

**ACUTE ARTERIAL STIFFNESS, TESTOSTERONE AND FORCE
PRODUCTION RESPONSES AND RECOVERY FROM DIFFER-
ENT COMBINED STRENGTH AND ENDURANCE LOADING
MODELS**

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ABSTRACT

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Much of the differences between strength (S) and endurance (E) exercise can be attributed to the contrasting endocrinological and molecular responses between the two exercise modes. From the current literature, it seems that aortic arterial stiffness, a reliable cardiovascular mortality predictor, also responds differently to these two modes of exercise. It is thus important to understand the acute responses that combined exercise loads may invoke, as acute responses are known to drive chronic adaptations. Furthermore, testosterone has been cited as a key hormone in cardiovascular protection and its effects may mediate blood flow and hemodynamics. Currently, there are very few studies investigating combined exercise loadings and its effect on central hemodynamic and endocrine response. Therefore, the purpose of the study was to determine the acute arterial stiffness and testosterone response to different concurrent strength and endurance models of exercises. In addition, the recovery profile from these loadings will also be elucidated to gain a better understanding of its time course.

A group of eight male (33.5 ± 5.9 years) recreationally endurance trained participants took part in the study. All participants took part in three loading sessions; one with S loading followed immediately by E loading (S+E), vice versa (E+S), and integrated (INT), where E and S alternated during the session. Participants were tested for their E (maximal oxygen consumption; VO_{2MAX}) and S performance (maximal bilateral dynamic leg press, 1RM) and performed all loadings in a randomized order. S primarily focused on leg extensor muscles including both maximal and explosive exercises (2 x 10 reps squat jumps, drop jumps, bounding and 3 x 10 reps leg press with 80% of 1 RM with 2min rest between the sets) and E was performed as continuous running with intensity between 80 – 85% VO_{2MAX} . Pulse wave velocity (PWV) and blood pressure values were determined pre (PRE), post (POST) and 30 minutes after (POST30). Serum testosterone concentrations, maximum voluntary contraction (MVC) and rapid force production (RFP) were determined for PRE and POST loadings and repeated after recovery of 24h and 48h.

The main findings were significant decreases in mean PWV PRE to POST (7.9 ± 0.7 m/s vs 7.3 ± 0.8 m/s, respectively) ($p = 0.017$) for combined exercise loadings and mean SBP POST to POST30min (128.0 ± 5.1 vs 134.6 ± 5.9 mmHg, respectively) ($p = 0.032$). Mean DBP had a statistically significant interaction effect between time and loading ($F(4, 28) = 3.677$, $p = 0.016$). There was a statistically significant reduction in MVC from PRE to POST (3291 ± 1007 N vs 2888 ± 804 N) ($p = 0.037$), as well as in RFP from PRE to POST (2182 ± 294 vs 1917 ± 239 N) ($p = 0.005$). In summary, the present results showed that an order effect may exist, when SBP and DBP are taken together into consideration with PWV. Combined exercise did not lead to detrimental effects in PWV and the ES order had the larger response. Additionally, INT showed the least amount of force production deficit among all three orders. These findings may be useful in assisting the exercise prescription in elderly, hypertensive and pre-hypertensive populations.

Keywords: arterial stiffness, PWV, order effect, combined exercise, blood pressure

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TABLE OF CONTENTS

ABSTRACT

ACKNOWLEDGEMENTS

TABLE OF CONTENTS

1	INTRODUCTION	5
2	MODES OF EXERCISE	8
2.1	Strength.....	8
2.2	Endurance	10
2.3	Concurrent/combined	11
2.3.1	Differences in single session construct (Acute)	14
2.3.2	Differences in training construct (Chronic)	15
3	EXERCISE STRESS	17
3.1	Acute response vs chronic adaptation	17
3.2	Hormonal responses and mechanisms.....	19
4	ARTERIAL STIFFNESS	21
4.1	Effects of Exercise.....	21
4.2	Combined Exercise Response	23
5	PURPOSE.....	27
5.1	Research hypothesis	27
6	METHODS	28
6.1	Participants	28

6.2	Ethical Approval.....	28
6.3	Experimental design	29
6.3.1	Baseline measurements.....	29
6.3.2	Arterial Stiffness	32
6.3.3	Loading Protocols	33
6.4	Statistical Analysis	35
7	RESULTS	36
7.1	Vascular and hemodynamic changes	36
7.2	Testosterone.....	39
7.3	Force production.....	40
8	DISCUSSION.....	43
8.1	Arterial Stiffness.....	43
8.2	Blood Pressure.....	44
8.3	Testosterone.....	46
8.4	Force Production	47
8.5	Study Strengths and Limitations	50
9	CONCLUSION.....	52
10	REFERENCES	53

1 INTRODUCTION

Since the discovery of the interference effect from concurrent training more than two decades ago (Hickson 1980), the sports science community has expanded its research in the area, notably with the detection of the “order effect” (Schumann et al. 2014) and the comparisons between same and different day orders (Eklund et al. 2015). When comparing between exercise modes, it is imperative that the forms of exercise are distinguished clearly, as both acute responses and training adaptations take distinct and often divergent pathways primarily from the systemic level (Kraemer & Rogol 2006) down to the finer molecular level (Fyfe et al. 2014). Exercise modes may be broadly defined between endurance and strength.

Endurance exercise has been well documented to provide several health benefits (Tipton 2006) many of which stem from an increase in the rate of energy production from all the energy producing pathways (Levine 2008; Baker et al. 2010). These adaptations lead to increases in the utilization of oxygen, thereby increasing endurance-related markers such as VO_2 max, and exercise/running economy. Similar to endurance exercise, strength exercise has its host of benefits as well, primarily increases in muscle mass (hypertrophy), strength and/or power (Vingren et al. 2012). However, these improvements differ largely from endurance-induced increments, as studies have shown that endurance exercise causes more oxidative stress on the homeostatic environment (Baar 2014) thereby generating a different stress response from the endocrine system. Typically, endurance exercise loads create a relatively more catabolic environment as opposed to strength loads, which tend to be more anabolic (Daly et al. 2005).

These differences are brought upon by the opposing nature of the major hormones in question, testosterone and cortisol; due to the fact that the two share common upstream precursors in the form of pregnenolone and progesterone (Descheues 2000; Hackney 2001). Using that information, we can thus compare between testosterone and cortisol using the testosterone-to-cortisol ratio to gain a better understanding as to what the acute systemic responses are to different exercise loadings, especially since acute responses are what drives chronic adaptations (Kraemer & Ratamess 2004).

Schumann and colleagues (2014) have done an elegant study investigating acute neuromuscular and hormonal responses and recovery between different loading orders in a single session. In that study, the exercise loading order of strength followed by endurance (SE) and endurance followed by strength (ES) was thoroughly compared and evaluated. However, the question remains as to what kind of response would an integrated (INT) combined strength and endurance session elicit. Figure 1 illustrates the various different structures of training sessions.

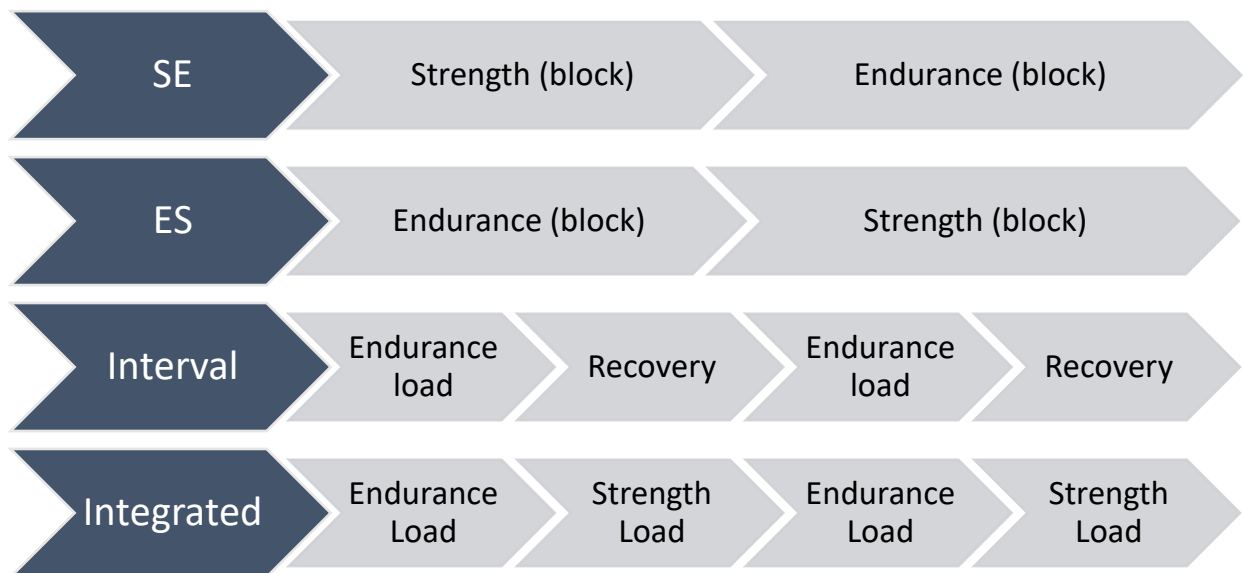


Figure 1. Different approaches to exercise session construct. Note: Hypothetically matched volume and total duration. All exercises are performed with rest in between sets except for endurance training blocks. Endurance training exercises and blocks performed at same relative intensity. For illustration purposes only; number of exercises in interval and integrated sessions are usually greater with short duration i.e. 3-5 minutes

Endurance interval training have been extensively studied (Billat 2001; Foster et al. 2015) and when strength training is performed in a continuous “circuit” or interval fashion (Monteiro et al. 2008; Wilmore et al. 1977), it mimics a response closer to that of endurance exercise (Camargo et al. 2008). Understanding the different responses to combined training session structures will provide a valuable framework to study integrated strength and endurance sessions.

Lately, different exercise modes and its effects on arterial stiffness have also been reviewed (Montero et al. 2015). The measurement of arterial stiffness through pulse wave velocity (PWV)

is the current gold standard and an independent predictor of cardiovascular events in patients with established cardiovascular disease as well as in healthy adults (Vlachopoulos et al. 2010). Indeed, exercise modality seems to exert an influence on arterial stiffness. Studies investigating arterial stiffness using strength training have shown that there is an increase in PWV in young adults, however, the physiological mechanisms underlying this effect is still unclear (Miyachi 2012). Furthermore, this effect is less pronounced in middle-aged adults. On the other hand, endurance training studies have unequivocally shown that PWV is significantly reduced (Montero et al. 2015), but it must be noted that this effect is only evident when there is a parallel decrease in blood pressure (Montero et al. 2014).

Currently, the majority of research regarding PWV have been done on the clinical population (hypertensive and obese), and these results may not translate accurately to the normal populations. Furthermore, most studies done reflect the long term adaptations to training, while the acute effects remains to be elucidated. It is of significance to understand what the acute mechanisms may be, considering that combined training intervention studies have seen differences in PWV with changes in training frequency (Miura et al. 2008), exercise order (Okamoto & Masuhara 2007), as well as structure (Guimarães et al. 2010).

To our best knowledge, no study on acute arterial stiffness and hormonal response has been done using an integrated exercise session structure, even though it is widely practiced by personal trainers on their clients, used by many recreationally active individuals and large exercise communities such as in Crossfit™. Given the benefits gained from using both strength and endurance exercise, understanding the acute effects of different combined exercise loadings on PWV will help us to establish a valuable framework which we can expand upon to optimize training prescriptions to both the healthy and clinical populations.

2 MODES OF EXERCISE

Broadly defined, sports science literature categorizes exercise into two common, but distinct modes, strength (resistance) training and endurance training (Hickson 1980; Leveritt et al. 1999; Tipton 2006). The various exercise performance and health adaptations between the two modes are summarized in Table 1. Although both modes provide numerous positive health benefits and performance adaptations, it is important to distinguish between the two forms as they both have intricate differences in cell signaling pathways, which leads to divergent acute responses (Beattie et al. 2014; Fyfe et al. 2014; Hawley et al. 2014).

2.1 Strength

Strength training typically involves the use of resistance to stimulate the skeletal and neuromuscular system, thus the term resistance training and strength training are often used interchangeably (Spiering et al. 2008, 2009). Typically, the acute responses of strength training include increases in serum testosterone, cortisol, growth hormone and insulin-like growth factor (IGF) levels, which in turn facilitate the increase in long term strength and hypertrophic gains through a cascade of signaling events on the molecular level (Hawley et al. 2014; Spiering et al. 2009). However, these increases and their magnitude of change may differ, based on exercise load, volume, intensity and even the type of contraction, as seen in previously well documented studies (Hakkinen & Pakarinen 1993; Kraemer & Rogol 2006; Paavolainen et al. 1999; Walker et al. 2013).

It has been well documented in research and practice that the process of strength training involves inducing mechanical shear stress on the muscle fibers to elicit acute responses which over a prolonged period of time (4 – 6 weeks), leads to positive chronic adaptations (Crewther et al. 2006; Kraemer & Ratamess 2004; Uchida et al. 2009). Strength training also leans heavily toward the use of type II muscle fibers, which is one of the reasons we often see improved neuromuscular adaptations through motor unit recruitment patterns, and resultant force changes with improved mechanical efficiency and force-velocity relationships (Farup et al. 2012; Shaw & Shaw 2009; Spiering et al. 2008).

