2018

Calf Venous Compliance in College Aged Male Smokers and Non-Smokers

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CALF VENOUS COMPLIANCE IN COLLEGE AGED MALE SMOKERS AND NON-SMOKERS

by

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B.S., Southern Illinois University, 2016

A Research Paper
Submitted in Partial Fulfillment of the Requirements for the
Master of Science in Education

Department of Kinesiology
in the Graduate School
Southern Illinois University Carbondale
May/2017

RESEARCH PAPER APPROVAL

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Master of Science in Education

in the field of Kinesiology

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April 5, 2018

AN ABSTRACT OF THE RESEARCH PAPER OF

JOCELYN ROTHSCHILD-FREY, for the Master of Science degree in KINESIOLOGY, presented on APRIL 5, 2018, at Southern Illinois University Carbondale.

TITLE: CALF VENOUS COMPLIANCE IN COLLEGE AGED MALE SMOKERS AND NON-SMOKERS

MAJOR PROFESSOR: Dr. Juliane Wallace

Smoking is a major independent risk factor for cardiovascular morbidity and causes endothelial damage and autonomic dysfunction which leads to decreases in arterial compliance. Similar to changes in arterial compliance with fitness and aging, venous compliance in the lower extremities of adults improves with higher fitness and declines with increasing age. In young adults, males have a higher venous compliance than females, a difference that does not appear related to hormonal fluctuations. While previous studies have compared smokers and non-smokers for changes in arterial wall properties, no research to date has investigated the impact of smoking on limb venous compliance. **PURPOSE**: To determine the calf venous compliance differences in college age smokers versus non-smokers. **METHODS:** 8 smokers (2-12 years of smoking; mean of 3 pack years; age = 23±3.3 yrs; mass = 83.76 ± 17.04 kg; ht = 180.66 ± 8.84 cm; body fat = 20.33±6.88 %; calf volume = 2487.18 ± 446.36 ml; VO2 submax = 31.98 ± 9.63 ml/kg/min) and 7 non-smokers (age = 22 ± 2 yrs; mass = 80.57 ± 9.52 kg; ht = 176.85 ±5.25 cm; body fat = 15.05±6.76 %; calf volume = 2389.13 ± 516.66 ml; VO_2 submax = 34.83 ± 8 ml/kg/min) were recruited for this project. Participants underwent anthropometric assessment, a graded exercise test, and assessment of calf venous compliance. Utilizing venous occlusion plethysmography, calf pressure-volume relations was determined using the quadratic regression equation [Δ limb volume) = $\beta_0 + \beta_1$*(cuff pressure) + β_2*(cuff pressure)^2]. Calf venous compliance was calculated as the first derivative of the pressure-volume relation during cuff pressure reduction [Compliance = $\beta_1 + (2 * \beta_2 *$ cuff pressure)]. Differences in anthropometric variables, fitness, and compliance (β_1, β_2, and the slope of the pressure compliance relationship) between smokers and nonsmokers were analyzed with a simple ANOVA. **RESULTS:** There were no significant differences between smokers and nonsmokers in anthropometric variables or fitness. There were no significant differences between smokers and non-smokers in calf volume or compliance [smokers; Δ volume = 0.6171 ± 1.40635 + 0.1084 ±0.0.5669 * (cuff pressure) - 0.0010 ± 0.00076* (cuff pressure)^2 vs. non-smokers; Δ volume = -0.1596 ± 1.31733 + 0.1168 ±0.06125 * (cuff pressure) - 0.0011 ± 0.00061* (cuff pressure)^2]. **CONCLUSION:** College age male smokers have similar calf venous compliance to non-smokers. It is likely that the chronic effects of smoking that would alter the vessel wall and subsequently decrease venous compliance have not had enough time to influence venous wall structure in men in their early 20's.

