The Role of Contemporary Echocardiography in the Management of Heart Failure

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A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy, Faculty of Medicine and Health Sciences, The University of Auckland, 2006

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Thesis Consent Form

Signed:

Date: 21 January 2006

Abstract

Heart failure (HF) is an increasing and leading cause of cardiovascular morbidity, hospitalisation and death. Echocardiography is often used in HF patients because it provides important aetiological, diagnostic and prognostic information to assist physician management at moderate cost. This thesis has explored contemporary echocardiographic techniques for assessment of both diastolic and systolic function to ascertain their effectiveness and optimal utility. Assessment of systolic function in HF patients is optimised by the use of harmonic imaging and not enhanced with the use of transpulmonary contrast agents, whilst diastolic filling is optimised by the use of preload manipulation. When optimised in this way, echocardiography can be used to stratify HF patients in terms of risk of death and/or hospitalisation after discharge from hospital. This was confirmed in a meta-analysis of more than 6000 patients (1000 deaths) with HF or after acute myocardial infarction (AMI), where the presence of restrictive filling pattern (the most severe form of diastolic dysfunction) was associated with a four-fold increase in mortality in both patient groups. In addition, restrictive filling pattern also predicted development of HF post AMI and hospitalisation in patients with HF. This meta-analysis also evaluated the intermediate stages of diastolic dysfunction and found a stepped relationship between each grade and prognosis. The last part of this thesis explored the role of contemporary echocardiography for management of symptomatic patients in the community and found that the diagnosis of HF in the community may be optimised by using brain natriuretic peptide (BNP) as a first test to “rule-out” heart failure and then echocardiography, which was superior to BNP in patients with intermediate BNP levels to diagnose HF. Furthermore, the systolic echocardiographic parameters were important for diagnosis, whilst the diastolic parameters predicted future hospitalisation. In summary, contemporary echocardiography in HF patients should include comprehensive assessment of systolic function (using tissue harmonics imaging) and diastolic filling (utilising preload manipulation). This approach will optimise both diagnosis and prognosis and in turn may aid physician management.

This thesis is dedicated to my father,

Alan Whalley,

who sadly passed aways before its completion.

Acknowledgements

A project such as this is never possible without the significant contribution of many individuals. Firstly, I would like to acknowledge my supervisor, Associate-professor Robert Doughty. I have been fortunate to work closely with Rob throughout this project and many others. Both Rob and my first supervisor, Professor Norman Sharpe have provided incredible collegial and academic support for more than a decade, whilst simultaneously allowing me to develop my own research interests and ideas.

I have been fortunate to work closely with some very exceptional individuals. Foremost among those has been Greg Gamble, who provided encouragement, support, statistical analyses and scientific advice. Next, I would like to thank Helen Walsh for her expert technical assistance, and Susan Wright, Cara Wasywich and Ann Pearl who provided medical collaboration on these studies. Several research nurses and technicians helped with patients recruitment and data collection: Renelle French, Jenny Koenders, Stephanie Muncaster, Jenne Pomfret and Graeme Orsbourne. I would also like to thank James Aoina who helped with the meta-analysis data collection and the individual authors who confirmed or provided additional data for the meta-analyses. Lastly, I would like to acknowledge the large number of patients and healthy volunteers who participated in these studies. Without their generous support, there would be little to write about.

I would also like to acknowledge the generous financial support that I have received from the National Heart Foundation of New Zealand in the form of a post-graduate scholarship and several travel grants that have enabled me to attend and present this data at international scientific meetings. I have also received generous product support from Philips Ultrasound (Australia) and Schering NZ Ltd.

And finally, I would like to acknowledge the truly wonderful support I have received from my entire family – my mum Catherine, my sister Janet, my husband Darryl and our two children Matthew and Ryan. Collectively they have orchestrated their own lives to support me - allowing me sufficient time to devote to this project.

With heartfelt appreciation to you all.

