



LEFT VENTRICULAR DIASTOLIC MECHANICS IN TRAINED ATHLETES DURING SUBMAXIMAL EXERCISE USING SPECKLE TRACKING ECHOCARDIOGRAPHY

Alexander Beaumont

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**LEFT VENTRICULAR DIASTOLIC MECHANICS IN
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USING SPECKLE TRACKING ECHOCARDIOGRAPHY**

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A thesis submitted to the University of Bedfordshire in partial fulfilment
of the requirements for the degree of Masters of Science by Research

December 2015

Author's Declaration

I declare that this thesis is entirely my unaided work. This thesis is being submitted for the degree of MSc by Research to the University of Bedfordshire. This work has not been submitted before for any degree or examination at any other university.

A handwritten signature in black ink, appearing to read 'A. Beaumont', with a long horizontal flourish extending to the right.

Alexander Beaumont

18th December 2015

Abstract

LEFT VENTRICULAR DIASTOLIC MECHANICS IN TRAINED ATHLETES DURING SUBMAXIMAL EXERCISE USING SPECKLE TRACKING ECHOCARDIOGRAPHY

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This thesis investigated sport specific responses of diastolic mechanics at rest and during submaximal exercise. Two-dimensional speckle tracking echocardiography (STE) was used to assess diastolic mechanics at rest and whilst triathletes (TRI, n=9, 32 ± 7 years), long distance runners (LDR, n=7, 34 ± 3 years), resistance trained (RT, n=5, 24 ± 5 years) and untrained controls (CON, n=5, 29 ± 5 years) performed dynamic and static exercise. Cycling consisted of 5 minute stages at 30% and 60% maximum workload (W_{max}), and leg extension involved 15 second contractions at 40% and 75% maximal voluntary isometric contraction (MVIC). Peak untwisting velocity (PUV), apical and basal rotation velocities did not differ between groups at rest or during exercise ($p > 0.05$). PUV increased in TRI from rest to 30% and 60% W_{max} ($p < 0.01$), remained unchanged in LDR, RT and CON from rest to 30% ($p > 0.05$, $p < 0.05$, $p > 0.05$, respectively) and 60% W_{max} ($p = 0.018$, $p > 0.05$, $p > 0.05$, respectively). PUV did not change from rest to 40% ($p > 0.05$) and 75% MVIC in TRI, LDR, CON ($p > 0.05$) and RT ($p < 0.05$). These findings suggest diastolic mechanics do not differ at rest or during exercise based on sport specificity, yet mixed training (TRI) athletes demonstrate augmented diastolic mechanics during dynamic exercise.

Key words: Speckle tracking echocardiography ; Left ventricular twisting mechanics; Athlete's heart; Diastolic function.

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List of Abbreviations

2-D	Two dimensional	ε	Strain
A'	Late tissue Doppler velocity	E'	Early tissue Doppler velocity
ACGS	Apical circumferential global strain	E/A ratio	Ratio of E and A wave
ANOVA	Analysis of variance	E wave	Early diastolic velocity through mitral valve
AP4CH	Apical 4 chamber		
AP2CH	Apical 2 chamber	EF	Ejection fraction
ASE	American society of echocardiography	HR	Heart rate
AVC	Aortic valve closure	IHG	Isometric hand grip
A wave	Late diastolic blood Flow velocity through mitral valve	IVPG	Intraventricular pressure gradient
BCGS	Basal circumferential global strain	IVRT	Isovolumetric relaxation time
BP	Blood pressure	IVS	Interventriular septum
d	Diastole		
CON	Controls	LA	Left atrium
CV	Coefficient of variation	LDR	Long distance runners
DT	Deceleration time	LV	Left ventricle
TDI	Tissue Doppler imaging	LVEDV	Left ventricular end diastolic volume
LVM	Left ventricular mass	LVESV	Left ventricular end systolic volume
LVID	Left ventricular internal diameter		

M-mode	Motion mode	STE	Speckle tracking echocardiography
MVIC	Maximal voluntary isometric contraction	SV	Stroke volume
MVO	Mitral valve opening	TRI	Triathletes
PAR-Q	Physical activity readiness questionnaire	TTP	Time to peak
PLAX	Parasternal long axis	UTR	Untwisting rate
PSAX	Parasternal short axis	VM	Valsalva manoeuvre
PUV	Peak untwisting velocity		
PWT	Posterior wall thickness		
Q̇	Cardiac output		
RER	Respiratory exchange ratio		
RPE	Rating of perceived exertion		
rpm	Revolutions per minute		
RT	Resistance trained		
s	Systole		
S'	Tissue Doppler velocity during systole		

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1.0 General Introduction

Normal left ventricular (LV) function requires efficient electrical stimulation and muscular contraction in order to facilitate the working needs of the human cardiovascular system (Sengupta et al., 2006). The thick walled LV provides a contractile force to eject blood out of the myocardium and through the systemic circulation (Smith and Fernhall, 2011). Myocardial emptying and refilling underpins the distribution of blood within one cardiac contraction, termed stroke volume (SV) (Levick, 2000). Diastole involves the process of active relaxation and compliance to enable filling, with the complex mechanical and physiological interaction between these elements known as diastolic function (George et al., 2010). In a closed loop system, diastolic function will greatly influence LV output (George and Somauroo, 2012).

Technological developments have established sophisticated methods over time to quantify cardiac structure and function; which include chest x-ray, electrocardiogram, magnetic resonance imaging and ultrasound echocardiography (Fagard, 2003, Prior and La Gerche, 2012). A novel method to measure myocardial function is speckle tracking echocardiography (STE). The novelty of STE is the ability to assess myocardial deformation (Bansal and Kasliwal, 2013) as the LV undergoes a complex array of deformation (strain ϵ) (Mor-Avi et al., 2011) in multiple directions throughout the cardiac cycle. The wringing motion of the LV is largely described by terms such as LV rotation, twist or torsion (Sengupta et al., 2008). Twisting which occurs during systole subsequently causes untwisting before aortic valve closure (AVC), which continues through diastole (George and Somauroo, 2012). The interaction between twisting and untwisting governs 'LV twisting mechanics', with LV untwisting serving as a useful indicator of diastolic function (Notomi et al., 2008).

The athletic heart is often described by physiological alterations in structural and functional parameters (Prior and La Gerche, 2012) following repetitive participation in exercise training (Baggish and Wood, 2011). Typically, adaptations may differ between 2 distinct categories of exercise, dynamic and static (Simsek et al., 2013),

leading to alternate forms of adaptation (Morganroth et al., 1975). Although athletes often demonstrate superior conventional diastolic function (Caselli et al., 2015), STE derived diastolic mechanics have shown contrasting athlete-control findings, with increases (Weiner et al., 2010a, Kovacs et al., 2014), no changes (Nottin et al., 2008, Lee et al., 2012, Maufrais et al., 2014) and decreases, with the suggestion of a functional reserve for effort (Zócalo et al., 2008, Santoro et al., 2014a, Santoro et al., 2014b). Based on a dichotomous classification, sport specific differences may be present given differences in peak untwisting velocity (PUV) have been observed between strength and endurance athletes (Santoro et al., 2014a).

Dynamic exercise involves changes in muscle length with a small magnitude in intramuscular force, whereas static induces large increases in intramuscular force with no changes in muscle length (Mitchell et al., 2005). When subjected to increasing cardiovascular demand, such as that found when exposed to an exercise stress, twist mechanics are augmented to enable normal LV function during dynamic exercise (Notomi et al., 2006, Doucende et al., 2010, Lee et al., 2012). Enhanced apical untwisting generates a pressure gradient despite a reduced filling period, to promote passive filling with low atrial pressures (Notomi et al., 2006). During isometric exercise, untwisting mechanics have failed to elicit alterations compared with rest, showing no enhancements in apical untwisting (Weiner et al., 2012, Balmain et al., 2015). The current understanding of diastolic mechanics during exercise has largely come from non-athletic population studies, thus more literature is required to establish the athletic responses to both preload and afterload mediated exercise modalities, which currently, is poorly understood.

2.0 Literature Review

2.1 The Athletic Heart

Differences between the trained and non-trained heart have been investigated since the late 1800's and early 1900's (D'Ascenzi et al., 2015), with Henschen in 1899 discovering that cross-country skiers possessed an enlarged heart (Fagard, 2003). Exercise training is associated with adaptive structural, functional and electrical cardiac remodelling (Baggish et al., 2009) and is characterised by morphological increases in the myocardial wall thickness, size and LV mass (LVM) (Pluim et al., 2000, Aksakal et al., 2013). These physiological adaptations are termed the 'athlete's heart' which occur to enable a superior standard of athletic performance (Prior and La Gerche, 2012), as a consequence of repeated exercise stimuli (De Luca et al., 2011).

The athletic heart may adapt structurally and functionally with sport specific remodelling. A sport categorisation outlined by Mitchell et al. (2005) provides a 9 box grid system dividing sports in accordance to the dynamic and static components required for the sporting movements (Figure 2.1). The two forms of exercise should be placed at polar ends of a continuum with sports that require both being placed in between (Barbier et al., 2006). A more comprehensive division of sports, as opposed to the dichotomous classification (endurance versus resistance) which is criticised for its oversimplification (Szauder et al., 2015), permits the assessment of potentially different cardiac adaptations as a consequence of sport specific myocardial loading.

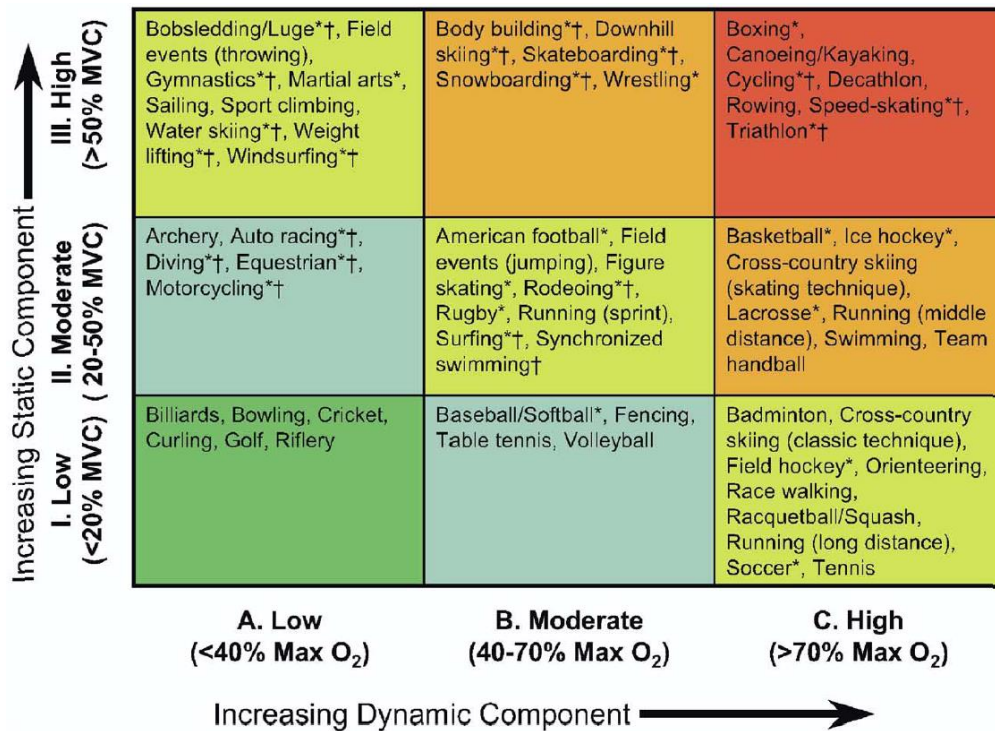


Figure 2.1 Sports classifications based on dynamic and static components. *Danger of body collision. † Increased risk if syncope occurs. Adapted from Mitchell et al. (2005).

2.1.1 The Morganroth Hypothesis

Further development from the concept of an athletic heart came from Morganroth et al. (1975) who investigated sport specific remodelling using motion-mode (M-mode) echocardiography. The study investigated endurance (swimmers, runners) and resistance (wrestlers, shot putters) athletes as they participated in alternate forms of exercise, dynamic and static respectively. The endurance group showed increases in LVM and LV dimensions ($p < 0.001$) with normal LV wall thickness. Contrasting findings were observed in the resistance group who demonstrated enhancements in wall thickness ($p < 0.001$) but not LV internal diameters (LVID). The notion that there are two morphological cardiac adaptations to different forms of exercise is now known as the ‘Morganroth hypothesis’ (Naylor et al., 2008). These two types of cardiac remodelling are termed eccentric and concentric hypertrophy, attributed to endurance and resistance hearts, respectively (Pluim et al., 2000) (Figure 2.2)). However, the Morganroth hypothesis is controversial with reviews and

meta-analyses concluding alternate findings which have supported (Pluim et al., 2000) and disputed the theory (Fagard, 2003, Naylor et al., 2008, Utomi et al., 2014). The inconsistency often comes from the lack of concentric remodelling in the resistance trained athletes (Haykowsky et al., 2000, Spence et al., 2011). Cardiac remodelling as a dichotomous concept does not exist but remains a relative concept as both endurance and strength training induce a volume and pressure challenge on the myocardium, but exerted at different magnitudes (Pluim et al., 2000, Fagard, 2003).

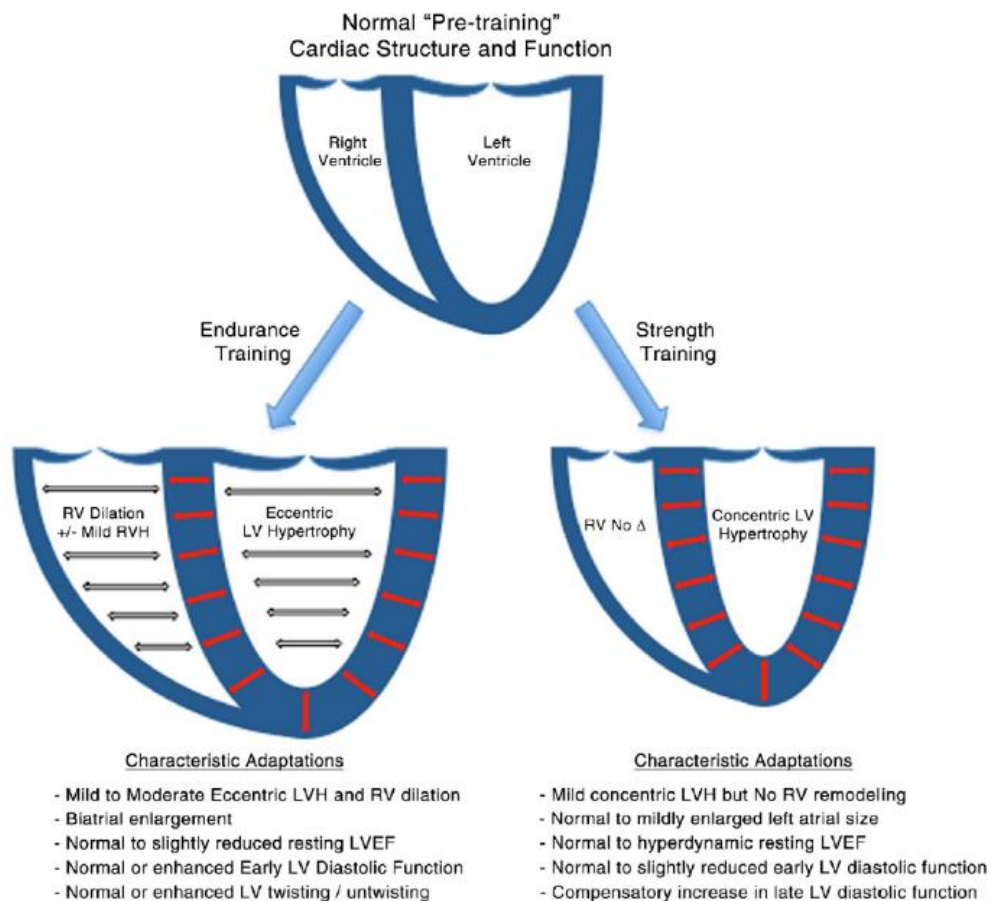


Figure 2.2 Summary of ventricular remodelling during sustained exercise training highlighting the sport-specific nature of exercise induced cardiac remodelling. Taken from Weiner and Baggish (2012).

2.1.2 *Left Ventricular Eccentric Hypertrophy*

Eccentric hypertrophy is typically characterised by chamber dilatation (King and Wood, 2013), determined by enhanced LVID during diastole (d), and proportional increases in posterior wall thickness (PWT) and interventricular septum (IVS) (Fagard, 2003). Sports such as cycling, triathlon and decathlon possess both high static (the cycling components) and dynamic components, therefore must adapt to both elements (Mihl et al., 2008). Increased LVM, LVIDd, IVS ($p < 0.001$) and PWT ($p < 0.01$) have all been shown in cyclists compared with healthy controls (Nottin et al., 2008). In addition, cyclists and triathletes (TRI) have demonstrated greater LVM and LVIDd than marathon runners (Hoogsteen et al., 2004). A mix of high dynamic and high static training may induce greater adaptations than high dynamic alone due to extreme blood volume and pressure overloads induced by these types of training for often long periods of time (Pluim et al., 2000). High static loading from the isometric components of cycling and swimming (triathlon) could enhance pressure loading and thus, trigger a secondary physiological adaptation of LV hypertrophy (Hoogsteen et al., 2004). Sports which are highly dynamic but low static (long distance running (LDR)) require adaptation to predominantly sustained elevations in venous return leading to a volume overload challenge on the myocardium (Paterick et al., 2014). The observation of structural changes to the LV diameter in those exposed to repeated dynamic exercise stimuli are consistent and evident throughout both cross-sectional (Morganroth et al., 1975, Vinereanu et al., 2002, Utomi et al., 2014) and longitudinal investigations (Spence et al., 2011), even after as little as 11 weeks of endurance training (Adams et al., 1981).

Preload refers to the degree of myocardial distention prior to shortening, which is influenced by the amount of ventricular filling (Vincent, 2008). Repetitive increases in venous return, and thus preload, results in eccentric hypertrophy (Naylor et al., 2008, Toischer et al., 2010). LV dilation occurs by way of applying new sarcomeres in-series (George et al., 2011), allowing the cardiomyocytes to increase in length and longitudinal dimension (Weeks and McMullen, 2011), subsequently leading to enlargements in LVIDd. Preload progressively increases during the diastolic filling

period until end diastole, when the LVEDV is established and causes myocyte stretching (Toischer et al., 2010). Greater LV fibre stretch enhances contractility during systole to eject a higher SV (Smith and Fernhall, 2011), due to the Frank-Starling law of the heart (Chan-Dewar et al., 2012). Findings from Otto Frank and Ernest Starling lead to the statement that, '... the larger the diastolic volume of the heart... the greater the energy of its contraction' (Konhilas et al. 2002, p.305).

Dynamic exercise causes vasodilation and initiates a drop in vascular resistance (decreased afterload) resulting in greater SV (Smith and Fernhall, 2011). During the initial stages of exercise, LVEDV increases compared to a resting state (Higginbotham et al., 1986). A 3-4 fold rise in systemic venous return ensures a stable filling volume by increasing preload, which then remains constant after the early increase (Rowland and Unnithan, 2013). An upper limit is evident in untrained individuals where LVEDV plateaued at ~30% (Stohr et al., 2011b) and SV at ~40-50% maximal capacity, respectively (Poliner et al., 1980, Higginbotham et al., 1986). During progressive exercise, due to a continual rise in heart rate (HR), cardiac output (\dot{Q}) plateaued at ~70% peak power (Stohr et al., 2011b). Beyond low work intensities (~30% maximal capacity), SV may not maintain \dot{Q} (Rowland, 2009) but increased HR may be responsible. A rise in HR occurs to match increased venous return and therefore, greater HR to 'defend' the lack of structural adaptations in untrained individuals (Rowland and Unnithan, 2013). If HR is unable to continually increase sufficiently, progressive LV dilatation occurs (Rowland and Unnithan, 2013). However, a disadvantageous reduction in wall tension and myocardial efficiency would ensue (Rowland and Unnithan, 2013), which may explain the plateau in \dot{Q} previously observed (Stohr et al., 2011b).

In contrast, trained endurance athletes exhibit greater maximal SV and \dot{Q} which may be due to larger resting LVIDd (Rowland, 2009). With incremental exercise SV, \dot{Q} and HR continue to increase without the observation of a plateau until maximal exercise (Gledhill et al., 1994, Warburton et al., 2002). Warburton et al. (2002) demonstrated that in 10 highly trained cyclists (26 ± 5 years), during both supine and upright

incremental exercise, SV increased which was accompanied by progressive enhancements in diastolic filling and LVEDV. Later work observed similar findings in 24 young (26 ± 5 years) endurance athletes (9 LDR, 10 cyclists, 3 cross-country skiers, 2 multisport) (Sundstedt et al., 2004). LVEDV increased from rest (175 ± 34 mL) to exercise (207 ± 27 mL) ($p < 0.001$) at $160 \text{ beats} \cdot \text{min}^{-1}$ by 18% and LV end-systolic volume (LVESV) decreased from rest (70 ± 25 mL) to exercise (58 ± 18 mL) by 21%. These observations suggest enhanced diastolic function enables more filling during the later stages of vigorous exercise, despite reductions in available filling time (Warburton et al., 2002). Therefore, the non-plateau in SV observed in elite endurance athletes may be governed by a progressive increase in LV diastolic filling and thus preload, enabling greater contractility via the Frank-Starling mechanism (Rowland, 2009).

2.1.3 Left Ventricular Concentric Hypertrophy

Afterload is the pressure which the LV must overcome to eject blood into the aorta (Rowland and Unnithan, 2013). The law of LaPlace is the proposed mechanism for adaptation, by which the LV muscular walls thicken to counter the external pressure exerted on the myocardium, expressed as wall stress (Naylor et al., 2008). Sarcomeres are added in-parallel to existing sarcomeres which increases wall thickness and consequently contractile force (Mihl et al., 2008).

Concentric hypertrophy is characterised as an increased ratio of wall thickness to radius (Pluim et al., 2000). This adaptation is thought to cause little change in LVIDd but increases in wall thickness (Barbier et al., 2006) and LVM when compared to matched controls (Fagard, 2003, Szauder et al., 2015). Findings of a concentric hypertrophic adaptation lack consistency (Naylor et al., 2008). Observations of concentric hypertrophy have come from cross-sectional studies (Vinereanu et al., 2002), longitudinal studies (~10-12 weeks in duration) (Lusiani et al., 1986) and meta-analysis investigations (Pluim et al., 2000).

