# Mechanisms of dyspnoea and poor exercise tolerance in a representative cohort of elderly patients with a relatively normal ejection fraction on echocardiography

Thesis submitted by

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# Publications and Presentations

## Publications and presentations related to the thesis

**Mahadevan G**, Davis RC, Frenneaux MP, Hobbs FDR, Lip GYH, Sanderson JE, Davies MK Viewpoint: Left ventricular ejection fraction – are the revised cut-offs for defining systolic dysfunction sufficiently evidenced based? *Heart*. 2008 Apr; 94(4): 426-8 (Review).

T T Phan, K Abozguia, G Nallur Shivu, **Mahadavan G**, I Ahmed, L Williams, M Frenneaux. Left ventricular torsion and strain patterns in heart failure with normal ejection fraction are similar to age-related changes. *European Journal of Echo Advance Access.*

T T Phan, K Abozguia, G Nallur Shivu, **G Mahadevan**, I Ahmed, L Williams, M Frenneaux Heart Failure with Preserved Ejection Fraction is characterized by dynamic impairment of active relaxation and contraction of the left ventricle. *J Am Coll Cardiol.* 2009 Jul 28; 54(5):402-9.

**Mahadevan G**, DwivediG, WilliamsL,SteedsRP, Frenneaux M. Epidemiology and diagnosis of heart failure with preserved left ventricular ejection fraction: rationale and design of the study. *Eur J Heart Fail.* 2012 Jan;14(1):106-12

### Invited speaker

Asia Pacific Doppler Echocardiography Congress 2009. Presentation **When is fibrosis important?** Diastology Symposium 3D workshop.

### Oral presentation of abstract

**Mahadevan G**, Williams LKW, Marsh AM, Weaver R, Palin T, Campbell R, Hobbs FDR, Frenneaux MP. Community prevalence of heart failure with preserved ejection fraction. British Cardiac Society 2007 and CSANZ 2008.

### Accepted abstracts

**Mahadavan G**, Dwivedi G, Williams L,Frenneaux M. How valid are the ESC echocardiographic criteria in diagnosing heart failure with normal ejection fraction? European Society of Cardiology (ESC) Congress, Paris 2011.

T T Phan, K Abozguia, G Nallur Shivu, **M Gnanadevan**, I Ahmed, L Williams, U Naidoo, R Weaver, M Frenneaux. Abnormal diastolic filling during dynamic exercise associated with impaired myocardial high energy phosphate kinetics in patients with heart failure with preserved ejection fraction (HFpEF): European Society of Cardiology (ESC) Congress 2008.

Thanh T. Phan, Ganesh Nallur Shivu, Khalid Abozguia, **Mahadevan G**, Ibrar Ahmed, Abdul Maher, Rebekah Weaver, Ross Campbell, Kunal Chudasama, Simon Anderson, Mohammad Nassimizadeh, Michael Frenneaux. Reduced cardiac energetics associated with impaired active relaxation during exercise in patients with heart failure with a preserved ejection fraction (HFpEF). American College of Cardiology. 2008.

# Declaration

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Signed …….

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# Abstract

Heart failure and preserved ejection fraction (HFpEF) is a syndrome that has experienced increasing interest over the last two decades, as there have been significant limitations in defining, diagnosing and treating the condition, as opposed to the great strides made in treating heart failure and reduced ejection fraction (HFrEF).

The limitations are related to the incomplete characterization of the affected individuals in epidemiological studies due to the lack of robust definitions for the syndrome, as well as the lack of easy to use and widely available investigational tools.

Most of the investigational tools measure resting cardiac physiological abnormalities, but the predominant symptom of HFpEF is exertional breathlessness, and therefore a robust investigational tool should be able to measure abnormal exercise physiology.

The contribution of subtle systolic impairment, despite a preserved overall ejection fraction to the pathophysiology of HFpEF, has not been fully established, which adds to the overall difficulties in diagnosis and establishing therapeutics.

The aims of this thesis were therefore to:

- establish the community prevalence and population characteristics of HFpEF
- determine the extent of correlation between the presence of abnormal exercise physiology of presumptive cardiac cause and that of impaired left ventricular relaxation/filling at rest
- determine whether minor impairment of left ventricular systolic function may represent a substantial contributor to the development of dyspnoea.

The studies from this doctoral thesis have established that not all patients with dyspnoea and a preserved ejection fraction are cardiac limited and dyspnoeic patients in a community setting are a heterogeneous group. The true prevalence of HFpEF in a community setting was established, albeit underestimated for reasons that are outlined in the thesis. The dyspnoeic group also have significantly more resting diastolic abnormalities than asymptomatic individuals, but the degree of difference was not strongly associated with symptomatic status.

Combining diastolic abnormalities had an incremental impact in predicting dyspnoea, but a significant number of dyspnoeic patients did not have more than one diastolic abnormality.

The significant but weak correlation between abnormal exercise physiology and that of impaired left ventricular relaxation/filling at rest was established. The correlation improved when abnormal exercise physiology was fully characterized with cardio-pulmonary exercise testing.

Finally, the presence of subtle systolic impairment in patients who were dyspnoeic with cardiac limitation was established. Combining resting systolic and diastolic abnormalities improved the correlation with abnormal exercise physiology.

Research from this doctoral thesis has contributed to the epidemiology, diagnostic algorithms and pathophysiology of HFpEF. Clinically this will help define the syndrome and aid in finding suitable therapeutics for the syndrome.