.0076
Left ventricular ejection time (sec)	0.28 ± 0.04	0.27 ± 0.03	0.5123
Left ventricular dP/dt Max, (mmHg/s)	1166.2 ± 181	1160.8 ± 164	0.1613
Left ventricular contractility (1/s)	15.13 ± 1.5	16.04 ± 1.6	0.0007
Cardiac output (L/min)	4.99 ± 1.2	5.31 ± 1.1	0.0008
Cardiac index (L/min/m^2)	2.8 ± 0.6	3.0 ± 0.5	0.0008
Stroke volume (mL)	67.31 ± 9.9	69.7 ± 10.4	0.0040
Stroke volume index (mL/m^2)	38.35 ± 3.2	39.8 ± 3.4	0.0044
Systemic vascular compliance (mL/mmHg)	1.3 ± 0.2	1.3 ± 0.2	0.0002
Systemic vascular resistance (dynes-sec/cm^5)	1521.8 ± 307.3	1281.1 ± 240	<0.0001
Brachial artery compliance (mL/mmHg)	0.078 ± 0.023	0.071 ± 0.02	0.0365
Brachial artery distensibility (%/mmHg)	6.52 ± 1.01	6.38 ± 0.94	0.2599
Brachial artery resistance (dynes-sec/cm^5)	188.2 ± 90.2	203.9 ± 94.3	0.2270

P-value is the paired *t*-test of significance between winter and summer.

Table 5 Generalized linear mixed-effect models for determinants of seasonal variations in blood pressure

Variables	SBP (mmHg)		DBP (mmHg)		cSBP (mmHg)		cDBP (mmHg)	
	Est.±S.E.	*P*-value	Est.±S.E.	*P*-value	Est.±S.E.	*P*-value	Est.±S.E.	*P*-value
Intercept	69.13 ± 9.19	< . 0001	42.55 ± 7.03	< . 0001	74.38 ± 9.89	< . 0001	39.20 ± 6.99	< . 0001
Age (years)	0.20 ± 0.08	0.0167	0.20 ± 0.06	0.0029	0.22 ± 0.09	0.0174	0.17 ± 0.06	0.0080
Male (yes)	3.02 ± 2.85	0.2939	3.01 ± 2.18	0.1728	3.31 ± 3.07	0.2852	3.15 ± 2.17	0.1516
Body weight (kg)	0.34 ± 0.10	0.0007	0.25 ± 0.07	0.0010	0.31 ± 0.10	0.0033	0.24 ± 0.07	0.0014
Smoking habit (yes)	−2.52 ± 2.19	0.2531	−3.05 ± 1.68	0.0726	−1.99 ± 2.36	0.4007	−2.59 ± 1.67	0.1235
Alcohol habit (yes)	0.51 ± 2.00	0.8006	0.87 ± 1.53	0.5701	−0.32 ± 2.16	0.8825	0.80 ± 1.52	0.6003
Temperature (°C)	−0.90 ± 0.19	< . 0001	−0.84 ± 0.15	< . 0001	−0.74 ± 0.21	0.0006	−0.80 ± 0.15	< . 0001
Non-sedentary work (yes)	−0.45 ± 1.79	0.8011	0.98 ± 1.37	0.4759	−0.70 ± 1.92	0.7168	0.95 ± 1.36	0.4872
Exercise habit (yes)	−1.34 ± 1.93	0.4890	−2.28 ± 1.48	0.1265	−1.16 ± 2.08	0.5771	−2.61 ± 1.47	0.0786
Fasting glucose (mg/dL)	0.21 ± 0.05	0.0001	0.14 ± 0.04	0.0006	0.20 ± 0.06	0.0006	0.13 ± 0.04	0.0016
Total cholesterol (mg/dL)	0.04 ± 0.03	0.1370	0.03 ± 0.02	0.1508	0.05 ± 0.03	0.0990	0.04 ± 0.02	0.0818
Anti-HTN medication (yes)	6.39 ± 2.48	0.0116	2.31 ± 1.90	0.2260	7.15 ± 2.67	0.0088	2.17 ± 1.89	0.2539