Despite the proposed mechanisms for physiological adaptation, a large quantity of studies have failed to evidence the theory (Pelliccia et al., 1993, Haykowsky et al., 2000, Naylor et al., 2008, Utomi et al., 2013, Utomi et al., 2014) including a study following 6 months strength training (Spence et al., 2011). The lack of adaptations reported during resistance training periods may be due to the initiation of the valsalva manoeuvre (VM), attenuating the increase in transmural pressure and wall stress (Haykowsky et al., 2002). The VM is the forced expiration against a closed glottis (Laborda et al., 2014) and becomes inevitable at intensities >80% maximal contraction (MacDougall et al., 1992). Haykowsky et al. (2001) found that when performing a leg press at near maximal (80% and 95% 1 repetition max) and maximal intensities with an accompanying brief VM, LV wall stress did not change from baseline. Intrathoracic pressure increased which protects the myocardium to neutralise LV wall stress (Haykowsky et al., 2001). The neutralisation conflicts with the LaPlace law that pressure loading induces concentric adaptation in resistance athletes (Haykowsky et al., 2002).

At rest, afterload is acknowledged as equal to aortic blood pressure (BP) (Chan-Dewar, 2012); however, both dynamic and static exercise influence the magnitude of afterload differently. Dynamic, aerobic exercise raises systolic (s) BP due to the augmentation of \dot{Q} , yet dBP remains unchanged or slightly decreases due to vasodilation (Tanaka et al., 2014). During resistance exercise both sBP and dBP increase compared with rest (Stefani et al., 2008, Weiner et al., 2012). Muscle fibres shorten, become stiffer and induce swelling which all contribute to increased intramuscular pressure (Hietanen, 1984). This pressure is transferred into the intramuscular blood vessels causing them to compress (Hietanen, 1984); ultimately occluding the vessels (MacDougall et al., 1985). Due to limited inflow and outflow of blood at the muscular level a progressive build-up of metabolites occurs. The sympathetic nervous system is stimulated to eject more blood to provide nutrients; therefore, suggesting it is the increase in \dot{Q} which raises BP (Hietanen, 1984), as opposed to the peripheral vascular resistance which does not change (Lind and McNicol, 1967, Chrysant, 1978).

Tanaka et al. (2014) investigated peripheral and central BP responses to static and dynamic exercise in healthy, middle-aged untrained subjects. DBP did not alter after isometric hand-grip (IHG) exercise at 30% maximal voluntary isometric contraction (MVIC) for 90 seconds; sBP increased but to a lesser extent than during cycling. Previous studies have shown IHG for 3 minutes at 30% (Stefani et al., 2008) and 40% MVIC (Weiner et al., 2012) increased DBP. Moreover, Laird et al. (1979) showed sustained IHG for 4 minutes increased both sBP and DBP with a lower intensity (25% MVIC) than used by Tanaka et al. (2014). Therefore, a short exposure (90 seconds) may not have been sufficient to enhance systematically detectable DBP. However, Tanaka et al. (2014) did show significant increases in systolic central BP ($p=0.002$), which may also be a superior index of cardiac load in comparison to peripheral BP (Tanaka et al., 2014). The change in central BP may be indicative of a haemodynamic afterload exposed during low intensity, short duration IHG.

Smolander et al. (1998) investigated BP responses to upper and lower body static exercise in 10 recreationally active males (26 ± 2 years). Mean BP was greater at 40% than 20% MVIC in both muscle groups ($p<0.05$), yet the knee extension produced a greater response compared to the IHG ($p<0.001$). Differences in MVIC (IHG (665 N) versus knee extension (924 N)) and thus the force generated at the same relative intensity may produce a greater BP response, and thus afterload, during lower body static exercise compared with IHG. Taken together, the BP responses to resistance exercise varies depending on the mode of exercise. In addition, the performance of a VM which may be accountable for the inconsistency in concentric hypertrophy observed following resistance training. With findings associated with the afterload effects from short duration exercise coupled with greater BP from lower body exercise, may advocate the usefulness of a lower body isometric modality to elicit physiological increases in response to a more representative 'real-world' exercise than IHG.

2.2 Speckle Tracking Echocardiography

Two-dimensional (2-D) STE was initially developed as an expansion to tissue Doppler imaging (TDI), to assess multiple planes of movement (Bansal and Kasliwal, 2013). STE is less angle-dependant than TDI (Perk et al., 2007) and quantifies deformation in any direction within the imaging plane (Mor-Avi et al., 2011). Notomi et al. (2005) validated the use of STE to examine LV functional deformation compared with TDI; suggesting STE may be an accessible and feasible approach to investigate LV diastolic function (Weiner et al., 2010a). Speckles are acoustic markers visible within the myocardium derived from ultrasound examinations (Kovacs et al., 2014), then analysed frame-by-frame which are used in an algorithm to determine cardiac mechanics (Bansal and Kasliwal, 2013).

2.3 Left Ventricular Mechanics

Complex patterns of LV deformation occur which enable it to efficiently fulfil its purpose. LV mechanics is an umbrella term used to describe strain and strain rate across three planes of motion, longitudinal, radial and circumferential (Blessberger and Binder, 2010) and the twisting mechanics, which concerns the rotational motions of the LV throughout the cardiac cycle (Figure 2.3).

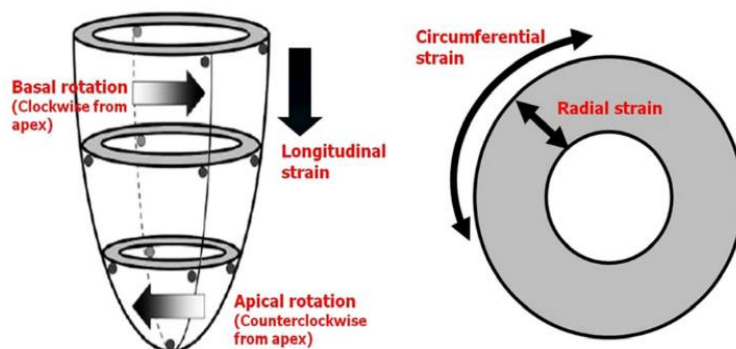


Figure 2.3 Different components of the left ventricular myocardial deformation that can be measured by speckle-tracking echocardiography. Taken from Bansal and Kasliwal (2013).

2.3.1 *Twisting Mechanics*

Circumferential rotations are expressed in degrees and refer to myocardial rotation of the short axis perpendicular to its long axis, with the net difference of apical and basal rotations during systole resulting in twist (Buckberg et al., 2011, Mor-Avi et al., 2011). Torsion is twist normalised to the distance between the two imaging planes (Voigt et al., 2015). LV untwisting is expressed as the opposite to twisting and the return to the original resting shape and size (Buckberg et al., 2011). Studies have used peak untwisting rate (UTR) when referring to PUV, with peak UTR defined as PUV occurring during early diastole (Weiner et al., 2012, Maufrais et al., 2014). UTR has also been defined as the average untwist (%) from peak twist velocity to the end of the isovolumic relaxation time (IVRT) (Takeuchi et al., 2006), expressed as %/ms (Kim et al., 2015). In addition, Vitarelli et al. (2013) defined peak UTR as $(LV_{\text{torsion}} - LV_{\text{torsion at mitral valve opening (MVO)}}) / (\text{time difference between the two events})$, expressed as $\text{deg} \cdot \text{sec}^{-1}$. All indices are measures of diastolic function, with UTR reflecting early diastole and PUV indicating the largest untwist velocity of during diastole.

2.3.2 *Myocardial Architecture*

LV architecture governs the mechanisms responsible for twisting and untwisting during systole and diastole, respectively (Mor-Avi et al., 2011). Work by Streeter et al. (1969) identified multiple layers of cardiac muscle that collectively make a continuum of myocardial tissue (Figure 2.4). Fibre geometry angle gradually changes from positive to negative (Sengupta et al., 2008), from the subendocardium ($\sim 80^\circ$) through the mid wall ($\sim 0^\circ$) and to the subepicardium ($\sim -60^\circ$) (Mor-Avi et al., 2011). The Torrent-Guasp model of the unscrolled myocardial band forms one apical and one basal loop (Biswas et al., 2013). The apical loop comprises of oppositely wound obliquely shaped fibres, consisting of a right (subendocardial) and left-handed (subepicardial) arm (Buckberg et al., 2011). The right-handed arm, also termed the descending segment has clockwise fibres, whereas the left-handed arm, also known

as the ascending segment has counter clockwise fibres (Biswas et al., 2013). The circumferential fibres of the basal loop encompass the upper two-thirds of the apical loop with the apex exposed (Biswas et al., 2013) and consist of the left and right sides (Buckberg et al., 2011) (Figure 2.5)). The combination and universal contraction of the helical structure and circular fibres enables LV rotational motion (Buckberg et al., 2011).

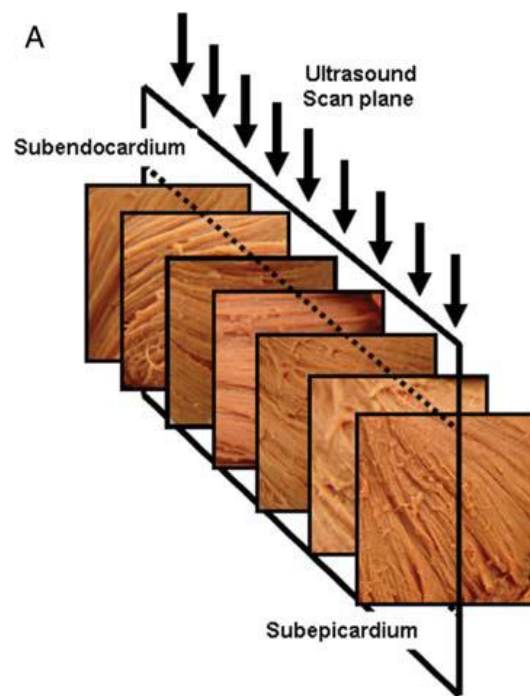


Figure 2.4 Multiple layers of myocardial fibers showing the geometry changes from right handed subendocardium to left handed subepicardium helices. Adapted from Mor-Avi et al., (2011).

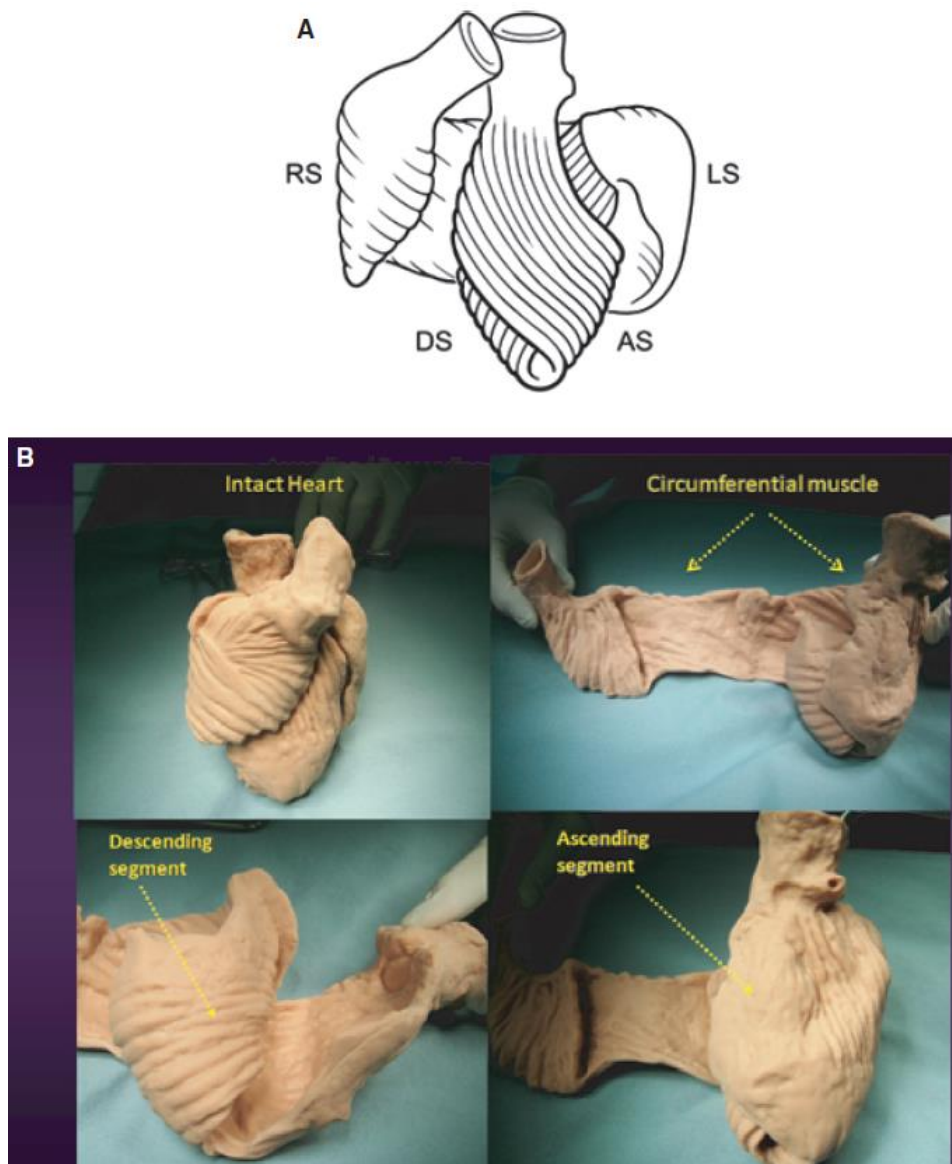


Figure 2.5 Schematic model and dissected heart model showing myocardial fiber arrangements. A. depicts the apical and basal loops. The apical loop consists of an outer ascending segment (AS) with oblique counterclockwise fiber orientation and an inner descending segment (DS). The basal loop fibers are oriented in a circumferential or transverse direction. It can be considered to have 2 segments – right (RS) and left (LS). B. depicts the way the circumferential fibers of the basal loop wrap around the ascending and descending segments. Taken from Biswas et al. (2013).

2.3.3 Twisting- Isovolumetric Contraction and Ejection

Initiation of the isovolumetric contraction period (pre-ejection) causes shortening of the circumferential fibres of the mid wall and subendocardial descending segment in the absence of ascending activation (Buckberg et al., 2008). A brief global counter clockwise rotation occurs (Buckberg et al., 2011) producing a 'cocking' motion in preparation for ejection (Buckberg et al., 2008). During the ejection phase, the ascending segment dominates the descending segment, resulting in an overall counter clockwise rotation of the apex due to its greater moment arm and thus radius (Biswas et al., 2013). The descending segment continues its contractual direction from the pre-ejection period causing the base to rotate clockwise (Buckberg et al., 2011). Although the subendocardial forces during contraction exceed that of the subepicardial, the greater torque of the epicardium dominates the direction of rotation due to its larger radius in a counter clockwise direction at the apex and clockwise at the base (Mor-Avi et al., 2011). Further midwall shortening results in fibre rearrangement of the subendocardial loop (Sengupta et al., 2008), heightening the magnitude of shearing (Sengupta et al., 2008). Shearing deforms the matrix and prompts the storage of potential energy (Mor-Avi et al., 2011) generated within both the ascending and descending segments of the right-handed helix (Buckberg et al., 2011) Figure 2.6)).

2.3.4 Untwisting- Isovolumetric Relaxation and Rapid Filling

Relaxation takes place at the later stages of systole, before AVC, and continues into early relaxation and filling (George and Somauroo, 2012). At the termination of contraction, the post-ejection isovolumetric period ensues with no contraction of the left and right segments of the circumferential muscle or descending segment, with the ascending segment continuing to shorten (Buckberg et al., 2011). Dominant subepicardial lengthening and subendocardial shortening causes brief global rotation in a clockwise motion at the base and apex (Mor-Avi et al., 2011). Although the ascending segment continues to contract counter clockwise, circumferential recoil

produces net clockwise and counter clockwise untwist at the apex and base, respectively (Buckberg et al., 2008). Further, elastic recoil within the highly sheared ascending apical loop (Buckberg et al., 2011) prompts the release of the stored energy within the spring like titin protein (Helmes et al., 2003), to cause untwisting (Notomi et al., 2008) which produces a ‘suction’ effect by creating an intraventricular pressure gradient (IVPG) (Notomi et al., 2006). The ability to create this gradient and facilitate passive filling is known as diastolic function (George and Somauroo, 2012). Lower ventricular pressure facilitates LV filling with low atrial pressures (Buckberg et al., 2008), with the relationship between IVPG and UTR shown to be positive ($r= 0.76$, $p<0.0001$) (Notomi et al., 2008). Apical unwinding is reliant on relaxation of all muscle segments so that the isovolumetric interval becomes a preclude element to the suction generated for rapid diastolic filling (Buckberg et al., 2011). LV untwisting occurs until just after MVO and precedes peak IVPG, which too precedes peak filling (Notomi et al., 2006). A large proportion (~50-70%) of untwisting takes place during the isovolumetric relaxation phase with the remainder taking place during early diastolic filling period (Mor-Avi et al., 2011). Due to untwisting taking place within the earliest phases of relaxation, LV untwist may be considered a determinant of diastolic function (Burns et al., 2009).

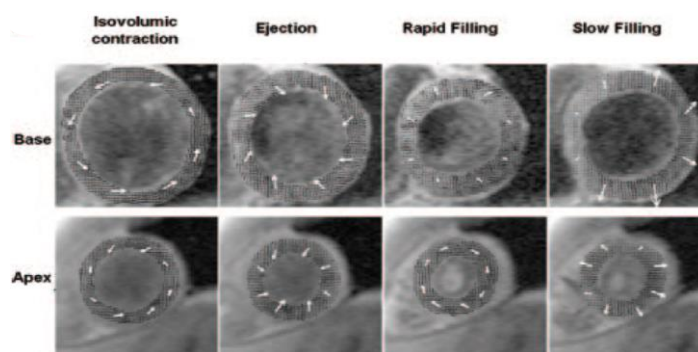


Figure 2.6 All motions are described in the text; the arrows show the clockwise (marker to right) and counter clockwise (marker to left) directions of transverse twisting motion during the shortaxis view and are obtained during isovolumic contraction, mid systole, isovolumic “relaxation” phase, and slower filling in mid diastole. Taken from Buckberg et al. (2008).

2.3.5 Influence of Preload and Afterload on Twisting Mechanics

LV twisting mechanics are influenced by the haemodynamic loading exerted upon it (Sengupta et al., 2008). Dong et al. (1999) independently manipulated preload and afterload, as LVEDV increased as did torsion ($p < 0.01$) and following the increase in LVESV, torsion subsequently decreased ($p < 0.001$). Controlled preload increases cause enhanced LV twist, while greater afterload results in reductions (Sengupta et al., 2008).

Human studies have shown contrasting findings following fluid administration to enhance preload (Burns et al., 2010, Weiner et al., 2010b). Burns et al. (2010) found that untwist decreased and PUV was delayed from pre-fluid (-37.0 ± 49.2 ms) to fluid (9.1 ± 46 ms), which occurred after MVO ($p < 0.01$). These findings may indicate that the diastolic component is not required due to the larger LV volumes being sufficient to facilitate the cardiovascular demands in a resting state. In contrast, Weiner et al. (2010b) showed that with increased preload, LV twist and peak early diastolic UTR increased ($p < 0.001$). The magnitude of preload infusion may underpin the differences, Weiner et al. (2010b) administered a greater volume of saline (2.1 ± 0.3 L) than Burns et al. (2010) (0.75L). A larger preload may have caused greater myocyte stretch and thus initiation of the Frank-Starling mechanism (Weiner et al., 2010b). Therefore, despite the contrasting findings, it may suggest that LV mechanics are influenced by haemodynamic loading conditions and the responses may be magnitude dependant.

2.4 Left Ventricular Untwisting

2.4.1 Untwisting Mechanics in Athletic Populations

Limited diastolic strain and untwist data investigating athlete-control differences has been published to date (George et al., 2010). Conflicting cross-sectional findings have been found, observing greater (Vitarelli et al., 2013, Kovacs et al., 2014), lower

(Zócalo et al., 2008, Santoro et al., 2014a, Santoro et al., 2014b) or no differences in untwist parameters (Nottin et al., 2008, Lee et al., 2012, Vitarelli et al., 2013, Maufrais et al., 2014, Santoro et al., 2015) (Table 2.1).

To the author's knowledge, only two studies have investigated untwist mechanics between endurance and strength-trained athletes (Vitarelli et al., 2013, Santoro et al., 2014a). The study by Santoro et al. (2014a) consisted of an endurance group of 33 elite male cyclists (24 ± 3 years), 36 male weight lifters (24 ± 5 years) and 17 non-physically active male controls (24 ± 3 years). Peak UTR was significantly lower in the cyclists ($-67.3 \pm 22.9^\circ/\text{s}$) compared with controls ($-103.3 \pm 29.3^\circ/\text{s}$) ($p < 0.05$), with a greater difference shown compared to the weight lifters ($-122.5 \pm 52.8^\circ/\text{s}$) ($p < 0.01$); no significant differences were observed between the weight lifters and controls. The variances are suggested to occur due to alterations in the diastolic apical rotations which mirrored the differences seen in UTR ($4.2 \pm 1.9^\circ$ vs. $6.3 \pm 2.8^\circ$ vs. $7.6 \pm 5.4^\circ$, respectively), indicative of a functional reserve (Santoro et al., 2014a). Myocardial relaxation is best quantified by the time constant of LV pressure decay (Tau) (Dong et al., 2001), which showed a strong association with UTR ($r = -0.66$, $p < 0.0001$) in dogs (Notomi et al., 2008). Additionally, HR was reduced in the cyclists which may also have contributed to lower UTR by lengthening the diastolic period; which were shown to be associated ($r = -0.35$, $p < 0.01$) (Santoro et al., 2014a). Therefore, the reduced untwist parameters in endurance athletes may be the result of a preserved LV pressure decay and reduced resting HR.

