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Research Paper

Effects of *Cinnamomum camphora* forest environment on elderly patients with hypertension: Implications for adjunctive therapy

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ABSTRACT

Increasing evidence demonstrates the benefits of forest environment on human health. However, the effect of tree-species-specific forest environment on human health has been rarely studied. As one of the medical plants, *Cinnamomum camphora* have been found to possess anti-inflammatory activities. Thus, the present study was conducted to investigate the effects of *C. camphora* forest environment on elderly patients with hypertension (HTN). 31 elderly patients with essential HTN were randomly divided into two groups. Blood pressure (BP), pulse oxygen saturation (SpO_2%), heart rate (HR), heart rate variability (HRV) and levels of plasma high-sensitive-reactive protein (hs-CRP), as well as profile of mood states (POMS) test, were measured. After three-day/ two-night forest bathing, patients in the forest group showed significantly lower levels of diastolic blood pressure (DBP), low frequency (LF), the ratio of low frequency and high frequency (LF/HF) and hs-CRP than in the control group. However, the levels of SpO_2% and high frequency (HF) were greatly higher than the control group. Furthermore, negative mood subscale scores of POMS were significantly lower following forest bathing, while the positive score was much higher. Our results demonstrated that *C. camphora* environment could significantly decrease the DBP and inflammatory level, balance the autonomic activity and improve the mood state of participates. These indicate that it might be an adjunctive therapy for HTN patients.

Key words: *Cinnamomum camphora*, cardiovascular diseases, forest bathing, hypertension, volatile organic compounds.

Abbreviations: BMI, body mass index; **CHF,** chronic heart failure; **COPD,** chronic obstructive pulmonary disease; **DBP,** diastolic blood pressure; **HTN,** hypertension; **HR,** heart rate; **HRV,** heart rate variability; **hs-CRP,** high-sensitive-reactive protein; **HF,** high frequency; **LF,** low frequency; **LF/HF,** the ratio of low frequency and high frequency; **POMS,** profile of mood states; **SBP,** systolic blood pressure; **SpO_2,** pulse oxygen saturation; **VOCs,** volatile organic compounds.

INTRODUCTION

At present, artificial stimulations in urban environments have been considered as a negative factor on human health. More attention has thus been paid on the natural environment, such as forest, which is an important factor in health promotion models (St, 2003). In the past decades, forest bathing (also named forest therapy) has been shown to alleviate stress and anxiety (Chun et al., 2016; Jung et al., 2015; Lee et al., 2011; Park et al., 2010; Park et al., 2014; Song, 2013), boost the immune function (Li, 2010; Li et al., 2008a; Li et al., 2008b) and increase the expression of anti-cancer proteins (Li et al., 2008b). In addition, our previous works have demonstrated that forest bathing have positive

influence on young healthy student, and that it might be used as an adjunctive therapy on elderly patients with hypertension (HTN), chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) (Huang et al., 2018; Jia et al., 2016; Mao et al., 2017; Mao et al., 2012a; Mao et al., 2018; Mao et al., 2012b; Wu et al., 2017).

In the forest environment, apart from numerous negative ions, abundant volatile and non-volatile substances called phytoncides (wood essential oil) were emitted from plants. Thus, different forest environment has different microenvironment with different phytoncides, which may have discrepancy influence on different subjects. *Cinnamomum camphora* is an evergreen broad-leaved tree belonging to the family Lauraceae, which is widely distributed in south China and often used as a virescent tree in urban gardens and streets. Due to its beautiful shape, it has become the "civic tree" in 19 cities in China, including Hangzhou (Qing et al., 2010). As one of the important economic trees in China, *C. camphora* has long been prescribed in traditional medicines for the treatment of inflammation-related diseases such as rheumatism, sprains, bronchitis, asthma, indigestion and muscle pains (Lee et al., 2006a). Therefore, it is reasonable to speculate that different forest environments, for example *C. camphora* forest environment, have discrepancy influence on different subjects. However, related study has not been reported. In the present study, we performed a forest bathing at *C. camphora* forest environment to determine the influence of tree-species-specific forest bathing, *C. camphora* forest, on elderly patients with HTN.

