



# A Comparative Study of Regional Cerebral Blood Flow Asymmetry Index in Stroke Patients with or without Poststroke Depression Using $^{99m}\text{Tc}$ -ECD Single-Photon Emission Computed Tomography

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## Abstract

**Introduction** Stroke is a major cause of death and disability around the globe. The development of depression following a stroke further increases the disability and impairs functional recovery. In recent decades, despite the advancement in structural and nuclear medicine imaging, the pathophysiologic basis of poststroke depression (PSD) is not well understood. Etiopathogenesis of PSD is multifactorial and afflictions of the frontal lobe, hippocampus, limbic region, and basal ganglia projections are implicated.

**Aim** The aim of this study was to assess the regional cerebral blood flow (rCBF) using  $^{99m}\text{Tc}$ -ethyl cysteinyl dimer single-photon emission computed tomography (SPECT) in patients with (PSD+) or without PSD (PSD-).

**Materials and Methods** To evaluate the hemispheric asymmetry, the percentage of asymmetry index (AI) was calculated for frontal, temporal, parietal, occipital, putamen, caudate, and thalamic regions of brain and compared between PSD+ and PSD-. The correlation between AIs over the different brain regions was also established in patients of PSD+ and PSD-. Our study cohort included 122 patients between 6 weeks and 1 year of stroke. Depression was present in 52 (42.6%) patients, assessed by hospital anxiety and depression scale (HADS) and general health questionnaire-28 items (GHQ-28) scale. The 28 patients with PSD+ and 18 PSD- gave consent for SPECT study.

**Results** Our results are based on 46 patients who underwent SPECT study. In patients with PSD+ and PSD-, the HADS and GHQ-28 scores were  $8.93 \pm 2.77$  vs.  $3.94 \pm 2.15$  ( $p = 0.001$ ) and  $40.96 \pm 9.48$  vs.  $17.72 \pm 5.38$  ( $p = 0.001$ ), respectively. A significant difference in rCBF AI was found in the temporal lobe ( $p = 0.03$ ) between patients of PSD+ and PSD-. On logistic regression analysis, the odds ratio of rCBF AI for temporal

## Keywords

- ▶ SPECT
- ▶ stroke
- ▶ depression
- ▶ cerebral blood flow

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lobe was 0.89 (95% confidence interval [CI]: 0.80–0.99;  $p = 0.04$ ) and caudate nucleus was 0.85 (95% CI: 0.73–0.98;  $p = 0.03$ ), which were statistically significant. PSD correlated with AI in temporal region ( $r = -0.03$ ;  $p = 0.03$ ) but did not show significant correlation with other regions of brain between PSD+ and PSD-.

**Conclusion** The presence of temporal lobe rCBF AI on SPECT is significantly associated with PSD. This may reflect the dysfunction of the limbic system and contribute to the occurrence of PSD.

## Introduction

Stroke is accountable for second common cause of death and considered to be a major reason for disability worldwide.<sup>1</sup> Despite recent advances in the management of stroke, functional disability remains to be significant among survivors.<sup>2</sup> Currently, with improved stroke care, the numbers of survivors continue to increase in future and a sizable number of patients continue to live with functional disability and impaired quality of life.<sup>2,3</sup> Apart from physical disability, stroke may lead to number of psychiatric symptoms like depression, anxiety, apathy, and sleep disorders.<sup>4</sup> The frequency of poststroke depression (PSD) reported to be variable across different studies; it ranges from 25 to 79%, most likely due to lack of distinct defined criteria in patient selection, and interval between stroke and time of assessment.<sup>5,6</sup> Pathogenic mechanism for development of PSD is perplexing and multifactorial; there is complex interplay between various neurotransmitters and neuronal network resulting from brain injury.<sup>4</sup> Neurobiological effect of brain dysfunction and psychological response to functional loss resulting from stroke, in isolation or combination, are major attributable factors for development of PSD.<sup>7,8</sup> Previous understanding of PSD relies on lesion location, stroke subtype and laterality, and various clinical parameters with anecdotal findings based on neuroimaging studies.<sup>5,9–11</sup> However, lesions located in frontal and temporal regions of brain are more commonly associated with PSD.<sup>12</sup> Study by Starkstein et al reported that lesions involving the left frontal or basal ganglia structures are more likely to cause PSD.<sup>13</sup> A systemic review to assess the relationship of PSD and lesion location concluded that right hemispheric stroke has significant association with incidence of PSD in subacute phase of stroke.<sup>6</sup> In recent decades, due to advent of newer imaging modalities like single-photon emission computed tomography (SPECT) and positron emission tomography, there have been growing interest to study the regional cerebral blood flow (rCBF) and metabolism in patients with PSD. The SPECT studies in PSD have shown the reduction in cerebral blood flow (CBF), which can occur at anatomically distant cortical zone from the real site of brain damage.<sup>14–17</sup> The different neuropsychiatric disturbances may be explained by the impaired functional connectivity between various gray matter structures caused by stroke at structurally distinct location.<sup>18–20</sup> Most of the SPECT studies have been done in ischemic stroke. In a study, 12 participants (with PSD = 5, without PSD = 7) were subjected to SPECT, which revealed reduction in CBF in frontal lobe in 100%

