

# Frequency of New Lesion in Brain after Carotid Stenting in Ischemic Stroke

DAS R<sup>1</sup>, RIZVI AN<sup>2</sup>, DEY SK<sup>3</sup>, AKHTER N<sup>4</sup>, MONDOL RK<sup>5</sup>, KAYSER MA<sup>6</sup>,  
BULBUL S<sup>7</sup>, ZANNAT T<sup>8</sup>, FOYSAL M<sup>9</sup>, GHOSH RK<sup>10</sup>

## Abstract

**Background:** Carotid angioplasty and stenting is an emerging treatment option for carotid stenosis to prevent stroke recurrence in ischemic stroke patients with carotid stenosis.

**Objective:** The purpose of the study was to observe the frequency of new brain lesions in ischemic stroke patients after carotid stenting. **Methodology:** This was a hospital based prospective longitudinal before – after study conducted in the department of neurology, BSMMU. We evaluated 31 ischemic stroke patients who had significant stenosis in the extracranial portion of internal carotid artery during September 2020 to August 2022. MRI of brain (including DWI sequence) was done to each patient to confirm the diagnosis. Vascular imaging by any of the modalities like Carotid Doppler, MRA, or cerebral DSA (Digital subtraction angiography) was done and the degree of stenosis was measured by the North American Symptomatic Carotid Endarterectomy Trial (NASCET) formulae. Those patients who got more than 50% carotid stenosis underwent carotid artery stenting procedure. Then all the patients were followed up by MRI (including DWI sequence) of Brain within 48 hours to see the occurrence of any new DWI lesion. Four patients were lost during follow up. **Results:** Total 31 patients were analyzed in the study. Mean age of the respondents were 60.2±8.79 years. Within 48 hours of stenting MRI of Brain showed new DWI lesion in 12.9% patients. After Stenting, 75% patients had single DWI lesion on MRI and 25% had multiple lesions. Most of the patients had MCA territory stroke (100%) where capsuloganglionic region was the most frequent location of infarction (100%). Among all the patients who underwent carotid stenting, only 3.2% patients had developed symptomatic new DWI lesion. **Conclusion:** Carotid stenting with or without angioplasty is a relatively safe procedure with few new DWI lesions on follow-up MRI.

**Keywords:** New lesion; brain; carotid stenting; ischemic stroke

## Introduction:

Stroke recurrence is a major problem around the world, leading to permanent and more severe disability<sup>1</sup>. Ischemic stroke survivors are at a risk for another stroke if cause of the first stroke is not treated<sup>1</sup>. The maximum incidence of recurrent stroke is within first 30 days after the initial stroke<sup>2</sup>.

Approximately 1 in 6 survivors (15%) of a first-ever stroke experience a recurrent stroke over the next 5 years, of which 25% were fatal within 28 days<sup>3</sup>. Risk of recurrence of stroke in patients with 50-90% carotid stenosis is 5.2% within 2 days, 7.9% within 7 days, 11.2 % within 14 days, 18.6% within 90 days of the previous events<sup>4</sup>. In Bangladesh

1. Dr. Rajib Das , Resident, Department of Neurology, BSMMU
2. Dr. Abu Nasir Rizvi, Professor and Chairman, Department of Neurology, BSMMU
3. Dr. Subash Kanti Dey, Professor, Stroke and Interventional Neurology Division, Department of Neurology, BSMMU
4. Dr. Nahid Akhter, Resident, Department of Neurology, BSMMU
5. Dr. Rakesh Kumar Mondol, Resident, Department of Neurology, BSMMU
6. Dr. Monsur Ahmed Kayser, Resident, Department of Neurology, BSMMU
7. Dr. Shahida Bulbul , Consultant Neurologist
8. Dr. Tahira Zannat , Consultant Neurologist
9. Dr. Md. Foysal, Resident, Department of Neurology, BSMMU
10. Dr. Ranjit Kumar Ghosh, Medical officer, department of Neurology, BSMMU.

one study shows that, carotid stenosis may be a source of ischemic stroke, which is also responsible for stroke recurrence. The risk of further stroke may be as high as 5% within the first week, 20% within the first month and 28.2% within one year of their first ischemic stroke event, out of which 66.7% patient had prior significant carotid stenosis<sup>5</sup>.

Recurrence of stroke due to atherosclerotic carotid stenosis is prevented by medical therapy alone or in combination with carotid intervention<sup>6</sup>. Although carotid endarterectomy had been the gold standard treatment for carotid stenosis, endovascular treatment of carotid stenosis by percutaneous transluminal balloon angioplasty or insertion of a stent (CAS) is an accepted alternative to carotid endarterectomy (CEA)<sup>7</sup>. CAS may have better outcome than CEA in selected patients<sup>8</sup>.

