Effects of Heat Stress on Arterial Compliance in Smokers: A Pilot Study

Erin Dougherty

Department of Health, Human Performance, and Recreation
College of Education and Health Professions
University of Arkansas, Fayetteville AR

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Major Advisor: Matthew S. Ganio, Ph.D.

Committee Members: Bart J. Hammig, MPH, Ph. D. & Tyrone A. Washington, Ph. D.

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Abstract

Arterial compliance (i.e., arterial elasticity) is a major contributor to the pathophysiology of cardiovascular disease (CVD) and has been recognized as an independent risk factor for CVD. Smokers have poor arterial compliance compared to non-smokers. In non-smokers, passive heat stress has been shown to acutely improve arterial compliance. It is unknown how passive heat stress affects arterial compliance in smokers. The purpose of this pilot study was to test the hypothesis that passive heat stress improves arterial compliance in smokers to a greater extent than non-smokers. This pilot study involved 2 male smokers and 2 male non-smokers, ages 18-21. Smokers and non-smokers underwent a control (no heat) and passive heat stress trial in a randomized, counter-balanced fashion. Passive heating was achieved by circulating hot water through a water-perfused, tube-lined suit that covered the entire body except the head, face, hands, feet, and right forearm. Measures were obtained prior to heating and after a 0.5, 1.0, and 1.5°C elevation in core body temperature or equivalent time points in the non-heated control trial. At each time point, mean skin temperature was measured via thermocouples and heart rate and blood pressure were measured using an automated sphygmomanometer with ECG. Arterial compliance was assessed with pulse wave velocity (PWV) measured from a Doppler ultrasound. During heat stress in the smokers, central PWV tended to decrease from 681.36 ± 31.21 cm/s at baseline to 634.91 ± 96.87 cm/s at the 0.5°C time point. From 1.0°C to 1.5°C there was an increase in central PWV (699.33 ± 135.46 to 747.11 ± 0.00 cm/s). The non-smokers central PWV tended to decrease during the heat stress from 660.03 ± 86.49 cm/s at baseline to 562.89 ± 23.41 cm/s at 1.5°C. Peripheral PWV in the smokers decreased from 724.00 ± 23.46 cm/s at baseline to 701.73 ± 5.43 cm/s at 0.5°C and 703.77 ± 23.22 cm/s at 1.0°C, but there was a later increase in peripheral PWV at 1.5°C (725.95 ± 43.45 cm/s). For the non-smoker heat stress
trial, peripheral PWV saw a steady decrease from 701.73 ± 1.52 cm/s at baseline to 603.30 ± 30.64 cm/s at 1.5°C. In conclusion we observed decreases in PWV (i.e., increases in arterial compliance) in non-smokers, but relatively no change in smokers when heat stressed. Future research should investigate the mechanisms by which arterial compliance may or may not change during passive heat stress in smokers and non-smokers.
Arterial compliance is a major contributor to the pathophysiology of cardiovascular disease (CVD) and has been recognized as its own independent risk factor for CVD (1, 4). The distensibility and compliance of the artery walls are both important in affecting the load on the arterial wall (4). Arterial compliance, noted as the inverse of arterial stiffness, is a good index of arterial health (13). A decrease in arterial compliance is increasingly being recognized as an important cardiovascular risk factor and an independent predictor of all-cause and cardiovascular death (2,3).

Smoking is a known risk factor for the progression of cardiovascular disease. Additionally, cigarette smoking has been linked to coronary artery disease and atherosclerosis and accounts for 25% of all cardiovascular deaths (5, 6). Changes to the arterial wall, such as decreased arterial compliance, increase the risk of developing cardiovascular disease. Importantly, there is evidence that smoking one cigarette can lead to a decrease in the arterial compliance of both large- and medium-sized arteries (4, 50-51). Recent studies have shown that in habitual smokers, after smoking one cigarette there can be hemodynamic changes in sympathetic activation leading to a decrease in the compliance of both elastic and muscular arteries (4). With a decrease in arterial compliance there can be an increase in one’s blood pressure which would, in turn, put an individual at risk for a cardiovascular event.

