Heart rate and systolic blood pressure response to workload during an incremental sub-maximal exercise test in healthy individuals

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by

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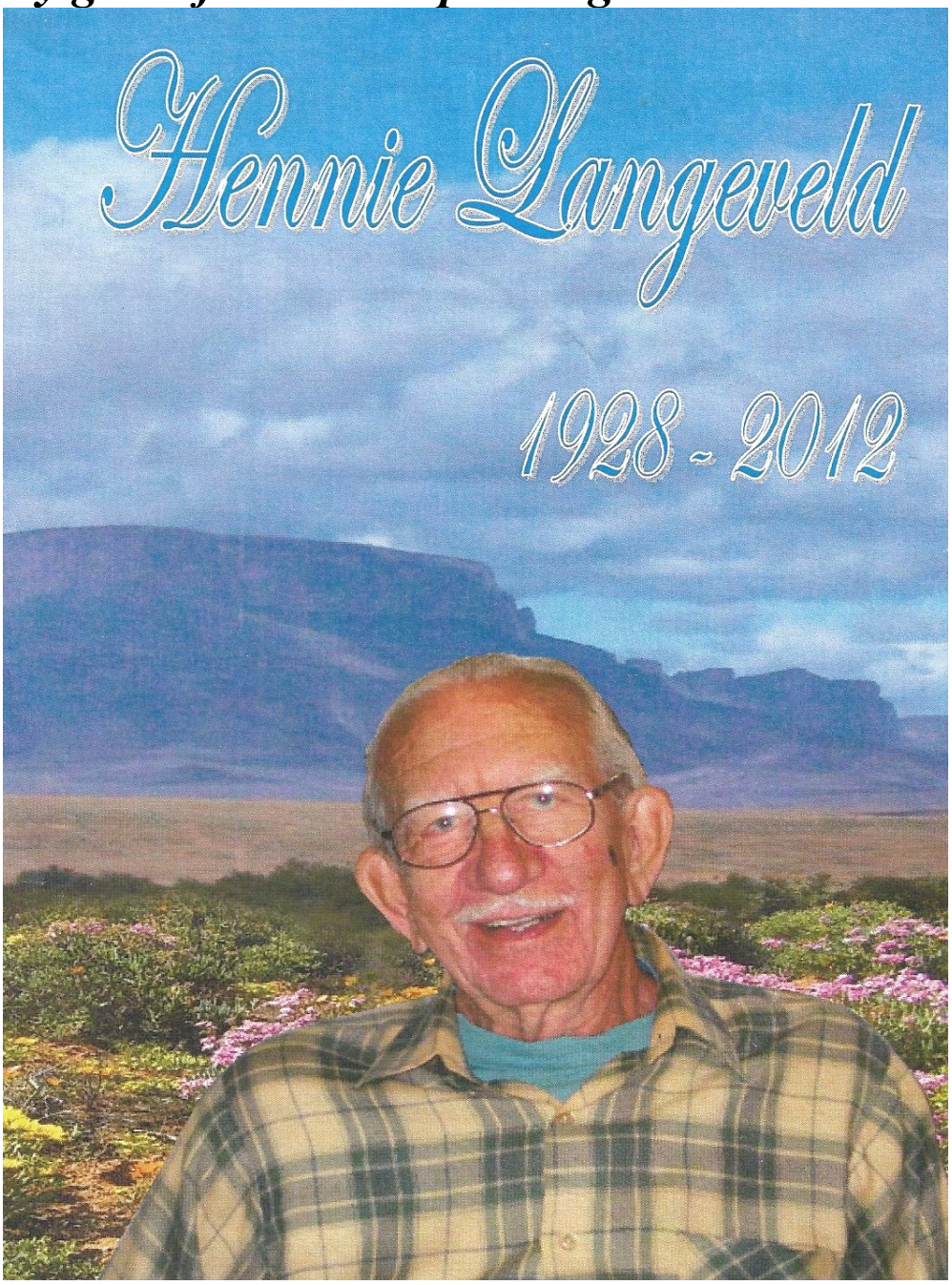
In loving memory of:

My grandfather – Oupa Langes



DECLARATION

The co-author of the two articles, which form part of this dissertation, Prof. S.J. Moss (Supervisor), hereby gives permission to the candidate, Mr H.L. Basson to include the two articles as part of a Masters' dissertation. The contribution, both advisory and supportive, of the co-author was within reasonable limits, thereby enabling the candidate to submit his dissertation for examination purposes. This dissertation, therefore, serves as fulfilment of the requirements for the M.Sc. degree in Biokinetics within Physical Activity, Sport and Recreation (PhASRec) in the Faculty of Healthy Sciences at the Potchefstroom Campus of the North-West University

Prof. S.J. Moss

Supervisor and co-author

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"The dictionary is the only place that success comes before work. Work is the key to success, and hard work can help you accomplish anything."

~ Vince Lombardi Jr.

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"No matter what you achieve as a human, you can only be humbled by nature"

~ Mike Horn

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ABSTRACT

Heart rate and systolic blood pressure response to workload during an incremental sub-maximal exercise test in healthy individuals

Healthcare practitioners, whom perform accurate sub-maximal exercise tests in healthy individuals, need to understand the physiological demands and normal cardiovascular (CV) responses with exercise. Exercise testing delivers valid information about the physiological systems of individuals that may identify healthy individuals at risk of developing future cardiovascular disease (CVD). Exercise is a common way to assess physiological stress experienced by an individual, because CV abnormalities that are not present at rest, can be elicited during exercise testing and be used to determine the adequacy of cardiac function. Cardiovascular markers like, resting heart rate (HR) and systolic blood pressure (SBP) have been used as simple non-invasive and useful biomarkers of the fundamental status of blood circulation and the CV system in healthy individuals.

Studies have contributed to exercise under sub-maximal and maximal stress testing. Modern-day literature lacks information on the safe HR and SBP responses to an increase in workload during a sub-maximal exercise protocol in healthy individuals.

Consequently, the first purpose of this study was to identify the current evidence in the literature on CV response during a sub-maximal incremental exercise protocol. Different protocols and modalities contribute to various CV responses over a wide age group and gender. Heart rate and SBP increases in a linear fashion with an increase in workload, irrespective of protocol and modality. The amount of this increase, or the response of these markers, is still a grey area in the literature, especially in healthy individuals.

The second purpose of this study was to analyse the HR and SBP response in healthy adults during a sub-maximal incremental exercise test, with an increase in workload (watt). The systematic review found mean changes from baseline for HR and SBP to be 75.7% and 63.5% respectively, on bicycle protocols (N = 3). The treadmill protocols (N = 2) found similar mean changes from baseline of 113.3% for HR and 36.1% for SBP. Descriptive

measures as well as Linear regression analyses were performed, using Generalised estimated equations (GEE). An independent t-test was used to compare the males with the female participants: HR and SBP response to an increase in workload (watt). GEE adjustments were made for age, body mass index (BMI) and workload (watt). Significant difference levels were set at $p \leq 0.05$.

The present once-off subject availability results revealed that male subjects were heavier and taller than their female counterparts ($p \leq 0.05$). They also had a noteworthy higher SBP_{rest}, as well as BMI ($p \leq 0.05$). The results from the GEE analyses we presented prediction equation, with all variables significant, except for the BMI ($p = 0.972$ females; $p = 0.169$ males).

In conclusion, the literature review indicated a lack of information on the HR and SBP response with workload in healthy adults. It is advised that further research is needed to test the prediction equations in healthy individuals to determine the validity and reliability. They need to be tested in a controlled clinical environment, where the participants are monitored more thoroughly. By putting these predicted equations to the test, healthcare practitioners will be able to identify an exaggerated HR and SBP response with an increase in workload. If the individual's response is exaggerated, the healthcare practitioner can intervene to prevent future cardiovascular events.

Key words: Cardiovascular, heart rate, systolic blood pressure, workload, healthy, incremental

OPSOMMING

Die respons van harttempo en sistoliese bloeddruk met ‘n toename in werkslading tydens ‘n sub-maksimale inkrementele oefentoets in gesonde individue.

Fisiologiese eise en normale kardiovaskulêre (KV) response met oefening moet begryp word, en is dus noodsaaklik vir gesondheidsorg-praktisyns om sodoende akkurate sub-maksimale oefentoetsings op gesonde individue uit te voer. Oefentoetsing lewer geldige inligting oor die fisiologiese sisteem van die individue, wat kan bydrae tot vroeë identifisering van moontlike KV siekte, asook die risiko’s daarvan. Oefentoetsing is `n algemene manier om fisiologiese sisteme te evalueer. Dit kan KV onreëlmatighede, wat nie teenwoordig is onder rustende toestande nie, aanvuur en ook die werking van die kardiovaskulêre sisteem (KVS) bepaal. Kardiovaskulêre merkers soos harttempo (HT) en sistoliese bloeddruk (SBD) word gebruik as eenvoudige, dog geldige merkers, om die status van die bloedsirkulasie en KVS in gesonde individue te ondersoek.

Verskeie studies het al geldige bydraes gemaak tot oefening, deur gebruik te maak van sub-maksimale en maksimale inspanningstoetse. Hedendaagse literatuur toon gebrek aan inligting oor die veilige HT en SBD response met `n verhoging in werkslading tydens `n sub-maksimale oefenprotokol in gesonde individue.

Die eerste doel van die studie was om die huidige bewyse in die literatuur oor KV response tydens `n sub-maksimale inkrementele oefenprotokol te identifiseer. Verskillende protokolle en modaliteite dra by tot verskeie KV response oor wye ouderdomsgroepe en geslag. Harttempo en SBD verhoog liniêr met `n verhoging in werkslading, ongeag die protokol of modaliteit.

Tweedens, het die studie die HT, SBD en werkslading (watt) se verwantskap evalueer, tydens `n sub-maksimale inkrementele oefenprotokol in gesonde volwassenes. Die literatuuroorsig het gemiddelde verhoogde veranderinge van 75.7% vir HT en 63.5% vir SBD gevind, tydens `n fietsprotokol (N = 3). Tydens die trapmeulprotokol (N = 2) was ooreenstemmende gemiddelde verhogings vanaf basislyn 113.3% en 36.1% vir HT en SBD onderskeidelik.

Beskrywende statistiek, asook liniêre regressie analises is bereken deur gebruik te maak van "Generalised estimated equations" (GEE). Onafhanklike t-toetse is gebruik om geslagsverskille te vergelyk in die lig van die bogenoemde response met `n verhoging in werkslading (watt). Daar was gekorrigeer vir ouderdom, liggaamsmassa-indeks (LMI) en werkslading. Betekenisvolheid is gestel op $p \leq 0.05$.

Die huidige eenmalige beskikbaardheid studie se resultate het bevestig dat mans swaarder en langer as vrouens was ($p \leq 0.05$). Mans het `n betekenisvolle hoër rustende SBD, asook LMI gehad ($p \leq 0.05$). Die resultate van die GEE analises is voorgestel as voorspellingsvergelykings, waar alle veranderlikes betekenisvol was, behalwe vir LMI (p = 0.972 dames; p = 0.169 mans).

Om saam te vat, die literatuuroorsig benodig meer inligting oor HT en SBD response met `n verhoogde werkslading in gesonde volwassenes. Dit word voorgestel dat verdere navorsing gedoen moet word om die voorspellingsvergelykings te toets ten einde die geldigheid en betroubaarheid te bepaal. Die toetsings moet plaasvind onder gekontrolleerde kliniese omstandighede, waar die deelnemers meer deeglik gemonitor word. Deur die vergelykings te toets, sal die praktisyn in staat wees om `n abnormale HT en SBD respons met `n verhoogde werkslading te identifiseer. As die individue `n abnormale respons toon, kan intervensies in plek geplaas word om toekomstige KV insidente te voorkom.

Sleutelwoorde: Kardiovaskulêr, harttempo, sistoliese bloeddruk, werkslading, gesonde, inkrementeel

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LIST OF ABBREVIATIONS

A

ACSM	American College of Sports Medicine
ANS	Autonomic nervous system

B

BP	Blood pressure
bpm	Beats per minute

C

CI	Confidence interval
cm	Centimetre
CO	Cardiac output
CV	Cardiovascular
CVD	Cardiovascular disease
CVS	Cardiovascular system

D

DBP	Diastolic blood pressure
DP	Double product / Dubbel-produk

E

et al.	And others
ExBPR	Exaggerated blood pressure response

G

GEE	Generalised estimated equation
GXT	Graded exercise test

H

HR	Heart rate
HR_{rest}	Resting heart rate

HT	Harttempo
HTN	Hypertension

I

ISAK	International Society for the Advancement of Kinanthropometry

K

kg	Kilogram
kg/m^2	Kilogram per metre square
KV	Kardiovaskulêr
KVS	Kardiovaskulêre sisteem

L

LMI	Liggaamsmassa-indeks

M

METs	Metabolic equivalents
min	Minute
mmHg	Millimetre mercury
$M\dot{V}O_2$	Myocardial oxygen consumption

N

NO	Nitric oxide

P

PAR-Q	Physical Activity Readiness Questionnaire
PNS	Parasympathetic nervous system

R

RPE	Rate of perceived exertion
RPP	Rate-pressure-product

S

SBD	Sistoliese bloeddruk

SBP	Systolic blood pressure
SBPR	Systolic blood pressure recovery
SNS	Sympathetic nervous system
SV	Stroke volume

T

THR	Target heart rate
TPR	Total peripheral resistance
TOD	Target organ damage

V

$\dot{V}O_2$	Oxygen uptake
$\dot{V}O_{2max}$	Maximum oxygen uptake

W

W	Watt

Symbols

%HR	Percentage heart rate
%SBP	Percentage systolic blood pressure
$\%HR_{rise}$	Percentage heart rate rise
$\%SBP_{rise}$	Percentage systolic blood pressure rise

Chapter 1: Introduction

1.1 Introduction

Easily measured hemodynamic variables, like heart rate (HR) and blood pressure (BP), are valid predictors of relative myocardial oxygen consumption ($M\dot{V}O_2$) during exercise in different populations (Gobel *et al.,* 1978:551; Hermida *et al.,* 2001:475). However, the double product (DP), defined by the product of HR and systolic blood pressure (SBP), (Gobel *et al.,* 1978:551; Lai *et al.,* 2004:607; ACSM, 2006:119; Nogueira *et al*., 2007:106; Suzuki *et al.,* 2007:20), is the index which best correlates with relative $M\dot{V}O_2$, and is, therefore, the critical measurement in defining the response of the coronary circulation to myocardial metabolic demands in healthy people (Gobel *et al.,* 1978:555).

