Lower Limb Venous Compliance in 10-Year Old Boys and Girls

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LOWER LIMB VENOUS COMPLIANCE IN 10-YEAR OLD BOYS AND GIRLS

by

Trey Beckerman

B.S., Southern Illinois University, 2012

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

Department of Kinesiology
in the Graduate School
Southern Illinois University Carbondale
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RESEARCH PAPER APPROVAL

GENDER EFFECTS OF LOWER LIMB VENOUS COMPLIANCE IN YOUNG ADOLESCENT CHILDREN

By

Trey Beckerman

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

Approved by:

Juliane Wallace, Chair

(Philip Anton)

Graduate School Southern Illinois University Carbondale August 2014
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While there has been extensive research investigating the proper health and function of the arteries within the human body, much less focus has been given to the venous vasculature until recent years. Veins are different from arteries in a number of aspects, an important one being their elastic properties. Veins are approximately 30-50 times more compliant than arteries. This increased level of compliance allows the venous vasculature to hold roughly 70% of the total blood volume that falls below the heart upon standing, and also helps maintain blood pressure during this position change. With this increase in lower-limb blood volume comes a decrease in central blood volume, which triggers sympathetic activity in an effort to maintain stroke volume and cerebral blood flow (Rothe, 1983; Rowell, 1993).

Venous compliance is represented by the relationship between venous volume and venous transmural pressure. The pressure-volume relationship is important in the maintenance of homeostasis through maintaining venous return. This results in attenuated decreases in arterial blood pressure as a result of orthostatic stress (Halliwill, Minson, & Joyner, 1999; Rowell, 1993).

Past studies have shown that venous compliance decreases with age, (Hernandez, Karandikar, & Franke, 2005; Lanne & Olsen, 1997; Lindenberger & Lanne, 2007a; Monahan, Dinneno, Seals, & Halliwill, 2001) and is higher in more physically fit individuals (Hernandez & Franke, 2005, Hernandez & Godar, 2009; Monahan et al., 2001). Recently, researchers have found differences in venous compliance between
the sexes (Hernandez & Godar, 2009; Hernandez & Franke, 2005; Lindenberger & Lanne, 2007b; Meendering et al., 2005; Monahan & Ray, 2004).

While many studies have investigated the effects of age on venous compliance, to the best of our knowledge none have looked at compliance in children. There are however studies showing a decreased arterial elasticity in children as young as 8 (Gardner & Parker, 2011) and 10 years old (Riley et al., 1986). These studies found decreased arterial compliance in children with lower fat-free mass and functional abnormalities associated with an increase in cardiovascular disease risk, respectively. Because these observations of altered arterial characteristics have been found in children at this age, it is possible that similar decreases in function may be found within the venous vasculature in the same age group.

To the best of our current knowledge, there have been no studies investigating the venous compliance in children as young as 9-12 years old. Therefore, the purpose of this study was to determine the venous compliance in young female and male children. We hypothesized that female children would have lower calf venous compliance compared to male children, following observations previously found in young adult comparisons of compliance between the sexes (Hernandez & Godar, 2009; Hernandez & Franke, 2005; Lindenberger & Lanne, 2007b; Meendering et al., 2005; Monahan & Ray, 2004).
CHAPTER 2
LITERATURE REVIEW

2.1 Introduction

Over the past century, a dramatic shift has been observed from physically active to sedentary lifestyles as the new and accepted “norm”. These changes have made it more challenging to maintain healthy lifestyles and a healthy heart through exercise and physical activity. A common result of the sedentary lifestyle is an increase in cardiovascular risk factors such as increased arterial stiffness. This structural adaptation is associated with a greater occurrence of myocardial infarctions and stroke (Blacher et al., 1999; Laurent et al., 2001). While there has been substantial evidence charting the effects of changes in arterial structure on our health, investigations into venous vasculature are not as common, but of equal importance to the current state of knowledge of vascular function.

