ORIGINAL ARTICLE

Comparison of Outcome in Different Types of Stroke Due to Cerebral Ischemia

Asif Husain Osmani, Rasheed Khan Durrani and Jamal Ara

ABSTRACT

Objective: To compare the outcome in different types of stroke according to cerebral ischemic region.
Study Design: Descriptive study.
Place and Duration of Study: Medical Unit-I (Ward 5), Jinnah Postgraduate Medical Centre, from June 2006 to April 2007.
Methodology: A total of one hundred and forty seven patients of first ever cerebral infarcts admitted through emergency and medical OPD were included in the study and diagnosed on the basis of clinical findings and scan of brain. Detailed history and relevant examination was done. Causes of death during hospital stay were assessed. Discharged patients were followed-up in medical OPD and progress was monitored by modified Rankin scale at 1,3 and 6 months poststroke.
Results: One hundred and forty seven patients were studied. Their average age was 56.47±15.8 years. There were 80 (54.4%) males and 67 (45.6%) females. The stroke syndromes inculded partial anterior circulation stroke in 43 (29.25%), posterior circulation stroke in 30 (20.41%), total anterior circulation stroke (TACS) in 36 (24.49%) and lacunar stroke in 38 (25.85%). During their hospital stay, 45 (30.6%) patients expired and 102 (69.3%) were discharged.The total mortality rate was 36.05% at one month, 40.1% at third month and 43.5% at sixth month poststroke. Mortality was significantly high in patients with TACS (n-26, 72.2%, p-0.0001), Furthermore, at the time of incidence, 27.8%, 19.7% and 14.2% cases respectively were functionally dependent. Twenty five (65.7%) patients of lacunar stroke were independent (p=0.002) at the end of the sixth month poststroke.
Conclusion: TACS had the worst outcome with the highest number of mortalities, whereas lacunar stroke had a better outcome, i.e. a majority of the patients were functionally independent by the end of 6 months.

Key words: *Total anterior circulation stroke. Partial anterior circulation stroke. Posterior circulation stroke. Lacunar stroke. Modified Rankin scale.*

INTRODUCTION

Stroke is defined according to World Health Organization as rapidly developing symptoms and/or signs of focal and at times global loss of brain functions, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.[1] Acute stroke is the second leading cause of death in industrialized countries.[2] The cost of related care is among the fastest growing expenses for medicare.[3] Prevention of stroke (and indeed diagnosis and therapy) requires an in-depth understanding of the stroke subtypes and etiological factors which differ by geographic region, and even by ethnicity within the same region.

Bamford *et al.* using data from the Oxford Community Stroke Project (OCSP), defined four sub-categories of cerebral infarction on the basis of presenting symptoms and sign; lacunar stroke, total anterior circulation stroke, partial anterior circulation stroke and posterior circulation stroke.[4] Classification was based upon bedside clinical features and the label attached to each sub-category is anatomical, which reflects the close correlation between symptoms and signs and site of cerebral infarction. This classification is of prognostic significance.

A major point of discussion is how to define outcome in acute stroke trials with disability and handicap scales.[5] The most widely used scales are Modified Rankin scale (MRS) and Barthel Index.[6] The MRS has proved to be valid and reliable for defining outcome in stroke patients. Extensive evidence on the validity, reliability and sensitivity of the MRS exists across broad but fragmented literature.[7] The MRS defines 6 different grades of disability, from 0 for "no symptoms at all" to 5 for "severe disability or bedridden, incontinent, and requiring constant nursing and care and attention", and 6 for death.[8] This study was conducted to determine the outcome and progress of patients suffering from four types of acute ischemic stroke as described above.

METHODOLOGY

This longitudinal study of patients with first ever clinical stroke due to cerebral infarction was carried out in

Medical Unit 1, Ward 5, Jinnah Postgradute Medical Centre, Karachi.

Correspondence: *Dr. Asif Husain Osmani, H. No. 76/II, 14th Street, Khayaban-e-Badar, Phase 6, DHA, Karachi.*
E-mail: osmaniasif@yahoo.com

Received February 26, 2008; accepted September 02, 2009.