As carotid artery stenting is a less invasive procedure and does not involve cervical dissection, the patient may experience less periprocedural discomfort and a lower risk of cardiac and pulmonary complications. However, the major risk of CAS is the possibility that, it may result in dislodgment and distal embolization of plaque and thrombotic debris into the brain or eye vessels which may result in another stroke. Again, during angioplasty, the balloon may obstruct the carotid blood flow long enough to cause low-flow ischemic lesions. Cerebral vasospasm may also occur<sup>9</sup>. So, to assess the safety and efficacy of this approach, it is desirable to have a noninvasive method for demonstrating areas of acute ischemia with certainty. Diffusion-weighted MRI (DWI) of Brain is very sensitive to early brain ischemia. This is becoming widely available and might therefore serve this purpose<sup>10</sup>. In fact, DWI is currently the most sensitive tool to detect early cerebral ischemia and offers the possibility of making even small and thus asymptomatic lesion visible shortly after their emergence. In one study, among 124 patients, it is found that after carotid stenting, 50% (62 patients) developed at least one new ischemic brain lesions, which were detected by DWI sequence of MRI of brain 1 day after the procedure. But all of these lesions were clinically asymptomatic<sup>11</sup>.

### **Methodology:**

**Study Settings and Population:** This was designed as prospective longitudinal before- after study. This present study was carried out from September 2020 to August 2022 for a period of two years. The Study was conducted in IPD (in patient department) of Department of Neurology, BSMMU, Dhaka, Bangladesh. All the patients presented with ischemic stroke in the presence of more than 50% carotid artery stenosis on vascular imaging, with the age group of more than or equal to 18 years with both sexes who was admitted in the IPD of the department of Neurology at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, were selected as study population. Subjects were selected by purposive sampling method. Patients age more than 18 year, patients of ischemic stroke, patients with carotid stenosis 50% or more in vascular imaging (DSA, measured by NASCET method) were included in this study. Hemorrhagic stroke patients, patients with posterior circulation stroke, ischemic stroke patients in whom carotid endarterectomy or stenting had been already done, presence of carotid stenosis less than 50%, patients with total carotid occlusion, patient with previous history of coronary artery disease including ischemic heart disease (IHD), myocardial infarction (MI), heart failure, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) or heart failure were excluded from this study.

**Study Procedure:** Proper history was taken, physical and neurological examination was done meticulously, keeping in mind of the demographic and clinical variables. All relevant investigations were obtained including MRI of brain, vascular imaging like MRA or CTA of brain and neck vessels or carotid duplex study, random blood sugar and HbA1C, serum creatinine, serum lipid profile etc. mRS score (Modified Rankin Score) was also calculated before the procedure. Then vascular imaging in the form of cerebral digital subtraction angiography (DSA) was performed by the interventional neurologist to assess the percentage of internal carotid artery (ICA) stenosis according to the NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria. After cerebral

DSA, patients were selected according to inclusion and exclusion criteria. Patients with posterior circulation stroke and total carotid occlusion were excluded from the study. The indication for revascularization was approved by interventional neurologist. Counseling was done to the suitable patients for carotid artery stenting (CAS) with explaining the risks and benefits. Fitness of the patient for carotid artery stenting (CAS) was assessed and CAS was done in the Pediatric Catheter Laboratory of Bangabandhu Sheikh Mujib Medical University (BSMMU). All patients were pre-treated with aspirin and clopidogrel. During procedure 2500 IU unfractionated heparin was administered. Angiography was performed using 5F diagnostic catheter. Digital subtraction angiography of each vessel was obtained at cervical and intracranial level. The stenting procedure was performed with either a 7F guiding catheter advance over a 300 cm microwire with telescoping technique or a 8F 90 cm long sheath. No distal cerebral protection device was used during the procedure. Self-expandable nitinol stents were used. Patients with more than 90.0% carotid stenosis, both angioplasty and stenting were done whereas patients with less than 90.0% stenosis, only carotid stenting was done. Finally follow up angiogram of the stented lesion as well as intracranial views was obtained. After the procedure all patients were monitored in the neurology ward. The sheath was removed on the same day. LMW heparin 40 IU was given in 12 hourly doses for 3 days. Patients were closely monitored during and after carotid artery stenting (up to 48 hour). Recurrent stroke and other complications that developed during this period were recorded in data collection sheet. MRI of brain was done 1 day after (within 48 hours) the procedure at BSMMU using 1.5 T Sonata Magnetom scanner (Siemens, Erlangen, Germany). Abnormal DWI lesions were identified in each patient by visual inspection of the MRI scans. New DWI lesions were determined by slice to slice comparison of the new DWI image with the previous DWI image and were reviewed by the interventional neurologist. Enlargement of a previous lesion was not considered as a new ischemic lesion. All new DWI lesions were

described by their number, location in the brain and arterial territory. The patients were discharged with aspirin and clopidogrel 75mg for three months and aspirin 75 mg for indefinite period.