Veins differ from arteries in many ways, one of the most important being their elastic properties. Veins are approximately 30 to 50 times more compliant than arteries. This level of compliance allows the venous vasculature to accommodate the roughly 70% of total blood volume that falls below the level of the heart upon standing and maintain blood pressure. This shift in blood volume causes a decrease in central blood volume, placing a stress on the cardiovascular system to maintain stroke volume and cerebral blood flow. In order to counteract this stress, there is an increase in sympathetic modulation and an activation of the skeletal muscle pump (Rothe, 1983; Rowell, 1993).
Venous compliance is the relationship between venous volume and venous transmural pressure (Rowell, 1993). Venous compliance is altered by many variables including fitness level, age, and sex. As we age, venous compliance decreases (Lanne & Olsen, 1997; Lopes et al., 2013; Monahan, Dinneno, Seals, & Halliwill, 2001). Men and women with higher fitness levels have exhibited increased venous compliance when compared to their age-matched counterparts (Hernandez & Franke, 2005; Hernandez & Godar, 2009; Monahan et al., 2001). Chronic endurance training improves venous compliance levels in older adults (Hernandez & Franke, 2005; Monahan et al., 2001). More recent research suggests that venous compliance may be affected differently by sex at various ages (Hernandez & Franke, 2005; Meendering et al., 2005; Monahan & Ray, 2004).

The purpose of this review of literature is to examine the current knowledge on the topic of venous compliance, as well as the effects of age, fitness level, and sex on venous compliance levels. Issues related to venous compliance that have not yet been investigated will also be discussed.

2.2 Assessment of Venous Compliance in Humans

As previously stated, venous compliance is the relationship between venous volume and venous transmural pressure. As pressure increases, compliance tends to decrease as a result of the increase in venous volume (Rowell, 1993). The initial increase in blood volume within the limb is called the capacitance response and is defined as the relationship between transmural pressure and total volume within the vasculature. It is possible for capacitance to change without a measurable change in compliance (Rowell, 1993). The capacitance response is a rapid process that is typically
completed with ~3 minutes, while capillary filtration, which is a much slower process, is defined from the filtration slope between 3 and 8 minutes (Lindenberger & Lanne 2007a; Lundvall et al., 1989; Schnizer et al., 1978). Capillary filtration is a gradual and continuous rise in leg volume that reflects the net transcapillary fluid transfer from the blood to the tissue (Lanne and Olsen, 1997). According to Lindenberger and Lanne (2007b), total changes in calf volume are dependent upon the capacitance response in addition to the total capillary filtration.

Venous occlusion plethysmography uses strain gauges to measure the overall changes in calf circumference, which provides us with a change in limb volume. A 1% change in gauge resistance is equivalent to a 0.5% increase in gauge length, which is proportional to a 1% increase in limb volume (Whitney, 1953). To measure compliance in the calf, a venous collecting cuff is placed around the thigh, proximal to the knee. The strain gauge is wrapped around the calf at its max circumference. With the limb elevated above the heart and the increase in cuff pressure proximal to the knee, calf volume increases. The methodology after this point, including the timing used for cuff pressure increases and decreases, along with other assumptions concerning compliance measurements, has changed over time. Prior to the current methodology of venous occlusion plethysmography developed by Halliwill, Minson, and Joyner (1999), there were multiple limitations with the noninvasive methods of measuring venous compliance.

Robinson and Wilson (1968) measured compliance through inflation of a collection cuff to 60 mmHg until intravenous pressure reached similar levels (55-215 seconds). Following this rise in intravenous pressure, cuff pressure was decreased at
1mmHg/s to 0 mmHg and the decrease in intravenous pressure and volume was recorded. This methodology incorrectly assumes resting pressure is equal to 0 mmHg. Halliwill and colleagues (1999) found it to be below 10 mmHg, suggesting the only pressure ranges that should be analyzed are those within the 10 mmHg – 60 mmHg range.

Buckey et al. (1992) measured compliance using multiple collecting cuff pressures inflated in sequence to 20, 40, 50, and 60 mmHg followed by decreasing pressure in 2-minute intervals. The lack of extended rest period between cuff inflation led to a shift to higher volumes in the pressure-volume relationship following venous distention that occurs with multiple increases in cuff pressure. This methodology also takes considerable amounts of time, and is difficult to observe compliance measurements within a small time frame.

Melchoir and Fortney (1993) followed similar increases and decreases in cuff pressure as Buckey et al. (1992) but decreased cuff pressure directly to 0 mmHg following each increase in pressure. While this methodology can be time consuming, it also assumes that an observer can determine when intravenous pressure has reached steady state following a step increase in cuff pressure. Halliwill and colleagues (1999) found this is not possible to accomplish accurately.

