

Carotid doppler evaluation in patients with ischemic stroke and its association with high risk factors

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ABSTRACT

Background: Strokes are the second largest cause of death and dementia and the leading cause of disability. With the rise of incidence in developing nation, primary and secondary prevention of strokes is of paramount importance. Carotid Doppler could be invaluable in achieving this, especially because its result can dictate future treatment plan. **Objectives:** Our study aims to highlight the importance of Carotid Doppler Sonography in this stroke prevention efforts as well as exploring how various risk factors may be associated with carotid Doppler findings. **Materials and Methods:** In this observational study, 46 patients with ischemic strokes were studied. Carotid Doppler was performed in all patients with emphasis on carotid artery stenosis and Intima thickening. Association of various risk factors was studied in detail. **Results:** Higher degree of stenosis was associated with hypochoic plaques and cortical strokes. Hypertension was the most common and most significant risk factor. Multiple risk factors also appear to have synergistic actions. **Conclusion:** Various modifiable risk factors provide valuable target for primary and secondary prevention of stroke. Carotid Doppler is a very cheap and highly effective tool for further management of stroke patients. Even in asymptomatic patients, risk factors may warrant precautionary carotid Doppler, and may result in significant reduction in disease burden on the families and the community, and should be encouraged.

KEY WORDS: Carotid Doppler; Carotid Intima Media Thickening; Ischemic Stroke


INTRODUCTION

Strokes, ischemic, and hemorrhagic, are the second leading cause of death (after Ischemic heart disease), also the second leading cause of dementia and the leading cause of disability. By sex, they are the third leading cause of death in men, (after ischemic heart disease and lung cancer), whereas in women they are the primary cause.^[1]

Internationally, as much as 70% of strokes and 87% of both stroke-related deaths and disability-adjusted life years

happen in low- and middle socio-economic nations.^[2-4] Over the last four decades, the stroke incidence in low- and middle socioeconomic nations has more than doubled while stroke incidence has declined by 42% in high-income countries.^[2] On average, stroke occurs 15 years earlier in when compared to those in high-income countries and has a far higher mortality (84% in low and middle socioeconomic nations vs. just 16% in developed nations in first three years after stroke).^[5] South Asian population, in particular has strokes at a significantly younger age compared to whites on average.^[6]

Strokes affect individuals in periods of activity, even peak activities in case of low- and middle socioeconomic nations. Not only it robs a family of their provider most of the times, it also creates dependents. And that creates an enormous impact on countries' socioeconomic development, this growing crisis has received very little attention to date.

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Even in developed nations, management and prevention of strokes get very little attention compared to ischemic heart disease or cancer. Total spending on research per person in the UK was just 48 dollars for stroke vs. 241 dollars for cancer.^[7]

This has led WHO to issue a notice that a global response is needed in their editorial in the "Bulletin of the world health organization."^[8] And we must respond accordingly. Of course, modern medicine has to concentrate on the prevention of stroke itself, be it primary or secondary.

Now, ischemic stroke is the more prevalent than hemorrhagic stroke (66% in developing nations vs. 91% in developed nations)^[5] and requires our urgent attention. Artery to artery embolism appears to be the dominant vascular mechanism causing ischemia rather than cardiac embolization or in situ arterial thrombosis, i.e. atherosclerosis. Most common source of embolism is the carotid bifurcation, but may arise from the aortic arch, common carotid, internal carotid, vertebral, and basilar artery also.

About 30% of stroke survivor will have another episode of stroke and transient ischemic attack,^[9] which is a figure that must be addressed as soon as possible. For ischemic strokes, carotid intima-media thickness has emerged as a reliable independent marker and must be targeted. The NASCET study has shown, carotid endarterectomy produces absolute reduction of 17% stroke at 2 years as compared to medical therapy in patients of >70 years, especially in presently symptomatic patients with internal carotid lumen diameter narrowing of >70%.^[10]

Unfortunately, this is an area where medical community is much less active than it should be. Very few centers have it in their protocol itself to do a carotid artery study (be it angiography or Doppler) to ascertain the stenosis and/or CIMT. Result is, most patients are sent home just with Aspirin and Statins, while the ticking time bomb of a carotid artery is ready in a large number of them, ready to cause another event that the patient may not recover from. This is even worse in private hospitals, compared to institutions.