patients with PSD, while this correlation was observed in 29% without PSD.<sup>21</sup> Another study demonstrated that bilateral basal ganglia hypoperfusion may lead to poststroke apathy, a frequent neuropsychiatric symptom in stroke patients.<sup>22</sup> The present study was aimed to compare the rCBF in stroke (ischemic and hemorrhagic) patients with or without depression.

## Aim

The aim of this study was to compare rCBFs using <sup>99m</sup>Tc-ethyl cysteinate dimer (ECD) SPECT in patients with or without PSD.

## Materials and Methods

Consecutive patients were recruited in our study cohort after obtaining informed written consent. The study was approved by the institute ethics committee (IEC no.26/14).

## Inclusion Criteria

All the consecutive adult patients aged 18 to 70 years with a definitive diagnosis of stroke (ischemic and hemorrhagic) attending to our neurology department were included in the study after 6 weeks to 1 year from the onset of stroke.

## Exclusion Criteria

Patients with history of hypothyroidism, HIV, hepatic failure, renal failure, heart failure, respiratory failure, aphasia, altered consciousness, history of psychiatric illness, use of antidepressant, and cerebellar lesion were excluded.

## Clinical Assessment

The patients were subjected for detailed medical history and neurological examination. Cranial nerve palsy and focal neurological deficit were noted. Type of stroke on computed tomography (CT) and or magnetic resonance imaging (MRI) was documented. Lesion locations were noted with respect to frontal, temporal, parietal, occipital, caudate, putamen, and thalamus. Ischemic strokes were further classified according to the Oxfordshire Community Stroke Project (OCSP) classification system.<sup>23</sup> This system of classification categorizes ischemic stroke into: total anterior circulation infarcts (TACI) that encompasses both cortical and subcortical infarct; those lesions that are more restricted as cortical infarcts (partial anterior circulation infarcts, PACI); the

infarcts confined to vertebra-basilar territory (posterior circulation infarcts, POCI); and deep perforating artery lesions classified as lacunar infarcts (LACI). For the assessment of depression, hospital anxiety and depression scale (HADS) and general health questionnaire-28 items (GHQ-28) were advocated and applied. HADS has correlation coefficient of 0.79 for depression and 0.54 for anxiety. HADS has approximately 80% sensitivity and specificity. The cut-off value of  $-8/21$ , on 0–3 scale, was taken for depression.<sup>24</sup> The GHQ-28 has correlation coefficient of 0.67 to 0.83 with sensitivity and specificity of around 81% to detect depression. The cut-off value of  $23/24$ , on 0–3 scale, was taken in our study.<sup>25</sup> Those patients with or without PSD who gave consent for SPECT study were analyzed.

### SPECT Study

#### Patient Preparation

All eligible patients were instructed to avoid caffeine and alcohol, which affect CBF.