Table 1. Differences in adaptations between strength and endurance exercise (Adapted from “Exercise Metabolism and the Molecular Regulation of Skeletal Muscle Adaptation,” by Egan & Zierath, 2013)

	Aerobic (Endurance)	Resistance (Strength)
Skeletal Muscle Morphology and Exercise Performance		
Muscle hypertrophy	↔	↑ ↑ ↑
Muscle strength and power	↔ ↓	↑ ↑ ↑
Muscle fiber size	↔ ↑	↑ ↑ ↑
Neural adaptations	↔ ↑	↑ ↑ ↑
Anaerobic capacity	↑	↑ ↑
Myofibrillar protein synthesis	↔ ↑	↑ ↑ ↑
Mitochondrial protein synthesis	↑ ↑	↔ ↑
Lactate tolerance	↑ ↑	↔ ↑
Capillarisation	↑ ↑	↔
Mitochondrial density and oxidative function	↑ ↑ ↑	↔ ↑
Endurance capacity	↑ ↑ ↑	↔ ↑
Whole-Body and Metabolic Health		
Bone mineral density	↑ ↑	↑ ↑
Body composition		
Percent body fat	↓ ↓	↓
Lean body mass	↔	↑ ↑
Glucose metabolism		
Resting insulin levels	↓	↓
Insulin response to glucose challenge	↓ ↓	↓ ↓
Insulin sensitivity	↑ ↑	↑ ↑
Inflammatory markers	↓ ↓	↓
Resting heart rate	↓ ↓	↔
Stroke volume, resting and maximal	↑ ↑	↔
Blood pressure at rest		
Systolic	↔ ↓	↔
Diastolic	↔ ↓	↔ ↓
Cardiovascular risk profile	↓ ↓ ↓	↓
Basal metabolic rate	↑	↑ ↑
Flexibility	↑	↑
Posture	↔	↑
Ability in activities of daily living	↔ ↑	↑ ↑

Aerobic exercise training generally encompasses exercise durations of several minutes up to several hours at various exercise intensities, incorporating repetitive, low-resistance exercise such as cycling, running, and swimming. Resistance training generally encompasses short-duration activity at high or maximal exercise intensities, and increases the capacity to perform high-intensity, high-resistance exercise of a single or relatively few repetitions such as Olympic weightlifting, bodybuilding, and throwing events. ↑, values increase; ↓, values decrease; ↔, values remain unchanged; ↑ or ↓, small effect; ↑ ↑ or ↓ ↓, medium effect; ↑ ↑ ↑ or ↓ ↓ ↓, large effect; ↔ ↑ or ↔ ↓, no change or slight change.

Training status seems to also have an influence on the acute strength training induced physiological change, and it has been shown that in a relatively untrained state, these changes are greater. This may possibly be attributed to the larger disturbance to homeostasis (Damas et al. 2015; Hausswirth & Mujika 2013, 5). Nutrition status of an individual is another factor that warrants consideration, as fed and fasted states can either amplify or attenuate the responses respectively (Beattie et al. 2014; Wilkinson et al. 2008). The pathway from acute response to adaptations to strength training are illustrated in Figure 2.

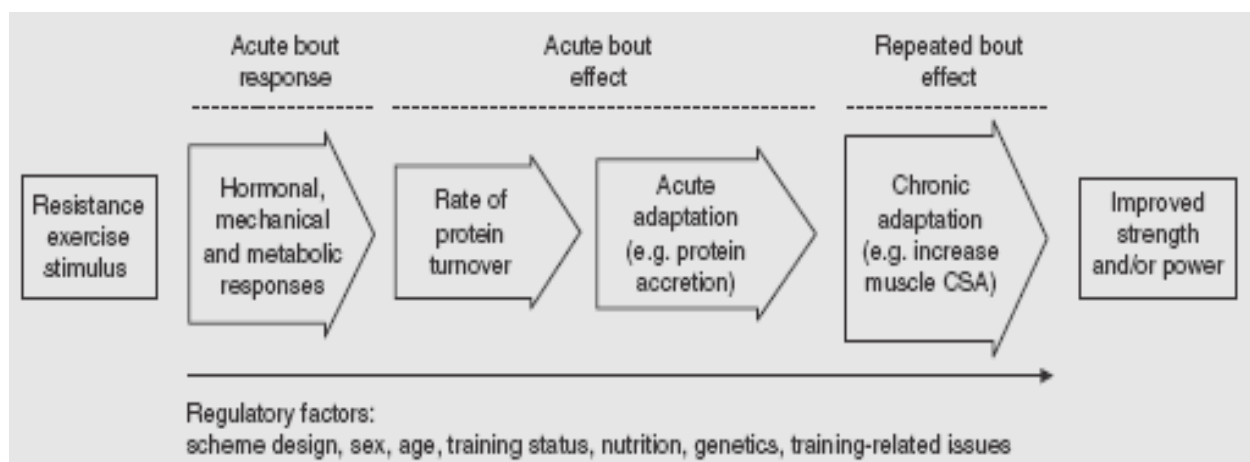


Figure 2. Pathway to resistance exercise adaptation. From “Acute Metabolic Responses,” by Crewther et al. 2006.

2.2 Endurance

As opposed to strength training, endurance training relies more heavily on the cardiovascular system, and as such, is often deemed to be more physiologically demanding (Amann 2012; Volek et al. 2015; Wilkinson et al. 2008). Where the key to positive changes through strength training is more neuromuscular and mechanical in nature, endurance training is dependent on the effective use of the three major energy pathways as a result of the metabolic stress placed on the system (Baker et al. 2010; Gastin 2001).

Benefits of endurance training include the more efficient use of oxidative pathways for adenosine triphosphate (ATP) regeneration and production, improved H⁺ (hydrogen) buffering capacity and exercise economy through lowered cardiac output (Baker et al. 2010; Midgley et al. 2007; Tipton 2006). Muscle fiber use and phenotype shift is also an important factor to acknowledge with regards to the two forms of training.

Endurance training engages more of the type I slow twitch muscle fibers, and chronic adaptations include an improved oxidative capacity of these fibers and more effective utilization of fat and triglycerides for fuel. (Billat 2001; Farup et al. 2012; Volek et al. 2015). While strength exercises typically induces higher levels of fatigue due in part to a higher level of muscular activation, endurance training requires lower levels of force production at a more repetitive rate (Taipale & Häkkinen 2013; Wilson et al. 2012).

2.3 Concurrent/combined mode

In spite of the differences outlined, strength and endurance training are often performed concurrently by the vast majority of physically active populations; with the goal of improving both performance capabilities, and work economy. Indeed, several exercise prescription guidelines by major health organizations such as the American College of Sports Medicine (ACSM) (Pescatello et al. 2013) have recommended the use of concurrent training. Table 2 compares the physiological outcomes between strength, endurance, and combined exercise.

Consequently, the importance of utilizing concurrent training in the athletic population should not be overlooked as well, as performance benefits from both strength and endurance training are fundamental for sporting success (Baar 2014; Hawley et al. 2014; Leveritt et al. 1999). However, because of overtraining concerns (Descheues 2000; Hausswirth & Mujika 2013, 9), the constraint of time (Schumann et al. 2015), and the prevalence of the interference effect, much of the research has been directed towards investigating ways to optimize performance gains through a “minimization” of the interference effect whilst maximizing the effective use of concurrent training (Baar 2014; Beattie et al. 2014; Hawley et al. 2014; Robineau et al. 2014).

Table 2. Comparison of data from large clinical trials (Adapted from “Combined Aerobic and Resistance Training Effects on Glucose Homeostasis, Fitness, and Other Major Health Indices: A Review of Current Guidelines” by Johannsen et al. 2016)

Health outcome	Resistance exercise	Aerobic exercise	Combined exercise
Body weight	↔	↓	↓
Total body fat	↓	↓↓	↓↓
Intra-abdominal fat	↓↔	↓↓	↓↓
Lean body mass	↑↑	↔	↑↔
Resting metabolic rate	↑↑	↑	↑
Peak VO ₂	↑↔	↑↑↑	↑↑↑
Submaximal and maximal endurance	↑↑	↑↑↑	↑↑↑
Muscular strength	↑↑↑	↔	↑↑
Muscular power	↑	↔	↑
Glycated hemoglobin (HbA _{1c})	↓↔	↓↓	↓↓↓
Insulin sensitivity	↑↑	↑↑	↑↑↑
SBP at rest	↓	↓↓	↓↓
DBP at rest	↓	↓↓	↓↓

↑ indicates increased, ↓ indicates decreased, ↔ indicates negligible effect; 1, 2, and 3 arrows indicate small, moderate, and large effects, respectively

DBP diastolic blood pressure, *HbA_{1c}* glycated hemoglobin A1c, *SBP* systolic blood pressure, *VO₂* oxygen uptake

Studies have shown that the frequency of endurance training in a concurrent training program has a strong bearing on the interference effect, especially on hypertrophy (Wilson et al. 2012). Although unwarranted, this compromise on hypertrophy is often overlooked as the addition of strength training in an endurance athlete’s program has been shown to lead to better performance both in runners (Paavolainen et al. 1999) and in cyclists (Rønnestad & Mujika 2014). Figure 3 is a simple representation of the sequence of molecular events leading to the likely outcomes of hypertrophy for strength exercise, and mitochondrial biogenesis for endurance exercise.

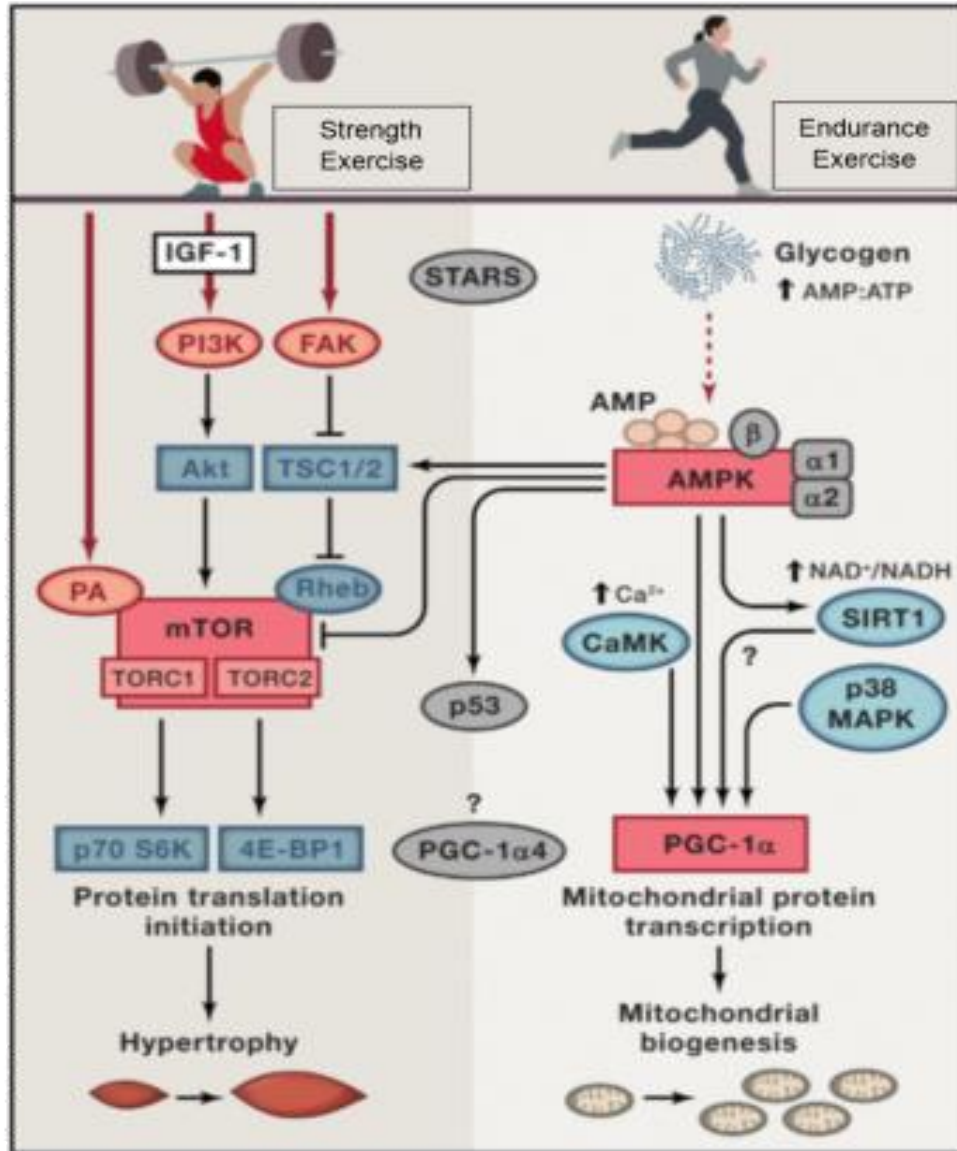


Figure 3. Differences in molecular signaling pathways between strength and endurance training (From “Integrative biology of exercise,” by Hawley et al., 2014)

At the onset, many of these studies focused on understanding the long term effects of concurrent training when strength and endurance sessions were performed on different days (Häkkinen et al. 2003; Hennessy & Watson 1994; Hickson 1980). With a growing trend in the scarcity of training time, this gradually evolved into experiments where combined strength and endurance training sessions were conducted on the same day (Gravelle & Blessing 2000; Robineau et al. 2014), to the more prevalent single session construct; where the differences in the ordering of

strength and endurance protocols were examined (Schumann et al. 2013, 2014). More recently, Eklund and colleagues (2015) conceived a novel study that investigated the differences between same day concurrent training with different orders together with different day concurrent training.

2.3.1 Differences in single session construct (Acute)

The question of whether the order of endurance and strength training combined in a single session plays a role with regard to neuromuscular and endocrine changes and recovery have received much attention in recent years (Cadore et al. 2012; Eklund et al. 2015; Schumann et al. 2013, 2014), and has led to many useful practical recommendations. In Cadore's (2012) study, testosterone and cortisol responses were found to be higher after the first exercise modality compared to the second, regardless of the order, but the response of testosterone after performing endurance-strength sessions (ES) were greater than strength-endurance sessions (SE). Additionally, they postulated that cortisol may have an inhibitory effect on testosterone, suggesting that an order effect may exist. It was concluded that ES may be better in terms of optimizing muscular hypertrophy when considering combined training. However, the authors cautioned that the results may have been due to increased receptor binding after the SE order and not from a decrease in secretion per se.

Schumann and colleagues (2013) proceeded to thoroughly investigate the order effect, and found that it takes a longer time for the endocrine system to recover from an ES order as opposed to an SE order, although no significant differences in neuromuscular recovery were found. The authors discovered that endocrine function represented by testosterone, cortisol and thyroid stimulating hormone remained suppressed even after 48 hours for the ES order. The study was able to clearly show that the true recovery status of the endocrine system may not be related to, or reflected by the neuromuscular indices; in that the time course of recovery may be different between the endocrine and neuromuscular system.

2.3.2 Differences in training construct (Chronic)

After having found the acute responses of the order effect, this same group of researchers followed up with a training intervention study to determine what the long term effects would be between training using SE and ES orders (Schumann et al. 2014). However, the research found no difference between SE and ES orders after 24 weeks, although the authors did conclude that a high training frequency especially in the early phase, may have a negative impact on training outcomes due to the prolonged requirement of recovery from the ES order.