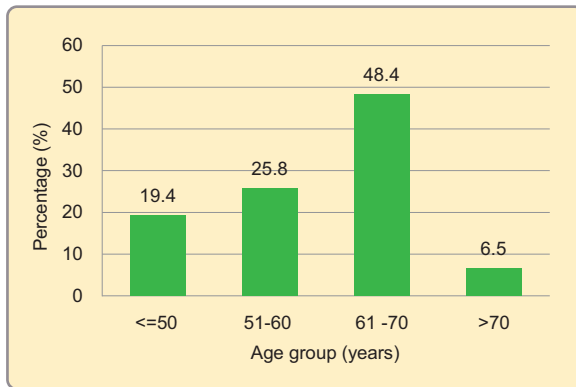
**Statistical Analysis:** All the data was checked and edited after collection. Statistical analysis was performed by Windows based software named as Statistical Package for Social Science (SPSS), versions 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Continuous data that were normally distributed were summarized in terms of the mean, standard deviation, minimum, maximum and number of observations. Categorical data were summarized in terms of frequency counts and percentages.

**Ethical Consideration:** Ethical permission was obtained from the Institutional Review Board (IRB) of BSMMU, Dhaka, Bangladesh. In this study written consent was taken from patients and guardians of all study participants. They had the right not to answer any question which made them uncomfortable. The aims and objectives of the study along with its procedures, risks and benefits were explained to the respondents in easily understandable local language and informed written consent were taken from each respondent.

### **Results:**

A total number of 35 patients were recruited after the fulfilling the inclusion and exclusion criteria among which 4 patients were lost during follow up. Therefore, total 31 patients were enrolled in the study. This was a hospital based prospective longitudinal before – after study conducted in the department of Neurology, BSMMU. Majority of study sample were in 61-70 years (48.4%) of age followed by 51-60 years (25.8%). Mean age of the respondents were  $60.2 \pm 8.79$  years with age ranging 40 to 75 years (Figure I).

A total number of 4 cases (12.9%) were reported as new DWI lesion (Figure II). Among these 4 cases, 3 (75%) cases were single and 1 (25%) cases were multiple. Most of the new DWI lesions were in the ipsilateral side than contralateral side which was 3 (75.0%) cases and 1 (25.0%) cases respectively. Considering arterial territory, all 4 (100.0%) new cases were in middle cerebral



**Fig.-1:** Distribution of study sample according to age group (n=31)

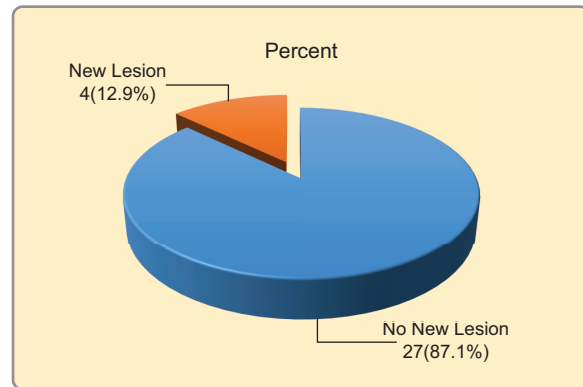
artery territory. Capsuloganglionic region was the most frequent location (100.0%) (Table 1).

**Table-I**

*Distribution of Study Population according to characteristics of New DWI lesion After Stenting*

Characteristics	Frequency (n=4)	Percentage
Number of Lesions		
Single	3	75.0
Multiple	1	25.0
Location of Lesion		
Contralateral	1	25.0
Ipsilateral	3	75.0
Arterial Territory		
Water Shade	0	0.0
MCA	4	100.0
ACA	0	0.0
Location of Infarction*		
Frontal	0	0.0
Parietal	1	0.0
Temporal	0	0.0
Occipital	0	0.0
Capsuloganglionic region	4	100.0
Brain Stem	0	0.0

