Short term mortality predictors in acute stroke

Sukdeb Das, Kartick Chandra Ghosh, Mainak Malhotra, Ujjal Yadav, Shib Sankar Kundu, Prasanta Kumar Gangopadhyay

Calcutta National Medical College and Hospital, Kolkata INDIA

KEY WORDS

Predictors
Mortality
Acute Stroke

Corresponding Author:

P. K. Gangopadhyay, MD
Tel : +91-33-24114771
E-mail : pkganguly100@yahoo.com

ABSTRACT

Background: Numerous studies have been done for last 20 years regarding the predictors of mortality in acute stroke. **Purpose:** This pilot study was designed for advancing our understanding the most influential factors involved in 4 wks mortality in Acute Stroke. **Methods:** 440 patients were included in the study. We studied the patients by 32 variables (clinical-12, radiological-3, complications-11 and previously handicapped-6). **Results:** Out of 32 variables (analyzed by Decision Tree Technique) complications like delay in recovery of consciousness and new onset AMI/CCF and aspiration pneumonia were found to be the most significant predictors of mortality. In the next grade of factors influencing morality, we found age (>60 years), severity of neurodeficit (GCS<7, grade I/V motor weakness), size of lesion (infarct>1 lobe. hemorrhage>60 ml) to be important variables. **Conclusions:** Scoring criteria and multicenteric study with a larger sample will be a better choice for assessing such predictability.

doi : 10.5214/ans.0972.7531.12190203

Introduction

In 2020, stroke will be the leading cause of death and disabilities after cancer throughout the world.[1] Numerous studies have been going on for the past 25-30 yrs, yet there is no uniform consensus regarding the most important predicting factors for mortality.

To reduce the overall burden of stroke in the society an organized approach is needed to predict mortality and morbidity in stroke especially aggressive management for complications of stroke.[2,3]

In contrast to myocardial infarction the data for stroke patients provided by multicentre studies comprising of large patients population with uniform perspective is lacking. In literature the most accepted scale for predicting outcome after ischemic stroke is NIH Stroke scale by Adam HF et al[5] in 1999. NIHSS score>25 (out of 42) caries grave prognosis and this scale is silent about other factor like neurological and medical complications e.g.; recurrent stroke, delayed recovery, raised ICT, increased mass effect and size of lesion or new onset AMI/AF/CCF or aspiration pneumonia during hospital stay.

German stroke study[6] in 2004, predicted that mortality in ischemic stroke increases with i) NIHSS score>25 ii) higher age iii) fever>380c. Henon H et al9 from France in March 1995 observed that in ischemic stroke 8 day mortality is increased with male gender, lower orgagozo score (<60), GCS<5, AF, dysphagia, hemianopia. Weimer et al[7] in 2006 proposed a new prognostic model of hemorrhagic stroke termed Essen ICH score in which he utilized the following variables, i) Age, ii) NIHSS Score, iii) Level of consciousness score > 7 (out of 10) has the poorest outcome. In this background we tried to include all the important factors in stroke including clinical, radiological aspects along with complications, risk factors and previous handicaps in stroke (either ischemic or hemorrhagic).

Methods

All the data in the present study was collected from patients admitted in Calcutta National Medical Mollege, Dept. of Medicine, from 8.1.2005 to 7.1.2010.

440 patients were included in the study who were admitted with a diagnosis of CVA (ischemic/hemorrhagic) with the help of CT Scan of brain within 24hrs of a symptomatic event.

The patients were selected with the following inclusion criteria: (i) must have been confirmed by CT Scan at Brain, (ii) admitted within 24hrs of onset of symptoms, (iii) age limit 15-90 yrs.

Following exclusion criteria were applied - I) SAH / Subdural Hematoma (ii) Malignancy, Diabetes with complications, hypoglycemia, (iii) Asymptomatic CVA/ TIA/ onset of symptoms>24 hrs, iv) complete heart block, head injury, gross anemia, (v) left the hospital within 28 days or not traceable, (vi) previous brain lesions like NCC, Tuberculoma, Meningitis, Encephalitis or Hydrocephalus, (vii) CRF/AMI, (viii) not affordable of - minimum investigation or drugs.

The registrars used as a standardized data sheet for all patients during the whole 28 days in-hospital study. In the patient study the following 32 variables were assessed to follow the early (28 days) outcome of a stroke (hemorrhagic or ischemic).

We maintained a supportive treatment like oxygen inhalation, intravenous fluid and electrolytes, catheterization, nasogastric feeding and mannitol infusion. Measures were taken for hypertension, diabetes, IHD, CCF, ARF and other complications. Antibiotics were given only in case of UTI, Aspiration pneumonia or fever. Ethical approval was obtained for the study.