With a well-designed study, Eklund et al (2015) took another step forward and compared the differences between orders (SE and ES) and combined training of different modalities on different days (DD) in the week. This 24 week training study found that voluntary activation increased with SE and DD order and that SE had an increase in maximal EMG. It is evident from these results that favorable neural adaptations may have been compromised through the long term use of ES order. It was thus concluded that a larger training volume, longer period of training and/or training frequency, stands to result in a more severe neural inhibition, when using the ES order. Table 3 shows a short list of studies and the different combined session constructs they have investigated and compared.

Table 3. Comparison of different combined training session structures

Study, year of publication	Endurance Training (E)		Strength Training (S)	Structure Comparison
	Mode	Duration	Description	
	Monteiro et al., 2008	Treadmill	30 sec @ 60% HR _{MAX}	
Cadore et al., 2012	Cycling	30 min @ 75% HR _{MAX}	4 exercise, 3 sets, 8 reps @ 75% 1RM; bench press, squat, lat pull-down, knee extension	ES vs SE
Schumann et al., 2013	Cycling	30 min @ 65% Watts _{MAX}	30 min; 3 sets, 10 reps @ 40% 1RM (explosive); 3 sets, 3 reps @ 90% 1RM (strength); 4 sets, 10 reps @ 75%-85% 1RM (hypertrophy)	ES vs SE
Rosa et al., 2015	Treadmill	32 min; 2 min @ 2mmol/L Bla, 1 min @ 4mmol/L Bla	6 exercise, 3 sets, 10 reps @ 70% 1RM for bench press, squats, leg press, lat pull-down; 3 sets, 30 reps for abdominal crunch and back extension (bodyweight)	ES vs SE
Eklund et al., 2015 (training study)	Cycling	30-45 min @ HR-based thresholds (aerobic/anaerobic)	Progressive periodized; circuit to hypertrophy to maximal strength; leg press, knee extension and flexion	ES vs SE vs DD

Note: INT, integrated; E, endurance; S, strength; DD, different day; HR_{MAX}, maximum heart rate; reps, repetitions; 1RM, 1 repetition maximum.

3 EXERCISE STRESS

Athletes use regular training to overload their physiological and cognitive systems, to induce acute responses that promote positive adaptations in attempts to improve performance. Physical training and exercise is thus, a significant source of physiological and psychological stress for the body which could be muscular, energetic or hormonal in nature (Issurin 2010). The demands of such training and stimuli are exceptionally large for most athletes, therefore, it is critical that the most ideal adaptation is ensured for both short and long-term performance success. (Hauswirth & Mujika 2013, 4; Roose et al. 2009). The physically active population however, are not usually subjected to such levels of exercise stress; a result of which means optimum well-being and health benefits through exercise need to be accounted for.

Physical exercise is a stressor to the human body and is often an activator of the neuroendocrine system, especially when the exercise load is sufficient; be it volume, intensity and/or duration. This usually generates a variety of stress responses within the endocrine system, such as increases in circulating testosterone, growth hormones and cortisol (Gomes et al. 2013; Hackney 2006). However, chronic exercise training is also known to cause a gradual decline in exercise stress responses of the endocrine system, where there is an inadvertent reduction in hormonal stress response to submaximal exercise (and sometimes even maximal exercise), accompanied by reduced circulating basal hormone levels (Daly et al. 2005; Hackney 2001; Kraemer & Rogol 2006). It is, therefore, vital to identify and understand the hormonal mechanisms which govern exercise training responses acutely and chronically for both strength, endurance, and combined exercise loads.

3.1 Acute response vs chronic adaptation

Hormonal adaptations to exercise training can be denoted under four general classifications: 1) acute changes during exercise and post-exercise; 2) chronic changes in resting concentrations, as a result of long-term training; 3) chronic changes in the acute response to an exercise stimulus, as a result of long-term training; and 4) acute and chronic changes in receptor content (Daly et al. 2005; Kramer & Hakkinen 2008; Hauswirth & Mujika 2013, 4; Willoughby & Taylor 2004).

Other noteworthy factors, such as nutrition, training experience, sex, age and/or maturity, interaction with other modes of training (e.g., endurance training), diurnal variations, as well as the training program design, affect the hormonal responses and adaptations to exercise (Ratamess et al. 2005). Figure 4 is a simplistic outline of the process.

Hormones are produced by glands in the endocrine system and are released to the blood stream in response to the different stresses that the body is put under. They bind to very specific receptors to dictate and regulate cellular activity, as well as bodily functions (Brownlee et al. 2005; Hackney 2001; Borer 2013, 5). The two key hormones which determined that are testosterone and cortisol, respectively.

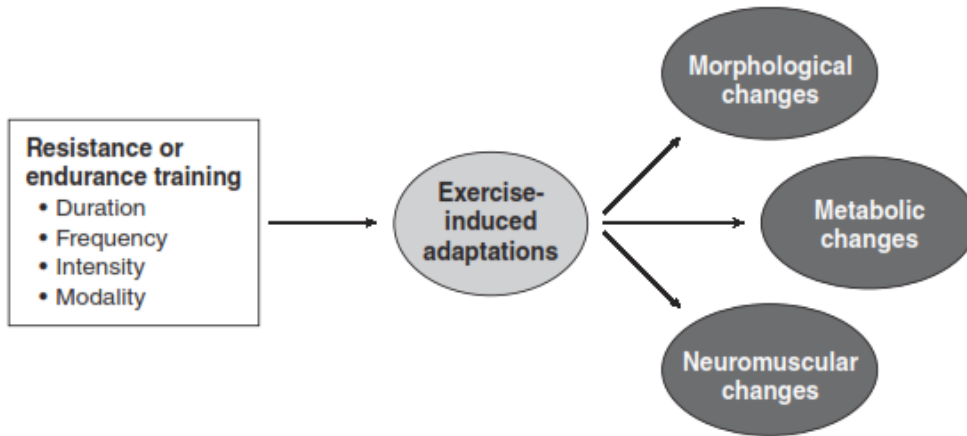


Figure 4. Pathway to exercise adaptation (From “Recovery from performance in sport,” by Hausswirth & Mujika, 2013)

Although the endocrine system is tightly governed by these hormones to maintain a constant state of homeostasis, its internal environment may be described as a continuum between anabolic and catabolic states (Brownlee et al. 2005). With elevated levels of testosterone, the system can be considered anabolic, where there is protein synthesis and cell proliferation. High levels of cortisol usually leads to catabolism and protein degradation, whereby structures are broken down (Descheues 2000; Hawley et al. 2014; Hill et al. 2008; Kraemer & Rogol 2006).

3.2 Hormonal responses and mechanisms

It has been well documented that testosterone plays a vital role in the homeostasis of the endocrine system. Substantial research has established that testosterone is a key factor in determining body composition, and in particular, muscle mass (Herring et al. 2013; Vingren et al. 2012; West & Phillips 2010). Current research has shown that testosterone deficiency is a risk factor in cardiovascular disease (Aversa & Morgentaler 2015), and increases in testosterone mediate improved endothelial vasomotor function, possibly lowering blood pressure and arterial stiffness (Hayes et al., 2015; Kumagai et al., 2014). Thus, the influence of exercise on hormonal response and possible long term changes cannot be ignored.

Testosterone may be determined in a few ways, by measuring serum levels, through the use of sex-hormone binding globulin (SHBG), to detect levels of free testosterone, or going a step further and identify the levels of biologically active testosterone (BAT). BAT is made up of unbound free testosterone and albumin-bound testosterone (weak bound). It has been suggested that BAT has access to all cells, thereby making it more androgenic and helpful in a larger number of applications, especially in sports and exercise science (Vingren et al. 2012).

Testosterone also controls the expression of important regulatory proteins involved in glycolysis, glycogen synthesis, and lipid and cholesterol metabolism (Kelly & Jones 2013; Rao et al. 2013). Thus, testosterone deficiency often leads to increased fat mass, reduced insulin sensitivity, and impaired glucose tolerance amongst other ailments. Conversely, elevated endogenous basal testosterone levels have been shown to reduce cardiovascular risk (Kvorning et al. 2006; Ong et al. 2000). This is made possible via several mechanisms, namely cardio-protection, vasodilation and testosterone's interaction with insulin and lipids (Herring et al. 2013).

Given that greater cardiovascular benefits can be achieved through improved metabolic function associated with higher testosterone levels (Kumagai et al. 2014; Ohlsson et al. 2011), the exercise science community has focused much of its research on this hormone. Numerous studies

have shown that exercise raises testosterone levels (Häkkinen et al. 2003; Paavolainen et al. 1999; Taipale & Häkkinen 2013). In this regard, it must be noted that strength exercise has a greater effect on testosterone than endurance exercise (Ahtiainen et al. 2009; Hakkinen & Pakarinen 1993; Schumann et al. 2014), and increases in serum basal testosterone levels arising from concurrent training may be attributed to the strength component.

Cortisol on the other hand, is catabolic in nature and is released from the adrenal cortex in response to both physical and psychological stress. It has previously been shown that a significant negative relationship exists between cortisol and testosterone post exercise (Brownlee et al. 2005); and this is further augmented with increases in the intensity or duration of exercise (Daly et al. 2005). It has been postulated that workloads resulting in high metabolic stress will lead to increases in cortisol, regardless of modes (Hackney 2006), and that hypertrophic resistance training provokes cortisol levels the least, with a concurrent increase in testosterone (Kraemer & Rogol 2006; Kraemer & Ratamess 2004). However, some forms of heavy resistance training have also been shown to elicit a parallel increase in both testosterone and cortisol (Häkkinen et al. 1985; Häkkinen et al. 2003; Vingren et al. 2012), proving the volatility and difficulty in establishing a consensus on their relationship and the influence of exercise.

Nevertheless, studies have shown that an increase in basal cortisol levels is associated with reduced strength and muscle mass (Cadore et al. 2012; Kraemer et al. 1995). Because of the differences in responses and actions of these hormones, results from studies on these hormones should be interpreted with caution as hormonal measurements can be influenced by several factors such as age, gender, variations (diurnal, circadian and rhythmic), physical state of the individual(s), as well as training status (Descheues, 2000). The endurance trained population were found to have suppressed levels of resting testosterone (Daly et al. 2005; Hackney 2006), while individuals exposed to long term resistance training had heightened resting levels. However, the endurance trained population had a larger hormonal response from resistance training than their resistance trained counterparts (Vingren et al. 2012). Thus, confounding factors associated with hormonal responses should be carefully considered when applying to practical situations.

4 ARTERIAL STIFFNESS

Arterial stiffness has recently been recognized as a risk factor in cardiovascular disease and mortality (Mitchell 2009; Sakuragi & Abhayaratna 2010). Studies have shown that arterial stiffness is better in predicting cardiovascular mortality than brachial blood pressure (Franklin 2008; Vlachopoulos et al. 2010), and increased arterial stiffness is independently associated with adverse cardiovascular events (Dekker et al. 2014; Elias 2011). Arterial stiffness can be determined from a number of arterial sites, such as between the brachial artery and the arteria dorsalis pedis or between the femoral and tibial artery. However, carotid-femoral pulse wave velocity (PWV) remains the gold standard in the measurement of arterial stiffness both in clinical and daily practice (Mitchell 2009; Van Bortel, Luc et al. 2012; Vlachopoulos et al. 2010), as it corresponds best to the propagative model of the arterial system (Elias 2011; Franklin 2008; Laurent et al. 2006).

4.1 Effects of Exercise

Regular physical activity as well as exercise training seems to be effective in reducing arterial stiffness (Montero et al. 2014; Padilla et al. 2013), although results from these studies indicate that populations suffering from hypertension or obesity do not share the same benefits. In normal healthy populations, however, endurance training is frequently associated with lower arterial stiffness (Montero et al. 2013), although the influence of endurance training modality on these results and the mechanisms by which they operate still remain very much unclear (Alkatan et al. 2016; Montero 2016).

On the contrary, strength training studies have frequently reported an unfavorable response (Li et al. 2015; Montero et al. 2014; Romero et al. 2011). This difference in arterial stiffness response between strength and endurance exercise also seems to exist in acute settings. For instance, in a study comparing acute responses, eight resistance exercises performed at moderate intensity (10 repetition max 90 seconds rest between sets) showed an increase in PWV, while 30 minutes of stationary cycling at 65% VO_{2PEAK} had a significant reduction (Heffernan et al. 2007).

Although evidence from the literature suggests that it is high intensity strength training that increases arterial stiffness, and that moderate training intensity may not have the same effects (Miyachi 2012), results from acute studies seem to consistently show increases in PWV through strength exercise in spite of the exercise intensity. Figure 5 shows a meta-analysis of strength training and its effect on arterial stiffness. In a study done by DeVan and colleagues (2005), arterial stiffness showed an increase in response to acute resistance exercise at moderate intensity (75% 1RM), although this effect did not last longer than 60 minutes. In a more recent experiment, eight resistance exercises performed at 60% of 1 repetition max also registered an acute increase in PWV in young healthy men (Yoon et al. 2010). Indeed, these experiments highlight the fact that acute responses and chronic adaptations may not always be in parallel.