These issues lead Halliwill and colleagues (1999) to develop a novel noninvasive method for measuring whole-limb venous compliance. This method consisted of a 4-minute period of cuff inflation to 60 mmHg followed by a decrease in cuff pressure of 1 mmHg/s over 60 seconds. This allowed for faster compliance measurements, and also allowed researchers to observe smaller time frames of compliance measurements,
easing the process of testing the effects of sympathetic activation on venous compliance.

In addition to Halliwill’s method of measuring whole-limb venous compliance, lower-body negative pressure (LBNP) chambers are often used to induce blood pooling in the lower limbs (Hernandez and Franke, 2005; Lanne and Olsen, 1997; Lindenberger and Lanne, 2007a; Lindenberger and Lanne, 2007b; Monahan and Ray, 2004). By causing blood to pool in the lower limb, calf venous compliance, capacitance response, capillary filtration, and overall change in limb volume can be measured using strain-gauge plethysmography. When comparing venous compliance measurements with and without the use of LBNP, there are some important factors to consider. LBNP has been shown to elicit an increase in sympathetic activity, but there is conflicting evidence as to its effect on limb venous compliance (Halliwill et al., 1999; Monahan and Ray, 2004). Another concern with LBNP is the fact that it is designed to simulate the orthostatic stress that occurs in the human body upon standing, but because there is not an actual position change, the results must be interpreted with care while comparing them with real-world orthostatic stress.

2.3 Age and Venous Compliance

As humans age, the cardiovascular system encounters a number of changes that are part of the process of aging. While these changes cannot be prevented from occurring, they do not occur at the same rate in everyone. These changes include increased arterial stiffness and decreased arterial elasticity. Arterial stiffness is inversely related to arterial compliance. Decreases in arterial compliance as a result of aging have been associated with cardiovascular diseases such as coronary heart
disease (Bertovic et al., 1999; Hirai, Sasayama, Kawasaki, & Yagi, 1989;) and hypertension (Van Merode, Hick, Hoeks, Rahn, & Reneman, 1988). Changes in arterial function lead to an increased afterload on the left ventricle, increasing systolic blood pressure. With an increase in systolic blood pressure we see left ventricular hypertrophy. Aging also leads to decreased responses in baroreceptors and chemoreceptors, both of which are vital to hormone regulation (Cheitlin, 2003).

Many studies have found that venous compliance decreases with age (Hernandez & Franke, 2004; Hernandez, Karandikar, & Franke, 2005; Monahan et al., 2001). Bassett, Frey, and Hoffler (1988) originally found no changes in capacitance response with age, but observed a very small age range in their study. Lanne and Olsen (1997) studied a larger age range of participants and found a decreased capacitance response with aging when using lower-body negative pressure to induce lower limb blood pooling. They proposed this finding as an explanation for the declining sympathetic reflex response that typically occurs with aging and can lead to orthostatic intolerance. They proposed that the decreased capacitance response would result in lower venous compliance, leading to a decreased loss in central blood volume upon standing. If central blood volume does not decrease, the sympathetic nervous system is not triggered through activation of the baroreceptors and heart rate and blood pressure cannot increase to account for the shifts in blood volume as a result of postural change. The decrease in capacitance response is a potential explanation for the decreased venous compliance seen in older adults (Lanne and Olsen, 1997).

Although venous compliance has been found to decrease with age, there is evidence that the decline can be attenuated through increases in physical activity.
Monahan and colleagues (2001) observed calf venous compliance in young and old sedentary and endurance-trained men. They found that while calf venous compliance is reduced with age in all fitness levels, it is better preserved in endurance-trained men. Hernandez and Franke (2005) found meaningful improvements in venous compliance following a 6-month endurance training program. These studies provide support for the importance of maintaining a physically active lifestyle as we age. Further effects of physical activity and exercise will be discussed in detail in the next section of this review.

### 2.4 Fitness Level and Venous Compliance

Multiple studies have found higher levels of venous compliance in individuals of a higher fitness level (Convertino, Montgomery, & Greenleaf, 1984; Louisy, Jouanin, & Guezennec, 1997; Olsen & Lanne, 1998). Monahan and colleagues (2001) found that exercise could not only improve venous compliance by ~70-120% compared to age-matched sedentary men, but could attenuate the age-associated reductions in compliance. They found endurance trained older males exhibited ~30% greater compliance than young sedentary males.