The exact mechanism by which exercise improves cardiovascular health is not well understood, but one hypothesis is that arterial compliance is improved with exercise (15, 16). Arterial compliance can be affected by acute exercise depending on the duration, intensity, and mode of exercise performed (14). With 30 minutes of aerobic intensity exercise at a moderate
intensity it has been shown that there is an increase in both central and peripheral compliance that remains elevated for 60 minutes post-exercise (15, 16). It is possible that arterial compliance improvements with exercise are due to increases in core temperature often experienced during exercise. A recent study investigated the independent effects of increasing core temperature on arterial compliance. It was shown that individuals who had lower arterial compliance at baseline had greater changes with passive heating versus those with greater arterial compliance at baseline (14). This occurs in both central and peripheral arteries (14). One explanation for why baseline compliance affects the degree of improvement in arterial compliance with heating is that those with greater compliance at baseline have little room to improve because their arteries are already at a healthy level of compliance. However, when one has lower arterial compliance at baseline, there is more room to improve and thus more drastic changes can be observed with passive heating (14).

It is unknown if this same negative association occurs with smokers who have poor arterial compliance at rest. The purpose of the current study is to investigate the effects of passive heat stress on arterial compliance in smokers versus non-smokers. It is hypothesized that smokers, with poor arterial compliance at rest, will have greater improvements with passive heat stress versus non-smokers. The findings of this study will provide further evidence for possible mechanisms of improved arterial compliance with heat stress.
Chapter 2 - Literature Review

Arterial compliance is a major contributor to the pathophysiology of cardiovascular disease (CVD) and has been recognized as its own independent risk factor for CVD (1, 4). The compliance of the artery walls is important in affecting the load on the arterial wall (4). An artery with less compliance will have increased load or pressure with each heartbeat. Arterial compliance, noted as the inverse of arterial stiffness, is a good index of arterial health (13). Specifically, arterial stiffness is noted as a risk factor for cardiovascular morbidity and mortality (2). Arterial compliance, or stiffness, is a regional measure; central compliance is the area between the carotid and femoral artery, while peripheral compliance is the area between the carotid and radial artery. Arterial stiffness is increasingly becoming recognized as an important cardiovascular risk factor and an independent predictor of all-cause and cardiovascular death (3).

Overall, studies have shown that physically active individuals have a lower average mortality rate than those who do not participate in at least moderate physical activity regularly (34-41). Additionally, studies have shown that smokers who are physically active at a vigorous level have a lower cardiovascular mortality rate than smokers who are sedentary or only slightly active (29, 34-40, 42). One study reported that non-physically active smokers have the highest mortality rate compared to physically active and non-smoker counterparts (29). Lower mortality rates among physically active smokers may be due to the counteractive effects of exercise against atherosclerosis and thrombus formation (43-49, 50).

Arterial Compliance and Smoking

Cigarette smoking has been linked to coronary artery disease and atherosclerosis and accounts for 25% of all cardiovascular deaths (5, 6). Studies have shown that cigarette smoke exposure increases myocardial demand (9) while reducing coronary blood flow through
vasoconstriction to the coronary arteries (10). While this mechanism is not fully understood, it is assumed that vascular dysfunction can occur from the absorption of tobacco smoke that has an effect on endothelial cell function (9, 11-12).

There are several physiological changes associated with chronic smoking. These include an increase in blood pressure, heart rate, cardiac index, muscle blood flow, and a decrease in skin blood flow (18). All-in-all, these results can be explained by the nicotinic-induced sympathetic activation (18). Smoking is a known risk factor for the progression of cardiovascular disease. This can occur by decreasing arterial compliance. Recent studies have shown that after smoking one cigarette, there can be an immediate decrease in compliance of both large and medium-sized arteries (4, 51-52). There is also a decrease in arterial compliance in chronic smokers (3). After smoking one cigarette there are influences to the vessel wall properties of the elastic carotid artery and the muscular brachial artery. There is no change in compliance at the carotid artery, but at the peripheral brachial artery there is a significant reduction in compliance (19%) (4). Any changes in compliance of large- and medium-sized arteries may be due to changes that occur within the muscular content of the arterial wall (4). The detrimental effects of smoking on arterial health are independent of age, gender, and fitness level (3). When an individual smokes a cigarette there is ganglionic stimulation and its associated release of norepinephrine. Epinephrine is released from the adrenal medulla, and there also is an increase in the stimulation to the central nervous system, which leads to an enhanced neural discharge (4). There is also an increase in heart rate associated with smoking that lasts for 75 minutes post-cigarette (18).