Statistical methods

Frequency of various categorical variables, mean and standard deviation of various numerical variables were used. Chi-square Test (or Fisher's Exact Test where chi-square was not applicable) was used to test association between stroke outcome and various categorical variables. Monte Carlo Approximation was done if Fisher's Exact Test was not possible to evaluate completely.

Statistical analysis was done with SPSS9.0 for windows software and numerical interval date comparison was done using Mann-Whitney's Test. In order to predict stroke outcome from other measures we used Tree Classification technique.[13,14]

	VARIABLES	GRADE I	GRADE II	GRADEIII
i)	Age	18-40	40-60	60-90
ii)	***Clinical Examination*** GCS level of consciousness	10-14	7-9	<7
iii)	Clinical severity of Neurodeficit	a) Motor deficit of one limb power<4/5 b) No facial palsy	a) One limb power<3/5 or two limb deficit b) Facial palsy ± speech/ cognitive defect	a) Both limb power<3/5 b) Facial palsy c) speech or cognitive defect ± sensory deficit
iv)	Features of raised ICT	Headache or Papilloedema	a) Headache b) Papilloedema	a) Headache b) Papilloedema c) Conjugate eye dev. and/or VIth nerve palsy
v)	***Risk Factor*** Hypertension	a) SBP=140-180 or DBP= 90-110 (without drug) b) SBP/DBP<150/90 (with drug)	a) SBP=140-18 b) DBP=90-110 (with regular or irregular drug)	a) SP>180 or b) DBP>110(with drug)
vi)	Diabetes (^BS without IV DNS)	a) RBSL>200 (without drug) b) RBSL<200 (with drug)	RBSL=200-300 With drug or without drug in known diabetic	BSL>300(known diabetic with or without drug)
vii)	Hyperlipidemia	isolated TCH>250 or Isolated TGL>200 (without drug)	Isolated TCH>250 or Isolated TGL>200 (with drug)	a) TCH>250 b) TGL>200 (with drug)
viii)	***Complications*** Site of Lesion A) Ischemic	a) Cortical or b) Subcortical	a) Brain Stem b) Cerebellum	Cortical+ Subcortical ± Infratentorial
	B) Hemorrhagic	a) Lobar b) Basal Ganglia / Thalamus	a) Brain Stem b) Cerebellum	Lobar+Basal Ganglia/Thalamus ± ratentorial
ix)	Size of Lesion A) Ischemic	lobar<$^1/_2$ lobe <20ml (3cm dia.)	<$^1/_2$ -1lobe [3-7.5 cm dia.) (20-200ml)	>1 lobe (200ml) (7.5 cm dia)
	B) Hemorrhagic	Lobar<11 ml <2 cm dia.	a) Lobar (11-60 ml) (2-5 cm dia.) b) Cerebellum<8ml c) Pontine<1cm dia.	a) Lobar>60ml (5cm dia.) b) Cerebellum>8ml (2.25 cm dia.) c) Pontine>1 cmdia.
x)	Mass Effect	Sulcal effacement or Ventricular without shift	Midline shift 2-5 cm	Midline shift>5 cm compression
xi)	Delay in recovery of GCS	<3 days	3-7 days	>7days
xii)	New onset IHD	ST depression	Infarction Complications	
xiii)	New onset CCF	CCF without shock/ dyspnoea	CCF dyspnoea or shock	
xiv)	New onset Arrhythmia	SVE/VE	SVT/VT/MAT/AF	
xv)	Stress Ulcer	Vomiting+ epigastric tenderness	Hematemesis epigastric and/or Melena	
xvi)	Aspiration Pneumonia	Creps in Localized area	Creps upto midzone / upper zone	
xvii)	Electrolyte imbalance	Na<130		
		K<3.5		
xviii)	ARF	Urea>80 Creatinine>2		
xix)	Fever	Axillary Temperature>98.400F		
xx)	Dysphagia	Needs naso-gastric feeding		
xxi)	Bed sore	Ulcer deep to dermis		
	Previous Handicap: 1) Old CVA 2) Old AMI 3) Old valvular defect 4) Old Hemorrhagic diathesis 5) Old AF 6) Old CRF			

A classification Tree is an empirical rule for predicting the class of an object from values of predictor variables. The goal is to produce subsets of the data which are as homogenous as possible with respect to target variables. For each split, each predictor is evaluated to find out the best cut point (continuous predictor)/ grouping of categories (nominal and ordinal predictor) based on improvement score or reduction of impurity and then the predictors are compared.