In contrast, Vitarelli et al. (2013) found that PUV was not different between marathon runners ($n=35$, 29 ± 11 years), powerlifters ($n=35$, 30 ± 9 years), martial artists ($n=35$, 29 ± 10 years) and untrained controls ($n=35$, 28 ± 11 years). However, UTR, when defined as the average from peak torsion to torsion at MVO, was observed to be significantly greater in the marathoners ($94.2 \pm 29^\circ/\text{sec}$) and martial artists ($80.6 \pm 31^\circ/\text{sec}$) when compared to controls ($61.7 \pm 24^\circ/\text{sec}$) ($p=0.03$). The authors indicated that the martial artists performed both endurance and strength training, yet according to the classification by Mitchell et al. (2005), martial arts is

considered a high static, low dynamic activity, suggesting that the sporting division is more closely associated with the dichotomous classification. Similar to Vitarelli et al. (2013), a later study found, in a group of 106 mixed endurance athletes (marathon and ultra-trail runners (n=28), cyclists (n=41) and triathletes (n=37)), PUV did not differ to 75 healthy controls (Maufrais et al., 2014). However, athletes did demonstrate greater %untwist during IVRT ($p < 0.001$), suggesting greater untwist during early diastole to facilitate a pressure gradient and enhance LV filling through greater suction effect. Based on findings by Vitarelli et al. (2013) and Maufrais et al. (2014), it may appear athletes demonstrate enhanced early untwist but peak untwist remains unchanged compared with untrained controls. However, as opposed to endurance based athletes, concentrically adapted professional water polo players (39 ± 7 years) (relative wall thickness (RWT)= 0.45 ± 0.3) showed reduced peak untwist when compared to patients with increasing levels of afterload, hypertension (47 ± 8 years) and aortic stenosis (48 ± 9 years) (Santoro et al., 2014b). Similar to previous studies, HR was significantly lower in the water polo players ($p < 0.05$) which may aid in the explanation for differences in diastolic mechanics.

Combined power-endurance athletes consisting of 28 elite rowers, canoeists and kayakers (26 ± 8 years) demonstrated significantly greater UTR at MVO compared with controls (30 ± 5 years) and hypertrophic cardiomyopathy patients (33 ± 14 years) (Kovacs et al., 2014). Enhanced UTR during the earliest phase of relaxation implies that a greater IVPG occurs sooner, causing rapid early untwist. However, the authors did not report PUV therefore the events occurring later in diastole cannot be determined.

Weiner et al. (2010a) did measure PUV and is the only longitudinal exercise study to date, which has measured LV diastolic mechanics following an exercise training programme. Ninety days of rowing training was conducted using 15 male (19 ± 1 years) university student athletes. The intentions of the training were to optimise 5 km distance, which was implemented with 1-3 hours training per day. Training duration and frequency increased from 8.5 ± 6.2 hours/week (before the training

programme) to 13.0 ± 0.9 hours/week (during the training programme). Significant alterations were observed in untwisting parameters which showed increased systolic twist, apical untwist ($p=0.01$) and PUV from pre (-110.6 ± 41.8 °/sec) to post (-148.0 ± 29.8 °/sec) ($p<0.01$), yet no changes in basal untwist.

The findings of Weiner et al. (2010a) appear to contradict the aforementioned cross-sectional studies investigating peak untwist; one suggestion for this discrepancy may be the age of the sample. With advancing age peak UTR has shown to decrease, potentially owing to a reduction in LV compliance (Takeuchi et al., 2006). Also, geometric adaptations to the fibre orientations following power-endurance rowing training is a suggested rationale (Kovacs et al., 2014), with alterations in the titin isoforms potentially responsible for the changes in untwist observed (Weiner et al., 2010a). Although, PUV occurred prior to MVO both before and after training, the greater PUV in early diastole may facilitate a pressure gradient to enhance early LV filling. A three year follow up with maintained training showed twist regressed to baseline whilst PUV remained increased (Weiner et al., 2015). The changes in twist were proposed to be augmented by changes in loading conditions and subsequent morphological adaptations to enhanced preload, PUV may be a reflection of less load dependant measures and more dependent on intrinsic myocardial efficiency. Although other studies have used high dynamic and high static athletes (cyclists) (Nottin et al., 2008, Santoro et al., 2014a), both longitudinal studies (Weiner et al., 2010a, Weiner et al., 2015) observed increases in resting diastolic mechanical parameters having recruited power-endurance athletes associated with rowing based training. Therefore, it may be suggested that sports evoke differing functional adaptations despite being categorised similarly (Mitchell et al., 2005) (Figure 2.1)). Together, athlete-control alterations in diastolic mechanics may be sport specific but not confined to absolute static and dynamic components, yet more research to establish the sport specificity in diastolic mechanics is required.

Table 2.1 Summary of studies that have investigated athlete-control differences in speckle tracking derived diastolic parameters at rest.

Study	# Subjects (age ± SD years)	Athlete Type	Diastolic Parameter			
			Apical Rot Vel.	Basal Rot Vel.	Peak Untwisting Velocity /Untwist Rate	TTP
Kovacs et al. (2014)	A: 28 (26 ± 8) HCM: 15 (33 ± 14) CON: 13 (30 ± 5)	A- National kayaking, canoeing, rowing (combined power- endurance)	-	-	UTR: EA > HCM, CON (Measured at MVO)	-
Maufrais et al. (2014)	Young- NC: 30 (21 ± 3) A: 25 (23 ± 2) Middle- NC: 19 (38 ± 5) A: 46 (38 ± 5) Senior- NC: 26 (56 ± 6) A: 35 (54 ± 7)	A- Endurance trained (Marathon, ultra-trail runners, triathletes, cyclists)	NS	NS	PUV: NS	NS
Nottin et al. (2008)	A: 16 (25 ± 5) CON: 23 (23 ± 5)	A- Cyclists	NS	NS	PUV: NS	NS
Santoro et al. (2014a)	ET: 33 (24 ± 3) ST: 36 (25 ± 5) CON: 17 (25 ± 3)	ET- International cyclists ST- Weight lifters	-	-	PUV: ET < ST, CON	-

A= athlete; EA= endurance athlete; HCM= hypertrophic cardiomyopathy; CON= controls; NC= normal controls; YU= young untrained; MU= middle-aged untrained; MT= middle-aged trained; ET= endurance trained; ST= strength trained; MA= martial artists; H= hypertensive; AS= aortic stenosis; y= years; NS= non-significant; S= sedentary; Rot= rotation; Rot/R= rotation rate; TTP= time to peak; MVO= mitral valve opening; PUV= peak untwisting velocity; UTR= untwisting rate.

Study	# Subjects (age ± SD years)	Athlete Type	Diastolic Parameters			
			Apical Rot Vel.	Basal Rot Vel.	Peak Untwisting Velocity /Untwist Rate	TTP
Santoro et al. (2014b)	A: 45 (40 ± 7) CON: 17 (40 ± 9) H: 22 (48 ± 8) AS: 47 (48 ± 10)	A- Professional water polo	-	-	PUV: A < NC, AS	-
Santoro et al. (2015)	Young (16-26 y)- S: 35 A: 53 Adult (27-37 y)- S: 30 A: 46 Old (38-48 y)- S: 30 A: 26	A- Amateur swimmers	-	-	PUV: NS	Young A < Old A Young S < Adult S Young S < Old S
Lee et al. (2013)	YU: 11 (24 ± 4.1) MU: 9 (55 ± 4) MT: 12 (54 ± 4)	MT- Endurance (cyclists, triathletes, speed skaters)	-	-	PUV: NS	MU > YU MT < MU
Zocalo et al. (2008)	PSP: 17 (25 ± 5) NC: 10 (27 ± 6)	PSP- Professional soccer player	-	-	Mean Untwisting Velocity: PSP < CON	-

A= athlete; EA= endurance athlete; HCM= hypertrophic cardiomyopathy; CON= controls; NC= normal controls; YU= young untrained; MU= middle-aged untrained; MT= middle-aged trained; ET= endurance trained; ST= strength trained; MA= martial artists; H= hypertensive; AS= aortic stenosis; y= years; NS= non-significant; S= sedentary; Rot= rotation; Rot/R= rotation rate; TTP= time to peak; MVO = mitral valve opening; PUV= peak untwisting velocity; UTR= untwisting rate.

Study	# Subjects (age ± SD years)	Athlete Type	Diastolic Parameters			
			Apical Rot Vel.	Basal Rot Vel.	Peak Untwisting Velocity /Untwist Rate	TTP
Vitarelli et al. (2013)	ET: 35 (28 ± 11) ST: 35 (29 ± 11) MA: 35 (30 ± 9) CON: 35 (29 ± 10)	ET- Marathon runners ST- Powerlifters MA- Martial Artists	-	-	PUV: NS UTR: ET, MA > CON	-

A= athlete; EA= endurance athlete; HCM= hypertrophic cardiomyopathy; CON= controls; NC= normal controls; YU= young untrained; MU= middle-aged untrained; MT= middle-aged trained; ET= endurance trained; ST= strength trained; MA= martial artists; H= hypertensive; AS= aortic stenosis; y= years; NS= non-significant; S= sedentary; Rot Vel= rotation velocity; TTP= time to peak; MVO = mitral valve opening; PUV= peak untwisting velocity; UTR= untwisting rate.

2.4.2 Alterations in Untwist Mechanics during Exercise

2.4.2.1 Dynamic Cycling

Alterations in LV mechanics during submaximal exercise is a compensatory mechanism that is necessary to maintain \dot{Q} (Drury et al., 2012), and thus exercise performance. Compared with a resting state, titin compression and myocyte shortening is greater at the onset of exercise (Notomi et al., 2006) (Figure 2.7)). Diastolic function and filling must augment to maintain LVEDV in a shorter duration of time (Esch et al., 2009).

Doucende et al. (2010) observed that peak UTR progressively increased from rest (-88.7 ± 34.2 °/sec) to 20% (-119.3 ± 42.8 °/sec), 30% (-157.1 ± 53 °/sec) and 40% (-189.9 ± 53.5 °/sec) maximal aerobic power in 20 young, healthy men (25 ± 9 years). Additionally, a strong correlation was evident between peak LV torsion and peak UTR ($r=0.61$, $p<0.001$). The reduction in LVEDV which occurs due to reduced filling time likely results in greater LV twist which subsequently causes greater LV untwist to adequately support SV (Doucende et al., 2010). These results represent a systolic-diastolic coupling and the augmentation was mainly due to enhancements in apical untwisting. During exercise, time to peak (TTP) apical UTR reduced which occurred further into systole and closer to MVO, whereas peak basal UTR occurred afterwards. Earlier augmentation of diastolic filling velocities would facilitate a greater IVPG, necessary to generate greater suction and passively fill the LV (Esch et al., 2009). The progressive increases in UTR within this study without a plateau suggests there may still be more of a reserve for even greater exercise intensities (Doucende et al., 2010).

A later study extended the findings of Doucende et al. (2010) by investigating LV mechanics and their relation to SV during continuous and discontinuous incremental semi-supine cycling in 9 recreationally active males (26 ± 4 years) (Stohr et al., 2011b). The exercise intensities were 10, 30, 50, 70 and 90% peak power with stage lengths of 4 minutes. During both continuous and discontinuous protocols, UTR progressively increased until it plateaued at 50% peak power which exceeded the plateaus observed in LVEDV (30%) and SV (50%). Similar to Doucende et al. (2010), a

systolic-diastolic coupling existed with the greater UTR being predominantly driven by enhanced and early apical UTR, simultaneously with MVO. The plateau in LVEDV cannot be attributed to LV mechanics as twist and PUV continued to increase beyond 30% peak power (Stohr et al., 2011b). The authors proposed that pericardial constraints preventing further end-diastolic distension, and thus filling time as a consequence of increased HR, may suggest why LVEDV plateaued prior to twisting mechanics (Stohr et al., 2011b). However, the levelling off in twisting mechanics likely contributes to the plateau observed in SV (Stohr et al., 2011b). Rather than a reduction in diastolic untwisting performance, the lack of structural cardiac adaptations may thus provide a limitation to LV filling in untrained individuals (Stohr et al., 2011b). Therefore, myocardial remodelling due to exercise training may account for the continual increase in hemodynamic components during incremental exercise until maximum (see section 2.1.2); however, this is simply a theoretical proposal based upon findings in untrained populations, and an incremental study using trained athletes has yet to be conducted.

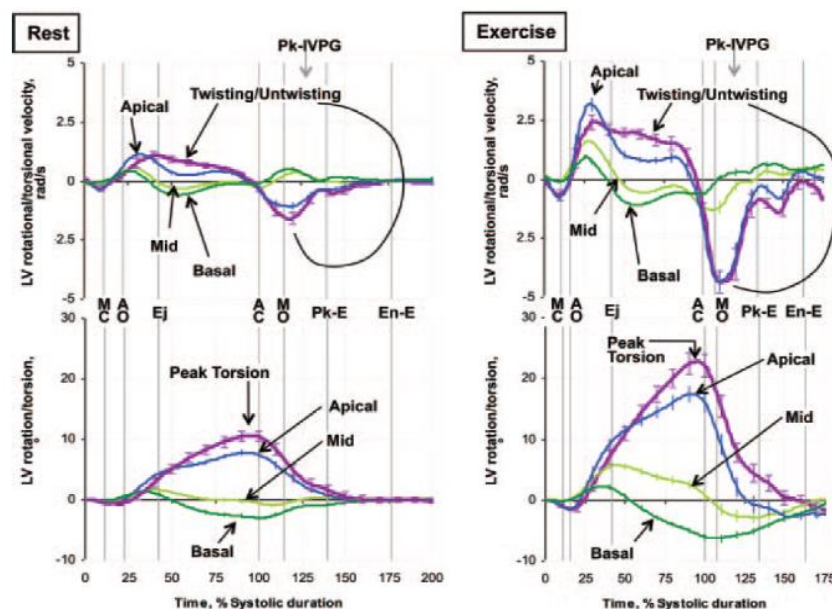


Figure 2.7 LV torsional behaviour at rest and during exercise in normal subjects. Upper panels: LV rotational and torsional velocity profiles at rest and during exercise. Lower panels: LV rotation and torsion profiles at rest and during exercise (obtained by integrating each velocity). Taken from Notomi et al. (2006).

Another recent study investigated LV twisting differences in healthy, subjects that were divided into high ($63 \pm 7 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) or moderate ($49 \pm 5 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) aerobic capacity groups (Stohr et al., 2012). In regards to PUV, there was no significant difference between the high and moderate aerobic capacity groups at rest or during exercise. However, in both groups PUV did significantly increase during the semi-supine cycling when compared with resting values ($p < 0.001$). A potential reason for the lack of differences between groups may be due to the ages of participants (21 ± 2 years and 21 ± 3 years, respectively), as both groups were < 40 years old, which has previously been demonstrated to be a threshold for augmentation of diastolic mechanics (Drury et al., 2012), and thus would have been able to augment diastolic function.

Research into athlete-control STE derived differences during exercise is sparse. Lee et al. (2012) studied the differences in untwisting velocities, between middle-aged untrained (55 ± 4 years), middle-aged endurance trained (54 ± 4 years) and young untrained (24 ± 4 years) groups. There were no significant differences between groups in PUV at rest or during supine submaximal exercise; however, middle-aged untrained showed a delayed TTP untwisting velocity when compared with young untrained and middle-aged trained. More specifically during exercise, a significant delay in obtaining PUV may inhibit aerobic capacity (Lee et al., 2012); which could partially explain why $\dot{V}O_{2\text{max}}$ was significantly lower in middle-aged untrained ($33.8 \pm 5.0 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) than in middle-aged trained participants ($47.9 \pm 4.3 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). However, the authors did not include young-trained athletes; therefore, it remains elusive whether young-trained athletes present dissimilar diastolic functioning during exercise in comparison to a young untrained cohort.

2.4.2.2 *Static Hand Grip*

To the authors' knowledge, only two studies have assessed LV mechanics during static exercise (Weiner et al., 2012, Balmain et al., 2015). Both investigations

performed an IHG exercise for 3 minutes at 40% maximum effort using healthy subjects (n=15 males, 3 females, 30 ± 3 years (Weiner et al., 2012); n=19 males, 23 ± 2 years (Balmain et al., 2015)). In the study by Weiner et al. (2012), from rest to peak IHG, sBP and dBP both significantly increased (both $p < 0.001$), accompanied by an increase in LVESV ($p = 0.005$) and reduction in SV ($p < 0.001$). These haemodynamic results are all evidence that an afterload challenge has been exerted. Similar to prior animal studies where afterload has been manipulated, Weiner et al. (2012) showed that apical rotation during systole significantly reduced ($p < 0.001$). However, this reduction did not translate into a reduction in peak apical UTR, suggesting a systolic-diastolic uncoupling (Weiner et al., 2012). However the authors indicated that peak apical untwist occurred before peak basal untwist, which is the opposite at rest. Although HR significantly increased ($p < 0.001$), the reductions in apical systolic rotations and lack of alterations in diastolic mechanical indices following IHG are suggested to have a negative impact (Weiner et al., 2012).

Balmain et al. (2015) observed similar findings, showing that systolic apical rotation decreased, yet UTR remained unchanged from rest ($-100.8 \pm 8.6^\circ/\text{s}$) to during IHG ($-108.2 \pm 9.4^\circ/\text{s}$) ($p > 0.05$). Following the IHG, Balmain et al. (2015) conducted a 3 minute period of circulatory occlusion to increase arterial BP whilst allowing HR to reduce. This method allowed the researchers to isolate afterload by removing the influence of HR on twisting mechanics. Apical UTR further reduced after the occlusion, which had previously remained unchanged during the IHG with no alterations in basal rotations. Impairment of diastolic apical rotation caused a resulting decrease in UTR ($-79.3 \pm 5.3^\circ/\text{s}$) compared with rest and IHG (both $p < 0.05$). The greater impairment following occlusion may indicate that twisting mechanics could possess greater sensitivity to resistance-mediated increases in arterial BP (Balmain et al., 2015). Therefore, the rise in HR likely confounded any effect that increased arterial pressure had on peak untwist during IHG (Balmain et al., 2015). However, both studies by Weiner et al. (2012) and Balmain et al. (2015) were conducted in healthy populations and it still remains unknown how specific populations, such as athletes respond during a static stimulus.

2.5 Overall Summary

Repetitive exercise training often results in structural and functional cardiac adaptations, which appears to be more pronounced in the endurance athlete by way of volume overload, resulting in eccentric hypertrophy. Contrasting findings regarding concentric hypertrophy associated with the resistance athlete have often disputed the Morganroth hypothesis (Naylor et al., 2008). Currently, it is not known whether the physiological adaptations of the athletic heart cause different untwisting mechanics, especially when subjected to cardiovascular stresses.

It may be suggested that athletes possess enhanced untwist during the earliest phases of relaxation. However, it remains unknown as to what effect exercise training has on peak untwist parameters due to the inconclusive, diverse findings to date; a conclusion on the athlete-control differences at rest cannot yet be determined. Different sports appear to demonstrate alternate untwisting responses when compared with healthy controls; therefore, sport specific functional adaptations may be present. With the onset of exercise, preload and afterload components alter LV output depending on the type of exercise stimuli; dynamic exercise typically evokes greater preload (Higginbotham et al., 1986), whereas static activity initiates enhanced BP response and thus afterload (Weiner et al., 2012). During dynamic exercise, PUV appears to increase in accordance with a reduced diastolic filling time, mediated by enhanced apical mechanics (Doucende et al., 2010). Larger untwist during diastole happens as a product of greater elastic recoil due to augmented apical twist, therefore suggestive of a systolic-diastolic coupling to facilitate LV filling and thus output. Conversely during sustained IHG exercise, PUV appears to remain unchanged with enhanced afterload, however peak apical alterations have been observed (Weiner et al., 2012, Balmain et al., 2015).

STE analysis is capable of providing a greater means than TDI for assessing myocardial deformation. The myocardial architecture and complex arrangement of the fibre geometry facilitate movement and permit contraction and relaxation throughout the cardiac cycle. The interaction between the structures of the basal and apical loops

enable LV twisting, and subsequent untwisting mechanics during contraction and relaxation, respectively.

2.6 Thesis Rationale

Based on the literature presented there is a lack of conclusive evidence regarding the athlete-control differences in untwisting parameters at rest. Further to this, no study to date has investigated untwisting mechanics between types of athletes based on dynamic and static components, including pure endurance (high dynamic, low static), pure resistance (high static, low dynamic) and mixed trained (high dynamic, high static). Therefore, a study to establish the influence of sports with varying dynamic and static components, in accordance with the sports categorisation (Mitchell et al., 2005) (Figure 2.3)), on STE derived diastolic function is warranted.

Although an upper limit and subsequent plateau has been observed in PUV during incremental exercise in normal individuals, it is unknown how athletic populations respond. Athletic studies during dynamic exercise are extremely sparse, with no study to the authors' knowledge having explored how the untwisting mechanics of various athletes respond and differ during either dynamic or static exercise. Also, it is unknown whether a lower body static exercise intended to induce greater afterload over a short duration of time, whilst minimising the elevation in HR, would elicit different untwisting responses than what has previously been observed during IHG. Therefore, more research is required to gain further insight into how both healthy and athletic individuals' diastolic function is augmented when subjected to various types of exercise stimuli, evidenced by preload and afterload.

2.7 Aims and Hypotheses

Using 2-D STE, the present study aims to investigate untwisting mechanics at rest and during submaximal exercise in athletes adapted to different forms of exercise training, in addition to athlete-control differences. Using incrementally elevated preload (dynamic) and afterload (static) exercises, the current study aims to establish the diastolic responses elicited by athletes during familiar and unfamiliar exercises. Therefore, based on the literature reviewed and the aim of the current investigation, the following hypotheses were tested:

Hypothesis 1

At rest, both endurance (high dynamic, low static), and mixed trained (high dynamic, high static) athletes will demonstrate significantly reduced PUV compared with healthy controls and resistance (high static, low dynamic) athletes.

Hypothesis 2

During submaximal dynamic exercise, PUV will significantly increase progressively in all athletic and non-athletic groups, with no differences between groups.

Hypothesis 3

During submaximal static exercise, PUV will demonstrate no significant alterations, with therefore no significant differences between groups.

3.0 General Methods and Reliability of Echocardiography

3.1 Ethical Approval

Before the commencement of the study, ethical approval was gained from the ethics committee of the Institute of Sport and Physical Activity Research (ISPAR) at the University of Bedfordshire (approval number: 2015ISPAR003). All procedures were conducted in accordance with the Declaration of Helsinki.

