Utility of cardiac magnetic resonance imaging after ST-segment elevation myocardial infarction and in-lab predictors of microvascular dysfunction

A thesis submitted by

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BSc (Med), MBBS (Hons), FRACP

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THESIS SUMMARY

In this thesis, our aims were to address some specific novel areas advancing the utility of cardiac magnetic resonance (CMR) imaging in three major areas of interest. These areas included the utility of CMR early after STEMI, assessment of infarct size and microvascular obstruction post ST-segment elevation myocardial infarction (STEMI) by CMR and 'in-lab' predictors of 'no-reflow' phenomenon.

The introduction of this thesis included 3 review articles. The first review article summarised the evolution of treatment strategies for STEMI over the last few decades. In our second review article, we reviewed the role of CMR after acute myocardial infarction. We highlighted the potential of CMR in offering the prospect of performing a 'triple vital assessment' of left ventricular remodelling, ischemia in the non-culprit territory and myocardial viability after acute myocardial infarction. In our third review article, we reviewed the 'no-reflow' phenomenon. In this review article, we summarised the diagnosis, pathophysiology and treatment of the 'no-reflow' phenomenon.

In our results section, we included five original articles. In our first original article, we set out to determine the safety and utility of adenosine stress CMR post STEMI. As up to 40% of patients presenting with STEMI have multivessel disease, it is important to have a safe and accurate assessment of non culprit territory stenosis. Visual assessment of adenosine stress CMR is

routine clinical practice. However, the semi-quantitative assessment of adenosine stress CMR based on myocardial perfusion reserve index (MPRI) has never been tested in patients post STEMI. We found that adenosine stress CMR allowed accurate detection of non-culprit territory stenosis in patients successfully treated with primary percutaneous intervention post STEMI. We also found that semi-quantitative analysis may be required for improved accuracy.

In our second original article, we continued to assess the utility of CMR early after STEMI. We addressed the ongoing debate about which is the best method for quantifying microvascular obstruction (MVO) on CMR. The established methodology of first pass perfusion technique (early MVO) has previously been compared to the late gadolinium enhancement technique (late MVO). Nonetheless these methods were never compared against the semi-quantitative assessment of resting and stress myocardial blood flow in the infarct region. We found that of all the characteristics of microvascular injury studied, CMR-derived extent of late MVO was the strongest predictor of LVEF at 90 days following STEMI. We also reported for the first time that quantitative CMR perfusion assessment of resting and stress infarct region myocardial blood flow correlates strongly with left ventricular function 90 days post-primary PCI.

In our third original article we sort to validate a simple and novel 'in-lab' tool, intracoronary-ECG as an accurate predictor of myocardial injury. We aimed to define the most robust and accurate method for defining ST-segment resolution on intracoronary-ECG (IC-ECG). Previous studies have used

different cut-offs such as >1mm, >50% and > 2mm to define ST-segment resolution on intracoronary ECG. However no studies have compared the different cut-offs against infarct size evaluated on cardiac MRI. To achieve this in our study, we assessed 4 different methodologies for defining ST-segment resolution on IC-ECG at 2 time points during primary-PCI. We then assessed scar mass and left ventricular function on CMR. Myocardial injury was assessed by biochemical analysis (peak CK) and CMR. The primary end-point of this study was infarct size on CMR. We found that the degree of early intracoronary ST-segment resolution (defined by IC-STR > 1-mm or <30%) successfully predicts myocardial damage following primary angioplasty for an acute STEMI.

Having established our technique and the most accurate method to define ST-segment resolution on IC-ECG, we then sort to compare IC-ECG with other established angiographic assessments of 'no-reflow' such as TIMI myocardial perfusion grade (TMPG) and myocardial blush grade (MBG) for assessment of microvascular obstruction (MVO). Previous studies have reported the correlation between TMPG and MBG with MVO. However no studies have compared the three 'in-lab' predictors of microvascular obstruction. In our study, we found that intracoronary-ST-segment resolution is a strong 'in-lab' predictor of MVO assessed 4 days after STEMI on CMR. Furthermore, IC-STR correlates with infarct size and left ventricular remodelling at 3 months.

In our fifth and last original research chapter, we assessed the hypothesis that CMR utilising grid-tag myocardial strain evaluation and late

gadolinium enhancement can characterise peri-infarct left ventricular dysfunction and identify patients at risk of ventricular arrhythmia. As previous studies have demonstrated that re-entrant ventricular tachycardia commonly originates from the peri-infarct region which may precipitate cardiac arrest, identification of these regions by CMR would provide incremental prognostic value beyond left ventricular volume or ejection fraction. In addition, we also sort to determine the effect of MVO and transmurality of scar mass on regional systolic and diastolic strain. We found that grid-tagged CMR-derived myocardial strain accurately characterises the mechanical characteristics of 'border zone' peri-infarct region. The presence of 'border zone' peri-infarct region was strongly associated with a recognised surrogate marker of heightened risk of ventricular arrhythmia.

