

**EVALUATION OF ALTERATIONS IN CARDIOVASCULAR  
STRUCTURE AND FUNCTION IN  
END-STAGE RENAL FAILURE**

**BENJAMIN KANE DUNDON**

**MBBS FRACP**

**DOCTOR OF PHILOSOPHY**

**DISCIPLINE OF MEDICINE**

**SCHOOL OF MEDICINE**

**UNIVERSITY OF ADELAIDE**

**ADELAIDE, SOUTH AUSTRALIA**

**AUSTRALIA**

*Submitted in the total fulfilment of the requirements*

*for the degree of Doctor of Philosophy*

*March 2013*

*To Annabel, without whom  
none of this would have been possible.*

# TABLE OF CONTENTS

<b>TABLE OF CONTENTS .....</b>	<b>III</b>
<b>FIGURE LEGEND: .....</b>	<b>IX</b>
<b>TABLE LEGEND .....</b>	<b>XIII</b>
<b>ABSTRACT .....</b>	<b>XIV</b>
Background:.....	xiv
Methods / Results: .....	xiv
Conclusions:.....	xvi
<b>DECLARATION .....</b>	<b>XVII</b>
<b>ACKNOWLEDGMENTS .....</b>	<b>XVIII</b>
<b>ABBREVIATIONS .....</b>	<b>XXI</b>
<b>BACKGROUND.....</b>	<b>1</b>
<b>CHRONIC KIDNEY DISEASE.....</b>	<b>2</b>
<i>Glomerular Filtration Rate.....</i>	<i>2</i>
<i>Disease Burden .....</i>	<i>6</i>
<i>Financial Burden of CKD .....</i>	<i>7</i>
<i>Aetiology.....</i>	<i>8</i>
<i>Co-Morbid Conventional Cardiovascular Risk Factors .....</i>	<i>10</i>
Diabetes Mellitus .....	11
Hypertension.....	12
Smoking.....	12
Hyperlipidaemia .....	13
Obesity .....	14
<i>Disease-Specific Cardiovascular Risk Factors.....</i>	<i>14</i>
Anaemia.....	14

Disordered Calcium / Phosphate Metabolism.....	16
Uraemia .....	19
<b>CARDIOVASCULAR SEQUELAE OF CKD.....</b>	<b>26</b>
<i>Left Ventricular Disease in CKD .....</i>	<i>27</i>
Congestive Cardiac Failure.....	32
<i>Atrial Disease in CKD .....</i>	<i>36</i>
<i>Valvular Disease in CKD.....</i>	<i>38</i>
<i>Endothelial Dysfunction in CKD .....</i>	<i>41</i>
Pathobiology of Endothelial Dysfunction in CKD .....	42
Assessment of Endothelial Function.....	44
Endothelial Dysfunction and Cardiovascular Risk in CKD .....	44
<i>Coronary Artery Disease in CKD.....</i>	<i>46</i>
Coronary Endothelial Function .....	46
Coronary Atherosclerosis.....	52
<i>Vascular Disease in Chronic Kidney Disease.....</i>	<i>56</i>
Arterial Function .....	56
Atherosclerosis.....	58
Arteriosclerosis.....	59
Vascular Calcification .....	60
Non-invasive Evaluation of Arterial Stiffness .....	62
<b>ARTERIO-VEINUS FISTULAE AND CARDIOVASCULAR STRUCTURE AND FUNCTION.....</b>	<b>69</b>
<i>Arterio-venous Fistula Creation .....</i>	<i>69</i>
Pulmonary Hypertension in Patients with Arterio-venous Fistulae.....	71
<i>Arterio-Venous Fistula Ligation.....</i>	<i>72</i>
<b>EFFECTS OF RENAL TRANSPLANTATION ON CARDIOVASCULAR STRUCTURE AND FUNCTION</b>	
.....	73
<b>EVALUATION OF CARDIOVASCULAR RISK PRIOR TO RENAL TRANSPLANTATION.....</b>	<b>76</b>
Tachycardia Stress Methodologies .....	78
<b>NON-INVASIVE IMAGING OF CARDIOVASCULAR STRUCTURE AND FUNCTION IN CKD.....</b>	<b>80</b>