3.2 Participant Recruitment and Inclusion Criteria

Recruitment for the present study included the distribution of posters to local sports clubs, in addition to advertisements on social media. The target participants were those trained in various disciplines based on training regime. Following interest, potential participants were provided with written information sheets, which fully detailed all procedures involved and the necessary requirements of each participant. From initial contact and throughout the course of the study, participants were encouraged to ask any questions. All participants took part in the study voluntarily.

Before testing began, formal written consent was gained and participants were required to complete a medical questionnaire (Appendix 1), Physical Activity Readiness Questionnaire (PAR-Q), followed by a training history and frequency questionnaire (Appendix 2). Training frequencies reported were based on weekly hours expressed as an average over the past month.

All participants were considered healthy, were non-smokers and did not have a history of cardiovascular disease. Participants were excluded from the study if previously diagnosed with any of the following diseases; coronary heart disease, hypertension (sBP >139 mmHg or dBP >89 mmHg (Chobanian et al., 2003)), diabetes mellitus, angina, myocardial infarction or peripheral artery disease. Additionally, if an

immediate family member had a history of sudden cardiac death, this would also lead to immediate exclusion.

A past use of any anabolic steroids also led to exclusion as it has been previously documented that anabolic agents consequently result in cardiac hypertrophy (Dickerman et al., 1997). In addition, anabolic steroid use has shown to cause impairments in cardiac ϵ and rotational mechanics (Angell et al., 2012). Participants were asked whether they had ever previously used anabolic steroids, there were no reported instances of any past or present medication use capable of inducing cardiac hypertrophy.

Information derived from the training history and frequency questionnaires aided in the determination of group inclusion. LDR were required to perform at least 50 km/week (Szauder et al., 2015) and perform ≤ 2 hours/week of resistance exercise. TRI must have been active in all three triathlon disciplines (running, cycling and swimming) within the past 6 months and completed ≤ 2 hours/week resistance exercise. On the contrary, those who were RT must have performed ≤ 2 hours/week of any aerobic based exercise. Any breach of the above criteria led to exclusion from the study, which subsequently amounted to 7 participants.

3.3 Study Population

Twenty-seven individuals were used for the present investigation and analysis, 22 were non-professional athletes and 5 non-active, healthy controls (CON). The athletic participants were divided into 3 groups based on training regimes, which consisted of long distance runners (LDR) (n= 7), triathletes (TRI) (n= 9) and resistance trained (RT) (n= 5). The LDR included 5 marathon and 2 ultramarathon (up to 145 miles) distance athletes with the TRI including those who competed in events ranging from Olympic to Ironman distance. The resistance group consisted of 3 body builders and 2 strength trained categorised by self-reported repetitions and sets in accordance

with the American College of Sports Medicine categorisation for resistance training (American College of Sports Medicine., 2013). The group separations were based on the dynamic and static components for sport categorisation as described by Mitchell et al. (2005) (see Figure 2.3)).

3.3.1 Training Regimes

All athletes had participated in their respective disciplines for at least 1 year. LDR trained regularly (8.29 ± 2.63 hours/week) and had done so for at least 1 year, completed 66.01 ± 6.51 km/week of running, cycled 8.57 ± 15.74 km/week and performed 1.08 ± 0.66 hours/week of resistance exercise. RT athletes had a training history of at least 3 years, trained 9.00 ± 3.61 hours/week and took part in only 0.70 ± 0.97 hours/week of aerobic based exercise (e.g running, cycling, rowing, swimming, soccer). All TRI trained ≥ 5 days per week and had done so for at least 2 years. For running, cycling and swimming the TRI performed 38.48 ± 25.25 , 127.19 ± 39.22 and 4.13 ± 3.38 km/week, respectively. Also, TRI performed 0.72 ± 0.67 hours/week of resistance exercise. CON were healthy but sedentary and completed ≤ 30 minutes of physical activity per week (0.1 ± 0.2 hours/week), which is below the current recommended physical activity guidelines advised by the United Kingdom government (≥ 150 minutes) (Department of Health., 2011)). Physical activity habits remained consistent and did not change for at least 6 months (De Luca et al., 2011).

3.4 Experimental Protocol

3.4.1 Overview

The study was a quasi-experimental research design that required all participants to attend the University of Bedfordshire's Sport Science Laboratories on 2 occasions. Prior to both visits participants were asked to abstain from any vigorous physical activity and alcohol for at least 24 hours and caffeine for 12 hours. The 2 visits were

at the same time of day within 7 days of each other. One individual was excluded after admitting a breach of the caffeine and physical activity requirements.

Visit 1 was initiated with completion of the documentations; following this, basic anthropometric measures (age (years), height (cm) and body mass (kg)) were recorded. After a 5 minute rest in the supine position HR and BP were measured. Subsequently, a resting baseline echocardiographic assessment was performed, with participants completing a $\dot{V}O_{2\max}$ test at the conclusion of the first visit. The second visit began with the completion of a PAR-Q, before performing a submaximal bout of cycling, a MVIC test after a rest period of 10-15 minutes then a series of submaximal static contractions. Echocardiographic assessments of the basal and apical levels were conducted during both methods of submaximal exercise. See Figure 3.1 for a schematic representation of the study overview and procedures.

3.4.2 Submaximal Cycling

The submaximal cycling was performed on a dedicated eBike (eBike-L, ergoline GmbH, GE Healthcare) (Figure 3.2A)), which was positioned semi-supine at 45°. The protocol consisted of 10 minutes (2 x 5 minutes) continuous cycling at 2 intensities equating to 30% and 60% work rate maximum (W_{\max}) derived from the $\dot{V}O_{2\max}$ (see Section 3.5.3). Participants were asked to maintain a fixed cadence of 60 revolutions per minute (rpm) whilst ultrasound images were collected during the last 3 minutes of each stage (Stohr et al., 2012), with HR, sBP and dBP also recorded at the end of each stage. Figure 3.2B illustrates the submaximal cycling protocol.

3.4.3 Submaximal Leg Extensions

All single leg static contractions were completed on an isokinetic dynamometer (Kin-Com 125E Plus, Chattecx Corporation, Chattanooga, USA). A MVIC was performed prior to the submaximal leg extensions (see Section 3.5.4). All contractions were

performed at a knee extension angle of 130° in the supine position using the dominant leg. The joint centre was aligned with the axis rotation point of the crank arm (Kong and Van Haselen, 2010). The ankle pad connected to the load cell was strapped proximal to the malleoli (Marginson and Eston, 2001). A thigh and hip strap was secured to prevent unnecessary movement (Marginson and Eston, 2001), however caution was taken to ensure that the thigh strap was not excessively tight, restricting blood flow to the lower limb. All participants were instructed to keep their back flat, without arching their backs and to generate force from the quadriceps.

After a 5-minute rest following the MVIC, participants performed 2 x 15 seconds contractions at both 40% and 75% MVIC separated by 2 minutes between each contraction. A visual digital value was displayed which indicated the force being exerted, participants were told a number to maintain which corresponded to the relative intensity for that particular contraction (for example; MVIC=1000N, 40%=400N and 75%=750N). A contraction time of 15 seconds was chosen as this was the necessary time required to obtain both dBp and sBP. Also, the exercise intentions were to limit the rise in HR yet still induce a pressure challenge on the myocardium. An upper intensity of 75% MVIC was chosen as MacDougall et al. (1992) found that VM only occasionally aided exercise when intensities were <80% MVIC, whereas static exercise that surpass 85% MVIC induces an inevitable VM (MacDougall et al., 1992). Therefore, an intensity of 75% would provide the highest relative intensity where only an occasional VM may be necessary (MacDougall et al., 1992), but subjects were still instructed to breathe normally and avoid the VM. Echocardiographic images were collected at the end of each contraction. See Figure 3.2C for an illustration of the static leg extension exercise.

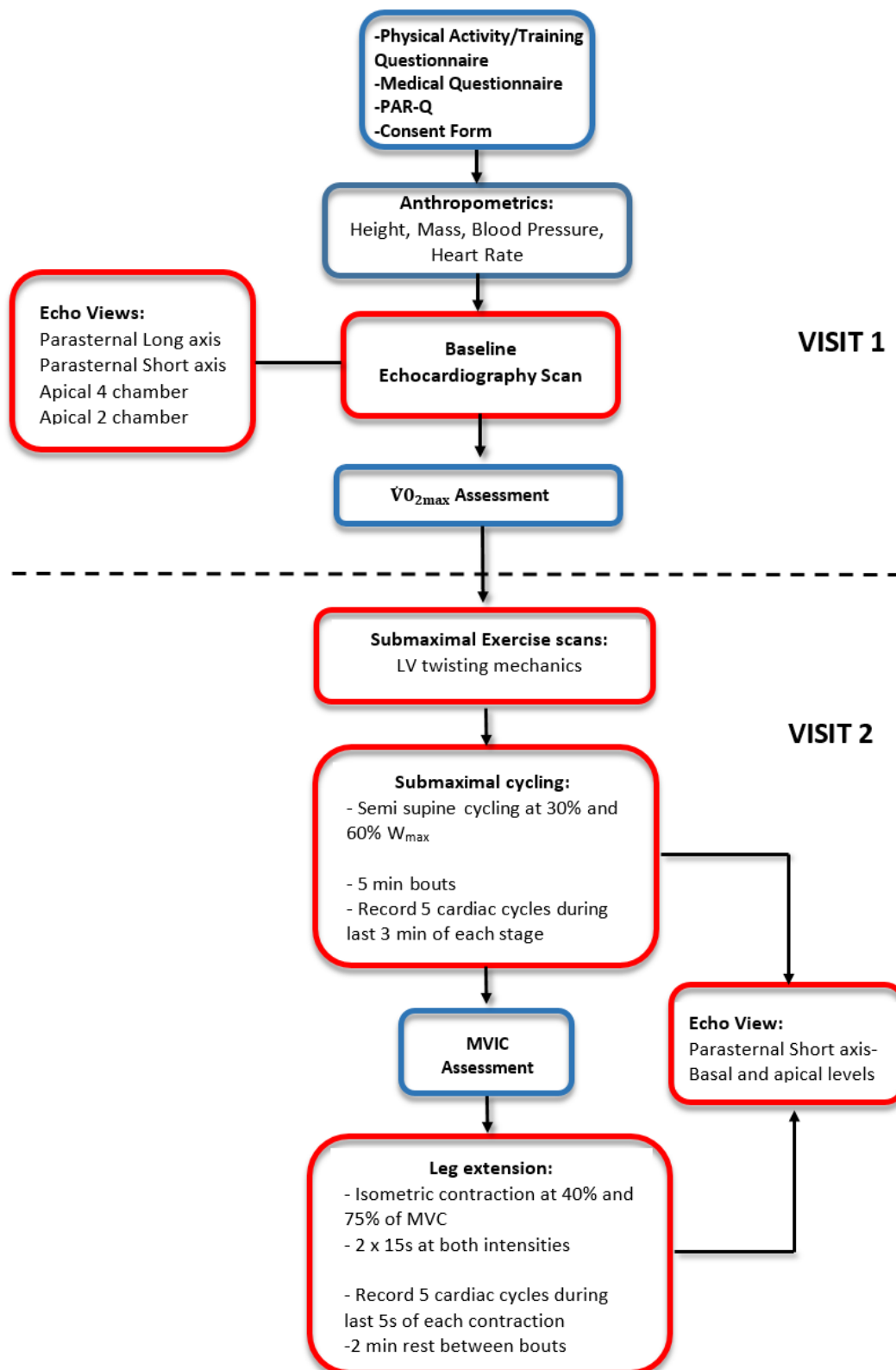


Figure 3.1 A schematic representation of the experimental protocols.

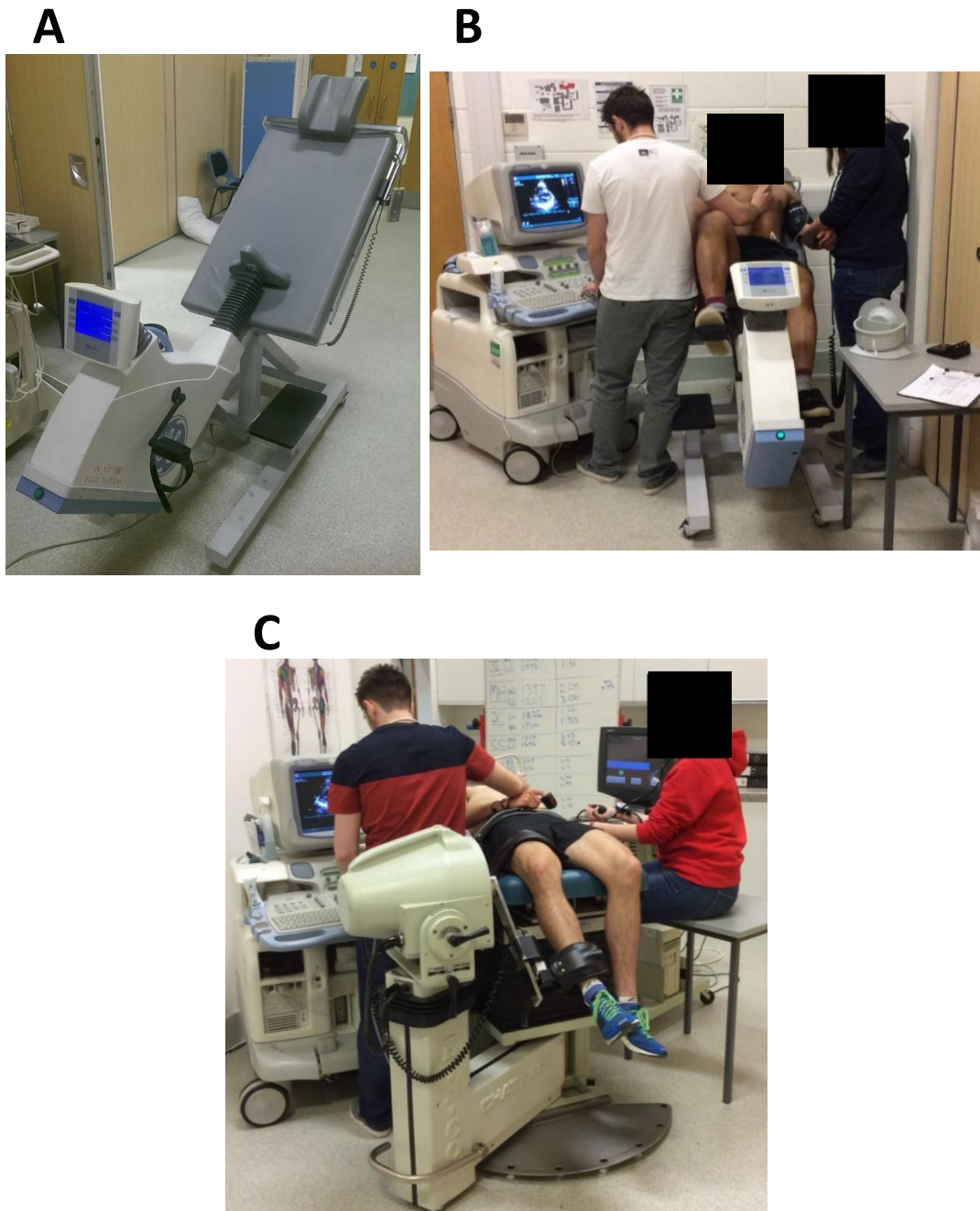


Figure 3.2 Illustrated of the semi-supine cycle ergometer (e-bike) (A) used for the submaximal cycling protocol (B). The protocol setup for the submaximal static leg extension is also illustrated (C).

3.5 Data Collection and Analysis

3.5.1 Anthropometrics

Basic anthropometric measures height (cm) and body mass (kg) were recorded with participants instructed to remove footwear and upper body clothing. To measure height, a wall mounted stadiometer (HAR-98.602, Harpenden, Holtain Ltd, Crymych) was used and required participants to stand in the anatomical position with a straight back and the calcaneus in contact with the floor. Body mass was measured using electronic, digital scales (BWBO800, Tanita, Netherlands).

3.5.2 Heart Rate and Blood Pressure

At rest, participants were fitted with a HR monitor (FS1, Polar Electro Oy, Kempele, Finland), recording HR after the supine rest period. During the submaximal cycling and leg extension protocols, a pulse oximeter (9590, Nonin Medical, Netherlands) was placed on the index finger to record exercising HR, in favour of the polar HR monitor and electrocardiogram. The HR monitor would have been in an obstructive position during the ultrasound scanning and interference from the electrocardiogram leads, due to movement, subsequently produced an inaccurate HR reading. The use of a pulse oximeter has been validated as an accurate method of estimating HR during submaximal cycle intensities (Iyriboz et al., 1991). The authors did conclude an under estimation when intensities exceeded a mean maximal heart rate of 89% and suggest that oscillation of the device at the higher work rates may have been responsible. Therefore, participants during the cycling protocol were instructed to refrain from any unnecessary motion to avoid any under estimation of HR.

All BP measurements were collected by individuals trained in using manual sphygmomanometers. Three BP measurements were collected at rest in the supine position, each separated by 2 minutes. Participants were asked to remain as relaxed as possible and to keep their legs and arms uncrossed with the palms faced up.

During exercise, BP was recorded during the last 15 seconds of each stage within the cycling protocol and throughout the 15 second contraction of the leg extension.

3.5.3 Maximal Oxygen Uptake

A preliminary $\dot{V}O_{2\max}$ assessment was performed on a semi-supine cycle ergometer to ensure that the relative intensities would be suitable and relevant for the submaximal procedure. Breath-by-breath online gas analysis was utilised to measure the expired air (Metalyser 3B, Cortex, Germany). A pre-programmed ramp protocol was employed which began with a 3 minute warm up at 70 Watts (W), before the maximal test ensued at a starting intensity of 120 W, or 100 W if HR exceeded 120 beats.min⁻¹ after the warm up period. The adjustment in starting intensity was chosen to ensure that the test concluded within 8-12 minutes (Boone and Bourgois, 2012), which has previously been documented to be the optimal duration for achieving the highest $\dot{V}O_{2\max}$ (Buchfuhrer et al., 1983). Additionally, this would enable the same protocol to be used for all athletic groups in addition to CON. The exercise intensity was increased by 20 W/minute until volitional exhaustion. Participants were required to maintain a cadence between 60-100 rpm and should the cadence fall below 60 rpm and could not be recovered then the test was terminated. For the duration of the test, the participant's back was to remain flat to the bed. All participants were provided with encouragement toward the latter part of the test.

Towards the end of each stage HR, respiratory exchange ratio (RER), volume of oxygen consumption and rating of perceived exertion (RPE), using the Borg scale (Borg, 1970), were recorded. Primary and secondary criteria for achieving $\dot{V}O_{2\max}$ were used in accordance with the British Association of Sport and Exercises Science criteria guidelines (Cooke, 2009). The primary criteria of a plateau was described as an increase of <2mL.kg⁻¹min⁻¹ or 3% despite increasing intensity and the secondary criteria consisted of an RPE ≥19, RER ≥1.15, participant subjective physical exhaustion

and a HR within ± 10 beats.min⁻¹ of age predicted maximum (220-age (years)). Three out of the five criteria, of which one was the plateau, were required in order for data to be reported as $\dot{V}O_{2max}$.

Each participant's W_{max} was calculated using the following formula with information derived from the incremental exercise test:

$$W_{max} = W_{com} + (t/60) * W$$

(Kuipers et al., 1985 cited by Arts et al., 1993)

' W_{com} ' refers to the last workload completed, 't' refers to the time (seconds) during the last uncompleted stage and 'W' refers to the workload increment (Arts et al., 1993, Jeukendrup et al., 1996).

3.5.4 *Maximal Voluntary Isometric Contraction*

Procedures were carried out in accordance with the American Society of Exercise Physiologists' recommendations for MVIC testing (Brown and Weir, 2001). Prior to the MVIC test, participants completed 5-10 submaximal leg extensions in order to ensure an increase in muscle temperature and thus reduce the risk of injury when conducting the maximal efforts. The warm up contractions also allowed a familiarisation with the static contraction. To establish MVIC participants were required to complete 3 maximal static contractions at an angle of 130° knee extension. Each maximal effort was 5 seconds in duration with a 1 second transition period from rest and each separated by 2 minutes passive recovery (Bojsen-Møller et al., 2005). MVIC was defined as the highest force produced from the 3 efforts (Adler et al., 2008) and was recorded in Newtons (N). Participants were instructed to keep their arms on their chest to prevent them from holding the sides of the equipment. Also, during the test, subjects were heavily encouraged throughout the duration of the contraction. Intensities of 40% and 75% were subsequently calculated

from the peak contraction to then be used during the submaximal protocol (see Section 3.4.3).

3.5.5 Echocardiography

All participants underwent 2-D transthoracic echocardiographic examinations at rest, during submaximal cycling and leg extension exercise, using commercially available ultrasound equipment (Vivid 7, GE Medical, Mius Ltd), with a phased array transducer (3S 1.4-3.8 MHz Phased Array). For the assessments, participants were asked to undress from the waist up and lie in the left lateral decubitus position. Imaging of the apical 4 chamber (AP4CH), apical 2 chamber (AP2CH), parasternal long (PLAX) and short axis views (PSAX) was performed in order to complete a full baseline assessment at rest. During both the submaximal exercises, participants were semi-supine and supine (cycling and leg extension, respectively) where a cushion was placed under the right shoulder producing a small amount of rotation to aid in image quality. However, attention was given to ensure that the hips remained neutral to allow for normal lower body movement.

All of the measurements and views used, outlined below, were conducted in accordance with well established guidelines (Feigenbaum et al., 2005, Lang et al., 2006, Nagueh et al., 2009, Mor-Avi et al., 2011) and the recommendations outlined by the American Society of Echocardiography (ASE) (Gottdiener et al., 2004). The same sonographer completed all echocardiographic assessments (see Section 3.6 for reliability). Measurements were collected at end-expiration and analysed using 3 consecutive cardiac cycles, however when unavailable a minimum of 2 cardiac cycles were used.