In the majority of situations, the physiological response of the SBP to an increase in workload is determined with a sub-maximal stress test, known as a graded exercise test (GXT), using either the treadmill or cycle ergometer (Tavel, 2001:907). A basic aim of sub-maximal exercise testing is to determine the HR and BP response to sub-maximal workloads (ACSM, 2006:68) in order to determine risk for exercise prescription and to monitor and implement progression in the exercise programme prescription.

Neder *et al.* (2001:1485) found that gender and age should also be considered in the assessment of the normality of dynamic exercise responses such as cardiovascular (CV) indices. In general, females exhibited increases in BP through greater myocardial reactivity relative to males, while males showed increases in BP through more enhanced vascular reactivity (Girdler *et al*., 1990:585). Males demonstrated significantly higher SBP levels at rest than females (Girdler *et al*., 1990:578; Ryan *et al*., 1994:1702). Males (aged 29 - 48 y)

had considerably higher resting mean SBP than in females of similar age (Ryan *et al*., 1994:1702). Overall elderly subjects (Male = 78 ± 2; Female = 73 ± 2) had a significantly higher resting SBP than younger subjects (Ryan *et al.,* 1994:1702).

Current findings show resting HR decreases with age for males and females (Ehrman *et al.,* 2009:137; Ostchega *et al*., 2011:12). The exception is for people 80 and over, where the average female's mean resting HR was higher than for males (Ostchega *et al*., 2011:12). The main effect regarding gender was marginally significant where females were greater HR reactors compared to males (Girdler *et al*., 1990:580). Ryan *et al.* (1994:1702) established that there was no difference in resting mean HR between males and females at any age. Females demonstrated greater increases in HR and cardiac output (CO) than their male counterparts (Girdler *et al*., 1990:585).

Normal SBP response to exercise shows gender differences amongst healthy people (Dimkpa *et al.,* 2008:24). The ACSM (2006:118) expresses that a normal response to exercise is a progressive increase in SBP, typically 10 ± 2 mmHg.MET^{-1}, with a possible plateau at peak exercise (Knight-Maloney *et al.,* 2002:40; ACSM, 2006:316; Suzuki *et al.,* 2007:23). However, according to the literature, the tempo of this increase is not defined at this point in time (Sieira *et al.,* 2010:197). A drop in SBP (> 10 mmHg from resting SBP despite an increase in workload), or failure of SBP to increase with increased workload, are considered abnormal responses (Sieira *et al.*, 2010:197). Basset *et al.* (1998:459) found that resting SBP correlated positively with maximal SBP during incremental cycle ergometry ($r = 0.64$, $p < 0.0001$). Patients who had a higher SBP response to exercise (> 220 mmHg) also had a higher resting SBP (126 ± 3 mmHg) than the normotensive patients (116 ± 2 mmHg) (Basset *et al.,* 1998:459).

Healthy individuals who exhibit an exaggerated SBP response to exercise have an increased risk of future hypertension (HTN) (Basset *et al.*, 1998:457). Tavel (2001:908) expresses that an abnormal rise in exercise systolic pressure to a level ≥ 214 mmHg in a subject with a normal resting SBP predicts increased risk for future sustained HTN, estimated at approximately 10% to 26% for the next 5 to 10 years. After cessation of exercise, the normal response for SBP will drop by an average of ≥ 15% at 3 minutes after terminating exercise (Tavel, 2001:908).

Dimkpa *et al.* (2008:22) established that the percentage systolic blood pressure rise ($\%SBP_{rise}$) and percentage heart rate rise ($\%HR_{rise}$) increased 39.82 ± 9.52% and 174.47 ± 20.32% respectively with incremental aerobic exercise in healthy individuals. When exercise was terminated, the %SBP decline in 1 minute and 3 minutes were 17.02 ± 5.99% and 23.46 ± 4.91%. The %HR decline in 1 minute, and decline in 3 minutes were reported as 43.94 ± 4.93% and 64.53 ± 3.5% respectively (Dimkpa *et al.,* 2008:22).

The DP, or rate-pressure product (RPP), is a well-established surrogate marker for relative $M\dot{V}O_2$ and has been used in a clinical rehabilitation setting (Hargens *et al.,* 2011:317). At a given CO, a decrease in sympathetic activity results in a lower HR and, therefore, lowers DP (Hargens *et al.,* 2011:317). Resting HR and BP have been used as simple and useful biomarkers of the fundamental status of blood circulation and the CV system in healthy people (Nagaya *et al*., 2010:215).

Nagaya *et al.* (2010:221) noticed that an increase in sympathetic activity elevates HR and SBP. The onset of exercise, HR increase is primarily as a result of parasympathetic nervous system withdrawal (Hargens *et al.,* 2011:317). With higher intensities, HR increases to maintain CO through sympathetic activity (Hargens *et al.,* 2011:317). Nagaya *et al.* (2010:219) on the other hand found that resting HR, like body weight, might be a simple and self-assessable predictor for diabetes mellitus in general populations. Heart rate increases in a linear fashion with the workload and relative oxygen uptake ($\dot{V}O_2$) during dynamic exercise (ACSM, 2006:68).

1.2 Problem Statement

The literature lacks information on the safe SBP and HR responses to an increase in workload during a sub-maximal exercise protocol. Therefore, this study aims to answer the following research question: What is the normal HR and SBP response in healthy adults during an incremental increase in workload during a sub-maximal exercise test?

The results obtained from this study will expose what a normal HR and SBP response with an increase in workload should be, and will aid healthcare practitioners performing sub-maximal stress testing to identify health risks regarding the CV response to incremental sub-maximal exercise before the presence of pathology.

1.3 Objectives

The objectives of this study are to determine:

- The current evidence in the literature on cardiovascular response during a sub-maximal incremental exercise protocol;
- The relationship between HR, SBP and workload during a sub-maximal incremental exercise protocol in healthy individuals.

1.4 Hypotheses

The following hypotheses were formulating for this research:

- There is only evidence of cardiovascular responses in diseased population during a sub-maximal incremental exercise protocol.
- The HR, SBP and workload will have a positive linear relationship during a sub-maximal incremental exercise protocol in healthy individuals.

1.6 Structure of the Dissertation

This dissertation is presented in four major parts, namely an introduction (Chapter 1), a systematic review, which is also one manuscript (Chapter 2), and the findings of the study as the second manuscript (Chapter 3). Subsequently a summary with conclusions, limitations and recommendations will follow (Chapter 4).

Chapter 1 presents the problem, and states the aim and hypotheses of this study, as well as the structure of the dissertation. The literature review (Chapter 2), is presented as a systematic review manuscript. The cardiovascular markers' response to incremental exercise is reviewed with the specific focus on the current evidence in the literature on cardiovascular response (HR and SBP) during incremental exercise. Chapter 3 presents the empirical findings of the study and is also presented as a manuscript: "Heart rate and SBP response to sub-maximal incremental exercise in healthy individuals." Both manuscripts will be prepared for submission to peer-reviewed journals namely: *Sports Medicine* and the *European Journal of Physiology*. The fourth and ultimate chapter will end with the summary, conclusions, limitations and recommendations and future research of both manuscripts. Chapter 4 is

followed by a list of appendices. Each chapter will be followed by the references. References for Chapter one will be according to the Harvard style. Chapter two and three will be according to the guidelines for authors as included in the appendices.

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Chapter 2: Cardiovascular markers' response to incremental exercise testing: a systematic review

Cardiovascular markers' response to incremental exercise testing: A systematic review

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Abstract

Background:

Exercise testing provides valid information about the physiological systems of apparently healthy individuals at risk of developing future cardiovascular (CV) disease. Researchers have indicated a linear relationship between heart rate (HR) and blood pressure (BP) during an increase in workload. An equation predicting the normal HR and systolic blood pressure (SBP) response in healthy individuals during an incremental exercise test, will assist in identifying abnormal HR and SBP response that is considered a predictor of future risk for developing hypertension (HTN).

Objectives:

The objective was to determine the scientific evidence available on the relationship between HR and SBP during an incremental increase in workload of healthy individuals.

Data sources:

The following electronic databases were searched: Academic search planner, CINAHL, E-journals, ERIC, Health source (academic edition), MEDLINE, Sportdiscus and cross-referencing. The literature searched included the period January 2000 to September 2012.

Study selection:

Full-length peer reviewed journal articles in English were eligible for inclusion. Studies from 2000-2012 that reported on randomised control trials (RCT`s), systematic reviews, cohort studies, longitudinal studies and meta-analysis of HR and BP response in relationship to an increase in workload were included. Two authors independently determined eligibility for inclusion. Articles were excluded if they had relevance to adolescents, diseases (diabetic, hypertension, cancer, obesity) disabilities, animals, resistance or strength training (isokinetic or isometric) or patients on any CV medication.

Study appraisal and synthesis methods:

The literature that assessed the CV responses to incremental exercise testing was searched.

Results:

From the 1711 relevant publications found, seven trials fulfilled our inclusion criteria. Randomisation was adequately concealed in a minority of studies (RCT`s, review, cohort, longitudinal), where SBP and HR was reported. The seven trials compared different SBP and HR responses to different exercise modalities and protocols. Systolic BP increased by 31.4% (mean resting baseline: 123.8 ± 12.5 mmHg; mean max.: 182.6 ± 17.9 mmHg) and HR by 85.8% (mean resting baseline: 72.6 ± 10 bpm; mean max.: 155.1 ± 11.6 bpm).

Limitations:

In the included studies, most of the participants were men. The studies lacked the acute response and most reported the training effect on the CV parameters. Rather small study groups were used that could influence the significance of the results.

Conclusions:

An increase in workload resulted in a linear increase in HR, as well as SBP. The response to the increase in workload is, however, influenced by gender, age, physical activity levels, exercise testing modality, body composition and lifestyle. No objectively determined equations predicting HR and SBP response to an increase in workload were reported. Future research should determine the normal response in HR and SBP in healthy individuals in order to identify abnormal responses.

Key words: Cardiovascular, exercise, incremental, workload

2.1 Introduction

Exercise testing provides valid information about physiological systems of individuals that may help identify healthy individuals at risk of developing future cardiovascular disease (CVD).[1] Cardiovascular markers such as, resting heart rate (HR) and blood pressure (BP) have been used as simple non-invasive and useful biomarkers of the fundamental status of blood circulation and the cardiovascular (CV) system in healthy people.[2] Exercise, which is the increase in bodily movement involving all major muscle groups, challenges all physiological systems including the cardiovascular system (CVS). Exercise would be referred to as an acute session, and training, the chronic effect (repeated acute bouts that lead to a conditioning effect). Heart rate and BP are hemodynamic variables that are easily measured during exercise in different populations.[3]

With the afore-mentioned descriptions, we can assume that the physiological response of the CVS of healthy individuals will give a reflection of the changes observed during exercise. Factors affecting BP are multiple, pervasive and difficult to quantify and pose a challenge in the attribution to BP solely to exercise.[4] One of the many mechanisms that control BP involves actions and stimulation of the autonomic nervous system (ANS).[5] The sympathetic drive to the heart and periphery is one part of the ANS.[5] The sympathetic activity's control by reducing vasomotor tone could be evoked to account for a lowered BP.[6] Furthermore, reductions in vasoconstrictor state of peripheral vasculature by less sympathetic neural state or greater local vasodilator influence are examples of neural and local changes that would reduce peripheral resistance and lowers BP.[7] The reduced BP is based on a reduced sympathetic vascular resistance and the sympathetic nervous system (SNS) and the renin-angiotensin system might be involved.[8]

One of the several mechanisms that could also play a role in BP regulation is the baroreceptor activity.[6,9] The BP responsiveness may be a protective regulatory mechanism, such as the arterial baroreflex that become particularly essential in buffering the very high BP observed during maximal exercise.[9] As the BP increase, the firing of the baroreceptor also increases.[10] The increased baroreceptor firing inhibits vasoconstrictor action and result in vasodilation of the blood vessels and a decrease in BP.[10]

Other researched mechanisms regarding regulation of BP includes impairment of endothelial function,[9,11] changes in systemic vascular resistance,[12-14] an increased peripheral vascular resistance,[5,7,15] impaired capacity for exercise-induced vasodilatation,[1] or abnormalities of autonomic control.[12] According to this research, it is clear that more than one mechanism regulates BP response.

When the sympathetic drive is stimulated, the result is an increase in the contractility of the heart (myocardial contractile force), which leads to an increase in HR and stroke volume (SV).[5,10] It is believed that vasodilatation is a passive process mediated by sympathetic withdrawal.[6] The level of parasympathetic activity affects the CV responsiveness to training[16] and the vagal nerve activity (parasympathetic branch of ANS) is considered to be a CV protective factor.[17] The intrinsic HR may have protective effects on CV events.[18] The above-mentioned leads to the assumption that the body has protective mechanisms when confronted with different stressors like exercise.