Trans-thoracic Echocardiography .....	81
Single Photon Emission Computed Tomography .....	83
Cardiovascular Computed Tomography .....	83
Cardiovascular Magnetic Resonance Imaging .....	84
AIMS OF THIS THESIS .....	88
<b>METHODS .....</b>	<b>89</b>
RESEARCH ETHICS CONSIDERATIONS.....	90
STUDY 1: EVALUATION OF ALTERATIONS IN CARDIOVASCULAR STRUCTURE AND FUNCTION FOLLOWING ELECTIVE ARTERIO-VEIN FISTULA CREATION IN PRE-DIALYSIS END-STAGE RENAL FAILURE .....	90
<i>Subjects</i> .....	90
Inclusion Criteria.....	90
Exclusion Criteria.....	90
<i>Study Investigations</i> .....	91
STUDY 2: EVALUATION OF ALTERATIONS IN CARDIOVASCULAR STRUCTURE AND FUNCTION FOLLOWING ELECTIVE ARTERIO-VEIN FISTULA LIGATION FOLLOWING SUCCESSFUL, STABLE RENAL TRANSPLANTATION .....	92
<i>Subjects</i> .....	92
Inclusion Criteria.....	92
Exclusion Criteria.....	92
<i>Study Investigations</i> .....	93
<i>Cardiovascular Magnetic Resonance Protocol – Studies 1 and 2</i> .....	94
Cardiac Protocol.....	94
Vascular Protocol .....	97
Summary of CMR Investigations for Arterio-Vein Fistula Studies.....	101
STUDY 3: EVALUATION OF THE DIAGNOSTIC ACCURACY OF DOBUTAMINE-STRESS CARDIAC MRI IN THE DETECTION OF ANGIOGRAPHICALLY-SIGNIFICANT CORONARY ARTERY DISEASE PRIOR TO RENAL TRANSPLANTATION .....	103

<i>Subjects</i> .....	103
Inclusion Criteria.....	103
Exclusion Criteria.....	103
<i>Study Investigations</i> .....	104
Dobutamine Stress Cardiac MRI.....	104
Invasive Coronary Angiography .....	105
<b>STUDY 4: EVALUATION OF DYNAMIC CORONARY ENDOTHELIAL FUNCTION IN END-STAGE</b>	
<b>RENAL FAILURE</b> .....	107
<i>Subjects</i> .....	107
Inclusion Criteria.....	107
Exclusion Criteria.....	107
<i>Study Investigations</i> .....	108
Coronary Endothelial Function.....	108
Quantitative Coronary Angiography.....	109
Coronary Blood Flow / Microvascular Function.....	110
<b>STATISTICAL METHODS</b> .....	111
<b>RESULTS</b> .....	113
<b>STUDY 1: EVALUATION OF ALTERATIONS IN CARDIOVASCULAR STRUCTURE AND FUNCTION</b>	
<b>FOLLOWING ELECTIVE ARTERIO-VEIN FISTULA CREATION IN PRE-DIALYSIS END-STAGE</b>	
<b>RENAL FAILURE</b> .....	114
<i>Introduction</i> .....	114
<i>Methods</i> .....	117
Statistical Methods .....	117
Power Calculation .....	117
<i>Results</i> .....	119
Clinical Results .....	121
Cardiac Results .....	121
Vascular Results: .....	125
<i>Discussion</i> .....	130