Convertino, Doerr & Stewart (1989) found an increase in leg venous compliance following 30 days of simulated microgravity. They found an inverse relationship between leg compliance and the size of the muscle compartment, which tended to decrease as a result of the simulated microgravity, suggesting that a decrease in calf muscle mass can lead to an increase in venous compliance. Convertino and colleagues stated that a decrease in muscle mass reduced the amount of mechanical compression on the veins, resulting in attenuated resistance to venous stretching and therefore allowing venous
compliance to increase. Subsequent studies involving increases in muscle mass as a result of resistance training have suggested otherwise. Hiroshi (2011) found that an increase in muscle mass had no significant effect on venous compliance. They found that forearm venous compliance was higher in resistance-trained men compared to sedentary men. However, they found that venous volume, not forearm muscle mass, held a significant positive relationship with venous compliance. This suggests that changes in muscle mass are not responsible for changes in venous compliance. To further contrast the findings of Convertino et al. (1988), Hiroshi (2011) found that forearm venous compliance increased with an increase in muscle mass, even though the relationship was not significant. Hiroshi and colleagues discuss these differences in the findings and suggest the greater amount of muscle mass in the lower limb compared to the forearm could potentially be responsible for the opposing muscle mass and venous compliance observations.

Other research in the area of resistance training and venous compliance has used low-intensity blood-flow-restricted (BFR) exercise to simulate high intensity resistance training. BFR exercise uses occlusive cuff pressure that is greater than the exerciser’s systolic blood pressure. The intensity can then be at 20-30% of maximal voluntary contraction, while blood pressure increases are enhanced and fast-twitch muscle fiber recruitment increases (Manini & Clark, 2009; Suga et al., 2009). Multiple studies have shown increases in muscle hypertrophy and strength as a result of BFR exercise (Abe et al., 2005; Moore et al., 2004; Shinohara, Kouzaki, Yoshihisa & Fukunaga, 1998; Takrada, Sato & Ishii, 2002; Takrada et al., 2000).
Exercise using BFR has found to increase venous compliance following a 6-week training program in untrained older adult female participants, while no changes were found in the control group or arm compliance measurements (Iida et al., 2007). In direct contrast to Convertino et al. (1988) and Convertino, Doerr, and Stein (1989), Iida and colleagues (2007) observed a significant increase in calf girth measurements following the 6-week program as well as a significant increase in calf venous compliance. This suggests that calf muscle mass may not directly affect calf venous compliance. A more recent study done by Fahs and colleagues (2014) found low-load BFR resistance training on lower limbs did not elicit changes in venous compliance in middle-aged men and women. However, venous compliance has been shown to increase in the forearm in resistance-trained men when compared to an age-matched control group (Hiroshi et al., 2010).

### 2.5 Sex and Venous Compliance

Young females have been found to have ~48% lower calf venous compliance when compared to age-matched male counterparts, and calf venous compliance may decrease in men, but not women as a result of baroreceptor unloading caused by lower-body negative pressure (Monahan & Ray, 2004). Monahan and Ray (2004) also found similar decreases in capacitance response as a result of lower-body negative pressure, suggesting capacitance response can be observed with no changes in venous compliance. Meendering and colleagues (2005) found a sex effect on calf venous compliance, with females exhibiting 19-26% lower venous compliance than males. This study observed venous compliance during the early follicular, ovulatory, and midluteal phases of the menstrual cycle, but found no differences. They also found no
compliance differences in oral contraceptive users between high and low hormone phases. These findings, along with the greater venous compliance found in males, suggest that sex differences in compliance are not a result of fluctuating hormone levels. Lindenberger and Lanne (2007a) investigated the sex differences in calf venous compliance at various transmural pressures. Females exhibited lower compliance at lower pressures, but with increased pressures this sex difference was not seen. Lower-body negative pressure was used to increase transmural pressures and induce baroreceptor unloading, similar to Monahan and Ray (2004). Therefore, it is not surprising that Lindenberger and Lanne (2007a) also found a reduced venous compliance in males with increased pressure, erasing the sex differences found at lower pressures. This study, along with the Hernandez and Godar study (2009), has found that females exhibit higher capillary filtration levels than males. Lindenberger and Lanne (2007a) found that the sex differences in calf venous compliance disappeared when capillary filtration was not subtracted from the overall compliance calculation, suggesting capillary filtration is the driving force behind the observed sex differences in venous compliance. In a follow up study completed by Hernandez and Godar (2009) the increased capillary filtration was also observed. However, in place of lower-body negative pressure methodology, which does not account for capillary filtration in the venous compliance measurement process, venous occlusion plethysmography was used. This methodology includes a swift pressure reduction of 5 mmHg/5 seconds, which should be quick enough to account for the effects of capillary filtration on venous compliance measurements (Halliwill et al., 1999).
While endurance-trained males consistently exhibited higher venous compliance than their sedentary peers (Hernandez & Franke, 2005; Monahan et al., 2001), past studies found untrained females to have lower venous compliance when compared to untrained males (Meendering, Torgrimson, Houghton, Halliwill, & Minson, 2005; Monahan & Ray, 2004). Hernandez and Godar (2009) investigated this training effect previously seen in males, in a group of endurance-trained female athletes. They found endurance-trained females had ~40% higher venous compliance than the females of average fitness, as well as higher net capillary filtration and capacitance volumes; however, when they compared females of above average fitness to males of average fitness they found females had higher venous compliance. This would suggest that capillary filtration is not the sole reason for sex differences observed in venous compliance. If it were, then all males, despite fitness levels, should have greater venous compliance than all age-matched females. This proposes two possibilities: 1) Venous occlusion plethysmography procedures do not accurately account for capillary fluid filtration, or 2) Capillary filtration is not affecting compliance measurements. Further investigation is needed in this area of sex and venous compliance.

