

Depression and Quality of Life after Cerebral Venous Sinus Thrombosis

Aralikatte O. Saroja, Ninad N. Thorat, Karkal R. Naik

Department of Neurology, Jawaharlal Nehru Medical College, Nehru Nagar, Belagavi, Karnataka, India

Abstract

Introduction: Cerebral venous sinus thrombosis (CVST) is an important cause of stroke in young and has a favorable outcome. Long-term sequelae of CVST include motor disability, cognitive impairment, depression, anxiety, fatigue, impaired employment and poor quality of life. **Objective:** To evaluate depression and quality of life after CVST. **Methods:** Patients who completed at least 1 year after discharge were recruited for this cross-sectional observational study from our CVST cohort. Quality of life was assessed using Stroke-Adapted Sickness Impact Profile (SA-SIP 30) and depression using Hamilton Depression scale (HAM-D). **Results:** A total of 100 patients (60 men and 40 women) were included in the study. Their age ranged from 14 to 60 years (34.97 ± 10.06). The interval from discharge to assessment of quality of life was 2.2 ± 1.6 years. In all, 98% of patients had good modified Rankin score at follow-up. SA-SIP 30 did not reveal any functional disability for physical functioning. Seven had impairment for psychosocial domain despite having good modified Rankin scores. Thirty patients had depression. Patients with higher mRS at discharge had increased presence of depression. Quality-of-life scores did not correlate with presence of seizure, headache, infarction and sinuses involved. **Conclusion:** This is the first Indian study demonstrating depression in patients with CVST and use of SA-SIP to assess quality of life in them. Occurrence of depression in CVST is as high as in arterial strokes.

Keywords: Cerebral venous sinus thrombosis, Hamilton Depression scale, post-stroke depression, quality of life

INTRODUCTION

Stroke is the leading cause of disability^[1] and according to the World Health Organization, one-third of the 15 million patients affected per year are permanently disabled due to stroke.^[2] Prevalence of stroke in India is increasing leading to more people being left with some degree of disability.^[3] Cerebral venous sinus thrombosis (CVST) accounts for up to 1% of all strokes worldwide.^[4] However, Indian studies have documented higher incidence of CVST. In hospital-based studies from India, 15-20% of stroke patients less than 40 years, had CVST.^[5,6] Cardinal presentations of CVST include raised intracranial pressure, focal neurological deficits, epileptic seizures and altered sensorium.^[7] Residual impairment of physical, psychological, social and cognitive functions can occur secondary to sequelae of CVST due to infarctions, seizures, and raised intracranial tension.^[8]

Outcome in CVST patients has been evaluated in terms of morbidity and mortality in majority of the studies most often using modified Rankin score (mRS) which does not reflect the subtle cognitive, physical and psychosocial impairments. Specific instruments to evaluate the quality of life (QOL) are needed.^[9] Health-related quality of life (HRQOL) covering physical, cognitive and social functions is an important index of outcome after stroke.^[10] Studies on QOL in CVST patients are sparse. There is a single study in children with CVST on QOL using Child Health Questionnaires which is not applicable to adult patients.^[11] Availability of QOL data would be essential to improve their functional outcome after discharge. Considering the sparse data on QOL in CVST, we conducted this study to evaluate the QOL in patients with CVST.

METHODS

This is a cross-sectional descriptive study. Patients were recruited from our CVST cohort who were diagnosed clinically and confirmed on cranial imaging. Patients who had completed at least 1-year follow-up for CVST attending out-patient clinic were selected after obtaining informed consent. Their baseline clinical and laboratory data were obtained from the hospital records. The mRS from 0 to 2 was graded as good outcome and scores above 2 were considered poor outcome. Patient recruitment was done consecutively from May 2017 to November 2018. Participants were interviewed by a single researcher. Addenbrooke's cognitive examination - III (ACE-III) was administered in local languages prior to inclusion of the participants.^[12] Patients with ACE-III score ≥ 88 were included in the study as poor

Address for correspondence: Dr. Ninad N. Thorat,
Department of Neurology, Jawaharlal Nehru Medical College, Nehru Nagar,
Belagavi - 590 010, Karnataka, India.
E-mail: drninadthorat@gmail.com

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cognition may interfere with interviewing these individuals. The questionnaires were downloaded from the official website of the University of Sydney.