Medical Unit I (Ward 5), Jinnah Postgraduate Medical Centre, Karachi, from June 2006 to April 2007. A total of 147 patients above the age of 15 years of either gender were included in the study and diagnosed on the basis of clinical findings and investigations. The diagnosis of clinical sub-types of ischemic stroke were rated according to Bamford's classification (Oxfordshire Community Stroke Project) criteria as total anterior circulation stroke (TACS), partial anterior circulation stroke (PACS), lacunar stroke (LACS) and posterior circulation stroke (POCS).

All patients of cerebral ischemia were included in the study and categorized into the four sub-types on the basis of clinical findings and location of infarcts on CT brain scan. Patients with total anterior circulation stroke (TACS) presented with a combination of higher cerebral dysfunction (e.g., dysphasia, dyscalculia, visuospatial disorder); homonymous visual field defect; and ipsilateral motor and, or sensory deficit of at least two areas of the face, arm, and leg.[9] If the conscious level was impaired and formal testing of a higher cerebral function or the visual field was not possible, a deficit was assumed. Patients with PACS presented with two, out of the three components of TACS, with higher cerebral dysfunction.[4] LACS patients presented with a pure motor stroke, pure sensory stroke, sensory-motor stroke, or ataxic hemiparesis without higher cerebral dysfunction.[4] Patients with POCS presented with any of the following;[10] ipsilateral cranial nerve palsy with contralateral motor and or sensory deficit; bilateral motor and or sensory deficit, disorder of conjugate eye movement; cerebellar dysfunction without ipsilateral long-tract deficit (i.e., ataxic hemiparesis) or isolated homonymous visual field defect. Patients suffering from haemorrhagic stroke, sub-arachnoid haemorrhage, head trauma, space occupying lesion in brain, previous old cerebral infarctions on imaging incidently found while investigating for the current infarct, demyelinating disease and vasculitis were excluded from the study.

The deaths during hospital stay were due to direct neurological sequelea, acquired infections and cardiac cause. The progress of the discharged patients was monitored on the basis of the functional outcome derived from Modified Rankin scale into three groups as (a) capable of independent existence, (b) dependant on others and (c) dead. The outcome was assessed at 1, 3 and 6 months poststroke respectively in the medical OPD. The data was entered and analyzed on SPSS version 10.0. The outcome was presented as a frequency table. A chi-square test was applied to compare proportion difference of outcome in different strokes. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study was carried out on 147 patients of cerebral infarction meeting with inclusion criteria and diagnosed on the basis of clinical finding and investigation. Their average ages were 56.47±15.8 years (ranging form 15 to 102 years). Out of 147 patients, there were 80 (54.4%) males and 67 (45.6%) females. The stroke syndromes were partial anterior circulation stroke in 43 (29.25%), posterior circulation stroke in 30 (20.41%), total anterior circulation stroke in 36 (24.49%) and lacunar stroke in 38 (25.85%).

During the hospital stay, 45 (30.6%) patients expired and 102 (69.3%) were discharged and advised for follow-up in the medical OPD of Medical Unit 1. Out of 45 deaths, 33 (22.4%) were due to direct neurological sequelea, 11 (7.5%) were due to infection and 1 (0.68%) patient died due to cardiac causes.

The outcome at one month is shown in Table I. The overall mortality was 53 (36.05%); 41 (27.8%) patients were dependant and 53 (36.05%) patients were independent. At this time, mortality was significantly high in patients with TACS which was 26 (72.2%, p=0.0001), where as 23 (60.5%) patients of lacunar stroke were independent (p=0.001).

Outcome at third month is shown in Table II. The overall mortality was 59 (40.1%); 29 (19.7%) patients were dependant and 59 (40.1%) were independent. Mortality at the third month was significantly high in patients with TACS (n=29, 80.5%, p=0.0001). Twenty five (67.7%) patients with lacunar stroke were independent (p=0.001).