3.5.5.1 Conventional Echocardiography

The probe was positioned on the left upper chest at the third intercostal space (Feigenbaum et al., 2005) below the clavicle to obtain the PLAX. The PLAX was used to measure the linear LVID via an M-mode image. The IVS was manoeuvred horizontally, enabling an M-mode cursor to intersect perpendicular to the IVS and posterior wall between the tips of the mitral valves (Nagueh et al., 2009). LVID, IVS and PWT were determined during diastole and systole. Attention was taken to ensure that the moderator bands of the right ventricle were not included in the measurement of the IVS which would lead to overestimation (Teske et al., 2010). LVIDd, PWTd and IVSd were all used to determine LVM using the ASE convention then implemented using the following calculation:

$$\text{LV Mass} = 0.8 * (1.04[(\text{LVIDd} + \text{PWTd} + \text{IVSd})^3 - (\text{LVIDd})^3]) + 0.6 \text{ g}$$

(Lang et al., 2006)

RWT was used to categorise either concentric (≥ 0.42) or eccentric (≤ 0.42) hypertrophy based on the linear dimensions collected from the M-mode image using the equation, $\text{RWT} = ([2 * \text{PWTd}]/\text{LVIDd})$ (Lang et al., 2006).

LV volumes were measured from the AP4CH and AP2CH views. To obtain an AP4CH, the probe was placed upon the apical beat then subsequently adjusted until a clear view of all 4 chambers was visible. The IVS was adjusted until it was vertically aligned to enable accurate measurements and avoid any instance of apical foreshortening. Following this, the probe was rotated 90° counter-clockwise to gain an AP2CH. End diastole and end systole were defined as the point at which the cardiac dimension appeared to be the largest and smallest, respectively (Lang et al., 2005). To assess LVEDV and LVESV, the modified Simpson's Biplane rule was used by tracing the endocardial border of the LV excluding the papillary muscles, delineated with a straight line connecting the lateral and septal mitral annulus (Lang et al., 2005).

Conventional diastolic function was determined using TDI and mitral inflow velocities. Mitral annular tissue velocities were recorded in the AP4CH view using pulsed-waved Doppler (Gottdiener et al., 2004). A sample volume was placed within 1 cm at the basal segment where the septal and lateral points intersect the mitral annulus (Gottdiener et al., 2004, Nagueh et al., 2009). The sample was adjusted so that it remained within the myocardium throughout both systolic and diastolic phases of the cardiac cycle (Mor-Avi et al., 2011). The spectral trace scale was adjusted to ± 20 cm/s (Nagueh et al., 2009) at baseline to enable the determination of septal and lateral E' and A' as the peak markers. 2-D gain settings were adjusted to aid in analysis, as annular velocities have high signal amplitude (Nagueh et al., 2009), where-by the most concentrated peaks were the point of measurement. Using the AP4CH view, a volume sample was placed between the tips of the mitral valves to assess transmitral inflow velocities (Nagueh et al., 2009). Pulsed-waved Doppler produced a spectral trace which was used to measure peak E and A waves with the adjustment of gain, to ensure accurate measurement of peak markers from the trace (Nagueh et al., 2009); the E/A ratio was subsequently produced. Deceleration time (DT) was measured from the peak of the E wave form, down the slope to the baseline.

3.5.5.2 Speckle Tracking Echocardiography

LV deformation and mechanical indices were assessed using STE from previously saved 2-D images at rest and during each of the intensities during both exercise protocols (see Section 3.4).

The PSAX was used for image acquisition of the apical and basal levels at 70-80 frames per second (Stohr et al., 2012). A 90° clockwise rotate of the probe from the PLAX revealed the basal level of the PSAX (Feigenbaum et al., 2005). The basal level has been described as the highest imaging plane at which full myocardial thickness is present with the observation of surrounding mitral valve at end systole (Weiner et al., 2010a). The LV cavity was positioned as circular as possible with no visible

papillary muscles (Notomi et al., 2005). To obtain an apical view, the probe was tilted and moved distally and laterally until a cavity was observed with no papillary muscles present (Weiner et al., 2010a). The cross-section of the ultrasound beam when obtaining an apical level has been shown to generate alternate apical rotation values (van Dalen et al., 2008). A more caudal position of the transducer produced greater apical rotation (van Dalen et al., 2008), therefore it was taken that the apical imaging plane was proximal to the obliteration of the LV cavity. During the exercise bouts, specifically the leg extensions, the transducer was maneuvered during the exercise in order to maintain a circular LV cavity.

Analysis of LV mechanics was performed using offline semi-automatic software (EchoPac software, GE Healthcare, United Kingdom). The 3 most defined consecutive cardiac cycles were selected, where full myocardial thickness was visible. Initially, the endocardial boarder was manually detected, followed by the software automatically tracking motion. When the automatic region of interest did not correctly track, the region of interest was manually adjusted until the epicardal border was correctly aligned (Blessberger and Binder, 2010); to therefore encompass the entire LV wall thickness whilst avoiding the echogenic pericardium of the base and apex (Mor-Avi et al., 2011) (Figure 3.3)). After the software divided the myocardium in 6 segments, global basal and apical circumferential strain was recorded (Figure 3.4). Following the analysis of a basal and apical level image to determine rotations (Figure 3.5) torsion (Figure 3.6) and torsion rate graphs (Figure 3.7) could be generated. Due to the basal and apical levels being unable for analysis during the same cardiac cycle, HR was required to be ± 10 beats.min⁻¹ between basal and apical levels to account for intra-subject variability. Frame by frame raw data files were exported to Excel 2013 (Microsoft Corporation, Seattle, Washington) where a cubic spline add-in (SRS1 Software, Boston, MA, USA) was implemented, generating 300 data points from systole and diastole (Burns et al., 2009). Due to inter-subject variations in HR, rotational mechanics data were normalized to percentages of systole and diastole with 5% increments. Deformation and mechanical measurements were then taken from the spreadsheet calculations which consisted of PUV, basal and apical rotation

velocities during diastole. PUV was determined as the largest negative deflection following peak twist velocity (Stohr et al., 2011b). TTP untwisting velocity was expressed as the %diastole generated from the automatically defined AVC from within the EchoPac software.

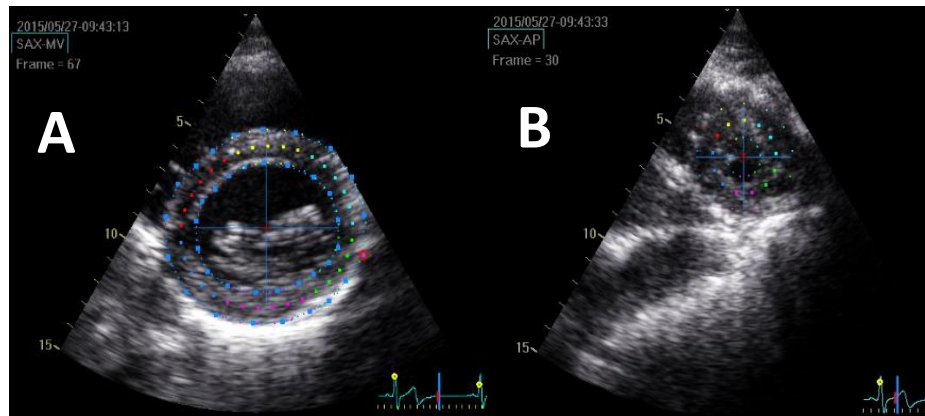


Figure 3.3 Basal (A) and apical (B) images showing a generated region of interest following the alignment of the endocardial and epicardial borders to encompass the entire wall thickness, whilst excluding the pericardium

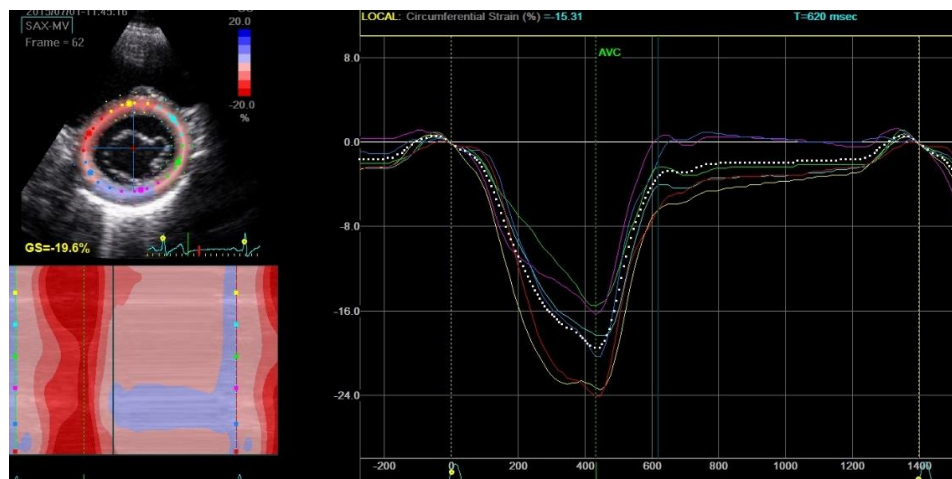


Figure 3.4 Global circumferential strain of the basal level indicating -19.6%.

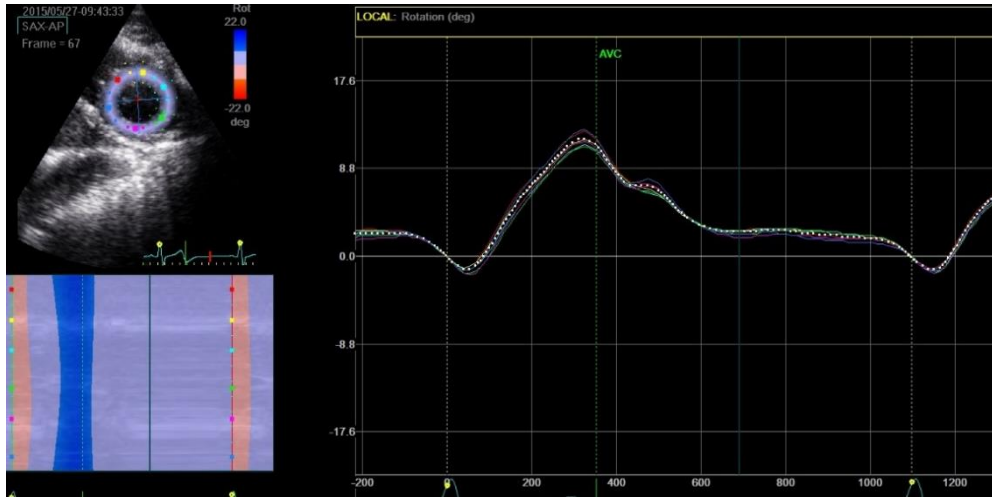


Figure 3.5 Example of a rotation/time graph generated within EchoPac of the apical level

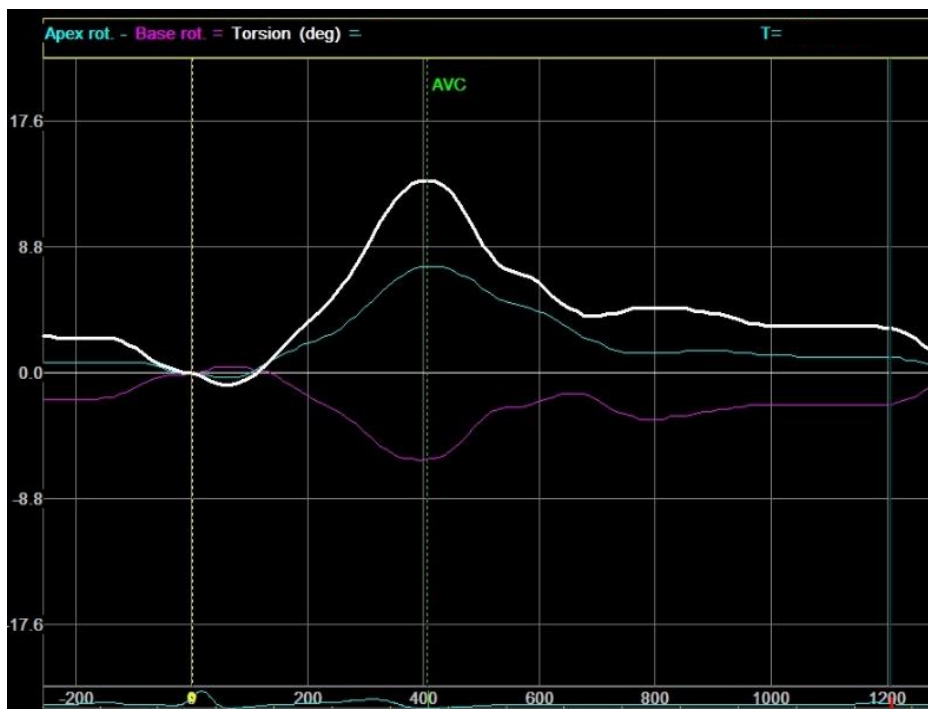


Figure 3.6 Example of a torsion/time graph automatically generated from EchoPac software. Apical and basal rotations are indicated by the blue and pink lines, respectively. The white line shows the net torsion. Red circle indicates peak twist. AVC= aortic valve closure.

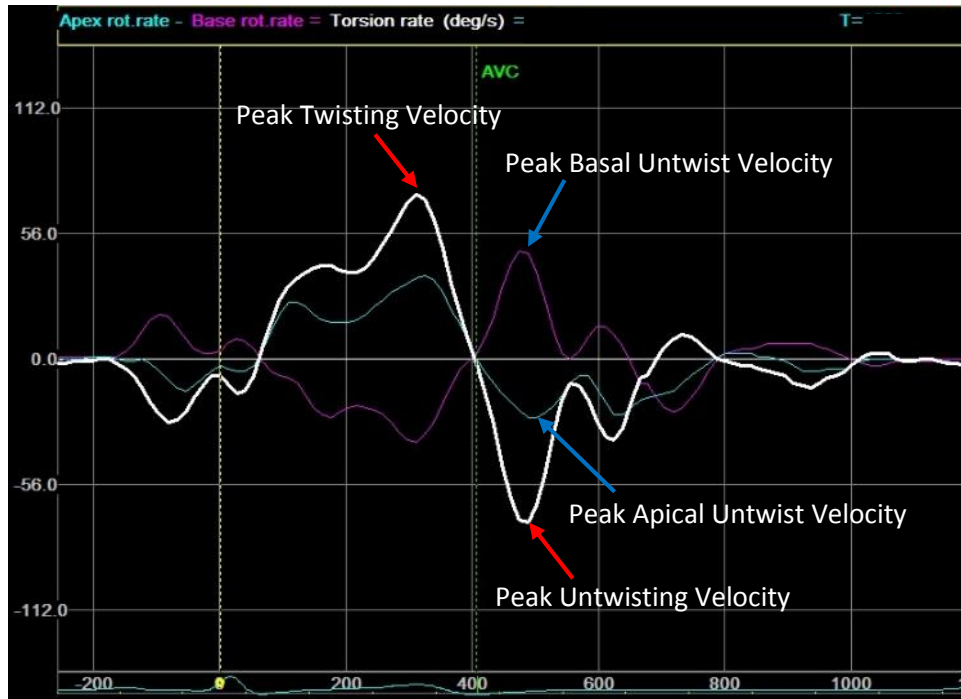


Figure 3.7 Example of a torsion rate/time graph automatically generated from EchoPac software in a 27 year old triathlete at rest. Apical and basal rotation rates are indicated by the blue and pink lines, respectively with peak untwist velocities indicated (blue arrows). The white line shows the net torsion rate with peak twisting and untwisting velocities identified (red arrows). AVC= aortic valve closure.

3.6 Reliability of Echocardiographic Images

Echocardiographic reliability was assessed at rest, during submaximal cycling and leg extension. PUV, apical and basal circumferential global strain (ACGS and BCGS, respectively) were analysed during all conditions, due to PUV being the main outcome variable of the present investigation, with ACGS and BCGS representing the reproducibility of single image acquisition. Images were acquired and analysed as previously outlined (see Section 3.5.5.2), PUV was however observed from the automatically generated torsion rate/time graph (Figure 3.7). Coefficient of variations (CV) were then determined from an existing spreadsheet (Hopkins, 2011) to assess intra-observer test-retest reliability. Table 3.1 indicates the CV observed for resting and exercising conditions.

All participants used for reliability data collection were university students. At rest, participants were required to attend the Sport Science Laboratories on one occasion for within-day variability assessment. During both cycling and leg extension exercise, individuals attended twice at the same time of day within 7 days of each other. Prior to all trials, participants were provided with an information sheet and testing did not take place until informed consent was provided. Moreover, subjects were asked to abstain from vigorous physical activity and alcohol for 24 hours and caffeine for 12 hours prior to testing.

For reliability of baseline images 14 individuals were recruited and initially rested for 5 minutes in the supine position before being scanned (trial 1), then following a further 5 minutes, scanned again (trial 2). Basal (n=1) and apical (n=2) images were not deemed suitable for analysis due to poor image quality; therefore, 11 cases were available for analysis of BCGS, ACGS and PUV.

For the submaximal cycling, 12 participants performed 2 x 4 minute stages (70 W and 170 W) of continuous semi-supine cycling on an e-bike. Echocardiographic images were recorded at the end of each stage. All acquired images of the base and apex, required HR to be ± 10 beats.min⁻¹ of each other. At the lower intensity, 1 participant was excluded due to both poor image quality and HR mismatch (≥ 10 beats.min⁻¹), enabling n=11 for BCGS, ACGS and PUV at 70 W. During the higher intensity, apical (n=4) and basal (n=4) images were excluded, thus preventing the determination of PUV in 4 participants. Further, for 1 participant PUV exceeded the scale of the torsion/time graph, so thus could not be determined. Therefore, at 170 W n=8 was used for ϵ measures and n=6 for PUV.

Twelve participants took part in the static leg extension protocol at 40% and 75% MVIC; the procedures employed are outlined in sections 3.4.3 and 3.5.4. At 40% MVIC, due to HR mismatch, apical and basal images could not be analysed in 3 participants. Consequently, BCGS, ACGS (both n=9) and PUV (n=8) was used for analysis. Similarly, at the higher intensity, basal and apical levels were not

determined in 2 and 3 subjects, respectively, which prevented the generation of PUV for 4 individuals. Therefore, analysis was performed with 10 (BCGS), 9 (ACGS) and 8 (PUV) participants.

To the author's knowledge, test-retest reliability data using STE has only been reported during resting conditions and no data has currently been published during exercise. Therefore, CV during rest and exercising conditions within the present investigation can only be compared to previously published resting data. During all conditions CV for BCGS and ACGS are within the criteria for acceptable CV of <10% (Atkinson et al., 1999), which are also favourably in agreement with published literature (Doucende et al., 2010, Oxborough et al., 2012, Monte et al., 2015, Santoro et al., 2015). PUV is comparable with another study (Burns et al., 2010) at rest, 170 W, 40% and 75% MVIC but not 70 W. Despite the low CV in BCGS and ACGS, PUV showed greater variance during all conditions, even though PUV is derived from the same images. However, these differences may be due to the algorithm within the software itself (Gustafsson et al., 2009), which therefore cannot be avoided.

Table 3.1 Coefficient of variations of test-retest reliability observed during rest (**A**), semi-supine cycling (**B**) and leg extension (**C**).

A LV measure		n	Trial 1&2 Mean	Trial 1&2 SD	CV (%)
Basal Circumferential strain (%)		13	-17.76	± 3.33	1.4
Apical Circumferential strain (%)		12	-23.47	± 6	2.2
Peak Untwisting velocity (deg·sec ⁻¹)		11	-75.17	± 24.47	18.1

B LV Measure	70 W				170 W			
	n	Trial 1&2 Mean	Trial 1&2 SD	CV (%)	n	Trial 1&2 Mean	Trial 1&2 SD	CV (%)
Basal Circumferential strain (%)	11	-20.08	± 3.18	2.8	8	-19.86	± 4.6	2.5
Apical Circumferential strain (%)	11	-28.48	± 4.46	3.2	8	-34.81	± 7.46	5.4
Peak Untwisting velocity (deg·sec ⁻¹)	11	-144.21	± 48.74	36.3	6	-192.83	± 50.25	24.5

C LV Measure	40% MVIC				75% MVIC			
	n	Trial 1&2 Mean	Trial 1&2 SD	CV (%)	n	Trial 1&2 Mean	Trial 1&2 SD	CV (%)
Basal Circumferential strain (%)	9	-16.22	± 4.61	2.9	10	-12.04	± 4.48	2.9
Apical Circumferential strain (%)	9	-23.73	± 5.32	3.1	9	-25.16	± 4.81	2.6
Peak Untwisting velocity (deg·sec ⁻¹)	8	-85.38	± 22.33	16.4	8	-140.41	± 49.65	23.1

CV = coefficient of variation; SD = standard deviation; MVIC = maximal voluntary isometric contraction; W = watts

3.7 Statistical Analysis

All data analysis was conducted using SPSS (V.21; IBM Company, SPSS Inc., Chicago, USA) and data presented as means \pm standard deviation. Normal distribution for all variables was assessed by the Shapiro-Wilk test and homogeneity of variance by Levene's test. If normality was not granted or variance violated, a log transformation was conducted. Statistical tests were then performed on the log transformed data if normality and variance had altered favourably. Group differences in baseline characteristics and conventional echocardiographic parameters were compared by one-way analysis of variance (ANOVA). For haemodynamic and diastolic mechanical parameters a 4x3 mixed repeated measures general linear model was employed for within and between subject analyses. Following the ANOVA, a post hoc Bonferroni correction was performed to identify pairwise comparisons. Non-parametric between groups assessments were analysed by a Kruskal-Wallis H test with Mann-Whitney U post hoc comparisons. Friedman test was used for within groups differences with a Wilcoxon signed-rank test used for post hoc analysis. Bonferroni corrected post hoc analyses were completed where appropriate, in which significance was granted at $p \leq 0.008$ and $p \leq 0.017$ following the Mann-Whitney U and Wilcoxon signed-rank tests, respectively. Effects sizes were calculated from Cohen's *d* and *r*. Statistical significance was set at $p \leq 0.05$.

4.0 Results

4.1 Anthropometric Characteristics

Age was significantly lower in the RT group compared to LDR but not TRI or CON (both $p > 0.05$); no other group differences were found ($p > 0.05$). There were no statistical differences in body mass ($p > 0.05$) or height ($p > 0.05$) between groups.

