Original Article

Prediction of Clinical Outcome in Acute Hemorrhagic Stroke from a Single CT Scan on Admission

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Abstract

Background: From a single CT scan in primary intracerebral hemorrhage (ICH), clinical outcome can be assessed on admission by using the CT scan parameters. **Aims:** The study aims to find out how hematoma volume, location of stroke, midline shift, intraventricular extension of bleed and ventricle compression influence the clinical outcome in patients with acute ICH. **Materials and Methods:** Non-contrast CT scan was done on admission in hospital for every patient with acute hemorrhagic stroke and was analyzed accordingly. Clinical assessments were done in National Institute of Health Stroke Scale (NIHSS). Chi-square test and multiple logistic regression analysis were used for statistical analysis. **Results:** Mean hematoma volume associated with death before 30 days is 33.16 cm^3 ($P < 0.0001$), with survived after 30 days is 15.45 cm^3 ($P < 0.0001$), with NIHSS score ≥16 is 29.03 cm^3 ($P < 0.0001$) and with NIHSS score <16 is 13.69 cm^3 ($P < 0.0001$). Independent poor prognostic factors were hematoma volume > 30 cm^3 (OR = 27.857), brain stem hemorrhage (OR = 6.000), intraventricular extension of bleed from other location (OR = 7.846), presence of ventricular compression alone (OR = 2.700) and in combination with midline shift of ≥ 5 mm (OR = 2.124). **Conclusions:** From a single CT scan during hospital admission, mortality and morbidity in next 30 days can be predicted. A hematoma volume >30 cm^3, brain stem hematoma, intraventricular extension of bleed and ventricular compression along and with midline shift are associated with early mortality in ICH.

Keywords: Clinical outcome prediction, CT scan parameters, Intracerebral hemorrhage

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Introduction

Brain imaging is the cornerstone for diagnosis of ICH. Although MRI is an excellent tool for considerable information on the process of acute stroke; MRI is not readily available to the most patients presented with acute stroke to a rural or community hospital. CT scan is the imaging modality of choice in patients presented with acute stroke, which can detect ICH within few minutes of onset of stroke.[1] It is safe and non-invasive, helps to measure the hematoma size, location of the hemorrhage and the presence of intraventricular, subarachnoid or subdural blood, or to find out any mass effect in primary non-traumatic ICH. All these information are extremely useful in assessing the clinical and functional outcome in acute ICH, which cannot be obtained by clinical examination itself.[2,3] In rural area where resources are limited, CT scan cannot be done repeatedly.

Therefore, it is an important task for the physician to predict the functional outcome from a single CT scan of the brain done at the time of the hospital admission. The purpose of this study is to find out how we can predict a short-term in-hospital mortality and morbidity from these CT scan findings; how hematoma volume, location of stroke, midline shift, intraventricular extension of bleed, ventricle compression, etc., influence the clinical outcome in patients with acute stroke.

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Materials and Methods

It is a prospective observational study done in Burdwan Medical College, which is situated in the eastern part of India from the time period of January 2010 to June 2011.

This was approved by the institution ethics committee. The study includes 150 patients with an acute non-traumatic ICH - all were CT scan proved. All patients were randomly selected irrespective of the age and sex and a signed, informed consent was obtained. Following patients were excluded from the study- (i) patients who had prior stroke with established neuro-deficit. (ii) time gap from the onset of stroke to the presentation to the hospital been more than 24 hours, (iii) hemorrhagic stroke due to trauma, sub-arachnoid hemorrhage and rupture aneurysm.