cSBP and cDBP central end systolic and diastolic blood pressure, respectively, *Smoking habit*: current smoker and ex-smoker, *Alcohol drinking habit* alcohol drinking at least once per week, *Exercise habit* exercise at least 3 times/week and 30 min each time, *Non-sedentary work* defined as grade 3 or 4 of physical activity during work day; grade 1 almost sitting, grade 2 sometimes walking, grade 3 sometimes physical exertion, and grade 4 mostly physical exertion.

Data were presented as Est. ± S.E. after adjusting age, male, body weight, smoking, and alcohol habit, temperature, non-sedentary work, exercise habit, levels of fasting glucose and total cholesterol, and anti-HTN medication.

49.36 dynes-sec/cm^5 with smoking habit, and 24.94 ± 4.38 dynes-sec/cm^5 per 1 °C increase in seasonal variation of temperature changes. As to the true difference of SVR in different seasons, supplementary table 1 showed lower mean SVR in summer among smokers compared with nonsmokers but without significant differences. Furthermore, mean SVR in winter was significantly lower among smokers (1419.97 ± 286.83 dynes-sec/cm^5) compared with

Table 6 Generalized linear mixed-effect models for determinants of seasonal variations in cardiovascular functional assessments

Variables	HR (beat/min)		CO (L/min)		SVR (dynes-sec/cm^5)		BAD (%/mmHg)		baPWV (cm/s)	
	Est.±S.E.	*P*-value	Est.±S.E	*P*-value	Est.±S.E.	*P*-value	Est.±S.E.	*P*-value	Est.±S.E.	*P*-value
Intercept	53.52 ± 8.62	<0.0001	0.45 ± 0.68	0.5118	2035.54 ± 206.89	<0.0001	8.83 ± 0.92	<0.0001	1088.78 ± 146.65	<0.0001
Age (years)	−0.03 ± 0.08	0.7171	0.00 ± 0.01	0.4585	5.34 ± 1.89	0.0058	−0.02 ± 0.01	0.0516	9.53 ± 1.34	<0.0001
Male (yes)	−4.89 ± 2.67	0.0722	−0.42 ± 0.21	0.0550	130.92 ± 64.14	0.0458	0.65 ± 0.28	0.0249	133.27 ± 45.47	0.0048
Body weight (kg)	0.02 ± 0.09	0.8001	0.05 ± 0.01	<0.0001	−9.08 ± 2.17	<0.0001	−0.01 ± 0.01	0.3141	0.01 ± 1.54	0.9938
Smoking habit (yes)	2.72 ± 2.06	0.1888	0.26 ± 0.16	0.1212	−108.59 ± 49.36	0.0303	−0.19 ± 0.22	0.3840	−40.46 ± 34.99	0.2505
Alcohol habit (yes)	−1.13 ± 1.88	0.5492	−0.04 ± 0.15	0.8016	16.65 ± 45.12	0.7130	0.17 ± 0.20	0.4039	2.94 ± 31.99	0.9271
Temperature (°C)	0.29 ± 0.18	0.1110	0.03 ± 0.01	0.0241	−24.94 ± 4.38	<0.0001	−0.02 ± 0.02	0.2143	−11.47 ± 3.11	0.0004
Non-sedentary work (yes)	−2.19 ± 1.68	0.1948	−0.25 ± 0.13	0.0687	63.91 ± 40.26	0.1158	0.12 ± 0.18	0.5133	−40.56 ± 28.54	0.1585
Exercise habit (yes)	–1.58 ± 1.81	0.3847	0.03 ± 0.14	0.8539	−32.98 ± 43.47	0.4499	−0.13 ± 0.19	0.4856	−16.39 ± 30.82	0.5960
Fasting glucose (mg/dL)	0.11 ± 0.05	0.0315	0.009 ± 0.004	0.0208	0.52 ± 1.17	0.6615	−0.01 ± 0.01	0.0711	2.71 ± 0.83	0.0016
Cholesterol (mg/dL)	0.05 ± 0.03	0.0835	0.001 ± 0.002	0.5985	0.37 ± 0.63	0.5631	0.0001 ± 0.003	0.9688	−1.12 ± 0.45	0.0138
Anti-HTN medication (yes)	−3.08 ± 2.33	0.1883	−0.19 ± 0.18	0.3077	88.23 ± 55.87	0.1176	−0.48 ± 0.25	0.0556	120.32 ± 39.60	0.0031