What is more, there is no concept of performing a carotid artery study as a tool for primary prevention tool. We are missing an important trick by screening at high-risk patients with at least a carotid Doppler.

The objective of our study is to understand the importance of carotid Doppler Sonography in this stroke prevention efforts through surveillance for carotid disease which predisposes the patient to ischemic stroke.

Another main objective here is the risk factors and their analysis. Factors such age, sex, and ethnicity are non-modifiable, but hypertension, diabetes, dyslipidemia,

smoking, etc. provide us with important targets to help in our goal of stroke prevention. Our study also considers the relationship between these risk factors and CIMT and/or stenosis, with which we hope to establish that controlling these modifiable risk factors may help prevention of recurrence. Our studies also explore individual risk factors to look into which would be the most dangerous risk factor here and should be watched out for the most. We also consider how to utilize even the non-modifiable risk factors in our effort to prevent ad/or treat ischemic stroke patients. We aim to show how making a carotid artery Doppler a part of routine investigations in ischemic stroke patients can be invaluable.

MATERIALS AND METHODS

Our study was observational and single site study. We recruited 46 patients with clinical history of cerebrovascular stroke randomly, from patients who were admitted in medical wards in Shri Sayajirao General Hospital, Vadodara, within study period from June 2016 to November 2016. The study was approved by scientific review committee and institutional ethical committee of Baroda Medical College. All the patients were informed about the design of the study, and informed consent was taken.

Patients were included based on detailed history and clinical signs/symptoms suggestive of stroke, after which, ischemic stroke was established via neuroimaging (computed tomography [CT] or magnetic resonance imaging [MRI]).

Patients with hemorrhagic stroke, with rheumatic heart disease or intracardiac clots, with vasculitis/connective tissue disorders, on statin therapy already and recurrent strokes were excluded from the study.

Each patients enrolled in the study were asked in details history regarding the present complaints, past history, addiction history including smoking and drug history. Detailed menstrual and obstetric history in the female patients were obtained.

Thorough general examination followed by detailed and complete neurological has been performed, including examination carotid pulsation, peripheral nerve, and vessels. Dilated Fundus examination and thorough systemic examination was carried out in all patients too. All routine blood investigations, including lipid profile, electrocardiogram and two-dimensional D echo, were done in all patient. CT scan/MRI has been done according to patient profile to label patients with ischemic stroke.

Carotid ultrasound with color Doppler has been performed. Extracranial carotid system including common carotid, external carotid, and internal carotid arteries of both sides have been evaluated in all patients. Each case has been evaluated

for intimal thickness, presence of plaque and its character or calcification, % of stenosis and arterial malformation like dissection or aneurysm.

Patients were also evaluated for risk factors such as diabetes (on treatment or diagnosed by OGTT), hypertension (on treatment or by three separate blood pressure measurement above 140/90 mm Hg), smoking, dyslipidemia, and previous stroke.

Statistical Analysis

Data were entered into Microsoft Excel 2010 and Epi Info 7. Data analysis was performed, and chi-square test was used to show the significance relation between various risk factors and carotid intima-media thickening/stenosis as required and possible. $P < 0.05$ was considered to be statistically significant and $P < 0.001$ was considered to be statistically highly significant.

RESULTS

In our study, data on our 46 patients were evaluated and following observations were made. The findings of the study were depicted in Tables 1-7 and Figure 1.