Table 4.1 Demographics of the study population

Demographic Variable	LDR (n = 7)	TRI (n = 9)	RT (n = 5)	CON (n = 5)
Age (years)	34 ± 3 *	32 ± 7	24 ± 5	29 ± 5
Height (cm)	179.9 ± 8.2	175.2 ± 2.9	171.7 ± 11.7	182.4 ± 6.6
Mass (kg)	75.0 ± 6.9	70.6 ± 4.3	83.4 ± 9.1	79.0 ± 16.5

LDR = long distance runners; TRI = triathletes; RT = resistance trained; CON = controls. * Significantly different to RT

4.2 Maximal Exercise and Work Rate Intensities

LDR and TRI had greater $\dot{V}O_{2peak}$ values than RT ($p = 0.01$, $d = 1.68$ (LDR), $p < 0.001$, $d = 3.52$ (TRI)) and CON ($p < 0.001$, $d = 2.50$ (LDR), $p < 0.001$, $d = 5.21$ (TRI)). There was no difference between CON and RT ($p > 0.05$). Similarly, W_{max} was higher in LDR and TRI than CON ($p < 0.001$, $d = 2.77$ (LDR), $p < 0.001$, $d = 4.78$ (TRI)) with W_{max} being higher in TRI compared to RT also ($p = 0.05$, $d = 2.51$). No other differences in W_{max} were found. RT athletes demonstrated significantly larger MVIC compared to all other groups (LDR $p < 0.01$, $d = 2.17$; TRI $p = 0.01$, $d = 1.78$; CON $p = 0.05$, $d = 1.86$), with no other alterations evident between any groups ($p > 0.05$).

Table 4.2 Maximal exercise test and relative percentage intensities.

Maximal and Work Rate Intensities	LDR (n = 7)	TRI (n = 9)^a	RT (n = 5)	CON (n = 5)
$\dot{V}O_{2peak}$ (mL.kg ⁻¹ .min ⁻¹)	52.4 ± 11.5 *#	55.6 ± 5.0 *#	37.4 ± 5.3	30.6 ± 4.6
W_{max} (W)	301.1 ± 42.8 *	307.8 ± 19.7 *#	258.4 ± 33.0	206.2 ± 22.7
30% W_{max} (W)	90.3 ± 12.8 *	92.4 ± 5.9 *#	77.4 ± 9.8	61.8 ± 7.0
60% W_{max} (W)	180.6 ± 25.7 *	184.7 ± 11.7 *#	155 ± 20.0	123.8 ± 13.4
MVIC (N)	950.6 ± 215.7	1047.8 ± 207.8	1454.4 ± 247.6 *†‡	1066.8 ± 160.2
40% MVC (N)	380 ± 86.4	419.1 ± 83.1	581.4 ± 99.3 *†‡	426.4 ± 64.0
75% MVC (N)	713 ± 161.3	786.0 ± 156.0	1090.8 ± 185.9 *†‡	800.0 ± 120.3

LDR = long distance runners; TRI = triathletes; RT = resistance trained; CON = controls. $\dot{V}O_{2peak}$ = peak oxygen consumption; W_{max} = work rate maximum; MVIC = maximal voluntary isometric contraction. ^a n = 8 for $\dot{V}O_{2peak}$. # Significantly different to RT; * Significantly different to CON; † Significantly different to LDR; ‡ Significantly different to TRI.

4.3 Haemodynamic Kinetics

Within and between group differences in HR, sBP and dBP during cycling and leg extension are illustrated in figure 4.1 (A-F). sBP and dBP was not collected during all exercise conditions and dBP was not collected during 75% MVIC in LDR for 1 participant and RT for 1 participant, respectively.

4.3.1 Heart Rate

At rest, TRI (53.1 ± 7.7 beats.min⁻¹) had significantly lower HR than CON (73.0 ± 16.6 beats.min⁻¹) ($p < 0.05$, $d = 1.51$) but not LDR (55.4 ± 8.3 beats.min⁻¹) or RT (61.0 ± 6.8 beats.min⁻¹) ($p > 0.05$). No further groups differences were found (all $p > 0.05$).

During cycling, HR did not differ between TRI (93.2 ± 4.4 beats.min⁻¹), LDR (93.6 ± 7.2 beats.min⁻¹), RT (105.8 ± 23.1 beats.min⁻¹) and CON (104.8 ± 6.7 beats.min⁻¹) at 30% W_{max} ($p = 0.06$), yet at 60% W_{max} the Kruskal-Wallis analysis identified between group differences ($p < 0.05$). Following post hoc analysis, no statistical differences were observed (LDR (122.6 ± 10.0 beats.min⁻¹) vs. CON (137.8 ± 7.9 beats.min⁻¹) ($p = 0.03$, $r = -0.64$); LDR vs. TRI (129.1 ± 7.8 beats.min⁻¹) ($p = 0.03$, $r = -0.56$); TRI vs. CON ($p = 0.03$, $r = -0.57$); LDR vs. RT (138.6 ± 21.2 beats.min⁻¹) ($p > 0.05$, $r = -0.40$); TRI vs. RT ($p > 0.05$, $r = -0.29$); RT vs. CON ($p > 0.05$, $r = -0.09$).

During the leg extension, at 40% MVIC HR was lower in TRI (69.6 ± 11.84 beats.min⁻¹) and LDR (74.4 ± 10.6 beats.min⁻¹) compared with CON (97.2 ± 7.0 beats.min⁻¹) (TRI $p < 0.01$, $d = 2.84$; LDR $p < 0.05$, $d = 2.54$ (LDR)) with TRI also being lower when compared with RT (95.0 ± 16.8 beats.min⁻¹) ($p < 0.01$, $d = 1.75$). No other group differences were found ($p > 0.05$). At 75% MVIC, LDR (83.7 ± 13.6 beats.min⁻¹) and TRI (90.6 ± 14.7 beats.min⁻¹) showed significantly lower HR than CON (114.6 ± 13.2 beats.min⁻¹) (LDR $p < 0.01$, $d = 2.31$; TRI $p < 0.05$, $d = 1.72$) but not RT (103.0 ± 12.3 beats.min⁻¹). No other group differences were found ($p > 0.05$).

Within group differences during the cycling protocol were analysed by Friedman's test, which revealed that HR in all groups statistically increased with progressive intensity (LDR $p = 0.001$; TRI $p < 0.001$; RT $p < 0.01$; CON $p < 0.001$). Following post hoc analysis significant increases from rest to 30% W_{max} (93.2 ± 4.4 beats.min⁻¹) and 60% W_{max} (129.1 ± 7.8 beats.min⁻¹) were found in TRI ($p < 0.01$, $r = -0.63$), with no significant increases in the LDR ($p = 0.018$, $r = -0.63$), RT ($p = 0.04$, $r = -0.64$) and CON ($p = 0.04$, $r = -0.64$). Similar findings were also found between exercise intensities (TRI ($p < 0.01$, $r = -0.64$); LDR ($p = 0.018$, $r = -0.64$); RT ($p = 0.04$, $r = -0.64$); CON ($p = 0.04$, $r = -0.64$).

During the leg extension, HR significantly increased in all groups from rest to 40% (all $p < 0.001$, LDR ($d=1.99$); TRI ($d=1.71$); RT ($d=3.12$); CON ($d=1.90$) and 75% MVIC (all $p < 0.001$, LDR ($d=2.57$); TRI ($d=3.29$); RT ($d=4.6$); CON ($d=2.66$). Additionally, from 40% to 75% MVIC significant increases were observed in LDR ($p < 0.05$, $d=0.77$), TRI ($p < 0.001$, $d=1.57$) and CON ($p=0.01$, $d=1.70$) but not RT ($p > 0.05$, $d=0.66$).

4.3.2 Systolic Blood Pressure

sBP was found not to differ between LDR, TRI, RT and CON at rest (112.3 ± 7.3 mmHg, 115.3 ± 6.0 mmHg, 126.0 ± 8.4 mmHg, 122.8 ± 10.1 mmHg, respectively), 30% W_{\max} (134.5 ± 8.6 mmHg, 146.3 ± 8.8 mmHg, 136.2 ± 7.3 mmHg, 142.6 ± 7.9 mmHg, respectively), 60% W_{\max} (171.0 ± 28.6 mmHg, 173.8 ± 15.2 mmHg, 168.4 ± 31.4 mmHg, 173.8 ± 10.6 mmHg, respectively) cycling or at 40% (128.0 ± 11.4 mmHg, 128.4 ± 5.2 mmHg, 136.6 ± 15.7 mmHg, 129.0 ± 10.5 mmHg, respectively) and 75% (144.7 ± 20.4 mmHg, 143.8 ± 11.3 mmHg, 133.6 ± 27.3 mmHg, 146.0 ± 18.9 mmHg, respectively) leg extension (all $p > 0.05$).

During the cycling bouts, sBP progressively increased from rest to 30% W_{\max} in LDR ($p < 0.001$, $d=2.79$) TRI ($p < 0.001$, $d=4.12$) and CON ($p=0.001$, $d=2.43$) but not RT ($p > 0.05$). Continual increases from rest to 60% W_{\max} were found in all groups (LDR ($p < 0.001$, $d=2.81$); TRI ($p < 0.001$, $d=5.05$); CON ($p < 0.001$, $d=4.94$); RT ($p=0.001$, $d=1.85$)), in conjunction with a significant increase from 30% to 60% W_{\max} in all groups (TRI ($p < 0.01$, $d=2.21$); CON ($p < 0.01$, $d=3.34$); LDR ($p=0.001$, $d=1.73$); RT ($p=0.001$, $d=1.41$)). In LDR and TRI, the static exercise elicited an enhanced sBP response from rest to 40% MVIC ($p=0.01$, $d=1.64$; $p < 0.01$, $d=2.33$ respectively), with no changes in CON or RT ($p > 0.05$). Compared to rest, sBP at 75% MVIC was significantly greater in all groups (LDR ($p < 0.001$, $d=2.11$); TRI ($p < 0.001$, $d=3.13$); RT ($p < 0.01$, $d=1.37$); CON ($p < 0.05$, $d=1.53$)); whilst also observing similar alterations between the 40% and 75% MVIC workloads (LDR ($p < 0.01$, $d=1$); TRI ($p=0.001$, $d=1.74$); RT ($p < 0.01$, $d=0.76$); CON ($p < 0.01$, $d=1.11$)).

4.3.3 Diastolic Blood Pressure

dBp was found not to differ between LDR, TRI, RT and CON at rest (71.4 ± 6.0 mmHg, 75.6 ± 5.6 mmHg, 76.4 ± 6.2 mmHg, 77.0 ± 4.6 mmHg, respectively), 30% W_{\max} (79.5 ± 1.4 mmHg, 82.2 ± 6.7 mmHg, 79.4 ± 6.6 mmHg, 81.6 ± 4.1 mmHg, respectively), 60% W_{\max} (81.5 ± 0.8 mmHg, 85.6 ± 6.3 mmHg, 83.4 ± 2.4 mmHg, 86.4 ± 4.1 mmHg, respectively) cycling or at 40% (77.2 ± 4.9 mmHg, 77.8 ± 5.5 mmHg, 78.8 ± 8.4 mmHg, 80.6 ± 2.4 mmHg, respectively) and 75% (81.5 ± 0.8 mmHg, 86.6 ± 7.4 mmHg, 91.3 ± 20.3 mmHg, 84.6 ± 5.4 mmHg, respectively) leg extension (all $p > 0.05$).

Friedman's assessment of dBp during cycling showed significance within all groups (LDR $p < 0.01$; TRI $p < 0.001$; RT $p < 0.05$; CON $p < 0.01$). Following Bonferroni post hoc correction, no significant changes were seen from rest to 30% W_{\max} in LDR ($p = 0.05$, $r = -0.55$), RT ($p > 0.05$, $r = -0.34$) and CON ($p = 0.04$, $r = -0.64$) and from baseline to 60% W_{\max} (LDR ($p = 0.03$, $r = -0.61$); RT ($p = 0.04$, $r = -0.64$); CON ($p = 0.04$, $r = -0.64$)). dBp also remained constant between 30% and 60% W_{\max} in LDR ($p = 0.04$, $r = -0.59$), RT ($p = 0.04$, $r = -0.64$) and CON ($p > 0.05$, $r = -0.59$). TRI demonstrated significant increases across all conditions (all $p < 0.01$, $r = -0.63$).

Analysis of dBp during the leg extension using Friedman's test displayed significant increases within all groups (LDR $p < 0.05$; TRI $p = 0.001$; RT $p < 0.05$; CON $p < 0.01$). Post hoc with Bonferroni correction identified no significant changes from rest to 40% MVIC in all groups (LDR ($p = 0.05$, $r = -0.55$); TRI ($p > 0.05$, $r = -0.28$); RT ($p > 0.05$, $r = -0.29$); CON ($p = 0.04$, $r = -0.64$)). TRI was the only group to demonstrate a significant change from rest to 75% MVIC ($p < 0.01$, $r = -0.63$), whereby RT ($p > 0.05$, $r = -0.61$), LDR and CON ($p = 0.03$, $r = -0.61$; $p = 0.04$, $r = -0.65$, respectively) all demonstrated no significant alterations. Similar findings were observed between exercise intensities, with significant progression in TRI ($p < 0.01$, $r = -0.63$) and non-significance between LDR, RT ($p > 0.05$, $r = -0.51$; $p > 0.05$, $r = -0.61$, respectively) and CON ($p = 0.04$, $r = -0.65$).

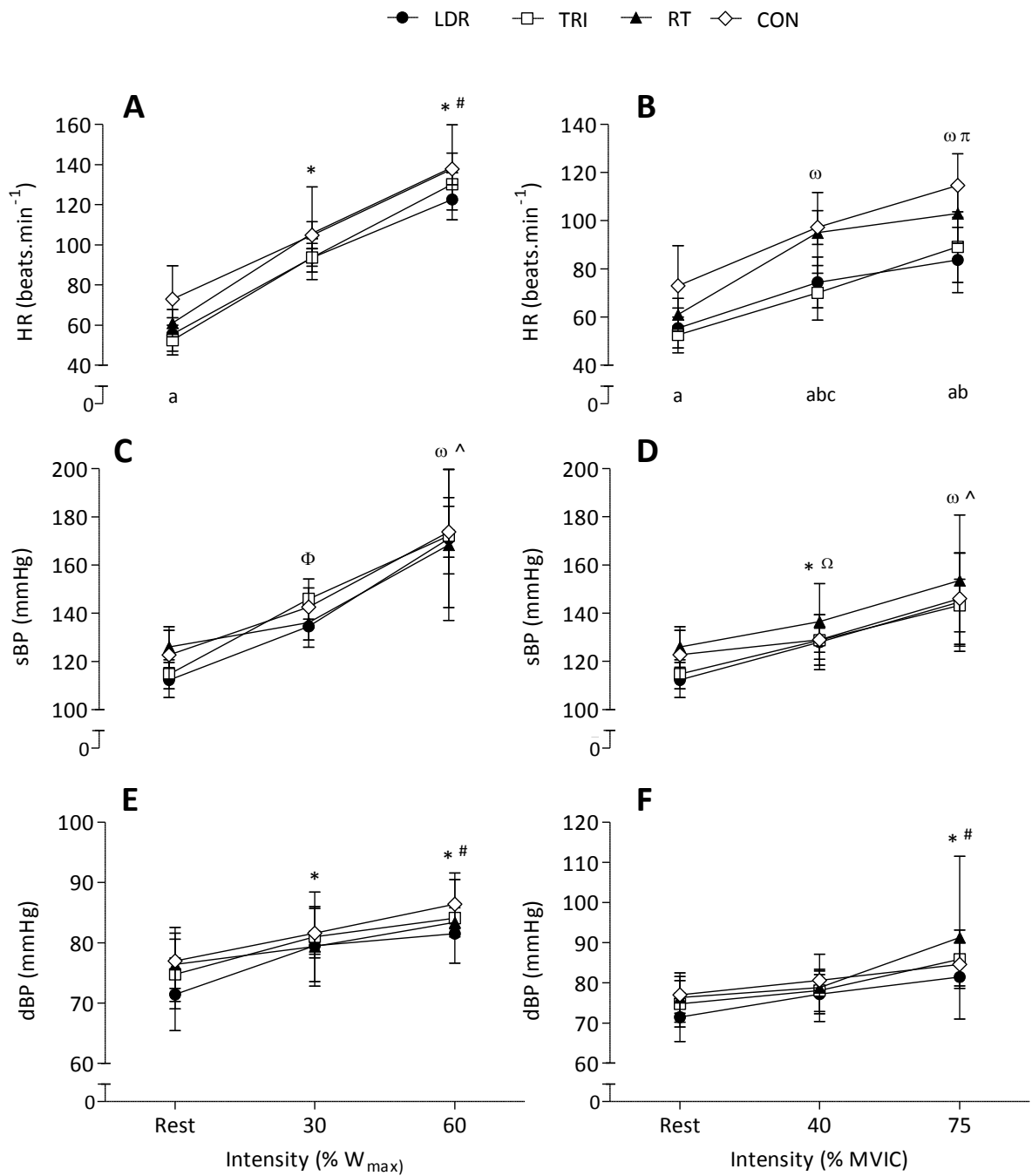


Figure 4.1 Haemodynamic parameters during 2 intensities of cycling and leg extension exercise, showing heart rate (A, B), systolic blood pressure (C, D) and diastolic blood pressure (E, F). HR= heart rate; sBP= systolic blood pressure; dBP= diastolic blood pressure. W_{max} = workload maximum; MVIC= maximum voluntary isometric contraction. * Significantly different to rest in TRI. Ω Significantly different to rest in LDR. ω Significantly different to rest in all groups. φ Significantly different to rest in all groups except RT. # Significantly different to previous intensity in TRI. π Significantly different to previous intensity in all groups except RT. ^ Significantly different to previous intensity in all groups. a= TRI significantly different to CON, b= TRI significantly different to RT, c= LDR significantly different to CON.

4.4 Conventional Resting Echocardiographic Parameters

4.4.1 Left Ventricular Structure

Between group comparisons identified that TRI had significantly greater IVSd compared with CON ($p < 0.05$, $d = 2.78$), with no further statistical differences between groups ($p > 0.05$). TRI and LDR demonstrated superior PWTs compared with CON ($p = 0.01$, $d = 1.96$ (TRI), $p < 0.05$, $d = 1.61$ (LDR)), no additional differences were observed ($p > 0.05$). It was found that LDR had larger LVEDV than CON ($p = 0.01$, $d = 2.04$), with no further differences between groups (TRI vs. CON ($p = 0.06$), all remaining $p > 0.05$). Compared with CON, LVM was significantly greater in the LDR ($p < 0.01$, $d = 2.57$) and TRI ($p < 0.01$, $d = 2.17$) but no further group differences were shown (all $p > 0.05$).

RWT statistically differed between groups ($p = 0.05$), however upon post hoc comparisons no significant differences were observed (TRI vs. CON ($p > 0.05$, $d = 1.36$), (TRI vs. LDR ($p > 0.05$, $d = 1.14$); TRI vs. RT ($p > 0.05$, $d = 0.49$); LDR vs. RT ($p > 0.05$, $d = 0.67$); LDR vs. CON ($p > 0.05$, $d = 0.62$); RT vs. CON ($p > 0.05$, $d = 1.74$)). It was found that PWTd was significantly greater in the TRI compared with CON ($p < 0.05$, $d = 1.49$) with no further between groups differences ($p > 0.05$). No significant differences were observed between groups for structural measures LVIDd, LVIDs, LVESV and IVSs (all $p > 0.05$).

Table 4.3 Resting echocardiographic structural measures of the study population.

Structural Parameters	LDR	TRI	RT	CON
IVSd (mm)	11 ± 1	11 ± 1 *	10 ± 1	9 ± 0
IVSs (mm)	14 ± 3	14 ± 1	12 ± 2	11 ± 1
LVIDd (mm)	56 ± 4	52 ± 3	54 ± 5	51 ± 2
LVIDs (mm)	37 ± 3	36 ± 3	37 ± 5	35 ± 4
PWTd (mm)	10 ± 1	11 ± 2 *	10 ± 1	8 ± 2
PWTs (mm)	16 ± 22 *	16 ± 2 *	16 ± 2	12 ± 3
LVEDV (mL)	139.7 ± 24.5 *	130.0 ± 14.3	129.9 ± 32.4	95.1 ± 18.7
LVESV(mL)	54.4 ± 13.6	52.4 ± 6.6	59.6 ± 13.1	41.3 ± 13.4
LVM (g)	225.0 ± 27.7 *	216.9 ± 30.4 *	201.3 ± 26.4	154.9 ± 37.0
RWT	0.34 ± 0.02	0.41 ± 0.08	0.37 ± 0.06	0.32 ± 0.05

LDR= long distance runners; TRI= triathletes; RT= resistance trained; CON= controls. IVSd= left ventricular septum in diastole; IVSs= left ventricular septum in systole; LVIDd= left ventricular internal diameter in diastole; LVIDs= left ventricular internal diameter in systole; PWTd= posterior wall thickness in diastole; PWTs= posterior wall thickness in systole; LVEDV= left ventricular end diastolic volume; LVESV= left ventricular end systolic volume; LVM= left ventricular mass; RWT= relative wall thickness. * significantly different to CON.

4.4.2 Left Ventricular Diastolic Function

No statistically significant differences were found between groups for any conventional diastolic functional variables (all p>0.05).

Table 4.4 Conventional diastolic functional parameters.

Diastolic Functional Parameters	LDR	TRI	RT	CON
E wave (cm.s ⁻¹)	68.4 ± 3.9	73.6 ± 11.1	76.0 ± 11.8	71.4 ± 10.8
A wave (cm.s ⁻¹)	32.9 ± 6.1	37.2 ± 6.7	40.8 ± 8.1	39.6 ± 8.3
E/A ratio	2.2 ± 0.5	2.1 ± 0.7	1.9 ± 0.4	1.8 ± 0.3
DT (ms)	271.0 ± 98.8	226.5 ± 47.6	268.4 ± 17.3	295.6 ± 29.7
Lateral E' (cm.s ⁻¹)	19.0 ± 4.1	18.2 ± 2.6	19.2 ± 3.3	17.8 ± 1.9
Septal E' (cm.s ⁻¹)	11.7 ± 2.4	11.7 ± 1.7	13.8 ± 0.8	13.6 ± 1.7
Lateral A' (cm.s ⁻¹)	8.3 ± 2.1	7.3 ± 1.3	7.6 ± 2.7	8.8 ± 1.6
Septal A' (cm.s ⁻¹)	7.4 ± 1.8	8.2 ± 1.4	7.6 ± 2.2	8.6 ± 1.1

LDR= long distance runners; TRI= triathletes; RT= resistance trained; CON= controls. E= mitral inflow early diastolic velocity; A= mitral inflow late diastolic velocity; E/A= ratio between early and late diastolic mitral inflow velocities; DT= deceleration time; E'= tissue Doppler early diastolic velocity; A'= tissue Doppler late diastolic velocity.

