HEART RATE VARIABILITY IN HEALTHY AND HEART FAILURE POPULATIONS: ASSOCIATIONS AND RESPONSES TO EXERCISE AND SPECIFIC INTERVENTIONS

A thesis submitted for the degree of Doctor of Philosophy
by

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Abstract.

Autonomic function is severely disrupted in heart failure. Depressed heart rate variability (HRV) in these patients is associated with an increased risk of cardiac events and death. Studies from 24 h HRV assessments demonstrate an improvement following exercise training as part of cardiac rehabilitation. At the most severe level, a need to transplant has been offset following structural recovery as a result of mechanical support to the failing heart yet the effect on autonomic dysfunction is unknown. The aim of this thesis was to examine the effects of cardiac rehabilitation (CR) and mechanical support on short-term measures of HRV in heart failure patients of varying disease severity.

The first few chapters and subsequent papers assessed the reliability and agreement of newly developed wireless technologies and measurement software in healthy participants. The findings revealed agreement was poor between systems but the new technologies demonstrated similarly fair reliability compared to each other and criterion measures.

A potential role for resting HRV underlying the physiology and prediction of higher risk heart rate (HR) responses to graded exercise testing was then explored. The consequent chapter found that resting vagally mediated HRV measures were able to predict a low risk but not a high risk HR recovery accurately. Lower HRV also underlined an increased risk profile based on known prognostic HR measures in healthy populations.

An observation was made for a lack of normative data with which comparisons could be made. A review of all papers publishing short-term HRV data in healthy adults revealed poor methodological standards in many of the studies, limiting the final outcomes. For all measures of HRV, data from the literature were lower than previously published norms but known age and gender differences remained. These data provide a new source for identification of so called normal and abnormal HRV.

Reviewing the literature concerning the diagnostic and prognostic use of HRV in heart failure identified gaps in the literature. There were no data available relating to the effect of differing exercise training modalities on autonomic function. A randomised trial of 12 weeks aerobic or resistance CR training was successful in increasing functional and aerobic capacities but did not significantly alter resting absolute HRV values. However, the harmony between HR and HRV was favourably altered and better matched that of healthy participants.

Prior to this thesis, there were no data relating to the autonomic profile of patients receiving mechanical support via left ventricular assist device (LVAD) therapy. The study of patients recovered and currently undergoing LVAD treatment revealed significantly higher HRV in the former and latter compared with heart failure patients receiving standard care. Patients recovered from LVAD therapy demonstrated a decreased risk for known HRV markers and a normalisation of autonomic modulations.

In conclusion, a depressed HRV remains a significant risk factor in heart failure patients. Exercise training may afford a beneficial effect in mild-to-moderate patients. In more severe patients, HRV risk factors are favourably altered by mechanical support and should be considered in the assessment of these patients.

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LIST OF ABBREVIATIONS.

ACE	Angiotensin converting enzyme
ACSM	The American College of Sports Medicine
AHA	American Heart Association
AR	Aerobic (exercise group)
ARB	Angiotensin receptor blocker
BMI	Body mass index.
BP	Blood pressure
BPV	Blood pressure variability
BRS	Baroreflex sensitivity
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CHF	Chronic heart failure
CO	Cardiac output
CR	Cardiac rehabilitation
CV	Coefficient of variation
DBP	Diastolic blood pressure
DCM	Dilated cardiomyopathy
ECG	Electrocardiogram
EF(%)	Ejection fraction
GXT	Graded exercise test
HR	Heart rate
HRR	Heart rate recovery
HRV	Heart rate variability
HUT	Head up tilt

ICC	Intraclass correlation coefficient
IDCM	Idiopathic dilated cardiomyopathy
ISHLT	International society for heart and lung transplantation
LVAD	Left ventricular assisting device
LVD	Left ventricular dysfunction
MET	Metabolic equivalent
MI	Myocardial infarction
MSNA	Muscle sympathetic nerve activity
NA	Noradrenaline
NYHA	New York Heart Association
PAD	Peripheral artery (or arterial) disease
PTCA	Percutaneous transluminal coronary angioplasty.
PVCs	Premature ventricular contractions
RER	Respiratory exchange ratio
RPE	Ratings of perceived exertion
RSA	Respiratory sinus arrhythmia
RT	Resistance (exercise group)
SCD	Sudden cardiac death
VPC	Ventricular premature contractions

GLOSSARY OF TERMS.