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CHAPTER 1

INTRODUCTION

The human vascular system (also referred to as the circulatory system) is composed of arteries and veins that are responsible for oxygen and nutrient delivery to the body's tissues and then excretion of tissue waste matter. An important function of arteries and veins is the ability of a blood vessel wall to passively expand and contract with pressure changes within the system. Venous compliance (VC) is the vessel's ability to distend and increase volume with increasing transmural pressure (pressure inside minus pressure outside of the vessel). VC is quantified by dividing the change in volume (ΔV) within the vessel by the change in pressure (ΔP). According to Rowell (1993), the venous vasculature is a volume reservoir which contains about 70% of total blood volume. Venous return to the heart is achieved because variations in blood volume can be overcome by altering the total capacity of the venous system to maintain pressure. Cardiovascular (CV) homeostasis relies on this pressure-volume relationship. When a human stands in the upright position, 70% of blood volume falls below the level of the heart due to gravity and the veins are 30-50 times more compliant than the arteries. This translocation of blood away from the heart causes a stress to the cardiovascular system that is counter-regulated by sympathetic modulation (Rowell, 1993). Cigarette smoking has been shown to have multiple adverse effects on the CV system. According to Li et al. (2005) cigarette smoking is a major risk factor for CV disease, and contributes to as much as 30% of all CV disease mortality in the U.S. each year. Though the effects of cigarette smoking on the CV system have been widely researched concerning arterial compliance, there is no known research done to date that looks at how cigarette smoking effects calf VC specifically.

We know from previous research that VC in the lower limb of humans' decreases with increasing age (Lanne & Olsen, 1998; Monahan et al., 2001; Tsutsui et al., 2002; Hernandez & Franke, 2004). According to a study completed by Länne and Olsen (1998), when comparing young and older adults, VC was reduced by 45% in the lower limbs of the older adult population. A similar reduction in the capacitance response during lower body negative pressure (LBNP) was also noted. We also know that VC is higher in those who engage in chronic endurance exercise (Convertino et al., 1984; Louisy et al., 1997; Pawelczyk et al., 1988; Monahan et al., 2001; Hernandez & Franke, 2004). There have been controversial findings on sex differences in VC. Some studies have found higher VC in men than women (Monahan & Ray, 2004; Lindenberger & Länne, 2007), but this difference does not appear to be related to fluctuating hormone levels (Meendering et al., 2005). Lindenberger and Länne (2006) found that calf VC was significantly lower in women compared to men, however, these differences were only seen at lower transmural pressures, no sex differences were seen at higher transmural pressures. Monahan and Ray (2004) also found that calf VC was lower in women than men, but only at rest. During baroreceptor unloading, VC was equally reduced in men and women.

There is extensive research done on both acute and long-term effects of cigarette smoking on arterial compliance. Cigarette smoking has repeatedly shown to decrease small and large arterial wall compliance and distensibility in both acute and chronic smoking (Doonan et al., 2010; Li et al., 2005; Kool, Hoeks, Struijker Boudier, Reneman, & Van Bortel, 1993; Benetos et al., 2002). There has been much less research done on the effects of smoking cessation on arterial wall properties. Jatoi, Jerrard-Dunne, Freely, & Mahmud (2007) investigated the impact of smoking and smoking cessation on arterial stiffness, and found that smoking cessation was associated with a significant reduction in arterial stiffness. They also showed a reduction in arterial stiffness in former smokers to the level of non-smokers after 10 years of smoking cessation, however, using radial pressure waveform analysis they did not find any difference in large artery stiffness. Continued research needs to be conducted to better understand some of these findings on the effect of smoking cessation on arterial wall properties. As stated earlier, to the best of our knowledge there is no research on the effects of cigarette smoking on limb VC.

The purpose of this research is to investigate the effects of cigarette smoking on calf VC in college aged male smokers and non-smokers. Based on what we know from past research in VC, and the effects of cigarette smoking on arterial compliance, we hypothesize that calf VC will be lower in smoking individuals when compared to non-smoking individuals.

CHAPTER 2

METHODS

Participants

A total of 19 male students' ages 19-28 years from Southern Illinois University, Carbondale volunteered to participate in the present study. Eight of them smoked cigarettes regularly and 11 were non-smokers. For comparison, participants were either placed in a smoking or non-smoking group where they were matched for age and fitness levels (smoking n=8, non-smoking n=8). All participants signed an informed consent approved by the SIUC Human Subjects Committee and completed a medical history form. All participants were free of any diagnosed cardiovascular disease and not taking any cardiac medications. Participants were categorized as either cigarette smokers (smoking at least two cigarettes/day), or non-cigarette smokers (never smoking cigarettes).