4.5 Left Ventricular Diastolic Mechanics

At 30% W_{max} rotational mechanics could not be determined in 1 CON and 1 LDR participant due to no basal and/or unmeasurable apical images and no basal image, respectively. At the higher cycling intensity, data was absent in CON for 2 participants and RT for 1 participant due to no basal images and/or unmeasurable images. At 75% MVIC during the leg extension exercise, data is not present in 1 TRI subject and 1 CON individual both due to no basal image available. Additionally, a further 1 CON subject was unavailable for measurement due to electrocardiogram lead interferences leading to the inability of EchoPac software to accurately define consecutive cardiac cycles. All participant images were categorised for image quality on a 1-4 scale, being excellent (1), good (2), poor (3) and no image available/unmeasurable (4). Good-excellent quality images were considered to be 65.4%, 53.8%, 65.4%, and 69.2% for

exercise conditions 30%, 60% W_{max} , 40% and 75% MVIC, respectively. Figure 4.2 (A-F) illustrates diastolic mechanics within and between groups during the cycling and leg extension.

4.5.1 Diastolic Apical and Basal Rotation Velocities

Apical rotation velocity did not significantly differ between groups at rest, during either intensity of cycling or at 40% MVIC (all $p>0.05$). However, at 75% MVIC between group differences were observed ($p<0.05$). Mann-Whitney post hoc with Bonferroni, subsequently found no significant group differences ((TRI vs. CON ($p=0.01$, $r= -0.74$), TRI vs. RT ($p=0.06$, $r= -0.53$); TRI vs. LDR ($p>0.05$, $r= -0.12$); LDR vs. RT ($p>0.05$, $r= -0.49$); LDR vs. CON ($p>0.05$, $r= -0.54$); RT vs. CON ($p>0.05$, $r= -0.05$)).

Apical rotation velocity did not significantly increase during the leg extension within LDR and CON ($p>0.05$) but did in TRI ($p=0.01$) and RT ($p<0.05$) following Friedman's test. However, upon post hoc pairwise comparisons RT demonstrated no significant changes from rest to 40% ($p>0.05$, $r= -0.47$), 75% MVIC and between exercise intensities (both $p<0.05$, $r= -0.64$). TRI also demonstrated no significant increases from rest to 40% MVIC and between exercise intensities (both $p>0.05$, $r= -0.43$, $r= -0.24$, respectively) but did show a significant increase from baseline to 75% MVIC ($p=0.01$, $r= -0.61$).

Friedman's test indicated significance within all groups (LDR $p<0.05$; TRI $p<0.001$; RT $p<0.05$; CON $p=0.05$) during cycling protocol for apical rotation. Following post hoc analysis, no significant changes from rest to 30% W_{max} were evident in LDR, RT (both $p<0.05$, $r= -0.61$; $r= -0.64$, respectively) and CON ($p>0.05$, $r= -0.61$), which was also observed from rest to 60% W_{max} in LDR, ($p<0.05$, $r= -0.59$), RT and CON (both $p>0.05$, $r= -0.63$; $r= -0.57$). Consequently, apical rotation velocity remained constant between exercise intensities within LDR, RT and CON (all $p>0.05$, $r= -0.14$; $r= -0.61$; $r= -0.60$, respectively). In contrast, statistically significant augmentation occurred in TRI from

rest to 30%, 60% W_{max} (both $p < 0.01$, $r = -0.63$) and between exercise intensities ($p = 0.01$, $r = -0.60$).

Basal rotation velocity did not differ between groups at rest or during either cycling or leg extension intensities (all $p > 0.05$). Basal rotation velocity significantly increased in CON from rest to 30% W_{max} ($p = 0.05$, $d = 3.96$), with no further differences between conditions within each group ($p > 0.05$). All groups were seen to significantly increase from rest to 60% W_{max} (LDR ($p < 0.05$, $d = 1.46$); TRI ($p < 0.001$, $d = 1.79$); RT ($p = 0.01$, $d = 2.27$); CON ($p < 0.01$, $d = 3.68$), with only TRI showing a significant augmentation between exercise intensities ($p < 0.05$). Basal rotation velocity remained unchanged from baseline within all groups during the leg extension ($p > 0.05$).

4.5.2 Peak Untwisting Velocity

PUV was shown not to differ between groups at rest or either intensities during both the cycling or leg extension (all $p > 0.05$).

PUV significantly increased during the cycling using Friedman's test within all groups (LDR $p < 0.05$; TRI $p < 0.001$; RT $p < 0.05$; CON $p = 0.05$). The following post hoc analysis found no significant changes from rest to 30% W_{max} in LDR ($p > 0.05$, $r = -0.49$), CON ($p > 0.05$, $r = -0.62$) and RT ($p < 0.05$, $r = -0.64$). PUV remained unchanged from rest to 60% W_{max} in LDR ($p = 0.018$, $r = -0.63$), RT and CON (both $p > 0.05$, $r = -0.61$; $r = -0.57$, respectively). No changes between exercise intensities were seen in LDR, RT and CON (all $p > 0.05$, $r = -0.49$; $r = -0.49$; $r = -0.60$, respectively). TRI was the only group to demonstrate statistically increased PUV from rest to 30% and 60% W_{max} (both $p < 0.01$, $r = -0.63$), with a significant difference between exercise intensities ($p = 0.01$, $r = -0.60$).

During the leg extension, no changes were observed between conditions in LDR, CON and TRI ($p > 0.05$), but were in RT ($p < 0.05$) using Friedman's test. However, post hoc

analysis failed to evidence a significant change from rest to 40% ($p > 0.05$, $r = -0.38$), 75% MVIC and between exercise intensities (both $p < 0.05$, $r = -0.64$) in PUV.

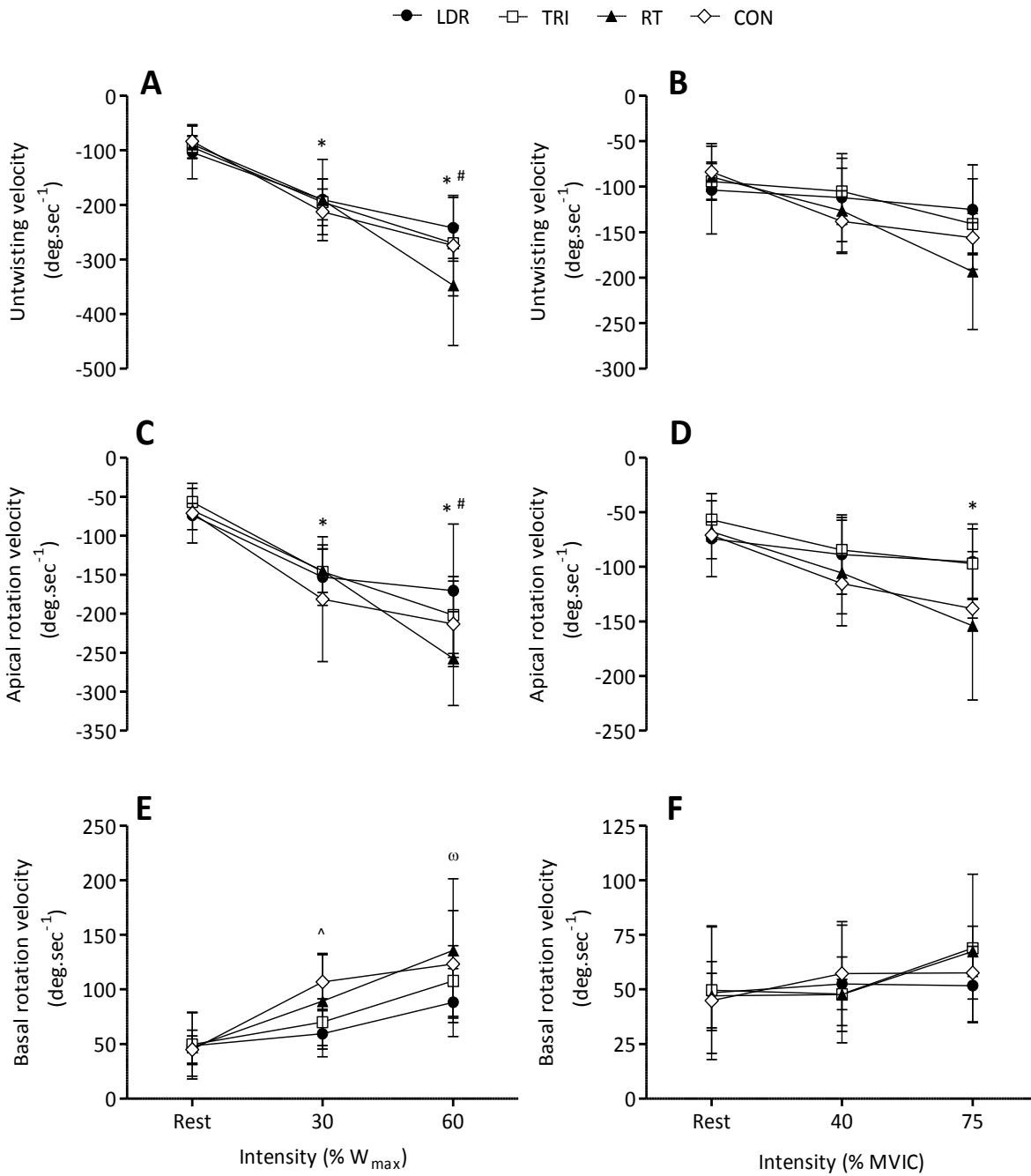


Figure 4.2 Peak diastolic rotational parameters during 2 intensities of semi-supine cycling and isometric leg extension exercise, showing peak untwisting velocity (**A, B**), apical rotation velocity (**C, D**) and basal rotation velocity (**E, F**). W_{max} = workload maximum; MVIC= maximum voluntary isometric contraction. * Significantly different to rest in TRI. ^ Significantly different to rest in CON. # Significantly different from previous intensity in TRI. ω Significantly different to rest in all groups.

4.5.3 *Time to Peak Untwisting Velocity*

No significant differences were seen between groups for TTP untwisting velocity, at rest or any intensities during the cycling and leg extension exercises ($p>0.05$).

During the cycling, Friedman's test showed no changes in RT and CON between conditions ($p>0.05$). However, both LDR and TRI demonstrated TTP increased significantly further into diastole ($p=0.01$, $p<0.001$, respectively). Post hoc analysis showed no significant differences in LDR from rest to 30%, 60% W_{\max} (both $p<0.05$, $r=-0.61$; $r=-0.59$, respectively) and between exercise intensities ($p>0.05$, $r=-0.14$). In contrast, TRI demonstrated PUV further into the diastolic phase at 30% ($p=0.015$, $r=-0.57$) and 60% W_{\max} compared with rest, in addition to a significant difference between the exercise intensities (both $p<0.01$, $r=-0.63$).

During the leg extension, no differences occurred between conditions within the CON and RT groups ($p>0.05$), yet significance within LDR ($p=0.05$) and TRI ($p<0.05$). TTP significantly increased from rest to 40% MVIC in TRI ($p=0.01$, $r=-0.60$) but not in LDR ($p>0.05$). In both LDR and TRI, TTP remained statistically unchanged from baseline to 75% MVIC ($p=0.06$, $p<0.05$, respectively). Additionally, no significant changes between intensities were observed in either group ($p>0.05$).

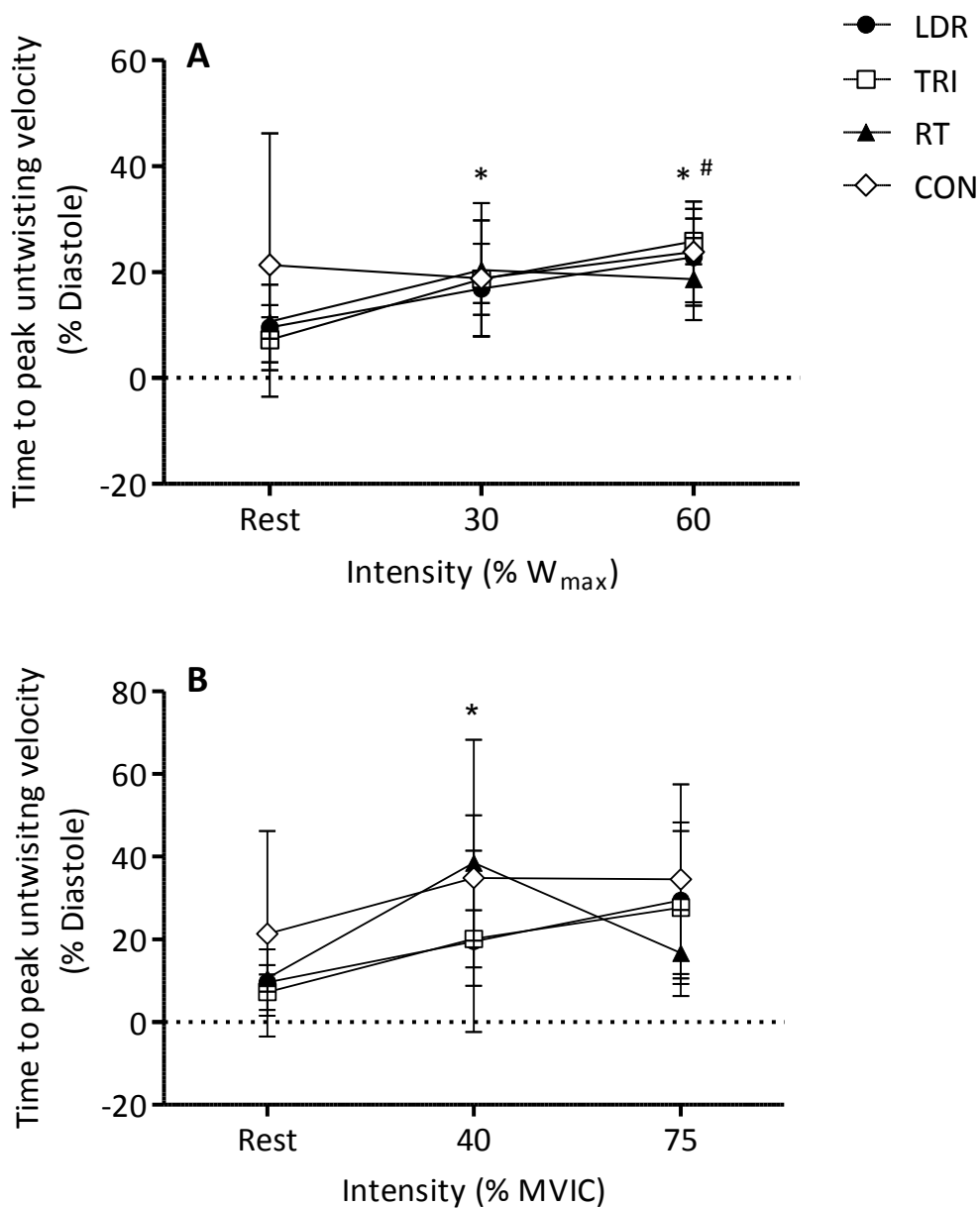


Figure 4.3 Time to peak untwisting velocity (% diastole) during 2 intensities of semi-supine cycling (**A**) and isometric leg extension exercise (**B**). W_{max} = workload maximum; MVIC= maximum voluntary isometric contraction. * Significantly different to rest in TRI. # Significantly different to previous intensity in TRI.

5.0 Discussion

5.1 Overview of Findings

The main aim of the present investigation was to study the untwisting mechanics in athletes adapted to alternate forms of exercise training in accordance with sports categorisation at rest. Also, to determine the responses of trained athletes and healthy non-trained CON when subjected to incremental preload and afterload challenges. To the best of the author's knowledge, this was the first study to differentiate athletic groups based on dynamic and static components and observe the responses when subjected to a volume and pressure overload, ultimately resulting in familiar and unfamiliar exercise modalities. The main findings were as follows: 1) PUV did not significantly differ between groups of athletes, based on sporting classifications, or those untrained at rest. Also, dynamic and static exercise aimed at increasing opposing haemodynamic loads, did not elicit differing diastolic mechanical responses between groups; 2) TRI showed a progressive and significant increase in PUV during incremental semi-supine cycling, with all remaining athlete and CON groups showing no statistically significant changes; 3) PUV remained constant within all trained and untrained groups presenting unchanged peak untwisting mechanics during static leg extension exercise.

5.2 Explanation of Findings

5.2.1 Rest

The main finding that STE derived diastolic function did not alter between athletes and CON is in contrast (Zócalo et al., 2008, Vitarelli et al., 2013, Kovacs et al., 2014, Santoro et al., 2014a, Santoro et al., 2014b) and agreement (Nottin et al., 2008, Lee et al., 2012, Vitarelli et al., 2013, Maufrais et al., 2014, Santoro et al., 2015) with previously published cross-sectional literature. Multiple factors, such as training level, population age and genetic predisposition may all influence deformation profiles (Kovacs et al., 2014).

Despite LDR showing larger LVEDV, in addition to both LDR and TRI demonstrating increased LVM compared to CON, chronic exercise training appeared to have no effect on PUV. Therefore, within the present athletic population, the theory of a functional reserve when compared to non-trained individuals may be refuted. Past literature which has also documented no changes in resting peak untwisting parameters, too have used non-professionally trained athletes (Lee et al., 2012, Maufrais et al., 2014, Santoro et al., 2015). Therefore, it may be suggestive that structural adaptations precede functional untwisting adaptations in amateur trained athletes, supported by the current results of increased LVM in LDR and TRI. In further support, no athlete-control differences were found for any conventional diastolic measure. PUV may consequently be indicative of an adaptation occurring in an elite trained athlete population, which may explain why functional reductions in professional soccer players (Zócalo et al., 2008), international elite cyclists (Santoro et al., 2014a) and professional water polo players (Santoro et al., 2014b), were observed compared with controls at rest.

Training volumes in the present study were similar to those reported in studies which also documented no changes in peak untwist parameters (Lee et al. 2012 (≥ 6 hours/week), Maufrais et al. 2014 (≥ 8 hours/week), Santoro et al. 2015 (6 hours/week)). It may be a plausible explanation that the population within the present study may not have been exposed to a high enough volume/intensity of training stress to require a functional reserve. Studies have shown lower systolic twisting mechanics in more highly trained individuals, without evidence of differences in diastolic mechanics (Nottin et al., 2008, Stohr et al., 2012). These findings may suggest that adaptations to untwisting mechanics be either less detectable or alterations may not occur in already healthy individuals when diastolic function is normal at rest.

In the present study, no differences in PUV were shown between LDR or TRI and RT, which is in contrast to Santoro et al. (2014a) who showed elite cyclists had significantly reduced UTR compared with weight lifters. Recruitment of the RT group

within the current study consisted of both hypertrophic (body builders) and strength trained (weight lifters) individuals. In the current study, PUV in the body builders was $-78.89 \pm 11.29^\circ/\text{sec}$, whereas PUV was larger in the weight lifters $-104.50 \pm 3.36^\circ/\text{sec}$; this observation may support previous findings (Santoro et al., 2014a), in addition to the current study. Body builders have demonstrated larger SV and \dot{Q} responses during dynamic resistance exercise compared with weight lifters (Falkel et al., 1992) and due to larger volume changes, a volume overload may be subjected to body builders. Long term training may lead to changes in LV morphology, resembling that of a more eccentric hypertrophic modification. This may explain why in the current study RWT in the RT group did not exceed the threshold of ≥ 0.42 (Lang et al., 2006) and thus, demonstrated a lack of concentric hypertrophy.

Exercise training was shown to have no effect on TTP untwisting velocity, expressed as a %diastole. HR was significantly lower in TRI than CON at rest ($p < 0.05$) and although non-significant, figure 4.3 shows that mean TTP untwisting velocity %diastole was greater in the non-trained group. Although the present study did not measure the untwist during IVRT, previous research has shown that in endurance trained individuals, a larger %untwist occurs during IVRT, despite no overall changes in absolute UTR (Maufrais et al., 2014). Early untwist is indicative of enhanced diastolic function by enhancing the ability to generate an IVPG (Notomi et al., 2006), enabling earlier, passive filling with low atrial pressures (George and Somauroo, 2012).

A reduction in peak untwist may be due to a reduction in torsion at rest, which has been shown to be lower with an accompanying decreased resting HR (Nottin et al., 2008). Within the current study, TRI had lower HR than CON, therefore it would have been expected that this reduction would translate into reduced PUV, which did not occur. However, the reductions in peak untwist in athletes may occur due to the myocardium requiring less torsion and thus untwisting to attain sufficient baseline cardiovascular functioning (Zócalo et al., 2008). The reduction in apical rotations (Nottin et al., 2008) and UTR observed in endurance athletes is suggested to be a

reserve mechanism for during exercise (Notomi et al., 2008, Zócalo et al., 2008, Santoro et al., 2014a). Despite the suggestion of an elongated diastolic period due to reduced HR and pressure decay, when PUV has been shown to be greater, HR has also been demonstrated to be lower (Weiner et al., 2010a). Therefore, other suggestions besides the influence of HR must contribute to the contrasting findings regarding LV untwisting, which may aid in the explanation for why TRI in the present study did not demonstrate a function reserve, despite lower HR than CON.