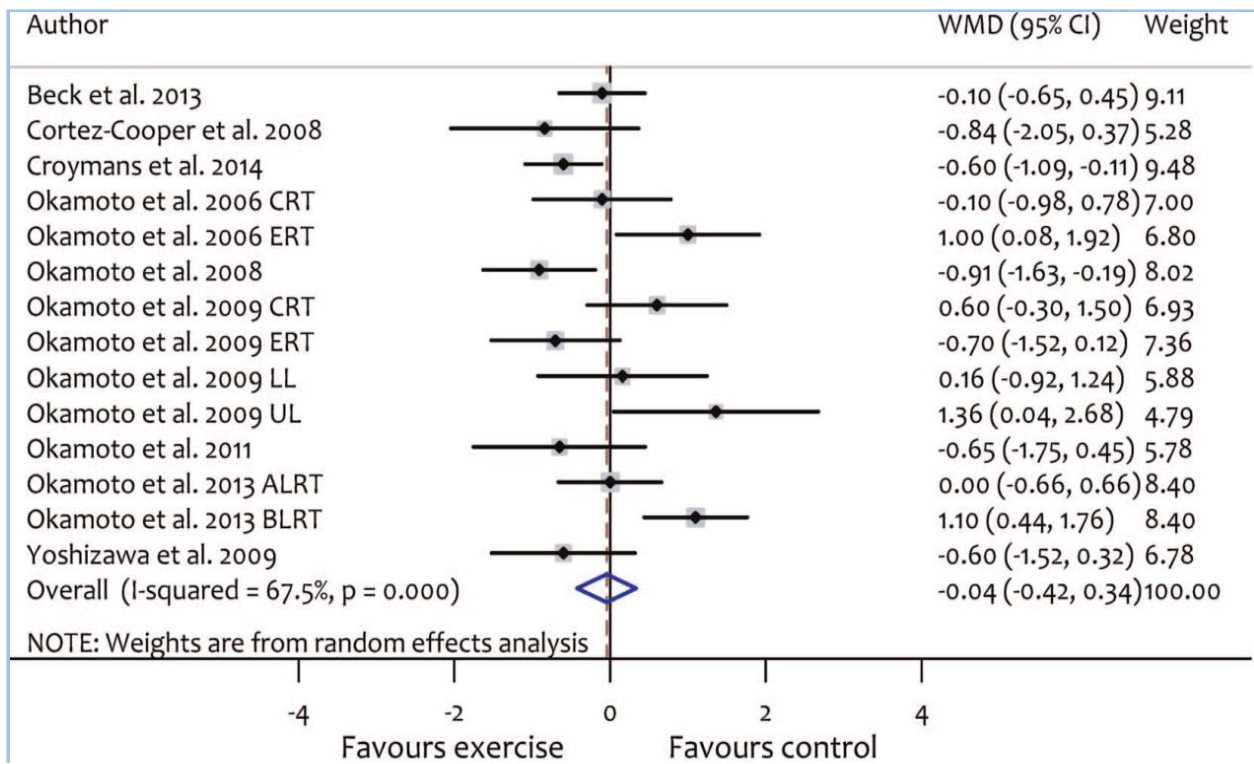


Figure 5. Comparison of strength training studies and its effect on PWV (From “Effects of Exercise Modalities on Arterial Stiffness and Wave Reflection: A Systematic Review and Meta-Analysis of Randomized Controlled Trials” by Ashor, Lara, Siervo, Celis-Morales, & Mathers, 2014)

However, in a more recent experiment, Li and colleagues (2015) found that compared to whole and lower body resistance exercise, it was upper body resistance exercise that resulted in an acute elevation of arterial stiffness, while lower body resistance exercise culminated with opposing results. The authors concluded that from a cardiovascular perspective, lower and whole body resistance training is preferred over upper body resistance training; especially in individuals with impaired arterial stiffness. Careful consideration of these findings should be made, as most endurance exercises involve the use of the lower limbs (cycling, running) and the exclusive use of lower limb resistance exercise in this study may have implicated the results.

4.2 Combined Exercise Response

Currently, there appears to be a lack of studies detailing the acute response of arterial stiffness to different training modes. Nonetheless, many long-term combined training studies investigating adaptations of arterial stiffness exist; these studies are helpful in providing insight into how exercise modality and session structure may be a factor influencing optimum exercise prescription. A summary of these studies are detailed in Table 4. In one of the first few studies investigating arterial stiffness and combined training, Kawano et al (2006) were able to show that the inclusion of an endurance training component to moderate intensity resistance training attenuated PWV when compared to resistance training alone. The authors thus concluded that endurance training should be performed with resistance training in order to prevent arterial stiffening.

From later studies, however, it seems that performing strength exercise (hypertrophic protocol) after endurance exercise has a negative effect on arterial stiffness after 8 weeks of training (Okamoto & Masuhara 2007); while a more recent study showed a modest decrease in arterial stiffness with the same session structure (Guimarães et al. 2010). Caution must be paid to the interpretation of these results, as the strength protocol used in the study was likely not of comparable intensity. Conversely, when endurance exercise is performed after strength, favorable results are consistently seen, even when strength training intensity was high (Okamoto & Masuhara 2007), and especially when training frequency was increased (Figuroa et al. 2011).

Table 4. Concurrent training studies and effects on arterial stiffness

Study, year of publication	Endurance Training (E)			Strength Training (S)		Construct	Sessions (weekly)	Study duration	Arterial stiffness
	Mode	Duration	Intensity	Description	Intensity				
	Figueroa et al., 2011	Treadmill	20 min	60% HR _{MAX}	9 EX, 1 set, 12 reps				
Guimaraes et al., 2010	Treadmill	60 min	60% HRR	20 min submaximal		E + S	3	16 weeks	↓
Loimaala et al, 2009	Jogging	> 30 min	65-75% VO _{2MAX}	8 EX, 3-4 sets, 10-12 reps	70% 1RM	Different day	2S + 2E	103 weeks	↓
Miura et al., 2008	Chair-based	20 min	75.4% HR _{MAX}	6-8 EX, 3-5 sets, 15-20 reps	50% 1RM	S + E	1	12 weeks	=
Miura et al., 2008	Chair-based	20 min	75.4% HR _{MAX}	6-8 EX, 3-5 sets, 15-20 reps	50% 1RM	S + E	2	12 weeks	↓
Cortez-Cooper et al., 2008	Cycling	30-45 min	60-75% HRR	10 EX, 2 sets, 8-12 reps	60% 1RM	Different day	2	13 weeks	↓
Okamoto et al., 2007	Treadmill	20 min	60% HRR	7 EX, 5 sets, 8-10 reps	80% 1RM	E + S	2	8 weeks	↑↑
Okamoto et al., 2007	Treadmill	20 min	60% HRR	7 EX, 5 sets, 8-10 reps	80% 1RM	S + E	2	8 weeks	↓↓
Stewart et al., 2005	Treadmill, cycling, stair stepper	43 min	60-90% HR _{MAX}	7 EX, 2 sets, 10-15 reps	50% 1RM	S + E	3	26 weeks	↑

Note: HR_{MAX}, maximum heart rate; HRR, heart rate reserve; VO_{2MAX}, maximum oxygen consumption; EX, exercises; reps, repetitions.

In this regard, it could be argued that the decrease in blood pressure as a result of resistance exercise training adaptation (Croymans et al. 2014; Cornelissen & Fagard 2005; Stone et al. 1991), might have led to the decreases in PWV. A training study done by Romero et al (2011) showed that PWV was unchanged after 12 weeks of whole body circuit training performed using resistance and endurance exercise at moderate intensity. This is in agreement with the literature, which showed that moderate intensity exercise, whether resistance-based (Miyachi 2012) or endurance-based (Montero et al. 2014), do not register significant changes to PWV. Similarly, in one of the few acute studies investigating PWV and combined strength and endurance exercise (Durocher et al. 2015), PWV did not show any significant changes from an acute bout of combined exercise. Furthermore, results from this experiment also seem to indicate that there was no order effect of exercise modality on arterial stiffness. Data from a systematic review of combined strength and endurance studies are shown in Figure 6.

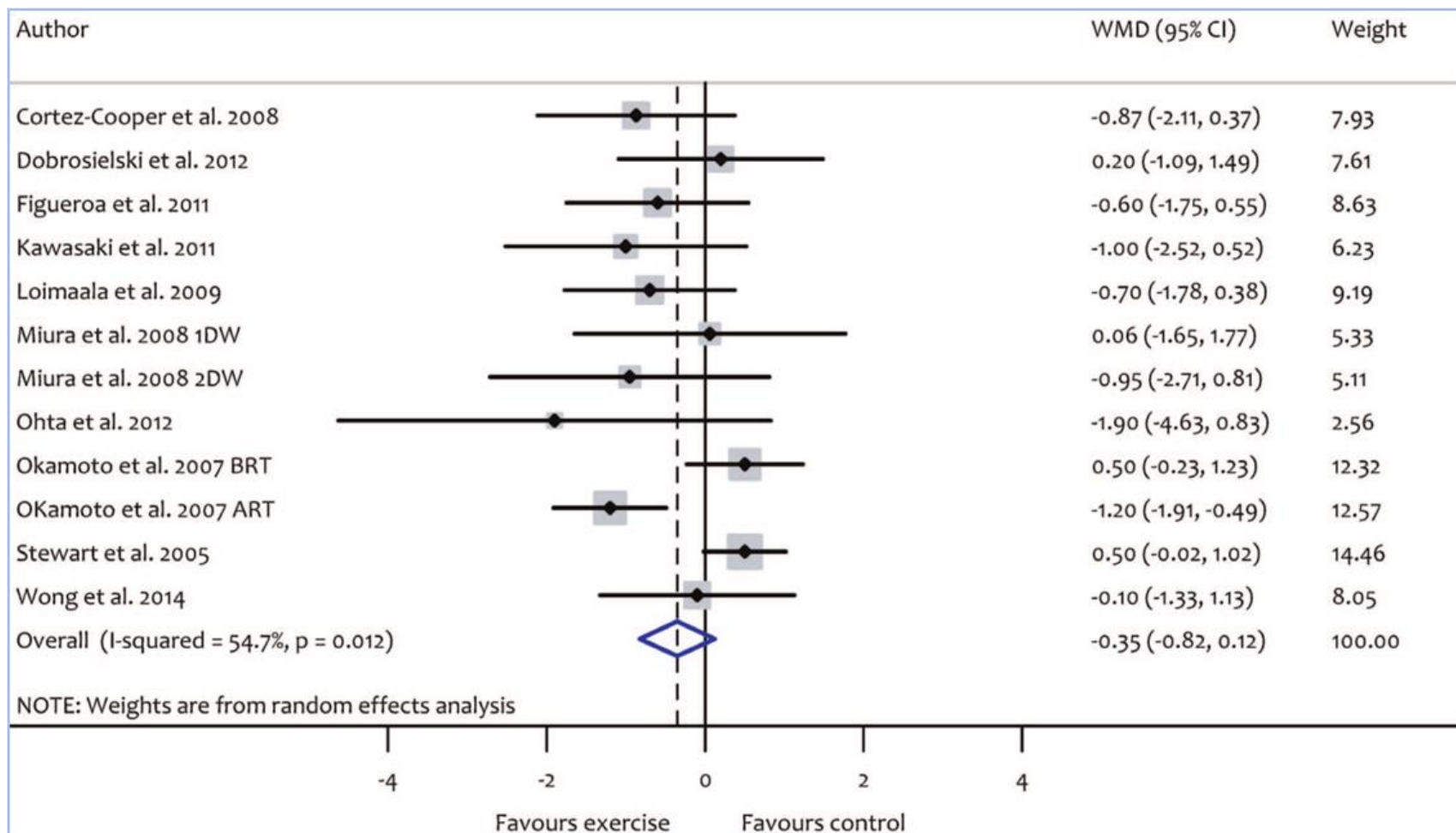


Figure 6. Combined strength and endurance exercise and its effect on arterial stiffness outcomes (From “Effects of Exercise Modalities on Arterial Stiffness and Wave Reflection: A Systematic Review and Meta-Analysis of Randomized Controlled Trials” by Ashor et al., 2014)

5 PURPOSE

The purpose of the present study was to examine acute changes in arterial stiffness, hemodynamics, force production, and testosterone responses to different orders of combined strength (S) and endurance (E) loadings when performed in a single session in young, recreationally trained men. Currently, there are very few studies investigating combined exercise loadings and its effect on hemodynamic and endocrine response. Furthermore, integrated (INT) exercise loading protocols have not been extensively studied. Therefore, the aim of the experiment in this thesis was to determine the acute arterial stiffness, testosterone and force production response to different concurrent strength and endurance exercise sessions. Specifically, this study evaluated the differences between SE, ES and integrated (INT) loading. In addition, the recovery profile from these loadings will also be elucidated to gain a better understanding of its time course.

5.1 Research hypothesis

From the current literature, it seems that arterial stiffness, a reliable cardiovascular mortality predictor, responds differently to strength and endurance exercise, respectively. Since acute responses are what drives chronic adaptations, it is thus fundamental, to understand the responses combined exercise loads may invoke. Furthermore, testosterone has been cited as a key hormone in cardiovascular protection and its effects may mediate blood flow and have an effect on arterial stiffness and hemodynamics.

The hypothesis with regard to the research objectives were as follows:

1. Integrated (INT) exercise loading will elicit the least response, particularly in force production, given that the potential effects of strength and endurance training “overlaps” one another before they can be taken as a block stimulus.
2. There will be clear differences in arterial stiffness and hemodynamic response, possibly mediated by testosterone, between the three exercise loadings, especially between SE and ES.

6 METHODS

6.1 Participants

Eight healthy male participants ($n = 8$) were recruited from Central Finland, in the Jyväskylä region through the website of the University of Jyväskylä. The characteristics of the participants are shown in Table 5. All participants were free of acute and chronic illness, diseases and injury. Additionally, they were required to abstain from using any form of medication that would influence or interfere with the performance of intense physical activity, neuromuscular function and endocrine metabolism.

Table 5. Characteristics of study participants

Variables	Mean \pm SD
Age (years)	33.5 \pm 5.9
Height (cm)	178.4 \pm 4.4
Mass (kg)	74.5 \pm 7.5
Body Mass Index (BMI)	23.4 \pm 2.4
Resting Systolic Blood Pressure (mmHg)	135 \pm 7
Resting Diastolic Blood Pressure (mmHg)	75 \pm 9
Resting Heart Rate (bpm^{-1})	55 \pm 5
HR_{max} (bpm^{-1})	189 \pm 9
$\text{VO}_{2\text{max}}$ (ml/kg/min)	50.5 \pm 2.9
PWV (m/s)	7.7 \pm 0.5

Note. HR_{max} , maximum heart rate; $\text{VO}_{2\text{max}}$, maximum oxygen uptake; PWV, pulse wave velocity.

6.2 Ethical Approval

All study participants had to complete a health questionnaire and attended a health screening where their resting electrocardiogram (ECG) was analysed and approved by a cardiologist as a part of the pre-test screening process. All of the participants received detailed information pertaining to the study design, measurements and procedures and were required to provide written informed consent prior to participation. The research protocol and study design received the ethi-

cal approval from the ethics committee of the University of Jyväskylä, Finland and was conducted in accordance with the declaration of Helsinki.