QOL measure used was Stroke-Adapted Sickness Impact Profile (SA-SIP 30) and depression was assessed by HAM-D after obtaining permission. Direct interview was performed in the application of the instrument of QOL due to the potential difficulty in reading and literacy among participants. No proxy interviews were done.

The SIP30 was developed from the original 136-item sickness impact profile (SIP-136) and assesses the QOL in patients who have suffered a stroke.^[13] The SA-SIP30 contains 30 items and each item consists of a statement describing changes in behavior that reflect the impact of illness on some aspect of daily life. The SA-SIP30 consists of eight subscales: Body Care and Movement, Mobility, Ambulation, Social Interaction, Emotional Behaviour, Alertness, Behaviour, Communication, and Household Management. All answers are in 'yes' or 'no' format. Scores are presented as a percentage of maximum dysfunction, ranging from 0 to 100%, with a higher score indicating poorer functioning. Patients with scores exceeding 33 are known to be impaired in activities of daily living (ADL), unable to live independently, experience difficulties in self-care, mobility and in performing their main activity. Although there is no specific cut-off for psychosocial subscale, values exceeding 22 in psychosocial dimension have been used to define patients with impaired psychosocial functioning.^[14]

The HAM-D is a widely used clinician-administered depression assessment scale. We used the 21-item version of the HAM-D scale and scoring is based on the first 17 items as the last 4 items are used to measure factors that might be related to depression, but are not thought to be measures of severity, such as paranoia or obsessional and compulsive symptoms.^[15] Scores of 0-7 are considered as being normal, scores of 8-16 as mild depression, 17-23 as moderate depression and more than 24 as severe depression.^[16]

Statistical analysis

Data were entered in Microsoft Excel and analysis was performed using R i386 3.5.1. The continuous variables were summarized as mean \pm SD. The comparisons were done using T-test for mean and Wilcoxon signed rank test for median. Chi-square and/or Fisher exact test were used as appropriate to study the association between categorical variables. *P* value <0.05 was considered as statistically significant.

RESULTS

One hundred patients with CVST were included in the study of whom 60 men and 40 women. Their age ranged from 14 to 60 years (34.97 \pm 10.06 years; median 34 years) majority under the age of 40 years. The interval from discharge to assessment of QOL ranged from 1 to 5 years (2.2 \pm 1.6 years). The Glasgow

coma scale (GCS) at admission was 13.02 \pm 2.84 (median 15). Their mRS at discharge was 1.37 \pm 1.12 (median 1) with 14 patients having poor mRS at discharge. [Table 1] At the time of QOL evaluation, their mRS was 0.3 \pm 0.6 (median 0) and only two patients had poor mRS. Thirty-one patients continued to have headache, 26 had recurrence of seizures and one patient had new onset seizure during follow-up. Seizures were controlled with monotherapy in 48, polytherapy was needed in 45 patients and seven did not receive antiepileptic medication. Three patients had deep venous thrombosis of lower limb. None of the patients had recurrence of CVST.

Headache was the commonest symptom of increased intracranial pressure (79%). Sixty-five patients had seizures with generalized seizures being the commonest. Multiple sinus involvement was common (76%) with superficial venous sinus system (89%) being the commonest. Left cerebral infarctions (36%) were twice as common as right (18%).

Hyperhomocysteinemia (61.67%), followed by alcohol and tobacco consumption (40%) were the most common etiological factors in men. In women anaemia, hormonal preparations, hyperhomocysteinemia and pregnancy-related CVST were the risk factors. Protein S deficiency was present in 17 of 32 patients tested for thrombophilia.

QOL scores did not change with presence of seizure at onset or during follow-up, presence of infarction and its laterality, persistence of headache and number of sinuses involved.