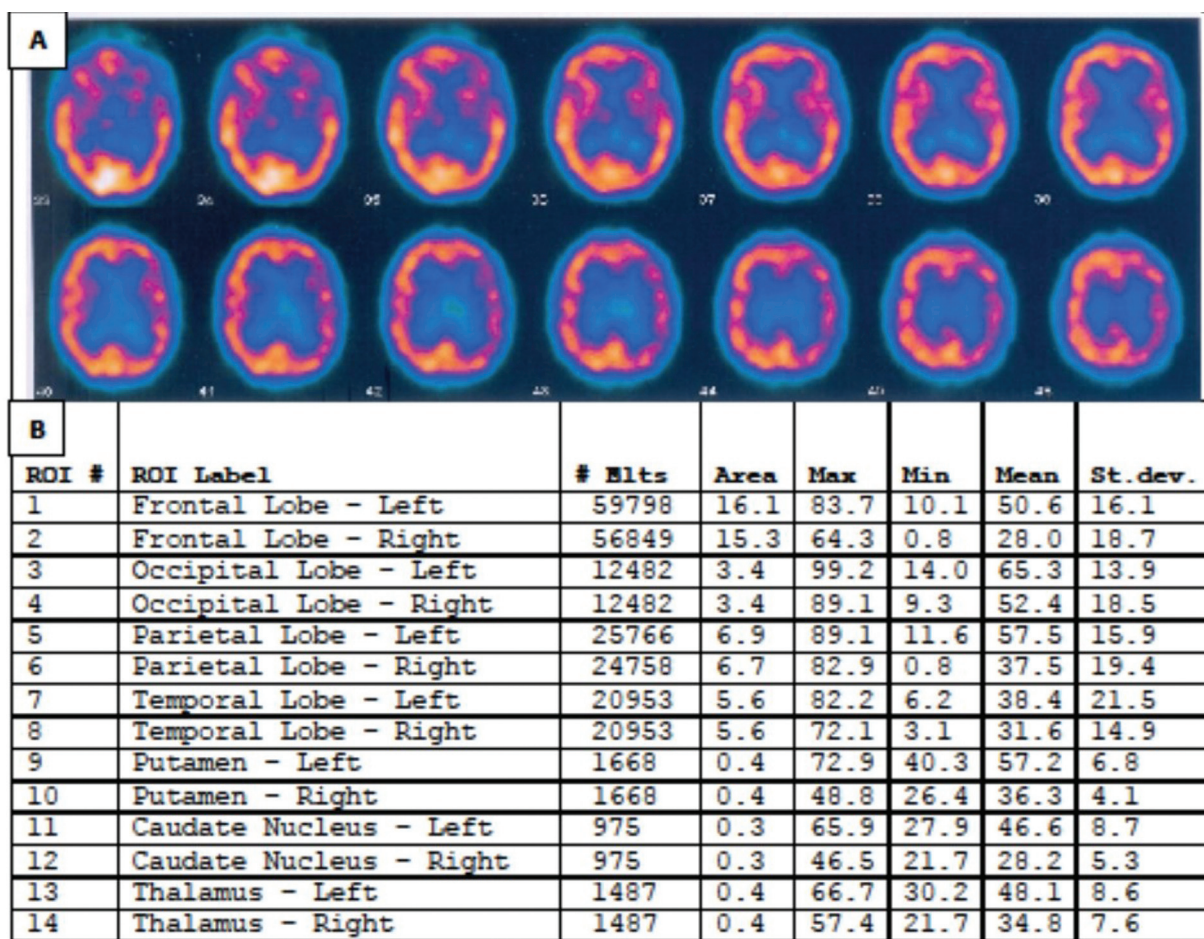
1. Radiopharmaceuticals: <sup>99m</sup>Tc-Bicisate (ECD).
2. Radiopharmaceutical injection: Tracer was injected no sooner than 10 minutes pre- and no more than 4 hours

postreconstitution. Patients were instructed to void within 2 hours postinjection to minimize radiation exposure.

3. SPECT-CT Imaging: Approximately 45-minute delay was assured from injection to imaging for best image quality. Imaging was completed within 4 hours postinjection.
4. Dosage: A 555–1,110 MBq (15–30 mCi) of <sup>99m</sup>Tc-ECD was injected after quality control of radiopharmaceuticals.