At the sixth month, the overall mortality was 64 (43.3%); as shown in Table III, 21 (14.2%) patients were dependent and 62 (42.1%) patients were independent. Mortality was significantly high in TACS (n=31, 86.1%, p=0.0001) and the 25 (65.7%) patients with lacunar stroke were still independent with (p=0.002).

The mortality rate was consistently high in patients with TACS while patients and patients with lacunar stroke had a significant consistently independent outcome. The overall mortality rate of the study was 43.5%.

Table I: Comparison of outcome of stroke after one month.

Stroke	Outcome (modified rankin scale)			Total	p-value
	Dead	Dependent	Independent		
PACS	14 (32.5%)	14 (32.5%)	15 (34.8%)	43	0.78
POCS	10 (33.3%)	2 (20%)	14 (46.6%)	30	0.434
TACS	26 (72.2%)	9 (25%)	1 (2.7%)	36	0.0001*
LACS	3 (7.8%)	12 (31.5%)	23 (60.5%)	38	0.001*
Total	53 (36.05%)	41 (27.8%)	53 (36.05%)	147	-

Table II: Comparison of outcome of stroke after third month.

Stroke	Outcome (modified rankin scale)			Total	p-value
	Dead	Dependent	Independent		
PACS	15 (34.8%)	10 (23.2%)	18 (41.8%)	43	0.741
POCS	11 (36.6%)	4 (13.3%)	15 (50%)	30	0.48
TACS	29 (80.5%)	6 (16.6%)	1 (2.7%)	36	0.0001*
LACS	4 (10.5%)	9 (23.6%)	25 (67.7%)	38	0.001*
Total	59 (40.1%)	29 (19.7%)	59 (40.1%)	147	-

Table III: Comparison of outcome of stroke after six months.

Stroke	Outcome (modified rankin scale)			Total	p-value
	Dead	Dependent	Independent		
PACS	16 (37.2%)	7 (16.2%)	20 (46.5%)	43	0.702
POCS	11 (36.6%)	3 (10%)	16 (53.3%)	30	0.45
TACS	31 (86.1%)	4 (11.1%)	1 (2.7%)	36	0.0001*
LACS	6 (15.7%)	7 (18.4%)	25 (65.7%)	38	0.002*
Total	64 (43.3%)	21 (14.2%)	62 (42.1%)	147	-

Data are given as no. of patients (%), Row wise percentage are computed for each stroke.

** Significant*

Strokes: Partial Anterior Circulation Stroke (PACS), Posterior Circulation Stroke (POCS) Total Anterior Circulation Stroke (TACS), Lacunar Stroke (LACS)

Outcome: Independent = (Ranking Grades 0-2), Dependent = (Ranking Grades 3-5), Death = (Ranking Grade 6).

DISCUSSION

Stroke is a global health problem. It is the leading cause of adult disability and the second leading cause of mortality worldwide.[11] In a population-based study among the Pasthun community in Pakistan, a high prevalence (4.8%) of stroke was observed.[12]

Sub-typing of the ischemic stroke to identify the underlying mechanism is essential for both clinical practice and research. Therefore, a reliable classification system for acute cerebral infarction is very important. Several clinical classification systems have been used to categorize the sub-types of cerebral infarction, but one of the most prevalent classifications is the Bamford's classification. In this study, the incidence and natural history of four clinically identifiable sub-types of cerebral infarction was described in 147 patients of first ever stroke. The outcome was monitored by the Modified Rankin scale (MRS), which is a clinician-reported measure of global disability and has been widely applied for evaluating recovery from stroke. Studies in small patient series have consistently shown significant relationships between lesion volume (measured by diffusion-weighted and other imaging methods) and Modified Rankin scale grades, with larger lesions predicting more severe disability.[13] As would be reasonably expected, improved brain perfusion and recanalization after thrombolytic therapy are also associated with improved Modified Rankin scale disability outcomes.[14-16] There are 6 grades of Modified Rankin scale, and all its grade transitions are considered to be clinically meaningful.[17]

The study was carried out on 147 patients of cerebral infarction diagnosed on the basis of clinical finding and investigation.

