Principal Investigator

First Name: Adnan
Last Name: Qureshi
Degree: MD
Primary Affiliation: University of Missouri
E-mail: qureshai@gmail.com

General Information

Key Personnel (other than PI):
First Name: Abdullah
Last name: Lodhi
Degree: MD
Primary Affiliation: University of Missouri, Columbia
SCOPUS ID:

First Name: Hamza
Last name: Maqsood
Degree: MD
Primary Affiliation: University of Missouri
SCOPUS ID:

First Name: Yilun
Last name: Huang
Degree: MA / MS / MSc
Primary Affiliation: University of Missouri
SCOPUS ID:

Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.
How did you learn about the YODA Project?: Colleague

Conflict of Interest

https://yoda.yale.edu/wp-content/uploads/2016/08/al.pdf
https://yoda.yale.edu/wp-content/uploads/2016/11/aiq.pdf
https://yoda.yale.edu/wp-content/uploads/2022/11/Coi_form_HM.pdf
https://yoda.yale.edu/wp-content/uploads/2022/11/coi_form_YH.pdf

Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

1. NCT00816166 - Phase III Study of Pharos Vitesse Neurovascular Stent System Compared to Best Medical Therapy for the Treatment of Ischemic Disease

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

Research Proposal

Project Title

Identification of Patients Who Can Benefit from Intracranial Stent Placement: analysis of Vitesse Intracranial Stent Study for Ischemic Stroke Therapy

Narrative Summary:

Intracranial atherosclerosis remains a major cause of ischemic stroke. Intracranial stent placement can reduce the risk of ischemic stroke by improving blood flow to the brain. The purpose of this study is to identify the patients who can benefit from stent placement. We will use the existing data to better understand the value of criteria including those specified by FDA in identifying high risk patients who may be considered for stent placement.

Scientific Abstract:

Background; Although previous randomized clinical trials have not shown a significant reduction in risk of ischemic stroke after intracranial stent placement in patients with symptomatic intracranial stenosis, there are patient subgroups which may potentially benefit from intracranial stent placement
Objective; To identify patient subgroups who may have a lower relative risk for primary outcome with intracranial stent placement compared with best medical treatment.
Study Design; Post hoc analysis of prospectively collected data as part of a randomized clinical trial
Participants; Patients with symptomatic high grade intracranial stenosis who were either treated with stent placement or best medical treatment.
Primary and Secondary Outcome Measure(s); 1/. Stroke or death within 30 days after enrollment; 2/. Ipsilateral stroke beyond 30 days; and 3/. Cumulative endpoint of stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or ipsilateral stroke beyond 30 days.
Statistical Analysis. We will perform Cox proportional hazards model to study the effect of treatment (stent placement versus best medical treatment) as a predictor of cumulative endpoint of stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or ipsilateral stroke beyond 30 days in the whole cohort.

Brief Project Background and Statement of Project Significance:

In 2005, the Wingspan intracranial stent system was approved under a Humanitarian Device Exemption (HDE). [1] The original indication was for treatment of refractory intracranial atherosclerotic disease with a stenosis of ?50% based on the results of a pilot study. [2] Due to higher than anticipated rates of 1-month stroke and death with Wingspan intracranial stent placement observed in the phase III Stenting Versus Aggressive Medical Therapy for Intracranial Arterial Stenosis (SAMMPRIS) trial, [3] the Food and Drug Administration (FDA) announced a more limited indication for Wingspan stent. On April 5, 2011, the trial's independent data and safety monitoring board recommended that enrollment be stopped because of safety concerns regarding the higher than anticipated risk of periprocedural stroke or death in the stent treated group which would prevent any chance (based on futility analysis) that a benefit from stent treatment would be identified at trial conclusion if enrollment continued. [2] In March 2012, the FDA advisory panel concluded that there was no evidence of benefit with use of the system in most patients with stroke or transient ischemic attack from intracranial stenosis. Some panel members believed that stent placement was still an important option for a small subset of patients. The FDA determined that the

Wingspan stent system remained an option for a more limited set of patients, specifically those with recurrent stroke despite medical management who have not had any new stroke symptoms within 7 days before treatment with Wingspan stent. [4] Recently, the results from the Wingspan Stent System Postmarket Surveillance (WEAVE) study were published. [5] The trial reported upon a total of 152 consecutive patients who met the FDA on-label usage criteria who underwent angioplasty and stenting with the Wingspan stent. The primary analysis reported a low rate of 2.6% for periprocedural stroke, bleed, and death rate within 72 hours of the procedure. However, the question remains regarding 1 and 12 month outcomes in such patients when treated with angioplasty and stent placement and when treated with high intensity medical treatment. We are proposing to reanalyze the data of the Vitesse Intracranial Stent Study for Ischemic Stroke Therapy (VISSIT) and compare the results of angioplasty and stent placement with best medical treatment in patients who would have met ?on label? criteria and those who would be considered ?off label? based on post-trial FDA advisory.