Atrial fibrillation	Irregular and insufficient contraction of the atrial muscle most often caused by atherelosclerosis, chronic rheumatic heart disease and hypertensive heart disease
Ambulatory monitoring	Continual recording of the ECG or blood pressure using a recording device worn by the subject during normal daily activities for 24 hours
Baroreflex sensitivity	The reactivity of the arterial baroreflex to alter blood pressure - usually in response to orthostatic challenge
Body mass index	The ratio of weight (kg) to body size (calculate as stature in m^2)
Borg Scale	6 – 19 point scale providing subject self reported ratings of perceived exertion.
Bridging to recovery	The use of an LVAD to allow the dilated myocardium of a CHF patient to recover.
Bridging to transplantation	The use of an LVAD to keep a patient alive until a suitable donor heart becomes available for transplantation
Cardiac output	The flow of blood from the heart in a given time period ($l \cdot min^{-1}$)
Cardiothoracic Ratio	The transverse cardiac diameter (the horizontal distance between the most rightward and leftward borders of the heart seen on a postero-anterior (PA) chest radiograph) divided by the transverse chest diameter
Cardioversion	A controlled direct-current electric shock given via a modified defibrillator placed on the chest wall designed to restore normal cardiac rhythm
Coronary artery bypass grafting	Operation to reroute blood flow from blood vessels of the heart using veins removed from other parts of the body
Ectopic beat	A heart muscle contraction that is outside the normal sequence of the cardiac cycle and stems from an impulse outside the usual focus of the sinoatrial node.
End diastolic diameter	Geometrical measure of the heart showing the diameter of the left ventricle at the end of diastole (mm)

End diastolic volume	The volume of blood in the ventricle at the end of diastole (ml)
End systolic diameter	Geometrical measure of the heart showing the diameter of the left ventricle at the end of systole (mm)
Ejection fraction	The fraction or % of blood (usually in the left ventricle) at the end of systole as a function of the volume during diastole
Heart rate turbulence	The return to equilibrium of heart rate after a ventricular premature contraction
Holter monitor	Recording device worn by subject to continually monitor ECG and/or blood pressure
Iodine-123 metaiodobenzylguanidine imaging	The infusion and monitoring of iodine-123 metaiodobenzylguanidine to observe the distribution of sympathetic nervous tissue
Left ventricular end systolic volume	Volume of blood remaining in the left ventricle at the end of systole
Neurohumoral	Relating to the transmitting, uptake and action of neurohormones in the body
Percutaneous transluminal coronary angioplasty.	Operation to increase blood flow in (coronary) blood vessels by increasing the internal diameter of the vessel. May involve stenting
Peripheral bypass surgery	Rerouting blood flow around damaged or occluded vessels using grafts from other healthy vessels
Premature ventricular contractions	Spontaneous depolarization of the ventricular myocytes prior to and without stimulation from the SA node resulting in ventricular contraction too early in the normal cardiac cycle – sometimes VPC
Remodelling	Change in size, shape and function of the heart after injury usually to the left ventricle
Reverse remodelling	An improvement in ventricular mechanics and function after a remote injury
Stenting	Insertion of a device into a previously occluded blood vessel to hold back plaque built up due to CAD
Stroke volume	The volume (ml) of blood leaving the left ventricle

	during each cardiac cycle
Tachycardia	A rise in the heart rate above the normal range at rest 60 to 100 beats per minute

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I dedicate this thesis to those hard working many who realise there is no big secret to it. To paraphrase a term that I have become very familiar with, it's a question of "just do it".

David Nunan.

Author declaration.

I take responsibility for all the material contained within this thesis and confirm that it is my own work.

David Nunan