<i>Conclusion</i> .....	140
STUDY 2: EVALUATION OF ALTERATIONS IN CARDIOVASCULAR STRUCTURE AND FUNCTION FOLLOWING ELECTIVE ARTERIO-VEIN FISTULA LIGATION FOLLOWING SUCCESSFUL STABLE RENAL TRANSPLANTATION .....	
	141
<i>Introduction</i> .....	141
<i>Methods</i> .....	143
Statistical Methods .....	143
Power Calculation .....	143
<i>Results</i> .....	145
Clinical Results .....	146
Cardiac Results .....	146
Vascular Results: .....	150
<i>Discussion</i> .....	156
<i>Conclusion</i> .....	161
STUDY 3: EVALUATION OF THE DIAGNOSTIC ACCURACY OF DOBUTAMINE-STRESS CARDIAC MRI IN THE DETECTION OF ANGIOGRAPHICALLY-SIGNIFICANT CORONARY ARTERY DISEASE PRIOR TO RENAL TRANSPLANTATION .....	
	163
<i>Introduction</i> .....	163
<i>Methods</i> .....	166
Statistical Analysis .....	166
<i>Results</i> .....	167
<i>Discussion</i> .....	172
Limitations .....	180
<i>Conclusion</i> .....	181
STUDY 4: EVALUATION OF DYNAMIC CORONARY ENDOTHELIAL FUNCTION IN END-STAGE RENAL FAILURE .....	
	183
<i>Introduction</i> .....	183
<i>Methods</i> .....	185

Statistical Analysis .....	187
Power Calculation .....	187
<i>Results</i> .....	<i>188</i>
<i>Discussion</i> .....	<i>191</i>
Limitations .....	198
<i>Conclusion</i> .....	<i>201</i>
<b>CONCLUSION</b> .....	<b>202</b>
THESIS SUMMARY .....	203
FUTURE DIRECTIONS .....	206
<b>BIBLIOGRAPHY</b> .....	<b>209</b>

## FIGURE LEGEND:

- Figure 1: Prevalence of ESRF patients in Australia in 2005, with relative contributions of dialysis (peritoneal and haemodialysis) and transplant renal replacement therapies (adapted from ANZDATA Annual Report, 2006).<sup>14</sup>..... 6*
- Figure 2: Prevalence of End-Stage Kidney Disease (ESKD) in relation to the Australian population between 1980 and 2004.<sup>15</sup>..... 7*
- Figure 3: Trends in patient age at commencement of Renal Replacement Therapy in Australia, 1981-2006.<sup>19</sup>..... 9*
- Figure 4: Age-specific prevalence of Diabetes diagnosis, by gender, 2004-5.<sup>19</sup>.....11*
- Figure 5: Active daily smokers, Australian population aged  $\geq 14$ , 1985-2004.<sup>26</sup> ..13*
- Figure 6: Age-standardised Rates of Death from Any Cause (Panel A), Cardiovascular Events (Panel B) and Hospitalisation (Panel C) according to eGFR among 1,120,295 ambulatory adults. (Reproduced from Go AS, et al, N Engl J Med, 2004 with permission. Copyright © [2004] Massachusetts Medical Society. All rights reserved.) .....27*
- Figure 7: Probability of overall survival (A) and cardiovascular event-free survival (B) amongst successful responders to the LVM reduction intervention, and non-responders (response defined by a  $>10\%$  change in LVM) ( $p < 0.001$  for both). (Reproduced from London et al, J Am Soc Nephrol, 2001, with permission from the American Society of Nephrology). .....32*

*Figure 8: Kaplan-Meier survival analysis for all cause mortality by NYHA Classification for 1322 patients with ESRF. (Reproduced from Postorino M, et al, Nephrol Dial Transplant., 2007, by permission of Oxford University Press).....35*

*Figure 9: Measurement of carotid-femoral PWV, utilising the foot-to-foot method, where ( $\Delta t$ ) represents the change in time, and ( $\Delta L$ ) represents the distance between waveform measurement sites. (Reproduced from Laurent S. et al. Eur Heart J, 2006;27:2592, with permission from Oxford University Press ).....64*

*Figure 10: Schematic representation of the method for determining arterial distensibility by measuring changes in arterial lumen cross-sectional area across the cardiac cycle ( $\Delta A$  = Maximal change in lumen area during cardiac cycle;  $D$  = diameter), as they relate to local pulse pressure. (Reproduced from Laurent S. et al. Eur Heart J, 2006;27:2593, with permission from Oxford University Press).....66*

*Figure 11: Representation of an illustrative central pressure waveform, demonstrating identification of the Augmentation Pressure; determined as the difference between the second ( $P1$ ) and first ( $P2$ ) systolic pressure peaks.  $AIx$  may then be calculated by evaluation of the augmentation pressure in relation to the pulse pressure. (Reproduced from Laurent S. et al. Eur Heart J, 2006;27:2595, with permission from Oxford University Press).....67*