<sup>99m</sup>Tc-Bicisate (ECD) scans were performed for all subjects using a Discovery NM-CT 670 SPECT-CT (16 Slice). SPECT acquisition was done in  $128 \times 128$  matrix size and parallel hole collimators. Images were acquired in 3-degree step-and-shoot mode, 360-degree acquisitions with a total count of  $5 \times 10^6$  or more. Multislice CT acquisitions of patient were done without any change in position. Image processing was performed first by filtered back projection using Butterworth filters. Images were reconstructed at high-pixel resolution and CT-based attenuation correction was performed in all patients. Reconstruction of CT images along with SPECT images was achieved using GE special fusion software and processed images were generated in three orthogonal planes in SPECT only, CT only, and SPECT-CT fused images.

Each SPECT study was analyzed by nuclear medicine physician blinded to clinical data using NeuroGam software



**Fig. 1** Brain perfusion single-photon emission computed tomography of a patient with left thalamic bleed with poststroke depression exhibiting hypoperfusion in left thalamus and parietal lobe. (A) Visual assessment and (B) quantitative analysis in different brain areas using NeuroGam software.

using a Talairach map, obtaining volumetric images and voxel-to-voxel assessment of regions of interest (ROIs).<sup>26</sup> The SPECT images were analyzed semi-quantitatively. ROI was placed on the ipsilateral and contralateral frontal, temporal, parietal, occipital, caudate, putamen, and thalamus. The quantitative results, including the mean/maximum/minimum pixel value, in each corresponding ROI were obtained (→ Fig. 1). The mean pixel value was chosen to quantify the perfusion. From the mean percent counts obtained from each region of brain using NeuroGam software, the asymmetry index (AI) was calculated by using the following equation:

$$AI = \frac{[(\text{mean pixel count in unaffected hemisphere} - \text{mean pixel count in affected hemisphere}) / (\text{mean pixel count in unaffected hemisphere} + \text{mean pixel count in affected hemisphere})] \times 100.}$$

**Statistical Analysis**

The statistical analysis of study data was performed using IBM SPSS version 20 software. The categorical variables were compared using Fisher’s exact tests and continuous variables by independent *t*-test or Mann-Whitney U test. Logistic regression analysis was performed to obtain the odds ratio to establish the association between variables. The relationship between AIs with mean count of different brain location was studied using Pearson’s correlation test. The variable was considered significant if the two-tailed *p*-value was less than 0.05.

**Results**

**Demographic and Clinical Characteristics**

Total 122 patients were recruited in our study cohort, from which 46 patients provided consent for SPECT study. The diagnosis of PSD was based on clinical criteria for depression using HADS and GHQ-28. Out of 46 patients subjected for SPECT study, 28 were PSD+ and 18 PSD-.

The mean age was 55 ± 8.85 years for patients with PSD+ and 50.78 ± 7.77 years for PSD- group. There were 21 males and 7 females in PSD+ group whereas 15 males and 3 females in PSD- group. The mean duration of stroke was 17.39 ± 11.06 and 21.22 ± 14.76 weeks in PSD+ and PSD- patients, respectively. The detailed demographic and clinico-radiological data are presented in → Table 1.

**Stroke Subtype**

The types of stroke were 20 ischemic and 8 hemorrhagic in PSD+ group and 10 ischemic and 8 hemorrhagic in PSD- group. The side of stroke on neuroimaging (CT and/or MRI) revealed right sided lesion in 17 (37%) and 11 (23.9%) left sided in PSD+ as compared with 11 (23.9%) right sided and 7 (15.2%) left sided lesion in PSD- group. The hypertension was most common comorbid illness in 23 (50.0%) versus 15 (32.6%) followed by diabetes mellitus 7 (15.2%) versus 5 (10.9%) in PSD+ and PSD- subjects, respectively. Smoking as a risk factor for stroke was present in 8 (17.4%) versus 7 (15.2%) and alcohol intake in 4 (8.7%) versus 6 (13%) in PSD+

