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RESEARCH ARTICLE

STUDY OF CAROTID INTIMA MEDIA THICKNESS AND APACHE II(ACUTE PHYSIOLOGICAL AND CHRONIC HEALTH EVALUATION) AND SHORT TERM MORTALITY IN ACUTE ISCHEMIC STROKE

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ABSTRACT

Objectives: The present study was carried out with an aim to detect correlation of CIMT, APACHE II and short-term mortality in patients with acute ischemic stroke.

Methods: After ethical considerations, this prospective observational study was conducted on 50 patients of acute is chenic stroke. The diagnosis of ischemic stroke was based on the clinical profile and confirmed by CT / MRI as defined by ASA/AHA.

Results: Among the 50 patients studied age of patients with acute ischemic stroke ranged from 45-78 years with a mean age of 61.18±7.59 years. Majority of patients were in 51-70 years of age (n=43; 86%).On day 1 of admission APACHE-II scores ranged from 11 to 33 with a mean value of 19.80±6.17.Day 3 APACHE score range expanded with minimum and maximum values being 8 and 34 respectively. Day 3 mean APCHE II scores were 19.50±6.80.On day 7, the range of APACHE II scores was 8 to 38 with a mean value of 22.54±9.71.Average CIMT value ranged from 0.055cm to 0.11cm with a mean value of 0.075±0.013. After one month, a total of 11 (22%) patients showed improvement, 13 (26%) showed survival without change in status. A total of 14 (28%) were lost to follow up and a total of 12 (24%) expired. Cause of mortality was ascertained as aspiration/pneumonia in majority (n=5; 41.67%), 2 (16.67%) expired owing to sepsis, 2 (16.67%) due to sepsis/AKI, 1 (8.33%) patient each died due to reinfarct/sepsis, atrial fibrillation/reinfarct and inability to feed respectively.

Conclusion: Carotid intima media thickness in acute ischemic stroke patients did not provide any useful information with respect to outcome (short term mortality). There was some association of constituents of APACHE-II scores and short term mortality.

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INTRODUCTION

Cerebrovascular diseases are ranked as the second leading cause of death after ischemic heart disease. In the year 2001 it was estimated that cerebrovascular diseases (stroke) accounted for 5.5 million deaths worldwide, equivalent to 9.6% of all deaths. Two-thirds of these deaths occurred in people living in developing countries and 40% of the subjects were aged less than 70 years. Additionally, cerebrovascular disease is the leading cause of disability in adults and each year millions of stroke survivors has to adapt to a life with restrictions in activities of daily living as a consequence of cerebrovascular disease. The situation is no less severe in India. A recent community survey in the eastern Indian city of Kolkata showed the prevalence rate of stroke to be 545 per 100,000 population. The average annual incidence rate of stroke in the same study was 145 per 100,000 persons per year. These rates, age standardized to world standard population, are similar to or higher than many Western nations. These rates are also much higher than those reported previously from the other parts of India. Stroke burden in India has been rising from last few decades, in contrast to developed countries, where stroke prevalence has decreased or plateaued. Based on the pathological background, the stroke may be either of ischemic or hemorrhagic type. Thrombotic cerebral infarction results from the atherosclerotic obstruction of large cervical and cerebral arteries, with ischemia in all or part of the territory of the occluded artery. This can be due to occlusion at the site of the main atherosclerotic lesion or to embolism from this site to more distal cerebral arteries. Several other causes of cerebral infarction exist and are of great practical importance for patient

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management. As they are relatively rare they can be ignored for most epidemiological purposes. Although mortality rates of ischemic stroke have been reported to be lower (25.9%) as compared to hemorrhagic stroke (49.2%), yet more than one-sixth (17.5%) of ischemic stroke patients have been reported not to survive beyond three months of stroke episode. In India, stroke accounts for nearly 1.2% of total deaths in country. This high mortality is concerning and has attracted the interest of many workers. It has been shown that stroke severity, age, sex, cardiovascular risk factors, smoking habit, atrial fibrillation, hypertension, atherosclerosis, hyperlipidemia, previous myocardial infarction, previous stroke and older age have been reported to be risk factors associated with mortality in stroke patients. The APACHE II system is the most commonly used scoring system for severity of illness (SOI) in North America. Age, type of ICU admission (after elective surgery vs. nonsurgical or after emergency surgery), a chronic health problem score, and 12 physiologic variables (the most severely abnormal of each in the first 24 h of ICU admission) are used to derive a score. APACHE and other critical care scoring systems have been used for prediction of the short-term mortality in acute ischemic stroke patients. Several features of the APACHE II score are associated with risk of death in this patient population. The findings suggest that increase in APACHE score are associated with, and may contribute to, increased mortality in patients with acute ischemic stroke. Carotid intima media thickness (CIMT or IMT) has emerged as a useful screening tool for detection of the presence of atherosclerosis, cardiovascular risk and associated mortality. 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 ischemicstroke, however, there are reports that suggest that carotid intima media thickness has nothing to do with the functional outcome after acute ischaemic stroke.

