

# Study of Early Predictors of Mortality in Acute Cerebral Ischemic Stroke

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## ABSTRACT

**Introduction:** Cerebrovascular diseases are ranked as the second leading cause of death after ischemic heart disease. Most these deaths occur in people living in developing countries. The objective of this research was whether a scoring system such as Acute Physiology and Chronic Health Evaluation II (APACHE-II) or Carotid Intima Media Thickness (CIMT) can be used effectively to predict short term mortality in cases of acute ischemic stroke.

**Material and methods:** The study included all consecutive indoor acute ischemic stroke patients more than 40 years. Patients with suspected stroke on the basis of history and clinical examination were further investigated to confirm ischemic stroke by computed tomography / Magnetic resonance imaging. These patients were subjected to laboratory investigations and B-mode (brightness mode) ultrasound for APACHE-II scoring and CIMT was measurements. The patients were followed up for 30 days after acute ischemic stroke for any mortality and cause of mortality.

**Results:** A total of 50 patients with acute ischemic stroke were enrolled in the study. During the study, 12 patients expired and 14 patients were lost in the follow-up after discharged from the hospital. For statistical analysis only 36 patients were included. In univariate analysis, age ( $p=0.013$ ), BMI ( $p<0.001$ ), diabetes mellitus ( $p<0.001$ ), APACHE II ( $p<0.001$ ), and length of hospital stay ( $p=0.009$ ) were associated with early mortality. Cox-proportional hazards survival regression revealed advanced age, BMI, and APACHE II score as independent predictors of early mortality.

**Conclusion:** This study suggests advanced age, high BMI, and APACHE II score on admission are the independent predictors of early mortality, while CIMT had no independent prognostic value.

**Keywords:** acute cerebral Ischemic stroke, APACHE II score, CIMT, early mortality

## MATERIAL AND METHODS

This prospective observation study was approved by the ethics committee and was performed at our tertiary care Centre from February 2013 to August 2014. The study included all fifty consecutive indoor acute ischemic stroke patients more than 40 years, admitted in the Department of Medicine of our tertiary care center. Patients with acute ischemic stroke of more than 3 days duration, transient ischemic attack, lacunar and hemorrhagic stroke were excluded from the study. The patients were followed up for 30 days after acute ischemic stroke.

A detailed history regarding the demographic details, physical activity, and personal habits were obtained from the patients after taking their written informed consent. After assessment of anthropometric parameters, these patients were subjected to laboratory investigations and B-mode (brightness mode) ultrasound.

The present study was done in two steps. Step I: All patients in inpatient suspected as stroke on the basis of history and clinical examination were further investigated to confirm ischemic stroke by CT/MRI imaging. They underwent routine investigations as and when required and for the APACHE II scoring system. Investigation included in the APACHE II scoring system were: complete blood count, Hematocrit, serum sodium, serum potassium, serum creatinine, arterial pH. CIMT measurements were made by using B-mode ultrasound (carotid duplex scanning with a 7.5 MHz linear superficial array probe in B-mode). In the present study, intima media thickness was measured just before the bifurcation of common carotid artery. Step II: Follow up of patients for 30 days after stroke for any mortality and cause of mortality.

All deaths occurring within 30 days after stroke were considered to be due to stroke, unless another cause of death (malignancy, accident, etc.) was the obvious cause of death.

## STATISTICAL ANALYSIS

Data so obtained was subjected to statistical analysis using Statistical Package for Social Sciences version 20.0. (SPSS Inc., Chicago, IL, USA). Data were presented as mean  $\pm$ SD or n (%). Student's t test was used for comparison of continuous variables. Differences between groups and the effect of patient characteristics on clinical outcome were assessed using the

## INTRODUCTION

The 1990 Global Burden of Disease showed that cerebrovascular diseases are the second leading cause of death, ischemic heart disease being on the first platform.<sup>1</sup> In 2001 it was estimated that cerebrovascular stroke accounted for 5.5 million deaths worldwide. Most deaths occurred in people living in developing countries and less than 50% of the subjects were aged less than 70 years.<sup>2</sup> Studies have used and compared Acute Physiology and Chronic Health Evaluation (APACHE) and other critical care scoring systems for the prediction of the short-term mortality in acute ischemic stroke patients.<sup>3-6</sup> Evidence has also emerged regarding the role of carotid intima media thickness in the prediction of major cardiovascular events or death after a first-ever ischemic stroke.<sup>7</sup> The objective of this research was to know whether a scoring system such as APACHE-II or Carotid Intima Media Thickness (CIMT) can be used effectively to predict short term mortality in cases of acute ischemic stroke.