During the hospital stay, 45 (30.6%) patients died. These deaths occurred in the first 7 days of their admission. The death rate in this study was higher than Vernino's study,[18] where 8% expired in the first week and in an Italian study 9.7% mortality occurred in hospital.[19]

Out of 45 (30.6%) deaths, 33 (22.4%) patients died of direct neurological sequelae and 11 (7.5%) patients died of infections such as aspiration pneumonia and septicemia secondary to urinary tract infection. Both these complications occur in the unconscious with urinary tract infections due to catheterization. Of 33 deaths due to direct neurological sequelae, 19 (57.5%) patients belonged to TACS. Patients with TACS have large vessel occlusion and often have acute cerebral edema caused by cortical ischemia.[20] Early deterioration is associated with a worse prognosis; Tei *et al.* found almost 42% of Japanese patients with TACS deteriorated within the first 7 days of acute stroke and more than one third of these were dead by 7 days.[9] The reason for early mortality could be the lack of thrombolytic therapy. Intravenous recombinant-tPA for treatment of acute ischemic stroke has been used in the developed world with favourable outcome, both in academic teaching hospitals as well as in community based medical centres.[21]

After discharge till one month outcome, 8 (5.4%) patients expired, and the total mortality was 53 (36.05%). Forty one (27.8%) patients were dependant and 53 (36.05%) patients were independent. The case fatality was higher than in other studies, i.e., in OCSP 10%, BROS study 29.8%,[22] 15.8% in a study conducted in Martinique,[23] 23.3% in a study conducted in Chille and 24 and 26% in the South London Stroke Register (SLSR).[25] At this time, 41 (27.8%) patients were functionally dependant, where as in OCSP 39% were dependant. Between one month and three months, 6 (4%) patients expired, and the total case fatality was 59 (40.1%) which was also high as compared to the South London Stroke Register where it was 32.7%.[25] At this time, 29 (19.7%) patients were functionally dependant. Between the third month and sixth month, 5 (3.4%) patients expired, and the total outcome in terms of case fatality was 64 (43.3%) which in comparison with the OCSP, Lavados study and SLSR was higher, where the mortalities were 18%, 33% and 36.1% respectively. At the 6th month, 21 (14.2%) patients were dependant which is lower than OCSP where 29% were dependant. The results show that the four groups do have distinctive features. In the TACS group the chance of a good functional outcome was negligible and mortality was significantly high. Poor outcomes after hemispheric infarctions are consistent with considerable damage to corticospinal tracts.[26] The observations of the LACS group showed that such strokes are "mild"; their mortality rates are low and a large portion show significant improvement. The case fatality secondary to LACS was higher then other studies conducted worldwide,[4,27,28] which therefore, justifies the need for further evaluation and management of diseases which lead to it. Mortality also depends on the type of neurological deficit at the time of presentation of the patient and the site and size of lacunar infarcts.[27]

The recovery patterns of LACI and PACI were distinctive in this study unlike in Smith's study,[29] where it does not distinguish distinctive recovery patterns. Finally, in the POCI group few patients died early, presumably due to interference with vital brainstem structures. The rate of death immediately after POCI is approximately 3-4%,[10] which is lower than this study.

There are several limitations of the present study. Not all tertiary care institutions taking care of stroke patients in Pakistan were included in this study. It is advisable to conduct a multicentre study on stroke in Pakistan that may help make future stroke management policy. However, to confirm any causalty, the present findings require an investigation in prospective studies. Therefore, future studies on risk factors of ischemic stroke should differentiate between stroke etiologies to unmask the role of particular risk factors for single subtypes. It is also recommended that future attempts to predict stroke outcome using acute clinical and imaging variables would be valuable in the management of ischemic stroke patients. Ischemic stroke is a polyetiologic disease with profound difference between subtypes regarding age and gender distribution, and outcomes. Several factors can contribute to this much increase rate of mortality in a hospital and at 1, 3 and 6 months poststroke in this study. Some of them can be effectively eliminated with standardization of stroke management in local institutions; e.g. introduction of IV tpA within 3 hours of the window period may decrease the poor outcomes in acute ischemic stroke patients. The importance of subsequent stroke risk assessment should be highlighted and every patient with stroke needs to have some preliminary investigation such as cardiac echography, carotid Doppler and lipid profile on admission, which is not routinely practiced in our institution. There is evidence that acute care and rehabilitation of stroke patients is best carried out in stroke units that offer an organized, multidisciplinary approach to care. All stroke patients should have access of such care. Dedicated stroke units with well equipped monitors and trained doctors and nursing staff may play a pivotal role in the management of acute ischemic patients. Improving general nursing care and reducing the number of complications like infections would probably decrease the death rate in stroke patients.