*Figure 12: Representation of CMR methodology for the use of the long axis reference images (horizontal long axis image shown on left) to enable acquisition of sequential, parallel ventricular short-axis images from the atrio-ventricular plane to the ventricular apices (end-diastolic images shown).....95*

<i>Figure 13: Sagittal oblique image of the aorta (left) with pictorial representation of the reference levels used in the acquisition of cross-sectional aortic images at the Ascending Aorta (AA), Proximal Descending Aorta (PDA) and Distal Descending Aorta (DDA) (right).</i> .....	98
<i>Figure 14: Alterations in Left Ventricular Structure and Function following successful AVF creation in ESRF.</i> .....	123
<i>Figure 15: Alterations in Right Ventricular Structure and Function following successful AVF creation in ESRF.</i> .....	124
<i>Figure 16: Alterations in Left and Right Atrial Area following successful AVF creation in ESRF.</i> .....	125
<i>Figure 17: Alterations in Aortic Distensibility following AVF creation in ESRF.</i>	126
<i>Figure 18: Aortic Distensibility by Aortic Level Prior to (Pre-), and Following (Post-) AVF creation in ESRF.</i> .....	127
<i>Figure 19: Alterations in Peripheral Endothelial Function following successful AVF creation in ESRF.</i> .....	128
<i>Figure 20: Alteration in CMR-assessed brachial artery blood-flow, ipsilateral and contralateral to the newly created arterio-venous fistula.</i> .....	129
<i>Figure 21: Alterations in Left Ventricular Structure and Function following AVF-ligation in the context of successful, stable renal transplantation.</i> .....	148
<i>Figure 22: Alterations in Right Ventricular Structure and Function following AVF-ligation in the context of successful, stable renal transplantation.</i> .....	149

*Figure 23: Alterations in Left and Right Atrial Area following AVF-ligation in the context of successful, stable renal transplantation. .... 150*

*Figure 24: Alterations in Aortic Distensibility following AVF-ligation in the context of successful, stable renal transplantation. .... 151*

*Figure 25: Aortic Distensibility by Aortic Level Prior to (Pre-), and Following (Post-) AVF ligation in the context of stable, successful renal transplantation. .... 152*

*Figure 26: Average Aortic Distensibility in ESRF subjects following AVF-creation compared to successful RTx recipients following AVF-ligation..... 153*

*Figure 27: Evaluation of Alterations in Endothelial Function following AVF ligation in the context of stable, successful renal transplantation. .... 154*

*Figure 28: Alteration in CMR-assessed brachial artery blood-flow, ipsilateral and contralateral to the ligated arterio-venous fistula in the context of stable, successful renal transplantation..... 155*

*Figure 29: Comparison of CMR-derived vs. SPECT-derived evaluation of LVEF. 171*

## TABLE LEGEND

<i>Table 1: Classification of Stages of Chronic Kidney Disease according to the National Kidney Foundation Kidney Disease Outcome Quality Initiative (K/DOQI) Advisory Board Findings.<sup>1</sup>.....</i>	<i>2</i>
<i>Table 2: Prevalence of echocardiographic findings of abnormalities in left ventricular structure and function at dialysis commencement (Reproduced from Parfrey PS, et al. Nephrol Dial Transplant., 1996;11:1277-1285, with permission of Oxford University Press). .....</i>	<i>28</i>
<i>Table 3: Subject Baseline Characteristics – Study 1 .....</i>	<i>120</i>
<i>Table 4: Subject Baseline Characteristics – Study 2 .....</i>	<i>145</i>
<i>Table 5: Subject Baseline Characteristics – Study 3 .....</i>	<i>167</i>
<i>Table 6: Diagnostic performance of DS-CMR and Stress-Perfusion SPECT in the detection of angiographically significant coronary stenoses.....</i>	<i>170</i>
<i>Table 7: Subject Baseline Characteristics – Study 4 ACEI = Angiotensin Converting Enzyme Inhibitor; ARB = Angiotensin Receptor Blocker.....</i>	<i>188</i>

