



RESEARCH ARTICLE

Clinical characteristics and radiological domains among patients with recurrent strokes-a descriptive cross-sectional study from a tertiary care center in central Nepal [version 1; peer review: 2 approved]

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Abstract

Background: Stroke is a significant global health hazard that ripples continuum multi-spectral effects to the patients as well their caretakers.

Methods: We studied 28 consecutive cohorts of patients with recurrent strokes managed in our centre within the last two years.

Results: The most common recurrence stroke pattern was of that of hemorrhagic to hemorrhagic subtype observed in 50% of the patients. The most common anatomical region of involvement was cortical – cortical seen in 39.28% of our cohorts. The surgical intervention was required in 17.85% whereas 42.85% of them were managed conservatively. Paradoxically, 39.28% of patients left against medical advice. The receiver operating curve (ROC) predicting mode of management was highest (area under the curve (AUC) =0.635) for compliance to therapy followed by stroke territory (AUC=0.578), age (AUC=0.457) and motor grading (AUC=0.374). The receiver operating curve (ROC) for influencing decision to leave against medical advice was highest (area under the curve (AUC) =0.861) for motor score followed by sex (AUC=0.701) and age (AUC=0.564). The analysis of variance (ANOVA) study pertaining to the mode of management was significantly connoted by the motor score and the stroke territory only. The ANOVA study pertaining to the decision to leave against medical advice was significantly governed by the motor score, stroke territory, and sex respectively. The multivariate analysis for variables governing mode of management was significant for motor score and the stroke territory only. The multivariate analysis for variables governing leave against medical advice was significant for sex, motor score and the stroke territory. **Conclusions:** This study aims to appraise early dichotomization of high-risk patients for recurrent strokes to reduce the continuum of neurological events as well as to mitigate the financial aspects

Open Peer Review

Reviewer Status  

Invited Reviewers

1

2

version 1

05 Aug 2021



report



report

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2. **Guoyi Gao**, Shanghai Jiao Tong University, Shanghai, China

Any reports and responses or comments on the article can be found at the end of the article.

governing stroke care.

Keywords

Recurrent, stroke, patterns, outcome

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Introduction

Stroke is a significant global health hazard^{1,2}. It is a silent epidemic that ripples continuum multi-spectral effects to the patients as well their caretakers. Recurrent stroke is slowly coming out of its shell with the reported incidence of up to 22.5% within 5 years³. Patients with recurrent stroke have greater disability and poorer outcomes than those with the first stroke⁴. Amidst the current paradox between the monumental stroke economy and the dismal provisions for rehabilitative strategies; these cohorts are most often compelled to lead a poor quality of life becoming socially aloof.

The sound knowledge on the incidence and the patterns of recurrent stroke paves the way to format necessary steps in mitigating them as well as improvise newer reforms in combating them in the future. This study aims to foster the pertinent need for national stroke database studies pertaining to strokes.

Methods

Consecutive cohorts of patients with recurrent strokes managed in the Department of Neurosurgery in College of Medical Sciences, Chitwan, Nepal within the last two years (January 2019–January 2021) were enrolled in this descriptive cross-sectional study. The recurrent stroke was defined either as:

- The stroke event occurring at the same anatomical location after 21 days of the index event or
- Different stroke event at another anatomical region within 21 days of the index event⁵.

Current smokers were defined as those who have smoked ≥ 1 cigarette per day for 6 months and have smoked in the last 28 days, whereas heavy drinkers were labeled as those who have consumed >2 and >1 standard drink per day (a glass of wine, a bottle of beer, or a shot of spirits, ~ 10 to 12 g of ethanol) for men or and women respectively⁶. Measurement of treatment adherence (compliance) was performed by the self reported and pills count methods.

The anatomical regions of involvement with the recurrent events were further categorized into subgroups as:

- Cortical and cortical
- Cortical and basal ganglionic
- Cortical and thalamic
- Basal ganglion and basal ganglionic
- Basal ganglionic and thalamic and
- Thalamic and thalamic

The demographical and the clinico-radiological variables comprising of age, sex, presenting clinical motor score, medical compliance, patterns of the index and recurrent strokes, anatomical distribution of the strokes, the mode of management, and those who left against medical advice (LAMA) were thoroughly appraised and analyzed.

The 'equipoise' governed from the recurrent events occurring in the same patient within the same geographical minimized the bias on the outcome from other confounding factors such as alcohol intake, smoking status and other medical comorbidities in our cohort study.