6.3 Experimental design

Baseline data was collected on a week prior to the experiment. All loading sessions were conducted at the same time of day for each participant, and were separated by at least 72 hours to avoid possible confounding factors such as accumulated fatigue, muscle damage and/or soreness. Figure 7 shows the process of the experiment for a single participant from start to finish.

6.3.1 Baseline measurements

One Repetition Maximum. 1RM of leg extensors was determined using a seated horizontal bilateral leg press (David 210; David Health Solutions Ltd., Helsinki, Finland). Participants completed a warm-up consisting of 3 sets using 5 repetitions with 70% of the estimated maximum, 2 repetitions at 80–85%, and 1 repetition at 90–95% with a one-minute rest between the sets. After this warm-up, they were allowed 5 attempts to reach 1RM. The starting knee angle for all subjects was below 60° ($57 \pm 1^\circ$). Participants were instructed to grasp the handles located on either sides of the seat and to keep constant contact with the seat and backrest during the complete extension to 180°. Verbal encouragement was given to promote maximal effort. The greatest weight that could be successfully lifted (knees fully extended) at the accuracy of 1.25 kg was accepted as 1RM.

Isometric Leg Press. Maximal isometric bilateral leg press force was measured on a horizontal dynamometer (Department of Biology of Physical Activity, University of Jyväskylä, Jyväskylä, Finland) in a seated position at a knee angle of 107° (Häkkinen et al. 1998). Participants were instructed to grasp the handles on both sides of the seat and keep constant contact with the seat and backrest to produce maximal force as rapidly as possible with both feet against the force plate for a duration of 3–4 seconds.

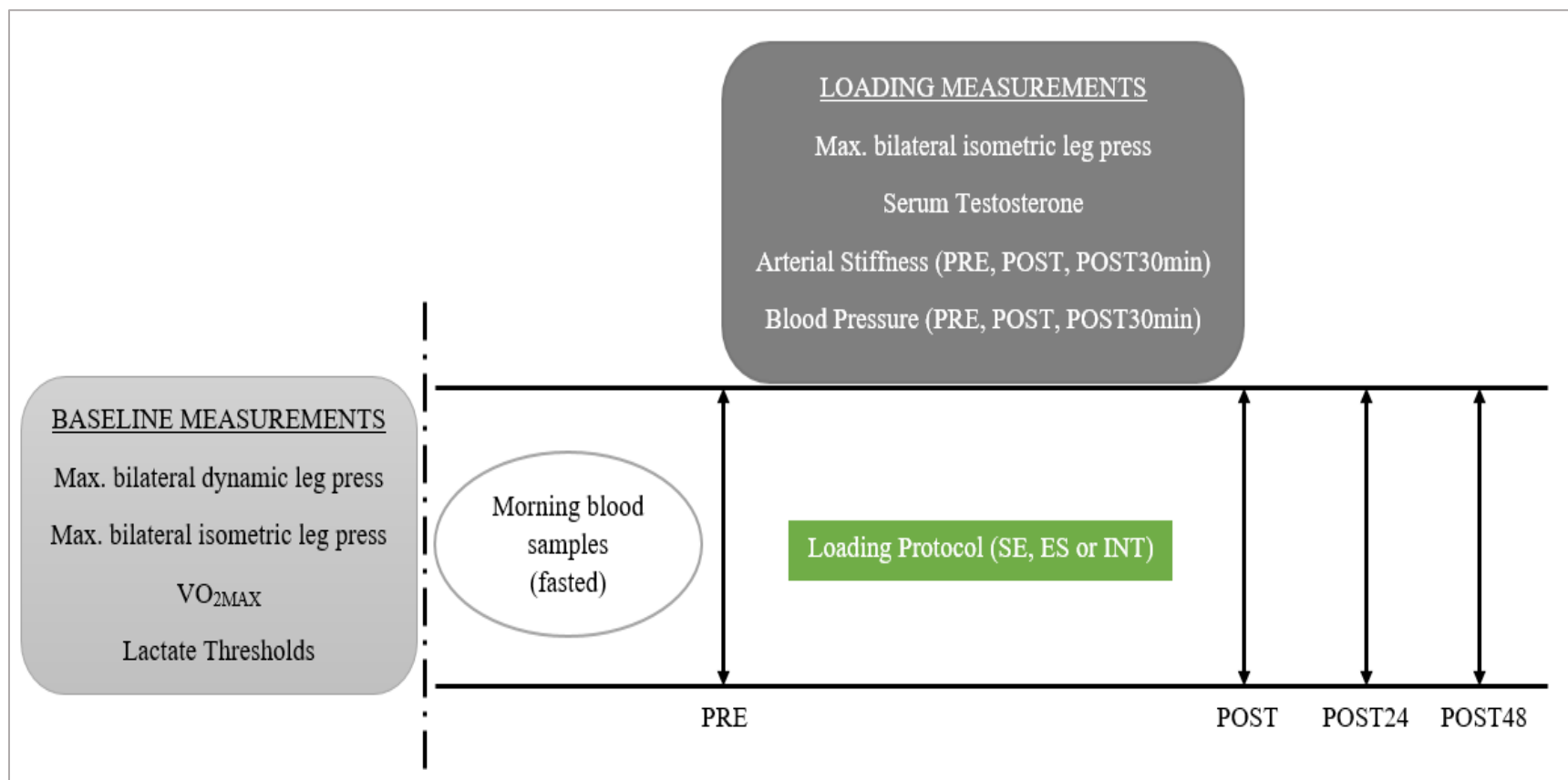


Figure 7. The experimental design from start to finish. PRE, pre loading; POST, 10 minutes post loading; POST30, 30 minutes post loading; SE, strength followed by endurance; ES, endurance followed by strength; INT, integrated strength and endurance. Note. force production variables from maximal isometric leg press (MVC and RFP) and testosterone responses were also measured 24 and 48 hours post.

Before the start of the loading (PRE) and at both follow-up measurements (24 and 48 hours), 3 trials with a resting period of 1 minute were conducted. At POST, only 2 trials separated by a resting period of 30 seconds were conducted. The force signal was low pass filtered (20 Hz) and analysed (Signal software, version 4.04; Cambridge Electronic Design Ltd., Cambridge, United Kingdom). In addition to maximal isometric force, rapid force production from 0 – 500 (RFP) were calculated from the force-time curve.

Maximal oxygen uptake. Maximal oxygen uptake (VO_{2max}) and maximal workload were determined using a graded maximal incremental test to volitional exhaustion on a horizontal custom-built motorized treadmill (University of Jyväskylä, Finland) set to a gradient of 1% (Jones & Doust 1996). A warm-up at $1 \text{ km}\cdot\text{h}^{-1}$ below the speed of the first stage was used. Each stage lasted three minutes with an increase of $1 \text{ km}\cdot\text{h}^{-1}$ for every stage. Heart rate was monitored continuously throughout the test (Polar V800; Polar Electro Oy, Kempele, Finland). Values for ventilation (VE), oxygen uptake (VO_2) and carbon dioxide (VCO_2) were collected via open circuit spirometry and analyzed using a breath-by-breath gas analyzer (Oxycon Pro, Jaeger, Hoechberg, Germany). The volume, flow, and gas analyzer were calibrated before the test according to the manufacturer's instructions using a certified gas mixture of 16% O_2 and 4% CO_2 . To ensure that VO_{2max} was reached, other criteria such as HR, blood lactate (Bla), and respiratory exchange ratio (RER) were monitored throughout the test. The highest 30 second VO_2 value was taken as VO_{2max} .

Blood sampling. Venous blood samples (10 ml) were collected by a qualified laboratory technician, using sterile needles into serum tubes (Venosafe; Terumo Medical Co., Leuven, Hanau, Belgium). Whole blood was centrifuged at 3500 rpm (Megafuge 1.0 R; Heraeus, Germany) for 10 minutes, after which serum was removed and stored at -80°C until analysis. Analyses of total serum testosterone was performed using chemical luminescence techniques (Immulite 1000; Siemens, New York, NY, USA) and hormone-specific immunoassay kits (Siemens). Capillary blood samples were taken from the fingertip and Bla concentrations were analyzed using a Biosen lactate analyzer (S_line Lab+; EKF, Magdeburg, Germany).

6.3.2 Arterial Stiffness

Arterial tonometry with simultaneous ECG was obtained from carotid and femoral arteries with the use of a commercially available tonometer (PulsePen, DiaTecne s.r.l., Milan, Italy; www.pulsepen.com) that has been well validated in previous studies (Joly et al. 2009; Boutouyrie et al. 2010; Salvi et al. 2004). Transit distances were assessed by body surface measurements using a tape measure from the suprasternal notch to each pulse recording site (carotid and femoral). Figure 8 shows how arterial stiffness was assessed.

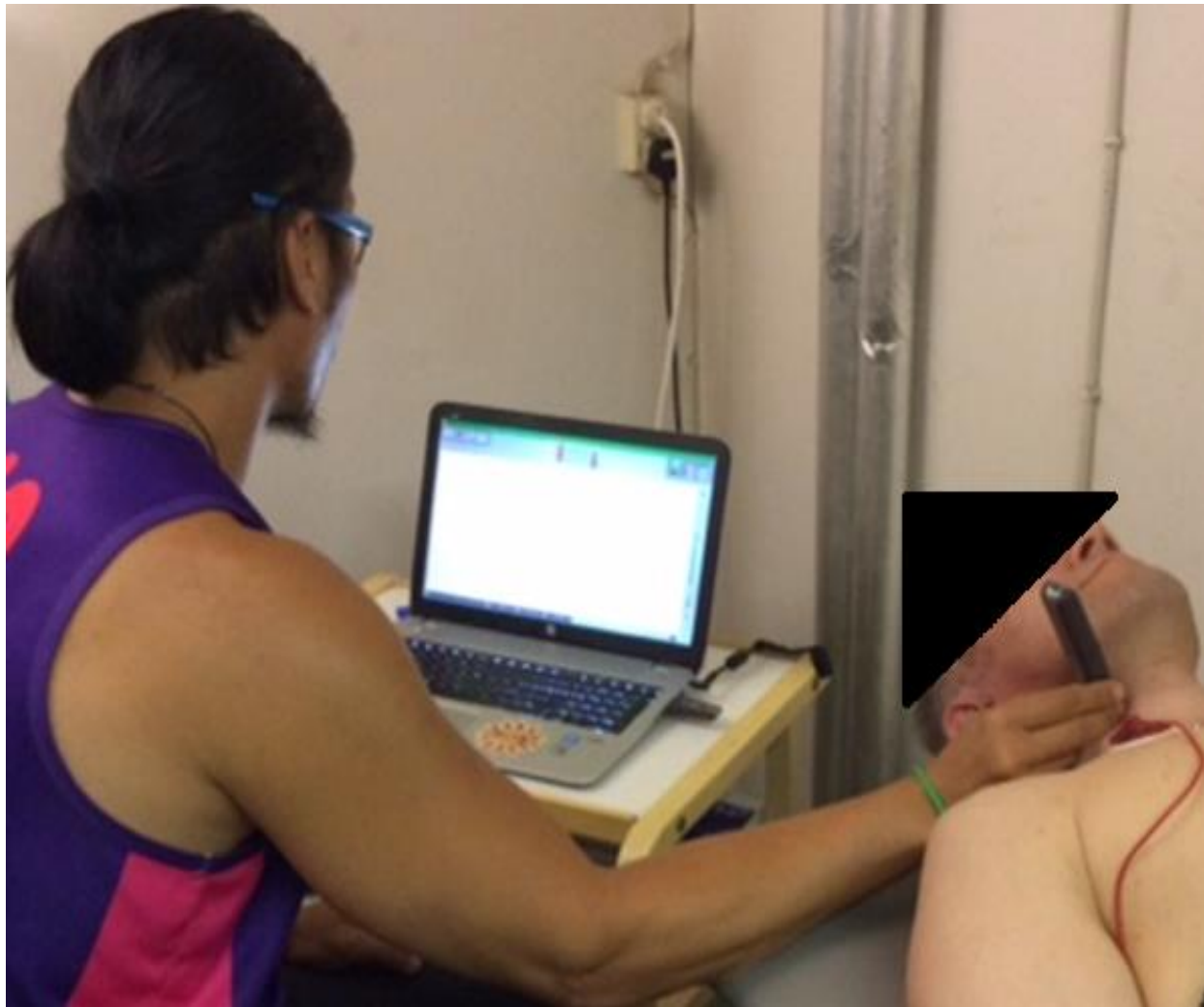


Figure 8. Assessment of arterial stiffness using applanation tonometry (carotid position)

Direct carotid to femoral measurement was adjusted to 80% (common carotid artery – common femoral artery x 0.8) for the calculation of pulse wave velocity (PWV) as recommended previously (Van Bortel et al. 2012). All arterial stiffness related measurements before and after the loadings were taken by a single trained operator of the tonometer and the same transit distances measured during baseline evaluation were used throughout the experiment for consistency and reliability. The measurement of PWV during this experiment adhered closely to the guidelines established (Tomlinson 2012); written and verbal instructions were given to all participants, informing them that no caffeine and smoking within 3 hours of the measurements were allowed, and that speaking and sleeping during the measurement was prohibited.

All measurements were taken in a quiet room with a stable temperature on the right side of the body in the supine position. The mean of two measurements was used as the individual baseline value; when the difference between the two measurements was more than 0.5 m/s, a third measurement was performed and the median value was used to calculate group mean at baseline. Supine brachial systolic and diastolic blood pressures (SBP and DBP respectively) were obtained using Microlife BP A200 (Microlife Corp., Taipei, Taiwan) for better sensitivity and accuracy (Wiesel et al. 2014). Two sequential readings were measured and the mean values were used. Participants rested in the supine position for 10 minutes before PWV was measured during baseline. However, due to the nature of the study, PWV after the loading (POST) was measured immediately after venous blood sampling.

6.3.3 Loading Protocols

Three different exercise orders comprising of the two distinct components of strength and endurance exercise modes were used. All loadings were balanced for volume, intensity and duration. A comparison of the loading orders are shown in Table 6. A 10 minute warmup consisting of dynamic stretches for the lower limbs (gluteus maximus, hamstrings, quadriceps, and hip flexors) were used to prevent the possibility of injury from the loading. All the participants were able to complete all three protocols successfully.