In the light of individuals that exercise regularly, there is a higher parasympathetic activity in well-trained fit individuals.[16] It is not evident whether well-trained athletes have better autonomic cardiac function or just a decreased intrinsic HR.[18] Fit individuals present a more effective autonomic activity than in sedentary individuals.[17] With this said it can be believed that the parasympathetic nervous system (PNS) of the SNS plays different roles in conditioned individuals and react differently to exercise.

Blood pressure and HR are also influenced by gender and age and should also be considered in the assessment of the normality of dynamic exercise responses.[19] Males and females with high-normal BP at baseline examination have a higher incidence of CVD on follow-up examination than those with optimal BP.[20] Cornelissen et al.[21] uncovered that systolic blood pressure (SBP) during recovery (SBPR) to be lower in females.[12] Males showed significantly higher peak-exercise SBP than females, because they can indulge in higher exercise workloads.[22] Dimkpa and Ugwu[22] drew attention to that in both genders a low resting HR would result in a faster SBP recovery and vice versa.

Older subjects revealed a lower resting HR[23,24] and lower peak-exercise HR than younger subjects.[23,25,26] In the older individual, there is a lack of improvement in aortic stiffness[27] with training, and it may be possible that the elderly are resistant to exercise-induced

improvements in SBP.[4] The explanation for this might be because older subjects have higher perception of effort during exercise;[28] diminished adrenergic responsiveness;[26] increased peripheral resistance and BP.[23,25,29] Singh et al.[12] concurred that exercise SBP was significantly higher in older subjects compared to their younger counterparts.

In the course of a 12 week aerobic training programme, SBP decreased following an accumulated training programme.[30] Similar noteworthy SBP results were also reported by Cornelissen et al.[21] for aerobic endurance training at low or high intensities where SBP at rest, during maximal exercise and during recovery reduced over 10 weeks. Cornelissen et al.[21] also looked into whether aerobic training at lower intensities had an effect on HR at rest, during exercise and after a maximal graded exercise test (GXTs). They uncovered that training forced reductions in HR during the maximal GXTs.[21] Therefore HR can be used as a variable in GXTs as it illustrates a very unwavering pattern throughout training.[31] Aerobic training reduced mean BP[6,15] by 4.9% at fixed relative workloads.[14] Aerobic training had a better effect on BP in patients with hypertension (HTN) than in normotensives.[8,32,33]

The American College of Sports Medicine (ACSM)[34] avows that a normal response to exercise is a progressive increase in SBP, typically 10 ± 2 mmHg/MET, with a potential plateau at peak exercise.[34-36] Fagard[14] observed in 68 study groups that the changes of SBP in response to exercise, after adjustment for the control observations, ranged from +9 to -20 mmHg for SBP. Exaggerated blood pressure response (ExBPR) to exercise signifies poor arterial compliance.[13,37] The ExBPR may impair endothelial function with the consequent restriction in vasodilatation in response to sheer stress.[4]

Sharabi et al.[38] and Singh et al.[12] carried out studies where they investigated whether ExBPR to exercise was a suitable predictor for development of future HTN. Future HTN has also been narrated by Pescatello et al.[7] to be correlated with an ExBPR during and after exercise. The probability for developing future HTN in normotensive healthy adults, with marginally elevated resting BP, is increased if they exhibit an ExBPR.[1] Sharabi et al.[38] and Miyai et al.[1] concluded that the chances of developing HTN or the usage of CV medication were significantly higher in individuals with an ExBPR. Individuals with ExBPR should be studied more thoroughly and lifestyle modifications should be indorsed which may postpone the development of CVD.[38]

Research from the late sixties and early seventies reported by Jones and Campbell[39] referred to Spiro et al.[40] and Sannerstadt et al.[41] that HR and SBP increased linearly with increasing workload during a sub-maximal exercise test in healthy normotensive subjects.

They derived a formula for SBP response from extensive studies done by Sannnerstadt et al.:[41]

$$SBP = 120 + 0.08\ W\ (\pm\ 2\ SD = 25\ mmHg)$$

where W is workload in kpm/min.[39] To date no formula exists for the HR response related to an increase in workload for normotensive persons.

Although various researchers have alluded to the existence of a relationship between HR and SBP with an increase in workload as reported by the ExBPR, the relationship in apparently healthy persons is not clear. In order to identify an exaggerated response, a relationship between HR and SBP in healthy persons should be known. Therefore, the purpose of this systematic review is to establish from the evidence available, the relationship between HR and SBP with an incremental increase in workload in healthy individuals. The findings of this systematic review will enable healthcare practitioners to identify an exaggerated response in order to identify future risk of HTN that may have detrimental future health consequences.

2.2 Methods

2.2.1 Literature Search Strategy

The present review of the literature examines the cardiovascular responses, in particular heart rate and systolic blood pressure, to incremental graded exercise testing. The literature search was conducted on research published from January 2000 to September 2012. The following electronic databases were searched: Academic search planner, CINAHL, E-journals, ERIC, Health source (academic edition), MEDLINE and Sportdiscus. The search engine EbscoHost was used for the search. Reference lists of relevant studies were also searched to identify further published work for eligibility. Two authors independently determined eligibility for inclusion. Criteria for inclusion were full-length peer reviewed journal articles in English language, in which cardiovascular responses were determined with an incremental graded

exercise test. During the search the following keywords were used: cardiovascular AND/OR exercise AND/OR response, systolic blood pressure AND/OR heart rate. Articles were excluded if they had relevance to adolescents, diseases (diabetic, hypertension, cancer, obesity) disabilities, animals, resistance or strength training (isokinetic or isometric) or patients on any cardiovascular medication.

2.2.2 Inclusion Criteria

i. Types of studies

Full-length peer reviewed journal articles in the English were eligible for reviewing. This included randomised control trials (RCT`s), systematic reviews, cohort studies, longitudinal studies and meta-analysis in the response of HR and SBP with an increase in workload.

ii. Types of participants

Only studies with apparently healthy male and female participants between the ages of 21 and 81 years from all ethnicities were included for eligibility.

iii. Exercise outcome measures

Graded exercise testing protocols that focus on cardiovascular responses in healthy individuals during any exercise test were included. Information on heart rate, blood pressure response and workload increase had to be available. Aerobic or continuous exercise, which challenged the cardiovascular system, like upright cycling, running and walking were included. The responses were evaluated with an increase in workload during the incremental exercise test.

a. Primary outcomes

1) Systolic blood pressure response to an increase in workload during incremental exercise.

2) Heart rate response to an increase in workload during incremental exercise.

2.2.3 Quality Assessment of Identified Studies

The methodological quality of the selected studies was assessed by a slightly modified Delphi list.[42] We used the Delphi list and added and left out certain questions. The questions included in Table 1 are no. 1,5,7,9,12,13,14. The questions that were left out of the original Delphi list is: 1. Was the care provider blinded? 2. Was the patient blinded? 3. Did the analysis include an intention-to-treat analysis? The questionnaire has been recognised to be an effective and valid assessment measure for RCT's when conducting a systematic review.[43-45] The questions were the following:

Table 1: Modified Delphi list

1. Was comprehensive research done to avoid bias?
2. Was a method of randomisation performed?
3. Was the treatment allocation concealed?
4. Were the groups similar at baseline (regarding the most important prognostic indicators)?
5. Was the number of test subjects enough to be conclusive?
6. Were the eligibility criteria specified?
7. Was the method description complete and repeatable?
8. Was the outcome assessor blinded?
9. Are the results complete?
10. Was there statistical significance to the results?
11. Were point estimates and measures of variability presented for the primary outcome measures?
12. Could a clear conclusion be derived from the results?
13. Were any inconsistencies in results interpreted?
14. Were the limitations of the study mentioned?

Each study was then given a score and the percentage could be calculated according to quality. The scoring system worked as followed: yes = 2; don`t know = 1; no = 0. A study could get a maximum of 28 points. Studies scoring ≥ 75% were regarded as most significant and eligible for inclusion. Two researchers individually completed the assessment, and a third researcher settled disagreements.

2.2.4 Data Extraction and Management

Data were extracted from the studies that were selected for inclusion. The information extracted were the author, study objective, measure instruments applied, modality of incremental exercise test and systolic blood pressure and heart rate as the outcome measures. The standardised mean difference was calculated for the cardiovascular variables (Systolic blood pressure and heart rate).

2.3 Results

2.3.1 Eligible Studies

The initial search strategy identified 1711 possibly relevant studies. The original subject search terms (Thesaures) were refined to: exercise, heartbeat, aerobic exercise, physical activity, and blood pressure. After the refined search, only 142 articles remained. We evaluated the titles and abstracts of these articles for inclusion. After evaluation of relevance according to the titles and abstracts, 57 articles remained that were narrowed to 12 articles when reading the full publication. Seven of the 12 articles, scored ≥ 75% in the quality assessment protocol step (Table 2). Two authors independently assessed the methodological quality of these studies. Disagreements between the two authors were resolved by discussion.

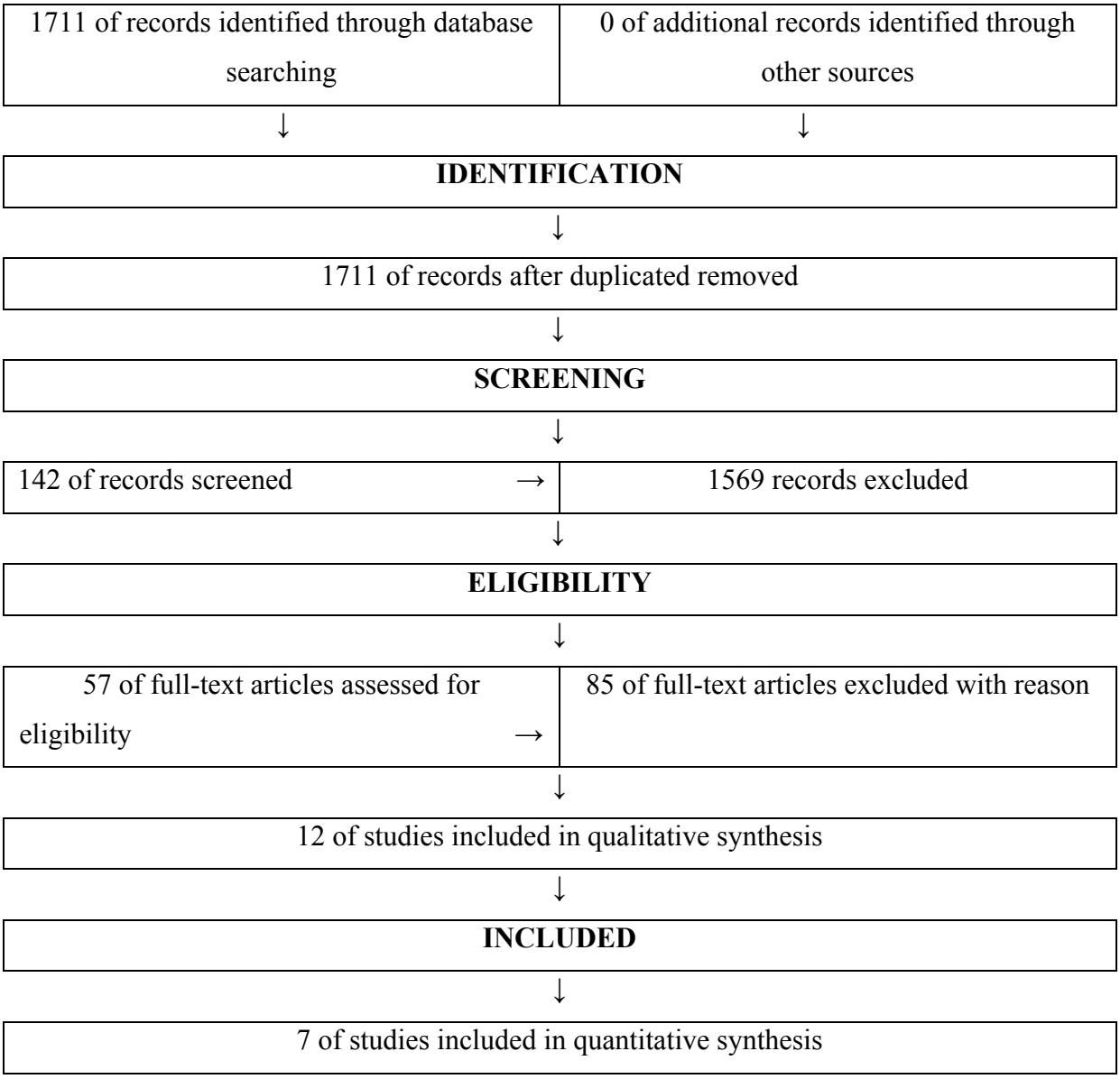

Figure 1: Prisma flow diagram – Relevant quality assessed studies for inclusion

Table 2: Quality assessment form for the 12 eligible studies according to relevancy

Criteria	Fagard 2005	Murphy *et al.* 2009	Cornelissen *et al.* 2010	Campbell *et al.* 2011	Dimkpa & Ugwu 2010	Lewis *et al.* 2008	Sharabi *et al.* 2001	Shim *et al.* 2008	Hamer *et al.* 2005	Achten & Jeukendrup 2003	Navalta *et al.* 2004	Dawson *et al.* 2007
Was comprehensive research done to avoid bias?	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was a method of randomization performed?	Yes	Yes	Yes	Yes	Yes	Don`t know	Don't know	Don't know	Yes	Don't know	Yes	No
Was the treatment allocation concealed?	Don't know	No	Yes	Yes	Don't know	Don't know	Don't know	Don't know	Don't know	Don't know	No	No
Were the groups similar at baseline (regarding the most important prognostic indicators)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Don't know	Yes	Yes
Was the number of test subjects enough to be conclusive?	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Don't know	No	No
Were the eligible criteria specified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No
Was the method description complete and repeatable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Was the outcome assessor blinded?	Yes	Don't know	Don't know	Yes	Yes	No	Don't know	Don't know	No	No	No	Don't know
Are the results complete?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was there statistical significance to the results?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Don't know	Yes	No
Were point estimates and measures of variability presented for the primary outcome measures?	Don't know	Yes	Don't know	Yes	No	Don't know	Yes	Don't know	Don't know	Don't know	Don't know	Don't know

Table 2: Quality assessment form for the 12 eligible studies according to relevancy (cont.)