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Fisher Exact test. The Cox proportional-hazards survival regression, which included variables that showed a statistical difference  $p \leq 0.1$  on univariate comparison, was performed. A result was deemed statistically significant when  $p < 0.05$ .

## RESULTS

A total of 50 patients with acute ischemic stroke were enrolled in the study. There were 21 males (42%) and 29 females (58%). The mean age (years) of the patients was  $62 \pm 7.14$  (45-78). The majority of patients were aged 51-70 years ( $n=30$ ; 82%). There were 2 (5%) patients aged  $<50$  years, and 4 (11.0%) patients were aged  $>70$  years (Table-1). The patients were treated according to the American Heart Association/American Stroke Association guidelines except for thrombolysis. During the study, 12 patients expired and 14 patients were lost in the follow-up after discharged from the hospital. For statistical analysis only 36 patients were included.

Among 36 cases, 29 (80%) had underlying comorbidities. The top two most common comorbidities were diabetes mellitus, and hypertension. Hypertension was the most common associated illness ( $n=21$ ; 58%) followed by diabetes ( $n=18$ ; 50%). History of smoking was recorded in 9 (25%) patients and alcohol use in 4 (11%).

The majority of patients were overweight and obese by BMI. The mean BMI ( $\text{kg}/\text{m}^2$ ) was  $30.31 \pm 4.36$  (21-39). On admission, mean APACHE II scores was  $19.80 \pm 5.18$  (11-31). CIMT values of left side ranged from 0.05 to 0.10 with a mean value of  $0.074 \pm 0.008$  cm. On the right side, CIMT values ranged from 0.06 to 0.12 with a mean value of  $0.08 \pm 0.009$  cm. Average CIMT value ranged from 0.055 to 0.11 with a mean value of  $0.073 \pm 0.007$  cm (Table-2). In the majority of cases ( $n=32$ ; 89%), the single vascular territory was involved. Two vascular territories involvement was observed in 4 (11%) patients. Among 36 cases, 30 (83%) had involvement of middle cerebral artery.

After 30 days, 11 (31%) patients survived with improvement

in neurological deficit, 25 (69%) survived without any improvement, and a total of 12 (24%) expired. The most common causes of mortality observed were aspiration pneumonia 6 (50%), sepsis 4 (33%), and re-infarction 2 (17%).

In univariate analysis, age ( $p=0.013$ ), BMI ( $p<0.001$ ), diabetes mellitus ( $p<0.001$ ), APACHE II ( $p<0.001$ ), and length of hospital stay ( $p=0.009$ ) were associated with early mortality. (Table-2) Cox-proportional hazards survival regression revealed advanced age, BMI, and APACHE II score as independent predictors of early mortality (Table-3).

## DISCUSSION

Considering the dynamics of factors affecting the mortality, it is important that newer relevant factors should be identified and reevaluated in view of clinical manifestation of acute ischemic stroke. The present study was carried out to evaluate the predictive value of a conventionally used predictive scoring system (APACHE II) and a new emerging parameter (CIMT), so that the predictive modeling of early mortality in elderly patients with acute ischemic stroke could be predicted.

12 (33%) patients expired within 30 days of acute ischemic stroke during the study period. The present study shows that advanced age, BMI, and APACHE II score were the only independent predictors of early mortality.

Relatively younger age of ischemic stroke patients has been reported in studies from Asian and developing countries as compared to western and developed countries.<sup>8-12</sup> The mean age of the patients in the current study, who presented with acute ischemic stroke are nearly similar to the earlier studies reported from Asian and developing countries.

Our study shows a higher ischemic stroke mortality rate (33%) compared to the previous studies where the case fatality rate range from 8-18%. In a study from the Department of Veterans Affairs (VA), 34 866 patients with first ever ischemic stroke were retrospectively identified. Collins et al reported 8.2% mortality at 30 days after the stroke.<sup>13</sup> De Jong et al observed

Characteristics	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	36	45.00	78.00	62.33	7.42
BMI ( $\text{kg}/\text{m}^2$ )	36	21.40	39.10	30.32	4.71
APACHE II (0-71)	36	11	31	19.80	5.18
CimtLeft (cm)	36	0.05	0.10	0.0747	0.0085
Cimtright (cm)	36	0.06	0.12	0.0807	0.0093
Length of stay (days)	36	6.00	21.00	11.4722	4.08