Table 6. Loading orders used in the experiment

Endurance + Strength (ES)	Strength + Endurance (SE)	Integrated (INT)
45 minutes run at 80-85% VO_{2MAX} + Jump squat 2 x 10 Drop jump 2 x 10 Alternate leg bounding 2x (2x5) Leg press 3 x 10 (80% 1RM)	Jump squat 2 x 10 Drop jump 2 x 10 Alternate leg bounding 2x (2x5) Leg press 3 x 10 (80% 1RM) + 45 minutes run at 80-85% VO_{2MAX}	A. 5 minute run at 80-85% VO_{2MAX} + B. Jump Squat 1 x 10 + C. 5 minute run at 80-85% VO_{2MAX} + D. Drop Jump 1 x 10 + E. 5 minute run at 80-85% VO_{2MAX} + F. Alternate leg bounding 2x5 + G. 5 minute run at 80-85% VO_{2MAX} + H. Leg Press 1 x 10 (80% 1RM) + (Repeat A – H) + 5 minute run at 80-85% VO_{2MAX} + Leg press 1 x 10 (80% 1RM)

Strength Loading. The strength component of the loading consisted of countermovement jumps, drop jumps (60cm drop) (Chu & Myer 2013), 5-step bounding (Bouhlel et al. 2006) and dynamic leg press at 80% of individual 1RM for 10 repetitions each. Two sets were performed for all exercises except for the leg press, which was done for three sets. There was a two minute rest in-between all sets.

Endurance Loading. A 45-minute run set at a gradient of 1% on the treadmill and at the velocity of 80-85% of individual VO_{2max} was performed either before (ES order) or after (SE order) the strength component was completed. For the integrated loading (INT), the endurance component was divided into 9 x 5-minute runs at the same intensity (80-85% of VO_{2max}) in-between all the strength sets. The in-between sets rest time of 2 minutes was maintained throughout the integrated loading.

6.4 Statistical Analysis

Results are presented as mean \pm standard deviation. Data was analyzed with IBM SPSS Statistics v.20 software (IBM Corporation, Armonk, New York, USA). All data were checked for normality using the Shapiro-Wilk test. Within-group differences for normally distributed variables were analyzed using repeated measures of analysis of variance (ANOVA) to assess differences over time. Within-group differences for non-normally distributed variables were analyzed using the Wilcoxon signed-rank test, and p -values were corrected for Bonferroni by multiplying all pairwise p -values with the number of comparisons conducted for each variable. The statistical significance for all tests was set for a baseline of $p = 0.05$, where $*p < 0.05$, $**p < 0.01$.

7 RESULTS

7.1 Vascular and hemodynamic changes

Arterial Stiffness. There was no interaction effect (Time x Loading) and main effect for loading. However, main effects for time was found. A repeated measures ANOVA with assumed sphericity determined that mean PWV differed statistically significantly between time points ($F(2, 14) = 5.774, p = 0.015$). Post hoc tests using the Bonferroni correction revealed that exercise loading elicited an acute reduction in PWV from PRE to POST (7.9 ± 0.7 m/s vs 7.3 ± 0.8 m/s, respectively), which was statistically significant ($p = 0.017$) (Figure 9).

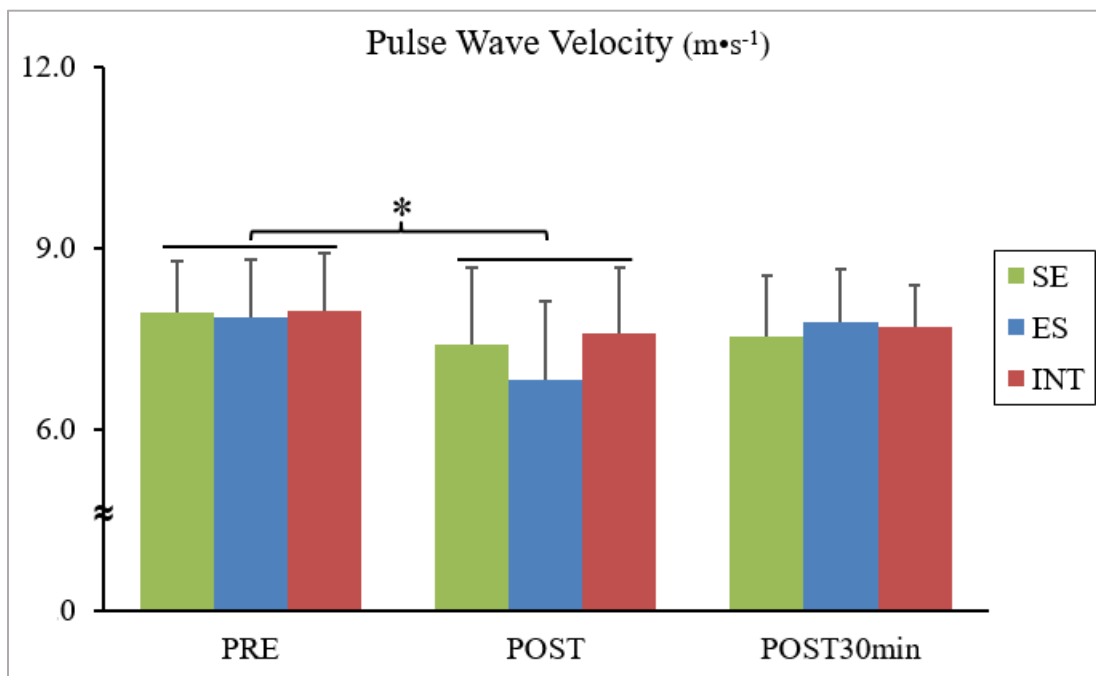


Figure 9. Arterial stiffness response between loading protocols across time points. SE, strength followed by endurance; ES, endurance followed by strength; INT, integrated strength and endurance.

However, PWV recovered to 7.7 ± 0.2 m/s at POST30, which was not statistically significantly different to PRE ($p = 1.0$) or POST ($p = 0.216$) levels. Although there was an overall difference in PRE to POST for ES loading, it was not statistically significant ($p = 0.021$) after a Wilcoxon signed-rank test conducted with a Bonferroni correction ($p \leq 0.017$) was applied. However, there was a statistically significant change in POST to POST30 ($Z = -2.521, p = 0.012$) (Figure 10). No significant changes for INT and SE loading between time points were found.

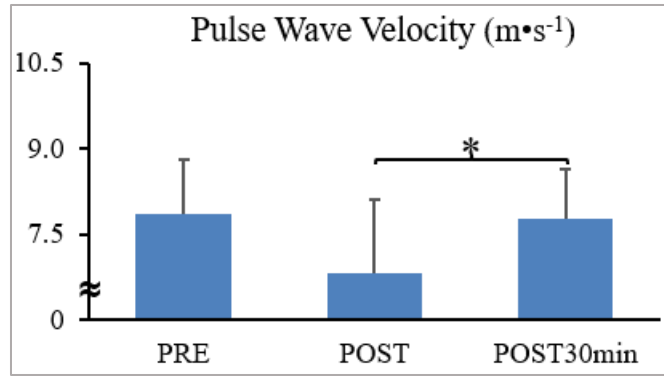


Figure 10. Arterial stiffness response to ES loading across time points (* $p = 0.012$)

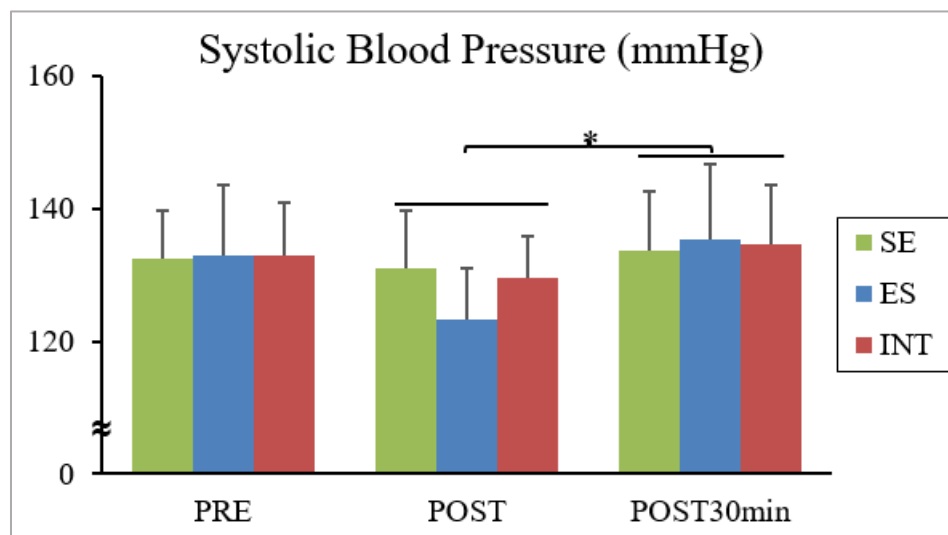


Figure 11. Systolic blood pressure response between loading protocols across time points

Blood Pressure. Mean SBP differed statistically significantly between time points ($F(2, 14) = 4.152, p = 0.038$). Post hoc tests using the Bonferroni correction revealed that this statistical difference in SBP was from POST to POST30 (128 ± 5 vs 135 ± 6 mmHg, respectively) ($p = 0.032$) (Figure 11). However, SBP PRE differed significantly to POST (133 ± 11 vs 124 ± 8 mmHg, respectively) ($p = 0.018$) only in ES loading (Figure 12), and this difference was not found for SE and INT. SBP PRE to POST30 was not statistically significantly between all loadings.

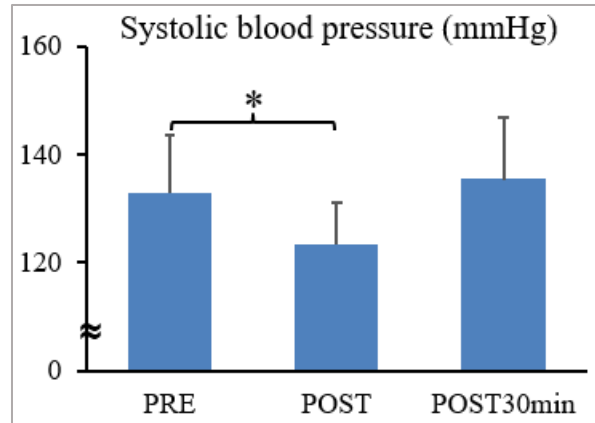


Figure 12. Systolic blood pressure response to ES loading across time points (* $p = 0.018$)

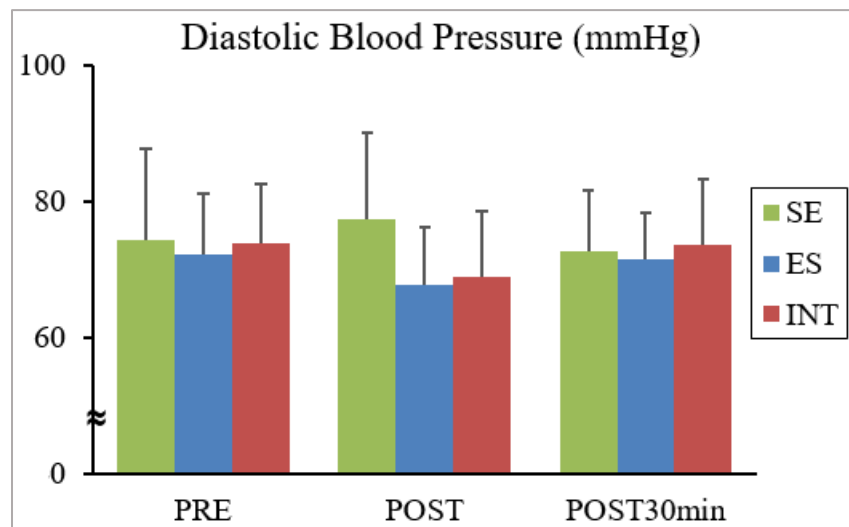


Figure 13. Diastolic blood pressure response between loading protocols across time points

A repeated measures ANOVA with assumed sphericity determined that there were no significant main effects for time, or loading for DBP. However, DBP response and recovery to SE loading differed from ES and INT (Figure 13). This was detected through a statistically significant interaction effect between time and loading ($F(4, 28) = 3.677, p = 0.016$) (Figure 14). DBP for SE was 74 ± 13 mmHg, 77 ± 13 mmHg and 73 ± 9 mmHg for PRE, POST and POST30, respectively, whereas DBP for ES was 72 ± 9 mmHg, 68 ± 8 mmHg, 72 ± 7 mmHg for the same time points. Similar to the ES loading, the response of the INT loading was 74 ± 9 mmHg for PRE, 69 ± 10 mmHg POST, and 74 ± 10 mmHg POST30. All DBP values were recovered by POST30 min and there were no significant differences.

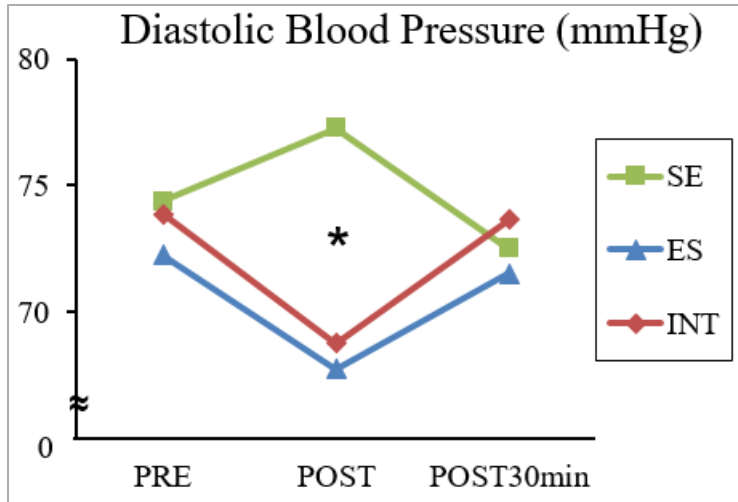


Figure 14. Diastolic blood pressure with a statistically significant interaction effect between time and loading (* $p = 0.016$) (Mean and SD are presented on page 38)

7.2 Testosterone

No interaction effect or main effect for loading was found. However, a main effect for time was found. A repeated measures ANOVA with assumed sphericity determined that mean serum testosterone levels differed statistically significantly between time points ($F(2, 10) = 5.108, p = 0.03$). Post hoc tests using the Bonferroni correction revealed that combined exercise loadings led to reductions in levels of serum testosterone levels from POST to POST24 (13.5 ± 1.6 nmol/L vs 10.5 ± 3.1 nmol/L, respectively), which was statistically significant ($p = 0.033$) (Figure 15). No significant correlations were found between serum testosterone levels and PWV.