Inclusion criteria

- Consecutive 28 patients presenting with recurrent strokes in our Neurosurgical unit

Exclusion criteria

- Failure of approval for participation in the study
- Simultaneous multiple intracerebral strokes
- Traumatic ICH
- ICH secondary to vascular malformation, aneurysm, or cavernoma.
- Transient ischemic attacks (TIA)
- Patients with missing data pertaining to the study variables

The sample size required for adequate statistical elaboration was calculated according to the formula

$$n = Z^2 \times p \times q/d^2 \text{ where}$$

$$Z=1.96 \text{ at } 95\% \text{ confidence interval,}$$

$$p = 7.4\% \text{ prevalence of recurrent CVA}^5$$

$$q = 1 - p \text{ and}$$

$$d = 10\% \text{ margin of error}$$

The required sample size calculated was 26.32

We analyzed the records of 28 patients.

Frequency distribution (counts and percentages) was undertaken for the studied variables of the cohorts included in our study. Data were recruited and analyzed using the SPSS version 16 software. Statistical analysis was done utilizing receiver operating curve (ROC) with area under curve (AUC) values, Analysis of variance (ANOVA) and multivariate logistic regression analysis among the pertinent variables applying mode of management and the decision to leave against medical advice as the final outcomes. P-value of <0.05 was considered significant. Patients who had missing data for variables were excluded from the analysis.

Ethical approval

All procedures performed in studies involving human participants followed the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Institutional Review Committee (IRC) of the College of Medical Sciences (COMS-IRC-2021-35), Chitwan in Nepal.

Consent

The article was based on a review of anonymous clinical data. Therefore, no patient consent was required.

Results

In our study, the prevalence of recurrent stroke was more common among male cohorts (M: F ratio of 1.54:1). The mean age of presentation of the studied population was 67.65 ± 10.39 for males and 61.64 ± 13.54 for females respectively.

Medical compliance was observed in only 64.28% of the patients. The smoking and alcohol consumption habit was seen in 35.71% and 64.28% of patients respectively.

The mean motor score of the patient at presentation was 1.46 ± 0.63 .

The recurrence pattern was observed to be of hemorrhagic to hemorrhagic (H-H) in 14/28 (50%), ischemic to hemorrhagic (I-H) in 12/28 (42.85%), ischemic to ischemic (I-I) in 2/28(7.14%) of the cohorts.

The pattern of recurrent stroke pertaining to the anatomical distribution was cortical – cortical in 11/28 (39.28%), cortical –basal ganglia in 2/28 (7.14%), basal ganglion- basal ganglion in 9/28(32.14%), basal ganglion-thalamic in 3/28(10.71%), thalamic–thalamic in 2/28 (7.14%) and cortical-thalamic in 1/28 (3.57%) of our cohort study.

The surgical intervention was required in 5/28 (17.85%) whereas 12/28(42.85%) of them were managed conservatively. Paradoxically, 11/28(39.28%) of patients left against medical advice. The relevant findings of our study have been summarized in [Table 1](#).

The receiver operating curve (ROC) of the study for predicting mode of management was highest (area under the curve (AUC) =0.635) for compliance to therapy followed by stroke territory (AUC=0.578), age (AUC=0.457) and motor grading (AUC=0.374) as shown in [Figure 1](#).

The receiver operating curve (ROC) of the study for influencing decision to leave against medical advice was highest (area under the curve (AUC) =0.861) for motor score followed by sex (AUC=0.701) and age (AUC=0.564) as shown in [Figure 2](#).

The ANOVA study pertaining to the mode of management was significantly connoted by the motor score and the stroke territory only as shown in [Table 2](#).

The ANOVA study pertaining to the decision to leave against medical advice was governed by the motor score, stroke territory, and sex as shown in [Table 3](#).

Table 1. Summary of pertinent findings in our study.

Variables	Frequency
Male: Female	1.54:1
Mean Age (years)	Male- 67.65 ± 10.39 Female- 61.64 ± 13.54
Medical Compliance	18 (64.28%)
Smoking Status	10(35.71%)
Alcohol Intake	18(64.28%)
Mean Motor Score at Presentation	1.46 ± 0.63
Patterns of presentation	
Hemorrhagic-Hemorrhagic	14(50%)
Ischemic-Hemorrhagic	12 (42.85%)
Ischemic -Ischemic	2 (7.14%)
Anatomical Categorization	
Cortical-Cortical	11 ± 0.67 (39.28%)
Cortical –Basal Ganglion	2 ± 0 (7.14%)
Basal Ganglion-Basal Ganglion	9 ± 0.72 (32.14%)
Basal Ganglion-Thalamic	3 ± 0.57 (10.71%)
Thalamic-Thalamic	2 ± 0.63 (7.14%)
Cortical-Thalamic	1 ± 0 (3.57%)
Management (Index Event)	
Surgical	5 (17.85%)
Medical	12 (42.85%)
Leave Against Medical Advice	11 (39.28%)

The multivariate analysis for variables governing mode of management was significant for motor score and the stroke territory as shown in [Table 4](#).