General Experimental Design

Participants reported to the laboratory on one occasion. They first completed a medical history form which asked if the participant smoked cigarettes and for how long. Similar to previous research (Rhee, Na, Kim, Lee, & Kim 2007) cigarette smoking frequency was determined as pack-year, which is calculated by multiplying the number of packs of cigarette smoked per day by the number of years the person has smoked. Anthropometric measures were then assessed. A balance scale and stadiometer were used to determine body mass (kg) and height (cm). Resting heart rate (RHR) was taken via palpitation, and resting blood pressure was taken manually with a stethoscope and blood pressure cuff. Body composition was estimated by a 3-site protocol using Lange Skinfold Calipers to measure body fat (BF) percentage. Strain gauge plethysmography (ECR5 Hokanson, Bellevue, WA) was used to assess changes in calf volume and a venous collecting cuff was used to control pressure (AG101 Hokanson, Bellevue, WA). Fitness status was assessed last, via submaximal oxygen consumption, which was measured during a graded treadmill exercise test following the Bruce Protocol until 85% of heart rate max was reached (ParvoMedics TrueOne, Metabolic System – QUSW 4.3.4 (20160305).

Venous Compliance

The chosen methods for the present study were a slightly modified version of the procedures validated by Halliwill et al. (1999), similar to those used previously by Hernandez and Franke (2004). Participants were placed in the supine position for a short period of time with the right leg elevated above heart level and supported at the ankle and thigh. By using the formula $\pi r^2 \cdot L$, calf volume was calculated from the mean of four girth measurements obtained equidistantly between the medial malleolus and the tibial plateau (r) and from one calf segment length, the distance between the medial malleolus and the tibial plateau (L). Changes in limb volume relative to baseline were measured noninvasively using strain gauge plethysmography at the maximal calf circumference. A venous collecting cuff was placed ~5 cm proximal to the knee on the right leg and inflated to 60 mmHg for 8 minutes and then reduced at a rate of 5 mmHg/5sec. (over 1 min) to 0 mmHg.

Analysis

Determination of venous compliance involved generating pressure-volume curves from the pressure-volume relationship as pressure was decreased at the rate of 5 mmHg/5sec. from 60 mmHg to 10 mmHg. Pressure-volume curves were compared by means of the quadratic regression model [(Δlimb volume) = $\beta_0 + \beta_1 \times$ (cuff pressure) + $\beta_2 \times$ (cuff pressure)^2] , where Δ is the difference between the limb volume at a given cuff pressure and the resting, pre-inflation, cuff volume, β_0 is the intercept, and β_1 and β_2 are slope components for each individual.

Regression models were calculated by using the general linear model procedure (SPSS), including between-participant classifications for smokers and non-smokers. The pressure-volume relation is not linear; therefore, a single number is not sufficient to characterize the slope of the pressure-volume curve. Thus the group averaged regression parameters β_1 and β_2, determined by the pressure-volume curves for each participant in the relevant groups, were used together as an estimate of compliance, such that compliance = $\beta_1 + 2 \times \beta_2 \times$ (cuff pressure) or the derivative of the pressure-volume curve, the coefficient of variation of this method has been reported to be 4.9% (Halliwill, Minson, & Joyner, 1999). Differences between smokers and non-smokers on anthropometric and compliance variables were determined using a one-way analysis of variance (SPSS 24).

CHAPTER 3

RESULTS

Participant Characteristics

Table 1 summarizes the participant characteristics. There was a significant difference in the pack-year amount of cigarettes smoked between the groups, where the non-smokers did not smoke any cigarettes and the smokers smoked 2.88±2.04 pack-year, but there were no other significant differences in the participant characteristic data. Participants were of similar age, mass (kg), and height (cm). The smokers tended to have a higher BF percentage (20.33±6.88% vs. 15.05±6.76%) and RHR (73±10.2 bpm vs. 65±13.65 bpm) than the non-smokers, but the differences were not significant (BF p = .144; RHR p = .205). There was no significant difference in the mean fitness level between groups, which was measured by estimated VO2max (mL/kg/min). Participants also had similar calf volume and systolic and diastolic blood pressure values.