Criteria	**Fagard 2005**	**Murphy *et al.* 2009**	**Cornelissen *et al.* 2010**	**Campbell *et al.* 2011**	**Dimkpa & Ugwu 2010**	**Lewis *et al.* 2008**	**Sharabi *et al.* 2001**	**Shim *et al.* 2008**	**Hamer *et al.* 2005**	**Achten & Jeukendrup 2003**	**Navalta *et al.* 2004**	**Dawson *et al.* 2007**
Could a clear conclusion be derived from the results?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were any inconsistencies in results interpreted?	Yes	Yes	No	No	Don't know	Yes	No	No	No	Don't know	No	No
Were the limitations of the study mentioned?	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No
Percentage score (%)	**92.9**	**89.3**	**85.7**	**78.6**	**78.6**	**75**	**75**	**71.4**	**71.4**	**60.7**	**53.6**	**42.9**

2.3.2 Cardiovascular Responses to Incremental Exercise

The 12 studies that met inclusion criteria are presented in Table 2. The summaries of cardiovascular responses of the seven studies are shown in Table 3. In the seven studies, the authors presented not all the results. The average systolic BP at baseline of the studies that reported the values, average SBP_{rest} was 123.8 ± 11.4 mmHg in six of the studies. The mean SBP_{rest} falls within the pre-hypertensive values according to the ACSM.[34] Systolic BP at maximum exercise was reported by only four studies and the mean SBP_{max} was 182.6 ± 17.9 mmHg. Heart rate at baseline was reported by six studies and the mean HR_{rest} was 72.6 ± 10 beats per minute (bpm). Heart rate at maximum exercise was reported by five studies and the mean HR_{max} was 155.1 ± 11.6 bpm. The exercise protocols applied for which these results were obtained differed. These studies reported on both males and females with a variety of age groups included. The differences in the populations, limits a comparison between the results of the studies.

(a) Modalities and protocols

The majority of the studies made use of a bicycle ergometer test. Fagard,[14] Murphy et al.[30] and Cornelissen et al.[21] reported on intervention studies that varied from four to fifty two weeks. Murphy et al.[30] and Fagard[14] reported the time of a single test, to be 20-40 minutes and 15-70 minutes respectively. The intensities on the bicycle ergometer varied amongst 30-85% of age-predicted HR_{max}. Lewis et al.[46] and Sharabi et al.[38] did maximum Bruce protocol treadmill tests to 85% and 90% of age-predicted HR_{max} respectively. Other modalities that were pointed out by authors were walking, dance and swimming.

(b) Co-variables

A substantial number of studies did not report details on the participants' gender.[9,14,21,30,38] Only in two of the studies were the gender of the participants reported, one being a bicycle test and the other a treadmill test. No significant discrepancies were reported between SBP and HR at baseline values, with regards to gender for both bicycle and treadmill protocols.[22,46] Dimkpa and Ugwu[22] found a 13.1% increase in SBP from baseline for men and 20.6% higher percentage increase

in SBP from baseline for females when compared with Lewis et al.[46] Both these studies performed a graded exercise test according to the Bruce protocol. On the other hand, Lewis et al.[46] had a 26.9% and 14.3% higher percentage increase in HR from baseline respectively for males and females when compared with Dimkpa and Ugwu.[22] Sharabi et al.[38] Fagard[14] and Lewis et al.[46] had the most similar age range of participants, which were between 42-44 years of age. Cornelissen et al.[21] only reported that the ages of their subjects varied between 55-71 years. The overall average of five studies, fully reported results, were 33.9 ± 8.6 years, and this rule out the study done by Cornelissen et al.[21] Most of the studies[9,14,22,38,46] did report the BMI of their participants, or we calculated[21] it ourselves where only height (cm) and weight (kg) were reported. The mean BMI of six studies were 25.1 ± 5.2 kg/m^2.[9,14,21,22,38,46] The combined BMI gender differences were 24.2 ± 5.9 kg/m^2 for males and 23 ± 6.1 kg/m^2 for females.[22,46] Campbell et al.[9] and Cornelissen et al.[21] used bicycle ergometer tests where workload increased from 40-120 W. Lewis et al.[46] only described that the participants attained stage 2 of the Bruce protocol. Three of the included studies had participants who were smokers.[22,38,46] Lewis et al.[46] reported that 43.5% of the males and 35.5% of the females were current tobacco users. Sharabi et al.[38] on the other hand reported that 62% were current smokers and 57% of their study and control groups were past cigarette smokers. Dimkpa and Ugwu[22] only obtained information on cigarette smoking verbally, and no results were reported.

Table 3: Summary of all relevant and high quality studies included in the systematic review

	Goal	Hypothesis and/or research questions	Study population	Intervention	Outcome measures	Conclusions	Implications in practice
Fagard 2005	To assess the effects of dynamic physical exercise on blood pressure.	None specified.	Healthy normotensive or hypertensive individuals. Age ranged from 21-79 (median: 44).	Duration ranged from 4-52 weeks (median: 16) with a frequency of 1-7 weekly sessions (median: 3) of 15-70 min each, including warm-up and cool-down activities. Exercise involved walking, jogging, running in 69%, cycling in 50%, swimming 3% and other exercises were included in 23% of training regimes. Intensities varied between 30-85% of maximal performance.	Mean blood pressure, cardiac output, heart rate, stroke volume, and systemic vascular resistance. Peak VO_2 and BMI were also measured.	Dynamic aerobic training is less effective than diet in lowering blood pressure and that exercise does not add to the blood pressure reduction by diet alone.	Diet and physical training can be more effective for blood pressure control than diet alone.
Murphy *et al.* 2009	They compared the effects of similar amounts of exercise performed in either one continuous or two or more accumulated bouts on a range of outcomes.	Physical activity increases adherence among the sedentary population at whom this patterns of exercise is targeted.	Studies included 836 subjects, predominantly females (N = 630). Physical activity levels varied between studies.	Majority of interventions were short, ranging in duration from 4-20 weeks, total daily exercise durations of between 20-40 min on 3-5days per week.	Long-term training responses: fitness, body composition (body mass, adiposity, BP, waist and hip circumference, blood lipids) and other health outcomes). Short-term responses: fasting blood lipids, postprandial lipaemia, fasting glucose and insulin.	Accumulated and continuous patterns of exercise training of the same total duration conferred similar benefits.	Short bouts of exercise, accumulated or continuous, is good for improving fitness levels.
Cornelissen *et al.* 2010	Effects of endurance training intensity (1) on SBP and HR at rest, during and after maximal exercise; (2) on measures of HRV at rest, during and after maximal exercise.	None specified.	Healthy sedentary non-smoking males or females who were at least 55 years old with SBP ≥120 mmHg or DBP ≥80 mmHg.	Three 10-week periods. First 10 weeks (training 33 or 66% HR_{res}); second 10 weeks (sedentary period) and third 10 weeks (training 66 or 33% HR_{res}).	Systolic blood pressure and heart rate at rest, during and after exercise by doing low (33% HR_{res}) or high intensity training (66% HR_{res}).	Lower and higher intensity training reduce SBP at rest, during and after exercise to similar extent. Aerobic endurance training does not affect the BP response to an acute bout of exercise in individuals with normal to high normal BP.	By doing aerobic exercise at low or high intensity you can lower the SBP to similar extent.
Campbell *et al.* 2011	They determine whether acute inhibition NO synthesis with L-NMMA would lead to ExBPR to maximal exercise.	Acute inhibition of NO synthesis with L-NMMA in healthy subjects would attenuate exercise-induced reductions in arterial stiffness.	Ten healthy male subjects (31 ± 5 years); weight (77 ± 9 kg); height (177 ± 1 cm); BMI (24 ± 3 kg/m^2).	Two separate laboratory sessions 7 days apart. Fifteen minutes rest, 10 min baseline measurements. Bolus infusion administered for 5 min, followed by 10 min post-infusion measurement period. Followed by maximal incremental exercise on an upright cycle ergometer.	Systolic BP, DBP, mean BP, HR, stroke volume, cardiac output. All parameters were with exercise and recovery. Also with saline and L-NMMA infused.	NO is an important contributor to reductions in artery stiffness after maximal exercise in healthy individuals. The NO influence on hypertensive response to exercise is intensity dependent.	Pharmacological inhibition of NO synthesis augments BP responses.
Dimkpa & Ugwu 2010	Evaluate the independent relationships of systolic blood pressure recovery (SBPR) with age, gender, BMI, waist circumference, resting HR, physical activity and cigarette smoking in healthy adults.	None specified.	Normotensive subjects (N = 337) between the ages of 18-66 years. They were all from Nigeria, 172 were males and 165 were females.	Subjects performed cycle ergometer exercise at progressive incremental workloads until subjects reached 80% of their age-predicted $HR_{max.}$	Peak exercise SBP and DBP, peak exercise HR, $SBPR_1$ and $SBPR_2$ responses to exercise.	There are independent relationships between SBPR and variables known to associate with cardiovascular abnormalities such as age, BMI and waist circumference, resting HR, physical activity and cigarette smoking in at least one gender-specific group of apparently healthy adults.	Systolic blood pressure recovery can be used as a useful tool to assess for any cardiovascular abnormalities.
Lewis *et al.* 2008	Determine the association of exercise BP response with risk of incident cardiovascular disease (CVD).	Exercise systolic and diastolic BP would predict long-term risk of CVD beyond BP at rest and other conventional risk factors.	In 1971, 5124 offspring and spouses of offspring were used. Second examination of the offspring cohort was conducted from 1979-1982 and consisted of 3863. Of the attendees, 3447 did an exercise treadmill test. They were all between 20-69 years old. After all exclusions 1437 (male) and 1608 (female) were used.	Bruce protocol aiming for attainment of 85% of target heart rates. Blood pressure assessed during stage 2 and recovery of this protocol. A 20-year follow-up examination was used.	Exaggerated systolic BP and diastolic BP and the risk of developing CVD. Exercise SBP and DBP and recovery SBP and DBP.	Dynamic BP provides incremental information to BP at rest and suggests that exercise diastolic BP may be a better predictor than exercise SBP in this age group (middle-aged adults).	Rather use the DBP during and after exercise to assess for future hypertension, than SBP.
Sharabi *et al.* 2001	Whether exaggerated blood pressure response to exercise was a good predictor for development of hypertension and target organ damage (TOD).	None specified.	190 male subjects; mean age of 42.6 years. ExBPR group (N = 73) and control group (N = 117).	Bruce protocol was used. 90% of age-adjusted $HR_{max.}$ BP was taken in the end of 3-min stage. Post-exercise recordings were obtained after 5 min.	The chances of developing hypertension or the usage of cardiovascular medication were significantly higher in ExBPR group than in control group. No differences for TOD were found in both groups.	ExBPR predicts the development of hypertension and CVD.	EXBPR should be followed more closely and be instructed for lifestyle modifications that may delay the development of CVD.

Table 3: Summary of all relevant and high quality studies included in the systematic review (cont.)