Results

The study comprised of 440 subjects (median age 60 yrs, mean age 60 ± 12 yrs), range 18-82 years 232 (52.7%) patients were male (mean age 59 ± 11 yrs) and 208 (47.3%) patients were female (mean age 61 ± 13 yrs).

Out of 440 patients, 262 (59%) patients presented with infarction and 178 (41%) with hemorrhage as detected by CT Scan.

Poor prognosis was observed in older patients, along with low GCS score, severely paralyzed, raised intracranial tension, increased size of lesion and with severe mass effect. Sex was not a statistically significant factor, although older male had suffered adversely than female. severe hypertension, uncontrolled Diabetes influenced the outcome adversely, but not so by hyperlipidemia.

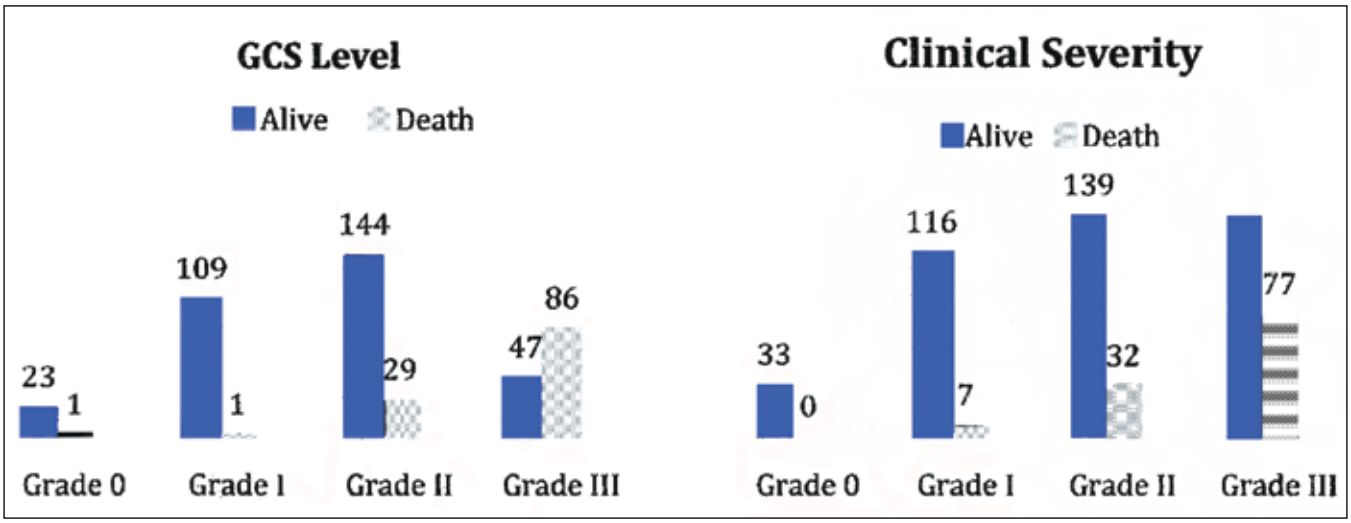
Between stroke related complications during hospital stay (28 days), adverse prognosis was observed in patients having delayed recovery of consciousness, new onset CCF, AMI, Aspiration Pneumonia and new onset Atrial Fibrillation, whereas fever, bed sore, electrolyte imbalance were statistically significant factors.

Out of all handicaps,history of past CVA and past AMI was very importment as an adverse prognostic marker.

This table demonstrates if the lesion is combined cortical and subcortical, the prognosis is worse whether it is hemorrhage

Table 1: Comparison of demographic and clinical features between alive and death patients.

	Alive (n = 323)				Death (n = 117)			
Age	Mean age = 57 ±11				Mean age = 68±10			
Sex	M/F ratio = 15:14				M/F ratio = 7:6			
CI.ftr.	Grade 0	Grade 1	Grade 2	Grade 3	Grade 0	Grade 1	Grade 2	Grade 3
ICT	137(42)	96(49%)	72(22%)	18(5%)	14(12%)	31(26%)	29(24%)	43(46%)
GCS sc	23(7%)	109(33%)	144(44%)	47(14%)	1(0.9%)	1(0.9%)	29(24%)	86(73%)
CL sev	33(10%)	116(35%)	139(43%)	135(10%)	0	7(6%)	32(27%)	77(65%)
Size	2(0.6%)	146(45%)	136(42%)	39(11%)	0	18(15%)	29(24%)	70(47%)
Mass eff.	145(44)	106(32%)	63(19%)	9(2%)	14(12%)	17(14%)	40(34%)	46(39%)
HTN	79(24%)	83(25%)	135(41%)	26(8%)	4(3%)	12(10%)	59(50%)	42(35%)
Diabetes	181(56)	65(20%)	68(21%)	9(2%)	31(26%)	21(17%)	41(35%)	24(20%)
lipid	177(54)	125(32%)	40(12%)	1(0.3%)	27(23%)	47(40%)	42(35%)	1(0.3%)



