Assessment of Left Ventricular Diastolic Function with Three Dimensional Cardiac Magnetic Resonance Imaging

Carissa Grace Fonseca

A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Auckland

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

Department of Anatomy with Radiology
Faculty of Medical and Health Sciences
The University of Auckland
New Zealand

2004

Primary Supervisor: Dr. Alistair A. Young
Department of Anatomy with Radiology
and The Bioengineering Institute
University of Auckland

Co-Supervisor: Dr. Ralph A. Stewart
Department of Cardiology
Auckland City Hospital
Auckland

Advisory Committee: Dr. Brett R. Cowan
(Department of Medicine, University of Auckland)

Associate Professor Bruce H. Smaill
(The Bioengineering Institute, University of Auckland)

Professor Colin R. Green
(Department of Anatomy with Radiology, University of Auckland)

I stand on the brink, on the edge of myself
and wonder at All that is beyond me
I am jealous of the Ocean and the Sky
that do not seem to end;
of the Universe itself
that holds so much Immensity.

I seek to comprehend all knowledge,
and I can't even know of all that has been written
I am a finite creature
but I ever struggle to hold within my grasp
the mystery of being
I want the power of knowing All,
of seeing All,
of having All

And I cannot even possess myself;
I have thoughts and fears and hopes
that I cannot often understand,
nor more frequently admit
I am not a comfortable creature
Even my most cherished dreams I cannot make come true
My heart cries out to me to be God!
and my life shouts out that I am not!
and my faith is based on the hope that
Someone else is!

I am left with the experience
that I exist beyond myself
but cannot contain my source
I am a grain of sand wanting to possess the ocean
and the miracle of Love is that I can
He has made me so small so that He can stretch me
to Immensity
He has made me so poor so He can fill me pressed down, and overflowing
with his Richness
He has made me so limited so that He can make me
Boundless
He has made me a creature
so he can make me God.
He has entered my heart and he has called me,
'Home'

~ Edward J Farrell

Abstract

Measurement of diastolic left ventricular (LV) function is vitally important in the assessment of cardiac disease. However, only limited information on tissue function can be obtained with current clinical techniques. This Thesis developed and investigated novel parameters of both global and regional myocardial function, using cardiac magnetic resonance imaging (MRI) with three-dimensional tissue tagging.

Multidirectional peak myocardial shortening strains and strain rates, as well as the peak systolic displacement and velocity of the mitral valve annulus plane (MVP), were considered as parameters of LV systolic function. The corresponding peak diastolic strain relaxation rates and peak diastolic MVP velocity were used to assess diastolic function. The effects of normal ageing were studied in people with no evidence of cardiac disease, and compared with the effects of disease in patients with type 2 diabetes mellitus (DM).

In normal healthy subjects, systolic strain parameters were preserved, while diastolic parameters were impaired, with age. DM patients showed impaired diastolic function on correction for age, and systolic functional parameters were also impaired, even though LV ejection fraction was normal. MVP systolic and diastolic motion were reduced both with age and in DM patients. Systolic LV torsion was increased with age and in DM, with no corresponding increase in torsional relaxation. Both systolic and diastolic function parameters were regionally heterogeneous. With normal ageing, diastolic function was impaired in a regionally non-uniform manner.

Thus, a complete assessment of LV function requires measurement of LV tissue mechanics as well as chamber haemodynamics. MRI provides valuable information regarding myocardial tissue behaviour, contributing to systolic and/or diastolic dysfunction, which cannot be obtained otherwise. Systolic tissue dysfunction may develop concomitantly in patients with diastolic dysfunction, even when global ejection fraction is preserved. Regional analyses provide important information on how local changes contribute to global function. The influence of age must be taken into account in studies of disease.

Acknowledgements

I have encountered some remarkable people, over the course of this doctoral degree, and have been fortunate to have friends, family, and colleagues who have offered encouragement and support throughout.