MATERIALS AND METHODS

Subjects and study design

From 19 October 2017 to 21 October 2017, 31 patients with HTN from Hangzhou city participated in the study. They were randomly divided into two groups consisting of 11 in the control group and 20 people in forest group according to the ratio of 1:2. The inclusion and exclusion criteria and experimental program were described in previous study (Mao et al., 2012a). All procedures of the present study are in line with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the ethics committee of Zhejiang Hospital. Informed consent was signed by every subject.

Blood pressure (BP), heart rate (HR), oxygen saturation (SpO_2%) and heart rate variability (HRV) measurement

Systolic, diastolic blood pressure (SBP, DBP) and HR were obtained from the right arm using a portable digital sphygmomanometer (HEM-7000-E, Omron, Kyoto, Japan). The fingertip pulse oximeter (YUWELL YX301) was used to measure pulse SpO_2%. HRV, including low frequency (LF), high frequency (HF) and the ratio of low frequency and high frequency (LF/HF), were assessed by SA-3000P (Medicore Inc., Seoul, Korea).

Bio-indicators determination

Plasma level of high-sensitive-reactive protein (hs-CRP) and testosterone were determined by an automatic biochemistry analyzer (Hitachi Model 7600 Series Automatic Analyzer, Japan).

Profile of mood states (POMS) evaluation

The standard version of the POMS questionnaire was used to measure the mood states (Pollock et al., 1979).

Data analysis

Categorical variables and continuous data were compared with Chi-square analysis and T-test, respectively. All statistical analyses were completed using the SPSS 19.0 software (SPSS China, Shanghai, China). $P<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

The clinical characteristics of the participants are shown in Table 1. No significant differences in the baseline characteristics of the participants, including gender, age, body mass index (BMI), SBP, DBP, HR, SpO2%, HRV, hs-CRP and POMS score, were observed between the two groups.

First, we measured the BP related indicators. It was found that, after experiment, the level of DBP was significantly lower in the forest group than in the control group (67.95±2.69 Vs 71.64±4.20, $P<0.05$; Figure 1). In contrast, the value of SpO_2% was significantly higher in forest group than in the control group (97.55±0.82 Vs 98.10±0.64, $P<0.05$; Figure 1). No obvious alteration was observed for HR and SBP.

As an important tool for studying autonomic control of the heart and autonomic dysfunction, HRV has been widely measured in heart diseases such as cardiac infarction, heart failure, arrhythmia and syncope (Im et al., 2010). Therefore, we determined the influence of forest bathing trip on the HRV of patients with HTN. As shown in Figure 2, *C. camphora* forest bathing significantly decreased the levels of LF (35.40±13.98 Vs 50.88±14.32, $P<0.05$) and LF/HF (0.68±0.52 Vs 1.36±1.29, $P<0.05$), when compared with the control group. Instead, HF level was significantly higher in

Table 1: Baseline level of the indicators of subjects before experiment (Mean±SD).

	Baseline of control group (n=11)	Baseline of forest group (n=20)	p-value
Age (year)	73.91±6.640	73.50±5.889	0.861
Gender (male/female)	12/8	7/4	0.106 [a]
BMI (kg/m2)	23.564±2.176	23.759±1.768	0.788
SBP (mmHg)	137.64±5.887	139.25±12.594	0.693
DBP (mmHg)	72.45±4.275	73.75±7.691	0.611
HR (bpm)	70.00±5.514	74.40±7.769	0.108
SpO2 (%)	97.09±1.700	97.85±1.089	0.202
LF (m/s^2)	39.786±21.766	40.681±15.888	0.896
HF (m/s2)	59.760±22.164	59.319±15.888	0.949
LF/HF	0.918±0.781	0.887±0.903	0.922 [b]
hs-CRP (mg/L)	3.064±1.777	3.135±2.968	0.943 [b]
Tension-anxiety (T)	14.874±1.794	14.686±1.489	0.757
Depression-dejection (D)	29.091±2.343	29.105±1.747	0.985
Anger-hostility (A)	23.18±1.328	24.00±1.170	0.086
Vigor-activity (V)	23.82±0.982	23.65±1.089	0.674
Fatigue-inertia (F)	15.45±1.214	14.55±1.234	0.059
Confusion-bewilderment (C)	16.00±0.775	15.60±1.095	0.294

Note: [a] the chi-squared test was used; [b] Mann-Whitney U test was used; others were analyzed by using the independent-samples *t* test.
Abbreviation: BMI, body mass index; SDP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; hs-CRP, high-sensitive-reactive protein.