Venous compliance was found to be lower in young females than males (Meendering et al., 2005; Monahan & Ray, 2004), but this sex effect was not seen in a more recent study (Hernandez & Godar, 2009) of a similar age group. In older adults the evidence suggests no differences in venous compliance between males and females (Hernandez & Franke, 2005, Wallace & Miller, currently unpublished).
2.6 Conclusion

The venous vasculature within the human body is responsible for holding 70% of total blood volume that falls below the level of the heart upon standing. The compliance within these veins allows us to maintain blood pressure and therefore maintain homeostasis (Rothe, 1983; Rowell, 1993). As humans age, venous compliance decreases (Lanne & Olsen, 1997; Lopes et al., 2013; Monahan et al., 2001), but increases in men and women with above average fitness levels (Hernandez & Franke, 2005; Hernandez & Godar, 2009; Monahan et al., 2001). Females have exhibited lower venous compliance at a young age compared to males (Meendering et al., 2005; Monahan & Ray, 2004), but this sex difference seems to disappear in older adults (Hernandez & Franke, 2005; Wallace & Miller, currently unpublished). To the best of our current knowledge, there are no studies that have looked at the sex effect on venous compliance in children.
CHAPTER 3

METHODS

Participants

Ten children with a mean age of 10.5 years old (SD±1.0) (5 male and 5 female) were recruited from a school in Carbondale, IL. Written informed consent was obtained from the participants as well as their parents or guardians according to the practices established by the Southern Illinois University Human Subjects Committee.

Experimental Procedures

Data collection was performed at a stable room temperature between 23-25° C. Anthropometric data was collected, followed by venous compliance measurements, and finally the sub-maximum exercise test was completed. Participant heart rate was monitored throughout using a Polar Heart Rate monitor. Resting blood pressure was assessed manually using a pressure cuff on the upper arm. Height (cm) and body mass (kg) were assessed using a stadiometer and balance scale. Body composition was estimated using a Bioelectrical Impedance Analysis device (Omron BF 306 Body Logic Pro Body Fat Analyzer, Lake Forest, IL). Participants completed a sub-maximum Bruce Protocol Treadmill test in order to estimate fitness level. Test termination criteria were reached when participants reached 85% of their age-predicted maximum heart rate. This criterion was met in all participants. Changes in calf volume were measured using strain gauge plethysmography (ECR5 Hokanson, Bellevue, WA) and a venous collecting cuff was used to control pressure (AG101 Hokanson, Bellevue, WA).
**Venous Compliance**

The methods used in the present study are similar to those used by Hernandez and Franke (2004), which was a slightly modified version of the procedures validated by Halliwill et al. (1999). Calf volume was calculated from four girth measurements taken equidistantly between the medial malleolus and tibial plateau and one calf segment length. Changes in calf volume were assessed non-invasively using strain gauge plethysmography. Participants began in the supine position with the right leg supported at the thigh and heel, holding the leg to a 45-degree angle and elevated above the heart to promote venous drainage. The venous collecting cuff was placed proximal to the right knee, and a mercury in-silastic strain gauge was placed around the maximal calf circumference. The participant was allowed to rest in this position for 30 minutes followed by an increase in venous collecting cuff pressure to 60 mmHg for 8 minutes. During the 60 seconds following the 8 minute period, pressure was reduced by 5 mmHg /5s.

