e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(11); 895-905

Original Research Article

Outcome Assessment by Single Photon Emission Computed Tomography after Revasularization Procedure in Patients with Moyamoya Disease

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Received: 05-09-2022 / Revised: 16-10-2022 / Accepted: 22-11-2022
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Conflict of interest: Nil

Abstract

Aim: The purpose of this study was to assess brain perfusion on SPECT in preoperative period. This area of hypoperfusion will be then compared with post-operative SPECT Thus the functional usefulness of revascularization procedure can be assessed.

Methods: The present study was conducted in the Department of Neurosurgery, Post Graduate Institute of Medical Education and Research, Chandigarh. The duration of the study was from July 2014 -December 2015 (1½year) and 22 patients were included in the study. The follow-up period was 6 months.

Results: Of the study population, 15 (68%) were males and 7 (32%) were females. There were 19 children and 3 adult patients who were all males. The number of patients below 13 years were 15 (68.2%), 14 – 20 years were 4 (18.2%) 21 – 40 years were 3 (13.6%). 18 (81%) patients presented with paresis which was unilateral in 11 (61.1%) and bilateral in 7 (38.9%).The distribution of symptomatology. Of the 21 patients, who underwent STA MCA bypass 8 (38%) patients underwent surgery on right side, 5 (23.8%) patients on left side, and 8 (38%) had bilateral surgeries done and one patient who underwent EDAMS alone underwent bilateral surgery.

Conclusion: Our study showed the efficacy of revascularizations procedure in moyamoya disease. Hence there is growing evidence that symptomatic patients should be offered revascularization therapy. SPECT is an important tool and can be used to optimize the treatment strategies for patients with moyamoya disease.

Keywords: Adult, Assessment, Outcomes, Combined Revascularization Surgery, Moyamoya Disease

Introduction

The term “moyamoya” means puff of smoke and describes the formation of collateral vessels due to high-grade stenosis of the distal internal carotid and proximal middle cerebral arteries. There are two related forms of the disease. Moyamoya disease is typically symmetric, genetically determined, prevalent notably in Japan and symptomatic at early stages in most cases. [1] In contrast, moyamoya syndrome or pattern is typically asymmetric, caused by a variety of underlying etiologies, more common in European countries with a prevalence of

3/1000000 and usually symptomatic only at later stages of the disease. [2,3] Extracranial-intracranial (ECIC ECIC) bypass is the most important surgical intervention, notably to prevent subsequent ischemic events and secondary hemorrhage. [2,4] The challenge in the follow-up of patients with moyamoya syndrome is the selection of the optimal time-point for the surgical intervention of the EC-IC bypass, as the benefit of prevention of stroke or hemorrhage contrasts the risk of peri-surgical complications of this difficult intervention. Moyamoya disease (MMD) is a progressive cerebrovascular disorder characterized by steno-occlusive changes at the terminal portion of the internal carotid artery and abnormal vascular network formation at the base of the brain.

Magnetic resonance (MR) imaging/ angiography noninvasively diagnoses various cerebrovascular diseases. The MMD guideline now approves MR imaging/angiography as an alternative technique for cerebral angiography for MMD diagnostics. The guideline states that when MR imaging and angiography findings meet all of the following criteria, cerebral angiography can be omitted: 1) MR angiography shows bilateral stenosis or occlusion of the terminal portion of the intracranial internal carotid artery or proximal portions of the anterior and the middle cerebral artery (MCA). 2) MR angiography shows bilaterally abnormal vascular networks in the basal ganglia, or MR imaging shows 2 or more visible flow voids in the basal ganglia. [5]

The criteria for diagnosis of moyamoya have been set forth by the Research committee on spontaneous occlusions of the circle of willis of the Ministry of Health and Welfare of Japan. [6] Patients with Moyamoya disease are generally investigated with angiographic study by digital substraction angiography (DSA), computed tomography angiography (CTA) or magnetic resonance angiography (MRA) to describe the occlusion of ICA and development of collaterals [7,8]

Single photon emission computed tomography (SPECT) is a long established whole brain radioisotope axial perfusion study that provides relative perfusion of brain1. SPECT involves injection of a radioactive radioisotope bound to a lipophillic pharmaceutical that can cross the blood brain barrier and can be performed with or without acetazolamide challenge.