**Table 1** Demographic and various clinico-radiological parameters of patients

Variables	Poststroke depression			p-Value	
		Present (28)	Absent (18)		
Age (mean ± SD)		55.00 ± 8.85	50.78 ± 7.77	0.10	
Gender	Male	21 (45.7%)	15 (32.6%)	0.71	
	Female	7 (15.2%)	3 (6.5%)		
Place of living	Urban	10 (21.7%)	6 (13.0%)	1.0	
	Rural	18 (39.1%)	12 (26.1%)		
Duration of strokes (wk)		17.39 ± 11.06	21.22 ± 14.76	0.32	
Type of stroke	Ischemic	20 (43.50%)	10 (21.70%)	0.34	
	Hemorrhagic	8 (17.40%)	8 (17.40%)		
Side of stroke on imaging	Right	17 (37.00%)	11 (23.90%)	1.00	
	Left	11 (23.90%)	7 (15.20%)		
Comorbidities	DM	Present	7 (15.20%)	5 (10.9%)	1.00
		Absent	21 (46.7%)	13 (28.3%)	
	HTN	Present	23 (50.0%)	15 (32.6%)	1.00
		Absent	5 (10.9%)	3 (6.5%)	
Risk factors for stroke	Smoking	Present	8 (17.4%)	7 (15.2%)	0.53
		Absent	20 (43.5%)	11 (23.9%)	
	Alcohol intake	Present	4 (8.7%)	6 (13.0%)	0.15
		Absent	24 (52.2%)	12 (26.1%)	

Abbreviations: DM, type-2 diabetes mellitus; HTN, hypertension; SD, standard deviation.

**Table 2** Comparison of various imaging parameters of stroke patients with or without depression

Variables	Poststroke depression			p-Value
		Present	Absent	
Size of ischemic stroke	Large cortical	2	0	0.69
	Medium size cortical	8	5	
	Small cortical	1	0	
	Large subcortical	2	2	
	Small subcortical	7	3	
Classification of stroke	Total anterior circulation	1	0	0.31
	Partial anterior circulation	15	6	
	Posterior circulation	0	1	
	Lacunar stroke	4	4	
Location of ischemic stroke (on imaging)	Frontal	2	1	0.39
	Temporal	7	2	
	Parietal	9	4	
	Occipital	0	1	
	Internal capsule	1	1	
	Thalamus	2	0	
Type of hemorrhagic stroke (on imaging)	Frontal	0	1	0.09
	Putamen	3	6	
	Thalamus	5	1	

and PSD- groups, respectively. There was no statistically significant difference between both groups regarding demographic and clinico-radiological parameters. The lesion characteristic in ischemic stroke revealed TACI in 1 versus 0, PACI in 15 versus 6, LACI in 4 versus 4, and POCI in 0 versus 1 in PSD+ and PSD- groups, respectively. The location of stroke in ischemic subtype were frontal in 2 versus 1, temporal in 7 versus 2, parietal in 9 versus 4, occipital in 0 versus 1, internal capsule in 1 versus 1, and thalamus in 2 versus 0 in PSD+ and PSD- patients, respectively. The hemorrhagic stroke subtype analysis revealed frontal 0 versus 1, putamen 3 versus 6, and thalamus in 5 versus 1 in PSD+ and PSD- subjects, respec-

tively. The lesion subtype and stroke location in ischemic and hemorrhagic stroke patients are summarized in ►Table 2.

### Depression Status and Stroke

For evaluation and quantification of depression, the HADS and GHQ-28 questionnaire was advocated. The details of HADS and GHQ-28 scores, along with their subscale in PSD+ and PSD- groups, are presented in ►Table 3. The PSD+ group has mean score for HADS  $16.39 \pm 4.35$ , and PSD- group  $7.11 \pm 3.67$ , which were statistically significant ( $p < 0.001$ ). The GHQ-28 score was (mean  $\pm$  standard deviation [SD])  $40.96 \pm 9.48$  and (mean  $\pm$  SD)  $17.72 \pm 5.38$  in PSD+ and