MATERIAL AND METHOD

The present study was prospective observational study done in total 50 patients of acute ischemic stroke. The diagnosis of ischemic stroke was based on the clinical profile and confirmed by CT / MRI as defined by ASA/AHA. Patients with stroke older than 3 days and hemorrhagic stroke were excluded. The selected patients underwent other investigations as and when required and for APACHE II scoring system. Investigation included in APACHE II scoring system were: CBC, Hematocrit, Serum sodium, serum potassium, serum creatinine, arterial pH, paO2. CIMT was measured on day 1 by using B-mode (brightness mode) ultrasound. In the present study intima media thickness was measured just before bifurcation of common carotid artery .All selected patients were again investigated on day four and seven of stroke again for the APACHE II scoring. Patients were followed for 30 days after stroke. Statistical analysis was done by SPSS software version 18 by using Pearson's Chi-square test and student t-test. P-value of less than 0.05 was considered significant.

RESULTS

Table 1 shows the distribution of cases according to age. Age of patients ranged from 45 to 78 years. Majority of patients were in between 51-70 years (n=43; 86%). There were only 3 (6%) patients aged ≤50 years, 11 (22.0%) patients were 66-70 years and 4 (8.0%) patients were aged >70 years. Mean age of patients was 61.18±7.59 years.

Table 1. Distribution of cases according to age

SN	Age Group	No. of cases	Percentage
1.	≤50 Yrs	3	6.0
2.	51-55 Yrs	9	18.0
3.	56-60 Yrs	11	22.0
4.	61-65 Yrs	12	24.0
5.	66-70 Yrs	11	22.0
6.	>70 Yrs	4	8.0
Mean Age±SD (Range in yrs)		61.18±7.59 (45-78)	

Table 2. APACHE II scores at day 1, day 3 and day 7 of admission

	N	Minimum	Maximum	Mean	Std. Deviation
Day 1	50	11	33	19.80	6.17
Day 3	50	8	34	19.50	6.80
Day 7	50	8	38	22.54	9.71

Table 2 shows APACHE II scores on day 1, day 3 and day 7 of admission. On day 1 APACHE II scores ranged from 11 to 33 with a mean value of 19.80±6.17. On day 3 APACHE score range expanded with minimum and maximum values being 8 and 34 respectively. Day 3 mean APCHE II scores were 19.50±6.80. On day 7, the range of APACHE II scores was 8 to 38 with a mean value of 22.54±9.71.

Table 3. CIMT Values

	N	Minimum (cm)	Maximum (cm)	Mean (cm)	Std. Deviation
Left	50	0.05	0.10	0.074	0.012
Right	50	0.06	0.12	0.077	0.017
Average	50	0.055	0.11	0.076	0.013

Table 3 shows CIMT values of left side ranged from 0.05cmcm to 0.10 with a mean value of 0.074±0.012. At right side, CIMT values ranged from 0.06cmcm to 0.12 with a mean value of 0.077±0.017 cm. Average CIMT value ranged from 0.055cm to 0.11 cm with a mean value of 0.075±0.013.

Table 4. Status after one month

SN	Status	No. of cases	Percentage
1.	Improvement	11	22.0
2.	Survival with no change	13	26.0
3.	Death	12	24.0
4.	Loss to follow up	14	28.0

After one month, a total of 11 (22%) patients showed improvement, 13 (26%) showed survival without change in status. A total of 14 (28%) were lost to follow up and a total of 12 (24%) expired.