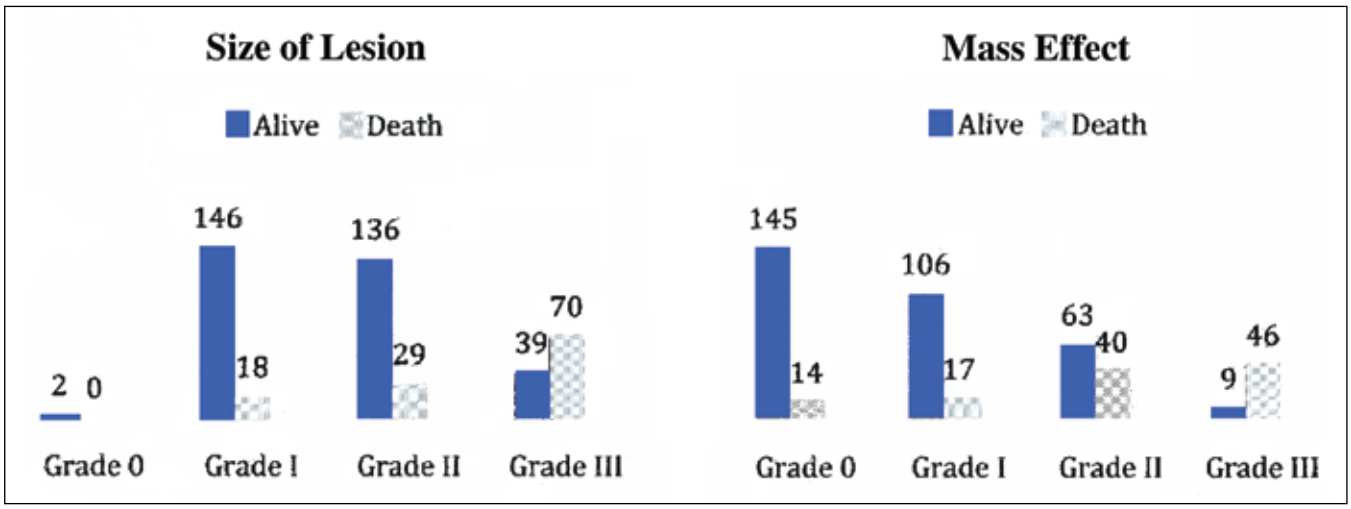


Table 2: Comparison of complications during hospital stay (28 days) between alive and death groups.

	Alive (n = 323)				Death (n = 117)			
Variables	Grade 0	Grade 1	Grade 2	Grade 3	Grade 0	Grade 1	Grade 2	Grade 3
Delayed recovery	25(7%)	152(47)	118(36)	28(8)		1(0.9)	32(27)	84(71)
New IHD	152(47)	159(49)	12(3%)		11(9)	71(60)	35(29)	
New CCF	258(79)	50(15%)	15(4%)		30(25)	39(33)	48(41)	
New Arrhythmia	109(61)	116(35)	8(2)		20(17)	88(75)	9(7)	
Asp. pneumonis	240(74)	58(18)	25(7)		21(17)	27(23)	69(59)	
Dysphagia	187(57)	136(42)			12(10)	103(88)	2(1)	
Stress ulcer	288(89)	25(7)	10(3)		59(50)	25(21)	33(28)	
Elect. imbalance	199(31)	124(38)			13(11)	104(88)		
ARF	288(89)	35(10)			55(47)	62(53)		
Bed sore	290(90)	33(10)			49(41)	68(59)		
Fever/UTI	257(86)	48(14)			65(55)	52(45)		

