## Original Article

# The Prevalence and Risk Factors of Significant Carotid Stenosis in Patients with Acute Ischemic Stroke in a Tertiary Hospital: A 5-Year Cross-Sectional Study

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**ABSTRACT:** The use of carotid duplex scan is recommended as part of routine screening among patients with acute ischemic stroke. Locally, however, significant stenosis is seldom seen and the rate of carotid intervention is low. This study aimed to: 1) find the prevalence of significant carotid stenosis; 2) identify risk factors for developing significant stenosis; and 3) detect the rate of carotid intervention among patients with acute ischemic stroke. A cross-sectional retrospective chart review was conducted among patients aged 18 years and above who suffered an acute ischemic infarct from January 2013 to August 2018 and were admitted at a Joint Commission International (JCI)-accredited tertiary hospital. Patients who did not undergo a duplex scan during admission were excluded. Data analysis was performed using Stata SE version 13. Quantitative variables were summarized as mean, median, and standard deviation, while qualitative variables as frequency and percentage. Factors associated with significant carotid stenosis were analyzed using logistic regression. The level of significance was set at 5%. Of the 1,607 patients admitted for acute ischemic stroke, 577 (35.9%) underwent a carotid duplex scan. Age ranged from 27-100 years, 56.67% were males, with a median National Institutes of Health Stroke Scale (NIHSS) of 3 and Modified Rankin Scale (MRS) of 0. Of the patients who underwent the duplex scan, 29 (5.0%) had significant carotid stenosis (70%). Only one underwent endarterectomy, and none underwent stenting. The most common risk factors for those with significant stenosis were hypertension (76%), smoking (38%), diabetes (34%) and alcohol (34%). On logistic regression, older age (OR 1.04, p=0.005) and higher NIHSS score (OR 1.07, p=0.026) were significant factors that increased the chance of having significant carotid stenosis. The prevalence of significant carotid stenosis among patients with acute ischemic stroke was low at 5% with risk factors including hypertension, smoking, and diabetes. In our cohort, the rate of carotid intervention was very low.

***Keywords:*** *carotid duplex scan, carotid stenosis, ischemic stroke*

## INTRODUCTION

Significant carotid stenosis (CS) is one potential source of an acute ischemic stroke, apart from the more common causes such as intracranial atherothrombosis, cardioembolic, and small-vessel diseases.[1] Acute stroke patients are worked up for possible etiologies and one of the procedures initially requested is a carotid duplex scan (CDS).[2] Woo et. al noted that the prevalence of atherosclerotic CS in Asian countries varies from one study to the other, ranging from 1.9-12.7% in males and 0.5-6.2% in females. In this study, the overall prevalence of acute ischemic stroke patients that had atherosclerotic CS was low at 1.1%.[3] There is no available local data on the prevalence of risk factors of significant carotid stenosis on acute ischemic stroke patients. There is a need to study the clinical profile of patients with significant CS and evaluate whether there are risk factors that can help identify patients who are at high risk. By doing so, we can refrain from requesting this procedure routinely, lessen hospital costs for these patients, and improve patient care. This study aimed to determine the clinical profile of acute ischemic stroke patients with significant CS. We hypothesized that the clinical profile of patients with significant CS is different from those with insignificant CS.

## METHODOLOGY

### Study design

The investigators conducted a cross-sectional retrospective chart review of patients who suffered an acute ischemic infarct from January 2013 to August 2018 who were admitted at a Joint Commission International (JCI)-accredited tertiary hospital. Review of stenting procedures and endarterectomy for acute ischemic stroke done at the operating room and catheter laboratory of the hospital was also done.

### Participants

Patients aged 18 years and above who were admitted between January 2013 to August 2018 for an acute ischemic stroke and who underwent a CDS and neuroimaging during the same admission were included in this study. The patients should have been referred to or admitted under the care of Neurology service. Patients with inaccessible CDS result and those with negative Magnetic Resonance Imaging (MRI) findings were excluded from the study. Figure 1 shows the study flow diagram.