On admission, clinical assessment of the patient was done via the prescribed format of NIHSS by a single neurologist in all cases. The total stroke score was obtained. This NIHSS score is the most useful predictor of mortality and it provides reliable information on patient's short-term mortality risk.[4] A non-contrast CT scan was done within few hours of the hospital admission. All CT scan analyses were done by a single CT scan machine (Hitachi ECLOS 16 slice, with a minimum scan time of 0.8 sec, and a maximum field of view of 500 mm). The following information were obtained from the scan (by the single neuro-radiologist to avoid interobserver bias) — (i) volume of hematoma, measured by the CT scan using the Analyze software (this procedure involved defining the zone of interest of ICH and defining the zone of edema at multiple sections). Then the Analyze software provided the area in mm^2 and volume in mm^3. The volume of ICH was calculated by multiplying the section thickness of the acquisition by the area, (ii) location of stroke, (iii) presence of intraventricular extension of bleed, (iv) midline shift, (v) presence of ventricular compression by hematoma. A midline shift of ≥5 mm was taken as a significant for mass effect and larger hematoma. NIHSS score ≥16 was taken as a very severe stroke.[5] Patients were divided into 2 groups on the basis of the NIHSS score – those with <16 and with ≥16. Again, for in-hospital mortality outcome, they are also divided into 2 groups – those who died before completion of day 30 and those who survived beyond 30 days. There were 5 groups of patients according to the location of stroke – (i) basal ganglia, (ii) thalamus, (iii) lobar, (iv) brain stem, (v) primary intraventricular bleed. Patients showing other important CT scan findings were put into 7 categories – (i) presence of intraventricular extension of bleed, (ii) midline shift, (iii) presence of ventricular compression by hematoma, (iv) combination of i and ii, (v) combination of ii and iii, (vi) combination of i and iii, (vii) combination of i, ii and iii.

Statistical analysis

Chi-square test was applied to calculate the mean value, 95% confidence interval of mean value and *P* value of hematoma volume of all groups. Linear regression analysis was done to see relationship between admission NIHSS score and hematoma volume. Multiple logistic regression analysis was done to calculate the odds ratio, 95% confidence interval, and *P* of location of stroke and CT scan findings, hematoma volume in respect to NIHSS score.

Results

Mean hematoma volume of 150 patients was 20.64 cm^3. Admission NIHSS score was significantly influenced by hematoma volume (P = < 0.0001, 95% CI = 0.305 – 0.600). Total 29.33% of the patients died before completion of day 30. Their mean hematoma volume was 33.16 cm^3 (SD- 9.04, 95% CI of 19.38 – 36.94, P < 0.0001) [Table 1]. Total 70.66% of patients survived beyond day 30. Their mean hematoma volume was 15.45 cm^3 (SD- 8.95, 95% CI of 13.04 – 36.94, P < 0.0001). Total 45.33% of patients had NIHSS score ≥ 16 (e.g., severe stroke). Their mean hematoma volume was 29.03 cm^3 (SD- 10.89, 95% CI of 25.37 – 32.69, P < 0.0001). Total 54.66% of patients had NIHSS score <16. Their mean hematoma volume was 13.69 cm^3 (SD- 7.86, 95% CI of 11.28 – 16.09, P < 0.0001). Total 29.33% of patients had hematoma volume more than 30 cm^3, out of them 26.66% patients had NIHSS score ≥ 16. A hematoma volume of more than 30 cm^3 was taken as a risk factor for adverse outcome (with NIHSS score ≥ 16); odds ratio for this relation was 27.857 (95% CI of 6.571 – 118.089, P < 0.0001). In respect to the location of stroke, 46.66% patients had a basal ganglia hemorrhage, 6.66% at thalamus, 20% at lobar, 13.33% at brain stem and 13.33% had a primary intraventricular hemorrhage (IVH). Taking location as a risk factor for higher NIHSS score, from logistic regression analysis, only brain stem hemorrhage was statistically significant for bad outcome (odds ratio = 6.000, 95 % CI of 1.347 – 26.718, P = 0.043). Other locations were not statistically significant for an adverse outcome with a higher NIHSS score. Among the important CT scan findings, 8% of total patients showed a significant midline shift, 18.66% had an intraventricular extension of bleed from another site, 10.66% had a ventricular compression by hematoma, 13.33% had a combination of midline shift and intraventricular extension, 5% had an intraventricular extension of bleed with ventricular compression, 10.66% had a combination of midline shift and ventricular compression, none had all 3 features, rest had no other features. Multiple logistic regression analysis showed that intraventricular extension of bleed was highly correlated with an adverse outcome (odds ratio = 7.846, 95% CI of 2.766 – 22.254, P < 0.0001)[Table 2]. Other 2 bad prognostic indicators were the presence of ventricular compression alone (odds ratio = 2.700, 95% CI of 1.619 – 4.669, P = 0.002) and in combination with a midline shift (odds ratio = 2.124, 95% CI of 1.834 – 4.139, P = 0.025).