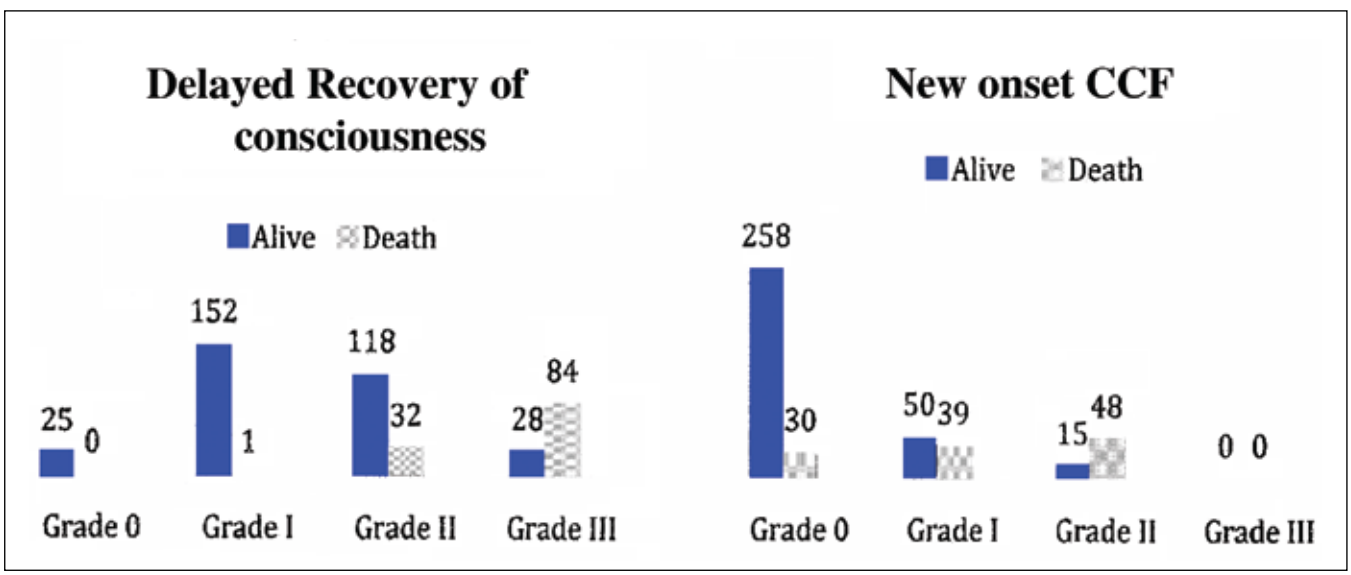
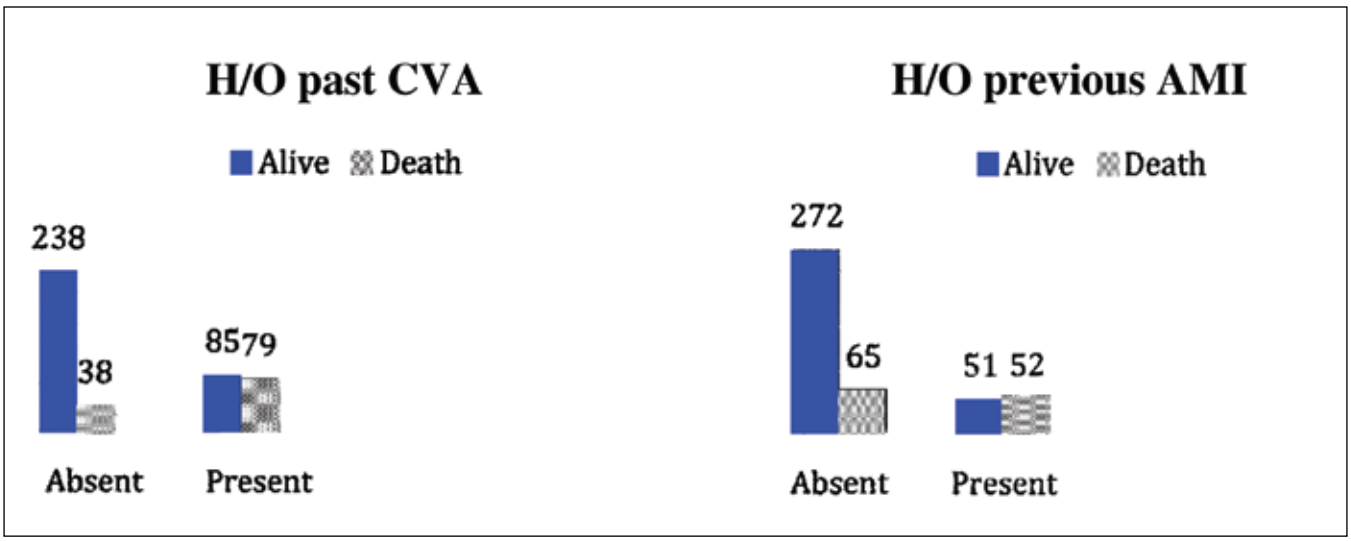
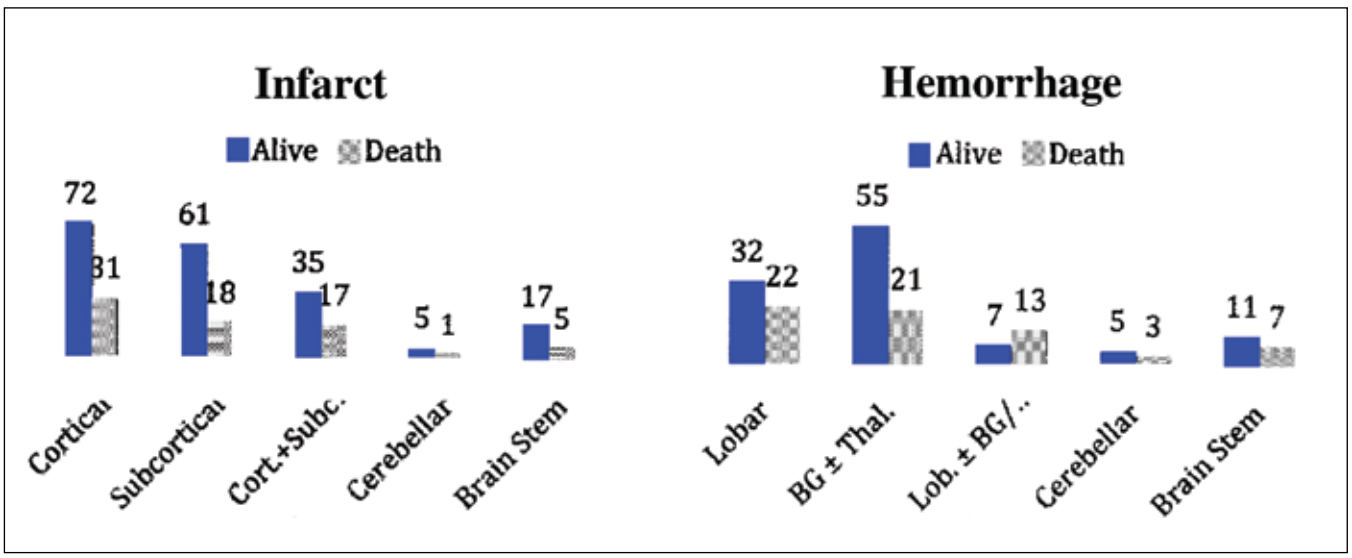