	Goal	Hypothesis and/or research questions	Study population	Intervention	Outcome measures	Conclusions	Implications in practice
Shim *et al.* 2008	Investigate the association between an exaggerated blood pressure response to exercise and augmented angiotensin (Ang) II rise during exercise.	An exaggerated BP response to exercise is associated with augmented Ang II rise during exercise.	Thirty-six subjects with an exaggerated BP response to exercise (group 2, 18 men, mean age (50 ± 16 years) and 36 age- and gender-matched control subjects with normal BP reactivity (group 1).	A variable bicycle ergometer was used at supine position. Pedalled at a constant speed which began at 25 W, with an incremental workload of 25 W every 3 min until limited by their symptoms.	Hemodynamic responses to exercise (total exercise duration, METs, SBP, DBP, HR) in both groups. Neurohormonal responses to exercise (norepinephrine, epinephrine, plasma renin activity, aldosterone, angiotensin) in male and females.	Exaggerated BP response to exercise was associated with augmented production of Ang II during exercise.	A rise in certain hormones can result in an exaggerated blood pressure during exercise and should therefore be monitored where possible.
Hamer *et al.* 2005	A systematic review that examined the effect of acute aerobic exercise on blood pressure responses to psycho-social laboratory tasks.	None specified.	N = 496 (46% female); 17-60 years.	60% VO_{2max} or 75% HRR. Sessions lasted 10min – 2 h; intensities of 50-100% $VO_{2max.}$ Cycle, treadmill or aerobic dance.	Systolic and diastolic blood pressure response to psycho-social stress.	An acute bout of aerobic exercise appears to have a significant impact on the BP response to psycho-social stressor.	Acute aerobic exercise could provide a buffer to real-life psycho-social stressors (e.g. exams public performance, daily work demands.
Achten & Jeukendrup 2003	The application and limitation of HR monitoring on physiological parameters.	None specified.	None specified.	None specified (Review article just reported other information with no information on interventions.)	Heart rate monitoring and heart rate variability.	Heart rate variability is associated with an increased mortality, but more research is needed towards interventions to increase HRV.	Monitor HR and HRV to prevent overtraining and use it to evaluate responses to different exercise stressors.
Navalta *et al.* 2004	Measure selected cardiovascular and metabolic responses in healthy older and younger individuals during downhill walking.	Activities that enhance physical movement (i.e. increasing walking speed), without producing undue cardiovascular or metabolic stress may be beneficial for older adults.	Twenty healthy subjects, ten older (64 ± 3 years) and ten younger (23 ± 3 years).	Six treadmill walking bouts, each lasting 6 min, with 2 min rest periods between bouts. Walking speed was 80.4 m/min at grades of 5, 0, -5, -10, -15 and -20% was administered at random order.	Heart rate, SBP, DBP, rate pressure product, oxygen consumption, pulmonary ventilation, rating of perceived exertion.	Metabolic responses of healthy older males and females are similar to younger individuals during downhill walking. Walking at negative grades reduces cardiovascular and metabolic responses in a curvilinear manner.	Incorporating downhill walking into exercise programs might be a safe alternative form of exercise in younger and older males and females.
Dawson *et al.* 2007	They examined whether left ventricular function was reduced during 3 h of semi-recumbent ergometer cycling at 70% of maximal oxygen uptake while preload to the heart was maintained via saline infusion.	Left ventricular function would not decline with exercise duration when central venous pressure was maintained.	Seven healthy trained male subjects participated in the study; age, 23 ± 3 years; height, 181 ± 7 cm; weight, 73 ± 10 kg; VO_{2max} 55.4 ± 5.4 $ml.min^{-1}kg^{-1}$.	Attend the laboratory on two occasions separated by a minimum of 3 days. On first occasion, they completed incremental semi-recumbent cycling to volitional exhaustion. On second visit, they completed a 3 h bout of semi-recumbent cycling at 70% of their $VO_{2max.}$	Heart rate, systolic and diastolic blood pressure, central venous pressure, stroke volume, cardiac output.	Central venous pressure was maintained throughout the 3 h exercise bout and blood pressure remained relatively stable. No significant increase in HR over exercise period. No evidence of exercise-induced cardiac fatigue in indices of left ventricular contractility assessed post-exercise.	Left ventricular function, specifically contractility, did not change significantly within a 3 h bout of semi-recumbent cycle ergometry at 70% of $VO_{2max.}$

Table 4: Summary of SBP response to various exercise protocols

Systolic BP (mmHg)							
Variables							
Author	**Intervention**	**Groups**	**Modality**	**Results**			
				Baseline (mmHg)	**Max. Exercise (mmHg)**	**% Change**	**BMI (kg/m^2)**
Murphy *et al.* 2009	4-20 weeks; 20-40 min; 3-5 d/week	N/R	Walking, running, dance	N/R	N/R	N/R	
Cornelissen *et al.* 2010	3x10 week periods; 40-120 W workloads	1. 33-66% HR_{res} (LI) 2. Sedentary 3. 66-33% HR_{res}	Bicycle ergometer	124.8±10.2 (LI) 126.9±9.4 (HI) 139±14.9 138±15.2 161.6±19.5 160.4±18.3 183.8±21.9 185.5±22	183.8±21.9 185.5±22	N/R N/R 11.4 8.8 29.5 26.4 47.3 46.2	26.5±6.1
Campbell *et al.* 2011	Max. incremental exercise	N/R	Bicycle ergometer	120±6 131±3 142±8 159±16	221±9	N/R 9.2 18.3 32.5	24±3
Fagard 2005	4-52 weeks (median = 16w); 1-7 p/week (median =3); 15-70min p/session; 30-85% HR_{max}	N/R	Treadmill (69%); Bicycle ergometer (50%); Swimming (3%); other (23%)	126.2 125.6 129.4	N/R	N/R	25.6
Dimkpa & Ugwu 2010**	20 W increments p/min; 80% HR_{max}	Male and Female	Bicycle ergometer	120±8.41 (m) 118±10.26 (f)	184±11.31 180±13	53.3 52.5	21.9±8.31 21.7±7.75
Lewis *et al.* 2008**	85% HR_{max}	Male and Female	Standard Bruce treadmill protocol	122±18(m) 116±18 (f)	171±25 153±23	40.2 31.9	26.5±3.5 24.2±4.4
Sharabi *et al.*2001**	90% HR_{max}	Exaggerated blood pressure response (ExBPR) and Control (C)	Standard Bruce treadmill protocol	133±13 (ExBPR) 124±9 (C)	N/R N/R	N/R N/R	27.9±5.1 27.2±3.5
All average results (x)±SD				**137.4±13.3**	**182.6±17.9**	**31**	**25.1±5.2**

**= Includes smoking participants; N/R = Not reported; SD = standard deviation; C = control group; ExBPR = exaggerated blood pressure response; m = male; f = female; LI = low intensity; HI = high intensity; HR_{res} = Heart rate reserve; HR_{max} = Heart rate maximum; BMI = Body Mass Index

Table 5: Summary of HR response to various exercise protocols

Heart Rate (bpm)							
Variables							
Author	**Intervention**	**Groups**	**Modality**	**Results**			
				Baseline (mmHg)	**Max. Exercise (mmHg)**	**% Change**	**BMI (kg/m^2)**
Murphy *et al.* 2009	4-20 weeks; 20-40 min; 3-5 d/week	N/R	Walking, running, dance	N/R	N/R	N/R	
Cornelissen *et al.* 2010	3x10 week periods; 40-120 W workloads	1. 33-66% HR_{res} (LI) 2. Sedentary 3. 66-33% HR_{res}	Bicycle ergometer	71.2±9.7 (LI) 70.6±8.2 (HI) 97.5±11.9 96.1±10.7 117.6±18.1 115.7±15.8 132.9±18.5 133.9±17.2	132.9±18.5 133.9±17.2	N/R N/R 36.9 36.1 65.2 63.9 86.7 89.7	26.5±6.1
Campbell *et al.* 2011	Max. incremental exercise	N/R	Bicycle ergometer	59±9 93±9 107±15 123±17	177±9	N/R 57.6 81.4 108.5	24±3
Fagard 2005	4-52 weeks (median = 16w); 1-7 p/week (median =3); 15-70min p/session; 30-85% HR_{max}	N/R	Treadmill (69%); Bicycle ergometer (50%); Swimming (3%); other (23%)	71.1	N/R	N/R	25.6
Dimkpa & Ugwu 2010**	20 W increments p/min; 80% HR_{max}	Male and Female	Bicycle ergometer	73±9.57 (m) 75±6.29 (f)	151±7.75 150±8.89	106.9 100	21.9±8.31 21.7±7.75
Lewis *et al.* 2008**	85% HR_{max}	Male and Female	Standard Bruce treadmill protocol	71±11(m) 77±11 (f)	166±12 165±12	133.8 114.3	26.5±3.5 24.2±4.4
Sharabi *et al.*2001**	90% HR_{max}	Exaggerated blood pressure response (ExBPR) and Control (C)	Standard Bruce treadmill protocol	80±13 (ExBPR) 78±12 (C)	158±12 162±7	97.5 107.7	27.9±5.1 27.2±3.5
All average results (x)±SD				**91.7±12.4**	**155.1±11.6**	**86**	**25.1±5.2**

**= Includes smoking participants; N/R = Not reported; SD = standard deviation; C = control group; ExBPR = exaggerated blood pressure response; m = male; f = female; LI = low intensity; HI = high intensity; HR_{res} = Heart rate reserve; HR_{max} = Heart rate maximum; BMI = Body Mass Index; bpm = beats per minute

2.4 Discussion

The results of this systematic review of the literature on the relationship between changes in HR and SBP during an increase in workload with an incremental exercise test revealed that very limited peer reviewed studies have been published for apparently healthy populations. The majority of published studies available are on persons with non-communicable diseases such as type-2 diabetes, hypertension (HTN), obesity, and other CV diseases. The results obtained from seven relevant papers, reveal that in all instances the HR and SBP responded in a linear fashion to an increase in workload. Different types of incremental exercise testing modalities resulted in different responses. Different intervention protocols, difference in age and gender also resulted in different responses in HR and SBP with an increase in workload.

The main results of this literature review indicate aerobic exercise increased the SBP and HR as the workload increased in different modalities used. With the bicycle protocols (n = 3) we found that there was a mean increase from baseline of 63.5% for SBP and 75.7% for HR. The treadmill protocols (n = 2) found similar mean changes from baseline of 36.1% for SBP and 113.3% for HR. The treadmill protocol, the SBP increased to a lesser extent (27.4%) and HR increased more (37.6%). According to these given results, HR increases about 1.5 times more during the treadmill protocol compared to the bicycle ergometer. When the attention is turned to SBP, it increases 1.75 times for the cycle ergometer protocol compared to the treadmill.

Three of the included studies reported with incremental increase in workload, but the protocols were not similar, even though all three were done on a bicycle ergometer.[9,21,22] The minimum increase in SBP and HR was 8.8% and 36.1% respectively when there was an increase in the workload of 40 W. The maximum increase of SBP and HR was 47.3% and 108.5% respectively in these reported studies when there was an increase of 120 W in the workload.

Insufficient relevant information to calculate the mean changes in SBP and HR were reported by three studies.[14,30,38] The explanations for different responses with the most reported modalities, bicycle ergometer and treadmill, are multi-factorial. With any treadmill protocol you will engage in weight bearing exercise, where most likely you would utilize upper, as

well as lower limbs and thus increasing muscles involvement in walking. Cycling, on the other hand, which is non-weight bearing includes primarily only lower limbs which result in a lower muscle involvement, and this leads to a diminished response compared to weight-bearing activities when it comes to SBP and HR. This means that the body requires less oxygenated blood flow to the functioning muscles to meet their metabolic demands.

According to Skime and Boone[47], the HR is responsible for an increase in cardiac output (CO). This happens through the fundamental sympathetic nervous system (SNS), with the onset of exercise.[48] The inactive muscles experience vasoconstriction, which diverts more blood flow to the active skeletal muscles to meet metabolic demands.[48] A higher HR increase the work of the heart ($M\dot{V}O_2$).[47] Heart rate increases because of the vasodilatation of the blood vessels, transporting more oxygenated blood to the working muscles.[48-51] This transported O_2 to active tissue is usually interpreted because of the increased vasodilatation.[49] The endothelium of the blood vessels becomes stimulated through shear stress, and nitric oxide (NO), adenosine and acetylcholine (Ach) acts as potent vasodilators.[50] Ultimately, blood flow of contracting and working skeletal muscle is a balance between metabolic vasodilatation and sympathetic vasoconstriction.[51]

Two studies, one bicycle protocol (20 W/min increase) and one treadmill protocol (Stage 2 Bruce protocol), indicated results of gender differences.[22,46] These protocols exerted their participants to 80% and 85% HR_{max} respectively. Males had a 46.8% and females a 42.2% mean increase from baseline for SBP. The mean HR increase from baseline was 120.4% and 107.2% respectively for males and females. According to these two studies, males' SBP increase 4.6% and HR increase 13.2% more than females. Under conditions of cardiovascular stress, such as exercise, males respond by increasing mainly total peripheral resistance (TPR).[5] This might be a reason why males reported a higher SBP at rest, and with exercise, than females. Females on the other hand predominantly increase HR thereby increasing cardiac output (CO).[5] This corresponds with the higher resting HR in the women compared to the males.[46] The studies included in this systematic review indicated that the females had less significant SBP and HR responses to incremental exercise than the males.

When considering the SBP response to an incremental increase in workload, resting SBP, was the strongest predictor of maximal exercise SBP in both genders.[4] In both genders there is a substantial increase (63.3% in male; 53.8% in female) in exercise SBP, but males reached

higher exercise workloads which were not reported.[4] The reason for the higher workload in males may be due to the overall higher muscle strength and endurance compared to their female equals.

At all ages, female's sympathetic activity is reduced (reflected by lower TPR and BP) and the parasympathetic activity is enhanced, relative to those of males.[5] With the abovementioned statement by Huxley[5], there are differences in autonomic nervous system (ANS) in gender, and thus the CV response with incremental exercise is gender-specific.[10] These gender-specific ANS differences may contribute to a lower CV risk and increase longevity in females.[10] The lower exercise SBP and HR are less strain on the heart and CV system with exercise, emphasizing the lower CV risk for females. The differences in gender, according to CV responses (SBP and HR), cannot be done extensively in our study, because most of the studies were only done on males.

As stated previously, females have an increased parasympathetic nervous system (PNS) and thus they have a decreased sympathetic nervous system (SNS) control of HR.[10] They may also have an increased overall complexity of the heart, and its dynamics, compared to males.[10]

Aerobic endurance training has the same response on the CV parameters (SBP and HR) in the elderly than in younger individuals. In the older individual, there is a lack of improvement in aortic stiffness with training, and it may be possible that the elderly are resistant to exercise-induced improvements in SBP.[4] Reasons for this could be that the amount of work is overall lower in the older individual, as well as a decrease in elasticity of arteries and stiffened vasculature.[52] When the elderly do aerobic exercise on a regular basis, smaller increases in arterial stiffness occur.[53] The maximum output and physical capacity may also be lower in older individuals.

Physiological ageing is associated with a reduced PNS control of the heart; one reason for this can be a decrease in overall physical fitness with age.[10] The older the individual the more reduced the range of both PNS and SNS with any physiological stress will be.[10] With physiological ageing, physical characteristics (muscle fibers, muscle contraction, endurance, and strength) lowers, all of this can lead to earlier fatigue and less power output. Amano et al.[54] declare that it is not only the PNS, but also the SNS activity that withdraw as you age.

With this said, the ANS and thus the SNS and PNS are physiologically less active in older individuals than in their younger counterparts.