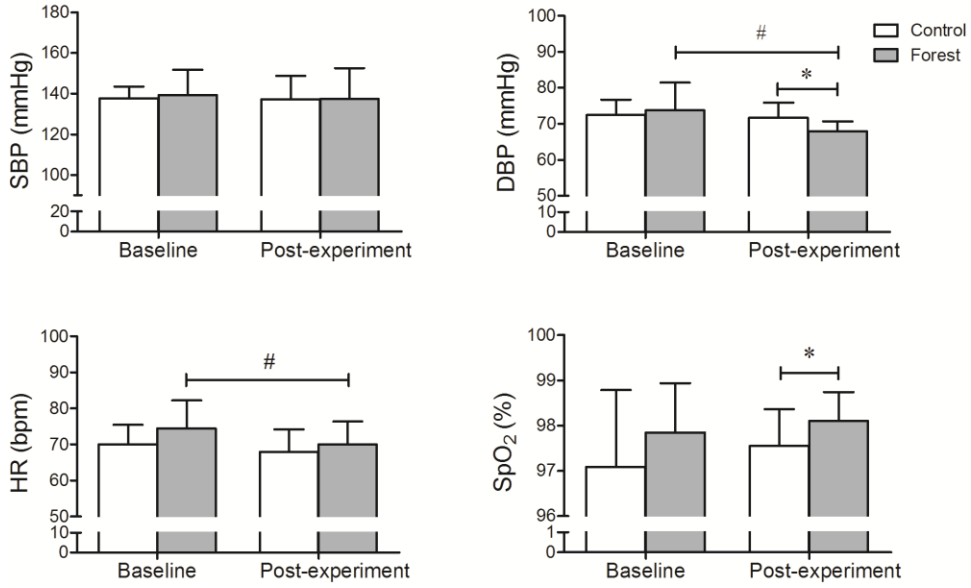

Figure 1: Effects of *C. camphora* Forest Bathing on BP-related Indicators. *p<0.05; #p<0.05, analyzed by the Kruskal-Wallis test followed by the Dunn-Bonferroni test. SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; SpO_2%, pulse oxygen saturation.

forest as compared with the control's (60.54±14.26 Vs 48.37±14.42, P<0.05). These results suggested the more balanced autonomic activity of elderly patients after forest bathing. Interestingly, similar HRV response were often seen in yoga therapy (Khattab et al., 2007; Shapiro et al., 2007).

C. camphora has long been prescribed in traditional medicines for the treatment of inflammation-related diseases (Lee et al., 2006a). In the present study, we analyzed the effects of forest bathing on the inflammatory factors, hs-CRP. As shown in Figure 2, at the end of the experiment, subjects experiencing forest bathing showed a significantly lower level of hs-CRP than that of the control group (1.77±1.09 Vs 3.34±1.80, P<0.05). These data