Table 3: Outcome of different previous handicaps between two groups.

	Alive (n = 323)		Death (n = 117)	
Variables	Absent	Present	Absent	Present
H/O Past CVA	238(73%)	85(26%)	38(32%)	79(67%)
H/O Past AMI	272(85%)	51(15%)	65(55%)	52(49%)
H/O AF	301(93%)	22(6%)	110(94%)	7(6%)
Valvular Heart Desease	317(98%)	5(2%)	103(89%)	14(11%)
H/O Hgic. Diathesis	312(96%)	11(3%)	100(88%)	17(12%)
H/O CRF	310(95%)	17(5%)	95(80%)	22(20%)





or infarct. But temporal profile shows that incase of infarct initially in conscious patients may go downhill gradually, whereas in case of hemorrhage, initially in deeply unconscious patients outcome is good.

Discussion

Stroke is the leading cause of death throughout the world among elderly. This study was designed to find out the important factors which influence the mortality of these patients admitted to hospital and followed up for 28 days after acute stroke. In our study the overall \in-hospital death is 26% (out of which 23% occurred in 7 days, 50% acute in 7-14 days and rest 27% occurred in 14-28 day). Heuschman P.U et al[12] in a series of 13,440 patients, observed that 10 days hospital mortality in stroke is 4.9% (out of which 34% occurred in first 3 days and remaining 66% in first 7 days).

Commonly cited data shows that[9] overall mortality in ischemic stroke is 4.9% and 18% in hemorrhagic stroke. In this study we observed in ischemic stroke mortality is 27% while in hemorrhagic stroke contributes upto 38%. We speculate that different management protocol of complications impacted results. The admission of patients at different stages of stroke may also be one of the reasons of this outcome. Mortality steadily increased beyond the age at 60 yrs. The death ratio between male and female was 11:9. In other studies mortality in stroke has been reported to steadily increase in men beyond 60 years while in females mortality after 60 yrs attains a plateau and slopes down with age of 70 years.