The multivariate analysis for variables governing leave against medical advice was significant for sex, motor score and the stroke territory as shown in [Table 5](#).

Discussion

Stroke is a significant global health hazard⁷. The continuum impact of the associated morbidity and mortality is mostly observed in low and middle-income nations⁶. With the concurrent increment in the lifespan of the population alongside adaptations of unhealthy lifestyle and living habits, the prevalence of stroke will certainly show an upward curve in the coming future⁷.

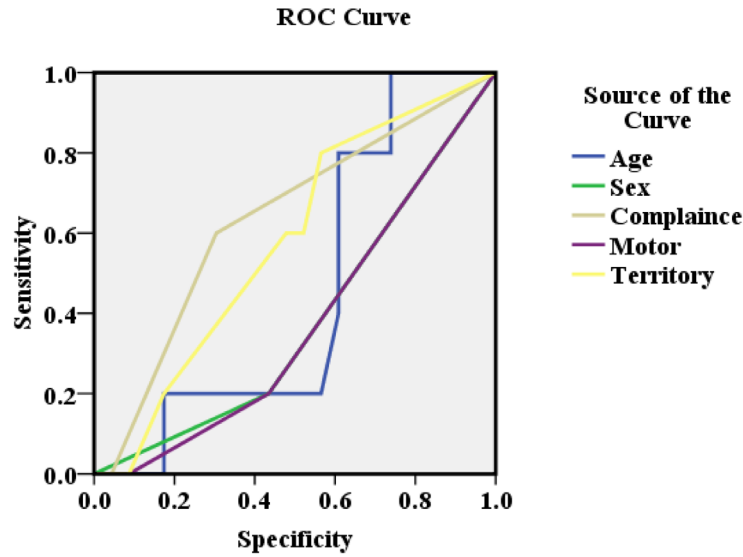


Figure 1. The receiver operating curve (ROC) of the variables governing mode of management.

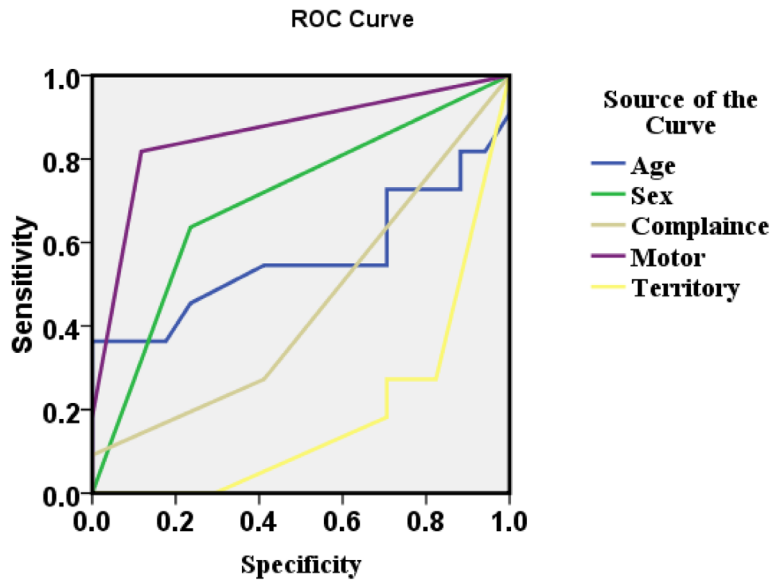


Figure 2. The receiver operating curve (ROC) of the variables governing leave against medical advice.

The reported incidence of recurrent stroke despite preventive measures is above 20%⁸. The risk of such adverse events is estimated at 5.4% and 11.3% during the first and the fifth years respectively, with an overall risk of 1.2/100/year for both hemorrhagic and the ischemic subtypes^{9,10}.

The “cortical–cortical” is the most common pattern of anatomical involvement in recurrent hemorrhagic strokes. This

has largely attributed secondary to cerebral amyloid angiopathy and coagulation disorders¹⁰. The similar anatomical pattern of involvement (39.28%) was seen in our study. The hemorrhagic-hemorrhagic patterns of the index and the recurrent stroke events were observed in 50% of the cohorts.

Hypertension is the strongest risk factor for both subtypes of recurrent stroke with an overall relative risk of almost 5.43^{7,9}.

Table 2. ANOVA analysis of variables governing mode of management.