## **ABSTRACT**

### Background:

Chronic renal dysfunction is associated with myriad alterations in cardiovascular structure and function, resulting in markedly elevated rates of cardiac and vascular morbidity and mortality. Utilising advances in cardiovascular magnetic resonance imaging (CMR), we evaluated the cardiovascular sequelae of arterio-venous fistula formation in advanced chronic kidney disease, and the impact of elective arterio-venous fistula ligation following successful renal transplantation. Furthermore, we undertook to evaluate the diagnostic accuracy of dobutamine-stress CMR in the detection of haemodynamically-significant coronary artery disease prior to renal transplantation. Finally, we invasively evaluated coronary endothelial function in the presence of advanced renal dysfunction, and compared this to subjects with preserved renal function.

### Methods / Results:

*Study 1:* CMR was undertaken to evaluate cardiac structure and function, brachial artery endothelial function (as assessed by flow-mediated dilatation) and aortic distensibility in twenty-four subjects at baseline, and 6-months following, clinically indicated arterio-venous fistula creation in preparation for the commencement of haemodialysis for end-stage renal failure. Following arterio-venous fistula creation, mean cardiac output increased by 25.0% ( $p < 0.0001$ ), with substantial associated increases in left and right ventricular volumes, left and right atrial area and left ventricular mass (12.7% increase,

p<0.0001). Peripheral endothelial function was significantly impaired at follow-up (9.0±9% vs. 3.0±6%, p=0.01). No significant change in aortic distensibility was identified.

*Study 2:* Cardiac and vascular function were similarly assessed utilising CMR in eighteen subjects prior to, and 6-months following, clinically indicated arterio-venous fistula ligation in the context of successful, stable renal transplantation. Following AVF-ligation, mean cardiac output fell by 15.6% (p=0.004), with significant attendant decreases in atrial and ventricular chamber dimensions. Notably, left ventricular mass fell by 9.7% (p=0.0001) at follow-up. Aortic distensibility was unchanged following AVF-ligation, though endothelial function improved significantly (2.5±6.5% vs. 8.0±5.9%, p=0.043).

*Study 3:* Dobutamine-stress CMR was performed in twenty-one subjects prior to clinically-indicated invasive coronary angiography before potential renal transplantation. Dobutamine-stress CMR demonstrated 100% sensitivity and 93% specificity for the detection of angiographically significant coronary disease (≥70% stenosis severity). This compared favourably to results for the institutional-standard (SPECT: sensitivity 67%, specificity 38%; p<0.0001 compared to CMR).

*Study 4:* At invasive coronary angiography, endothelium-dependent and endothelium-independent coronary endothelial and microvascular function were evaluated amongst eight pre-renal transplant subjects with only minimal coronary artery disease (≤20% epicardial coronary stenoses). Utilising intra-coronary infusions of acetylcholine (10<sup>-7</sup>M and 10<sup>-6</sup>M), adenosine (48mcg) and glyceryl tri-nitrate (100mcg), results were compared to thirteen control subjects with minimal coronary artery disease but comparatively preserved renal

function. There was no significant difference in endothelium-dependent or endothelium-independent coronary endothelial function between the cohorts. Microvascular function (as assessed by coronary flow reserve following adenosine administration) was markedly impaired in subjects with advanced renal impairment compared to controls ( $1.9\pm 0.4$  vs.  $3.0\pm 1.1$ ,  $p=0.01$ ).

### Conclusions:

Chronic kidney disease is associated with substantial alterations in cardiovascular structure and function. Arterio-venous fistulae, though necessary for the performance of haemodialysis, appear to contribute significantly to the high burden of cardiovascular maladaptation present in this condition. Recent advances in CMR and stress-CMR may play a significant role in improving the detection of sub-clinical cardiovascular disease in these high-risk patients.