### Study size

Using Epi Info Version 7, the minimum sample size requirement was set at 380 based on the percent significant

stenosis among patients with acute ischemic stroke =1% with margin of error = 1%.[3]

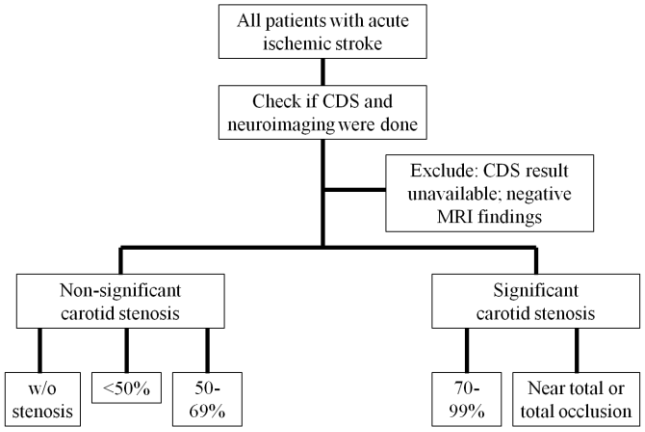


**Figure 1.** Diagrammatic framework of the study

## Variables

Acute ischemic infarct was defined as a sudden focal neurologic deficit with imaging-confirmed cerebral infarction.[4] Factors noted to be associated with developing significant carotid stenosis were included. Demographic profile such as age and gender were also taken into account.

To measure stroke severity, the modified National Institutes of Health Stroke Scale (NIHSS) was determined.[5] The individual scores from each item were added up, with a maximum possible score of 42 and a minimum score of 0. To assess the functional capacity of a person prior to the stroke, the Modified Rankin Scale (MRS) was used.[6] It is an ordinal scale with 6 categories ranging from 0 (no symptom) to 5 (complete physical dependence).

Co-morbidities were noted such as diabetes mellitus, hypertension, coronary artery disease, atrial fibrillation, dyslipidemia, and chronic kidney disease (CKD). Diabetes Mellitus was defined as a fasting blood sugar level of 7.0 mmol/L or a 2-hour plasma glucose value of >11.1 mmol/L.[7] Hypertension was defined as having a BP >140/90 mmHg.[8] Coronary artery disease was the narrowing of the coronary arteries due to plaque build-up that was noted on electrocardiogram (ECG) or coronary angiogram.[9] Atrial fibrillation was considered as a supraventricular arrhythmia confirmed by ECG showing an absence of P waves.[10] Dyslipidemia was defined as blood levels of total cholesterol >200 mg/dL.[11] Lastly, CKD was defined as abnormalities of kidney structure or function present for > 3 months with a GFR <60 ml/min.[12] Personal history of smoking, drinking alcoholic beverages, and using illicit drugs were also recorded. In this study, significant carotid stenosis was defined as stenosis of 70% or more of the internal carotid artery as reported on CDS. The presence of carotid stenosis was further classified into one of the following: <50%, 50-69%, 70-99%, and near total or total occlusion.

## Data measurement

Age, gender, handedness, NIHSS, MRS, past medical history, social history, CDS results, and neuroimaging results were gathered and recorded on a patient data form based on the details found in their medical records.

## Statistical methods

Data analysis was performed using Stata SE version 13. Quantitative variables were summarized as mean, median, and standard deviation, while qualitative variables as frequency and percentage. Factors associated with significant carotid stenosis were analyzed using logistic regression. The level of significance was set at 5%.

## Ethics and data privacy

This study underwent ethical and technical review and was approved by the Institutional review board (IRB) of the hospital. Data was kept confidential in accordance with the Data Privacy Act.

## RESULTS

A total of 1,607 patients were admitted due to an acute ischemic stroke between January 2013 to August 2018. Among these patients, 579 (36%) underwent a CDS. Results of the CDS were available for all patients, but there were two patients who had a negative MRI finding of stroke, hence these two were excluded. A total of 577 patients (35.9%) were included in the study.