The purpose of this study was to assess brain perfusion on SPECT in preoperative period. This area of hypoperfusion will be then compared with post-operative SPECT Thus the functional usefulness of revascularization procedure can be assessed.

Materials and Methods

The present study was conducted in the Department of Neurosurgery, Post Graduate Institute of Medical Education and Research, Chandigarh. The duration of the study was from July 2014 -December 2015 (1½year) and 22 cases of moyamoya disease were included in the study. The follow-up period was 6 months.

Study design: Prospective and retrospective observational study.

A). Retrospective: Patients of moyamoya disease who have been operated in the past were included. The hospital records of these patients were analysed and all patients were contacted and asked to report for follow-up. Only those patients who reported for follow-up were included.

B). Prospective: All patients diagnosed with moyamoya disease and those who underwent surgery were included.

Inclusion Criteria

1. Patients diagnosed to have moyamoya disease of any age group.
2. Patients who have been planned for or have undergone revascularization surgery.

3. Patients who gave informed consent for participation in the study.

Exclusion Criteria

1. Patients of moyamoya disease who have not got operated.
2. Patients of moyamoya disease who have not undergone SPECT preoperatively and postoperatively.

Methodology

22 patients of moyamoya disease who satisfied the inclusion and exclusion criteria were enrolled in the study. The demographic profile and clinical symptomatology were recorded and analysed. Preoperative investigations included CT head/DSA/MRA/ CTA/SPECT (as per Performa).After analyzing clinical and radiological data, patients were taken up for surgery. Surgical revascularization procedures included were:

1) STA –MCA anastomosis

2) Encephaloduroarteriosynangiosis

3) Encephalo myo synangiosis

4) Encephaloduroarteriomyosynangiosis

SPECT was done preoperatively and 3 months postoperatively after revascularization procedure. All patients were followed up for a period of at least 6 months from surgery. The effectiveness of revascularization procedure was assessed in terms of brain perfusion by SPECT and clinically which was based on the questionnaire to patients /attendents regarding halting of symptoms and improvement in scholastic performance.

Methodology of Spect

All patients underwent baseline technicium -99m - ethyl cysteinate dimer (Tc99m-ECD) brain perfusion scintigraphy as per the established procedure guidelines.

A intravenous line was secured, patient was placed in a quiet dimly lit room. Tc99m –ECD in a dose of about 15 – 20 mci was injected intravenously. Patients were instructed not to speak and their head was immobilzed by strapping. For preparation of ECD, Tc 99m was obtained from a generator that was diluted previously within 24 hours. Images were acquired 45 minutes after the injection for best image quality. Tomographic images of the brain were acquired in 128 x 128 matrix, circular orbit and continuous 360 acquisitions. The acquired data was processed using butter worth filter, order 0.5, cutoff 10 and Chang attenuation correction method was applied. Images were displayed on 256 continuous color scales in transverse, sagittal and coronal sections. Segmentation of data acquisition into multiple sequential acquisitions was done to permit exclusion of bad data i.e. removing segments of projection data with patient motion, visual interpretation of perfusion state was made.

Applying manually drawn regions of interest in the region with perfusion defect to corresponding contralateral normal cerebral cortex was determined. The perfusion defect was graded as mild, moderate, severe, negligible and absent.< 20% decrease in tracer uptake with no associated decrease in cortical thickness compared to corresponding contralateral normal cerebral cortex was considered as mild defect, 20 – 50% decrease in intensity of tracer uptake with associated decrease in cortical thickness was considered as moderate defect, >50% decrease in intensity of tracer uptake with associated significant reduction in cortical thickness is considered severe defect .Negligible tracer uptake and nil tracer uptake with significant cortical thickness is considered negligible and absent perfusion defect respectively.

Statistical Analysis

The data (continuous) were presented as mean + SD or median and interquartile range. Mann-Whitney U-test was used for statistical analysis of scores. For time

related scores Wilcoxon signed rank test was applied. When data was considered as categorical; these were described as frequencies and proportions. Proportions were compared using Chi square or Fisher's exact test whichever was applicable. McNemar Test was applied for comparison between preopeative to post-operative values. P value <0.05 was considered to indicate statistical significance. All calculations were performed using SPSS® version 17 (Statistical Packages for the Social Sciences, Chicago, IL).