Mechanistic changes in the titin isoforms may be responsible for the theoretical functional reserve in endurance athletes, in addition to the earlier untwist previously observed (Maufrais et al., 2014). Titin, a bidirectional myocardium filament contributes a crucial role in storing forces necessary for untwisting mechanics (Weiner et al., 2010a). Movement of the thick myosin filament extends the springs generating stored energy, upon relaxation the springs recoil (LeWinter and Granzier, 2010). Titin based restoring forces are described as reverse extension following a myocardial contraction and are estimated to be accountable for 50% of restoring forces (LeWinter and Granzier, 2010). Passive stiffness is greater when the N2B isoform (short spring) is predominant, whereas N2BA titin (long spring) is more compliant (Wu et al., 2002), with the length of titin's spring segments inversely related to passive stiffness (Methawasin et al., 2014). High N2B titin myocyte expression is likely to result in greater restoring forces (LeWinter et al., 2007), with the direct relationship between titin passive stiffness and restoring forces expressed as proportional (LeWinter and Granzier, 2010). A favourable shift in endurance athletes to a more elastic isoform (i.e greater N2BA) may increase the quantity of energy released during the early phase of diastole (Maufrais et al., 2014). In a recent rat model, following 3 weeks of daily exercise, cardiac stiffness decreased via altered proline-glutamine-valine-lysine (PEVK) phosphorylation (Hidalgo et al., 2014). More elastic titin produce less passive force and thus restoring forces, however due to a reduction in stiffness, untwist may occur early following the cessation of contraction (Methawasin et al., 2014). In regards to a functional reserve for effort, due to the compliance of the N2BA isoform, additional stretch may be obtainable following a

more vigorous contraction during exercise. Diastolic function is influenced by increases in titin-based compliance which manifests into increased LV chamber compliance (Methawasin et al., 2014). Therefore, adaptation to a more compliant titin isoform may produce less absolute untwist, at any given intensity when comparing endurance and untrained populations. Taken together, the lack of athlete-control differences in PUV in the present study may be suggestive of a lack of elastic isoform adaptations within TRI and LDR; however, this suggestion requires substantial investigation.

Titin isoforms may modify with cardiac adaptations, a previous study demonstrated shifts towards titin stiffness within the diseased heart of purpose-bred mongrel dogs following tachycardia-induced cardiac failure (Wu et al., 2002). Changes in titin, compliant versus stiff, isoform ratios may explain why a cross-sectional (UTR at MVO) (Kovacs et al., 2014) and longitudinal study (Weiner et al., 2010a) observed increases in peak early UTR at rest compared with controls following power-endurance rowing exercise training (Weiner et al., 2010a). In a recent mouse model, greater compliance attenuated the Frank-Starling mechanism, whereas stiffer titin isoforms showed length-dependant activation of the Frank-Starling mechanism (Methawasin et al., 2014). Stiffer titin may produce enhanced passive force and consequently greater restoring forces; this could then lead to greater LV untwist. This type of chronic adaptation may resemble that of a diseased heart with greater myocardial stiffness, however much research is required to identify the changes in titin isoforms following various types of exercise training and their subsequent influences on twisting mechanics.

5.2.2 Semi-Supine Cycling

As expected, no group differences in any untwisting measurements occurred during either of the cycling intensities. The present findings cannot be directly compared with past literature as this is the first study to the authors' knowledge which has differentiated athletic type during cycling. However, an investigation conducted by

Stohr et al. (2011a) showed no differences in PUV from a group of recreationally active students divided into moderate and high aerobic capacity during semi-supine cycling at 40% peak power output. Additionally, during steady state cycling (HR 105-110 beats.min⁻¹), recoil velocity was also shown to remain unchanged between young untrained, middle aged untrained and middle aged endurance trained groups (Lee et al., 2012). Therefore, although only loosely comparable, findings from Lee et al. (2012) and Stohr et al. (2012) confirms that of the present study in showing no training effect on peak untwist parameters during steady state, preload inducing cycling.

Similar to the findings of this study, neither study by Lee et al. (2012) or Stohr et al. (2012) observed athlete-control differences in peak untwist at rest, therefore whether a functional reserve at each relative intensity exists within endurance athletes cannot be determined thus far. Due to untwist being the consequential net difference of apical and basal rotations; in the current study, no differences were observed between groups at either exercise intensity for basal or apical measures. Due to the lack of differences, no compensatory increases in apical or basal rotations occurred, suggesting untwist was sufficient to ensure normal diastolic filling during dynamic exercise within all groups. No group differences were observed in HR, sBP or dBP at either exercise intensity, which therefore indicates similar biological responses occurred between all groups. Collectively, the lack of differences in haemodynamic and untwisting mechanical parameters shows that during relative intensity dynamic exercise, no beneficial diastolic function is present in trained endurance (high dynamic, high static or high dynamic, low static) or resistance (high static, low dynamic) non-professional athletes when compared to untrained individuals.

Findings observed for HR ($p<0.01$), sBP ($p<0.001$) and dBP ($p<0.01$) demonstrated TRI was the only group to increase in all haemodynamic parameters, whereas the remaining groups showed significantly increased sBP from rest to 60% W_{max} (all $p\leq 0.001$), but non-significant trends for HR and dBP. HR and sBP are consistent;

however, during semi-supine cycling dBP responses have shown some variation during exercise compared with a resting state, with increases (Lee et al., 2012), no changes (Stohr et al., 2012), and a study failing to report BP during exercise (Doucende et al., 2010). Although the current study found sBP and dBP enhanced during the cycling exercise, PUV still augmented in TRI, which therefore may suggest LV untwist to be a volume dependant measure based on HR responses, with increased afterload appearing to have minimal influence during dynamic exercise.

As anticipated, PUV statistically increased with progressive exercise intensity within the TRI group ($p < 0.01$). Although all other groups showed no significant changes from rest to both exercise intensities, effect sizes were medium and large in the LDR, RT and CON from rest to 30% W_{max} . Equally, large effect sizes were observed from rest to 60% W_{max} in each group. Sample sizes of the groups may be accountable for a lack of significance, however upon observation of the effect sizes and figure 4.2 it is evident of a continual increase with exercise within all groups. The finding of increased PUV with progressive intensity is in agreement with what has previously been observed (Notomi et al., 2006, Lee et al., 2012, Stohr et al., 2012). During diastole, apical rotation velocity significantly increased from rest to 30% W_{max} and a further augmentation to 60% W_{max} in TRI but non-significant increase in the remaining groups. In contrast, basal rotation rate only increased at 60% W_{max} when compared with rest. It has been frequently documented that enhances in peak untwist are driven mainly by enhanced diastolic apical rotation velocities, reaching peak earlier and closer to MVO than rest and before peak basal rotation (Doucende et al., 2010). The findings in the present study confirm those of previously published literature (Doucende et al., 2010, Stohr et al., 2011b). Peak UTR closely followed that of peak apical rotation resulting in earlier onset of suction to generate the IVPG necessary to ensure adequate filling, despite the reduction in the diastolic period due to greater HR (Doucende et al., 2010). Rapid apical diastolic rotation reduces wall stress and causes a greater decline to create the IVPG, thus blood can rapidly be pulled towards the apex (Notomi et al., 2006). During exercise, IVRT is reduced as a consequence of an increased rate in LV pressure decay and with no elevation in left

atrial pressure, the 'suction' phase prolongs from IVRT and into filling (Notomi et al., 2006). The complex fibre arrangement and larger radius of the epicardium around the long axis may facilitate the earlier peak apical rotation. The apex is considered to permit a more dynamic behaviour when the myocardium is subjected to physiological demands (Stohr et al., 2012). Moreover, the continual contraction of the ascending segment which surpasses the termination of the descending segment (Buckberg et al., 2011), may also explain why diastolic basal rotation peaks later than apical, due to the onset occurring later.

Previously, it has been shown that progressive increases in untwist mechanics are correlated to enhanced systolic torsion (Doucende et al., 2010). Titin based restoring forces may aid in ventricular suction especially during exercise when diastolic filling rate is required to markedly increase (LeWinter et al., 2007). Stiffer titin is likely to cause activation of the length-dependant Frank-Starling mechanism, which during exercise when preload is increased, is an important process required for elevated \dot{Q} (Methawasin et al., 2014). Dynamic posttranslational modifications via phosphorylation causes changes in the elastic I-band regional titin domains N2-Bus and PEVK (Müller et al., 2014). In a rat model, Müller et al. (2014) showed that following a single acute bout of 15 minutes treadmill running, PEVK increased and thus demonstrated increased titin based stiffness. An acute response appears to differ from a chronic adaptation when conducting dynamic exercise (Hidalgo et al., 2014, Müller et al., 2014). However, increased stiffness can be considered as an augmentation to the positive inotropic effect due to the onset of exercise (Müller et al., 2014). As previously discussed, passive tension and restoring forces are proportional to the titin stiffness, therefore during exercise the Frank-Starling mechanism is likely to become activated to produce a more forceful contraction. This may suggest why twist and thus untwist enhance, due to greater restoring forces which is a direct reflection of enhanced contraction.

Diastolic timings were not measured in the current study; however, it was observed that TTP untwisting velocity occurred later in diastole within TRI (Figure 4.3A). These

results may not suggest a delay in obtaining peak untwist but a product of reduced overall diastolic time. This observation is in agreement with Doucende et al. (2010), who showed with incremental cycling at 20, 30 and 40% maximum aerobic power, diastole progressively declined from 586ms at rest to 334, 300 and 269ms, respectively. An overall reduction in the availability to fill the LV subsequently requires an efficient myocardium to facilitate re-filling to ensure adequate SV for the ensuing ejection. However, the %untwist during the isovolumetric relaxation period was not measured, therefore it is only suggested that greater untwist occurred earlier within diastole and that greater TTP untwisting velocity is simply a reflection of a reduction in diastole.

5.2.3 Leg Extension

The present investigation has demonstrated that untwisting parameters do not alter between varying types of trained and untrained populations during static exercise. Although HR differed, shown to be less in the LDR and TRI at both intensities compared with CON, these alterations did not translate into greater untwist in the CON. This indicates that HR may not contribute to alterations in untwisting mechanics when performing static exercise. Despite lower body leg extension being a highly static, resistance exercise which may be more familiar to RT, mechanical responses during incremental exercise did not differ. Therefore, it is suggested that chronic resistance training does not translate into enhanced diastolic function when performing a familiar exercise compared to athletes undertaking an unfamiliar exercise; however, the RT did not display concentric hypertrophy. In addition, TRI who are categorised as high dynamic, high static (Mitchell et al., 2005) also appear to demonstrate similar responses. Therefore, it may be concluded that chronic training provides no additional enhancements or determinants in diastolic function when performing static exercise. These findings cannot be compared to previously published literature because no other study has investigated the athlete-control differences in untwisting mechanics, more specifically multiple types of athlete groups with varying sporting demands.

Prior studies have demonstrated significant increases in sBP, dBP and thus mean arterial pressure during IHG exercise at 40% MVIC (Weiner et al., 2012, Balmain et al., 2015), which is in partial agreement with the current study. A progressive increase from rest was evident to 40% and 75% MVIC for sBP but only a significant change occurred from rest to the higher intensity for dBP; differences in experimental protocols may explain these discrepancies. In the current study, the static exercise was completed following the dynamic exercise. This may explain why an afterload may be considered absent in the current study. Post-exercise hypotension has been shown to cause significant decreases in both sBP and dBP following moderately intense cycling after as little as 10 minutes exercise (MacDonald et al., 2000). The reduction in BP could have therefore blunted the BP response observed during leg extension, detected peripherally. Also, the contraction time used was purposely kept to the shortest duration possible, whereby BP could be measured whilst attempting to limit a rise in HR, which has been shown to independently increase twist/untwist mechanics (Gibbons Kroeker et al., 1995). However, due to a short, 15 second contraction time, increases in peripheral dBP may not have been detectable, yet, a centrally elevated afterload may have occurred. Tanaka et al. (2014) showed that during 90 seconds IHG, peripheral dBP did not increase, whereas central BP increased in IHG but not dynamic exercise, which involved graded exercise until 80% maximal HR was achieved. Thus, suggesting that changes in dBP may not always be detectable when a central BP response to static exercise may be present, therefore the possibility of an increase in central afterload within the present study cannot be neglected.

The onset of static exercise elicited increased HR responses from rest compared with the 40% and 75% MVIC intensities within all groups. Although this is the only study to date which has studied static exercise with multiple intensities, the finding parallels that of Weiner et al. (2012) and Balmain et al. (2015).

The current observation of no changes in untwisting measures during static exercise is a finding which is in agreement with past literature (Weiner et al., 2012, Balmain

et al., 2015). Weiner et al. (2012) and a recent study by Balmain et al. (2015) used IHG exercise at 40% MVIC for a duration of 3 minutes to induce afterload. At the same relative intensity (40% MVIC), the present study confirms that of Balmain et al. (2015), showing no changes in peak apical or basal UTR compared with rest. However, in the current study, as exercise intensified to 75% MVIC, apical UTR significantly increased compared with rest in TRI ($p=0.01$) but basal UTR remained unchanged. A further progression in HR between intensities may indicate that the inotropic effect of greater HR may have enhanced apical untwist. However, peak UTR did not significantly change which therefore may indicate that an afterload effect is preventing PUV augmentation. It remains unknown as to why apical rotations did not increase at the higher intensity in each group, despite significant HR rises within all athlete and non-athlete groups.

It was suggested by Balmain et al. (2015) that the reduction in HR following circulatory occlusion may have enhanced contractility, causing a subsequent decreased UTR. This suggestion was based on findings by Gibbons Kroeker et al. (1995) who found that when maintaining HR at ~ 100 beats.min⁻¹, but enhancing the chronotropic effect of increased contractility, greater untwist occurred during the isovolumetric contraction phase and less during isovolumetric relaxation phase. However, this does not explain the findings from Balmain et al. (2015) as apical UTR decreased as opposed to the increase found by Gibbons Kroeker et al. (1995). Therefore, an alternative suggestion to explain why lower systolic and diastolic apical rotations occurred may be related to myocardial architecture (Balmain et al., 2015). The apex is suggested to be more 'free' than the base due to its greater elasticity and not being tethered to the right ventricle (Stöhr et al., 2015). Therefore, the enhanced surrounding pressure limiting the magnitude of LV twist and untwist may be governed by diminished apical rotational ability, given the known dominance of the apex on twist mechanics. The findings by Balmain et al. (2015) may explain the current study findings in suggesting that increasing afterload, a consequence of incremental static exercise, results in decreased diastolic function. The lack of adjustment observed may be due to an increased HR facilitating the un-coupling in

twist/untwist (Balmain et al., 2015) to normalise untwist by maintaining normal diastolic function when subjected to an afterload challenge. In support, it has been suggested that the effects of preload on LV mechanics are two thirds as great as that of afterload (Sengupta et al., 2008). However, a limitation of the study is that occlusion occurred directly after IHG, therefore there was collectively an afterload effect for 6 minutes, as opposed to the 3 minutes intended. More research is required to establish whether independent afterload mediated increases from occlusion reduce LV untwist; this will help determine whether an increase in HR occurs to normalise untwist and thus diastolic function during static exercise.

The present study cannot confirm the findings of Weiner et al. (2012) in regards to the uncoupling of apical and basal timing events as these were not measured. However, TTP showed initial significance in LDR and significant change in TRI from rest to 40% MVIC, showing PUV occurring later in diastole. This may be due to a reduction in the diastolic period in accordance with the increased HR. However, RT and CON also showed increased HR from rest to 40% MVIC however, TTP remained unchanged from rest. Earlier untwist necessary to facilitate normal function, whereas the high dynamic sports may not have been required to generate a greater IVPG due to sufficient untwist at the given intensity to support SV. Although the LDR and TRI groups appear to demonstrate alternate responses to RT and CON, no between group differences were found. With the progression to the higher intensity, no group changes in TTP untwisting velocity occurred; peak untwist may have occurred closer to MVO to enhance early diastolic filling as a compensatory mechanism. However, further data would have been required to justify this suggestion.

5.3 Limitations

The present study contains several limitations which must be acknowledged. A cohort of young, trained and untrained healthy subjects were studied, which limits the findings to this specific healthy and trained populations. The RT group was not

age matched to the remaining groups, however past literature using 2D STE has found that PUV is not altered with advancing age (Takeuchi et al., 2006, Maufrais et al., 2014). Further, the influence of body size on LV morphology was not accounted for in this study. Given LVM increases in proportion with body size (Brumback et al., 2010), 'scaling' LVM, chamber dimensions and volumes to body surface area, as suggested in current recommendations, would allow for the direct comparison between groups with different body sizes (Lang et al., 2015). Although no statistical differences were observed between groups in height and weight, scaling morphological parameters to body size may eradicate some of the absolute structural differences found. Further, sample sizes between groups were unequal and small in the RT and CON groups, which limits the inference of the present findings and the ability to detect true effects due to low statistical power (Button et al., 2013). Only morphological differences between groups were observed without changes in conventional or STE derived diastolic function, it is possible that the effect may have been overestimated and somewhat exaggerated based on sample sizing in CON, with the possibility of a false-positive result due to random error (Hackshaw, 2008, Button et al., 2013). Taken together, the observation of morphological changes in the TRI and LDR groups is to be interpreted with care with the suggestion that participants within the study may not be different.

The protocol order may have influenced the BP response during the static exercise, as previously discussed, which could have limited the magnitude of afterload detected. Although relative exercise intensities were used for both exercise protocols and images were acquired at the end of each stage/contraction, HR of the basal and apical images did differ $> \pm 10$ beats.min⁻¹ during the cycling ((30% (n=1), 60% W_{max} (n=1)) and leg extension ((40% (n=5), 75% MVIC (n=3)) exercises.

Although STE is a more feasible approach to assess LV ϵ as opposed to TDI derived (Weiner et al., 2010a), it is not without its limitations especially in regards to exercise. The use of STE derived ϵ has not yet been widely validated for its use during stress echocardiography (Lee et al., 2012). Image acquisition is also a limitation of

echocardiographic studies, especially during exercise. Section 3.6 may indicate that the intra-observer reliability for PUV reflects poor test-retest reproducibility during exercise. However, single image acquisition (ACGS and BCGS) is considered acceptable. In an attempt to reflect the image quality, the grading system used by the current sonographer considers 63.5% of images collected during all exercising conditions to be of a good-excellent quality. However, more research may be required to assess the measurement and biological variation associated with ϵ indices. The location of the basal and apical imaging planes may vary between subjects (Doucende et al., 2010), every attempt was made to obtain similar planes between rest and exercise conditions. Between exercise intensities, the imaging planes may have differed slightly, potentially due to enhanced myocardial shortening and overall deformation, therefore enhancing the difficulty of consistent imaging. Care should be taken when obtaining the apical image especially, and a standardised plane should be developed due to various imaging planes distal to the termination of the papillary muscles having shown variations in apical rotation values (van Dalen et al., 2008).

6.0 Conclusion

The current study investigated the impact of progressive dynamic and static exercise on diastolic function in sport specific groups, assessed by 2-D STE. The present findings show that no athlete-control differences in untwisting mechanics existed at rest or during incremental cycling and leg extension exercise. These results have shown that untwisting mechanics are not sport specific in non-professional athletes based on sporting categorisation, despite some morphological adaptations in high dynamic sports associated with the athletes' heart. Alterations in diastolic mechanics may only be evident in highly trained athletes; however, future research should address the sport specific differences in elite level athletes.

During progressive cycling, the present findings demonstrate enhanced diastolic function with increased preload. The ability to augment diastolic function was driven mainly by apical mediated enhancements. Conversely, during leg extension exercise, diastolic mechanics remained unchanged despite a rise in HR. It appears that static exercise does not influence diastolic function; however, HR may neutralise untwisting mechanics to maintain normal functioning. Still, far more literature is warranted to investigate responses to afterload induced exercise, in addition to whether various highly trained athletes differ.

Taken together, the current study has extended existing literature to investigate athlete-control differences in diastolic mechanics; by highlighting the diastolic responses to two forms of haemodynamic loading. Additionally, these findings have provided a foundation for future studies to investigate LV deformation in specific populations and address any potential implications that may occur during preload and afterload exercise.

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Appendices

Appendix 1 – Medical Questionnaire



MEDICAL QUESTIONNAIRE

1 Have you been unwell in the past 7 days?

Yes

No

2 Please mark the category and inform the Echocardiogram Operator.

Stomach illness

Cold

Flu

Virus

Muscular injury

Wounded (Cuts/Grazes)

Skin

Headache/Migraine

3 Do you consider yourself to be in good health today?

Yes

No

4 Do you have any allergies to Electrode Gel or Ultrasound Gel that you are aware of?

Yes

No

5 Is there any medical reason why you think you might not be able to have an Echocardiogram taken? Please give details below.

Former

Current

Never

11 If you answered 'Former' to question 9 please state how long you have been stopped

_____ **years**

_____ **months**

12 Do you currently or have you ever taken anabolic steroids?

Yes

No

Please provide your GP's details below

Name

Address

Postcode

Tel. Number

Signature

Date

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

_____ **days per week**

No vigorous physical activities



Skip to question 3

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

_____ **days per week**

No moderate physical activities → **Skip to question 5**

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

No walking → **Skip to question 7**

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

Don't know/Not sure

Training History and Frequency Questionnaire

We are interested in finding out about your current training history, sports you participate in and how frequently you do so. Please try and answer the questions as best you can providing the most accurate information.

8. How often do you take part in endurance based exercises, which may include running, football, hockey, tennis (excluding rowing, canoeing, cycling and swimming)?

_____ **hours per week**

9. How often do you take part in swimming?

_____ **hours per week**

10. How often do you take part in other endurance based exercises such as rowing and cycling?

_____ **hours per week**

11. How often do you take part in strength based exercises, which may include weight lifting, body building, shot put, wrestling, gymnastics etc?

_____ **hours per week**

The next series of questions are about your participation in specific sports. If you do not regard yourself as a trained individual then the questionnaire is complete, otherwise please proceed to answer the following questions.

12. What sport/event do you participate in?

13. Do you participant in any **other** sports? (If yes, please state):

14. How often do you train for your sport?

_____ **days per week**

_____ **hour per day**

_____ **minutes per day**

15. How many months of the year do you routinely train? (Please circle appropriate):

<1

1-3

4-6

7-9

>9

16. How long have you been routinely training? (Please circle appropriate):

<1 year

1 year

2 years

3 years

4 years

>5 years

17. What is the highest level of competition that you compete at? (Please circle appropriate):

Recreational Club National International Olympic

The next series of questions are about your training volume. If you do not regard yourself as a trained individual then the questionnaire is complete, otherwise please proceed to answer the following questions.

Endurance Training:

How many miles do you run per week on average?

How many miles do you cycle per week on average?

What distance do you swim per week on average?

_____ (meters/km/miles)

Resistance Training:

Typically, how many repetitions and sets do you do and how much rest period do you have between each set?

_____ reps

_____ sets

_____ time between (mins)