Stroke adapted - sickness impact profile (SA-SIP30)

Seven patients (five men and two women) had abnormal SA-SIP scores in psychosocial subscale. The mRS at discharge in these patients was low (range 0-2; median 1) and at the time of QOL evaluation was 0 to 1 (median 0). Five of these

Table 1: The demographic and clinical data in 100 patients with cerebral venous thrombosis. Numbers in the parenthesis are the percentages. GCS=Glasgow coma score, mRS=modified Rankin score

	Men n=60	Women n=40	All patients n=100
Age (years)			
≤20	3 (5)	2 (5)	5 (5)
21-30	20 (33.33)	17 (42.5)	37 (37)
31-40	19 (31.67)	11 (27.5)	30 (30)
41-50	12 (20)	8 (20)	20 (20)
51-60	6 (10)	2 (5)	8 (8)
Seizures	40 (66.67)	25 (62.5)	65 (65)
Generalized	28 (46.67)	19 (47.5)	47 (47)
Focal	12 (20)	6 (15)	18 (18)
Status	2 (100)	-	2 (2)
Cluster	16 (26.67)	9 (22.5)	25 (25)
Headache	49 (81.67)	30 (75)	79 (79)
GCS	13.05 \pm 2.72	12.975 \pm 3.04	13.02 \pm 2.84
mRS at discharge			
≤2	55 (91.67)	31 (77.5)	86 (86)
≥3	5 (8.33)	9 (22.5)	14 (14)

patients had depression. None of the patients had limitation in carrying out ADL, physical functioning or feeling of incapacitation, as depicted in the normal scores for the physical subscale. [Table 2].

Hamilton depression rating scale (HAM-D)

Scores on HAM-D scale were normal in 70 patients. [Table 2] Twenty-nine patients had mild depression and one had moderate depression without any gender difference. Ten of the 18 patients with frontal infarctions had depression and none of six patients with deep venous thrombosis had depression. Among 31 patients with persistent headache, 10 had depression. Twenty-six patients had recurrence of seizures of whom seven were depressed. Out of the 30 patients with depression, 23 (76.7%) had seizures. Among the 58 patients receiving antiepileptic monotherapy, 16 (27.59%) had depression and 14 of 48 patients (29.17%) on polytherapy had depression. Twelve patients (25%) receiving levetiracetam had depression and nine of 23 (39.13%) patients on levetiracetam with additional antiepileptic drugs had depression. Three of the seven patients (42.87%) with postpartum CVT had depression whereas only seven of the 33 patients (21.21%) with nonpuerperal CVT had depression ($P < 0.01$). There was increased presence of depression in patients with higher mRS at discharge ($P < 0.0001$). Among 86 patients with good mRS, 21 (24.41%) were depressed and among 14 patients with poor mRS, 9 (64.28%) were depressed. There was no gender difference in the presence of depression.

DISCUSSION

CVST is an important and treatable cause of stroke affecting the young more than the elderly. Unlike arterial strokes CVST has a good outcome when diagnosed and treated early.^[9] Physical disability assessment can be easily done using modified Rankin Scale. QOL in these patients may not be evident using mRS, and hence, detailed assessment requires the use of specific tools such as the SF36 and SA-SIP 30. The SF-36

is more of a subjective assessment, on the contrary SIP 30 has items that concentrate on a particular behaviour relating to restrictions or recent alterations in functionality instead of subjective feelings or perceptiveness.^[17] In the present study, 86% had good outcome with mRS score < 2 at discharge and at the time of assessment of QOL 98% had mRS of < 1 . We assessed QOL using SA-SIP 30 and demonstrated normal scores for physical domain which bears good correlation with mRS at the time of assessment of QOL. All the patients achieved functional independence in ADL as seen with normal SIP30 scores for physical subscale, which is in accordance with larger studies like the ISCVST.^[9] In spite of achieving functional independence, 30% had depression highlighting the need to look at depression in these patients after discharge. Among seven patients in our study with lower scores in the psychosocial domain, five had depression. SA-SIP30 has not been recommended for assessment of depression and the cut-off scores for its psychosocial dimension are not clearly defined. Hence, the results of this dimension were not evaluated further. CVST affects younger people hence it is essential to assess long-term sequelae and QOL using appropriate scales.