		Sum of Squares	df	Mean Square	F	Sig.
Motor	Between Groups	5.200	1	5.200	23.451	.000
	Within Groups	5.765	26	.222		
	Total	10.964	27			
Territory	Between Groups	24.614	1	24.614	10.655	.003
	Within Groups	60.064	26	2.310		
	Total	84.679	27			
Ictus event	Between Groups	.037	1	.037	.140	.712
	Within Groups	6.963	26	.268		
	Total	7.000	27			

Table 3. ANOVA analysis of variables governing leave against medical advice.

		Sum of Squares	df	Mean Square	F	Sig.
Motor	Between Groups	5.200	1	5.200	23.451	.000
	Within Groups	5.765	26	.222		
	Total	10.964	27			
Territory	Between Groups	24.614	1	24.614	10.655	.003
	Within Groups	60.064	26	2.310		
	Total	84.679	27			
Ictus event	Between Groups	.037	1	.037	.140	.712
	Within Groups	6.963	26	.268		
	Total	7.000	27			
Age	Between Groups	2.228	1	2.228	.015	.903
	Within Groups	3803.487	26	146.288		
	Total	3805.714	27			
Sex	Between Groups	1.074	1	1.074	4.984	.034
	Within Groups	5.604	26	.216		
	Total	6.679	27			

Similarly concurrent transient ischemic events and the radiological presence of chronic infarction have shown to prognosticate increased odds of recurrent ischemic strokes⁵. Such epiphenomenon have been shown to increase the mortality risk by almost 17 folds⁹. Increased age is also a risk variable for stroke recurrence with the estimated hazard ratio of 1.02/year⁹. The average age of patients in a study ranged

from 54 to 66 years¹⁰. However, both age and sex were not found to be linked to harbinger subsequent IS¹⁰. Male genders have shown to have a higher cumulative risk for recurrent stroke¹¹. Our study showed male gender preponderance with a ratio of 1.54:1. Age ≥ 65 years have been found to be an independent predictor of long-term mortality¹². The average age of the patients in our cohort study was 65.45 years. In addition to

Table 4. Multivariate analysis of variables governing mode of management.

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	Age	8.502 ^a	2	4.251	.028	.972
	Sex	1.083 ^b	2	.542	2.420	.109
	Motor	5.248 ^c	2	2.624	11.474	.000
	Territory	26.030 ^d	2	13.015	5.548	.010
Management	Age	8.502	2	4.251	.028	.972
	Sex	1.083	2	.542	2.420	.109
	Motor	5.248	2	2.624	11.474	.000
	Territory	26.030	2	13.015	5.548	.010

Table 5. Multivariate analysis of variables governing leave against medical advice.

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	Age	2.228 ^a	1	2.228	.015	.903
	Sex	1.074 ^b	1	1.074	4.984	.034
	Motor	5.200 ^c	1	5.200	23.451	.000
	Territory	24.614 ^d	1	24.614	10.655	.003
LAMA	Age	2.228	1	2.228	.015	.903
	Sex	1.074	1	1.074	4.984	.034
	Motor	5.200	1	5.200	23.451	.000
	Territory	24.614	1	24.614	10.655	.003

having higher stroke risk, women have poorer post-stroke outcomes. However, in the literature, these differences in sex are not consistent¹².

Smoking habit has been attributed as a risk factor for ischaemic strokes only⁷. The smoking status was observed in 35.71% whereas the alcohol intake habit was seen in 68.28% of patients. Hypertension and diabetes mellitus are other documented independent risk factors. Moreover, hypertension at admission during index stroke events prognosticate the risk of early mortality¹².

One study showed that only 45% of patients were aware of their hypertension, and approximately 30% of them were compliant with their medications⁷. Another study revealed that only 12% of patients with atrial fibrillation were receiving appropriate prophylactic anticoagulation therapy⁹. In our study, adherence to medication was found in 64.28% of patients.

The neurological improvement to compensate for carrying out activities of daily living is further compromised among patients with contralateral recurrence, further hampering their quality of life⁸.

Mortality among patients with recurrent strokes have been documented to be above 35% with a hazard ratio of 2.55⁹. The all-cause mortality at five years pertaining to hemorrhagic strokes is almost twice comparing to the ischemic counterpart. The result mirrors the risk of mortality among patients with non-lacunar infarction comparing to that of the lacunar subtypes¹¹.

Patients with large vessel atherosclerosis and cardio-embolism have an early risk of stroke recurrence¹³.

