



## RACP Foundation Research Awards

### YEAR 2 PROGRESS REPORT

<b>Project / Program Title</b>	Cardiovascular dysfunction in advanced liver failure and after liver transplantation	
<b>Name</b>	Dr Anoop N Koshy	
<b>Award Received</b>	2018 RACP NHMRC CRB Blackburn Scholarship	
<b>Report Date</b>	16 April 2020	
<b>Chief Investigator / Supervisor</b>	A/Prof Omar Farouque	
<b>Administering Institution</b>	The University of Melbourne	
<b>Funding Period</b>	Start Date:	1 February 2018
	Finish Date:	1 February 2021

#### PROJECT SUMMARY

Liver disease affects at least 20% of the population of Australia. Liver transplantation (LT) is the only curative treatment option for patients with life-threatening liver disease. It is well recognised that cardiovascular disease is one of the leading causes of morbidity and mortality in patients after LT. The scarcity of donor organs means that LT is a limited and valuable resource. Therefore, potential transplant candidates undergo detailed cardiac assessment prior to LT to exclude those with significant underlying cardiovascular disease. This study will examine a new approach to improve detection and early treatment of heart disease in LT candidates, which integrates screening with CT imaging of coronary arteries and assessment of heart function with stress testing. Follow-up CT imaging of heart arteries will be performed to assess if LT itself predisposes to rapid progression of coronary heart disease. Patients with advanced liver disease can also have structural changes in the heart that predispose them to heart failure before and after LT. We aim to further investigate this phenomenon called 'cirrhotic cardiomyopathy' and assess what cardiac abnormalities characterize this condition.

#### PROJECT AIMS / OBJECTIVES

- Report the burden of cardiovascular disease in patients undergoing liver transplantation
- Assess the role of an impaired cardiac reserve in the diagnosis of cirrhotic cardiomyopathy and hepatorenal syndrome
- Risk stratification of patients for noncardiac surgery including liver transplant
- Prospective study evaluating the progression of coronary artery disease in liver transplantation

## SIGNIFICANCE AND OUTCOMES

- We have demonstrated through the ANZLTR registry that cardiovascular death is the commonest cause of early mortality following liver transplantation. Cardiovascular mortality also occurs significantly later than non-cardiac aetiology of death highlighting the need for long-term cardiac follow-up in this cohort
- In our study of stress testing in liver transplant, we have shown that patients with an impaired cardiac reserve have a four-fold higher risk of developing a life-threatening condition called hepatorenal syndrome.
- We have demonstrated that QT-interval prolongation in patients undergoing liver transplantation significantly increases risk of cardiac arrest in this cohort and we propose a novel risk score to stratify patients at risk for these events
- Two studies have also demonstrated that post-operative atrial fibrillation following noncardiac surgery and following liver transplantation increases the risk of stroke
- We are also undertaking analyses of a prospective study assessing whether liver transplantation leads to accelerated atherosclerosis.

## PUBLICATIONS / PRESENTATIONS

### Publications

Koshy AN, Gow PJ, Han HC, et al. Cardiovascular Mortality Following Liver Transplantation: Predictors and Temporal Trends Over 30 Years. *Eur Heart J Qual Care Clin Outcomes*. Feb 3, qcaa009. 2020

Koshy AN, Ha FJ, Gow PJ, et al. Computed Tomography Coronary Angiography for Risk Stratification of patients prior to Non-cardiac Surgery: a systematic review and meta-analysis. *Heart*; Sep; 105(17): 1335-1342; 2019.

Koshy AN, Farouque OF, Gow PJ et al. Impaired cardiac reserve on dobutamine stress echocardiography predicts the development of hepatorenal syndrome. *Am J Gastroenterol*. 2019, Oct; B316(14309): 1-10; 2019

Koshy AN, Cailles B, Gow PJ et al. Inducible Left Ventricular Outflow Tract Obstruction in Patients Undergoing Liver Transplantation: Prevalence, Predictors and Association With Cardiovascular Events. *Transplantation*. 2020, March 10.1097/TP.0000000000003245.

Koshy AN, Hamilton G, Theurele J, et al. Perioperative atrial fibrillation after noncardiac surgery increases risk for stroke. *American Journal of Medicine*. 2019, Aug; S0002-9343(19): 30702-30708.

Koshy AN, Ramchand J, Farouque O. Functional Capacity Prior to Noncardiac Surgery. *Lancet*; 20, 393 (10181):1593, 2019

Koshy AN, Farouque O, Gow PJ. Diagnosis of Cirrhotic Cardiomyopathy: Role of an Impaired Cardiac Reserve. *Hepatology*. 2019, Nov; 11(2): 34-35.