**Table 3** HADS and GHQ-28 score in patients with or without poststroke depression

Variables	Poststroke depression			p-Value
		PSD+ (28)	PSD- (18)	
HADS	HADS total	$16.39 \pm 4.35$	$7.11 \pm 3.67$	0.001
	HADS-anxiety	$7.46 \pm 2.72$	$3.17 \pm 2.09$	
	HADS-depression	$8.93 \pm 2.77$	$3.94 \pm 2.15$	
GHQ-28	GHQ-28 total	$40.96 \pm 9.48$	$17.72 \pm 5.38$	0.001
	Somatic symptoms	$9.25 \pm 2.41$	$6.28 \pm 3.14$	
	Anxiety and insomnia	$9.75 \pm 3.91$	$3.17 \pm 2.17$	
	Social dysfunction	$12.75 \pm 3.05$	$5.78 \pm 3.05$	
	Severe depression	$9.21 \pm 4.45$	$2.89 \pm 2.80$	

Abbreviations: GHQ-28, general health questionnaire-28 items; HADS, hospital anxiety and depression scale score.

Note: Data are presented as the mean  $\pm$  standard deviation.

**Table 4** Relationship of asymmetry index/regional cerebral blood flow of different brain regions on <sup>99m</sup>Tc-ECD SPECT with poststroke depression status

Asymmetry index	Poststroke depression	n	Mean	Standard deviation	p-Value
Frontal	Present	28	15.05	14.23	0.08
	Absent	18	5.41	23.40	
Parietal	Present	28	15.08	20.72	0.21
	Absent	18	6.84	23.34	
Temporal	Present	28	7.95	16.46	0.03
	Absent	18	-4.98	22.66	
Occipital	Present	28	12.58	24.66	0.12
	Absent	18	-1.67	37.83	
Caudate	Present	28	10.14	11.63	0.46
	Absent	18	7.16	15.81	
Putamen	Present	28	6.87	13.70	0.74
	Absent	18	8.44	18.85	
Thalamus	Present	28	1.52	16.15	0.09
	Absent	18	9.24	13.19	

Abbreviation: <sup>99m</sup>Tc-ECD SPECT, technetium-99m ethyl cysteinate dimer single-photon emission computed tomography.

PSD- groups, respectively. The HASD and GHQ-28 score showed statistically significant difference in PSD+ and PSD- groups ( $p < 0.001$ ).

**Comparison of AI over Different Brain Regions with PSD Status**

The comparison of AI between the PSD+ and PSD- patients showed significant difference in temporal lobe ( $p = 0.03$ ) but did not in other regions of brain, as analyzed in ▶Table 4. The logistic regression analysis revealed that the odds ratio for temporal lobe AI was 0.89 (95% confidence interval [CI]: 0.80–0.99;  $p = 0.04$ ) and caudate nucleus was 0.85 (95% CI: 0.73–0.98;  $p = 0.03$ ), which were statistically significant but not significant for other regions of brain; the odds ratio for frontal lobe was 1.00 (95% CI: 0.88–1.14;  $p = 0.98$ ), for parietal lobe 0.99 (95% CI: 0.90–1.10;  $p = 0.97$ ), for occipital

lobe 1.00 (95% CI: 0.94–1.07;  $p = 0.85$ ), for putamen 1.03 (95% CI: 0.94–1.14;  $p = 0.43$ ), and for thalamus 1.12 (95% CI: 0.98–1.28;  $p = 0.07$ ). Among the demographic and clinical features, the modified Rankin Scale (mRS) score predicted the PSD but not for age and duration of stroke (▶Table 5).

**Correlation of AI with PSD Status at Different Brain Regions**

PSD correlated with AI in temporal region ( $r = -0.03$ ;  $p = 0.03$ ) but did not for frontal ( $r = -0.25$ ;  $p = 0.08$ ), parietal ( $r = -0.18$ ;  $p = 0.21$ ), occipital ( $r = -0.22$ ;  $p = 0.12$ ), caudate ( $r = -0.11$ ;  $p = 0.46$ ), putamen ( $r = 0.04$ ;  $p = 0.74$ ), and thalamic ( $r = 0.24$ ;  $p = 0.09$ ) regions (▶Table 6).