**Arterial Compliance and Acute exercise**
Arterial compliance can be affected by acute exercise depending on the duration, intensity, and mode of exercise performed (14). After 30 minutes of moderate intensity aerobic exercise it has been shown that there is an increase in both central and peripheral compliance that remains elevated for 60 minutes post-exercise (15-16). Conversely, with higher intensity and short duration anaerobic exercise there are acute decreases in central compliance while peripheral compliance increases (14, 16-17).

The mechanisms by which acute exercise influences arterial compliance are not entirely understood. It is possible that heat stress during exercise plays a role. Exercise at a moderate-intensity has also been shown to increase one’s core temperature up to 1.0°C with exercise as short as 30 minutes (24, 25). A recent study investigated the independent effects of increasing core temperature on arterial compliance. It was shown that individuals who had lower arterial compliance at baseline had greater changes with heating versus those with greater arterial compliance at baseline (14). This occurs in both central and peripheral arteries (14). One explanation for why baseline compliance affects the degree of improvement in arterial compliance with heating is that those with greater compliance at baseline have little room to improve because their arteries are already at a healthy level of compliance. However, when one has lower arterial compliance at baseline, there is more room to improve and thus more drastic changes can be observed with passive heating (14).

The mechanism by which passive heating improves arterial compliance is not entirely understood. Passive heating increases cardiac output which leads to an increase in blood flow through the large arteries of the body. Following these physiological responses there is also a reduction in resistance in the systemic vasculature, which leads to an increase in shear stress (30). Nitric oxide has a linear relationship with shear stress. Therefore, when there is an
increase in shear stress there is also nitric oxide released with leads to vasodilation, improved arterial elasticity, and arterial compliance (31, 32, 33). One exercise bout can acutely increase arterial compliance via the adjustment of the tone of the smooth muscle cells by endothelial cells (53). The endothelium plays a significant role in the regulation of nitric oxide, an intrinsic vasodilator. The release of nitric oxide contributes to the regulation of arterial compliance during acute exercise (31, 54-55).
Chapter 3 – Methods

Adult males were recruited for this pilot study from the University of Arkansas and surrounding area. The study included only males to conserve homogeneity of data. Participants were categorized as either smokers or non-smokers based off of responses to a questionnaire. Smokers were defined as those who smoke at least \( \frac{1}{2} \) pack a day for a minimum of two years. Non-smokers were those who have smoked less than 100 cigarettes in their lifetime. The researchers ensured that participants fully understood that their participation was completely voluntary and failing to participate would not lead to any repercussions. The participants completed a medical history questionnaire and an international physical activity questionnaire before participation in the study.

Participants participated in two separate trials, and the order of the trials was randomized and counter-balanced. The trials were separated by at least 48 hours. 24 hours prior to testing subjects refrained from alcohol and exercise. Participants abstained from food for four hours and caffeine 12 hours prior to testing. To ensure compliance a pre-test questionnaire was administered before testing. Additionally, euhydration was encouraged prior to each test; this included consuming 500 mL of water the night before testing and 2-3 hours prior to testing. Participants were given a temperature sensor pill (CoreTemp Inc., Palmetto, FL) the night prior to their participation in the study. The pill measures core body temperature and transmits the temperature to a receiver that is positioned within 40 cm of the sensor. The pill was swallowed with water and passes harmlessly through the gastrointestinal tract.