Specific Aims of the Project:

Specific aims
1. To identify patients who are most likely to benefit from intracranial stent placement after stratification based on criteria such as age, severity of stenosis, qualifying event (stroke versus transient ischemic attack) and time interval between qualifying event and procedure.
2. To determine whether using the FDA on label criteria can identify patients with lower ischemic stroke risk over 2 years compared with those who would be classified as off label when stent placement is compared with best medical treatment.
3. To perform a combined analysis with SAMMPRIS data to study the above-mentioned specific aims.
Hypothesis
We hypothesize that intracranial stent placement may reduce the risk of ipsilateral stroke compared with best medical treatment in certain patient subgroups of patients with symptomatic intracranial stenosis.

Study Design:

Individual trial analysis

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:

Inclusion criteria
We will be analyzing the data from VISSIT, which was an investigator-initiated randomized trial. We will include the following patients in our analysis:
1. Patients aged ? 22 years and ? 80 years, who suffered from transient ischemic stroke or stroke in less than 30 days prior to enrollment related to high grade (70% to 99% in severity) stenosis;
2. Stenosis is located in a major intracranial artery (internal carotid artery, proximal middle cerebral artery (M1), vertebral artery, or basilar artery).
3. Patients were randomized and completed both the trial intervention and clinical follow up.
Exclusion criteria
1. Patient with incomplete data;
2. Patients who were not compliant with allocated treatment.
Patients randomized in the VISSIT trial are divided into ?on label? and ?off label? based on clinical characteristics of patients at time of recruitment (see Table 1). All the other patients are classified as ?off label? (Table 1).
Table is attached in the document file attached.

Primary and Secondary Outcome Measure(s) and how they will be categorized/defined for your study:

The outcomes for study are:
1/. Stroke or death within 30 days after enrollment; 2/. Ipsilateral stroke beyond 30 days; and 3/. Cumulative endpoint of stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or ipsilateral stroke beyond 30 days between patients who were randomized to intracranial stent placement and those to best medical treatment alone.

Main Predictor/Independent Variable and how it will be categorized/defined for your study:

Effect of treatment (stent placement versus best medical treatment) as a predictor of cumulative endpoint of stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or ipsilateral stroke beyond 30 days in the whole cohort.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:

Age: ?22 years and ? 80 years versus ? 30 years and ? 80 years
Ischemic event: ?2 ischemic events in the vascular territory of the stenotic lesion with at least 1 ischemic event while on medical therapy versus Transient ischemic attack (TIA) or non-severe stroke within 30 days of enrollment
Stent placement: ?8 days after the last ischemic event versus ?1 days after last ischemic event

Statistical Analysis Plan:

We will perform Cox proportional hazards model to study the effect of treatment (stent placement versus best medical treatment) as a predictor of cumulative endpoint of stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or ipsilateral stroke beyond 30 days in the whole cohort. We will enter age and ?on label? status in the Cox proportional hazards model and test the interaction between ?on label? status and randomized to intracranial stent placement to identify any modifying effect of ?on label? status.
We will match the variables with SAMMPRIS data to create pooled data and perform the labove-mentioned analysis to validate the results with larger number of patients and determine any heterogeneity between balloon expandable stents or self-expanding stents.

Project Timeline:

Data acquisition and import into statistical software ?01 month
Data analysis and validation of results -02 months
Manuscript preparation ?02 months
Submission and publication -06 months

Dissemination Plan:

Provide a description of anticipated products and target audience(s), including expectation for study manuscript(s) and potentially suitable journals for submission of the completed research project.
The target audience is medical professionals involved in treating patients with stroke which include vascular neurologists, interventional neurologists, endovascular neurosurgeons, and neuroradiologists.
The target journals would be Stroke, Neurology, International Journal of Stroke, and Neurosurgery.

Bibliography:

1. Humanitarian Device Exemption (HDE). (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfhde/hde.cfm?id=h050001).
2. Bose A, Hartmann M, Henkes H, et al. A novel, self-expanding, nitinol stent in medically refractory

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3. Chimowitz MI, Lynn MJ, Derdeyn CP, et al. Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis. New England Journal of Medicine 2011;365(11):993-1003. DOI: 10.1056/NEJMoa1105335.
4. FDA Revises Indications for Use of Stryker's Wingspan Stent System. (https://evtoday.com/news/fda-revises-indications-for-use-of-strykers-win...).
5. Alexander MJ, Zauner A, Chaloupka JC, et al. WEAVE Trial: Final Results in 152 On-Label Patients. Stroke 2019;50(4):889-894. (In eng). DOI: 10.1161/strokeaha.118.023996.