Our results show that early death (1 week) is more prevalent in PICH, although it sharply comes down from second week onwards; whereas the mortality in ischemic stroke is not so high in first week but it increases in later days (2-4 week). Similar observation was found in other studies[11] showing PICH is characterized by mortality in early days than ischemic stroke.

In this study we have observed that overall mortality is increased in the patients who are deeply unconscious with GCS levels ≤7 (73%), whether it is ischemic or hemorrhagic. In the study of Henon H et al[9], out of 18 variables, they concluded that only the level of uncosciousness has been the most important predictors. Concerning 3 months outcome-the severity of clinical deficit, presence of previous stroke and age>60 years were established as independent predictors. One of the study[10] showed that mortality rate in Ischemic Stroke is 90%; if GCS level ≤8. In our study, we found that in stroke patients with grade III neurodeficit mortality rate is 65%. In another study[6] the risk of death with a severe focal neurodeficit is 53%. In our study we observed that raised intracranial tension (ICT) was an important predictor of mortality. In grade II rise of ICT, mortality was found to be 24% and in case of grade III, it rose to 36%. Heuschman P.U. and colleagues in their study[12] observed that raised ICT is an important predictor of mortality (53%) in Ischemic stroke. He concluded highest attributable death rate was due to raised ICT followed by pulmonary embolism and pneumonia (in ischemic stroke).

When site of lesion was analysed as predictor, we found cortical lesion as contributing upto (30%) mortality than subcorrical lesion (22%) and 32% when combined. The subtentorial infarct contributed more towards mortality with brain stem infarct (25%) than in cerebellar infarct (16%). In homorrhagic lesion, mortality is more in lobar hemorrhage (40%) than in subcortical hemorrhage (i.e. basal ganglia ± tha lamus) (27%). But it is 65% if the hemorrhage is both lobar and basal ganglia / thalamus. In one local study[16] in lobar hemorrhage the mortality is 30%, in subcortical hemorrhage or combine lobar and basl ganglia/ thalamic hemorrhage it is 40% and in infratentorial hemorrage it is only 4%. Overall conclusion is that mortality increases when the lesion is combined i.e. cortical and subcortical, whether it is ischemic or hemorrhagic. We found that in the lobar hemorrhage, if the size of hematoma is >60 ml. the mortality is 57%. However, if there are associated basal ganglia hemorrhage and intraventricular extension the mortality increases to 90%. In Cerebellar hemorrhage we observed mortality to be kept 40% but in another study[15] they observed mortality is only 4%. In this context, we have very poor resources of surgical evacuation in Cerebellar hemorrhage>8ml.

Hypertension and Diabetes have earlier been found to be more frequently associated with in lacunar stroke, compared with non-lacunar stroke. Our observation is also similar. We found lower rate of in hospital death (28 days) among hypertensive women[12]. Petty G et al[8] demonstrated that lacunar stroke predicted a better outcome independent of stroke severity, which is also observed in our study. Henon H et al in a study of 492 patients dislinked the influence of hyperglycemia on infarct size as controversial and hyperglycemia speculating to result from stress induced by stroke. Overall negative, effect of hypertension & diabetes in early outcome after stroke is 50% in grade II & 35 % in grade III hypertensive, in moderate & severe diabetes the mortality is 35 % & 20 % respectively. Because other important determinants comes into play such as strategic location and size of stroke, complicated by infection, heart failure, etc.

Regarding complications, delayed recovery of consciousness>7 days is an independent predictor of mortality (71%) in our study. It is also observed by Henon H et al9 (mortality is 60%).

In our observation, if there is new onset AMI,CCF,atrial fibrillation, the mortality becomes 89%, 72% and 82% respectively. Pretty G et al in 1998 amongst 1111 resident of Rochester in Minnesota observed that recent onst CCF & IHD were the strongest predictor of death after stroke. Recent onset AMI was a bad prognostic marker in a few studies[8,12,11,15], as well as recent onset atrial fibrillation.[8,11] We found in stress ulcer and aspiration pneumonia mortality is 49% and 82% respectively. It is also observe. This is also been suggested in other studies.[6, 11, 14]

Hankeys et al[11] in their study of 492 patients showed that during first 30 days after stroke approximately 66% of deaths were due to direct neurological effect of stroke and 17% due to recurrent stroke.

Baird A. E. et al in his study[10] of 66 patients has shown that imaging predictors used in combination with clinical markers were more accurate in predicting the early outcome than using either of them alone. Our observation is also in accordance with it.