Upon arrival to the Human Performance Laboratory at the University of Arkansas the participants were instructed to void their bladder while providing the researcher a small urine sample. From this sample specific gravity was measured using a refractometer (ATAGO SUR-
NE refractometer) to ensure euhydration (urine specific gravity <1.028). Thermocouples were then taped on the right side of the participant’s body in the following locations used to calculate mean skin temperature: lateral subdeltoid, pectoral, lateral calf, and quadriceps. A heart rate monitor (Polar, Inc.) was used to measure heart rate. ECG was also attached to the participants and integrated to the ultrasound for the measurement of pulse wave velocity (PWV). The participants were then dressed in a water-perfused, tube-lined suit that covered the entire body minus the head, face, hands, and feet (Allen-Vanguard Technologies). This suit controls both skin and core temperature by adjusting the temperature of the water perfused through the suit. Local skin blood flow was measured using laser Doppler (moorLAB). The laser was attached to the participant’s right forearm once the participants were fully dressed in the suit and had lied down. The participant’s were instructed to keep this arm as still as possible so an accurate skin blood flow reading could be measured. Skin blood flow was recorded as a percentage of max for the individual. Maximal skin blood flow was obtained by 30 min of local heating at 42°C performed at the end of each trial.

Before baseline measurements, participants lied supine for ~30 minutes. During this time 34°C water was perfused through the suit. After 30 minutes, baseline measures were acquired and participants were exposed to either – hot water (49°C - experimental trial) or room temperature water (34°C - control trial). During heating in the experimental trial, measurements were obtained after a 0.5°C, 1.0°C, and 1.5°C increase in core temperature. Heating lasted ~70 min. During the control trial, since no heat was administered, measurements were obtained at 30, 50, and 70 minutes. At each time point participants were asked their thermal perception (57). The thermal perception scale ranges from 0.0 (unbearably cold) to 8.0 (unbearably hot). Pulse wave velocity (PWV) was measured with a Doppler ultrasound (GE Goldseal LOGIQ e BT08) and
used as an index for arterial compliance; PWV is the inverse of the square root of compliance (56). Central PWV was determined from measurements taken at the carotid and femoral arteries; peripheral PWV was determined from the carotid and radial arteries. These measurements were all taken on the left side of the body, and consistency was maintained by markings on the skin.

The distance between arterial measurements was calculated by taking the distance from the carotid measurement location to the femoral or radial site. PWV was calculated by measuring time between the peak of the R-wave and the foot of the pulse within the same heart beat. This was averaged across 10 heartbeats. Once this value was found Central PWV was determined by dividing the distance from the carotid to femoral artery by the average time of the pulse wave at the femoral artery subtracted from the average time at the carotid artery times 1,000. Peripheral PWV was calculated in the same manner with the exception being that the radial artery was used instead of the femoral. Arterial blood pressure was measured at the brachial artery via an electrosphygmomanometry (SunTech, Raleigh, NC).

To minimize the possibility of a type I error with low subject numbers, a t-test was performed between non-smokers and smokers at each time point. Significance was set at P < 0.05.
Chapter 4: Results

Subject demographics are in table 1. There were no significant differences between smokers and non-smokers hydration status between trials ($P > 0.05$). USG at arrival to the lab for the non-smoker control trial was $1.026 \pm 0.000$ and in the heat stress trial it was $1.004 \pm 0.001$. For the smoker control trial USG was $1.023 \pm 0.006$ and for the heat stress it was $1.011 \pm 0.013$.