DISCUSSION

Ischemic stroke is one of the most important causes of mortality, morbidity, and disability. It is of paramount importance for us to do our best for the primary and secondary prevention of this dangerous disease. Where we start this battle is the risk factors. Majority of the patients were age of 41–60 years, and there was male predominance. Among the various modifiable risk factors, hypertension had the most striking association with stroke in our study. (69%) hypertension was closely followed by smoking and dyslipidemia. (61%) Diabetes and previous history were present in 12 patients

each. (26%) Important to note that significant stenosis above >40% increased with the number of risk factors that. In the 19 patients with 0.40% stenosis, as many as 15 patients had three risk factors or more. In the 17 patients who had cortical strokes, 16 (95%) had stenosis >40%. In 46 patients,

Table 1: Age and gender distribution

Age	Male	Female	Total
<30	0	4	4
31–40	2	0	2
41–50	10	4	14
51–60	11	3	14
61–70	7	1	4
Total	33	13	46

Table 2: Modifiable risk factors

Risk factor	Number of patients
Hypertension	32
Diabetes mellitus	12
Smoking	28
Dyslipidemia	28
Previous stroke	12

Table 3: Plaque morphology and percentage of stenosis

Plaque morphology	Percentage of Stenosis (56 carotids involved in 92 carotid systems in 46 patients)			Total
	>70%	50–70%	<50%	
Hypoechoic	5	5	30	40
Hyperechoic	2	2	12	16
Total	7	7	42	56

Table 4: Pattern of infarct and percentage of stenosis

Pattern	Stenosis<40%	Stenosis>40%	Total
Subcortical	26	3	29
Cortical	1	16	17
Total	27	19	46

Table 5: CIMT and hypertension

CIMT	Hypertension	
	Present	Absent
Present	30	7
Absent	2	7

CIMT: Carotid intimamedia thickness

Table 6: CIMT and smoking

Smoking	CIMT		Total
	Present	Absent	
Present	28	4	32
Absent	8	6	14

CIMT: Carotid intimamedia thickness

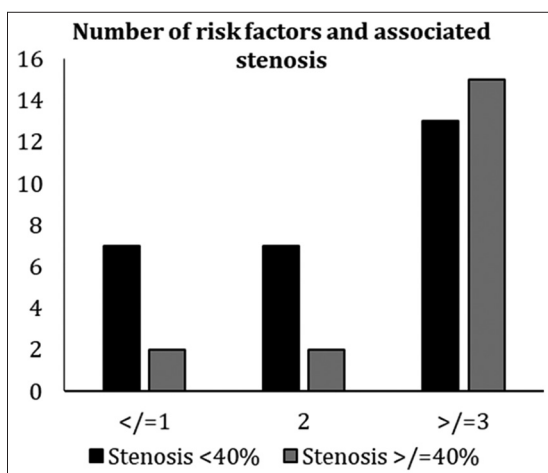


Figure 1: Synergy of risk factors

Table 7: CIMT and dyslipidemia

Dyslipidemia	CIMT		Total
	Present	Absent	
Present	27	5	32
Absent	8	6	14

CIMT: Carotid intima-media thickness

(92 carotid arterial systems) 56 arteries showed plaque. Out of these, 40 (71%) plaques were hypoechoic (echolucent) and 16 (29%) plaque were hyperechoic. Out of 32 patients were found to have hypertension, CIMT was present in 30(93%) from 32 hypertensive patients. ($P < 0.02$) 27 out of 32 smokers, and 27 out of 32 patients with dyslipidemia had CIMT as well. ($P < 0.05$) In the present study, out of 46 patients of ischemic stroke, 33 (62%) patients were treated with medical management whereas 13 (28%) patients who had major stenosis (>50%) within carotid arterial system required carotid intervention.

Age is the strongest determinant of stroke, which is less common before 40 years old. According to data obtained from Framingham study, incidence of stroke increased steeply with age, becoming double in each successive decade from 55 years old on.^[11] Hence, we have a comparatively younger age group. Which is falling in pattern with the data that suggest Asian population are susceptible to stroke at younger age.^[6] There is a significant male gender preponderance, which lines in with the previous studies, which state a male preponderance, especially in younger ages.^[11-13] Our analysis that shows hypertension as the most common and most significant risk factor lines well with previous studies in western population suggesting that Hypertension may be the most consistent risk factor for ischemic stroke.^[14-16] Smoking was also clearly a major behavioral risk factor among our patients. The explanation for which is that it causes a decrease in high-density lipoprotein, and fibrinogenemia.^[17] Dyslipidemia contributes significantly here by accelerating atherosclerosis.^[18]