Table 1 shows the characteristics of the subjects. Age ranged from 27-100 years with a mean of 60 years. There was a slight male preponderance (56.67%). Median NIHSS score was 3 and median MRS was 0. The most common comorbidities among those who had a CDS were hypertension and diabetes. More than half of the subjects were non-smokers and non-alcoholic beverage drinkers.

**Table 1:** Demographic characteristics of the subjects

| **Characteristics (N=577)** | **Mean ± SD or n (%) or Median (IQR)** | |
|---|---|---|
| Age in years | 59.75 ± 13.54 | |
| Gender | | |
| Male | 327 (56.67) | |
| Female | 250 (43.63) | |
| NIHSS | 3 (1 to 4) | |
| MRS | 0 (0 to 1) | |
| **Co-morbids** | **Present n (%)** | **Absent n (%)** |
| DM | 252 (43.67) | 325 (56.33) |
| HTN | 459 (79.55) | 118 (20.45) |
| CAD | 73 (12.65) | 504 (87.35) |
| Atrial Fibrillation | 64 (11.09) | 513 (88.91) |
| Dyslipidemia | 133 (23.09) | 443 (76.91) |
| CKD | 26 (4.51) | 551 (95.49) |
| Stroke | 139 (24.09) | 438 (75.91) |
| On Anticoagulant | 7 (1.22) | 569 (98.78) |
| On Antiplatelet | 87 (15.10) | 489 (84.90) |
| **Social History** | **Yes (%)** | **No (%)** |
| Smoker | 222 (38.47) | 355 (61.53) |
| Alcohol Drinker | 238 (41.25) | 337 (58.61) |
| Illicit Drug Use | 3 (0.52) | 574 (99.48) |

Of the patients who underwent CDS, only 29 (5.0%) had significant CS. Characteristics of patients with significant CS included the following: age ranged from 35-96 years; 18 were males and 11 were females; median NIHSS was at 3 and MRS at 0. Table 2 shows the characteristics of the 29 patients with significant stenosis. Of all these patients, only one underwent endarterectomy. No one was managed with stenting. The most common risk factors for those with significant stenosis were hypertension (76%), smoking (40%), and diabetes (36%).

**Table 2:** Demographic characteristics of patients with significant carotid stenosis

| Characteristics (N=29) | Present n (%) | Absent n (%) |
|---|---|---|
| **Co-morbids** | | |
| DM | 10 (34.48) | 19 (65.52) |
| HTN | 22 (75.86) | 7 (24.14) |
| CAD | 3 (10.34) | 26 (89.66) |
| Atrial Fibrillation | 4 (13.79) | 25 (86.21) |
| Dyslipidemia | 5 (17.24) | 24 (82.76) |
| CKD | 3 (10.34) | 26 (89.66) |
| Stroke | 7 (24.14) | 22 (75.86) |
| On Anticoagulant | 1 (3.45) | 28 (96.55) |
| On Antiplatelet | 4 (13.79) | 25 (86.21) |
| **Social History** | Yes (%) | No (%) |
| Smoker | 11 (37.93) | 18 (62.07) |
| Alcohol Drinker | 10 (34.48) | 19 (65.52) |
| Illicit Drug Use | 0 | 29 (100) |

Four hundred thirty seven patients (75.74%) had abnormal findings on CDS, while the rest of the 140 patients (24.26%) had a normal result. Patients with abnormal findings had predominantly bilateral ICA stenosis accounting for 77.12%, with majority having <50% stenosis (64.76%) (Table 3).