Table 1: Participant Characteristics

Variables	Non-Smokers (n=8)	Smokers (n=8)
Pack-year*	0	2.88±2.04*
Age (yr)	22±2	23±3.3
Body Mass (kg)	80.57±9.52	83.76±17.04
Height (cm)	176.85±5.25	180.66±8.84
Body Fat (%)	15.05±6.76	20.33±6.88
VO2submax (mL/kg/min)	34.83±8	31.98±9.63
Calf Volume (mL)	2389.13±516.66	2487.18±446.36
Systolic BP (mmHg)	124.75±6.56	126.25±12.17
Diastolic BP (mmHg)	80.25±6.25	76.25±9.16
Resting Heart Rate (bpm)	65±13.65	73±10.2
Compliance @ 20mmHg	0.0749±0.039	0.0695±0.036
Capacitance	2.85±1.34	3.05±0.68
Capillary Filtration	2.88±0.78	3.19±0.74
Slope of Capacitance	0.075±0.03	0.085±0.02

Values are means ±SD. * $p<.05$. BP, blood pressure.

Venous Compliance

Table 2 presents the pressure-volume regression parameters β_0, β_1, and β_2 calculated (means ±SD) for male non-smokers and smokers. There were no statistically significant differences found between these variables. When comparing the pressure-volume curves (figure 1), and the compliance-pressure relationship (figure 2) between the non-smokers and smokers, no significant differences were found. Figure 3 displays the calf venous compliance at 20mmHg cuff inflation, the non-smokers did tend to have a higher compliance but the differences were not significant (p = .772). Figure 4 compares the capacitance and capillary filtration volumes between the non-smokers and smokers, there were also no significant differences found here.

Table 2: Pressure-Volume Regression Parameters

	β0	**β1**	**β2**
Non-Smokers	-0.16±1.317	0.117±0.613	-0.001±0.0006
Smokers	0.617±1.406	0.108±0.057	-0.001±0.001

Values are means ±SE ΔCalf Volume = $\beta_0 + \beta_1$ *(cuff pressure) + β_2 *(cuff pressure)^2

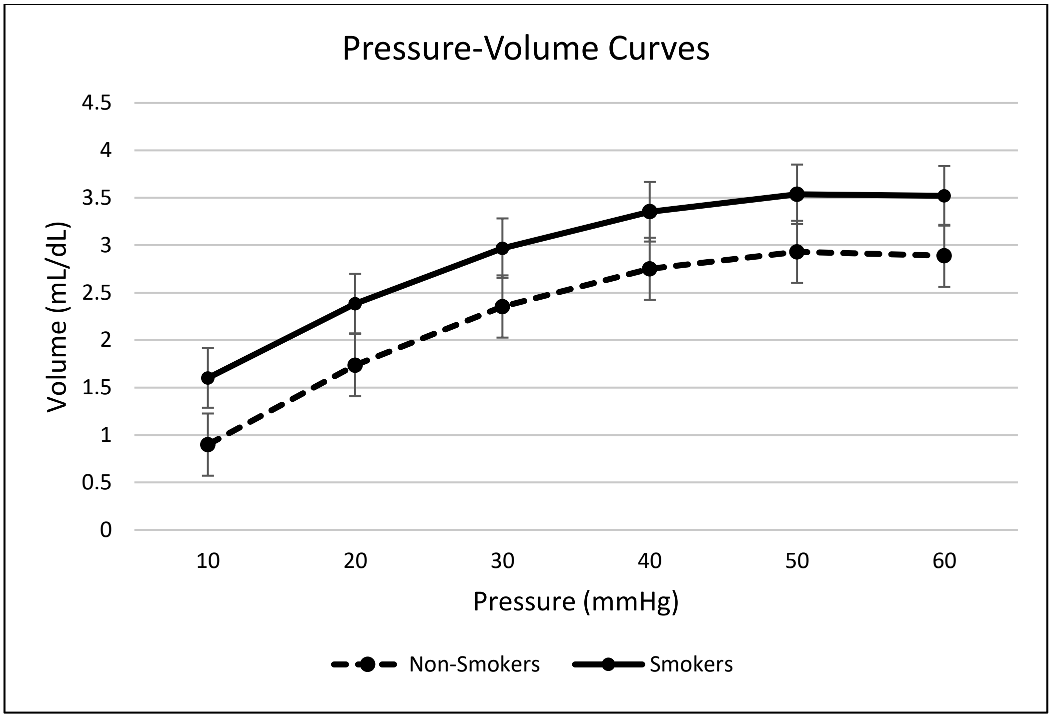

Figure 1. Pressure-Volume curves in non-smokers and smokers.