Our results clearly show that the chance of carotid arterial involvement increases significantly when multiple risk factors are involved. Which suggests that some synergy exists among the risk factors and that makes them more dangerous in group. We have to keep in mind that atherosclerosis is the most common cause of craniocerebral vascular stenosis in adults. Most of the infarction is due to occlusion of internal carotid artery (ICA), middle cerebral artery, and posterior cerebral artery.^[19] Atherosclerotic changes most commonly occur in 1st part of the ICA. It causes stroke due to stenosis or embolus. Carotid Doppler has increasing role in diagnosis of extracranial cerebral vessel atherosclerosis, as 88% of plaques responsible for stroke originate at carotid bifurcation.^[20] Hypoechoic plaques showed up as a major red flag sign in our study. Heterogeneous plaques have a hypoechoic component and are associated with the presence

of intra-plaque hemorrhage, ulceration and lipids, more likely to result in adverse events such as embolization.^[21,22]

With this data, we were able to guide our patients for proper management with the help of carotid Doppler, a much cheaper investigation compared to CT/MR angiography. Plus, it is completely non-invasive compared to other methods, especially the conventional angiography. Which is why carotid ultrasound has become the pivotal examination in majority of the patients for carotid endarterectomy. Hence, role of angiography is decreasing, and in many centers, carotid ultrasound is the only imaging technique.^[23] In acute infarcts. CT brain may be normal if the study is done within 6 hours, but carotid Doppler can detect flow abnormality after stroke. Sometimes carotid angiography underestimates the degree of stenosis while Doppler gives better reliable results.^[18,24] It also helps in distinguishing between occlusion and stenosis. Accuracy of Doppler threshold rates is similar with most centers reporting. Accuracy between 85% and 90% has been noted when compared to angiography Carotid Doppler has 90% specificity and sensitivity relative to angiography.

The strength of our study was that we were able to show off the importance of Carotid Doppler study and risk factors associated with ischemic stroke at the same time. We were able to also show the relationship that risk factors for stroke themselves have with carotid stenosis and/or carotid intima-media thickening, and with that, we can show that presence of these risk factors, especially if multiple, makes carotid Doppler absolutely essential.^[25] Carotid Doppler analysis can be vital in establishing atherosclerosis and its degree itself.^[26] Using this data from our carotid Doppler studies and analysis of risk factors, we were able to get much needed surgical intervention in our patients.

However, major limitation of our study is that we could not compare the conventional carotid angiography with Carotid Doppler. Due to relatively less number of patients with diabetes and smoking as a risk factor, we were unable to show their significance in causing CIMT.

CONCLUSION

We conclude that various risk factors for ischemic stroke may be very important target for prevention of stroke. Not only do they have extremely strong association with Ischemic stroke but also they have synergistic actions. Moreover, they have strong association with the carotid intimal thickening, a factor that dictates the surgical management of Ischemic stroke.

We conclude that these risk factors must be considered red flag signs for stroke. Their presence, especially if multiple, warrants thorough clinical auscultation, and if any suspicion, a carotid Doppler even in patients without stroke. Moreover, any patient with one or more risk factors must undergo carotid Doppler if they develop stroke.

While we may not be able to do anything about the non-modifiable risk factors, it is very important to note that South Asian population like ours is more vulnerable to Ischemic stroke at a younger age than Caucasians. Male sex at younger age is also something that we must keep in mind.

We also conclude that significant carotid artery stenosis has a very strong association with cortical strokes. Our study also shows that a hypoechoic lesion on Doppler in carotid artery is a very dangerous sign for stroke.

We also conclude that carotid Doppler is a highly efficient, very cheap, and non-invasive procedure to gain insight into the carotid vasculature. It can be extremely useful as an early warning for stroke in high-risk populations (which are rising day by day 2),^[8] as well as sometimes providing indirect evidence of stroke itself in early stages. We recommend carotid Doppler should be performed in all confirmed cases of stroke as well as high-risk patient with suspicion to guide us in the management. It might not be wrong to advise carotid Doppler in high-risk population, even without suspicion at regular interval as an early warning radar.

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