**Table 3**. Frequency of ICA stenosis based on severity

| Degree of ICA stenosis (N=437) | Right ICA (%) | Left ICA (%) | Bilateral ICA (%) |
|---|---|---|---|
| <50% | 55 (12.59) | 41 (9.38) | 283 (64.76) |
| 50-69% | 1 (0.23) | 0 | 27 (6.18) |
| 70-99% | 1 (0.23) | 0 | 11 (2.52) |
| Near total occlusion | 1 (0.23) | 1 (0.23) | 7 (1.60) |
| Total occlusion | 0 | 0 | 8 (1.83) |
| Total | 58 (13.27) | 42 (9.61) | 337 (77.12) |

Age and NIHSS were both statistically significant factors that increased the chances of having a significant CS. For every increase in age by one year, the odds of having significant carotid stenosis increased by 4.30 (OR=1.0430) (Table 4). Sensitivity analysis showed that 64 years was the cut-off above which there was a tendency to have significant carotid stenosis. For every increase in NIHSS score, the odds of having significant carotid stenosis also increased by 7.14% (OR=1.0714). Sensitivity analysis showed that an NIHSS >4 increased the tendency towards having significant CS. Other factors associated with an increased risk of developing significant stenosis but were not statistically significant included: gender (OR 1.27; p=0.55), MRS (OR 1.28, p=0.18), Atrial Fibrillation (OR 1.30, p= 0.64), CKD (OR 2.63; p=0.13), stroke (OR 1.01, p=0.99), and use of anticoagulant (OR 3.23; p=0.286).

**Table 4:** Linear regression analysis for possible predictors of having significant CS

| Variable | With significant carotid stenosis (n=29) Mean ± SD or Frequency (%) or Median (IQR) | w/o significant carotid stenosis (n=548) | Odds ratio (95% CI) | P-value |
|---|---|---|---|---|
| Age (years) | 66.8 ± 14.99 | 59.38 ± 13.37 | 1.04 (1.01 to 1.07) | **0.005** |
| Gender (male) | 18 (62.07) | 309 (56.39) | 1.27 (0.59 to 2.73) | 0.548 |
| NIHSS | 4 (3 to 6) | 3 (1 to 4) | 1.07 (1.01 to 1.14) | **0.026** |
| MRS | 0 (0 to 1) | 0 (0 to 1) | 1.28 (0.89 to 1.85) | 0.181 |
| **Co-morbids** | | | | |
| DM | 10 (34.48) | 242 (44.16) | 0.67 (0.30 to 1.46) | 0.309 |
| HTN | 22 (75.86) | 437 (79.74) | 0.80 (0.33 to 1.92) | 0.614 |
| CAD | 3 (10.34) | 70 (12.77) | 0.78 (0.25 to 2.43) | 0.674 |
| Atrial Fibrillation | 4 (13.79) | 60 (10.95) | 1.30 (0.44 to 3.87) | 0.635 |
| Dyslipidemia | 5 (17.24) | 128 (23.36) | 0.68 (0.26 to 1.83) | 0.448 |
| CKD | 3 (10.34) | 23 (4.20) | 2.63 (0.74 to 9.34) | 0.134 |
| Stroke | 7 (24.14) | 132 (24.09) | 1.01 (0.42 to 2.40) | 0.995 |
| Anticoagulant | 1 (3.45) | 6 (1.09) | 3.23 (0.38 to 27.7) | 0.286 |
| Antiplatelet | 4 (13.79) | 83 (15.15) | 0.90 (0.30 to 2.64) | 0.843 |
| **Social History** | | | | |
| Smoker | 11 (37.93) | 211 (38.50) | 0.98 (0.45 to 2.11) | 0.951 |
| Alcohol Drinker | 10 (34.48) | 229 (41.79) | 0.73 (0.34 to 1.58) | 0.430 |
| Illicit Drug Use | 0 | 3 (0.55) | 1 | - |

## DISCUSSION

Stroke etiology differs according to race and ethnicity.[13] In Western countries, cardioembolism or extracranial large arteries are common; while in Asian countries, small-vessel occlusion or intracranial atherosclerosis predominate. Despite this difference, work up for acute ischemic stroke patients remains the same across different populations as we follow the guidelines set by American and European countries.