Table 1: Hematoma volume and its mean value in different situations

Hematoma volume	Number of patients	Mean value (in cm^3)	SD	95% CI of mean value	*P*
All patients with ICH	150	20.64	12.06	17.91-23.37	<0.0001
Patients who died within 30 days	44 (29.33%)	33.16	9.04	19.38-36.94	<0.0001
Patients who survived beyond 30 days	106 (70.66%)	15.45	8.95	13.04-17.86	<0.0001
Patients with NIHSS score ≥ 16	68 (45.33%)	29.03	10.89	25.37-32.69	<0.0001
Patients with NIHSS score < 16	82 (54.66%)	13.69	7.86	11.28-16.09	<0.0001

Table 2: Logistic regression analysis of different CT scan parameters with their statistical significance in respect to NIHSS score ≥16 (severe stroke)

Parameters	Total number of patients %	Odd ratio	95% Confidence interval	*P*
Anatomical location of stroke				
Basal ganglia	70 (46.66)	1.278	0.519-3.143	0.598
Thalamus	10 (6.66)	0.254	0.121-1.156	0.168
Lobar	30 (20.00)	0.364	0.110-1.207	0.149
Brain stem	20 (13.33)	6.000	1.347-26.718	0.043
Primary IVH	20 (13.33)	1.241	0.346-4.454	0.750
Hematoma volume				
Size of hematoma more than 30 cm^3	44 (29.33)	27.857	6.571-118.089	<0.0001
CT scan findings				
Midline shift ≥ 5 mm	12 (8.00)	1.688	0.646-4.413	0.167
Intra ventricular extension of bleed from other site	28 (18.66)	7.846	2.766-22.254	<0.0001
Ventricle compression by hematoma	16 (10.66)	2.700	1.619-4.669	0.002
Combination of 1 and 2	20 (13.33)	1.367	0.210-3.207	0.139
Combination of 2 and 3	8 (5.33)	1.388	0.735-3.569	0.993
Combination of 1 and 3	16 (10.66)	2.124	1.834-4.139	0.025
Combination of 1, 2 and 3	0	-	-	-

Discussion

This is one of the few studies that calculates the in-hospital mortality and morbidity of stroke patients with ICH from single CT scan during hospital admission. In this study, we have found that initial hematoma volume is an independent predictor of the clinical outcome and the higher hematoma volume is associated with the higher NIHSS score. Patients with a large volume hematoma (around 30 cm^3) have higher NIHSS score and mean hematoma volume of 33.16 cm^3 is associated with early death (before day 30). In contrast to that, patients with smaller hematoma volume (around 13 cm^3 to 15 cm^3) are associated with low NIHSS score and prolonged survival.

A number of studies showed a direct relationship of hematoma volume with a clinical outcome in ICH.[6,7] A study by Molshatzki *et al*. demonstrated that patients with moderate to severe stroke had 2.3-fold higher hematoma volume as compared to mild stroke patients.[8] In one of the trial for the recombinant activated factor VII in ICH it was seen that the initial ICH volume and IVH were associated with an increased mortality and initial ICH volume (OR 0.94, $P < 0.0001$) predicted outcome. According to their observation, hematoma growth is an independent determinant of both mortality and functional outcome after ICH.[9] But what should be the size of hematoma based on which we can say this is "large" or "small" hematoma? According to Molshatzki *et al*. the mean hematoma volume for a severe stroke was 50.2 ml.[8] "The FUNC score" by Rost *et al* said that the hemorrhage size is used frequently in clinical decisions in patients with ICH, and scores predicting mortality and good functional outcome have been developed using ICH volumes categorized as <30 cm^3, 30 to 60 cm^3, and >60 cm^3.[10] A study by Broderick and his colleagues also stated that a hematoma volume more than 60 cm^3 could be a predictor of high 30-day mortality.[11] All these values are quite different from our observation. Our study

suggests that 60 cm^3 hematoma volume is too high to call it a severe stroke, if the hematoma is as large as 33 cm^3, it can be stamped as a very severe stroke. This also supports the view of Hemphill *et al.* in "The ICH score" published in Stroke 2001 where they have mentioned that hematoma volume >30 cm^3 is an independent poor prognostic factor for 30-day mortality and morbidity.[12] Moreover, this is further validated for a 1-year functional outcome where it is seen that the hematoma volume >30 cm^3 is prognostically poor for a 1-year functional outcome.[13]