Results

Table 1: Demographic profile of study cohort, prevalence of symptoms in study cohort and frequency of various surgeries performed

Category	n = 22
Sex Male	 15 (68%)
Female	7 (32%)
Prevalence of symptoms	
Paresis	18(81 %)
Seizure	12(54.5 %)
Aphasia	1(4.5 %)
Chorea	1(4.5 %)
Delayed milestones	1 (4.5 %)
Gait impairment	1(4.5 %)
Surgery performed	
STA MCA + EDAMS	21 (95.4 %)
EDAMS ALONE	1 (4.5%)
STA MCA alone	0

Of the study population, 15 (68%) were males and 7 (32%) were females. There were 19 children and 3 adult patients who were all males. The number of patients below 13 years were 15 (68.2%), 14 – 20 years were 4 (18.2%) 21 – 40 years were 3 (13.6%). 18 (81%) patients presented with paresis which was unilateral in 11 (61.1%) and bilateral in 7 (38.9%).The distribution of symptomatology. Of the 21 patients, who underwent STA MCA bypass 8 (38%) patients underwent surgery on right side, 5 (23.8%) patients on left side, and 8 (38%) had bilateral surgeries done and one patient who underwent EDAMS alone underwent bilateral surgery.

Table 2: Post-operative clinical outcome and Post-operative spect

Post-operative clinical outcome		
	Valid	**Percent**
Improvement	14	63.6
No improvement	8	36.3
Deterioration	0	0
Post-operative spect		
Improvement	13	59.1
No improvement	9	40.9
Deterioration	0	0

It was found that 14 (63.6%) patients showed improvement in clinical outcome and there was no improvement in 8 (36.3%) patients. To summarize 13 (59.1%) patients had improvement on SPECT postoperatively. However this

improvement was not statistically significant (P=0.297) and 9 (40.9%) patients showed no improvement on SPECT at 3 months.

Table 3: Comparison of preoperative and postoperative spect findings for each individual patient and co –relation with clinical improvement

S No.	Right Side SPECT			Left Side SPECT			Clinical Status
	Pre-operative	Post-operative	p-value	Pre-operative	Post-operative	p-value	
1.	7	2	P=0.044*	4	1	P=0.203	Same
2.	3	3		13	12		Improved
3.	12	12		15	10		Improved
4.	2	2		6	6		Improved
5.	2	0		3	1		Same
6.	6	6		14	16		Same
7.	3	3		12	12		Improved
8.	12	8		0	0		Same
9.	0	0		4	1		Same
10.	9	3		9	7		Improved
11.	11	9		7	9		Same
12.	16	16		3	6		Improved
13.	0	0		3	0		Improved
14.	8	8		0	1		Same
15.	14	11		3	0		Improved
16.	0	0		6	6		Improved
17.	15	11		11	11		Improved
18.	6	6		1	2		Same
19.	3	0		20	14		Same
20.	3	2		11	2		Improved
21.	6	9		14	16		Improved
22.	8	12		11	6		Improved

P = 0.044 indicates that there is significant improvement in severity of perfusion defect on the right side.There was no correlation between clinical outcome and SPECT findings.

Table 4: Paired sample correlation between clinical outcome and total score (pre–operative and post-operative severity grading on spect)

Clinical Outcome	n	Pre-operative and Post-operative total score	Correlation
IMPROVEMENT	14	Right side	0.848
		Left side	0.909
NO IMPROVEMENT	8	Right side	0.874
		Left side	0.791

No correlation was found between clinical outcome and pre-op and post-operative SPECT findings.

