

# **ATRIAL ARRHYTHMOGENESIS DURING MYOCARDIAL INFARCTION**

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**To my children Ali & Rami  
and my mum Jamilah**

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## Abstracts

Atrial fibrillation (AF) is the most common cardiac arrhythmia encountered in the clinical practice. However, the underlying mechanism or pathophysiology is not fully understood despite our extensive research on AF. Furthermore, AF is commonly complicated by myocardial infarction (MI) with an incidence rate as high as 22%. Atrial fibrillation is also associated with poor short and long-term outcome after acute myocardial infarction. Although the association between myocardial infarction and AF is well established, our knowledge of the underlying mechanism by which MI leads to AF remains incomplete. This thesis focused on the pathophysiology of AF during MI in the clinical and bench-side setting. It also examined the prognostic value of AF post MI.

Chapter 2 is a systematic review and meta-analysis showing us the trend in AF incidence and prognosis over the last three decades with our advancement in both intervention and pharmacological therapy. The study reveals a significant declining in AF incidence post MI; however, mortality remains higher compared to non-AF even during the interventional era (2000s). This may be attributed to the fact that AF patients are older with more comorbidities and had less invasive procedures compared to non-AF patients but clearly more work is required in this area.

Chapter 3 focused on the mechanism of AF during the acute phase (60 minutes) of myocardial infarction. This was ovine model of myocardial infarction which was induced by percutaneous approach via the right femoral artery using angioplasty technique to induce infarct. The study involved 36 sheep divided into 3 groups; the first group included 12 animals with proximal left circumflex occlusion (LCX) to induce myocardial infarction with left atrial infarction or ischaemia. The second group included 12 animals with proximal occlusion of the left anterior descending artery (LAD) to induce myocardial infarction without left atrial ischaemia or infarction, and the third group included 12 sham animals which underwent the same procedure without induction of myocardial infarction. This model was unique as both LAD and LCX supply almost equivalent myocardium but the LCX only supplies the left atrium. The study found that occlusion of the LCX (MI with LA ischaemia) resulted in significant conduction slowing, greater

inhomogeneity in conduction and more AF inducibility and duration compared to LAD group or controls. On the other hand, occlusion of LAD resulted in only moderate conduction slowing with a slight inhomogeneity in conduction compared to controls. The study concludes that atrial ischaemia is the dominant substrate for AF after MI. However, there is additional contribution to this substrate due to raised intra-atrial pressure with diastolic dysfunction which is associated with left ventricular infarction.

Chapter 4 examined the role of atrial branches (left atrial ischaemia) disease on AF genesis during acute myocardial infarction in humans. This is a case-control study in which cases and controls were selected from a pool of 2460 patients who presented with AMI between 2005 and 2009. A total of 42 patients with left atrial branches disease (proximal lesion in right coronary artery or left circumflex artery) were matched with 42 control patients (MI patients with lesion distal to the left atrial branches). Both groups were also matched for left ventricular ejection fraction, age and sex. The study concluded that coronary artery disease affecting the atrial branches was an independent predictor for the development of atrial fibrillation after MI.

Chapter 5 focused on characterisation of left atrial remodeling of patients with coronary artery disease affecting the left atrial branches (atrial ischaemia) after AMI. In this case-control study, 26 consecutive patients with acute myocardial infarction and coronary artery lesion affecting the left atrial branches were matched with another 26 patients with MI without LA branches disease according to age, sex, body mass index and left ventricular ejection fraction. The study highlighted the importance of left atrial branches disease or atrial ischaemia results in left atrial structural remodeling characterised by atrial enlargement and this was independent of end diastolic pressure load (1), age, sex or left ventricular ejection fraction. It provides further evidence for the importance of atrial ischemia to the development of the substrate for AF.

Chapter 6 looked at the association between new onset AF and post MI ventricular fibrillation and the long-term outcome. From a prospectively collected cohort of 3200 patients with MI, 96 patients with new onset AF were matched 1:3 with 288 patients with no AF on the basis of left ventricular ejection fraction. The incidence of VF arrest during admission and long-term mortality was significantly higher in AF patients independent of LVEF.