The visual findings revealed hypoperfusion in the ipsilateral side over the region of stroke in 25 versus 15, contralateral side to stroke in 2 versus 0, and no perfusion defect in 2

**Table 5** Predictors of poststroke depression including various clinical and laboratory parameters by logistic regression analysis

Variables	Odds ratio (95%CI)	p-Value	
Asymmetry index	Frontal lobe	1.00 (0.88–1.14)	0.98
	Parietal lobe	0.99 (0.90–1.10)	0.97
	Temporal lobe	0.89 (0.80–0.99)	0.04
	Occipital lobe	1.00 (0.94–1.07)	0.85
	Caudate	0.85 (0.73–0.98)	0.03
	Putamen	1.03 (0.94–1.14)	0.43
	Thalamus	1.12 (0.98–1.28)	0.07
Duration of stroke (in weeks)	1.03 (0.95–1.12)	0.37	
Age (in years)	0.85 (0.71–1.01)	0.07	
mRS score	0.12 (0.02–0.59)	0.01	

Abbreviation: CI, confidence interval; mRS, modified Rankin scale.

**Table 6** Correlation between poststroke depression status and asymmetry index of different brain region on perfusion <sup>99m</sup>Tc-ECD SPECT

Correlation between poststroke depression and asymmetry index of different brain region	Pearson's correlation coefficient	p-Value
Frontal lobe	-0.25	0.08
Parietal lobe	-0.18	0.21
Temporal lobe	-0.03	0.03
Occipital lobe	-0.22	0.12
Caudate	-0.11	0.46
Putamen	0.04	0.74
Thalamus	0.24	0.09

Abbreviation: <sup>99m</sup>Tc-ECD SPECT, technetium-99m ethyl cysteinate dimer single-photon emission computed tomography.

versus 3 in PSD+ and PSD- cases, respectively. However, there was no statistically significant difference achieved in PSD+ and PSD- patients, respectively ( $p=0.32$ ).

The cortico-cerebellar ratio was calculated for unilateral frontal and hemicortical regions from opposite side of stroke. The cortico-cerebellar ratio for frontal location was  $0.82 \pm 0.19$  versus  $0.83 \pm 0.19$  ( $p=0.86$ ) and for hemicortical region was  $0.76 \pm 0.17$  versus  $0.77 \pm 0.17$  ( $p=0.88$ ) in PSD+ and PSD- groups, respectively. There was no statistically significant difference in PSD+ and PSD- groups (►Table 7).

## Discussion

PSD has unfavorable long-term consequences on the prognosis of patients leading to greater disability, morbidity, and mortality on health outcome measures.<sup>9,27</sup> The depression was found in 42.6% (52/122) of patients in our study cohort. Despite being an underdiagnosed condition, the occurrence of PSD ranges from 18 to 33% in stroke survivors.<sup>28</sup> The incidence and prevalence vary across the different studies, which may be due to various factors like time to stroke onset, ethnicity, and socioeconomic background. The prevalence varied from 17 to 73% in a systematic review on PSD from Middle East and North Africa.<sup>29</sup> Apart from poor social and family support, the PSD may have positive association with stroke severity and physical disability and possibly PSD might influence the functional outcome by lack of motivation and participation in rehabilitative strategies.<sup>30</sup>

In our study also, the patients with PSD have poor functional outcome on mRS score. Our study was performed with an aim to compare the CBF AI in the different locations of brain using <sup>99m</sup>Tc-ECD SPECT. In our study cohort, results

