**Research Protocol**

**STUDY TITLE**

*“A retrospective cohort study to evaluate outcomes in carotid endartertomy vs carotid artery stenting in carotid artery disease”*

**STUDY INVESTIGATOR(S)**

# Principal Investigator (A): Dr Rebekah Tan

# Ph: 0416009979

# Email: Rebekah\_2104@hotmail.com

# Principal Investigator (B): Dr Kishore Sieunarine

1. Royal Perth Hospital, Perth WA.
2. Hollywood Private Hospital, Perth WA.
3. Joondalup Health Campus, Perth WA.
4. St John of God Hospital, Murdoch, WA.

**1. BACKGROUND**

Stroke is the most common life-threatening neurologic disorder and the most important single cause of disability1-2. In patients with atherosclerotic internal carotid artery stenosis, distal embolization arising from degenerative break down or thrombotic occlusion of complex plaques are important mechanisms of stroke2. Carotid endarterectomy (CEA) is an established and effective treatment for both symptomatic and asymptomatic patients3-4. It is considered to the standard of care for the primary and secondary prevention of stroke related to carotid artery stenosis. Carotid artery stenting (CAS) is another option for treatment that is less invasive and is increasingly used in place of CEA. Although some case-series, industry sponsored registries and randomised controlled trials have indicated that CAS can be performed with acceptable complication rates, a high incidence of emboli shed to the brain has generated great concern regarding the safety of this technique, especially when considering the established low risk and durability of CEA3-4. Nonetheless, the results of randomised trials comparing prevalence of micro-emboli post CEA and CAS are still conflicting.

The ECA can be an important collateral for cerebral perfusion in patients with high grade ICA stenosis5-6. Another observed phenomenon is the increased risk of external carotid artery (ECA) stenosis or occlusion after interventions for common carotid artery and ICA that covers the ECA origin5-8. The incidence of ECA stenosis is between 5-11% after carotid endarterectomy. Comparably, there are higher rates of stenosis and progression of pre-existing stenosis in the ECA after ICA stenting5. There are very few studies describing the natural history of ECA patency after ICA interventions, as well identification of factors predictive of long –term ECA stenosis.

This multi-centre retrospective study compares the outcomes of CEA vs CAS using diffusion-weighted magnetic resonance imaging (DW-MRI), a sensitive tool in identifying new ischaemic cerebral lesion caused by emboli9. The secondary goal of this study is to evaluate ECA patency after ICA interventions and identify factors contributing to ECA stenosis.

**2. AIM(S) OF STUDY**

To compare the incidence of new ischemic lesions after both CEA and CAS and to define the role of DWI in identifying this adverse outcome.

**3. OBJECTIVES**

The primary objective of this study is:

1. to compare the prevalence of microembolic events using DW-MRI, after CAS vs CEA among patients with symptomatic or asymptomatic extracranial carotid stenosis.

The secondary objectives of this study are:

1. to compare the rates of stenosis and progression of pre-existing stenosis in the external carotid artery after CAS vs CEA
2. to compare patient outcomes with regards to timing of intervention after symptom and referral.

**4. HYPOTHESIS**

1. Null hypothesis: the outcomes for both CAS and CEA are equivalent
2. CAS as opposed to CEA is associated with a significantly greater incidence of any new DWI ischaemic lesion.
3. CAS as opposed to CEA is associated with higher rates of stenosis and progression of pre-existing stenosis in the external carotid artery
4. The shorter the time between initial presentation for symptomatic carotid stenosis and intervention, the better the outcome

**5. STUDY DESIGN**

In this muti-centre retrospective cohort study, patients who underwent either CAS or CEA performed by one vascular surgeon between the years 2006 and 2018 are included. Pre- and post-operative DW-MRI were performed and compared in these patients and the number of new microemboli, size and location of lesions compared.

**6. STUDY POPULATION/ELIGIBILITY CRITERIA**

The study population will consist of those with symptomatic and asymptomatic carotid artery stenosis who underwent either CEA or CAS. The decision to offer either procedure to patients was made on a clinical basis by the primary surgeon.