In summary, AF post MI remains a poor prognostic indicator despite our advancement in intervention and pharmacotherapy. Although AF patients are usually older with multiple comorbidities, AF remains an independent predictor of poor outcome after MI. This is probably related to the total ischaemic burden (involvement of left atrium) and rapid ventricular rate in already compromised ischaemic myocardium. The mechanisms of AF during MI are a combination of atrial ischaemia or infarction, atrial stretch due to raised end diastolic pressure with diastolic dysfunction during MI. In addition, there may be neurohumoral and autonomic factors that play an additive role in the pathophysiology of AF in patients with MI. Finally, the management of AF post MI is suboptimal with lack of evidence-based medicine. Further studies require determining the optimal antiarrhythmic as well as the best anticoagulation regime, especially in those who require dual antiplatelet therapy.

## **Declaration**

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

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Muayad Alasady

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# Publications and Communications to Learned Societies

## Chapter 1:

1. **Manuscript:** Lau DH, Alasady M, Brooks AAG, Sanders P. New-onset atrial fibrillation and acute coronary syndrome. **Expert Reviews: Cardiovascular Therapeutics 2010; 8: 941-948.**

## Chapter 2:

1. **Manuscript:** Muayad Alasady, MBChB;<sup>1</sup> Walter P. Abhayaratna MBBS, PhD;<sup>2,3</sup> Rajeev Pathak, MBBS;<sup>1</sup> Nicholas Chia;<sup>1</sup> Abhinav Mehta, MActSt;<sup>2</sup> Rajiv Mahajan, MD;<sup>1</sup> Han S. Lim; MBBS, PhD;<sup>1</sup> Dennis H. Lau, MBBS, PhD;<sup>1</sup> Stephen J. Nicholls, MBBS, PhD;<sup>1</sup> Matthew I. Worthley, MBBS, PhD;<sup>1</sup> Anthony G. Brooks, PhD;<sup>1</sup> Prashanthan Sanders, MBBS, PhD.<sup>1</sup> **Impact of Coronary Artery Intervention on the Incidence and Prognosis of Atrial Fibrillation after Acute Myocardial Infarction: A Systematic Review. Submitted to J Am Coll Cardiol 2014.**
2. **Presentation:** Presented at the Heart Rhythm Society 34<sup>th</sup> Annual scientific Meeting, May 2013, Denver, United States of America. *Heart Rhythm 2013;10: S307.*
3. **Presentation:** Presented at the Cardiac Society of Australia and New Zealand 60<sup>th</sup> Annual Scientific Meeting, August 2013, Gold Coast, Australia and published in abstract form (**Heart, Lung and Circulation 2012;21:S126-S127**).

## Chapter 3:

1. **Manuscript:** Muayad Alasady, MBChB;<sup>1</sup> Nicholas J. Shipp, PhD;<sup>1</sup> Anthony G. Brooks,<sup>1</sup> PhD; Han S. Lim, MBBS, PhD;<sup>1</sup> Dennis H. Lau, MBBS, PhD;<sup>1</sup> David Barlow;<sup>1</sup> Pawel Kuklik, PhD;<sup>1</sup> Matthew I. Worthley, MBBS, PhD;<sup>1</sup> Kurt C. Roberts-Thomson, MBBS, PhD;<sup>1</sup> David A. Saint, PhD;<sup>1</sup> Walter Abhayaratna, MBBS, PhD;<sup>2</sup> Prashanthan Sanders, MBBS, PhD.<sup>1</sup> **Myocardial Infarction and Atrial Fibrillation: Importance of Atrial Ischemia. Circulation: Arrhythmia and Electrophysiology. 2013; 6:738-745.**

2. **Presentation:** Presented at the Heart Rhythm Society 31<sup>th</sup> Annual scientific Meeting, May 2010, United States of America. Heart Rhythm 2010: 7: S420.
3. **Presentation:** Presented at the Cardiac Society of Australia and New Zealand 58<sup>th</sup> Annual Scientific Meeting, August 2010, Adelaide, Australia and published in abstract form (**Heart, Lung and Circulation 2010;19:S2**)
4. **Presentation:** Presented at the European Cardiac Society Congress, August 2010, Paris, France. European Heart Journal 2010: 31: S1041.
5. **Presentation:** Presented at the 3rd Asia Pacific Heart Rhythm Society Scientific session, October 2010, JeJu Island, South Korea. J Arrhythmia 2010: 26: 1.