Conclusion

Among 32 variables, by Decision Tree Technique, we arrived at a conclusion that 50% of death in acute stroke (within 28 days of hospital stay) is more due to compications like delay in recovery of consciousness or new onset CGF,AMI, Atrial fibrillation or Aspiration pneumonia.

Among the residual 50% the following factors are more significant than others, like Age>60 years, size of lesion (infarct>1 lobe)/200ml, or hemorrhage>60ml), features of severely raised ICT (like 6th nerve palsy, conjugate deviation of eye), severity of neurodeficit (GCS level<7, grade III paralysis in both upper

lower limbs). Associated severe hypertension/ uncontrolled diabetes were also important prognostic factors but not much significance like previous variables.

Regarding previous clinical handicaps h/o recurrent CVA and hemorrhagic diathesis (like antiplatelet drugs) are very important factors predicting early death in stroke.

Early onset mortality is common in hemorrhagic stroke, where late mortality is prevalent amongst ischemic stroke.

At the end we admit that there are several strength and limitations of our study. We scanned every factor longitudinally as far as possible within our infrastructure, then we come to the conclusion by a standard statistical method i.e. decision Tree Technique. Hospital based study may not reflect true picture – extremely critical patients died before hospitalisation and patients with minimal dysfunction may not be hospitalisation.

However it would be more rational, if there is a scoring criterion regarding all these variables in relation with mortality which should be multicentric and large sample based.

The article complies with International Committee of Medical Journal Editor's uniform requirements for the manuscripts.

Competing interests: None, Source of Funding: None

Received Date : 24 March 2012; Revised Date: 17 April 2012

Accepted Date : 25 April 2012

References

1. Murray C J, Lopez A D. Alternative projection of mortality and disability by cause 1990–2020. Global burden of disease study, Lancet, 1997; 349: 1498–1504.
2. Stroke Unit Trialists collaboration, collaborative Systematic Review of the randomized trial of organized (Stroke unit) in patients care after stroke. BMJ, 1997; 317: 1151–1159.
3. Kennedy B S, Kasi S R, Brass L M Vacarino V. Trends in hospitalized strokes for blacks and whites in United states. 1980–1999. Neuroepidemiology, 2002; 21: 131–141.
4. Chandra N. C, Ziegelstein R C, Rogers W J. Observation of the treatment of women in the united states with myocardial infarction. Arch intern Med, 1998; 158: 981–988.
5. Adam H P Jr, Davis P H, Leira E C Baseline NIH stroke scale score strongly predicts the outcome after stroke: a report of trial of ORG 10172 in acute stroke treatment (TOAST) Neurology, 1999; 53: 126–131.
6. German Stroke study Collaboration, Predicting outcome after acute ischemic stroke: An external validation of prognostic model. Neurology, Feb 2004; vol 62 (4): 208–216.
7. Weimar C, Mieck T, Buchthal J, *et al.* for the German Stroke Study Collaboration.Neurologic worsening during the acute phase of ischemic stroke. Arch Neurol 2005; 62: 393–397.
8. Petty GW, Brown RD, Whishnant JD *et al*. Survival and recurrence after first cerebral infarction : A population based study in Rochester, Minnesota. 1975 through 1989, Neurology, Jan 1998; vol. 50 (1): 208–216
9. Henon H, Godefroy O, Leys D *et al*. Early prediction of death and disability after acute cerebral ischemic event. Stroke, March 1995; vol, 26 (3): 392–398.
10. Baird AE, Dambroria J, Janket SJ *et al*. A three item scale for early prediction of stroke recovery Lancet, June 2001; vol 357: 2095–2099.
11. Hankey G J, Jamrojik K, Broadband R J *et al*. Five year survival after first stroke and related prognostic factor in Perth Community Stroke Study, stroke, 2000; 31: 2080.
12. Heuschman PU, Kolominsky Rabus PL, Misselwitz B *et al*. German Stroke Registry Group: Predictiojn of in hospital mortality and attributable risk of death after ischemic stroke. Ach intern Med, sept 2004; vol. 164: 1407–1431.
13. Loh W Y, shih Y S. Split selection method for Classification Trees. Statistica Sinica, 1977; 7: 815–840.
14. Everit B S. Classification Trees, Statistica Sinica, 1977; 7: 815–840.
15. Victor M and Ropper AH. Principles of Neurology,7ed. Mc Graw Hills Publisher 2001.
16. Banerjee TK, Chowdhury D, Das A *et al*. Analysis of hospital based stroke registry in a neurological centre in Kolkata, JIMA; Dec 2001; Vol. 103 (12): 665–668.