I am especially grateful to my supervisor, Alistair Young, for giving me the opportunity to undertake this study. Thank you, not only for your guidance, and the invaluable research skills you have taught me, but also for your trust and belief in me, which has given me confidence in my own abilities. It has been an honour to work with you.

Ralph Stewart, my co-supervisor, and the members of my advisory committee – Brett Cowan, Bruce Smaill, and Colin Green – have been nothing but supportive. Sincere thanks to each of you for sound advice, for always being so approachable, despite your other commitments, and for providing extremely helpful and constructive criticism of my work.

Many thanks to Brett and Dr. Chris Occleshaw (Department of Cardiology, Auckland City Hospital) who performed the MR scans for all of the subjects examined in this Thesis (after-hours, more often than not!). Chris also contributed to discussions on much of the work presented here.

A special note of thanks must go to Dr. Helen Oxenham (currently at the Department of Cardiology, Royal Infirmary of Edinburgh) who recruited the older normal, healthy people for the studies on the influence of age, whilst working in the Department of Medicine in 2001, and to Dr. Tom Gentles (Department of Cardiology, Auckland City Hospital) for recruiting the younger normal, healthy subjects. Thanks also to Prof. Garth Cooper and Dr. John Baker (School of Biological Sciences) and Dr. Ajith Dissanayake (Middlemore Hospital, South Auckland Health) who recruited the patients with type 2 diabetes, and provided access to the data from this group.

I would like to thank Gillian Whalley from the Department of Medicine who performed many of the echocardiographic examinations and, along with Greg Gamble and Assoc. Prof. Rob Doughty (also from the Department of Medicine), contributed to helpful and stimulating discussions on the data resulting from these studies.

The Auckland MRI Research Group, which I have been a part of, for the last four years, deserves special thanks. In particular I would like to thank Kevin Augenstein - my fellow PhD student, and John Baek – our head software programmer, who helped me learn to use the MR image analysis tools, which were so necessary for obtaining the data presented in this Thesis. It was their company that made life in the 'dungeons' (the basement of the Medical school) bearable.

Many thanks to all staff and postgraduate students in the Department of Anatomy with Radiology for creating such a great atmosphere to work in. The post-graduate experience would not have been the same without my peers, especially Robert Huang, Maurice Curtis and Adèle Pope; their support and friendship made all the difference. Lily Yang, Jacelyn Loh and Nimali Withana (the 'dinner girls') have been such wonderful friends all the way through university, and ensured that I visited some of Auckland's best eating-places!

I have been blessed with two guardian angels – Prof. Colin Green and Assoc. Prof. Louise Nicholson! Colin and Louise introduced me to research and it was their infectious enthusiasm for science that led me to pursue this career. They are truly inspirational teachers, have been my mentors and, I am proud to say, have become two of my dearest friends. Thank you both for always being there for me, and for your constant encouragement.

I don't know how I could ever repay Dr. Denis Loiselle (Department of Physiology) for proof-reading the final draft of my Thesis, and adding valuable input, in the incredibly short period of time that I allowed him. Many, many thanks for doing this for me; it is so deeply appreciated!

I am grateful to the National Heart Foundation of New Zealand, which provided generous support in the form of a postgraduate scholarship and an award for travel to an overseas conference. The Royal Society of New Zealand also provided an award for overseas travel.

Finally, I would like to pay tribute to Cecil and Coral Fonseca (my parents), Celia and Caraliza (my sisters), Lawrie Miranda (my grandfather), Abigail Fonseca (my cousin), and Ashika Akhil (my best friend). You are my world – this would not have been possible without you!

List of Publications

The following publications have arisen from work done as part of this Thesis:

Fonseca CG, Dissanayake AM, Doughty RN, Whalley GA, Gamble GD, Cowan BR, Occleshaw CJ, Young AA. 3D Assessment of LV Systolic Strain in Type 2 Diabetic Patients with Diastolic Dysfunction and Normal LV Ejection Fraction. *American Journal of Cardiology. 2004, 94(11):1391-1395.* (Chapter 5).