**Data Analysis**

All data were recorded on a Dell PC (Biopac data acquisition software) for analysis. Resulting pressure-volume curves during the step down in pressure were described by the quadratic regression equation \[(\Delta \text{ limb volume}) = \beta_1 + \beta_2 \ast (\text{cuff pressure}) + \beta_2 \ast (\text{cuff pressure})^2\]. The group-average regression parameters \(\beta_1\) and \(\beta_2\) were used together as an estimate of compliance \[\text{compliance} = \beta_1 + 2\ast\beta_2 \ast (\text{cuff pressure})\]. The first derivative yields a linear pressure-compliance relationship and this slope was used to determine sex differences.
The capacitance response was calculated from the volume increase at the onset of cuff pressure to the line defined from the filtration slope between 3 and 8 minutes of cuff pressure application. Total capillary filtration during cuff pressure was calculated from the rate of filtration (ml/min) multiplied by the time of the cuff pressure application (8 min). Total calf volume increase was the sum of the capacitance and net capillary filtration volumes.

Anthropometric and compliance data between the two groups were compared using a one-way analysis of variance (IBM SPSS Statistics 22). Group differences were considered significant at the $p < .05$ alpha level.
CHAPTER 4
RESULTS

Participant Characteristics

Physical characteristics are summarized in Table 1. The female and male groups were of a similar age, height, and body mass. There were no differences in BMI or fitness between the two groups. Both systolic and diastolic blood pressures were similar between females and males. There were also no differences in resting heart rate and calf volume between groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Female Children</th>
<th>Male Children</th>
</tr>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>10.5±1.0</td>
<td>10.3±0.8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>142.0±16.7</td>
<td>150.5±4.7</td>
</tr>
<tr>
<td>Body Mass (kg)</td>
<td>42.9±14.5</td>
<td>42.4±9.9</td>
</tr>
<tr>
<td>BMI</td>
<td>19.4±4.3</td>
<td>18.9±3.2</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>111.2±2.0</td>
<td>107.0±6.8</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>68.7±9.8</td>
<td>66.8±8.6</td>
</tr>
<tr>
<td>Resting Heart Rate (bpm)</td>
<td>79.7±13.5</td>
<td>88.7±13.8</td>
</tr>
<tr>
<td>Calf Volume (ml)</td>
<td>300.30±49.45</td>
<td>292.78±78.90</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 10 (5 in each group). BP, blood pressure; BMI, body mass index. a_p < 0.05 vs. female children; b_p < 0.05 vs. male children.

Table 2. Pressure-Volume Regression Parameters

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<th>B2</th>
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<tr>
<td>Female Children</td>
<td>0.6800±0.3882</td>
<td>.0890±.0423</td>
<td>-</td>
</tr>
<tr>
<td>Male Children</td>
<td>0.7795±1.2536</td>
<td>.1210±.0441</td>
<td>.0007±.0005</td>
</tr>
</tbody>
</table>

Values are means ± SE. Δ Calf Volume = β0 + β1 *(cuff pressure) + β2 *(cuff pressure)^2; a_p < 0.05 vs. female children; b_p < 0.05 vs. male children.

Venous Compliance

Table 2 displays the regression parameters β0, β1, and β2 calculated (means ± SD) for female and male children. When comparing female and male pressure-volume curves derived from the calf, no significant differences were found, although the males
tended to have greater calf venous compliance ($p=.08$; Table 2 and Figure 1). No differences were observed in compliance-pressure curves between groups, suggesting calf venous compliance levels were similar in both males and females.

![Figure 1. Volume-Pressure curves (left) and Volume-Compliance Slopes (right) for female and male children. Means ± SD.](image)

The female group had significantly lower capacitance responses compared to the males (Figure 2). There were no significant differences observed in capillary filtration volumes between groups (Figure 2).