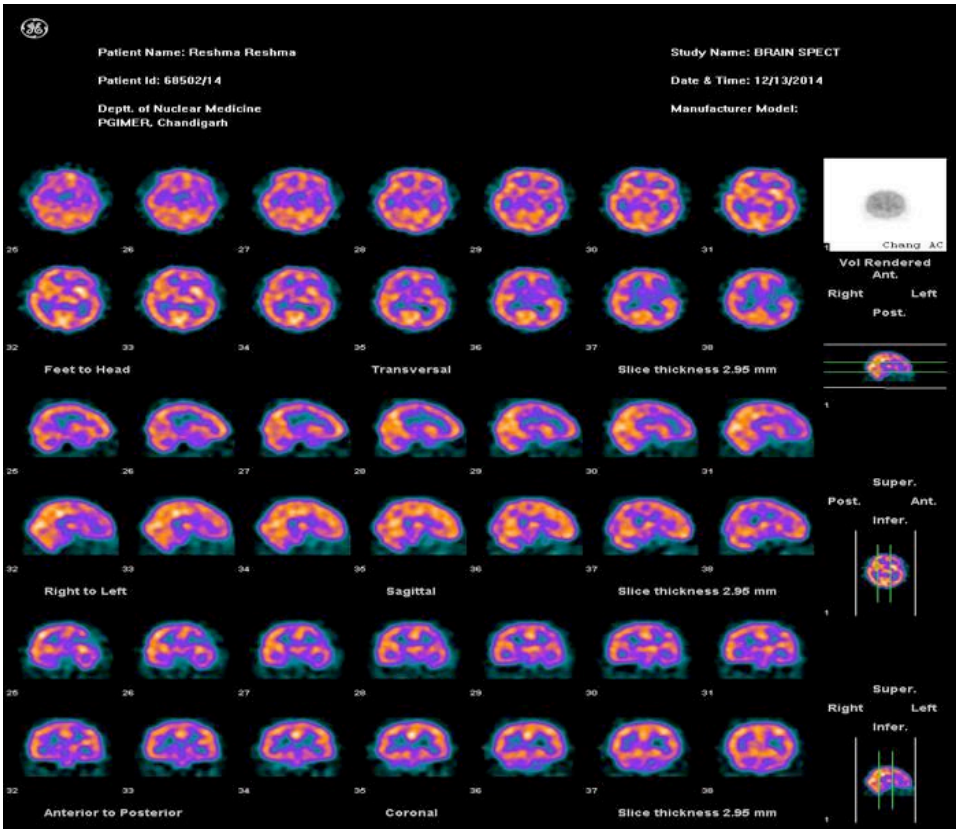

Figure 1: Pre-operative SPECT showing severely reduced perfusion in left frontal cortex