#### Chapter 4:

1. **Manuscript:** Alasady M, Abhayaratna WP, Leong DP, Lim HS, Abed HS, Brooks AG, Mattchoss S, Roberts-Thomson KC, Worthley MI, Chew DP, Sanders P. **Coronary artery disease affecting the atrial branches is an independent determinant of atrial fibrillation after myocardial infarction. Heart Rhythm 2011 July, 8 (7):955-960.**
2. **Presentation:** Presented at the Heart Rhythm Society 28<sup>th</sup> Annual scientific Meeting, May 2010, United States of America. Heart Rhythm 2010: 7: S59.
3. **Presentation:** Presented at the Cardiac Society of Australia and New Zealand 58<sup>th</sup> Annual Scientific Meeting, August 2010, Adelaide, Australia and published in abstract form. (**Heart, Lung and Circulation 2010; 2: S98**)
4. **Presentation:** Presented at the European Cardiac Society Congress, August 2011, Paris, France. European Heart Journal 2010: 31: S113.

#### Chapter 5:

1. **Manuscript:** Alasady M, Leong DP, Lim HS, Roberts-Thomson KC, Brooks AG, Worthley MI, Chew DP, Sanders P, Abhayaratna WP. **Left atrial structural remodeling as a consequence of myocardial infarction: relationship to adverse cardiovascular outcome. Submitted to American Journal of Cardiology (2014)**
2. **Presentation:** Presented at the Heart Rhythm Society 28<sup>th</sup> Annual scientific Meeting, May 2012, Denver, United States of America. Heart Rhythm 2010: 7: S217.



3. **Presentation:** Presented at the Cardiac Society of Australia and New Zealand 58<sup>th</sup> Annual Scientific Meeting, August 2010, Adelaide, Australia and published in abstract form (**Heart, Lung and Circulation 2010; 19:S188**)
4. **Presentation:** Presented at the European Cardiac Society Congress, August 2010, Stockholm, Sweden. European Heart Journal 2010: 31: S739-740.

#### **Chapter 6:**

1. **Manuscript:** Muayad Alasady, MBBS; Derek Chew, MBBS, MPH; Rajeev Pathak, MD; Rajiv Mahajan, MD; Anthony G. Brooks, PhD; Han S. Lim, MBBS, PhD; Dennis H. Lau, Kurt C. Roberts-Thomson, MBBS, PhD; Stephen J. Nicholls, MBBS, PhD; Matthew I. Worthley, MBBS, PhD; Walter Abhayaratna, MBBS, PhD; Prashanthan Sanders, MBBS, PhD. **New Onset Atrial Fibrillation is associated with Ventricular Fibrillation and Poor Long Term Outcomes after Myocardial Infarction. Submitted to Heart Rhythm Journal 214.**
2. **Presentation:** Presented at the Heart Rhythm Society 29<sup>th</sup> Annual scientific Meeting, May 2011, Boston, United States of America. Heart Rhythm 2011: 8: S138.
3. **Presentation:** Presented at the Cardiac Society of Australia and New Zealand 58<sup>th</sup> Annual Scientific Meeting, August 2010, Adelaide, Australia and published in abstract form (**Heart, Lung and Circulation 2010;19:S97-S98**).

## **Prizes and Award during Candidature**

1. Ralph Reader Prize (Young Investigator Award-Finalist) at the Cardiac Society of Australian and New Zealand 58<sup>th</sup> Annual Scientific Meeting 2010.
2. Best Paper Award Prize (3<sup>rd</sup> prize) at the 3<sup>rd</sup> Asia Pacific Heart Rhythm Scientific Meeting 2010.
3. Nimmo Prize , Royal Adelaide Hospital 2010.
4. National Health and Medical Council Postgraduate Scholarship 2009-2011.
5. National Heart Foundation Travel Grant 2010
6. Highest scoring abstract at the Annual Scientific Sessions of the Heart Rhythm Society 2010.
7. Dawes Scholarship, Royal Adelaide Hospital; 2008-2010
8. Earl Bakken Electrophysiology Scholarship from the University of Adelaide; 2008-2009.
9. Divisional Scholarship, University of Adelaide; 2008-2009.