CONCLUSION

TACS had the worst outcome with the highest number of mortalities, where as lacunar stroke had better outcome, i.e. a majority of the patients were functionally independent by the end of 6 months.

REFERENCES

1. Vohra EA. Stroke: the challenge and response. *Pak J Med Sci* 2001; **17**:65-6.
2. Mackay J, Mensah GA. The atlas of heart disease and stroke. Geneva: *World Health Organization*; 2004.
3. Centers for Disease Control. Public health and aging: hospitalizations for stroke among adults ages over 65 years -- United States, 2000. *JAMA* 2003; **290**:1023-4.
4. Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet* 1991; **337**:1521-6.
5. Young F, Lees KR, Weir CJ. Glycine Antagonist in Neuroprotection International Trial Steering Committee and Investigators. Strengthening acute stroke trials through optimal use of disability end points. *Stroke* 2003; **34**:2676-80. Epub 2003 Oct 16.
6. Uyttenboogaart M, Stewart RE, Vroomen PCAJ, DeKeyser J, Luijckx G. Optimizing cutoff scores for the Barthal Index and the modified rankin scale for defining outcomes in acute stroke trials. *Stroke* 2005; **36**:1984.
7. Wilson JT, Hareendran A, Grant M, Baird T, Schulz UGR, Muir KW, *et al.* Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified rankin scale. *Stroke* 2002; **33**:2243-6.
8. Banks JL, Marotta CA. Outcome validity and reliability of the modified rankin scale: implications for stroke clinical trials. *Stroke* 2007; **38**:1091-6.
9. Tei H, Uchiyama S, Ohara K, Kobayashi M, Uchiyama Y, Fukuzawa M. Deteriorating ischemic stroke in 4 clinical categories classified by the Oxfordshire community stroke project. *Stroke* 2000; **31**:2049-54.
10. Glass TA, Hennessey PM, Pazdera L, Chang HM, Wityk RJ, Dewitt LT, *et al.* Outcome at 30 days in the New England Medical Center Posterior Circulation Registry. *Arch Neurol* 2002; **59**: 369-76. Comment in: p. 359-60.
11. World Health Organization: The world health report 2003: shaping the future. Geneva: *WHO*; 2003.
12. Jaffar TH. Blood pressure, diabetes, and increased dietary salt associated with stroke- results from a community - based study in Pakistan. *J Hum Hypertens* 2006; **20**:83-5.
13. Derex L, Nighoghossian N, Hermier M, Adeleine P, Berthezene Y, Philippeau F, *et al.* Influence of pre-treatment MRI parameters on clinical outcome, recanalization and infarct size in 49 stroke patients treated by intravenous tissue plasminogen activator. *J Neurol Sci* 2004; **225**:3-9.
14. Molina CA, Alexandrov AV, Demchuk AM, Saqqur M, Uchino K, Alvarez-Sabin J. CLOTBUST investigators. Improving the predictive accuracy of recanalization on stroke outcome in patients treated with tissue plasminogen activator. *Stroke* 2004; **35**:151-6. Epub 2003 Dec 11.
15. Chalela JA, Kang DW, Luby M, Ezzeddine M, Latour LL, Todd JW, *et al.* Early magnetic resonance imaging findings in patients receiving tissue plasminogen activator outcome: insights into the pathophysiology of acute stroke in the thrombolysis era. *Ann Neurol* 2004; **55**:105-12.
16. Lui Y, Karonen JO, Vanninen RL, Nuutinen J, Koskela A, Soimakallio S, *et al.* Acute ischemic stroke: predictive value of 2-D phase contrast MR angiography-serial study with combined diffusion and perfusion MR imaging. *Radiology* 2004; **231**:517-27. Epub 2004 Mar 4.
17. Shuaib A, Lees KR, Lyden P, Grotta J, Davalos A, Davis SM, *et al;* SAINT II trial investigators. NXY-059 for the treatment of