## **DECLARATION**

This body of work contains no material which has been accepted for the award of any other degree or diploma in any university or tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Dr Benjamin Kane Dundon

Discipline of Medicine

School of Medicine

University of Adelaide

Adelaide

South Australia, 5000

AUSTRALIA

## **ACKNOWLEDGMENTS**

It was with no small amount of trepidation that I initially committed to the commencement of this PhD. Having never been exposed to meaningful research during my under-graduate education or post-graduate clinical training, as an advanced trainee in Cardiology the idea of removing myself from clinical medicine for three years seemed a path both onerous and of little lasting professional value – merely a hoop to be jumped through in order to “tick the research box”. It is with great gratitude and humility that I commit this Thesis to the numerous colleagues who have mentored, aided and supported me through an experience that has proven to be of immense professional and personal value.

To Professor Stephen Worthley, never could it be said that you lack for optimism. I am deeply indebted to you for your vision, support, mentorship and enthusiasm in supporting my research undertakings and, more broadly, my professional career. Few in number are the clinicians throughout medical education who truly shape with lasting effect the future path of their trainees. I consider myself extremely fortunate to have benefitted from your guidance and example as a clinician and a mentor. Invaluable is a leader who, by example, engenders a pervasive culture of teamwork and determination in the pursuit of excellence. Such has been my experience.

To Dr Matthew Worthley, for your boundless enthusiasm and limitless accessibility, I sincerely thank you. The path from doctor to academic clinician is besieged by obstacles, both small and large. I am extremely fortunate to have experienced in my primary supervisor a mentor infectious in his passion and commitment to medical

research and ceaselessly patient in his support of the fledgling steps of an early career researcher. Through humour, wisdom and enthusiasm, you form the heart of our research team. I am deeply indebted to you for all of your support.

To Professor Randall Faull and Associate Professor Kym Bannister, I am extremely grateful for your advice and support in the conduct of my research. I remain humbled by your commitment to the welfare of your patients and exceedingly thankful for your willingness to mentor a lowly Cardiologist within the realms of Renal and Transplantation Medicine. Through efficient systems and outstanding personnel, the cooperation of the Renal Unit was instrumental to the success of my research studies.

To Mr Kim Torpey, your contribution to the AV fistula research is peerless. I sincerely thank you for your tireless support and enthusiasm for these Projects and for your dedication to the success of our work together. My PhD has much to be grateful to you for your hard work, outstanding patient rapport and ever-present good cheer.

To my many colleagues within the Cardiovascular Research Centre of the Royal Adelaide Hospital, thank you for your immeasurable support. The two years of PhD research and training in Cardiovascular Magnetic Resonance Imaging were a busy but fulfilling period of my Cardiology career. Without the support and assistance of the many members of the CRC team however, the numerous tasks necessary in the completion of a PhD would surely have proven insurmountable. To Ms Kerry Williams, thank you for your tireless assistance in the booking and performance of the many CMR studies undertaken for my research. I am truly grateful for all of your hard work. To Dr Rishi Puri, thank you for your assistance in the performance of the

QCA measures for our invasive study. Your enthusiasm for research and your unwavering curiosity for new discoveries enabled the completion of many productive Projects together. To Mr Angelo Carbone, thank you for your commitment to the team and your constant willingness to help others in the department, wherever assistance was required. To Dr Adam Nelson, I remain truly humbled by your capacity for productivity despite your numerous clinical, research and administrative commitments. I look forward to watching and supporting your undoubtedly stellar career in the years to come. Thank you for all your help.

I thank the Cardiac Society of Australia and New Zealand, the National Health and Medical Research Council and the National Heart Foundation of Australia for their support of my research career, and I thank the Board of the Cardiovascular Lipid Research Grants for their support of my arterio-venous fistula ligation study. Without such support, the undertaking of meaningful research is greatly hampered.

I would also like to thank Dr Leo Mahar, whose mentorship during my Cardiology training I have valued above all others. I benefitted immensely from the example of your dignity and strength of leadership within our Department and greatly value the enormous library of highly educational (and often highly amusing) anecdotes you shared in your commitment to my education on the path to becoming a Consultant Physician. For your generosity and commitment to my career, I sincerely thank you.

But more than any other, I thank my wife, Annabel. For our wonderful boys James, William and Thomas and for your love and unwavering support through all of the challenges and hardships of this PhD, I thank you.