![Figure 2. Contribution of capacitance response and capillary filtration response to increase calf volume with cuff pressure application of 60 mmHg for 8 minutes. Means ± SD. $^a p<0.05$ vs. female children; $^b p<0.05$ vs. male children.](image)
CHAPTER 5
DISCUSSION

To the best of our current knowledge this is the first study to investigate differences in lower limb venous compliance between young male and female children. Based on previous observations in adult males and females (Lindenberger and Lanne, 2007b; Meendering et al., 2005; Monahan & Ray, 2004), we hypothesized female children would have lower venous compliance than their age-matched male counterparts. The findings of this study do not support our hypothesis due to the fact that no significant differences were observed in venous compliance between the female and male groups.

Sex

In 2004, Monahan and Ray found apparently healthy young females had ~48% lower calf venous compliance compared to age-matched male counterparts between the ages of 25 and 27 years old. They also observed capacitance response and found it to be lower in women compared to men at rest. Meendering et al. (2005) reported a similar finding of 26% greater calf venous compliance in males than an age-matched female group between 19 and 32 years old. While participant fitness levels were not reported, the study was limited to participants who exercised ~1-3 times per week for at least an hour per session. In 2007, Lindenberger and Lanne observed apparently healthy individuals and found females exhibited lower venous compliance than males and males had greater capacitance levels at low transmural pressures. Similar to the previous two studies discussed, fitness levels were not reported. Hernandez and Godar (2009) investigated the effects of endurance training on venous compliance, and found
that when comparing males and females between the ages of 20 to 23 of similar fitness levels, no sex differences were found in relation to compliance. The females exhibited similar venous compliance levels to their fitness-matched male counterparts. This suggests the possibility that previous findings in young adults of decreased venous compliance in females could be a result of fitness differences between the participants of each study. Hernandez and Godar (2009) also reported no sex differences in capacitance response when comparing similar fitness levels. In the current study there was not a significant difference in venous compliance between male and female children. However, male children did exhibit a greater capacitance response than the female children. According to Rowell (1993) and Monahan and Ray (2004), changes in capacitance response can occur independently of changes in venous compliance.

In 2007, Lindenderger and Lanne investigated sex differences in calf venous compliance at various transmural pressures in 22 and 23 year olds. They observed lower compliance levels in females at lower transmural pressures, but this sex difference disappeared at higher transmural pressures. The 19-26% decreased venous compliance in females reported in this study of 22 to 23 year olds is likely a result of capillary filtration being removed from the overall compliance equation. They found that when capillary filtration was not accounted for, the sex differences in compliance disappeared. It is likely that this method of quantifying differences in compliance is responsible for their findings of lower compliance in females. In the present study, capillary filtration was not accounted for. Therefore it is not a surprise that no sex differences were found in relation to compliance levels.
In a 2005 study, Meendering et al. pursued an explanation to the potential mechanisms behind the sex differences in compliance. This study observed compliance levels during the early follicular, ovulatory, and midluteal phases of the menstrual cycle, but found no significant differences. By measuring compliance levels during the various phases of the menstrual cycle, as well as comparing compliance levels in oral contraceptive users between high and low hormone phases, and finding no differences in lower limb compliance, it was concluded that fluctuating hormone levels are not responsible for increased compliance they observed in males. Other potential mechanisms responsible for changes found in previous studies in venous compliance include the structural components of the venous wall, such as elastin and collagen ratios (Lindenberger and Lanne, 2007b; Meendering et al., 2005; Monahan & Ray, 2004), as well as sympathetic stimulation, although there has been conflicting evidence in this area (Halliwill et al., 1999; Monahan & Ray, 2004).

Limitations

When interpreting the results of the current study, several things should be considered. To begin, by using venous occlusion plethysmography to assess venous compliance non-invasively, the venous collecting cuff pressure is used as a substitute for actual venous pressure. This results in a measurement of whole limb compliance, not just the lower limb, or calf, compliance. In an effort to minimize this concern, we did not analyze compliance levels when cuff pressure was below 10 mmHg.

Finally, the standard error of the compliance measurements calculated in the present study was very large, making it difficult to find statistically significant differences between groups. It is unclear as to why the large standard error was observed.
Conclusion

In conclusion, female and male children at the age of 10 years old do not exhibit significantly different calf venous compliance levels, but male children show greater capacitance volumes and a tendency toward greater compliance compared to female children. More investigation into the effects of fitness level and potential sex differences in venous compliance in this age group is necessary as the importance of venous function is continuously associated with improved cardiovascular health. With a better understanding of calf venous compliance in children we can potentially prevent issues seen in adulthood that are related to poor calf venous compliance.
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