Kelley et al.[32] importantly noted that one does not have to train at high intensity levels in order to reduce resting SBP. Loimaala et al.[18] found that a 5 month, well-controlled, high intensity (75% $\dot{V}O_{2max}$) exercise programme did not have substantial effects on cardiac autonomic function assessed by the baroreceptor-reflex sensitivity.

2.5 Conclusions

In conclusion, the response of the HR and SBP increase as workload increase and is influenced by numerous factors. These factors include gender, age, physical activity levels, exercise testing modality, body composition and lifestyle. The eligible studies included in this systematic review found that there was a gradual increase in HR and SBP with an increase in workload. Heart rate increased at a 2,7:1 ratio more rapidly than SBP. Males exhibited a higher overall workload and reflected overall a higher SBP response than females did. The SBP increased with incremental exercise and the SBP response was higher in males than in females, as well as in elderly compared to the younger participants. The same result was found in HR response to incremental exercise, with males exhibiting a higher HR with incremental exercise. The rate of increase in HR and SBP with an increase in workload could not be quantified as no studies found investigated these relationships. Future research is needed to determine a prediction equation for a normal and safe HR and SBP response for healthy individuals during an incremental workload increase. This will assist in early intervention of lifestyle factors to prevent the development of cardiovascular and lifestyle diseases.

2.6 Limitations and Implications

In the included studies, most of the participants were male. This makes the study more bias and in line with the literature, with the results more concentrated on males. The majority of studies examining CV adaptations to endurance training have been completed on males, and did not provide us with the acute exercise response.[10] The different interventions and exercise protocols the studies used, might not have been controlled correctly to minimize any chances of measuring faults, in particularly the measuring of cardiovascular variables we

used (SBP and HR). Some of the studies included rather small study groups that could also influence the outcome of the cardiovascular results. Not all available databases were searched for eligible studies, therefore certain studies could have been left out.

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Chapter 3: Heart rate and systolic blood pressure response to sub-maximal incremental exercise in healthy individuals

Heart rate and systolic blood pressure response to sub-maximal incremental exercise in healthy individuals

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Abstract

Abnormal responses in cardiovascular variables such as heart rate (HR) and systolic blood pressure (SBP), during a sub-maximal exercise test may predict future development of hypertension. The literature lacks predictive information on normal HR and SBP responses to an incremental increase in workload. The aim of this study is to determine the predictive equation for a normal HR and SBP response to an increase in workload. Data of subjects (N = 216 male; N = 388 female) were included in the study. HR and SBP response during the adapted YMCA bicycle ergometer protocol was measured at three workloads with four-minute increments. Age, gender, body mass and stature were recorded for each participant. Independent t-test determined significance between genders. Linear regression analyses, using Generalised estimated equations (GEE), was done to determine relationships between HR, SBP and workload. Males were significantly taller and heavier than females (p = 0.000). Males presented with significantly higher body mass index (BMI) (p = 0.002) than females. From GEE analysis an equation, predicting the expected HR and SBP for a known increase in workload (watt) was formulated. Predicted equation models for HR response to increasing workload, for both genders, were significant except for the BMI (p = 0.972 females; p = 0.169 males). For SBP significant prediction equations were derived for an increase in workload ($p < 0.05$).

Key words: Sub-maximal, incremental, exercise, cardiovascular, healthy, heart rate, systolic blood pressure, rate-pressure product

1 Introduction

Exercise, a common physiological stress, can elicit cardiovascular (CV) abnormalities that are not present at rest, and it can be used to predict the adequacy of cardiac function [13]. Cardiovascular function can be thoroughly described through a range of appropriately selected responses to incremental exercise as an incremental exercise test is excellent at exposing CV system abnormality [36]. The maximum workload obtained from an incremental exercise test is considered as a physiological variable that can give information to be used for a variety of purposes [5].

At fixed sub-maximal workloads in healthy individuals, steady-state conditions are generally achieved within minutes after the onset of exercise [13]. Sub-maximal aerobic exercise tests provide an alternative form of testing that can supply the researcher and participant with objective results that can be used as a benchmark for future comparison [49].

Several protocols are used for functional exercise analysis [3]. The purpose of the test and functional capabilities of the subject determine the protocol to be used [3]. These exercise protocols use easily obtained hemodynamic variables, such as heart rate (HR) and blood pressure (BP) to assess the health and functional capacity of an individual [1,17].

Heart rate is a practical and objective parameter of exercise workload [50]. The immediate response of the CV system to exercise is an increase in HR [21] due to a decrease in vagal tone [13]. During the course of dynamic exercise, HR increases linearly with workload, as well as oxygen consumption ($\dot{V}O_2$) [1,13]. When workload increases, the time for the HR to stabilise will gradually prolong [13]. Aspects that influence HR include the type of dynamic exercise, state of health, blood volume, sinus node function and environment [13].

Due to the dynamic and predictive response of heart rate to exercise, HR is often used to estimate maximum aerobic output ($\dot{V}O_{2max}$) during sub-maximal or maximal exercise tests [50]. A lower HR for a given workload is indicated to represent a higher level of aerobic fitness [50]. Aerobic fitness is normally reported as a person`s $\dot{V}O_{2max}$, the maximum amount of O_2 that can be transported and utilised by the functioning muscles [45,50] or for cellular metabolism [13].

With prolonged exercise, skeletal muscle blood flow increases as much as three-fold together with an increase in systolic blood pressure (SBP) [13]. Systolic BP augments with increasing dynamic workload as a result of the increase in cardiac output (CO) [13]. High intensity maximal workload generates a higher SBP response, as well as a higher CO [7] than in sub-maximal exercise intensities. The incremental increase in SBP observed during exercise is considered normal [13]. Resting BP, age, gender, smoking status, body surface area and the duration of exercise all contribute to the exercise SBP response [9].

In patients with reduced CV function or in elderly people, changes in physiological functions and structures related to disease and age may very well be of such implication that the above conclusions may not be observed [7]. It is, therefore, important that the gender, age and anthropometric characteristics of individuals be assessed during exercise testing to ensure the true normality of dynamic exercise response [20].

The relatively varied ranges of exercise response patterns during testing emphasise the large differences in individual responses [20]. Exercise testing is widely practiced in elderly patients and achieved lower workloads (6 METs) compared with younger patients (11 METs) [42], but higher exercise SBP results [9]. The exercise test offers incremental value over clinical variables as exercise capacity is the utmost important prognostic measurement and has the same association with mortality in elderly as in younger patients [42]. Elderly people may require reduced initial workloads and reduced changes in workloads during exercise testing [50].

Additional to HR and BP variables the double product (DP), or rate-pressure product (RPP), is a well-established surrogate marker for relative myocardial oxygen consumption ($M\dot{V}O_2$) [16]. Rate-pressure product is a variable which could evaluate CV function, for example the strain placed on the cardiac muscle [45], and it is determined by the product of SBP and HR [23,32,41,45]. The RPP if reported to increase with an increase in exercise intensity until fatigue sets in, signifying that relative $M\dot{V}O_2$ increase for the period of incremental maximal, and also sub-maximal, exercise [15]. An increase in relative $M\dot{V}O_2$ emits metabolic coronary vasodilation and is considered a key determinant of coronary blood flow [47].

The increase in RPP arises primarily because of the SBP response [8]. Maeder and partners [25] instead claim that RPP differences are due to HR response, although values for SBP did

not differ. A lower HR response during aerobic exercise would result in a lower RPP [6,37]. The RPP increases linearly in proportion to increases in the intensity of the exercise [45]. An increase in body mass index (BMI) in general corresponds to an increased RPP for all ages [41]. The maximal RPP was ominously lower in older subjects [23].

The CV reactivity during exercise sometimes responds in a negative way even in the absence of clinical disease [12]. The measurement of exercise BP is regarded as a valuable way of identification of an increased risk of developing future hypertension (HTN) in healthy normotensive adults [30]. The presence of an exaggerated BP (systolic and diastolic) with exercise (ExBPR) could indicate increased BP (systolic and blood pressure) values during resting and activities, sufficient to result in early target organ damage (TOD) [29]. An elevated SBP response with exercise was associated with impaired endothelium-dependent vasodilator function [28,43]. Thus, this impaired endothelial function might limit vasodilation in response to sheer stress of exercise [43]. This constant impairment may lead to an exaggerated response, spiralling into diseases like HTN and other CV abnormalities. Accordingly, the ExBPR can partially be explained by total peripheral resistance (TPR) which would influence the exercise-induced vasodilation [28].

The literature lacks information on the prediction of a safe or normal HR and SBP responses to an increase in workload during a sub-maximal exercise protocol in healthy individuals. Therefore, this study aims to determine the HR and SBP response to a standardised incremental increase in workload during a sub-maximal exercise test in healthy adults. The results obtained from this study will propose a prediction equation for normal HR and SBP response to an increase in workload in order to identify exaggerated HR and SBP responses to incremental exercise testing. This will aid healthcare practitioners performing sub-maximal stress testing to identify health risks regarding the CV response to incremental sub-maximal exercise before the presence of pathology.

2 Methodology

Study design

A once-off subject availability study was performed. Information was collected from the database of two practices in which the same sub-maximal exercise testing protocol was

performed between 1999-2011. Participants gave consent for the data to be used for research purposes and all measurements and data was collected and handled according to guidelines of the Helsinki declaration. Ethical approval was requested from the Ethics Committee of the North-West University, Potchefstroom Campus.

Participants

Data from apparently healthy people who requested exercise prescription guidelines were included in the analyses. From this availability population the data of 604 people (N = 216 male; N = 388 female) adhered to our inclusion criteria and gave consent that the data may be used for research. The inclusion criteria stated that the participants were Caucasian between the ages of 18 and 80. All participants were healthy and had no known cardiovascular risk factors, orthopedic limitations, mental illness, respiratory disease or cancer. Data from participants were excluded when they were using anti-hypertensive medication, medication for a heart condition, diabetes, cholesterol, as well as smokers.

3 Measuring instruments and equipment

Demographic information

Demographic information was collected by means of completing a Physical Activity Readiness Questionnaire (PAR-Q). Medical history, medicine usage, lifestyle habits (smoking, alcohol consumption and physical activity), gender and age as well as risk factors for coronary heart disease of participants were obtained by means of a questionnaire.

Body composition

Stature of the participants was measured using a Stadiometer (Rosscraft, Canada) according to the guidelines provided by the International Society for the Advancement of Kinanthropometry (ISAK) [26] to the nearest 0.1 cm. The participant stood with heels together and the heels, buttocks and upper part of the back touching the stadiometer. The head was placed and kept in the Frankfort plane, and did not need to touch the stadiometer. The participant was instructed to take a deep breath and the measurement was taken before the participant exhaled [26]. Body mass was measured to the nearest 0.01 kg with an

electronic scale (Goldbell A-5037, China) with a maximum capacity of 150 kg. The participant stood on the centre of the scale without support and with the weight evenly distributed on both feet, while wearing minimal clothing [26]. The body mass index (BMI) was used to assess weight relative to height and was calculated by dividing body weight in kilograms by height in metres squared (kg/m^2) [2].

Sub-maximal exercise protocol

The sub-maximal exercise protocol was performed according to the adapted YMCA protocol [2]. A cycle ergometer (Monark 874E Exercise AB, Sweden) was used for the exercise protocol. The cycle ergometer was calibrated before each test to ensure accurate readings. The participants were instructed to keep the speed of the cycle ergometer between 49-51 rpm, and the practitioner made sure that it was kept between the values for the duration of the test. All participants were seated in the exercise posture for three minutes before any measurements were taken. Resting HR and BP were obtained immediately prior to exercise in the exercise posture. The participant was in an upright posture, 5-degree bend at the knee at maximal leg extension, hands in a proper position on the handlebars. The protocol consisted of 4-min stages. Heart rate and BP were monitored in the last minute of each stage, and BP was verified in the event of a hypotensive or hypertensive response. Rate of perceived exertion (RPE) was monitored near the end of the last minute of each stage using the 0-10 scale [2]. The participant's appearance and symptoms were monitored and recorded regularly. The exercise protocol was terminated when the subject reached target heart rate (THR), which was calculated as 70% of their age predicted maximal HR as calculated by Karvonen's formula [19]. The workload was increased by increments of 25 W or 50 W (watt), so that the THR was attained after three stages of four minutes. A three-minute recovery period was initiated after THR was attained. During the recovery stage HR and BP were measured at one and three minutes of recovery [2].

Blood pressure

A mercury Baumanometer (WA Baum Co., Inc., USA) and a stethoscope (Littmann, USA) were used to measure the blood pressure (mmHg) before the sub-maximal exercise protocol started. The participant sat quietly for 5 minutes in a chair with back support, feet on the floor and arm supported at heart level. Participants were asked to refrain from smoking cigarettes

or ingesting caffeine during the two hours preceding the measurement. The cuff was wrapped firmly around the upper right arm at heart level and it was aligned with the brachial artery. The appropriate cuff size was used to ensure accurate measurement. The bladder within the cuff encircled at least 80% of the upper arm. The stethoscope was placed below the antecubital space over the brachial artery. The cuff was quickly inflated to 20 mmHg above the first Korotkoff sound. The pressure was slowly released at a rate equal to 2 to 5 mmHg per second. The systolic blood pressure (SBP) was noted as the point at which the first of two or more Korotkoff sounds were heard and diastolic blood pressure (DBP) was the last Korotkoff sound. Participants were informed of their specific BP volume verbally and in writing [2]. During the sub-maximal exercise protocol, the BP was taken with the participant sitting upright on the cycle ergometer, while they kept on cycling. The same procedure was followed to measure the BP. When the protocol was finished, the recovery BP was measured with the participant sitting upright on the cycle ergometer.