Table 1: Mean ± SD Subject Demographics

<table>
<thead>
<tr>
<th></th>
<th>Non-Smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Age (years)</td>
<td>21 ± 1</td>
<td>19 ± 1</td>
</tr>
<tr>
<td>Body Mass (kg)</td>
<td>77.8 ± 8.4</td>
<td>88.8 ± 50.8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.7 ± 8.1</td>
<td>177.2 ± 17.9</td>
</tr>
<tr>
<td>IPAQ</td>
<td>5,094 ± 1,133*</td>
<td>718 ± 665</td>
</tr>
</tbody>
</table>

*P<0.05 between groups
Table 2. Mean ± SD measures during control trial

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>~30 min post baseline  (28.96min ± 8.70)</th>
<th>~50 min post baseline  (49.24min ± 12.02)</th>
<th>~70 min post baseline  (68.83min ± 13.96)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-Smokers</td>
<td>Smokers</td>
<td>Non-Smokers</td>
<td>Smokers</td>
</tr>
<tr>
<td>Change in core temperature from baseline (°C)</td>
<td>--</td>
<td>--</td>
<td>- 0.07 ± 0.03</td>
<td>0.29 ± 0.29</td>
</tr>
<tr>
<td>Mean Skin Temperature (°C)</td>
<td>33.43 ± 0.41</td>
<td>33.39 ± 2.10</td>
<td>34.21 ± 0.31</td>
<td>34.11 ± 1.64</td>
</tr>
<tr>
<td>Heart Rate (BPM)</td>
<td>60 ± 21</td>
<td>78 ± 31</td>
<td>62 ± 21</td>
<td>71 ± 31</td>
</tr>
<tr>
<td>Skin blood flow (% max)</td>
<td>60.07 ± 6.87</td>
<td>59.00 ± 21.56</td>
<td>60.24 ± 6.67</td>
<td>58.84 ± 20.90</td>
</tr>
<tr>
<td>Mean Arterial Blood Pressure (mmHg)</td>
<td>94.41 ± 5.77</td>
<td>79.17 ± 17.68</td>
<td>93.17 ± 4.48</td>
<td>89.67 ± 5.42</td>
</tr>
<tr>
<td>Thermal Perception</td>
<td>3.5 ± 0.7</td>
<td>4.8 ± 0.4</td>
<td>4.0 ± 0.0</td>
<td>4.3 ± 0.4</td>
</tr>
</tbody>
</table>

*P<0.05 between groups at the given time point
Table 3. Mean ± SD measures during heat-stress trial

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>0.5°C</th>
<th>1.0°C</th>
<th>1.5°C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-Smokers</td>
<td>Smokers</td>
<td>Non-Smokers</td>
<td>Smokers</td>
</tr>
<tr>
<td>Change in core temperature from baseline (°C)</td>
<td>--</td>
<td>--</td>
<td>0.33 ± 0.06</td>
<td>0.32 ± 0.01</td>
</tr>
<tr>
<td>Mean Skin Temperature (°C)</td>
<td>33.91 ± 1.32</td>
<td>34.32 ± 0.57</td>
<td>39.44 ± 0.36</td>
<td>39.78 ± 2.33</td>
</tr>
<tr>
<td>Heart Rate (BPM)</td>
<td>61 ± 10</td>
<td>81 ± 13</td>
<td>86 ± 1*</td>
<td>110 ± 6</td>
</tr>
<tr>
<td>Skin blood flow (% max)</td>
<td>51.50 ± 37.04</td>
<td>48.37 ± 37.55</td>
<td>62.11 ± 45.95</td>
<td>60.68 ± 44.30</td>
</tr>
<tr>
<td>Mean Arterial Blood Pressure (mmHg)</td>
<td>92.75 ± 3.65</td>
<td>90.33 ± 0.47</td>
<td>83.42 ± 9.55</td>
<td>90.83 ± 1.65</td>
</tr>
<tr>
<td>Thermal Perception</td>
<td>4.3 ± 0.4</td>
<td>4.0 ± 0.0</td>
<td>6.3 ± 0.4</td>
<td>6.8 ± 0.4</td>
</tr>
</tbody>
</table>

*P<0.05 between groups at the given time point
Figure 1 – Central pulse wave velocity during control trial

![Central pulse wave velocity during control trial](image)

No significant differences between groups at each time point

Figure 2 – Central pulse wave velocity during heat-stress trial

![Central pulse wave velocity during heat-stress trial](image)

No significant differences between groups at each time point
Figure 3 – Peripheral pulse wave velocity during control trial