HR heart rate, *CO* cardiac output, *SVR* systemic vascular resistance, *BAD* brachial arterial distensibility, *baPWV* brachial ankle pulse wave velocity, *Smoking habit* current smoker and ex-smoker, *Alcohol drinking habit* alcohol drinking at least once per week, *Exercise habit* exercise at least three times per week and 30 min each time, *Non-sedentary work* defined as grade 3 or 4 of physical activity during work day; grade 1 almost sitting, grade 2 sometimes walking, grade 3 sometimes physical exertion, and grade 4 mostly physical exertion.

Data were presented as Est. ± S.E. after adjusting age, male, body weight, smoking, and alcohol habit, temperature, non-sedentary work, exercise habit, levels of fasting glucose and total cholesterol, and anti-HTN medication.

nonsmokers (157.21 ± 305.27 dynes-sec/cm^5). The seasonal changes of aortic stiffness in terms of baPWV were significantly and positively associated with age, male sex, fasting glucose level, and anti-hypertensive medication but negatively associated with temperature and total cholesterol level.

Discussion

This study is the first to demonstrate the health effects of seasonal variation on cardiac and vascular clinical parameters of workers in a forest environment. Higher incidence rates of cardiovascular disease-related morbidity and mortality during winter than in summer and/or other seasons have been reported [15, 16, 30]. The novel finding of this study was that the prevalence of hypertension and hypercholesterolemia, serum levels of cholesterol, complete blood count (WBC and RBC), BP components (SBP and DBP, and cSBP and cDBP), and aortic stiffness index of baPWV were significantly higher in winter than in summer. The higher levels of these parameters in cold season may be associated with multiple risk factors, such as lower temperature, higher air pollution, lack of physical activity, dietary habits resulting in higher energy intake, and increased risk of viral infection [15, 31, 32]. Among these, low temperature is the most important environmental factor leading to cardiovascular events in winter [31]. The influence of temperature on the onset and course of cardiovascular events is not well understood [31]. Possible mechanisms accounting for this association with winter include effects of thermoregulatory responses on vasoconstriction, high BP and blood flow resistance, and higher risk of thrombosis through increased RBC count, blood viscosity, and platelet count.

Our study demonstrated an increased BP and aortic stiffness in the winter season compared to the summer season. The possible mediating mechanisms might be due to increased sympathetic activity [33], and glucocorticoid activity may contribute to the observed seasonal variations in cardiovascular morbidity and mortality [34]. A study by Cuil et al. [33] found that resting sympathetic nerve activity varies along the seasons, with peak levels evident in the winter. Walker et al.reported on 105 healthy men, ages 24–33 years., during a 15-month period that included two winters. In winter, 0900-h plasma cortisol concentrations were higher than in summer, the ratio of metabolites of cortisol to those of cortisone was higher than in summer, and dermal glucocorticoid sensitivity was higher than in summer[34].