The yearly estimates of recurrent stroke, death, and cardiovascular events were reported at 3.6%, 10.5%, and 6.7%,

respectively in one study¹⁴. The 5-year rate event for MI is 41% for recurrent stroke comparing to only 2% after the first stroke. The cumulative event rates for major vascular events are 18% and 45% at 1 and 5 years respectively¹¹.

The pattern of stroke recurrence mirrored that of the index events more for the ischemic subtypes, compared to their hemorrhagic counterparts (90% Vs. 56%)¹¹.

Patients managed in dedicated stroke units have shown to have improved outcome⁵. However; the expenditure pertaining to stroke care has been projected to cross 150 billion dollars by 2030¹⁵. One of the salient findings in our study was the observation of almost 40% of patients who opted to leave against medical advice from the hospital. This reflects the poor perception about the disease and its impact upon the patient by their caretakers' superadded by the financial burden associated with stroke care. This further reinforces the imminent need of implementing primary and secondary preventive measures to prevent and mitigate such events.

Plaque stability in the extracranial group, whereas the progression of stenosis in the intracranial group determines the risk of recurrence¹⁶. Among stroke with no determined cause, intracranial stenosis was often found at the time of recurrence¹⁶. Timely and appropriate screening of these high-risk patients helps to reduce the short and long-term multispectral neurological and financial burden among such patients as well as their caretakers.

Limitations of the study

The true estimates of the recurrence may be underestimated owing to omission bias since our study reviewed medical records of admitted patients within the last two years only. We also have scarce data pertaining to the analysis of factors governing long-term morbidity and mortality. Finally, the results of our study may not mirror demographics from other topography.

Conclusion

A provision for nationwide hospital and community-based stroke register is therefore of paramount importance to monitor the patterns and quality of primary and recurrent stroke care. The early dichotomization of high-risk patients for recurrent strokes is essential to reduce the continuum of neurological events as well as to mitigate the financial aspects governing stroke care. This is even more relevant in our context wherein there is a high stroke burden with paradoxical minimal stroke care and rehabilitative facilities.

Data availability

Figshare. Clinical characteristics and radiological domains among patients with recurrent strokes-a descriptive cross-sectional study from a tertiary care center in central Nepal¹⁷. DOI: <https://doi.org/10.6084/m9.figshare.14923071.v1>

Data are available under the terms of the [Creative Commons Zero "No rights reserved" data waiver](https://creativecommons.org/licenses/by/4.0/) (CC BY 4.0 Public domain dedication).

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Reviewer Report 10 November 2021

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Guoyi Gao

Department of Neurosurgery, Shanghai Jiao Tong University, Shanghai, China

This is an interesting report on recurrent stroke in one center in Nepal. I believe that many colleagues are keen to learn the current status of neurological diseases and the treatment in this Southern Asia area. Thus I suggest this manuscript is suitable for indexing after revision.

1. The inclusion criteria could be rewritten.
2. In the demographic variables, I did not find the preexisting condition of hypertension, as well as the antihypertensive treatment. The author could add this information to strengthen the evidence.
3. The author should not neglect that the major limitation of this study is the small sample, this could be described in the part of limitations.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Neurosurgery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 31 August 2021

<https://doi.org/10.5256/f1000research.58514.r92803>

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Lekhjunga Thapa 

Department of Neurology, National Neuro Center (NNC), Maharajgunj, Kathmandu, Nepal

This is a good report highlighting characteristics of a group of stroke patients who presented to a neurosurgical unit of a tertiary care center with hemorrhagic stroke in 21 days, which the authors have considered as a recurrent stroke. Although the community prevalence of stroke report in Nepal is available¹, the prevalence of recurrent stroke is still lacking. The authors have used data from an international study to calculate the sample size and have studied 28 patients with hemorrhagic stroke who had an ischemic or hemorrhagic stroke in the past 21 days. After reading the article, I found it very interesting that a very high proportion (40%) of the patients left against medical advice which is very common in developing countries because of various unavoidable reasons like a financial burden, and moreover, a grim prognosis associated with recurrent stroke. This information highlights not only the need for a stroke registry as the authors have highlighted but also for secondary stroke prevention awareness programs.² Few suggestions for authors willing to conduct a similar study would be:

1. Incorporation of important clinical variables that are known to be risk factors for recurrent stroke such as data on hypertension, metabolic syndrome, dietary habits, stress, etc.
2. ICH score would be a more meaningful way to communicate in cases of ICH instead of motor score
3. Cardio-embolism (Rheumatic Heart Disease) is a unique cause of recurrent stroke in developing countries like Nepal and a note on it would be better as there is no risk

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2. Stroke: Knowing it better makes a difference. *Forbes India.* 2021. [Reference Source](#)

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Stroke

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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