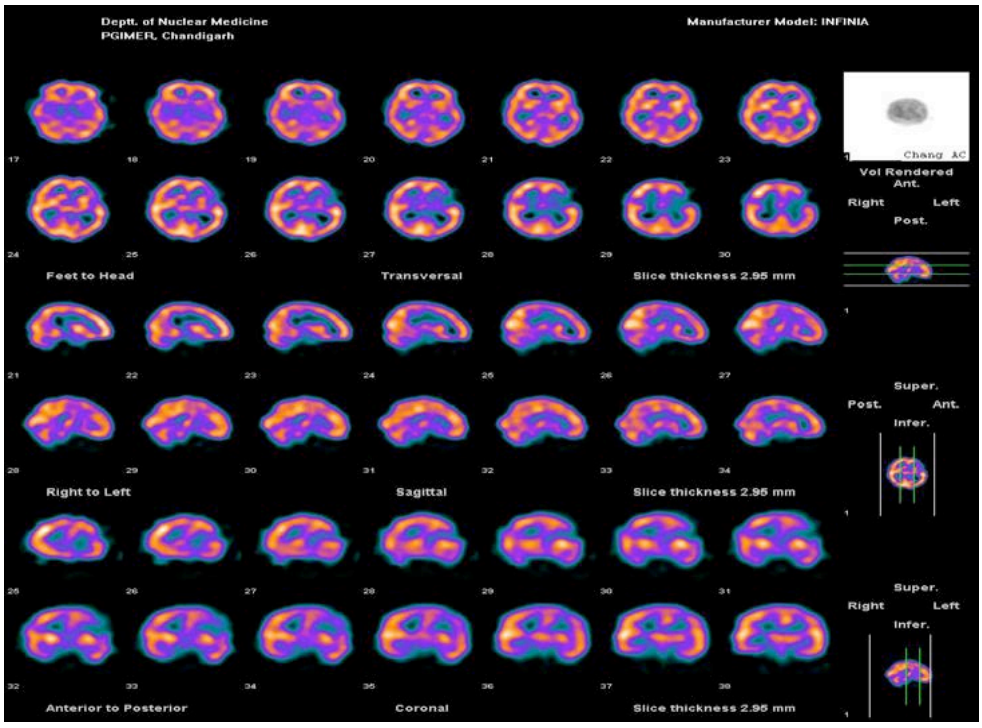

Figure 2: Post-operative SPECT showing severely reduced perfusion in left frontal cortex (mild improvement perfusion in left frontal cortex compared to pre-operative SPECT).

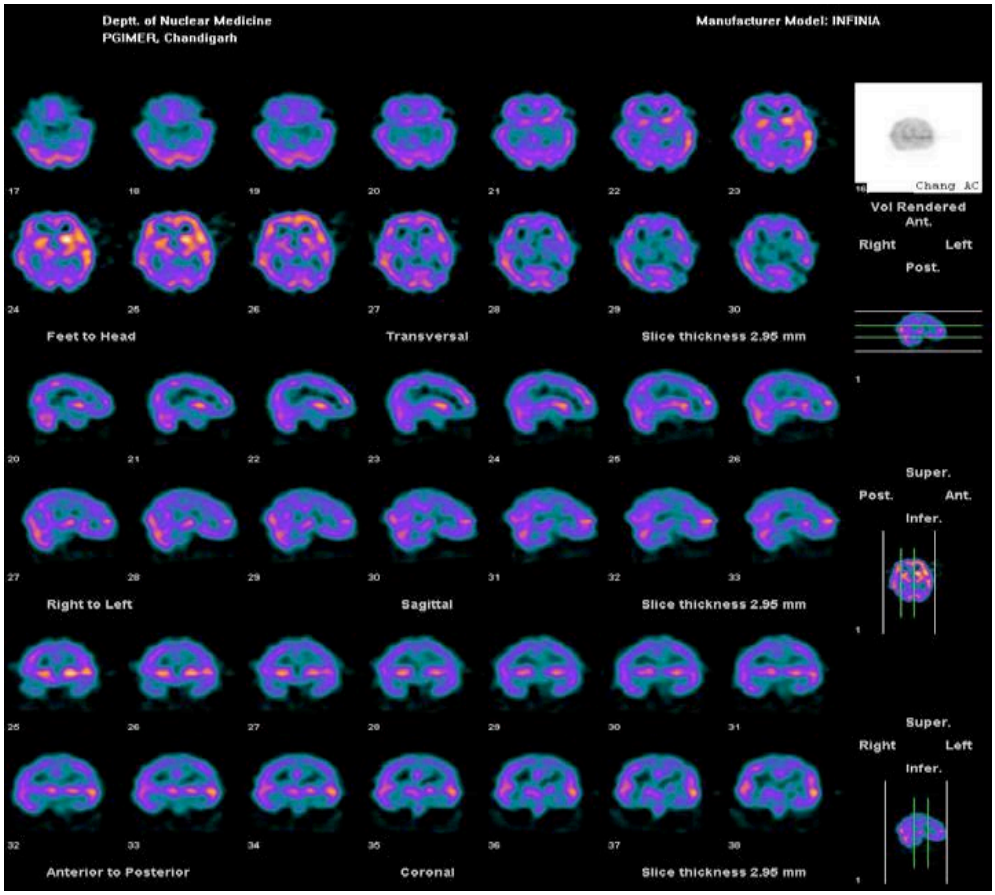

Figure 3: Pre-operative SPECT showing negligible perfusion in left posterolateral occipital lobe and mildly reduced perfusion in left inferior temporal lobe.