Table 5. Cause of Mortality (n=12)

SN	Status	No. of cases	Percentage
1.	Aspiration/Pneumonia	5	41.6
2.	Sepsis	2	16.67
3.	Sepsis/AKI	2	16.67
4.	Atrial fibrillation/Reinfarct	1	8.33
5.	Reinfarct/sepsis	1	8.33
6.	Inability to feed	1	8.33

Maximum number of cases (n=5; 41.6%) expired owing to aspiration/pneumonia, 2 (16.67%) expired owing to sepsis, 2 (16.67%) expired due to sepsis / AKI (acute kidney injury), 1(8.33%) patient each died due to atrial fibrillation/reinfarct, sepsis/Reinfarct, inability to feed respectively and 1(8.33%). No patient expired owing to cardiac event(MI) in present study.

DISSCUSSION

Acute ischemic stroke carries with it a huge burden of short-term mortality and disability throughout the world (WHO, 2002; Das *et al.*, 2007; Carter *et al.*, 2007; Xian *et al.*, 2011; Fonarow *et al.*, 2012; Chaudhuri *et al.*, 2013) (World Health Organization, 2002; Das *et al*., 2007; Carter *et al*., 2007; Xian *et al*., 2011; Fonarow *et al*., 2012; Chaudhuri *et al*., 2013). This huge burden of mortality has attracted the focus of healthcare community throughout the world to assess, evaluate and give weight age to different predictor variables that can predict a poor outcome and hence provide the basis for improvement. Thousands of studies throughout the world have been carried out on this issue and are still undergoing at different centres (Ellul *et al*., 2004; Hatano, 1976; Lanktree *et al*., 2009; Prati *et al*., 2008; Vaartjes *et al*., 2013). As a result, despite incline in incidence of ischemic stroke, the mortality rate has been on the decline (Vaartjes *et al.*, 2013). Considering the dynamics of factors affecting the mortality, it is important that newer relevant factors should be identified and reevaluated in view of changing environmental, infrastructural and clinical manifestation of acute ischemic stroke.

In present study, we attempted to detect correlation of CIMT, APACHE II and short-term mortality in patients with acute ischemic stroke. APACHE II is a predictive scoring system that was developed by Knaus *et al.* in the year 1985 and is used as a predictor of ICU mortality. In average Indian conditions; APACHE II is still being used as a performance measure of ICU (Rao *et al.*, 2008; Rapsang and Shyam, 2014). CIMT on the other hand is a new variable, relevance of which as a predictor of acute ischemic stroke itself and as a predictor of its outcome especially in Indian conditions (Sahoo *et al.*, 2009; Das *et al.*, 2015). With this background, 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 modelling for early mortality in elderly patients with acute ischemic stroke could be predicted precisely. For this purpose a total of 50 elderly patients with acute ischemic stroke were enrolled in the study. The age of patients ranged from 45 to78 years. Mean age of patient was 61.18±7.59 years which was nearly similar to the mean age of others, reported as in earlier study from India (Sahoo *et al.*, 2009) and a recent study from Bangladesh (Chowdhury *et al.*, 2013). Mean age of patients in present study was close to that reported in a recent study by Mapoure *et al*. (2014). Relatively younger age of ischemic stroke patients has been reported in studies from Asian and developing countries (Chowdhury *et al.*, 2013; Jeng *et al*., 2008; Sawalha *et al.*, 2009) whereas western and developed countries (Papazafiropoulou *et al.,* 2009; Ayazoglu *et al.*, 2011) have reported a much older mean age of ischemic stroke patients. Papazafiropoulou *et al.* (2009) have reported mean age of patients in their series to be above 77 years. Ayazoglu *et al.* (2011) reported the mean age of stroke patients in their series to be 76.5 and 72 years for male and female patients respectively. Difference in lifestyle and vulnerability to obesity in Asian population could be the reason for this. Williams and Jiang (2000) who reported association of age with mortality had 77% of patients who were above 65 years of age. However, in present study mean age of both survivors as well as expired patients was less than 70 years. In another study, Collins *et al*. (2003) reported an association of age 65 years and older with mortality which was nearly same as present study. In present study, there were 15 patients aged above 65 years. The other studies reported an association between age and mortality, the general age of patients was similar as compared to that in present study (Carter *et al*., 2007; Jeng *et al*., 2008; Sawalha *et al*., 2009; Nedeltchev *et al*., 2010; Hedna *et al*., 2013). In present study, mean day 1 and day 3 APACHE-II scores remained closely similar (19.80±6.17 and 19.50±6.80). Day 7, APACHE-II scores were slightly higher at 22.54±9.71. Higher scores are generally indication of a poor status suggestive of mortality, thus the APACHE-II scores of day 7 indicated a poor health status of patient as compared to that at day 1 and day 3. In another study, Bhalla *et al.* (2002) indicated a very low specificity of APACHE scores (53.85% only) for prediction of mortality among patients with acute ischemic stroke despite showing a high sensitivity (94.12%). This highlights the fact that APACHE II scores in acute ischemic strokes are generally of lower order and for a given cut-off, mortalities take place, however, a lower specificity indicates that even lower APACHE II scores have higher mortality rate, thus practically APACHE II scoring system is of less use for prediction of early mortality in stroke. This may be attributed to many confounding factors. The findings in present study did not match with the findings of Khalil *et al.* (2013) who found APACHE II scores to be significantly associated with short term mortality. In present study we found higher APACHE II score on day -7 in those patient who expired but no significant association with short-term mortality was found ($p>0.05$). In fact, APACHE II scoring system has become obsolete in contemporary evaluations. Ayazoglu *et al.* (2011) in a recent study used the most recent version of APACHE II scoring system, *viz.* APACHE IV and found it to be 94.7% sensitive and 94.4% specific. As per their conclusion APACHE IV (score of >84) gave probably a more reliable prediction of high risk of death in patients with stroke than APACHE II (score >24). In present study too, we feel that APACHE II scoring system was inefficient in prediction of mortality.