No significant differences between groups at each time point

Figure 4 – Peripheral pulse wave velocity during control trial

No significant differences between groups at each time point
**Figure 5** – Changes in Peripheral Pulse Wave Velocity versus Normothermic PWV

**Figure 6** – Changes in Central Pulse Wave Velocity versus Normothermic PWV
Chapter 5: Discussion

The purpose of this study was to measure arterial compliance during passive heating and to see if there were differences between two populations: smokers and non-smokers. Using a tube-lined water perfusion suit the participant’s were heated up to a ~1.5°C increase in core temperature while pulse wave velocity (PWV), an index of arterial compliance, was measured. PWV was measured centrally and peripherally.

The statistical findings should be interpreted with caution because of the low subject numbers in this pilot study. Nonetheless, during the control trial (i.e., no heat stress) heart rate was not significant between the two populations (Table 2). Mean skin temperature was not significantly different and neither was skin blood flow during the control trial. Mean arterial pressure was significantly different between the two populations during the third time point (60 minutes) in the control trial but was not significantly different at any other time point. Thermal perception was not significantly different at any time point during the control trial.

There were no significant differences in PWV between subjects and trials, but the directional changes are as follows. During the control trial peripheral PWV decreased in the smokers and increased in the non-smokers (Figure 3). For central PWV the smoker’s compliance greatly increased at the second time point (40min) and the decreased at the final time point (60min). The non-smoker’s compliance decreased at the first time point (20min) and then increased back to baseline by the final time point (60min) (Figure 1). Central PWV during the final time point may be slightly skewed because the final measurement for one of the smoker participants was not recorded. As expected the relatively short time of testing (~2 hrs total) resulted in relatively little changes in compliance under control conditions. This means that any changes during the heat stress trial where due to heat stress and not simply the passage of time.
Additionally, the smokers smoked their last cigarettes immediately prior to their arrival to the Human Performance Lab. This could potentially have an affect on the smoker’s baseline compliance levels due to the acute effects of smoking one cigarette (4).

During the heat stress trial, heart rate was significantly different between smokers and non-smokers at the 0.5°C time point, but was not significant at any other time point (Table 3). Mean skin temperature and skin blood flow were not significant at any point during the heat stress. Mean arterial pressure was not significantly different between smokers and non-smokers during the heat stress. Thermal perception was also not significant during the heat stress trial.

During the heat stress trial peripheral and central PWV decreased in the non-smokers as hypothesized (Figures 2 & 4). This confirms prior data investigating the effect of heat stress on non-smokers (14). Interestingly, and contrary to the hypothesis there was relatively little change in peripheral PWV for smokers and a slight increase in central PWV when heat stressed. More subjects will need to be tested to confirm this finding, but it is possible that increased central nervous system activation during heat stress was greater in smokers, thus overriding any effect of nitric oxide on the endothelium. It is also possible that nitric oxide release with increases in cardiac output was not as great in smokers or the endothelium was not as sensitive to the vasodilatory effect of nitric oxide compared to non-smokers.

Given prior data suggesting that baseline compliance (PWV) influences the amount of change observed during heating (14), we sought to examine that relationship in smokers when heat stressed. Independent of smoking status, the change in central PWV with heating was correlated to baseline, normothermic PWV (Figure 6). Specifically, the greater the normothermic PWV, the greater the improvement in arterial compliance with heating. This is
similar to previous findings (14). However, contrary to our hypothesis there does not appear to be differences dependent on smoking status. Furthermore this relationship is not present when examining peripheral PWV (Figure 5).

In conclusion we observed decreases in PWV (i.e., increases in arterial compliance) in non-smokers, but relatively no change in smokers. These findings are preliminary, and future subjects will need to be tested to confirm/refute these findings. Ideally, further research will also match physical activity level in smokers with non-smokers because it is known that exercise can improve the compliance of artery walls (15, 16). Lastly future research should investigate the mechanisms by which arterial compliance may or may not change during passive heat stress in smokers and non-smokers.
Acknowledgements:

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References