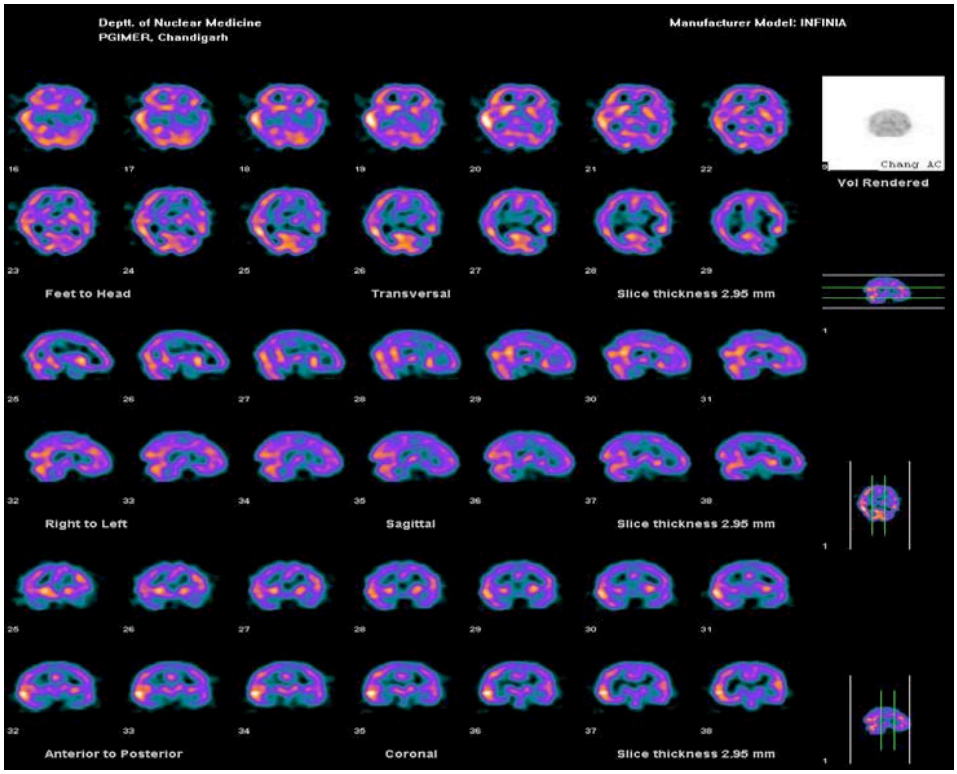

Figure 4: Post-operative SPECT showing severely reduced perfusion in left parietooccipital cortex.