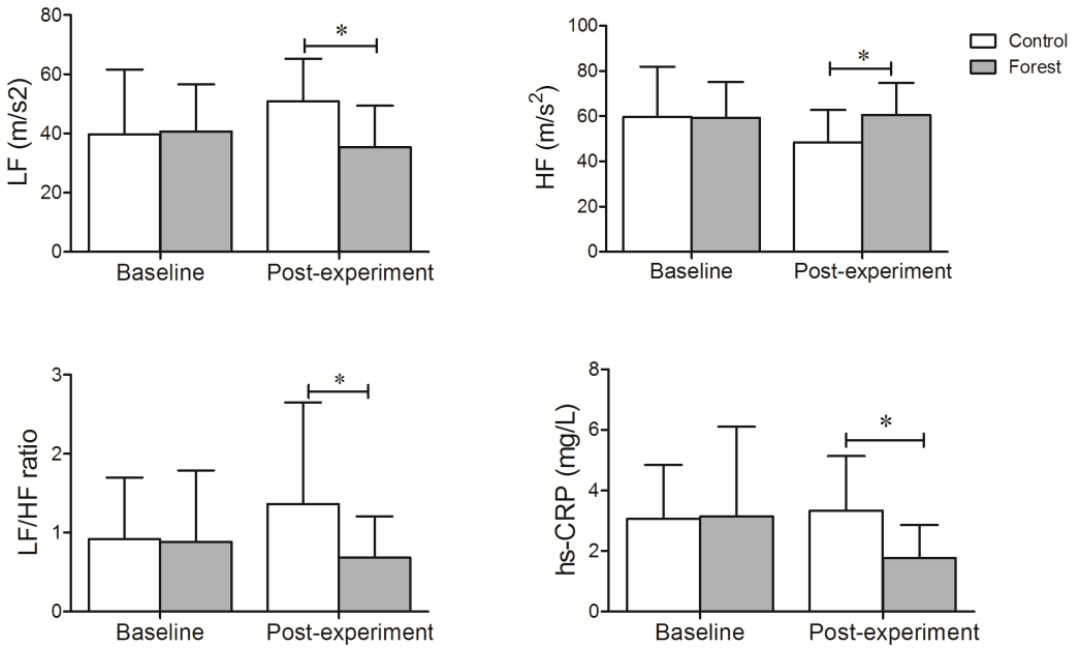

Figure 2: Influences of *C. camphora* Forest Bathing on HRV and Inflammatory Cytokines. *p<0.05, analyzed by the Kruskal-Wallis test followed by the Dunn-Bonferroni test. LF, low frequency; HF, high frequency; LF/HF ratio, low frequency/high frequency ratio; hs-CRP, high-sensitive-reactive protein.

suggested that *C. camphora* forest bathing alleviated the level of inflammatory response in elderly patients with HTN.

From the POMS subscale score, as shown in Figure 3, after forest bathing, much lower scores of tension-anxiety (T), depression (D), confusion(C) and fatigue (F) were found in the forest group as compared with the control group (T, 12.90±0.97 Vs 15.55±0.93, P<0.05; D, 25.72±1.45 Vs 29.82±1.08, P<0.05; C, 13.75±0.97 Vs 16.64±1.36, P<0.05; F, 13.80±1.11 Vs 15.55±0.69, P<0.05) or itself baseline scores (T, 12.90±0.97 Vs 14.69±1.49, P<0.05; D, 25.72±1.45 Vs 29.11±1.75, P<0.05; C, 13.75±0.97 Vs 15.60±1.10, P<0.05; F, 13.80±1.11 Vs 15.55±1.23, P<0.05), while it showed opposite trend in the score of vigor-activity (V, 26.90±1.59 in forest, 24.36±1.29 in control and 23.65±1.09 in forest baseline, P<0.05). These evidences indicated that *C. camphora* forest environment significantly improved the mood state of participates.

Generally, different species volatilize phytoncides with different constituents. *C. camphora* volatilizes a large number of compounds, which show strong property of anti-fungi and anti-inflammation (Lee et al. 2006a). It has been reported that the main component of phytoncides emitted from *C. camphora* is oxy-terpene, which accounts for the most abundant constituent in all volatile oils (flowers 50.83%, leaves 70.75%, branches 78.22%) (Shi et al., 2013). As one of the important natural products, most terpenes have multiple important physiological activities, such as BP modulator, anti-tumor, antifungal, anti-inflammatory, reducing blood lipid, etc (Lee et al., 2006b; Pragadheesh et al., 2013). Additionally, *C. camphora* leaves has also been reported as a biosorbent for the removal of copper ions, as well as for toxic air including SO_2, NO_2, and Cl_2, because it has satisfactory absorption (Chen et al., 2010).