Central BP is more relevant than brachial BP for the pathogenesis of cardiovascular disease [35]. Among the 3520 participants of the Strong Heart Study, central BP was more strongly related to cardiovascular events, extent of atherosclerosis, and vascular hypertrophy than brachial BP after the mean follow-up of 4.8 ± 1.3 years [36]. Central (aortic and carotid) BP information is very important for understanding systolic BP during systole (afterload) of left ventricle encounters, coronary perfusion during diastole of the aortic pressure, and predicting cardiovascular morbidity and mortality [37]. Brachial BP is measured for convenience and simplicity and usually serves as a surrogate for central BP. Central BP, which is the pressure exerted on the heart and brain, offers more accurate prediction for outcomes of antihypertensive drugs [37]. The Anglo-Cardiff Collaborative Trial II investigated 10,613 individuals aged between 18 and 101 years and reported relatively higher central systolic pressure in individuals with risk factors or diseases (i.e., hypertension, hypercholesterolemia, or smoking) compared with healthy individuals [38]. These studies support prospective examination of central BP as a treatment guide in the future.

In this study, arterial pulsation signals from a noninvasive cuff device were recorded using DynaPulse with automated monitoring and recording system. The pulse dynamic technique was employed to determine cSBP, cDBP, and mean arterial pressure using pulse wave analysis of the oscillometric cuff signal from the brachial artery [28]. It was found that levels of cSBP, cDBP, and MAP among participants were significantly higher in winter than in summer. Another important innovation of this study is using the mixed linear models to demonstrate a significant decrease in brachial and central BP among study subjects experiencing seasonal increase in ambient temperature after controlling associated covariates. Several studies have demonstrated that cooler weather in winter increases arterial BP, as evidenced by repeated or single measurements among hypertensive and healthy subjects including the elderly, adults, and children [39, 40]. Lower temperature has a direct impact on multiple CVFs. Specifically, living in a cooler environment can result in increased BP components, including SBP and DBP, and decreased cardiac workload parameters, including HR, SV, SVI, LV contractility, CO, and CI. According to the mixed linear models, both SVR and baPWV were negatively while CO was positively associated with temperature. In particular, average decrease in SVR was 24.94 ± 4.38 dynes-sec/cm^5 per 1 °C increase in seasonal variation of temperature changes. Regarding vascular function assessments, low-temperature winter increased peripheral vascular resistance by reducing SVC and increasing SVR; it also increased BAC compliance indices, including BAC and BAD, but decreased BAR in the human body. The negative impacts of winter on CVFs are associated with multiple factors, subsequently leading to increased risk of cardiovascular morbidity and mortality.

The present findings offer some possible explanations for the winter cardiovascular phenomenon observed. First, cooler temperature in winter is associated with relatively increased waist circumference as the human body instinctively needs to increase food intake to maintain body warmth. Second, winter decreases HR, LV contractility, and CO, showing that the human body must reduce cardiac activity to avoid energy consumption in cold weather. Our study showed the reduced heart rate is a real-world measurement of chronic adaptation of cardiovascular physiology in human. Evidence of physiological mechanism of animal hibernation in winter season indicates reduced metabolic rate and heart rate, an important cardiovascular adaptation while encountering the cold winter season [41, 42]. Thus, the heart rate reduction can be a phenomenon of cardiac physiology, with reduced metabolic consumption and preserved energy to meet the metabolic requirement of the winter season, which is a protective mechanism of keeping warm by reducing physical activity and preserving energy in winter season. Brown fat tissue increased in the winter season [43], an important protective factor in heat production, which might be a possible linking mechanism of reduced heart rate in winter.

Third, cooler winter induces vasoconstriction to preserve energy for central vital organs, leading to increases not only in brachial BP components but also in cSBP, cDBP, MAP, and SVR, as well as decreases in SVC. Fourth, elevated levels of RBC in winter would increase blood viscosity, and a trend of higher WBC counts in winter indicates the risk of inflammation that might increase the risk of developing atherothrombosis in the cold winter season.