showed that there was a significant difference in rCBF AI in temporal region among the PSD+ and PSD- patients. In a study of 15 patients after single-lesion subcortical stroke with depression ( $n=8$ ) and no depression ( $n=7$ ), the CBF values were lower in former group measured by <sup>99m</sup>Tc-hexamethylpropyleneamine oxime SPECT.<sup>17</sup> The study was supported by the hypothesis that the temporal lobe hypoperfusion may reflect the dysfunction of limbic system, which may be responsible for depression conceivably by influencing the interrupted cortico-subcortical connections. There is paucity of literature on PSD and rCBF using ECD SPECT. In study on patients with ( $n=37$ ) or without ( $n=65$ ) poststroke apathy, using *N*-isopropyl-*p*-[(123)I]-iodoamphetamine SPECT, it was found that there were reduced rCBF in basal ganglia of apathetic patients.<sup>22</sup> Though apathy differs from depression in clinical phenomenology, there is considerable overlap of symptoms. Apathy is also common after stroke and frequently accompanied with depression. In a longitudinal study that included 60 patients of stroke (ischemic and hemorrhagic), rCBF was measured using the <sup>133</sup>xenon inhalation method with an aim to evaluate the relation with severity of depression. In the above study, the authors concluded that the severity of depression was inversely correlated with rCBF value in parieto-occipital region in right hemisphere and anterior temporal region in left hemisphere.<sup>31</sup> However, the study recruited the patients with bilateral and large lesions. The temporal lobe, inferior frontal lobe, and subcortical limbic anatomical sites play a crucial role in the regulation of mood in normal and neurological disorders.<sup>32,33</sup> Remote anatomic location from the primary pathological site in manic patients following brain injury demonstrated hypometabolism of right inferior

**Table 7** Cortico-cerebellar ratios from different brain regions in PSD patients

Brain region	PSD+ ( $n=28$ )	PSD- ( $n=18$ )	p-Value
Cortico-cerebellar ratio: Frontal lobe	$0.82 \pm 0.19$	$0.83 \pm 0.19$	0.86
Cortico-cerebellar ratio: Hemicortex	$0.76 \pm 0.17$	$0.77 \pm 0.17$	0.88

Abbreviation: PSD, poststroke depression.

Note: Data are presented as mean  $\pm$  standard deviation.

temporal lobe.<sup>34</sup> This phenomenon supports the hypothesis that the focal brain lesion may be responsible for affective syndrome irrespective of primary location of brain insult.<sup>33</sup> Our study demonstrated that on logistic regression analysis, the odds ratio for temporal lobe AI was 0.89 (95% CI: 0.80–0.99;  $p=0.04$ ) and for caudate nucleus was 0.85 (95% CI: 0.73–0.98;  $p=0.03$ ). In a study of 102 patients with post-stroke apathy, hypoperfusion of basal ganglia on SPECT was demonstrated in 37 (36%) subjects.<sup>22</sup> There are several clinical, social, and demographic factors that determine the PSD, but the lesion location remains the main focus of researchers. In a preliminary study, Robinson et al have shown that patient with left frontal region had high risk of depression as compared with insult elsewhere in the brain.<sup>35,36</sup> Subsequent studies have also confirmed that the lesions in frontal lobe, basal ganglia, and temporal lobe are more commonly associated with PSD.<sup>37–40</sup> Recent studies on pathogenic mechanism of PSD have implicated the limbic-cortical-striatal-pallidal-thalamic (LCSPT) circuit in the development of depression.<sup>41,42</sup> It is postulated that this circuit may get affected indirectly by the distant primary lesion by surrounding edema and anterograde or retrograde neuronal degeneration. The growing body of evidence as suggested by recent meta-analysis did not find the role of hemispheric laterality on PSD.<sup>43</sup> The variability across the various studies on clinico-anatomic correlate can be explained by this hypothesis of LCSPT circuit involvement up to some extent. There is a need for more studies to get a robust data to support the effect of lesion location and laterality of stroke on PSD.

Our study included both ischemic and hemorrhagic stroke patients of cortical and subcortical locations, which is a real scenario encountered in clinical practice. A certain limitation in our study design is the exclusion of aphasic patients, who might be suffering from depression. The patients enrolled in our study cohort were between 6 weeks and 1 year post-stroke but PSD may even persist for longer duration and there may be variability in rCBF.

## Conclusion

Our study found that the presence of temporal lobe rCBF AI on SPECT is significantly associated with PSD. Abnormalities of rCBF/AI measured by SPECT may have utility in understanding the pathophysiologic basis of PSD.

### Note

The manuscript has been read and approved by all the authors.

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### Conflict of Interest

None declared.

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