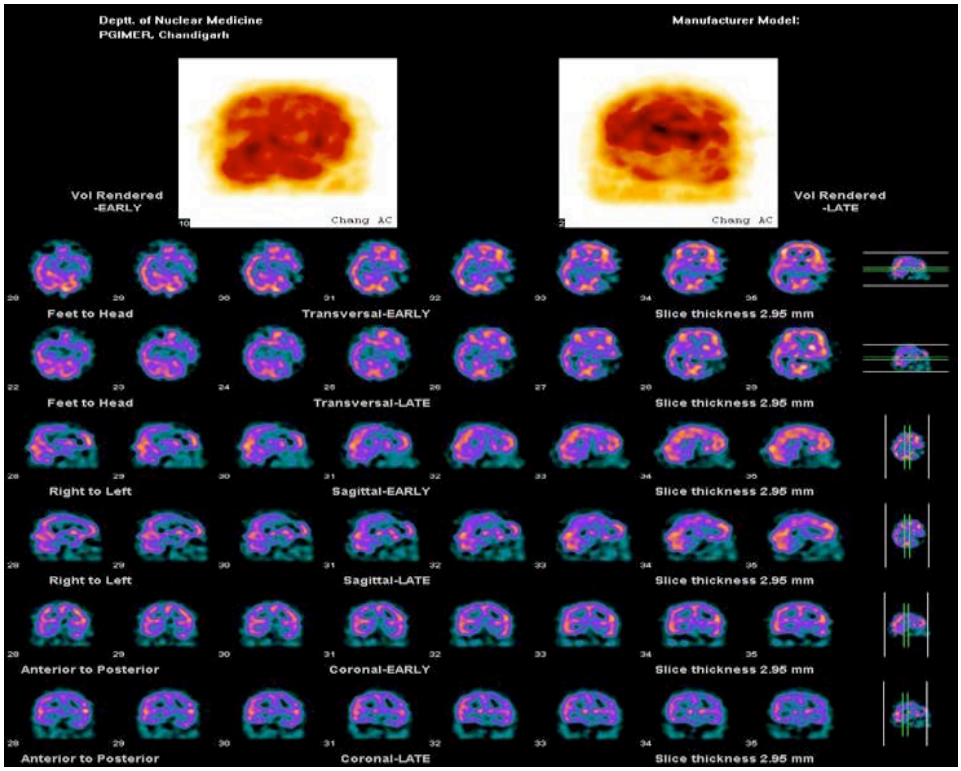

Figure 5: Pre-operative SPECT showing negligible tracer uptake in left parieto occipital cortex and left temporoparietal cortex.Severely reduced tracer uptake in right high frontal cortex. Mildly reduced tracer uptake in left basal ganglia

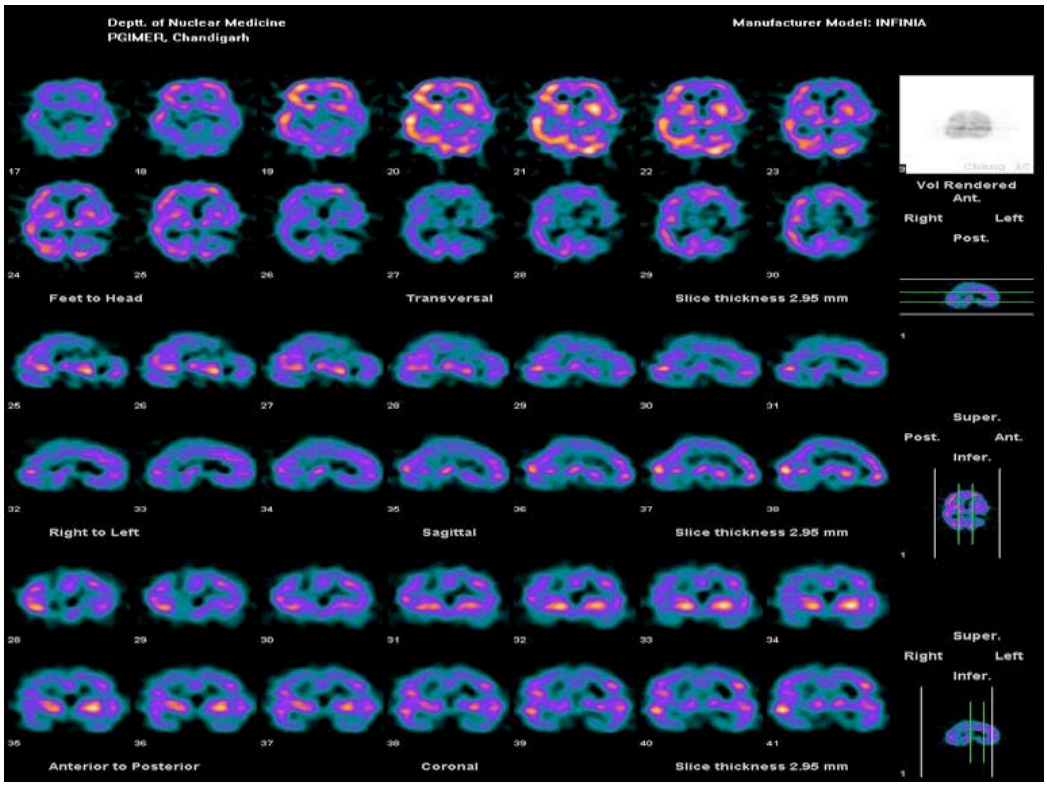

Figure 6: Post-operative SPECT showing negligible tracer uptake in left parietoccipital cortex and left temporoparietal cortex, severely reduced uptake in right high frontal cortex, Adequate tracer uptake in both basal ganglia and cerebellum.

Discussion

Moyamoya disease was first reported by Takeuchi and Schimizu in 1957. Kudo introduced the disease to English literature in 1968. The term Moyamoya disease was first used by Suzuki and Takaku in 1969. Moyamoya disease is a rare progressive cerebrovascular disease that is characterized by narrowing or stenosis of distal internal carotid and proximal portion of anterior and middle cerebral arteries. The etiology of moyamoya disease is unknown. The high incidence among the Japanese and Asian population, together with a familial occurrence of approximately 10–15% of cases, strongly suggest a genetic etiology.