Thus, in summary, we have confirmed the utility of CMR after acute myocardial infarction. We also confirmed the best methodology for quantification of MVO on CMR and correlated this with 'in-lab' predictors of MVO. In addition, we established the best criterion for defining ST-segment resolution on IC-ECG and correlated this criterion with MVO. The potential utility of this simple and novel 'in-lab' predictor of MVO requires further evaluation in future studies. Specifically, the work in this thesis has led to enthusiasm utilising 'in-lab' predictors for early identification of patients at high risk of 'no-reflow' during primary-PCI to potentially investigate future adjunctive therapies.

In this thesis, our aims were to address some specific novel areas advancing the utility of cardiac magnetic resonance (CMR) imaging in three major areas of interest. These areas included the utility of CMR early after STEMI, assessment of infarct size and microvascular obstruction post ST-segment elevation myocardial infarction (STEMI) by CMR and 'in-lab' predictors of 'no-reflow' phenomenon.

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DECLARATION

Name: Dennis Thiam Leong Wong Program: Doctor of Philosophy

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ACKNOWLEDGEMENTS

This thesis is a summary of my PhD journey filled with lots of memories and lessons learnt. This journey has reminded me that we learn the most from adversities and through trials and tribulations, we emerge wiser and stronger. The most important lesson I have learned is that in everything that I do, I should do it for God's glory and not my own. It took me 18 months to learn this valuable lesson and since then God has blessed my research journey abundantly, more than I can ever ask for or comprehend. This thesis would not have been possible without God's blessings and strength.

My wife, Jessica, has been my tower of strength and pillar of support. It would not have been possible juggling research, clinical work and having a young family without her selfless sacrifice of showering our daughters Chloe and Audrey with love and the attention they so deserve. To Chloe and Audrey, you are God's greatest gift to me and I love you dearly. To my mother-in-law, Vivien, thank you for your sacrifice of loving and caring for Chloe and Audrey. It would not have been possible for Jess and I to complete our theses without your help. To my mum and dad, thank you for your life long sacrifice of providing me with the best education. Your selfless sacrifice of sending me to medical school in Australia has empowered me to achieve greater heights.

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ABSTRACTS ARISING FROM THE THESIS

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PRESENTATIONS ARISING FROM THE THESIS

Cardiac Society (CSANZ) 2012 Oral Presentation

"Myocardial Grid-Tagging Is a Superior Predictor of Myocardial Viability than Late Gadolinium-Enhanced Magnetic Resonance Imaging Post STEMI"

SA Heart Cardiology Research Scholarship 2011 Presentation

"Cardiac magnetic resonance derived late microvascular obstruction assessment post ST-segment elevation myocardial infarction is the best predictor of left ventricular function: a comparison of angiographic and cardiac magnetic resonance derived measurements"

American Heart Association (AHA) 2011 -Oral Presentation

"Intracoronary ECG is novel predictor of myocardial injury and hyperaemic blood flow following primary coronary intervention: insights from a cardiac MRI study"

Nimmo Professor Prize for Part Time Research 2011 Oral Presentation

"TIMI Myocardial Perfusion Grade predicts myocardial salvage index: Insights from a cardiac MRI study"

RACP Trainee Research 2011 Award Oral Presentation

"Intracoronary ECG during Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction Predicts Microvascular Obstruction and Infarct Size"

Cardiac Society (CSANZ) 2010 Oral Presentation

"Intracoronary ECG during Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction Predicts Microvascular Obstruction and Infarct Size"

Cardiac Society (CSANZ) 2010 Oral Presentation

"Diagnostic Accuracy of Adenosine Stress Cardiac MRI (CMR) Following Acute ST Elevation Myocardial Infarction Post Primary Angioplasty Utility of Adenosine Stress MRI"

PRIZES ARISING FROM THE THESIS

SA Heart Cardiology Research Scholarship 2011 (Winner)

CSANZ McCredie / Wilcken AHA Travelling Fellowship 2010 (Top Ranked Candidate)

Nimmo Professor Prize for Part Time Research 2010 (Winner)

Genesis Research Award 2010 (Winner)

RACP Trainee Research Award 2010 (Winner)

SA Heart Cardiology Research Scholarship 2010 (Winner)