Fifth, cigarette smoking is known to impair arterial function in middle-aged and older adults. For healthy young adult smokers and nonsmokers that were race-, sex-, and age-adjusted, smokers ($n = 142$; average age of 35.6 years) had higher SVR compared with nonsmokers ($n = 145$; average age of 35.4 years), 1399.0 vs. 1325.5 dynes-sec/cm, respectively [44] However, another study showed that smokers ($n = 15$; average age of 47.6 years) had lower mean SVR compared with nonsmokers ($n = 15$; average age of 44.7 years) (1504.6 vs. 1531.0 dynes-sec/cm, respectively), with no significant difference [45]. Results obtained using mixed linear regression showed that SVR was significantly and negatively associated with smoking habit. The possible reasons for decreased SVR among smokers during winter in a forest environment are as follows. The average decrease in SVR of 24.94 ± 4.38 dynes-sec/cm^5 per 1 °C increase in seasonal variation of temperature changes (Table 6) indicates decreasing SVR level with increasing temperature. Higher body temperature after sauna or hot-tub bath has been demonstrated to have a positive effect on cardiovascular responses, such as increasing skin blood flow, HR, and CO, as well as decreasing SVR [46, 47]. Variations in SVR among smokers during winters with low temperatures was clearly observed; hence, it was hypothesized that smokers inhaling hot air will foster body temperature increases and promote systemic vasodilation. However, detailed studies to clarify the actual mechanism behind decreased SVR among smokers compared with nonsmokers, particularly in winter, are warranted.

There are two possible reasons for significant cardiac and vascular stress during cold winter in Taiwan. First, Taiwan is located in the subtropical and tropical climate zones, and has a hot and humid environment, especially in the forest region. In the Xitou Experimental Forest, 320 foggy days (visibility <1000 m) were recorded between April 2005 and March 2006 [48]. Humidity during winter in Taiwan is high; the average recorded in this study was 91.4%. Second, although the average temperature in winter in the Xitou Experimental Forest is 13 °C, the temperature will drop quickly below 10 °C during cold spells. In addition, houses in Taiwan, unlike those in cold countries, are not equipped with heating facilities; hence, people can feel the chill in winter even when staying indoors. This study observed that humid and cold winters posed a specific and large challenge to cardiovascular functions, revealing how local seasonal changes in temperature affect human health in a subtropical area, such as Taiwan. These findings may be applicable to other subtropical areas. Thus, the impact of seasonal changes on the cardiovascular system in other subtropical countries and cold countries merits further investigation.

This study has several strengths. First, this is the first study demonstrating the health effects of a cold winter on CVFs in a forest environment compared with summer for the same subjects. The intra-individual comparisons of seasonal variation on CVFs provide clear evidence of significant differences in CVFs between winter and summer. Second, the consistent response in both cardiac and vascular systems in winter also corroborates the importance of cardiovascular protection and energy preservation in cold winter. The seasonal variations in CVFs were consistent even after controlling potential confounding factors. In particular, ambient temperature is negatively associated with BP components, SVR, and aortic stiffness but positively associated with cardiac activity indices. Third, the whole spectrum of increased serum levels of lipids, liver enzyme, and complete blood count also indicates higher cardiovascular risk due to environmental stress caused by winter season.

However, this study also had some limitations. First, outcome of CVFs in winter may be associated with air pollution [15, 32, 49], physical activity [50], dietary habits [31], and infections [51]. Second, the significant difference in intra-individual comparisons of cardiovascular hemodynamics among subjects might overestimate or underestimate seasonal differences. Third, although this study demonstrated seasonal variation in cardiovascular hemodynamics of people working in a forest environment, the same among people working in the urban environment have not been considered.

In conclusion, this study has demonstrated the health effects of seasonal variation in subclinical CVFs among people working in a forest environment. The significant decrease in cardiac activity accompanied with increased peripheral vascular resistance in winter also indicates that energy preservation for protecting visceral organs is a very important autoregulation mechanism of the cardiovascular system. A large-scale cohort study on seasonal variation, particularly the effects of a cold winter on CVFs and human responses, among people living in an urban environment is warranted.

Perspectives of this study indicate that people must pay more attention to cardiovascular risk during winter season, particularly when exposed to extremely cold weather with marked temperature changes. People, especially the elderly and those at risk of cardiovascular disease, should keep their body warm and avoid exposure to cold environment in winter.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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