There are a large number of studies on arterial strokes which demonstrate poor QOL in females more than males.^[18-20] Women had lower QOL with lower SF36 scores and the domains involved were physical functioning, emotional well-being, vitality, energy and fatigue. They also demonstrated mean SIP 30 score of 24.3 at 1 year. Women with severe disability and depression had poorer scores on SIP 30.^[18] These scales have not been used in earlier studies on CVST.

Depression or anxiety has been documented in two-thirds of patients with CVST.^[21] Depression has been demonstrated in 18% using Beck depression inventory among 34 patients included in the study and none of them had cognitive or functional disability.^[22] Another study demonstrated cognitive impairment in 35%, poor functional outcome with dependency or restrictions in life-style in more than 40% of their patients with CVST.^[23] We observed depression in 30% of our patients and 31% had persistent headache. There was no gender preponderance for depression. We found a significant correlation between poor mRS at the time of discharge and presence of depression at follow-up. Post-stroke depression in arterial strokes has been reported in 18%-70%, and attributes to lower QOL.^[24-27] Depression in CVST patients needs to be treated to achieve better QOL in view of its high prevalence. It is also essential to evaluate the cause of depression in patients with CVST despite having good mRS and SA-SIP36 scores. We do not have pre-morbid evaluation for depression; hence, it is possible that the true prevalence of depression post-CVST may be over-estimated. Further studies are required for evaluating true prevalence of pre-morbid and post-CVST depression.

Literature survey revealed very few studies assessing outcome of cerebral venous thrombosis using QOL measures.^[21-23] Long-term sequelae included headache (43%), impaired concentration (75%), fatigue and depression in 30% of patients

Table 2: The HAM-D scores, ACE-III and SA-SIP in patients with cerebral venous thrombosis. Numbers in parenthesis are percentages for HAM-D and median values for ACE-III and SA-SIP scores

	Male	Female	Total
HAM-D			
Normal	43 (71.7)	27 (67.5)	70 (70)
Mild	16 (26.7)	13 (32.5)	29
Moderate	1	-	1
Severe	-	-	-
ACE-III	90.03±2.91 (90)	90.43±2.63 (90)	90.19±2.79 (90)
SA-SIP physical score	2.27±4.47 (0)	3.1±4.82 (0)	2.6±4.61 (0)
SA-SIP psychological score	8.08±8.89 (6.7)	6.6±8.52 (6.4)	7.49±8.73 (6.4)
SA-SIP total score	4.29±4.01 (3.50)	5.61±5.01 (4.25)	5.09±4.67 (4)

followed up after a year of occurrence of CVST.^[28] Other long-term sequelae of CVST documented include cognitive impairment in about 35% patients, dependency 6% and restriction of lifestyle in 40% and inability to achieve pre-morbid employment level in 40%.^[23] These studies have used cognitive tests, mRS, Barthel Index, Fatigue severity scales, European QOL and depression scales. In the present study, we included patients with normal ACE scores, and hence, cognitive dysfunction could not be commented upon. We inferred that the assessment of QOL could be difficult in cognitively impaired individuals. Other domains not assessed in our patients is the employment status which is known to be impaired in CVST.^[23]

CONCLUSION

CVST is an important and increasingly diagnosed cerebrovascular disease. QOL is an under-evaluated dimension of patient's well-being. In this study, we have demonstrated the utility of QOL assessment to bring to light the subtle impairments in the various dimensions of daily functioning. We have also demonstrated significant occurrence of depression which is as much as seen in arterial strokes and needs attention. Hence, it is imperative to assess long-term psychosocial, motor, cognitive outcome and QOL using specific tools in these patients. Assessment of disability, depression and their management would improve QOL in CVST patients. To the best of our knowledge, this is the first study to evaluate QOL in Indian patients with CVST. Occurrence of depression in CVST is as high as in arterial strokes.

Limitations of our study are selective inclusion of cognitively normal patients, underestimation of premorbid depression and confounding effect of anti-epileptic drugs.

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Conflicts of interest

There are no conflicts of interest.

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