Fonseca CG, Oxenham HC, Cowan BR, Occleshaw CJ, Young AA. Ageing Alters Patterns of Regional Non-Uniformity in LV Strain Relaxation: A 3D MR Tissue Tagging Study. *American Journal of Physiology – Heart and Circulatory Physiology. 2003, 285(2):H621-H630.* (Chapter 3).

Contents

List of Tables

List of Figures

List of Abbreviations

$\%s_C$	percent circumferential shortening strain
$\%s_L$	percent longitudinal shortening strain
α_{CL}	torsion angle (also 'α')
3D	three dimensional; in three dimensions
A	late diastolic transmitral flow velocity (due to atrial contraction) measured by Doppler echocardiography
A'	late diastolic mitral annular velocity measured by tissue Doppler imaging
AFP	echocardiographic abnormal filling pattern
ANCOVA	analysis of covariance (statistical)
ANOVA	analysis of variance (statistical)
ATP	adenosine triphosphate
B_0	magnetic field
BMI	body mass index
BP	blood pressure
BSA	body surface area
DBP	diastolic blood pressure
DENSE	displacement encoding with stimulated echoes (in cardiac magnetic resonance imaging)
DM	diabetes mellitus
E	early diastolic transmitral flow velocity measured by Doppler echocardiography
E	Lagrangian strain tensor
E'	early diastolic mitral annular velocity measured by tissue Doppler imaging
E:A	ratio of early to late transmitral flow velocity measured by Doppler echocardiography
ECG	electrocardiogram
ED	end-diastole
EDV	end-diastolic volume
EF	ejection fraction
e.g.	*exempli gratia (Latin)*: for example
ES	end-systole
ESV	end-systolic volume
FEM	finite element model
FID	free induction decay
FLASH	fast low angle shot

HARP	harmonic phase
HbA1c	haemoglobin A1c;
HR	heart rate
i.e.	*id est (Latin)*: that is
LV	left ventricle; left ventricular
MANOVA	multivariate analysis of variance (statistical)
mm Hg	millimetres of mercury
MR	magnetic resonance
MRI	magnetic resonance imaging
MVP	mitral valve (annulus) plane
n	sample size (statistical)
NC	normal control
NMR	nuclear magnetic resonance
NS	non-significant (statistical)
P	P-value; probability (statistical)
P^B	Bonferroni corrected P-value (statistical)
PFP	echocardiographic pseudonormal filling pattern
PWD	echocardiographic pulsed wave Doppler recording
r	correlation coefficient (statistical)
RAAS	renin-angiotensin-aldosterone system
R_C	peak rate of relaxation of circumferential shortening strain
RF	radiofrequency
R_L	peak rate of relaxation of longitudinal shortening strain
ROC	receiver operator curve analysis (statistical)
R_P	peak rate of relaxation of principal shortening strain
R_T	peak rate of relaxation of torsional shear strain
SBP	systolic blood pressure
S_C	peak value of circumferential shortening strain
S_L	peak value of longitudinal shortening strain
S_m	systolic mitral annular velocity measured by echocardiography
S_P	peak value of principal shortening strain
SPAMM	spatial modulation of magnetization
SR	strain rate
SRI	strain rate imaging
SSR_C	peak systolic circumferential strain rate
SSR_L	peak systolic longitudinal strain rate
SSR_P	peak systolic principal strain rate
SSR_T	peak systolic torsional shear strain rate
S_T	peak value of torsion
SV	stroke volume
T	tesla
T_1	T_1 Relaxation time
T_2	T_2 Relaxation time
TDI	tissue Doppler imaging

TE	echo time
TR	repetition time
tR_C	time from end-diastole to peak rate of relaxation of circumferential shortening strain
tR_L	time from end-diastole to peak rate of relaxation of longitudinal shortening strain
tR_T	time from end-diastole to peak rate of recovery of torsion
tS_C	time from end-diastole to peak circumferential shortening strain
tS_L	time from end-diastole to peak longitudinal shortening strain
tS_T	time from end-diastole to peak torsion
viz	videlicet; that is to say; namely
vs.	versus; as opposed to