Heart rate

Heart rate was measured during rest, at each of the incremental stages and at one and three minutes of recovery. The auscultation method was used where the ball of the stethoscope was placed to the left of the sternum just above the level of the nipple. Heart rate was counted for 15 seconds, multiplied by four, and then recorded in beats per minute (bpm) [2].

Statistical analyses

The Statistical Consultation Services of the North-West University was consulted for the statistical analysis of the data. The SPSS statistical software programme (IBM, SPSS v.2.0, USA) was used for the analyses. This once-off subject availability study implies that the participants were only tested once. Participant characteristics were determined with descriptive statistics reporting means and standard deviations (SD). An independent t-test was used to determine significant differences between males and females. Linear regression analyses, making use of General estimated equations (GEE) [48] was performed making use of unstructured correlation analyses to determine the relationship between the response in HR, SBP and an increase in workload (watt). The prediction equations were presented with the reporting of 95% confidence interval (CI). Adjustments were made in the analysis for age and BMI. Statistical significance was set at $p \leq 0.05$.

4 Results

Descriptive statistics, along with sub-maximal exercise data, for all male and female participants (N = 604) are presented in Table 1. Data of six hundred and four healthy participants, 216 male and 388 females were included in this study. The results are expressed as mean ± SD. Males had a 1.56 kg/m^2 higher BMI than females (p = 0.002). The male subjects weighed on average 16.2 kg more than their female counterparts (p = 0.000). The male participants were significantly taller than the females, with a mean difference of 12 cm (p = 0.000). A significant higher SBP_{rest}, by 3.9 mmHg (p = 0.003), as well as significantly higher DBP_{rest}, by 3.3 mmHg (p = 0.000) were observed between male and female with an independent two-tailed t-test.

Table 1: Participants' characteristics

Variables	All Mean±SD	Males (N = 216)	Females (N = 388)	*p-value*
Stature (m)	1.69 ± 0.09	1.77 ± 0.08	1.65 ± 0.06	0.000
Weight (kg)	79.4 ± 18.9	89.9 ± 19.1	73.6 ± 16.2	0.000
HR_{rest} (bpm)	79.3 ± 12.0	79.3 ± 11.8	79.3 ± 12.1	0.950
SBP_{rest} (mmHg)	123.9 ± 15.5	126.4 ± 14.9	122.5 ± 15.7	0.003
DBP_{rest} (mmHg)	81.6 ± 10.2	83.7 ± 10.9	80.4 ± 9.6	0.000
BMI (kg/m^2)	27.7 ± 5.9	28.7 ± 5.5	27.2 ± 6.0	0.002
Age (years)	42.3 ± 16.8	43.6 ± 17.7	41.6 ± 16.2	0.172

Values are means ± SD; N = number of subjects; m = meter; kg = kilogram; bpm = beats per minute; mmHg = millimetres mercury; kg/m^2 = kilogram per metre square; y = years of age; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; * $p \leq 0.05$

The results from the GEE analyses indicate a significant model for the relationship between HR and SBP and workload for males and females. In the prediction equations for HR response to increase in workload, for both genders, the BMI was the variable that was the least significant (p = 0.972 females; p = 0.169 males). In the prediction equations for the response of the SBP with an increase in the workload, BMI was significant (p = 0.000 both genders) in the model.

HR between males and females did not differ significantly, but the SBP between males and females differed significantly. The prediction equations for males and females were, therefore, determined separately.

Table 2: The relationship between HR response and workload (watt) in females

Variable	β	95% CI	*p-value*
Intercept	141.8	129.62 – 153.89	.000
[Measurement 1]	-25.5	-30.56 - -20.41	.000
[Measurement 2]	-9.8	-6.98 – 46.57	.000
[Measurement 3]	0[a]	.	
Age	-0.4	-0.30 – 76.7	.000
BMI	-0.004	0.23 - 0.001	.972
Watt	0.3	0.34 – 37.53	.000
(Scale)	235.5		

Dependent variable: HR; Model: Intercept, measurement, age, BMI, watt; *$p \leq 0.05$

a. Set to be zero because this parameter is redundant

The results in Table 2 convert to the prediction equation (Equation 1) where the applied workload in watt is included in the equation in order to predict the corresponding HR in females.

The prediction equation for predicted HR in response to increase in workload in females:

Y = [(141.8) + (-25.5)(M1) + (-9.8)(M2) + (age)(-0.4) + (BMI)(-0.004) + (watt)(0.3)]

(Equat. 1)

M1 = watt 1

M2 = watt 2

Table 3 indicate the results of the GEE analysis for the prediction equation for males for the HR response with an increase in the workload.

Table 3: The relationship between HR response and workload (watt) in males

Variable	β	95% CI	*p-value*
Intercept	153.0	140.14 – 165.81	.000
[Measurement 1]	-27.9	-33.43 - -22.28	.000
[Measurement 2]	-15.3	-12.2 – 92.5	.000
[Measurement 3]	0[a]	.	.
Age	-0.5	-0.43 – 90.02	.000
BMI	-0.2	0.08 – 1.89	.169
Watt	0.1	0.19 – 9.52	.002
(Scale)	264.45		

Dependent variable: HR; Model: Intercept, measurement, age, BMI, watt; *$p \leq 0.05$

a. Set to be zero because this parameter is redundant

The results in Table 3 convert to the prediction equation (Equation 2) where the applied workload in watt is included in the equation in order to predict corresponding HR in males.

The prediction equation for predicted HR in response to increase in workload in males:
Y = [(153.0) + (-27.9)(M1) + (-15.3)(M2) + (age)(-0.5) + (BMI)(-0.2) + (watt)(0.1)]
(Equat. 2)

M1 = watt 1
M2 = watt 2

The GEE analysis was also performed to determine the prediction equation for the response of the SBP with an increase in workload. Table 4 and Table 5 respectively formulate prediction equations for females and males. Most of the variables used are significant ($p < 0.000$). The least significant variable was measurement 2 in Table 4 ($p = 0.132$).

Table 4: The relationship between SBP response and workload (watt) in females

Variable	β	95% CI	*p-value*
Intercept	73.8	59.16 – 88.45	.000
[Measurement 1]	-11.2	-17.33 - -5.1	.000
[Measurement 2]	-2.5	0.76 – 2.27	.132
[Measurement 3]	0[a]	.	.
Age	0.8	-0.66 - 0.90	.000
BMI	1.1	0.83 – 1.45	.000
Watt	0.3	0.23 – 0.44	.000
(Scale)	360.2		

Dependent variable: SBP; Model: Intercept, measurement, age, BMI, watt; *$p \leq 0.05$

a. Set to be zero because this parameter is redundant

The results in Table 4 convert to the prediction equation (Equation 3) where the applied workload in watt is included in the equation in order to predict the corresponding SBP in females.

The prediction equation for predicted SBP in response to increase in workload in females:

Y = [(73.8) + (-11.2)(M1) + (-2.5)(M2) + (age)(0.8) + (BMI)(1.1) + (watt)(0.3)]

(Equat. 3)

M1 = watt 1

M2 = watt 2

Table 5: The relationship between SBP response and workload (watt) in males

Variable	β	95% CI	*p-value*
Intercept	114.23	98.23 – 130.24	.000
[Measurement 1]	-21.75	-27.88 - -15.63	.000
[Measurement 2]	-11.14	-14.46 - -7.81	.000
[Measurement 3]	0[a]	.	.
Age	0.35	0.21 - 0.49	.000
BMI	0.94	1.34 – 22.15	.000
Watt	0.17	0.25 – 14.63	.000
(Scale)	373.85		

Dependent variable: SBP; Model: Intercept, measurement, age, BMI, watt; *$p<0.05$

a. Set to be zero because this parameter is redundant

The results of Table 5 convert to the prediction equation (Equation 4) where the applied workload in watt is included in the equation in order to predict the corresponding SBP in males.

The prediction equation for predicted SBP in response to increase in workload:
Y = [(114.23) + (-21.8)(M1) + (-11.1)(M2) + (age)(-0.4) + (BMI)(0.9) + (watt)(0.2)]
(Equat. 4)

M1 = watt 1
M2 = watt 2

5 Discussion

The present study sought to identify the relationship between HR and SBP with an increase in workload in order to determine a prediction equation for the response of HR and SBP in healthy males and females. The participants in this study indicated similarity between males and females with regards to HR_{rest} (males 79.3 ± 11.8 bpm; females 79.3 ± 12.1 bpm) and age (males 43.6 ± 17.7 years; females 41.6 ± 16.2 years). The participants could be classified as overweight regarding their BMI measurements (27.7 ± 5.9 kg/m^2). The results are in line with Koch et al. [20] that demonstrate that gender and anthropometric characteristics should be considered in the assessment during dynamic exercise response.

Neder et al. (2001) claim that there are differences in HR and BP, and that the exercise response of these markers must not be ignored [31]. Heart rate increases in a linear fashion with the increase in workload and dynamic exercise [2]. The ACSM states that a normal response to exercise for SBP is a progressive increase [2]. Currently, to our knowledge, there is no equation to predict the response of the HR or SBP during an incremental exercise protocol with a gradual increase in workload. Sannerstadt published the only available equation regarding SBP [39], they derived it from their own extensive studies, and it was published in Jones & Campbell in the early eighties [18]:

$$SBP = 120 + 0.08\ W\ (\pm\ 2\ SD = 25\ mmHg)$$

In this formula, W (kpm/min) acts as the workload during exercise. To date no formula or equation exists for the HR response related to an increase in workload for apparently healthy normotensive persons. The abovementioned was formed by using minimal statistical models. Progress in the development of statistical models has increased the possibilities to perform more informative data analyses that will increase the understanding of relationships between variables.

The implementation of these predictive equations would aid healthcare practitioners to identify an exaggerated response with incremental exercise. This exaggerated response to incremental exercise increases the risk of developing future hypertension (HTN) or potential target organ damage (TOD). With a known abnormal response, interventions need to be put in place to act preventatively.

In our study, it was identified that adjustments for age, BMI and workload (watt) should be included in the prediction model. These variables, on their own, can influence the model. The older the participant, the lower your HR_{rest} [11,35], lower HR response to exercise, as well as the lower the peak-exercise HR will be [4,9,10,11,44]. The older participant might have a decreased sympathetic drive of the autonomic nervous system. They also have a higher SBP in resting circumstances [10,36], plus a higher peak exercise SBP [9]. The literature expresses that regular aerobic exercise is associated with smaller increases in arterial stiffness with aging and improves stiffness in older healthy males and females [36]. Aging,

although an unavoidable cardiovascular (CV) risk factor, may overcome all the other risk factors collectively [29].

As mentioned, our population was overweight regarding BMI, we can assume that their risk for CV disease is higher. This is in line with Thomas et al. [46] that reported that an increased body weight for a given height significantly increases the prevalence of associated risk factors, especially HTN, therefore the BMI should be considered as a major CV risk determinant [46].

The individual differences of the participants, like BMI, fitness level, gender and lifestyle will have an impact on these equations. Additionally, there is large inter-individual variation in exercise capacity that may result in different SBP response to exercise [23]. We propose the prediction equations for HR and SBP responses with an increase in workload in different genders. It has been documented that males have a significantly higher SBP_{rest} than their female counterparts [14,38]. Systolic BP at equivalent exercise intensities was lower in younger females than in males, regardless of their training status and capabilities [34]. These predicted equations support these findings as the intercept of the equations are higher in males than females for both HR and SBP.

These equations predict what a normal HR and SBP response should be, considering certain variables. We can assume that when the actual response exceeds the predicted normal response, that the individual may have underlying cardiovascular abnormalities. To reduce the impact of subsequent cardiovascular events and complications, the early identification of an exaggerated response is of utmost importance. Miyai et al. [30] performed a study where they evaluated the clinical significance of abnormal BP (systolic and diastolic) reactivity to physical exertion, which is considered an early marker of future hypertension (HTN) [30]. They found that an exaggerated BP response to HR increase during ergometric exercise was associated with a three- to four-fold greater risk for developing HTN [30]. Researchers speculate that neurohormonal mechanisms might be involved in an ExBPR to exercise [24,29].

When SBP responds like this, defined as an excessive acute increase in SBP from rest to exercise, it shows a strong association with a higher risk for future HTN, after adjusting for several factors [24,27]. Exercise BP (systolic and diastolic) measurement is a valuable tool

for the identification of an increased risk of future HTN in apparently healthy normotensive adults. Physical activity leads to an increase in cardiac output (CO), leading to a rise in SBP as a normal response to dynamic exercise [22,30]. Because so many adults are at risk for possible cardiac events, these predicted equations have broad clinical implications. Most of the reported literature, discussed the SBP response to exercise, and very few discussed the clinical significance of HR response to exercise.

6 Conclusion

The conclusion that can be drawn from this study is that different equations are present for the prediction of the HR response to an increase in workload for males and females. The predictive models included adjustment for age and BMI. The same was found for the predictive equation for SBP response to an increase in workload. The predictive equations for a normal HR and SBP response in healthy adults during incremental increase in workload during a sub-maximal exercise test can now be applied in practice and tested for reliability and validity.

The study limitations experienced with this study are that the sub-maximal testing protocol was only performed on bicycle ergometers, and results can only be applied to this modality. Only Caucasians were included in the study population, hence we can only apply these predictive equations to this population. The sample size should be increased in order to obtain stronger statistical power for the prediction equations.

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Chapter 4: Summary, conclusions, limitations and recommendations

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4.1 Summary

Exercise testing provides valid information about physiological systems of individuals that may help identify healthy individuals at risk of developing future cardiovascular diseases (CVD), like hypertension (HTN). Exercise can elicit cardiovascular (CV) abnormalities that are not present at rest. The purpose of this study was twofold – firstly, to identify and investigate the existing evidence in the literature on cardiovascular response during a sub-maximal incremental exercise protocol. The second aim was to determine the relationship between HR, SBP and workload during a sub-maximal incremental exercise protocol.