This study showed for the first time that the tree-species-specific forest environment, *C. camphora* forest, had positive influences on elderly patients with HTN. However, the exact mechanisms were not fully understood. This experiment was performed at a *C. camphora* forest area named Changle farm, which is located in Jingshan country, 42 km distant from Hangzhou city (Zhejiang province, China). Averagely, it is 200 m above sea level and the highest is 800 m, which covered a square of 86,658 m^2 and included 230 various camphor tree species. For comparison, a suburban area in Jingshan country was used. Except for the air humidity (83.48±2.39 in forest Vs 71.65±5.20 in control, P<0.05, Table S1), the other factors of air quality in two sites were similar. However, the main components of the VOCs in two sites were obviously different. In the suburban area (as control), the main components in the air were esters (35.74±10.52) and aromatics (48.99±9.06), along with lesser amounts of terpenes, ketones and others. In the forest area, the VOCs consisted of terpenes (29.26±6.84), aromatics (29.75±11.27), aldehydes (13.68±3.3), ester (14.79±6.89), organic acids (6.65±8.35) and others (Table S1). Therefore, the possible mechanisms which resulted in significant discrepancy results of the two experimental sites can be attributed to the different VOCs and the properties in two

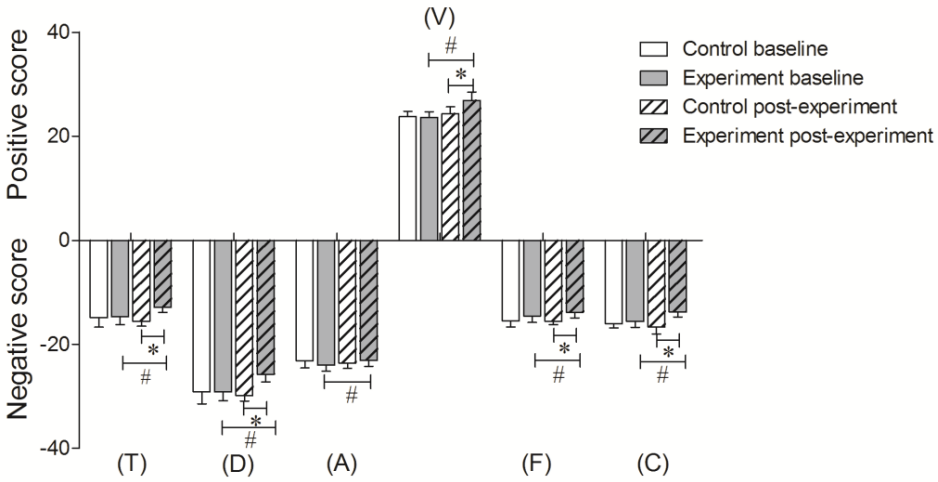

Figure 3: Impacts of *C. camphora* Forest Bathing on the Mood State of Subjects. *p<0.05; #p<0.05, analyzed by the Kruskal-Wallis test followed by the Dunn-Bonferroni test. T, tension-anxiety; D, depression; A, anger-hostility; F, fatigue; V, vigor-activity; C, confusion.

experimental sites.

Conclusion

In conclusion, although the sample size was small, it is worth noting that *C. camphora* forest environment can significantly decrease the level of DBP, LF and LF/HF, increase the levels of SpO_2%, HF and hs-CRP and promote the mood state of participants. This study showed for the first time that *C. camphora* forest bathing had an adjunctive therapeutic effect on elderly patients with HTN. Therefore, it is necessity to conduct a randomized clinical trial with larger sample sizes and longer intervention in the future.

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SUPPLEMENTARY MATERIAL

Table S1: The air quality and constituent of VOCs in two experimental sites.

	Suburban area	**Forest area**
Temperature	19.87±1.57	17.86±1.30
Humidity	71.65±5.20	83.48±2.39 *
Negative ions	304.68±150.42	492.99±97.50
PM2.5	0.04±0.02	0.03±0.01
PM10	0.05±0.01	0.04±0.01
Comfort index	72.33±3.51	69.00±3.00
Terpenes	2.66±3.34	29.26±6.84 *
Hydrocarbons	0	0
Aromatics	48.99±9.05	29.75±11.27 *
Aldehydes	0	13.68±3.30 *
Ketones	2.44±2.31	0
Alcohols	0	0
Esters	35.74±10.52	14.79±6.89 *
Organic acids	0	6.65±8.35
Others	10.17±2.92	5.86±6.18

Note: * independent –samples t-test were used.