\*Multiple response included



**Fig.-2:** Distribution of Study Population according to new DWI lesion after stenting (N=31)

### Discussion:

A total number of 35 patients were recruited after the fulfilling the inclusion and exclusion criteria among which 4 patients were lost during follow-up. Therefore, ultimately 31 patients were recruited for this study. The distribution of the study population according to age group was recorded. Most of the study populations were in the age group of 61 to 70 years which was 15(48.4%) cases followed by 51 to 60 years and less than 50 years which was 8(25.8%) cases and 6(19.4%) cases respectively. However, more than 70 years age group was only in 2(6.5%) cases only. The mean age with the SD was  $60.2 \pm 8.79$  years with a range of 40 to 75 years. Therefore, it is very clear that, old age is the most common age group for the carotid artery stenosis. Similar result has been reported by Schnaudigel et al<sup>13</sup>.

Another retrospective, observational study in Bangladesh showed that, patients with CAS had mean age of  $55 \pm 5.5$  years<sup>14</sup>. In another study, mean age in the CAS registry in 2878 patients from 31 hospitals was  $70.0 \pm 8.6$  years and it was  $75.2 \pm 7.6$  years among US Medicare population<sup>15</sup>. Mean age of western population undergone carotid stenting was higher than Asian may be due to poor life expectancy of Asian population compared to European or American.

Distribution of study population according to new DWI lesion after stenting was recorded. Among the total 31 patients, new lesion was reported in 4(12.9%) cases. Pinero et al., 2006 found that new DWI lesion



in 17.3% cases<sup>16</sup>. Van Heesewijk et al., 2002<sup>17</sup> got new DWI lesion in 23% cases. Bijuklic et al., 2013<sup>18</sup> found new DWI lesion in 32.8% cases. Bonati et al., 2010<sup>19</sup> got new DWI lesion in 50% cases.

Among patients with new DWI lesion, 75% patient had single and 25% had multiple lesions. Most of the DWI lesions were in the ipsilateral side than in contralateral side which was 3(75.0%) cases and 1(25.0%) cases respectively. Similar results have been reported by Gensicke et al<sup>20</sup> and has been added that DWI lesions and ischemic complications during stent placement are more common among patients with unstable plaques characterized by echolucent appearance on ultrasound and lipid-rich necrotic plaque and intraplaque hemorrhage on MRI. Another study showed that once atherothrombosis has occurred, the plaque may remain chronically unstable unless trigger factors such as inflammation or increased shear stress are removed. Unstable plaques might not only be present in the target artery but also in the access vasculature, including the aortic arch. Aortic arch lesions have been shown to increase the risk of cerebral embolism during carotid artery stenting<sup>21</sup>.

The current study found some similarities as well as dissimilarities with the previous studies. This may have occurred due to different study procedures and sample size. But according to this study, new DWI lesion after carotid stenting is not uncommon but most of them are asymptomatic and most of the patients achieved good functional outcome. So, carotid stenting was found to be feasible and safe, with acceptable levels of the outcome.

### Conclusion:

In conclusion, this study reveals that new DWI lesion in MRI of Brain after carotid artery stenting is not uncommon but most of these lesions are asymptomatic and has no impact on outcome. All the procedures were technically successful. So, in experienced hands carotid angioplasty and stenting without distal embolic protection device is a safe procedure with few new DWI lesions and significant good functional outcome.

### References:

1. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D,

Kamel H, Kernan WN, Kittner SJ, Leira EC, Lennon O. 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke*. 2021 Jul;52(7):e364-467.

2. Buenaflor FG. Recurrence rate of ischemic stroke: a single center experience. *Journal of the Neurological Sciences*. 2017 Oct 15;381:399.
3. Hankey GJ, Jamrozik K, Broadhurst RJ, Forbes S, Burvill PW, Anderson CS, Stewart-Wynne EG. Long-term risk of first recurrent stroke in the Perth Community Stroke Study. *Stroke*. 1998 Dec;29(12):2491-500.
4. Johnson W, Onuma O, Owolabi M, Sachdev S. Stroke: a global response is needed. *Bulletin of the World Health Organization*. 2016 Sep 9;94(9):634.
5. Dey, S.K., Bakshi, L., Patwari, K.K., Habib, A., Rahman, A., Hosen, M., Chowdhury, A., 2020. Carotid Stenosis and Recurrence in Patients with First Ever Ischemic Stroke. *Journal of Rangamati Medical College*, 3(2), 17-20
6. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC, Lennon O. 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke*. 2021 Jul;52(7):e364-467.
7. Ricotta JJ, Malgor RD. A review of the trials comparing carotid endarterectomy and carotid angioplasty and stenting. *Perspectives in vascular surgery and endovascular therapy*. 2008 Sep;20(3):299-308.
8. Massop D, Dave R, Metzger C, Bachinsky W, Solis M, Shah R, Schultz G, Schreiber T, Ashchi M, Hibbard R. Stenting and angioplasty with protection in patients at high risk for endarterectomy: SAPHIRE Worldwide Registry first 2,001 patients. *Catheterization and Cardiovascular Interventions*. 2009 Feb 1;73(2):129-36.