The dissertation was presented in three main parts, namely an introduction (Chapter 1), a systematic review (Chapter 2) as the first manuscript and the empirical investigation containing the background to the research, methods and results in the format of a research manuscript (Chapter 3). These two manuscripts were presented in agreement with the guidelines of the respective journal as indicated on the manuscripts.

In Chapter 1 a brief problem statement and introduction that culminated in the research questions of the study, the objectives and the related hypotheses as well as the structure of this dissertation were presented. Chapter 2 consisted of a systematic review titled "Cardiovascular markers' response to incremental exercise testing." This chapter was compiled in accordance with the guidelines of *Sports Medicine* journal. The purpose of this chapter was to provide

the reader with a brief background concerning the available literature on heart rate (HR) and systolic blood pressure (SBP) response during exercise and training (acute and chronic effect) using different protocols. The different protocols and results are discussed and analysed for further understanding of the different responses with different workloads and to determine if any predictive equations for HR and SBP response to workload are available in the literature.

In Table 3 a summary is presented of all relevant quality assessed studies, and Table 4 summarises the SBP, HR and workload changes with various exercise protocols. Seven included studies compared different SBP and HR responses to different exercise modalities and protocols. Systolic blood pressure increased by 31.35% and HR by 85.75% with increasing workload. Heart rate increases 2.7:1 ratio more rapidly than SBP. An increase in workload results in a linear increase in SBP and HR. The responses to these specific CV markers are, however, influenced by gender, age, physical activity, exercise testing modality, body composition and lifestyle.

As no predictive equations could be related from the existing literature as reviewed in Chapter 2, an empirical investigation was performed (Chapter 3) and the findings presented in the form of a research manuscript titled: "Heart rate and systolic blood pressure response to sub-maximal incremental exercise in healthy individuals." This chapter was compiled in accordance with the guidelines of the *European Journal of Physiology*. The aims of this study were to analyse the HR and SBP response in healthy adults during a sub-maximal incremental exercise test, with an increase in workload (watt). Prediction equations were formulated for both genders, regarding HR and SBP response with an increasing workload. Significant predictive equations were derived for males and females as well as for HR and SBP. BMI did not contribute significantly to the model in the case of the HR equations. The validity and reliability of the prediction equations need to be tested in controlled clinical environment. The presence of exaggerated SBP response during incremental exercise testing will be identified with this proposed equations, therefore, healthcare practitioners can intervene with lifestyle changes earlier to prevent future development of HTN.

4.2 Conclusions

The conclusions drawn from this research are presented in accordance with the set hypotheses (Chapter 1):

4.2.1 Hypothesis 1

There is only evidence of cardiovascular responses in diseased population during a sub-maximal incremental exercise protocol

Hypothesis 1 is rejected due to the fact that we gathered information regarding CV markers` responses during incremental exercise testing. It reveals that there is evidence available about apparently healthy individuals, free from CV or other abnormalities and diseases. The literature consists of various studies, including healthy normotensive adults. These studies use different modalities (bicycle ergometer, treadmill, arm-crank ergometer) and protocols (sub-maximal, maximal, intermittent) to assess certain CV markers' responses during exercise testing.

4.2.2 Hypothesis 2

The HR, SBP and workload will have a positive linear relationship during a sub-maximal incremental exercise protocol in healthy individuals

The results of this study have significant predicted equations regarding these CV markers for both males and females, according to the GEE analyses. In the prediction equations for the response of the SBP with an increase in the workload, BMI was significant (p = 0.000 both genders) in the model. Heart rate between males and females did not differ significantly, but the SBP between males and females differed significantly. The prediction equations for males and females were therefore determined separately.

The prediction equation for predicted HR in response to increase in workload in females:
Y = [(141.8) + (-25.5)(M1) + (-9.8)(M2) + (age)(-0.4) + (BMI)(-0.004) + (watt)(0.3)]
(Equat. 1)

The prediction equation for predicted HR in response to increase in workload in males:
Y = [(153.0) + (-27.9)(M1) + (-15.3)(M2) + (age)(-0.5) + (BMI)(-0.2) + (watt)(0.1)]
(Equat. 2)

The prediction equation for predicted SBP in response to increase in workload in females:
Y = [(73.8) + (-11.2)(M1) + (-2.5)(M2) + (age)(0.8) + (BMI)(1.1) + (watt)(0.3)]
(Equat. 3)

The prediction equation for predicted SBP in response to increase in workload in males:
Y = [(114.23) + (-21.8)(M1) + (-11.1)(M2) + (age)(-0.4) + (BMI)(0.9) + (watt)(0.2)]
(Equat. 4)

M1 = watt 1 (applicable to all equations)
M2 = watt 2 (applicable to all equations)

With the abovementioned significant predictive equations for both genders, we accept Hypothesis 2.

4.3 Limitations and Recommendations

This study is the first to have assessed the normal response of HR and SBP in normotensive healthy individuals, during a sub-maximal incremental graded exercise test. Furthermore, this is also the first study to propose predicted equations for HR and SBP response with an increasing workload, for both genders of apparently healthy individuals. With abnormal or exaggerated HR and SBP responses during incremental workload increase, intervention could be implemented early enough to intervene if CV abnormalities were evident. There are, however, certain limitations that need to be considered when interpreting the study results.

- The findings of this study are to be interpreted in the context of the population investigated. Only data of Caucasian individuals were used, so generalisation of these results for other ethnic groups is not possible. We recommend that larger studies, with different ethnic groups, be performed to formulate ethnic group specific prediction equations regarding HR and SBP responses.

- In this study bicycle ergometers were used as the testing modality and results can only be applied to this modality. It is recommended that studies should be repeated for treadmill testing, as well as arm-crank ergometers, to calculate prediction equations for each of the different modalities.

- The sample size we used was relatively small. We recommend larger sample size in order to obtain stronger statistical power for the prediction equations for both genders.

- The baseline level of fitness was not adjusted for in this study and could have an influence on the prediction equations. Future studies should investigate if adjustment for fitness should be included.

4.4 Future research

This study was a once-off subject availability design. In order to obtain a clear understanding of the relationship between HR, SBP and workload increase during a sub-maximal incremental exercise protocol, we can suggest that future research should investigate:

- similar cardiovascular data in a longitudinal research design, with a larger population
- perform exercise intervention studies to determine if the level of fitness has an influence on the HR and SBP response to an incremental exercise protocol
- apply these prediction equations to clinical practice, so that follow-up studies can be done on the same participants

It is, however, suggested that intervention programmes be implemented that focus on the prevention of CVD, such as HTN, in apparently healthy normotensive adults. It is possible that a lower HR and SBP response during incremental exercise could lower the individuals' risk of any cardiac event. Healthcare practitioners, like Biokineticists, are trained in the field of wellness, healthy lifestyle and physical activity. They could effectively assist in the prevention of CVD with exercise as intervention.

APPENDIX A

PAR – Q & YOU

(A Physical Activity Readiness Questionnaire for People Aged 18 – 81)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 18 and 81, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 81 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the question carefully and answer each one honestly: Check YES **or** NO

YES	NO		
☐	☐	**1.**	**Has your doctor ever said that you have a heart condition <u>and</u> that you should only do physical activity recommended by a doctor?**
☐	☐	**2.**	**Do you feel pain in your chest when you do physical activity?**
☐	☐	**3.**	**In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	**4.**	**Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	**5.**	**Do you have a bone or joint problem that could be made worse by a change in your physical activity?**
☐	☐	**6.**	**Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	**7.**	**Do you know of any other reason why you should not do physical activity?**

IF YOU ANSWERED

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- **You may be able to do any activity you want – as long as you start slowly and build up gradually. Or, you may need to restrict your activities to hose which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.**
- **Find out which community programs are sage and helpful for you.**

Please note**: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.**

DELAY BECOMING MUCH MORE ACTIVE**:**

NO to all questions

If you answered NO honestly to <u>all</u> PAR-Q questions, you can be reasonably sure that you can:

- **Star becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.**
- **Take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively.**

- **If you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or**
- **If you are or may be pregnant – talk to your doctor before you start becoming more active.**

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction.

NAME _____

SIGNATURE _____ DATE _____

SIGNATURE OF PARENT _____ WITNESS _____

Or GUARDIAN (for participants under the age of majority)

APPENDIX B

Instructions for Authors for Preparation of Manuscripts for *Sports Medicine*

General Information (http://adisonline.com/sportsmedicine)

ISI Impact Factor (2010)
5.072

Indexing
Sports Medicine is indexed in MEDLINE, EMBASE/Excerpta Medica, Current Contents/Clinical Medicine, SciSearch, Science Citation Index, Journal Citation Reports/Science Edition, Focus On: Sports Science & Medicine, CINAHL, PASCAL, SPORT, SportDiscus, SPONET, Focus On: Sports Science & Medicine, PsycINFO and Journals@OVID.

Journal Aim and Scope
Sports Medicine focuses on definitive and comprehensive commissioned review articles that interpret and evaluate the current literature to provide the rationale for and application of research findings in areas such as:

sports medicine and sports science (including performance research)

the medical syndromes associated with sport and exercise

the practical role that clinical medicine plays in sport, through injury prevention and treatment

the medical use of exercise for rehabilitation and health and the application of physiological and biomechanical principles to specific sports.

Please see Appendix B for the types of paper this journal considers for publication.

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Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Authors should meet all the following criteria: (i) conceived and planned the work that led to the manuscript or played an important role in the acquisition, analysis and interpretation of the data or both; (ii) wrote the paper and/or made substantive suggestions for revision and; (iii) approved the final submitted version. The corresponding author takes responsibility for the work as a whole, from inception to the published manuscript, and will be responsible for sign-off of the final proofs prior to publication.

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The potential for conflict of interest arises when authors have personal or financial relationships that could influence their actions. All authors should indicate potential conflicts of interest, including specific financial interests relevant to the subject of their manuscript, in section F of the Author Declaration Form (see Appendix C). To prevent ambiguity, authors must state explicitly whether potential conflicts *do* or *do not* exist. Details of relevant conflicts of interest (or the lack of) must be declared in the Acknowledgments section of the manuscript for all authors.

Role of the Funding Source

All sources of funding used to support the preparation of a paper should be declared in the Acknowledgements section of the manuscript.

Sports Medicine Instructions for Authors *Sports Medicine* Instructions for Authors

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To submit a manuscript to the journal you will need to go to the AdisOnline site (http://adisonline.com) and follow the links and instructions to our online submission system (Adis Editorial Manager; www.editorialmanager.com/adis). Step-by-step instructions are available on the website.
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Manuscript Format and Style

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A.

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B.
Acknowledgments: See Appendix A, point 4.
C.
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Table of contents
E.
Figure captions
F.
Key words: These should be words/terms that could be used in a searchable database, such as PubMed, to identify the manuscript.
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Abstract: The abstract should succinctly highlight, in an informative manner, the specific important points addressed in the main body of the text; it should not just describe the general areas covered in the manuscript. The aim is for the abstract to stand alone as a synopsis of the article to accommodate those readers who do not have access to the full article. The journal style is to not cite references in the abstract so as to provide a discrete synopsis of the article. The length can be up to 400-500 words.
H.
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I.
Footnotes
J.
Reference list (in Vancouver style)
K.
Tables (begin each table on a new page)
L.
Figures (place each figure in a separate file)
M.
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Please put sections A-K into a single file. *Sports Medicine* Instructions for Authors

Abbreviations and Symbols

Use SI symbols and recognised abbreviations for units of measurement. The first time an abbreviation appears in the abstract and the text it should be preceded by the full name for which it stands, followed by the abbreviation in parentheses. Generally, abbreviations should be avoided as much as possible, and used only when the full term would make the text unduly cumbersome.

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Generic names (International Nonproprietary Names [INN]) must be used. In review papers, brand names or trade names can be used in selected instances, e.g. when use of the generic name would be impractical or ambiguous. In original research a therapeutic intervention should be named by both its generic name and trade name (along with the manufacturer and location) in the methods section in order to precisely identify the product investigated.

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Tables and figures help to convey information to the reader. Please make every effort to include such items in your article. Tables can be used, for example, to summarise important points, to compare agents or treatment regimens, or to list information that would otherwise impede the flow of the text. Figures may be schematic diagrams, graphical representations of data, photographs or treatment algorithms. Large numbers of tables and figures and lengthy tables can be problematic in print – these can, however, be published online-only as supplemental digital content.

Tables

Tables should be comprehensible without reference to the text, and data given in tables should in general not be duplicated in the text or figures. Any necessary descriptions should appear in the table heading, and abbreviations and footnotes should be placed immediately below the table. Each table should be cited in the text. Please prepare tables in ‘table format', rather than using ‘tab' or ‘indent' commands. Do not format tables using word spaces. Number tables with Roman numerals (I, II, etc.) and provide a heading for each. Please put each table on a separate page. This is an example of the standard style for tables. **Table I.** Table heading

Heading	Heading[a]	Straddle heading	Reference
Subhead		Subhead	
Subheading			
Parameter			
Parameter			
Subheading			
Parameter			
Parameter			
Parameter			

APPENDIX C

A5

European Journal of physiology

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Respiratory control (cardio-respiratory control)
Synaptic transmission and integration
Physiology of neuronal networks
Neuromodulation

A6

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b) The title of the paper. (For bibliographic reasons, double titles are undesirable, particularly if the authors of the main and subsidiary parts are different.)

c) The names of the authors together with their respective affiliations. Addresses should be complete and may be given in the local language. An envelope symbol should be used to indicate to which author correspondence should be sent.

d) The fax and e-mail numbers of the corresponding
author.

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