### Abstracts

Koshy AN, Ko J, Farouque O, et al. Impact of liver transplantation on QT-Interval in patients with cirrhosis. *J Am Coll Cardiol*. 75(11):398. 2020

Koshy AN, Gow PJ, Han HC, et al. Diabetes is an independent predictor of sudden cardiac death following liver transplantation: Results from the Australian and New Zealand Liver Transplant Registry Over 30 years. *J Am Coll Cardiol* 75(11)3465. 2020

Ko J, Koshy AN, Farouque O et al. Effect of QT prolongation of ventricular arrhythmias and cardiac arrest following liver transplantation. *J Am Coll Cardiol*. 75(11):363, 2020

Koshy AN, Horrigan M, Gow PJ et al. Preoperative pulmonary hypertension is associated with risk of long-term major adverse cardiovascular events in patients undergoing liver transplantation. *J Am Coll Cardiol* 75(11): 2095. 2020

Enyati A, Koshy AN, Teh AW, et al. Post-operative atrial fibrillation following liver transplantation and association with adverse cardiovascular events. 75(11): 198. 2020

Enyati A, Koshy AN, Farouque O, et al. Long term risk of stroke in patients with new post-operative atrial fibrillation after liver transplantation. *J Am Coll Cardiol* 75(11): 403. 2020

Koshy AN, Gow PJ, Cailles B et al. Beta-blocker use is associated with an increased early risk of major adverse cardiovascular events after orthotopic liver transplantation. *J Am Coll Cardiol* 75(11): 1942. 2020

Koshy AN, Cailles B, Ramchand J, et al. *J Am Coll Cardiol*. Early Cardiovascular Mortality following Liver Transplantation: Temporal Trends from the Australian & New Zealand Liver Transplant Registry. *J Am Coll Cardiol Suppl*. Mar; 73(9): 1348; 2019

Koshy AN, Sajeev JS, Gow PJ et al. Impact of Cardiovascular Risk Factors on Survival after Liver Transplantation: Results from a Prospective Binational Multicentre Registry. *J Am Coll Cardiol Suppl*. , Mar; 73(9): 1848 2019

Koshy AN, Sajeev JS, Gow PJ et al. Role of Traditional Cardiovascular Risk factors in Predicting Long term Survival after Liver Transplantation. *Journal of Hepatology* 70 (1):e563; 2019

Koshy AN, Farouque O, Ramchand J, et al. *J Am Coll Cardiol*. Early Cardiovascular Mortality following Liver Transplantation: 30 year Temporal Trends from the Australian & New Zealand Liver Transplant Registry. *Journal of Hepatology* 70 (1):e563-e564; 2019

Koshy AN, Farouque O, Cailles B et al. Impaired cardiac contractile reserve on dobutamine stress echocardiography predicts development of hepatorenal syndrome. *Journal of Hepatology* 70(1); 346; 2019

Koshy AN, Farouque O, Cailles B et al. Impaired rise in cardiac output on on dobutamine stress echocardiography predicts development of hepatorenal syndrome. *J Am Coll Cardiol*. 73 (9):1614; 2019

Koshy AN, Farouque O, Cailles B et al. Impaired cardiac contractile reserve on dobutamine stress echocardiography predicts development of hepatorenal syndrome. *Journal of Hepatology* 70(1); 346; 2019

Koshy AN, Cailles B, Farouque O, et al. Cardiac Output Increases in End-Stage Liver Disease Proportional to the Severity of Liver Dysfunction. *Eur Heart J Suppl*. Oct; 40(1): 3466 2019

Cailles B, Koshy AN, Gow P, et al. Hepatorenal Syndrome: An Independent factor for Perioperative Cardiac Complications in Patients Undergoing Liver Transplantation. *Heart Lung Circ*. Suppl 2019

Koshy AN, Han HC, Teh AW et al. Atrial fibrillation after noncardiac surgery increases risk of stroke following noncardiac surgery. *Heart Lung Circ Suppl*. 2019

Cailles B, Koshy AN, Ko J, Farouque O et al.. Beta Blocker Use Increases The Risk of Perioperative Cardiac Events in Liver Transplant Patients. *Heart Lung & Circulation*. 2019, Jun; 1(28): 6. Pub Status: Published.

Cailles B, Koshy AN, Ko J, Gow PJ et al. Existing Models to Assess Perioperative Cardiac Risk Demonstrate Poor Predictive Validity in Patients Undergoing Liver Transplantation. *Heart Lung & Circulation*. 2019, Jun; 28(1): 429. Pub Status: Published.

Cailles B, Koshy AN, Ko J, Gow PJ, Farouque O et al.. Inducible left ventricular outflow tract obstruction is associated with a higher incidence of perioperative cardiac arrest in liver

transplantation. European Heart Journal Supplement. 2019, Oct; 40(1): 12. Pub Status: Published.

#### **ACKNOWLEDGEMENTS**

- Cardiac Society of Australia and New Zealand Young Investigator Cardiac Imaging Prize Finalist, Adelaide 2019
- European Association of Society of Liver: Young Investigator Prize, Vienna 2019
- National Heart Foundation Research and Collaboration Award, Awarded for Highest Ranked abstract at American College of Cardiology and research collaboration visit to UCSF 2019
- RACP Trainee Research Prize: Winner 2019 (co-author)