An inexpensive way to detect CS is through carotid auscultation for bruits. According to Lanzino et.al, it is a sufficient screening test for asymptomatic patients with vascular risk factors. However, for those who are already symptomatic, like patients with stroke, as in this paper, the evaluation for CS cannot be limited to auscultation of the neck because carotid bruits have relatively low sensitivity for detection of moderate or severe CS. This is because bruits are generated when there is turbulence in the flow of blood so they are best heard with mild stenosis. However, when the stenosis becomes severe, bruits tend to disappear because there is already marked restriction of blood flow. Hence, there is a need for carotid imaging such as CDS.[14]

In the UK National Stroke Strategy, part of the basic work up for acute ischemic stroke patients includes CDS within 24 hours of ictus. This is difficult to comply with in a third-world country such as ours because the procedure is relatively expensive; in our institution alone, this costs P6,540. Due to the limited finances of most of our patients and their sole reliance on HMO coverage, only 35.9% of acute ischemic stroke patients were able to undergo the said procedure even if it was requested.

In a study done by Woo, et. al, atherosclerotic carotid stenosis was defined as the presence of a plaque that has > 50% vessel diameter reduction and peak systolic velocity (PSV) >125cm/s or PSV ratio > 2.0. Carotid plaque on the other hand was defined as the presence of plaque that has <50% vessel diameter reduction.[4] In their study comprised of 3030 participants with acute ischemic stroke, atherosclerotic carotid stenosis was noted in 1.1% and carotid plaque in 5.7%. They found that old age, hypertension, and smoking were significant risk factors for developing atherosclerotic carotid stenosis. They also noted that age >80 years, male sex, hypertension, and hyperlipidemia were significant risk factors for developing carotid plaque.[4,15] In this paper, 5.0% of subjects had significant carotid stenosis, a value that is relatively high compared to previous studies, but still low overall. It can be due to the fact that only about one-third of stroke patients were evaluated with CDS. This is likely due to preference of attending neurologists: e.g. he/she chooses the procedures necessary to be done for a certain patient.

Our study also validated the finding that there seems to be a bigger risk of having a significant CS with increasing age. However, none of the known co-morbidities that pose as risk factors for significant carotid stenosis were significant in the logistic regression analysis in this study.

According to guidelines, patients with ICA stenosis > 70% but not totally occluded would benefit from carotid endarterectomy (CEA) within one week and ideally within 48 hours from ictus.[16,17] In this paper, we note that 21 of those with significant stenosis were candidates for carotid intervention but only one of them underwent the said procedure. This can be due to the fact that the procedure costs approximately P100,000, an amount that most Filipinos cannot afford. Also, this study did not take into account possible surgeries done at other hospitals beyond the current admission at our institution.

### Limitations and recommendations

This is a retrospective review and certain variables could not be changed or manipulated. For example, the decision of clinicians on whether to request for a carotid duplex scan could not be controlled. Future researchers may want to do a prospective study to further control the variables.

This study also did not take into consideration the presence or absence of intracranial or extracranial atherosclerosis found in neuroimaging. This can be a variable that can potentially be significant; a correlation between MR-angiography and/or CT-angiography findings with the degree of carotid stenosis measured by CDS could have been done.

### Implications of the study

Although guidelines recommend that CDS should be part of the initial evaluation for an acute ischemic stroke, the routine use of CDS may not be warranted as the prevalence of significant carotid stenosis appears to be low. Clinicians need to screen stroke patients who have a high risk for developing significant CS and limit doing CDS as part of the initial work up to avoid unnecessary patient expenses.

Even though we were able to obtain CDS results that would have required carotid intervention, the rate of interventional procedures was very low in our institution. Advising patients who are good candidates for surgical intervention should routinely be done to improve patient status.

### Conclusion

The prevalence of significant carotid stenosis is low at 5%. Age and NIHSS were statistically significant factors that increased the chances of having a significant CS. Gender, MRS, atrial fibrillation, CKD, stroke, and use of anticoagulant were other factors associated with an increased risk of developing a significant stenosis but were not statistically significant. Finally, the rate of carotid intervention was very low.

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