



## RACP Foundation Research Awards

### PROGRESS REPORT

<b>Project / Program Title</b>	Investigating the role of thrombosis biomarkers and prostheses geometry in the development and diagnosis of leaflet thrombosis following transcatheter aortic valve implant (TAVI)	
<b>Name</b>	Dr Hashrul Rashid	
<b>Award Received</b>	2020 RACP NHMRC Kincaid-Smith Scholarship	
<b>Report Date</b>	29/04/2021 – Year 1	
<b>Funding Period</b>	Start Date:	01/01/2020
	Finish Date:	31/03/2022

#### PROJECT SUMMARY

Severe aortic stenosis is stiffening of the aortic valve, which may lead to heart failure and death. It can be treated with transcatheter aortic valve implant (TAVI), usually through deploying a valve through the groin artery. Unfortunately, this valve may develop clot(s) at any time after insertion, with an incidence of 15 to 40% and may increase the risk of stroke. Echocardiography has been used to detect valve clots, but imaging artefact may impair visualisation of these clots. Computed tomography (CT) is highly accurate in detecting small sized clots on valve leaflets but it is a limited resource and it comes with the risk of contrast-related kidney impairment and radiation exposure. This research aims to predict which patients may develop valve clots. This allows 1) appropriate selection of patients requiring investigations, 2) reduction of unnecessary tests, 3) reduce the risks of regular CT to patients and 4) prevent stroke events.

One potential method to predict this is by measuring blood clotting markers, which is the first aim of the study. Blood samples are collected before the TAVI procedure, at discharge and at one month. Patients with valve clots may have higher levels of clotting markers such as D-dimer, similarly seen in patients with other clotting conditions. The shape of valve prosthesis may play a role in valve clots. Simulation studies have demonstrated abnormally shaped valve leads to leaflet damage and may lead to clot formation, but it has not been clearly demonstrated in real-world studies. With sophisticated 4-dimensional CT, our second aim is to determine the relationship between valve shape with developing valve clots.

#### PROJECT AIMS / OBJECTIVES

The aim of this study is to determine clinical, biochemical and prosthesis risk factors of developing leaflet thrombosis (LT) following transcatheter aortic valve implant (TAVI). This study will utilise 4-dimensional computed tomography (4DCT) to detect LT as it is highly accurate and allows volumetric assessment of LT. 4DCT also allows precise measurement of valve geometry and leaflet motion. Clotting biomarkers will be tested to determine its role in the pathophysiology and diagnosis of LT.

**To summarise, the main aims of this study are:**

- 1) To determine the role of clotting biomarkers in predicting and diagnosing LT.
- 2) To understand the pathophysiology and biomechanism of LT.
- 3) To determine the role of valve geometry (mal-expansion, circularity and depth) in the development of LT.

**Our main hypotheses are:**

- 1) Clotting biomarkers such as high D-dimer levels and platelet reactivity are associated with the development of LT.
- 2) Abnormal valve geometry (under-expanded valves, elliptical valves and deep implantation) is associated with the development of LT.

### SIGNIFICANCE AND OUTCOMES

Reduce risk of cerebrovascular events (CVE):

- Leaflet thrombosis (LT) following transcatheter aortic valve implant (TAVI) has been associated with CVE. Understanding the mechanism behind LT would allow earlier investigation and diagnosis of this condition. If detected early, this could reduce the risk of CVE by commencement of anticoagulation in suitable patients.

Promote longevity of TAVI prosthesis:

- LT is associated with earlier valve dysfunction and the need for future replacements. By detecting LT early, commencement of anticoagulation could prolong the longevity of these devices.

Reducing the risks of of regular computed tomography (CT):

- Even though CT is an accurate imaging modality, it comes with the risk of contrast nephropathy and radiation exposure. This project aims to predict patients who are at high risk of LT through abnormal clotting biomarkers. By selecting patients with high likelihood of LT, we can tailor our investigations and prevent harmful effects to our patients.

Prioritising investigations to reduce cost from unnecessary CT imaging.

- By selecting patients at high-risk of developing LT, we can prioritise investigation in these patients whilst prevent unnecessary CT scans in patients of low-risk of developing LT. This would be beneficial from a logistic and financial perspective.

### PUBLICATIONS / PRESENTATIONS

#### AWARDS

1. RACP Australian Trainee of the Year 2020
2. RACP Trainee Research Award 2020
3. ANZET Early Career Research Prize 2020
4. CSANZ Cardiac Imaging Award 2020
5. SCCT Young Investigator Award 2020 (finalist)
6. ACC Young Investigator Award 2021 (competition pending)
7. RACP Fellow's Poster Prize 2021 (competition pending)

#### PRESENTATIONS

1. Invited Oral Abstract (ACC Young Investigator Award): Association between Prosthesis Geometry and LT following TAVI Rashid HN, Michail M, Tan S, Khav R, Cameron JD, Nasis A, Gooley RP Presented at American College of Cardiology Annual Scientific Meeting 2021. Abstract published in J Am Coll Cardiol.
2. Invited Oral Abstract (TCTAP Late-Breaking Trial): Association between Prosthesis Geometry and LT following TAVI

Rashid HN, Michail M, Tan S, Khav R, Cameron JD, Nasis A, Gooley RP Presented at Transcatheter Cardiovascular Therapeutics Asia Pacific 2021, Seoul. Abstract published in J Am Coll Cardiol.

3. Invited Oral Presentation: OCT-Guided PCI: Szabo's Technique in Ostial LAD Disease Rashid HN, Sapontis J, Brown AJ.

Presented at Australia NZ Endovascular Therapeutics 2020, Brisbane.

4. Invited Oral Abstract (CSANZ Cardiac Imaging Prize - winner): Clinical Impact and Predictors of LT following TAVI

Rashid HN, Michail M, Tan S, Khav R, Cameron JD, Nasis A, Gooley RP Presented at Australia NZ Endovascular Therapeutics 2020, Brisbane. Abstract published in Heart Lung Circ.

5. Invited Oral Abstract (ANZET Early Career Research Prize - winner): Prostheses Geometrical Predictors and LT following TAVI Rashid HN, Michail M, Tan S, Khav R, Cameron JD, Nasis A, Gooley RP Presented at Australia NZ Endovascular Therapeutics 2020, Brisbane. Abstract published in Heart Lung Circ.

### **ACKNOWLEDGEMENTS**

I am extremely grateful at the support given to me by RACP. To receive one of the most prestigious PhD scholarship in the country is an honour and I have worked hard to ensure I fulfilled the trust given to me. I have strived hard and I have been very fortunate to have been awarded numerous research accolades. I have notably mentioned RACP in all of these prizes as I am eternally grateful to this foundation.