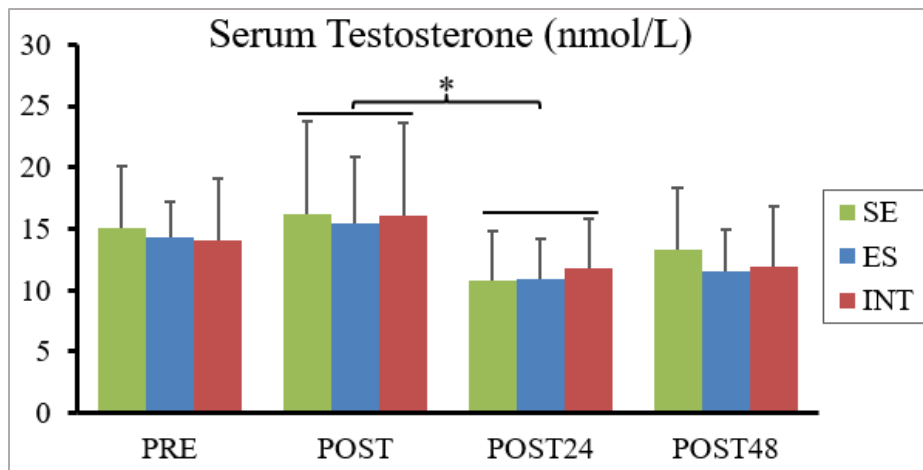


Figure 15. Serum testosterone levels across time points

7.3 Force production

Maximal Voluntary Contraction. No interaction (Time x Loading) and main effect for loading was found. However, there was a main effect for time. A repeated measures ANOVA with a Greenhouse-Geisser correction determined that mean MVC differed statistically significantly between time points ($F(1.166, 6.995) = 6.086, p = 0.04$). Post hoc tests using the Bonferroni correction revealed that exercise loading elicited a statistically significant reduction in MVC from PRE to POST (3291 ± 1007 N vs 2888 ± 804 N, respectively) ($p = 0.037$) (Figure 16).

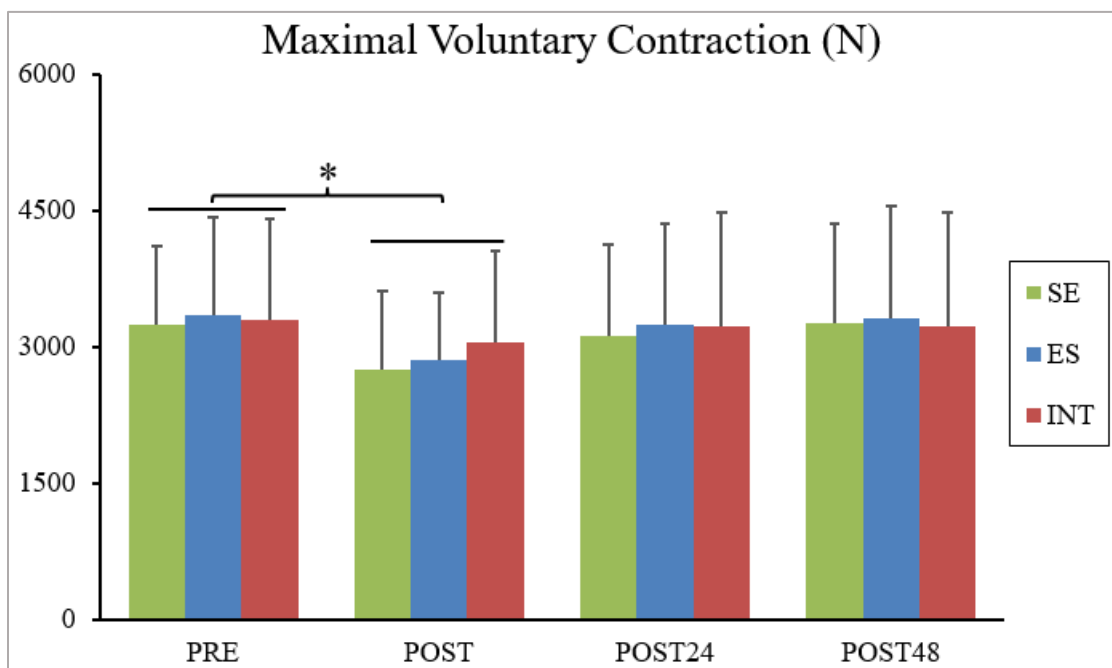


Figure 16. Force production response between loading protocols across time points

A difference in MVC for both ES [$\chi^2(3) = 9.900, p = 0.019$] and SE loading [$\chi^2(3) = 11.743, p = 0.008$] between time points were detected, and a post hoc analysis with Wilcoxon signed-rank tests was conducted. There was an overall difference in ES loading PRE to POST ($p = 0.025$) and POST to POST24 ($p = 0.017$). However, only POST to POST24 (2858 ± 741 vs 3237 ± 1109 N) was significant (Figure 17). There were no significant correlations between MVC and serum testosterone levels.

Similarly, there were differences for SE loading PRE to POST ($p = 0.017$) and POST to POST24 ($p = 0.025$), however, only PRE to POST (3248 ± 860 vs 2754 ± 852 N) was significant, after Bonferroni correction was applied, as this resulted in a significance level set at $p \leq 0.017$ (Figure 18).

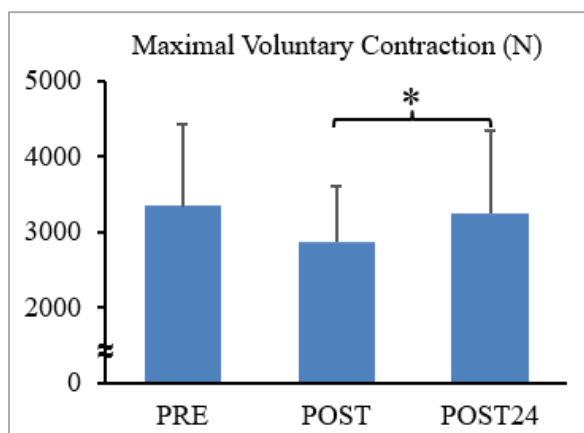


Figure 17. Force production changes in ES loading

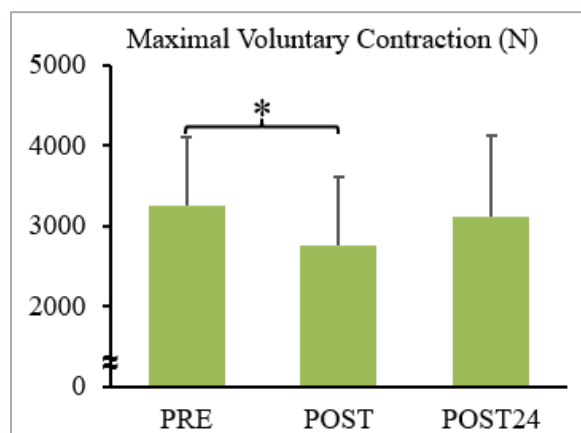


Figure 18. Force production changes in SE loading

Rapid Force Production. A repeated measures ANOVA with assumed sphericity determined that there were no significant interaction effect (time x loading) and main effects for loading in RFP. However, there was a main effect for time. Mean RFP differed statistically significantly between measurement time points ($F(2, 14) = 16.581, p = 0.0001$), from PRE to POST (2182 ± 294 vs 1917 ± 239 N) ($p = 0.005$), PRE to POST24 (2182 ± 294 vs 2083 ± 299 N) ($p = 0.043$), and POST to POST24 (1917 ± 239 vs 2083 ± 299 N) ($p = 0.042$) (Figure 19). No significant correlations were found between RFP and serum testosterone levels.

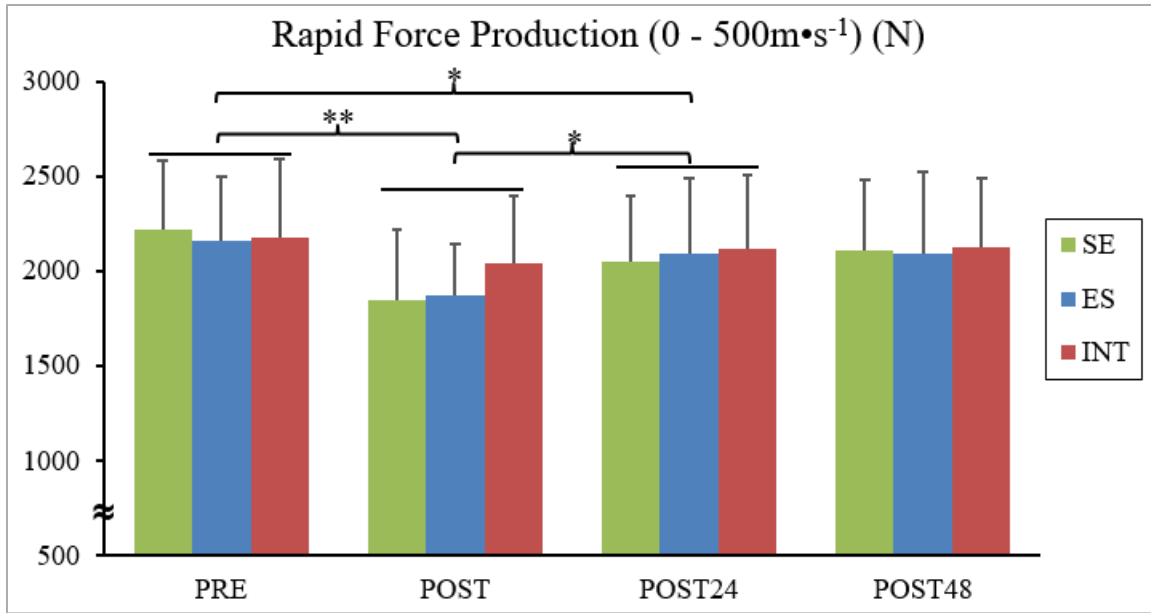


Figure 19. Rapid force production (RFP) response between loading protocols across time points

A difference within groups was detected from PRE to POST in both ES (2155 ± 342 vs 1871 ± 272 N) ($p = 0.033$) (Figure 20) and SE loading (2218 ± 365 vs 1845 ± 377 N) ($p = 0.035$) (Figure 21). There were no significant differences between time points for INT loading.

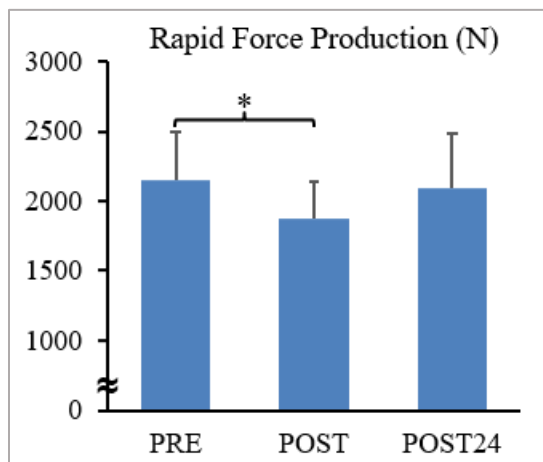


Figure 20. Rapid force production changes in ES loading

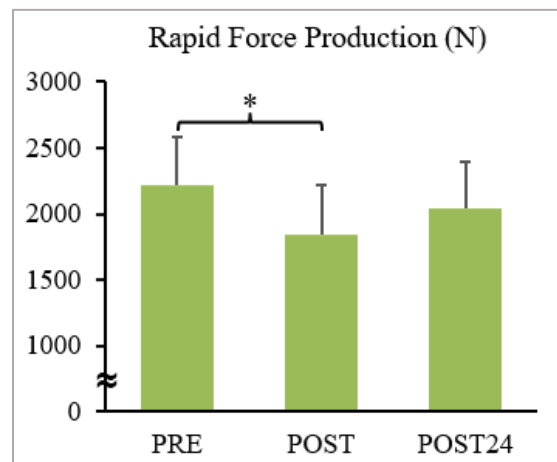


Figure 21. Rapid force production changes in SE loading

8 DISCUSSION

The present study investigated acute changes in vascular, hormonal and force production functions as well as their recovery to three different combined endurance and strength loading protocols in recreationally trained males. The results indicate that a possible “order effect” may exist in arterial stiffness as well as blood pressure between the SE and ES loadings. Most notable were the findings of the acute increase in diastolic blood pressure (DBP) in the SE loading, as well as the INT loading not incurring any significant force production impairments compared to the SE and ES loading.

8.1 Arterial Stiffness

The main finding from the study was that combined strength and endurance loadings was able to acutely reduce PWV in recreationally trained men, and these changes in arterial stiffness remained even after 30 minutes of exercise cessation for the SE and INT loadings. PWV is inversely-related to arterial compliance, in that a lower PWV value relates to better compliance (Heffernan et al. 2007; Kingwell et al. 1997; Montero et al. 2014). Our results showed a statistically significant reduction in PWV from PRE to POST, and is in agreement with the literature that acute exercise improves arterial compliance (DeVan et al. 2005; Green et al. 2004; Heffernan et al. 2007; Kingwell et al. 1997). These changes could be attributed to the short term mechanisms of endothelial function, such as exercise-related vasodilation to the large proximal vessels and vasa vasorum (Green et al. 2004; Kingwell et al. 1997), as well as vascular smooth muscle tone (McEniery et al. 2006)

It is important to note that while PWV levels remained depressed at POST30 for SE and INT loadings, it returned to PRE levels for ES loading. This may be due to a potential “order effect” of combined exercise session structure. It has previously been documented (Schumann et al. 2015) that this phenomenon exists for acute combined exercise loading conditions on hormonal responses. However, to our best knowledge, this has not been investigated in acute arterial stiffness responses previously. There has only been one training intervention study (Okamoto et al. 2007) that has investigated different combined exercise loading orders similar to our study (ES vs SE), and the authors concluded that performing endurance exercise after strength exercise

(SE) can prevent vascular function deterioration, and that performing combined exercise in the ES order did not show any improvements. The speculation was that strength exercise neutralized the favorable effect of endurance exercise in the ES order. However, we did not measure arterial stiffness in-between any of the loadings and thus lack the data to show any potential differences.