9. van Heesewijk HP, Vos JA, Louwerse ES, Van Den Berg JC, Overtoom TT, Ernst SM, Mauser HW, Moll FL, Ackerstaff RG. New brain lesions at MR imaging after carotid angioplasty and stent placement. *Radiology*. 2002 Aug;224(2):361-5.
10. Lövblad KO, Plüschke W, Remonda L, Gruber-Wiest D, Do DD, Barth A, Kniemeyer HW, Bassetti C, Mattle HP, Schroth G. Diffusion-weighted MRI for monitoring neurovascular interventions. *Neuroradiology*. 2000 Feb;42(2):134-8.
11. Bonati LH, Jongen LM, Haller S, Flach HZ, Dobson J, Nederkoorn PJ, Macdonald S, Gaines PA, Waaijer A, Stierli P, Jäger HR. New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: a substudy of the International Carotid Stenting Study (ICSS). *The Lancet Neurology*. 2010 Apr 1;9(4):353-62.
12. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. *Stroke*. 2007 Mar 1;38(3):1091-6.
13. Schnaudigel S, Groschel K, Pilgram SM, Kastrup A. New brain lesions after carotid stenting versus carotid endarterectomy: a systematic review of the literature. *Stroke*. 2008 Jun 1;39(6):1911-9.
14. Momenuzzaman NA, Begam F, Khan KN, Dey A, Adhikary DK, Ilius ZM, Sohail KM, Haque F, Amin MU, Rahman R, Mallick S. Percutaneous Angioplasty and Stenting of Carotid Artery: Study of 18 Cases. *Cardiovascular Journal*. 2010;2(2):218-22.
15. Lichtman JH, Jones MR, Leifheit EC, Sheffet AJ, Howard G, Lal BK, Howard VJ, Wang Y, Curtis J, Brott TG. Carotid endarterectomy and carotid artery stenting in the US Medicare population, 1999-2014. *Jama*. 2017 Sep 19;318(11):1035-46.
16. Pinero P, Gonzalez A, Mayol A, Martinez E, Gonzalez-Marcos JR, Boza F, Cayuela A, Gil-Peralta A. Silent ischemia after neuroprotected percutaneous carotid stenting: a diffusion-weighted MRI study. *American Journal of Neuroradiology*. 2006 Jun 1;27(6):1338-45.
17. van Heesewijk HP, Vos JA, Louwerse ES, Van Den Berg JC, Overtoom TT, Ernst SM, Mauser HW, Moll FL, Ackerstaff RG. New brain lesions at MR imaging after carotid angioplasty and stent placement. *Radiology*. 2002 Aug;224(2):361-5.
18. Bijuklic K, Wandler A, Varnakov Y, Tuebler T, Schofer J. Risk factors for cerebral embolization after carotid artery stenting with embolic protection: a diffusion-weighted magnetic resonance imaging study in 837 consecutive patients. *Circulation: Cardiovascular Interventions*. 2013 Jun;6(3):311-6.
19. Bonati LH, Jongen LM, Haller S, Flach HZ, Dobson J, Nederkoorn PJ, Macdonald S, Gaines PA, Waaijer A, Stierli P, Jäger HR. New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: a substudy of the International Carotid Stenting Study (ICSS). *The Lancet Neurology*. 2010 Apr 1;9(4):353-62.
20. Gensicke H, van der Worp HB, Nederkoorn PJ, Macdonald S, Gaines PA, van der Lugt A, Mali WP, Lyrer PA, Peters N, Featherstone RL, de Borst GJ. Ischemic brain lesions after carotid artery stenting increase future cerebrovascular risk. *Journal of the American College of Cardiology*. 2015 Feb 17;65(6):521-9.
21. Spagnoli LG, Mauriello A, Sangiorgi G, Fratoni S, Bonanno E, Schwartz RS, Piepgras DG, Pistolese R, Ippoliti A, Holmes DR. Extracranial thrombotically active carotid plaque as a risk factor for ischemic stroke. *Jama*. 2004 Oct 20;292(15):1845-52.