Patients were considered to be symptomatic if they had had transient ischemic attack, amorusis fugax or a minor non-disabling stroke involving the carotid artery. Asymptomatic patients were offered intervention if they had angiography proven stenosis of >80%. All patients were optimized medically before their procedures. CT angiography was also used as assessment tool to determine plaque type.

Exclusion criteria included allergy to heparin, aspirin or clopidogrel, contraindication to MRI, intracranial hemorrhage, dementia or neurologic illness that might confound neurological evaluation.

**7. STUDY PROCEDURES**

All patients who underwent CEA and CAS received maximum medical therapy and were optimized pre-procedure. The pre-operative assessment included a demographics information form filled in by patients during the initial consult, neurological examination and DW-MRI. Post operatively, neurological examinations are conduction and DW-MRI repeated 2-14 days after the procedure to assess for any new ischaemic events.

All patients who underwent CEA or CAS will be entered into a database set up by the primary surgeon. Data collected will include patient demographics, results of pre- and post-operative DWI-MRI results of any carotid ultrasounds if performed, neurological examination and any adverse outcomes in the follow up period. Data collection will occur prospectively for which consent has been obtained from all patients.

Baseline characteristics of study population to be collected:

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| --- | --- |
| All patients with carotid disease who underwent carotid endarterectomy or carotid stenting | * Right, left sided or bilateral * Degree of stenosis in carotid operated on, stenosis in contralateral side * Time between diagnosis and operation * Any neurological symptoms at time of diagnosis/pre operatively |
| Patient demographics | * Age (DOB) * Sex * Comorbidities (including ischaemic heart disease, hypertension, hyperlipidaemia, diabetes, peripheral vascular disease CVAS/Strokes/TIAs, amuerosis fugax) * Smoker |
| Medical treatment | * Antiplatelet before procedure * During procedure – heparin/vasopressors * Antiplatelet after procedure |
| Procedural characteristics | * Surgical technique – CEA or CAS * Access site * Sheath and/or guiding catheter placement technique (over-the-wire/telecsoping/coronary) * Use of embolic protection * Stent design * Concomitant occlusive disease and management (baloon dilatation, stent placement, arterial dilator) * Complications (converted to open, dissection, obstructed blood flow to distal carotid artery) |
| Imaging | * Pre-operative Doppler ultrasound, CT angiography and/or DW-MRI * Post operative DW-MRI |
| Follow up | * Restenosis of internal carotid artery * Stenosis or progression of existing stenosis of external carotid artery * Any new neurological symptoms * Any complications * 1 and 3 months USS, I year follow up from surgery |

**8. STUDY OUTCOMES**

The primary outcome is new ischaemic lesions as diagnosed on post-operative DW-MRI.

Secondary outcomes include development of stenosis or progression of pre-existing stenosis in the external carotid artery, any stroke, TIA and/or myocardial infarction.

**9. STATISTICAL ANAYLYSIS**

The primary end point is the evidence of new ischaemic lesions on postoperative DW-MRI. Continuous variables will be expressed as the mean and standard deviation. Categoric data will be compared using the fisher exact test and summarized as absolute frequencies and percentages. An unpaired student t-test will be used to compare continuous variables between the two cohorts and statistical significance is defined as p<0.5.

Binary regression models to compare DW-MRI measures between the two groups will be used. Interactions between the effect of intervention type on the primary outcome measure and selected variables (age, symptomatic status, stent type) will be investigated and adjusted for any significant imbalances in baseline characteristic.

**10. ETHICAL CONSIDERATIONS**

The study will be conducted in full conformance with principles of the “Declaration of Helsinki”, Good Clinical Practice. All patients have provided written consent for the procedures and verbal consent for collection and use of data in this study. Data extraction will be carried for all recruited patients, information will later be de-identified and stored as a password protected electronic file.

Plans for publication/presentation of the findings of this study include:

* Presentation at the 2019 RACS conference
* Publication in a pier reviewed journal

**References**

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