

S RTP - Project Description Form #242

PART I:

Name of Schulich faculty member who will supervise the project Chrysi Bogiatzi

Supervisor's Schulich, Western, Hospital or Lawson Email chrysi.bogiatzi@lhsc.on.ca

Schulich Department Clinical Neurological Sciences

PART II - Project Description

Title of Project Periodontal disease and high-risk atherosclerosis features in patients with ischemic stroke: an imaging-based study

Background

Periodontal disease is now recognized as a significant risk factor for cardiovascular and cerebrovascular disease.(1) The PREMIERS study failed to show a significant association between intensive dental care and secondary stroke prevention.(2) However, the subgroup of patients with large artery disease seemed to benefit from intensive dental care in addition to their standard medical care. Stroke patients with large artery atherosclerosis are better served by measuring atherosclerosis burden with total plaque area in carotid ultrasound, to reclassify the patients who have symptomatic non-stenotic large artery disease.(3) This reclassification dictates a more intensive and personalized medical management, with the overall goal to reduce the probability of recurrent stroke related to atherosclerosis. Our clinical observation during the coronavirus pandemic suggested that the control of vascular risk factors has been sub-optimal, mainly due to barriers in accessing health care resources. The pandemic had also a negative impact in maintaining adequate dental health by reducing the amount of dental follow up visits. In addition, we have observed an increase in uncontrolled atherosclerosis and strokes related to large artery disease. It remains unclear if the pandemic had an effect on periodontal disease and high-risk atherosclerosis features.

References:

1. Sanz M, Marco Del Castillo A, Jepsen S, Gonzalez-Juanatey JR, D'Aiuto F, Bouchard P, et al. Periodontitis and cardiovascular diseases: Consensus report. *J Clin Periodontol.* 2020;47(3):268-88.
2. Sen S, Curtis J, Hicklin D, Nichols C, Glover S, Merchant AT, et al. Periodontal Disease Treatment After Stroke or Transient Ischemic Attack: The PREMIERS Study, a Randomized Clinical Trial. *Stroke.* 2023;54(9):2214-22.
3. Bogiatzi C, Wannarong T, McLeod AI, Heisel M, Hackam D, Spence JD. SPARKLE (Subtypes of Ischaemic Stroke Classification System), incorporating measurement of carotid plaque burden: a new validated tool for the classification of ischemic stroke subtypes. *Neuroepidemiology.* 2014;42(4):243-51.

Hypothesis

We sought to investigate the effect of periodontal disease to high-risk features of large artery atherosclerosis-related strokes before and after the pandemic. We hypothesize that the prevalence of periodontal disease has increased during the pandemic, leading to an increase in atherosclerosis burden and high-risk features of the carotid plaque composition in patients with ischemic strokes.

Proposed Methodology

This is a descriptive case-series study of patients who presented to the Urgent Transient Ischemic Attack (UTIA) clinic between 2017 and 2023. We will analyze the presence of periodontal disease in computed tomography (CT) and we will correlate this with the presence of high-risk atherosclerotic plaque features on carotid duplex ultrasound (CDU) during three years before (2017 - 2020) and after the onset of the pandemic (2020-2023). This data will create a new

database that will be used for further analysis.

Data Collection:

1. Computed Tomography: we will use non-contrast CT head to measure the number of teeth and the presence of periodontal disease. These two variables will be then combined into one final variable indicating the presence or the absence of periodontal disease.
2. Carotid Duplex Ultrasound: where available, we will record total plaque area (TPA), degree of stenosis (symptomatic versus asymptomatic) and plaque texture analysis (degree of carotid atheroma calcification, presence of ulceration or intraplaque hemorrhage, plaque contour and shape, presence of carotid web or dissection, spontaneous microemboli). All these variables will be then combined into one final variable indicating high-risk versus low-risk features of carotid atherosclerotic disease.
3. Additional clinical information: age, sex, ischemic stroke subtype, vascular risk factors (hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease, atrial fibrillation, heart failure, coronary artery disease, peripheral vascular disease), lifestyle (smoking, lack of physical activity, egg yolk consumption, number of vegetarian days), medications, clinical outcomes after 6 months of initial presentation (recurrent stroke/TIA, myocardial infarction, peripheral vascular disease, death due to vascular etiology), recent COVID infection or vaccination, presence of autoimmune and inflammatory disease.

Statistical analysis:

All analysis will be completed using SPSS. Multivariable logistic regression will be used to assess the effect of periodontal disease and high-risk carotid atherosclerosis on clinical outcomes, adjusting for potential confounders.

Expected Outcomes

Our primary outcome includes a composite of stroke, myocardial infarction, peripheral vascular disease and death from vascular etiology in patients who have periodontal disease and high-risk features of carotid atherosclerosis. Secondary outcomes include ischemic stroke subtypes, hypertension, dyslipidemia, diabetes mellitus, atrial fibrillation, heart failure, intracranial atherosclerosis, autoimmune and inflammatory disorders, medications and medication compliance, recent COVID infection or vaccination.

Research Environment - Description of the number of research personnel, primary location of research, size of lab, etc

A successful candidate will be provided with a computer station at the Stroke Prevention and Atherosclerosis Research Centre (SPARC) to complete the database and save all data into our confidential server. The created dataset will include merging data from the London Stroke Registry (LOSR) and the SPARC database to capture all patients who were seen at the UTIA clinic and their vascular risk factors. The first summer will focus on patients who presented to UTIA prior to the pandemic and the second summer will conclude the project by including the remaining cases who presented after the onset of the pandemic.

The SPARC unit has dedicated research sections on the main floor (2 stations) of the Siebens Drake building as well as the basement (1 station). Given the need for imaging processing in an environment with lower light exposure, we will dedicate our computer station at the basement to allow for better visualization of CTs and CDUs. Statistical analysis software (SPSS) will be added in our computer station to analyse the data and provide with the final report.

Our research unit current has a research coordinator (Leslie Paddock) who is also the manager of our lab. In addition, the clinical aspect of our unit includes two carotid ultrasound sonographers (Maria DiCicco and Janine DesRoches) who examine approximately 7 patients per day, and two transcranial Doppler rooms that are used by the two Neurologists on an as-needed basis. There are also 2 additional rooms for clinical examination of our patients.

Names and titles of other individuals who will be involved with the research project?

1. Primary Investigator: Dr. Chrysi Bogiatzi
2. Research coordinator: Leslie Paddock
3. Vascular ultrasound sonographer: Maria DiCicco
4. Vascular ultrasound sonographer: Janine DesRoches
5. Medical Student: TBD

Can this project be done remotely? No

Duration of Project Two Summers

Expected Objectives/Accomplishments for Student for Year 1?

Complete literature review and data entry for all cases between 2017 to 2020.

Expected Objectives/Accomplishments for Student for Year 2?

Complete data entry, by including the clinical cases between 2020 to 2023 and presentation of the results.

PART III - Certifications

If the project will require any certification - Human Ethics approvals from one or more of the following offices, please check the appropriate box below.

Human Ethics: If you have the protocol information, please enter it below (or enter the status of the approval). This study is pending approval from the local Ethics board.

Note: certification approval should be obtained prior to the start of the summer. Projects without this approval will not be a priority for funding.