Although the results of this study showed that the ES loading induced the greatest change in arterial stiffness POST exercise, it was also the only exercise loading where arterial stiffness returned to PRE exercise levels POST30. It would thus be logical to assume that the results from this experiment supports the notion of Okamoto and colleagues (2007), that the strength training bout in the ES order may have accelerated the return of arterial compliance to pre-exercise levels within 30 minutes at POST30. Indeed, ample research has shown that acute bouts of strength exercise leads to decreased arterial compliance (DeVan et al. 2005; Heffernan et al. 2007; Yoon et al. 2010), and that conversely, acute bouts of endurance exercise was able to reduce arterial stiffness (Kingwell et al. 1997; Green et al. 2004; Heffernan et al. 2007). This was further supported by the fact that in our study, the SE order, though not statistically significant, had the lowest POST30 PWV values.

A possible reason that no statistical differences in PWV were found between the loading groups might have been because of the individual variation between participants. The participants performed each of their respective visits at the same time of day, visits varied from the mornings to the afternoons for different participants. However, it is unlikely that this had a large effect on the results though, as PWV has been shown to not exhibit significant diurnal variation (Li et al. 2014). In summary, combined exercise loadings can acutely reduce arterial stiffness, with ES loading eliciting the greatest magnitude of change and the INT loading the least.

8.2 Blood Pressure

The results indicate that combined strength and endurance exercise reduces blood pressure, and that the ES order had the greatest effect on SBP. This is consistent with the literature, in what is a generally accepted effect of endurance training on resting hemodynamics (Fagard 2005; Rowell 1974), although the persistence of these effects after an additional bout of strength training was

not anticipated. The decrease in SBP also may have been due to post-exercise hypotension (PEH) (Pescatello et al. 2004) from the preceding endurance component. However, this effect was not found for the SE loading.

In normotensive participants, such as the ones in our study, PEH has been attributed to a reduction in systemic vascular resistance (Halliwell et al. 1996; Bermudes et al. 2004; Forjaz et al. 2004), which is evident from the reduction in PWV from PRE to POST for all loading groups. Therefore, it could be reasoned that blood pressure, in particular SBP, may be influenced by the order of strength and endurance modes, and that the preceding mode exerts a stronger effect. This is substantiated by the differences in the DBP response, and in particular the SE order; in spite of performing an endurance bout after strength loading, DBP did not show a reduction like in the ES and INT loading. This ‘order effect’ is clear when comparing the results of both blood pressure measurements. In the ES loading, a reduction in both SBP and DBP POST ES loading can be seen, while a decrease in SBP POST and an increase in DBP POST was seen instead for SE loading.

Strength training has been documented to induce changes in sympathetic activity (Fagard 2005; Heffernan et al. 2007), and thus, a plausible explanation could be that the preceding strength training bout suppressed the sympathetic tone and set a precedence for the physiological response to the rest of the loading. As shown from the experiment conducted by Rezk and colleagues (2006), DBP only decreased with low intensity strength exercise, while high intensity strength exercise showed no change. Therefore, the increase in DBP seen in the SE group in our current study may have been a reflection of the intensity of both strength and endurance (85% VO_{2MAX}) components used in the study. However, the DBP responses POST for the ES and INT loadings differed to that of SE loading despite being matched for intensity, duration and volume. Thus, these factors alone are unable to account for the differences completely.

Overall, these results indicate that different combined strength and endurance loading orders invoke different DBP responses. This may have been due to a sustained response of increased

DBP from the strength component of the loading, which as a prior exercise stimulus, stressed the cardiovascular system differently. This is supported by the evidence that this effect was not seen in the ES group and INT group. Additionally, contrary to previous studies (Pescatello et al. 2004; Rezk et al. 2006), blood pressure returned to PRE exercise levels by POST30 minutes. The study population used in this study may have had an effect on the response of DBP as they were recreationally endurance trained men; other experiments have mostly used normotensive untrained men.

Collectively taken, the findings from blood pressure suggests that an order effect exists between the ES and SE loadings, in that the ES order provokes the greatest reduction in both SBP and DBP, while the SE order increases DBP. Additionally, the overall blood pressure responses to the INT loading more closely resembles that of the ES loading.

8.3 Testosterone

The current study showed that testosterone responses and recovery from combined exercise loading protocols did not differ significantly between each other. These results may be indicative of the matched volume and duration between the three different combined strength and endurance exercise loadings used in this study. And although there were elevations in testosterone levels from PRE to POST, it did not achieve statistical significance. This may be because the combined exercise load was not strenuous enough to provoke a significant anabolic response (Eklund et al. 2015, 2016; Schumann et al. 2015). However, the levels of serum testosterone remained similarly suppressed from POST to 24 hours of recovery and was statistically significant.

The prolonged recovery of the endocrine system in response to the loadings offers two possible explanations; that the exercise volume of used in the combined exercise loadings of this study (four lower body exercises with nine sets and a 45 minute run in total) may have been large enough to suppress the endocrine system (Eklund et al. 2016; Schumann et al. 2015), or, there may have been an excessive uptake of testosterone by the large muscles (West et al. 2016; Camera et al. 2015) of the lower body involved in the performance of combined exercise loadings.

Prolonged endurance exercise has been shown to suppress testosterone levels for up to 48 hours after the session (Billat et al. 2001; Hackney 2006; Millet & Lepers 2004), and this could be one of the plausible reasons for the reduced levels of serum testosterone levels seen post 24 hours in this study. The overall duration of the endurance component (45 minutes) may have been lengthy enough to elicit responses and changes to the endocrine system, yet not as stressful that they would remain after 48 hours of recovery.

The results of these testosterone levels differed to what was shown by Schumann and colleagues (2013), as well as Cadore and associates (2012). However, when taken into consideration with the results collected from force production, it supports the notion that was first suggested by Häkkinen (1995); that the time course of recovery between the neuromuscular and endocrine system occurs at different rates, with the endocrine system showing slower recovery profiles.

8.4 Force Production

Combined strength and endurance loadings has been well documented to show acute decreases in maximal voluntary force production (Eklund et al. 2015; Schumann et al. 2013, 2014). Our study showed similar force production deficits POST loading for MVC. These observed decreases in force production typically stem from the two different sources, each with its own unique mechanisms. For instance, strength exercise causes reduction of maximal voluntary neural activation due to centrally accumulated fatigue in the neuromuscular system (Häkkinen 1995), while endurance exercise, in particular running, leads to peripheral fatigue; postulated to be caused by the prolonged performance of the stretch shortening cycles (Avela & Komi 1998; Nicol & Komi 1991).

These decrements in force production capabilities were most prominent for the SE loading, both in MVC and RFP, although it did not achieve statistical significance when compared between ES and INT. Previous research (Eklund et al. 2015; Schumann et al. 2013, 2014) has shown that the ES order induces more acute neuromuscular deficit, which is contrary to the results found in the current study. One possible reason for this difference may be due to the mode of endurance exercise used. Because cycling exercise involves more continuous muscular effort from the quadri-

ceps, this may have impaired the force production capabilities in the ES order for earlier studies. Consequently, the use of cycling exercise in the SE order of earlier studies may have benefitted from the restorative effects of calcium flux and metabolite clearance (Hauswirth & Mujika 2013, 38) after lower body strength exercise.

Interestingly, the INT loading did not produce any significant change for both force production measures of MVC and RFP. This may be due to the alternating nature of the INT loading, where no one particular modality exerted a continuous, sustained amount of fatigue (Monteiro et al. 2008; Sforzo & Touey 1996) even though there was an accumulation of fatigue due to the loading duration and volume from the entire loading session (Simão et al. 2002, 2005; Zatsiorsky & Kraemer 2006). This may be one of the strongest possible reasons for the current results.

Another plausible explanation related to that may be the recovery time that each system receives. For instance, during the strength component, the stretch shortening mechanisms has a chance to recover, while during the endurance component, the neuromuscular system gets an opportunity to recuperate. Continuous running exercise has been postulated to result in a mechanical link “failure” in the excitation-contraction coupling (Ingalls et al. 1998; Martin et al. 2004), as well as significant central fatigue. Although central fatigue from endurance exercise has been shown to recover quickly enough to not exert a substantial effect on force production properties when compared to peripheral fatigue (Millet et al. 2011; Froyd et al. 2013). However, this remains speculative, as fatigue was not one of the emphases of the current study.

The form of endurance exercise used in our study may have also influenced the results, as running is an endurance exercise that more evenly distributes the forces required throughout locomotion through the entire lower limb, whereas during the movement of cycling, the quadriceps are more isolated in its usage (Ardigo et al. 2003; Bijker et al. 2002; Millet & Lepers 2004). Furthermore, because the testing protocol was focused on the quadriceps (seated leg press), using a stationary bike for cycling exercise as opposed to treadmill running exercise may result in an increase deficit to the force production capabilities of the lower limb in the INT loading. Indeed,

neuromuscular differences have been well documented between the two endurance exercise modes (Millet & Lepers 2004)

The current study did not show loading differences in the recovery at 24h and 48h in all the combined loadings in MVC. These results are consistent with the study conducted by Schumann et al (2013), who reported that neuromuscular deficits were mainly recovered for both the SE and ES orders after 24 hours. They further postulated that these results may have been due to the use of cycling exercise as their endurance mode; which does not involve stretch shortening (SSC) mechanisms. However, because the results from the current experiment showed a similar trend, in spite of using running exercise, SSC may thus be ruled out as a cause for force production reductions and recovery, particularly in the current study.

Similarly, in a more recent study from Eklund and colleagues (2016), maximal strength performance was found to be recovered by 24 hours as well. This group of researchers also found out that single session exercise-induced acute decreases in force production was the same before, and even after a combined training intervention. It must be pointed out however, that their study had involved female participants and thus, results from their study may not be directly comparable. Nevertheless, the current study showed that the INT order did not result in as much maximal strength reductions when compared to the SE and ES orders.

There were significant differences in RFP that demonstrated that it had yet to recover by POST24, but these changes were shown to be mainly from the SE and ES loading. The current study showed for the first time that, despite the overall volume and intensity of the sessions being matched, the INT order showed the least post loading neuromuscular deficit for RFP and is more rapid in its recovery. Although it has been well demonstrated that an acute bout of strength (Häkkinen 1995; Zatsiorsky & Kraemer 2006), endurance (Millet et al. 2011; Millet & Lepers 2004) or concurrent (Eklund et al. 2016; Schumann et al. 2015) exercise can have a negative effect on force production as well as its recovery, this effect does not appear to be as prominent

when the exercise session is structured in an intermittent fashion, such as in the INT order used in this study.

8.5 Study Strengths and Limitations

The study was able to show for the first time, the acute hemodynamic responses of a single combined exercise loading session. There has yet to be any acute studies done that assesses arterial stiffness and blood pressure responses to combined exercise sessions, especially when considering that the INT model was used for comparison in this study. Understanding these acute effects allows us to better appreciate the mechanisms involved in cardiac and metabolic tissue remodeling.

The experimental design and thus the results, also reduced the number of possible confounding factors, where statistical analyses were concerned. The repeated measures design with the consistent exercise loading times for each participant meant that there would be less fluctuations, especially for testosterone, within participants. The fact that the study was conducted in Finland also meant that participants were docile and complied very well with the instructions given during the whole research process.

There is an element of practical application from the results of this study as combined exercise sessions structured in the INT manner may be a solution to competing athletes or populations with lower exercise capacities, as the results of the study have shown, the impairment to force production capabilities was not nearly as much as the SE or ES orders. Still, it must be highlighted that the study population used were recreationally endurance trained males, and that may have had an influence on the results, and thus, its interpretation.

It is important to note several limitations in this study. One limitation of this study was that we did not measure changes in arterial stiffness and blood pressure during the different loading sub components, i.e. after the strength or endurance bout. Based on aerobic exercise studies and arterial stiffness, greater arterial compliance has been found in endurance-trained individuals

(Tanaka et al. 2000) and after acute cycling exercise (Kingwell et al. 1997). These acute changes have lasted up to 30 min post-exercise and thus reflect the body's response to the acute changes occurring during exercise.

Post-exercise measurements of arterial stiffness and blood pressure were taken after the subjects had given blood samples, which was approximately 10 minutes after the loading protocol. Although this was consistent across all protocols and for all participants, this delay in the procedure might have a bearing on post-exercise hemodynamic results, and at 30 min of recovery. Nevertheless, the procedure was the same for all loading protocols and would not have affected the between protocol comparisons. Another limitation was the relatively small sample size ($n = 8$). This may have affected the statistical analyses due to a lack of statistical power. Future studies should investigate arterial stiffness immediately after the exercise bout to get a more accurate indication of its response to different structures of combined exercise.

9 CONCLUSION

In conclusion, the results from this study showed that an acute single session of concurrent exercise did not have a detrimental effect on arterial compliance and that the ES order had the greatest positive effect on arterial stiffness. From a more comprehensive standpoint, combined exercise should still be encouraged and prescribed, given its superiorly beneficial effects on body composition and musculoskeletal health as well as its metabolic benefits compared with aerobic training alone. This holds especially true in older populations, where sarcopenia-related atrophy may be better managed through strength exercise, and cardiovascular health be better maintained via endurance exercise.

Nonetheless, when performing a concurrent strength and endurance exercise bout, acute changes in arterial stiffness and blood pressure appear to be affected by the order of the strength and endurance components. That is to say, an order effect for hemodynamics may exist, especially between the SE and ES orders. Additionally, the INT loading impairs force production function the least and could thus be recommended for a wider variety of populations. From an application standpoint, athletes may use this form of combined training during the pre-competition phase or during their tapering period. However, the lack of fatigue-induced impairment after the exercise loading session may result in reduced adaptations, when used as a long term training intervention.

Future studies should use the INT exercise loading model in an intervention study to understand its effects on long term arterial compliance, blood pressure changes and force production capabilities. Additionally, the INT and ES exercise loading models could be considered for future investigations, for example, in the hypertensive and pre-hypertensive cohorts based on its favorable acute responses on measures of vascular function.

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