The mean age of presentation in our study is 12.64+9.752 which is similar to other studies. The male to female ratio is 2.1: 1 which is not concordant with most of the studies ,in a survey conducted by Nadia et al (M:F 1:2.5)16, however series from Garg et al showed male predominance [9] and study from Chinchure et al also showed slight male predominance (M:F 1.2 : 1). [10,11] In MMD, most commonly children are affected. In our study, peadiatric age group (<16 years) constituted 19 (86.3%) subjects. Most commonly symptoms are related to ICA territory which includes sudden onset hemiplegia, aphasia, headache , seizures and involuntary movement. [12] The most common symptom in our study was paresis which was present in 18 subjects (81%) and seizures were present in 12 (54.5 %) patients and aphasia in 1 (4.5%) patient.

Angiography is the gold standard for the diagnosis of moyamoya disease. Angiographic criteria for diagnosis of moyamoya disease was described in 1998. [13] They include stenosis or occlusion of distal part of intracranial internal carotid artery and proximal part of anterior and middle artery as well as presence of collateral vasculature in regions of brain. In case of bilateral changes, diagnosis is unilateral as sure, bilateral changes are qualified as probable. SPECT generates a cerebral blood flow map which is compared with a normal control to represent regions of abnormal perfusion. It is often used in conjunction with vasodilatory challenge as an assessment of functional reserve. On the basis of perfusion studies, it was also found that in children with MMD, there is reduction in cerebrovascular reserve (CVR) which is evaluated by Acetazolamide challenge tests on SPECT. [14,15] However our study is limited only to baseline perfusion of SPECT (Qualitative analysis). Since vasodilatory challenge was done in only some patients, it was not included as a part of our study.

One study by Houkin and associates noted that indirect revascularizations through an EDAMS procedure proved effective in all pediatric patients while many adults responded poorly to the procedure. In their analysis, indirect revascularizations was found to be statistically less effective in adults as compared with children .These authors also noted that direct arterial bypass surgery was statistically more effective in adults than children. [11,16,17] However in our study, direct revascularization procedure (STA MCA anastomosis) was done in almost all patients (21 patients). In addition, all patients underwent indirect revascularization procedure (EDAMS) to accomplish the benefits of both. The rationale was to give a maximal chance for revascularization and STA MCA anastomosis was feasible in all the children included in our study. [18]

Postoperatively after three months, all patients were assessed clinically and was found that 14 (63.6 %) showed improvement in clinical outcome and 8 (36.3%) showed no improvement. SPECT was done again and perfusion defects were assessed. In patients who had underwent STA MCA with EDAMS, improvement in

perfusion defect on SPECT was seen in 12(42.8%) and in patient who had underwent EDAMS alone (1) also showed improvement on postoperative SPECT, overall improvement in SPECT irrespective of type of revascularization procedure was seen in 13(59.1%) patients but it was not statistically significant. However no correlation was found between post-operative clinical outcome and SPECT findings.

Improvement in severity of perfusion defect was more marked on the right side (P= 0.044) when compared on left side (P=0.203).

This study demonstrates that perfusion defect in moyamoya disease involve both anterior and posterior circulation unilaterally or bilaterally which is better delineated in perfusion imaging such as SPECT compared to anatomical imaging modalities. As almost all patients included in our study underwent direct as well as indirect revascularization, and time taken for revascularization after indirect procedure is more when compared to direct procedure and hence it is possible that SPECT at 6-9 months in postoperative period may show further improvement and moreover some patients already showed infarct in preoperative NCCT head and these patients may not show improvement in postoperative SPECT.

Conclusion

Our study showed the efficacy of revascularizations procedure in moyamoya disease. Hence there is growing evidence that symptomatic patients should be offered revascularization therapy. SPECT is an important tool and can be used to optimize the treatment strategies for patients with moyamoya disease. The limitations of our study were small sample size, lack of control, qualitative analysis of SPECT.

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