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Whalley, GA, Wasywich, CJ, Walsh, HJ, Doughty, RN. The role of echocardiography in the contemporary management of congestive heart failure. Expert Rev Cardiovasc Ther 2005;3(1):51-70

Chapter 2

Whalley, GA, Gamble, GD, Walsh, HJ, Wright, SP, Agewall, S, Sharpe, N, Doughty, RN. Effect of tissue harmonic imaging and contrast between observer and test-retest reproducibility of left ventricular ejection fraction measurement in patients with heart failure. Euro J Heart Failure 2004;6:85-93

Whalley GA, Doughty RN, Gamble GD, Sharpe N. Improved endocardial visualization with harmonics and contrast agents improves interpretation of wall motion score index. Euro J Echocardiography 2005;6:134-143.

Whalley, GA, Walsh, HJ, Gamble GD, Doughty, RN. Comparison of different methods for detection of diastolic filling abnormalities. J Am Soc Echocardiogr 2005;18:710-717.

Chapter 3

Whalley GA, Doughty RN, Gamble GD, Wright SP, Walsh HJ, Muncaster SA, Sharpe N. Pseudonormal mitral filling pattern predicts hospital readmission in patients with congestive heart failure. J Am Coll Cardiol 2002;39:1787-1795

Chapter 4

Whalley GA, Gamble GD, Doughty RN. Restrictive diastolic filling predicts death post acute myocardial infarction: A meta-analysis of prospective studies. Heart *(in press)*

Whalley GA, Gamble GD, Doughty RN. The prognostic significance of restrictive diastolic filling associated with heart failure: A meta-analysis Int J Cardiol *(submitted)*

Chapter 5

Whalley GA, Wright SP, Pearl A, Gamble GD, Walsh HJ, Richards AM, Doughty RN. Prognostic role of echocardiography and brain natriuretic peptide in symptomatic breathless patients in the community. J Am Coll Cardiol *(submitted)*

Abbreviations

A	late diastolic mitral valve inflow velocity
A Dur	mitral A wave duration
Aa	late diastolic tissue Doppler velocity of the mitral annulus
ACE	angiotensin converting enzyme
AF	atrial fibrillation
AMI	acute myocardial infarction
ANOVA	analysis of variance
ANP	atrial natriuretic peptide
AR	abnormal relaxation
AUC	area under the curve
AVPD	atrioventricular plane displacement
BNP	brain natriuretic peptide
CABG	coronary artery bypass graft
CHARM	Candesarten in Heart failure: Assessment of Reduction in Mortality and morbidity
CI	confidence interval
COMPANION	Comparison of medical therapy, pacing and defibrillation in heart failure
CV	coefficient of variation
D	pulmonary venous diastolic velocity
DT	deceleration time of early mitral inflow
E	early diastolic mitral valve inflow velocity
Ea	early diastolic tissue Doppler velocity of the mitral annulus
ECG	electrocardiogram
E:A ratio	early to late filling ratio
E:Ea ratio	ratio of mitral early filling velocity to early mitral annular velocity
E:Vp	ratio of mitral early filling velocity to mitral flow propagation velocity
EF	ejection fraction
FS	fractional shortening
GP	general practitioner
GTN	nitroglycerin
HF	heart failure
IHD	ischemic heart disease
IVRT	isovolumic relaxation time
JVP	jugular venous pressure
LA	left atrium/atrial
LOA	limits of agreement
LV	left ventricle/ventricular
LVEDP	left ventricular end-diastolic pressure
LVEDV	left ventricular end-diastolic volume

LVESV	left ventricular end-systolic volume
LVH	left ventricular hypertrophy
LVIDd	left ventricular end-diastolic internal dimension
LVO	left ventricular opacification
MI	myocardial infarction
MV	mitral valve
NT-proBNP	N terminal pro brain natriuretic peptide
NPC	natriuretic peptides in the community study
non-RFP	non-restrictive filling pattern
NYHA	New York Heart Association
PCWP	pulmonary capillary wedge pressure
PN	pseudonormal
pmol/l	picomoles per litre
PTT	pulmonary transit time
PV	pulmonary veins
PV AR	pulmonary veins atrial reversal
PW	pulsed wave
RFP	restrictive filling pattern
ROC	receiver operating characteristic
S	pulmonary venous systolic velocity
Sa	systolic tissue Doppler velocity of the mitral annulus
Tau	time constant of relaxation
TDI	tissue Doppler imaging
THI	tissue harmonic imaging
VO_2	oxygen uptake
Vp	mitral flow propagation velocity
WMSI	wall motion score index
2D	two-dimensional
3D	three-dimensional