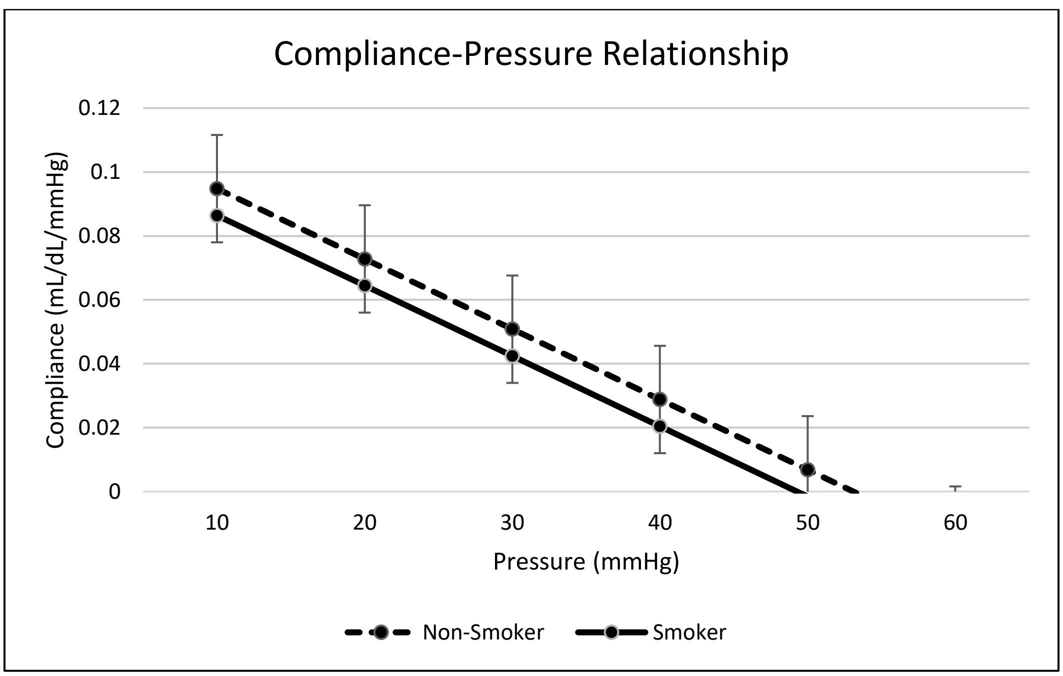

Figure 2. Compliance-Pressure Relationship in non-smokers and smokers.