A clinically significant difference was demonstrated in an early outcome as well as in the late functional recovery potential between lobar, basal ganglia, brain stem and thalamic bleedings. Hemorrhage location is important for prognosis−particularly for posterior fossa hemorrhage. We have found that only brain stem hemorrhage is statistically significant for poor prognostic factor with respect to the anatomical location of stroke. But this study has failed to identify any significant differences in the clinical outcome among the strokes at basal ganglia, thalamus or lobar hemorrhage by logistic regression analysis. This is in line with the study by Castellanos *et al.* where they found the cortical location of bleeding as an independent predictor of good short-term stroke outcome.[14] But in contrast to them, the deep location of stroke, which is a poor short-term outcome predictor according to their study, is not prognostically different from each other in our study. Many other studies described lobar hemorrhage as a predictor for severe stroke. Molshatzki *et al.* found >6-fold higher odds of lobar location of stroke in case of severe stroke as compared to mild stroke.[8] Why this discrepancy has occurred is not clear to us.

Though primary IVH has not statistically become significant for a poor outcome in our study, intraventricular extension of bleed from other anatomical location of hemorrhage is an independent poor prognostic factor (OR = 7.846, 95 % CI of 2.766−22.254, $P < 0.0001$). Ventricular compression by hematoma either alone or in combination with midline shift becomes statistically significant (OR = 2.700, $P = 0.002$ and OR = 2.124, $P = 0.025$, respectively). This also supports the view of Hallevi *et al.* They found that patients with IVH were twice as likely to have a poor outcome (OR 2.25, $P = 0.001$) when compared to patients without IVH.[15] A study on Japanese stroke patients also found that IVH along with hemorrhage size and ICH severity on admission is related to high mortality.[16] Another data by Daverat *et al.* showed similar type of result where it was seen that intraventricular spread of the hemorrhage (OR = 5.3) was the independent predictor of 30-day mortality.[17] Location of hemorrhage was not significantly correlated with survival either on 30 days or after 6 months in their study while other observations and morphological characteristics on initial CT scan are similar to our findings. Hemorrhage size, midline shift correlated well with early 30 days survival probably because acute IVH lead to raised intracranial tension and obstructive hydrocephalus, both contribute to lowering cerebral perfusion and damage to the reticular activating system resulting in a severe stroke outcome, but mere presence of blood in the ventricle is not the sole factor for the deleterious effect.[18]

In our study, a midline shift of more than 5 mm was not found as an independent predictor of bad outcome. It is prognostically poor only when coexisting with other mass effect like ventricular compression by hematoma. In a study by Fogelholm *et al.*, a midline shift >6 mm was a strong predictor of poor outcome.[19] Our study failed to prove this association, probably due to the fact that the midline shift is not a sole indicator of the mass effect; it is also indicated by ventricular compression, which is a significant factor in our study.

The major limitation of this study is that it is a 30-day in-hospital observational study. So, long-term follow-up and impact of the hematoma, location and other CT scan parameters on long duration functional outcome remains to be determined.

Conclusion

Primary spontaneous ICH, from a single non-contrast CT scan of brain gives a lot of information from which we can predict the functional outcome in stroke patients. A hematoma volume >30 cm^3 is an independent bad prognostic factor and is associated with higher NIHSS score on admission and early mortality. Except for brain stem hematoma, no other location of stroke is prognostically significant with respect to the functional recovery. Intraventricular extension of bleed and ventricular compression are 2 poor prognostic factors. Midline shift alone is not an independent poor prognostic factor for adverse outcome, but when it is present along with other mass effects like ventricular compression, it affects the functional recovery adversely.

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