acute ischemic stroke. *N Engl J Med* 2007; **357**:562-71. Comment in: *N Engl J Med* 2007; **357**:2198; author reply 2198-9.

18. Vernino S, Brown RD, Sejvar JJ, Sicks JD, Petty GW, O' Fallon WM. Cause- specific mortality after first cerebral infarction: a population-based study. *Stroke* 2003; **34**:1828-32. Epub 2003 Jul 10.
19. Sciolla R, Ferrari G, Leone M; SINPAC (Società INter-regionale Piemonte e Valle d'Aosta per le Cerebrovasculopatie) Group. Stroke and transient ischemic attack in 18 neurology departments from two Italian regions: the SINPAC database. *Neurol Sci* 2005; **26**:208-17.
20. Mead G, Wardlaw J, Dennis M, Lewis SC, Warlow CP. Relationship between pattern of intracranial artery abnormalities on transcranial doppler and Oxfordshire community stroke project clinical classification of ischemic stroke. *Stroke* 2000; **31**: 714-9.
21. Katzan IL, Hammer MD, Furlan AJ, Hixson ED, Nadzam DM; Cleveland clinic health system stroke quality improvement team. Quality improvemet and tissue-type plasminogen activator for acute ischemic stroke: a Cleveland update. *Stroke* 2003; **34**:799-800. Epub 2003 Feb 13.
22. Corbin DOC, Poddar V, Hennis A, Gaskin A, Rambarat C, Wilks R, *et al.* Incidence and case fatality rates of first-ever stroke in a black Caribbean population: The Barbados register of strokes. *Stroke* 2004; **35**:1254-8. Epub 2004 Apr 15.
23. Smadja D, Cabre P, May F, Fanon J, Rene-Corail P, Riocreux C, *et al;* Ermancia Study Group. Ermancia: epidemiology of stroke in Martinique, French West Indies. Part I: methodolgy, incidence, and 30-day case fatality rate. *Stroke* 2001; **32**:2741-7.
24. Lavados PM, Sacks C, Prina L, Escobar A, Tossi C, Araya F, *et al*. Incidence, 30-day case fatality rate, and prognosis of stroke in Iquique, Chile: a 2 years community-based prospective study (PISCIS project). *Lancet* 2005; **365**:2206-15.
25. Wolfe CDA, Rudd AG, Howard R, Coshall C, Stewart J, Lawrence E, *et al.* Incidence and case fatality rates of stroke in a Multi ethnic population: the South London Stroke register. *J Neurol Neurosurg Psychiatry* 2002; **72**:211-6.
26. Kwakkel G, Kollen BJ, Van der Grond J, Prevo AJH. Probability of regaining dexterity in the flaccid upper limb: impact of severity of paresis and time since onset in acute stroke. *Stroke* 2003; **34**:2181-6.
27. Sacco S, Marini C, Totaro R, Russo T, Cerone D, Carolei A. A population study of the incidence and prognosis of lacunar stroke. *Neurology* 2006; **66**:1335-8.
28. Michelli S, Agnelli G, Palmerini F, Caso V, Venti M, Alberti A, *et al.* Need for extensive diagnostic work-up for patients with lacunar stroke. *J Neurol* 2008; **255**:637-42.
29. Smith J, Brotheridge S, Young J. Patterns of hemiparesis recovery in lacunar and partial anterior circulation infarct syndromes. *J Clin Rehabil* 2001; **15**:59-66.