N = number

**Table-1:** Baseline Characteristic of Patients

Characteristics	Survivors (n=24)	Expired (n=12)	p-value
Age (mean $\pm$ SD)	60.20 $\pm$ 7.204	66.58 $\pm$ 6.097	0.013
BMI (mean $\pm$ SD)	28.58 $\pm$ 4.119	33.81 $\pm$ 3.904	<0.001
Hypertension (n %)*	12 (57)	9 (43)	0.141
Diabetes Mellitus (n %)*	7 (39)	11(61)	0.001
Smoking (n %)*	4 (44)	5 (56)	0.112
Alcoholism (n %)*	3 (75)	1 (25)	0.593
CIMT(Left) (mean $\pm$ SD)	0.074 $\pm$ 0.009	0.074 $\pm$ 0.006	0.93
CIMT (right) (mean $\pm$ SD)	0.081 $\pm$ 0.010	0.078 $\pm$ 0.006	0.34
APACHE II (mean $\pm$ SD)	17.58 $\pm$ 3.900	24.25 $\pm$ 4.614	<0.001
Length of Stay (mean $\pm$ SD)	10.25 $\pm$ 3.313	13.91 $\pm$ 4.521	0.009

\*Fisher Exact test

**Table-2:** Baseline Characteristic according to Outcome

Variable	Hazard ratio	95% CI	p-value
Age	1.22	1.02–1.47	p=0.023
BMI	1.90	1.24–2.91	p=0.003
Apache II	1.25	1.04–1.50	p=0.016

**Table-3:** Independent predictors of early mortality in patients

10% mortality at 30 days in 998 patients with first-ever cerebral infarction.<sup>14</sup> Rothwell et al in Oxford Community Stroke Project and Oxford Vascular Study reported case fatality due to initial stroke in 17.2% and 17.8% cases respectively.<sup>15</sup>

Several factors are known to influence early mortality in acute ischemic stroke. Among them, age and stroke severity have been consistently reported. A Framingham study had shown that advanced age at initial stroke was independently associated with a high 30-day mortality.<sup>16</sup> Advanced age, along with diabetes and stroke subtype, was also an independent predictor of 30-day case fatality in the study by de Jong et al.<sup>14</sup> In the current sample, advanced age was significantly associated as a hazard for early mortality (HR = 1.22; 95% CI 1.02–1.47; p=0.023).

In contrast to the previous studies, paradoxical role of increased BMI in protecting against mortality was not observed in the present study.<sup>17,18</sup> High BMI was significantly associated with 30 day mortality in both univariate and multivariate analysis. (HR=1.90; 95% CI 1.24–2.91; p=0.003) Similarly, high APACHE II score on admission was significantly associated as a hazard associated for 30-day mortality in multivariate analysis. (HR=1.25; 95% CI 1.04–1.50; p=0.016) Previous study have shown considerable variations of BP in the acute phase of ischemic stroke. Variables describing the course of BP over the first 2.5 days have a marked and independent relationship with the outcome at 30 days.<sup>19</sup> In a previous study on effect and prognostic value of hs CRP, severity scoring system (GCS and APACHE II score) and other risk factors on morbidity and mortality of ischemic stroke subjects it was found that GCS significantly decreased and APACHE II score significantly increased in deceased subjects as compared to those with uncomplicated and morbid subjects. While these parameters don't differ significantly in uncomplicated subjects as compared to morbid subjects.<sup>20</sup> In another study, association of only some features of APACHE II scores like body temperature, serum creatinine, and white blood cell counts were the main predictors of in-hospital mortality.<sup>21</sup> All of these findings indicate the importance of systematized assessments and proper management of coexisting medical complications in treating stroke patients, especially for those with more prominent disease severity.

Similar to observation seen in the previous studies where no association was found between CIMT and short term mortality in acute ischemic stroke.<sup>22,23</sup> We observed that average CIMT measurements of patients who expired was nearly similar compared to that of patients who survived, on multivariate analysis no relation was found between CIMT and short term mortality in patients with acute ischemic stroke.

## CONCLUSION

The present study reports a 33% mortality rate at 30 days after acute ischemic stroke. Advanced age, high BMI, and APACHE II score on admission were the independent predictors of early mortality, while CIMT had no independent prognostic value.

The major limitation of the present study was that follow-up data for mortality within 30 days were available only for 36 (72%) patients.

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