With respect to CIMT, although we had reviewed two studies showing association of acute ischemic stroke with CIMT (Mukherjee *et al.*, 2006; Sahoo *et al.*, 2009), but neither of two studies showed an association of CIMT with short term mortality in cases of acute ischemic stroke. In present study, we found that average CIMT measurements of patients who expired was nearly similar compared to that of patients who survived, thus indicating , no relation between CIMT and short term mortality in patients with acute ischemic stroke. After one month, a total of 11 (22%) patients showed improvement, 13 (26%) showed survival without change in status. A total of 14 (28%) were lost to follow up and a total of 12 (24%) expired. Thus the correlation of different variables with outcome could

be done in only 36 patients as the outcome of patients was not known in 14 patients who were lost to follow up. Effective mortality rate was thus 33.3%. This mortality rate is in agreement with the reported short-term mortality rate of 25.9% as reported by Andersen *et al.* (2009). A slightly lower mortality rate of 22.7% was reported by Bhalla *et al.* (2002). De Jong *et al.* (2003) in their study reported a mortality rate of 36% but over a 1-year long follow up. Basri and Ali (2003) in contrast reported a much lower case fatality rate of 11.7% but within an average follow up period of 7.5 days. In a much larger study, Collins *et al.* (2003) who reported a series of 34,866 patients of ischemic stroke reported the 30-day mortality to be merely 7.4%. In another evaluation of a big series of 13,440 ischemic stroke patients, Heuschmann *et al.* (2004) reported the in-hospital mortality rate of 4.9%. Sawalha (2009) (Lanktree *et al*., 2009) reported an in-hospital mortality rate of 17%. Smith *et al.* (2010) WHO, 2002 in another big series of 274, 988 ischemic stroke patients reported an in-hospital mortality rate of 5.5%. A 30-day mortality rate of 13% was reported by Nedeltchev *et al.* (2010). Similar to our study, Ayazoglu *et al.* (2011) reported a mortality rate of 34.54% in their series of fifty five patients of stroke. The limitation of present study was a huge loss to follow up. This huge loss to follow up limited the already small sample size and failed to establish a statistically significant association with categorical variables.

Conclusion

The findings in present study showed that carotid intima media in acute ischemic stroke patients did not provide any useful information with respect to outcome (short term mortality). There was some association of constituents of APACHE-II scores and mortality was found in present study. There was presence of an association of arterial pH, hospital stay, lipid levels and physical condition of patient (Bed sores) with mortality while, there was absence of association of APACHE-II scores and CIMT with mortality. Further study to clarify role of each factor is recommended on a larger sample size

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