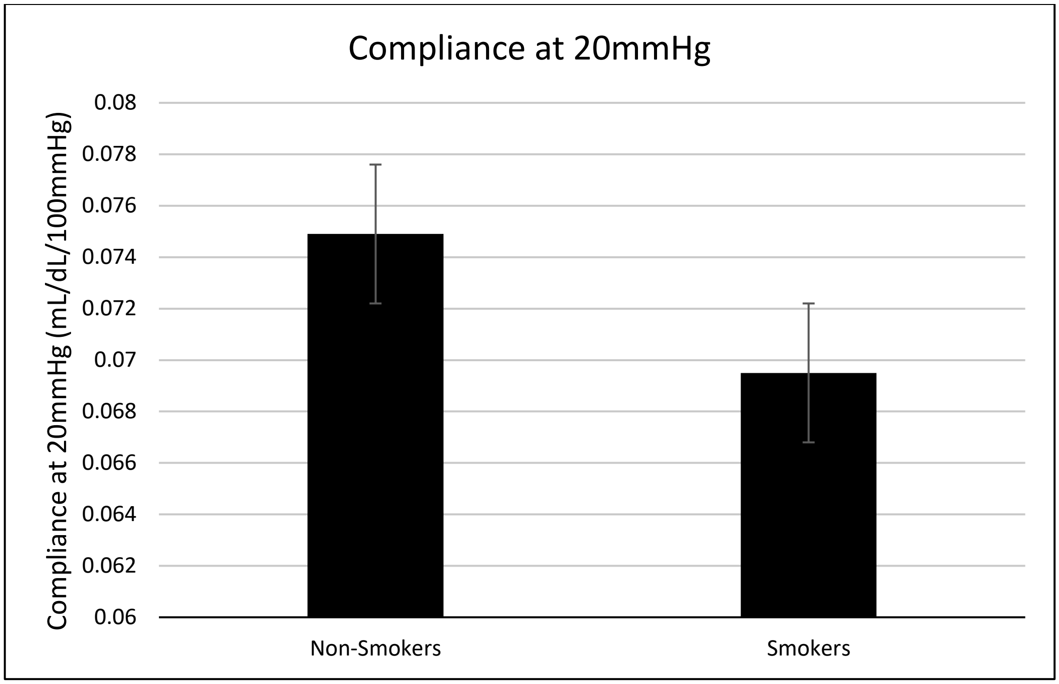

Figure 3. Calf venous compliance at 20mmHg cuff pressure.

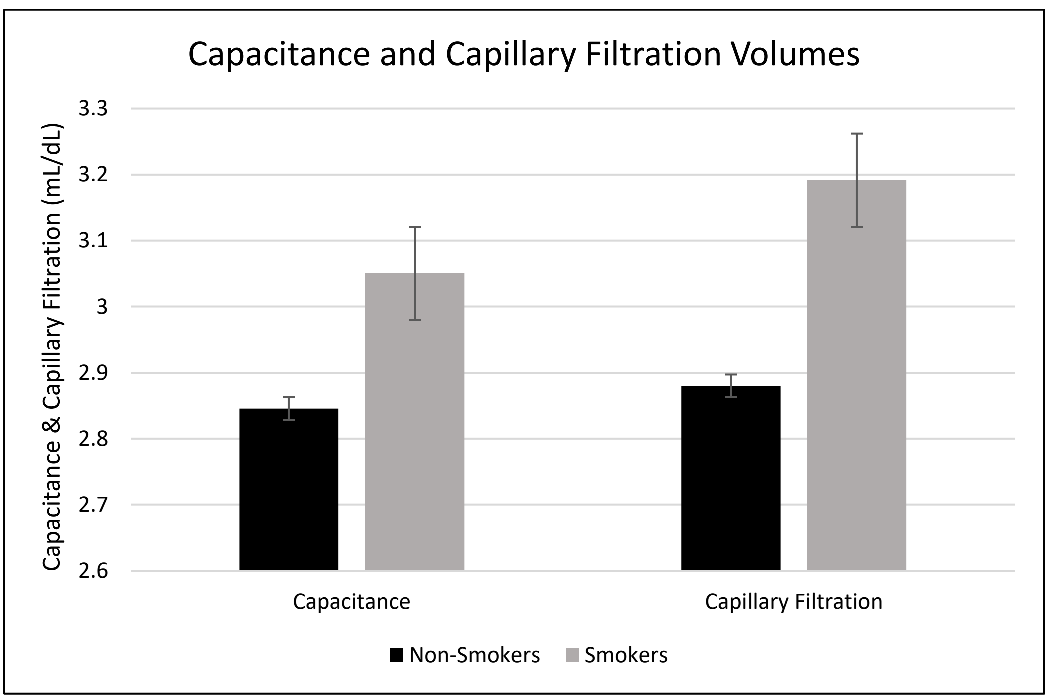

Figure 4. Capacitance and capillary filtration volumes during cuff inflation.