## **ABBREVIATIONS**

Ach	Acetylcholine
ACS	Acute Coronary Syndrome
ADMA	Asymmetrical dimethylarginine
AF	Atrial Fibrillation
AGE	Advanced Glycosylation End-products
Aix	Augmentation Index
ANP	Atrial Natriuretic Peptide
ANZDATA	Australian and New Zealand Dialysis and Transplant Registry
APV	Average Peak Velocity
ARVC	Arrhythmogenic Right Ventricular Cardiomyopathy
ASCOT	Anglo-Scandinavian Cardiac Outcomes Trial
AVF	Arterio-Venous Fistula
BMI	Body Mass Index
BNP	Brain Natriuretic Peptide
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CAFÉ	Conduit Artery Function Evaluation
CBF	Coronary Blood Flow
CCF	Congestive Cardiac Failure
CFR	Coronary Flow Reserve
CKD	Chronic Kidney Disease
CMR	Cardiovascular Magnetic Resonance Imaging
CO	Cardiac Output

CrCL	Creatinine Clearance
CT	Computed Tomography
CV	Cardiovascular
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
eGFR	Estimated Glomerular Filtration Rate
eNOS	Endothelial Nitric Oxide Synthase
EPO	Erythropoietin
ESKD	End Stage Kidney Disease
ESRF	End-stage Renal Failure
ET-1	Endothelin-1
FAME	Fractional Flow Reserve versus Angiography for Multivessel Evaluation
FFR	Fractional Flow Reserve
FISP	Fast-imaging with Steady State Free Precession
FMD	Flow-mediated Dilatation
FOV	Field of View
GFR	Glomerular Filtration Rate
GTN	Glyceryl Tri-nitrate
Hb	Haemoglobin
HDx	Haemodialysis
HMG-CoA	Hydroxyl-methylglutaryl coenzyme-A
HR	Heart Rate
ICA	Invasive Coronary Angiography
IHD	Ischaemic Heart Disease

IMR	Index of Microvascular Resistance
IQR	Inter-quartile Range
IVUS	Intravascular Ultrasound
K/DOQI	National Kidney Foundation Kidney Disease Outcome Quality Initiative
LA	Left Atrial
LAD	Left Anterior Descending Artery
LDL	Low Density Lipoprotein
LIFE	Losartan Intervention for Endpoint Reduction in Hypertension
LV	Left Ventricular
LVEDP	Left Ventricular End-Diastolic Pressure
LVEF	Left Ventricular Ejection Fraction
LVH	Left Ventricular Hypertrophy
LVM	Left Ventricular Mass
LVSV	Left Ventricular Stroke Volume
MDRD	Modification of Diet in Renal Disease Study Group
MI	Myocardial Infarction
MOD	Method of Discs
MPI	Myocardial Perfusion Imaging
NO	Nitric Oxide
NPV	Negative Predictive Value
NSF	Nephrogenic Systemic Fibrosis
NSTEMI	Non-ST-segment Elevation Myocardial Infarction
NYHA	New York Heart Association
oxLDL	Oxidised Low Density Lipoprotein

PAP	Pulmonary Artery Pressure
PCI	Percutaneous Coronary Intervention
PGI <sub>2</sub>	Prostacyclin (Prostaglandin I <sub>2</sub> )
PHT	Pulmonary Hypertension
PP	Pulse Pressure
PPV	Positive Predictive value
PTCA	Percutaneous Trans-luminal Coronary Angioplasty
PTH	Parathyroid Hormone
PWV	Pulse-wave Velocity
QALY's	Quality-Adjusted Life Years
QCA	Quantitative Coronary Angiography
RA	Right Atrial
RAAS	Renin-Angiotensin-Aldosterone System
RRT	Renal Replacement Therapy
RTx	Renal Transplantation
RV	Right Ventricular
SBP	Systolic Blood Pressure
SPECT	Single Photon Emission Computed Tomography
SSFP	Steady-State Free Precession
STEMI	ST-segment Elevation Myocardial Infarction
TIIDM	Type II Diabetes mellitus
TE	Echo Time
TR	Repetition Time
TTE	Trans-thoracic Echocardiography
TXA <sub>2</sub>	Thromboxane

UVB            Ultraviolet B

25(OH)VitD3   25-hydroxyvitamin D<sub>3</sub>