CHAPTER 4

DISCUSSION

To the best of our knowledge, the present investigation is the first to look at the differences in calf VC between non-cigarette smokers and cigarette smokers in college age males. Based on previous research on cigarette smoking effects on vascular wall properties (Doonan et. al., 2010; Jatoi, Jerrard-Dunne, Feely, & Mahmud, 2007; Mahmud & Feely, 2002; Li et. al., 2005), we hypothesized that the non-cigarette smokers would have higher calf VC than those who smoked cigarettes regularly. We found that the non-smoking group did tend to have higher calf VC than the smoking group, however these differences were not significant therefore the findings to this study do not support our hypothesis. There was also no significant differences found between the pressure-volume slopes or the capacitance and compliance volumes between the groups.

Proposed reasoning for the current findings is that it is likely that the chronic effects of smoking that would alter the vessel wall properties and subsequently decrease VC have not had enough time to influence venous wall structure in men in their early 20's. In a study by Kool et al. (1993) they found that compared to non-cigarette smokers, those who smoked cigarettes had increased arterial wall stiffness of both elastic and muscular arteries after smoking, however, these finding were in participants that were 25-55 years old and who on averages smoked 23 cigarettes a day for 17 years. Jatoi, Jerrard-Dunne, Feely, & Mahmud (2007) found that there was a direct linear relationship between smoking status and arterial stiffness in a population of 554 subjects ages 18 to 80 years old, where current smokers were defined as smoking >1 cigarette per day for ≥1 year. It may be possible that we would have seen greater differences in VC in the current study if we had a larger pool of participants who on average were older and smoked for a longer duration of time in order to have greater chronic effects on the venous wall properties.

VC is defined as the relationship between change in venous volume and distending (transmural) pressure. Although differences in calf VC have not previously been researched in cigarette smokers, there has been extensive research on VC in other populations (examining different variables). In 2007, Lindenberger and Läne found that in apparently healthy men and women, women had significantly reduced VC compared with men with a concomitant reduction in capacitance response during lower body negative pressure, however these differences were only seen at lower transmural pressures.

In 2001, Monahan, Dinenno, Seals, and Halliwill investigated calf VC in 32 healthy men who were “young” (20-35 yr old) and “old” (55-75 yr old) and were either “sedentary” or “endurance exercise trained”, they found that calf VC is reduced with age in both sedentary and endurance trained men, however compliance is better preserved in men who endurance train. The authors concluded that venous compliance decreases with increasing age but increases with increased fitness. Similarly, Hernandez and Franke (2004) found increased VC in those who participated in chronic exercise in both young and older participants and VC was reduced with age in both fitness categories. In a different study, Hernandez and Franke (2005) investigated the effects of a 6-month endurance-training program on VC and maximal lower body negative pressure in older men and women. It was found that a 6-month endurance training program increased the venous compliance in these individuals without affecting their tolerance to maximal lower body negative pressure. The results of these studies contributed to our reasoning for assessing fitness statuses in the current study.

Limitations

There are some limitations that should be taken into consideration in the present investigation. First, the technique of venous occlusion plethysmography to measure compliance is a measure of whole limb compliance, which varies with age (Dinenno, Jones, Seals, & Tanaka, 1999). The current method assumes that venous collecting pressure is equal to venous pressure and the use of the 8-minute collecting period accounted for any differences that may have been present in whole limb blood flow (Halliwill, Minson, & Joyner, 1999; Monahan, Dinenno, Seals, & Halliwill, 2001). Second, our participants in the current study were apparently healthy which should be considered when analyzing our findings and extrapolating them to clinical populations. Third, we had a relatively small sample size of only male participants in the present study. Continued research should be executed involving larger populations of both male and females to better contribute to the conclusions made in this study.

CHAPTER 5

CONCLUSION

In conclusion, to the best of our knowledge this is the first research study that investigates the effects of cigarette smoking on lower limb VC in college aged males. The current study concluded that cigarette smoking does not have any significant effects on lower limb VC in apparently healthy males in their 20's of similar body composition and fitness level. Although it was found that non-smoking males tended to have higher VC than smoking males, these differences were not statistically significant. Additional investigative research should be done in larger and older smoking populations who have been smokers for a longer period of time to better understand the effects of cigarette smoking on VC. Since improved VC is highly associated with cardiovascular health, having a better understanding of the possible adverse effects of cigarette smoking on VC could help healthcare professionals better detect cardiovascular abnormalities in those who smoke cigarettes.

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