

# Functional Outcome, Survival and Independent Risk Factors in Patients with Spontaneous Intracerebral Hemorrhage from Chronic Arterial Hypertension

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## Abstract

**Background:** Spontaneous intracerebral hemorrhage (spICH) from chronic arterial hypertension (CAH) carries high morbidity and mortality rate.

**Objective:** This study investigates the functional outcome, survival and predictors of severe disability or death following ICH from CAH.

**Methods:** A prospective study of 75 patients with spICH from CAH. The functional outcome was estimated using the modified Rankin Scale (mRS) before ICH and at 3, 6 and 12 months after ICH.

**Results:** 75 patients were included (mean age 52 years, 56% males). Percentage of mortality at 1 week was 20%, at 3 months 34%, at 6 months 38%, and at 12 months 42%. Median mRS score before ICH was 1; for survivors at 3, 6 and 12 months, it was 5, 4 and 3 respectively. Independent predictors of severe disability (mRS of 5) or death (mRS of 6) were mRS score before the ICH (RR 2.1, 95% CI 1.3-3.8,  $p=0.01$ ), Glasgow Coma Scale (GCS) on admission (RR 4.3, CI 2.1-6.6,  $p<0.001$ ), hematoma volume  $>60\text{ml}$  (RR 3.2, CI 1.8-6.2,  $p=0.005$ ), infra-tentorial location of ICH (RR 2.2, CI 1.3-5.5,  $p=0.03$ ), intraventricular hematoma (RR 3.4, CI 2.4-6.8,  $p<0.001$ ) and BP $>180/110$  mm Hg for  $>24$  hours after ictus (RR 3.2, CI 1.3-4.5,  $p=0.002$ ).

**Conclusion:** SpICH from CAH is associated with high mortality, and about one third of survivors end up with severe disability or death 3 months later. Predictors of severe disability or death were functional disability prior to ICH, low GCS on admission, larger hematoma volume, infratentorial location of ICH, persistently elevated BP and intraventricular hematoma.

**Keywords:** Spontaneous intracerebral hemorrhage • Chronic arterial hypertension • Functional outcome • Survival • Risk factors

## Introduction

Spontaneous intracerebral hemorrhage (spICH) is defined as non-traumatic bleeding into the brain parenchyma, [1,2] which can extend into ventricles and into the subarachnoid space [3]. ICH is the second most common subtype of stroke with worst prognosis [4], accounting for 10%-15% of all cases of stroke [5]. Between 25%-50% of patients with ICH die within the first month and half of the fatal cases occur in the first 48 hours after presentation [6-8]. Survivors are often left with severe disability [9], with less than 40% of patients regaining functional independence [10].

The most important modifiable risk factor in spICH is chronic arterial hypertension [11]. Chronic hypertension is present in 50-70% of patients who develop ICH [12]. Besides hypertension, cerebral amyloid angiopathy which is seldom seen in patients under 60 years of age is second most common cause of spICH [13]. Other etiologies like use of blood thinners (anti platelet and anticoagulants), hemorrhage from rupture of vascular malformation (e.g. cerebral aneurysm, AVM) and brain tumor bleed etc. are other common causes of spontaneous ICH.

Spontaneous ICH is a heterogeneous group of differing etiologies with distinct pathophysiology and probably variable prognosis. Incorporating them

in one basket of spontaneous ICH and deriving the risk factors which predict their functional outcome may not be accurate representation of individual etiology. For example, spICH from cerebral venous sinus thrombosis carries high morbidity, so does in a patient with use of oral antithrombotic drugs.

Accumulating literature over time have shown independent predictors of poor outcome in spontaneous ICH like level of consciousness and baseline volume of parenchymal hemorrhage [14-17]. However, the impact of

intraventricular extension of hemorrhage and hematoma location in the determination of the functional outcome remains more uncertain [18]. Despite advancement in better diagnostic and treatment modalities, the morbidity and mortality associated with this subtype of stroke has remained high over time.

The aim of this study is to investigate the predictors of functional outcome and survival in patients who present with spontaneous ICH from chronic arterial hypertension. Hypertensive brain bleed is the most common cause of spICH and it deserves a study solely focused on it. This study aims to determine accurate and reliable clinical and radiological predictors of ICH outcomes in patients with chronic arterial hypertension. This will ultimately lead to optimization of treatment and improve functional outcome.

This study is unique in that we have excluded patients with previous intracranial adverse events. It selectively includes only those patients who had good functional status and independent of care prior to ICH. This was designed to prevent the effect of pre-existing high morbid and neurological conditions in unduly influencing functional outcome and survival after ICH.

## Methods

### Study Population

Subjects for the study were admitted in Manmohan Memorial Medical College and Teaching Hospital which is a tertiary referral center for stroke with high resource setting. We have an average of 3-4 patients per week admitted to this institute with spICH from chronic arterial hypertension. Total sample size was 75 patients who met the eligibility criteria. The duration of the study was from January 2019 to September 2020.

### Ethical Clearance

Institutional ethical board clearance was obtained prior to commencing the study. Informed written consent was obtained from the patient or the next of kin in all cases. It is purely an observational study. Henceforth, no additional financial constraint, surgical intervention or tests were required to conduct this study. All the identifiable patient's information and privileged data like name, national identity number, date of birth etc. was not included in the data collection form designed for this study. A numerical code was given to each patient for data collection purpose.

### Eligibility criteria

Inclusion criteria: 1) Patients with spontaneous ICH due to chronic arterial hypertension who presented to our hospital were enrolled in the study 2) Patient who gave consent to participate in the study 3) A preset data collection form has been duly filled and complete 4) Patient should have follow up visit at 3, 6 and 12 months after ICH in outpatient setting 5) In case patient fails to follow up, the patient or next of kin is phoned to know the condition of the patient. They were approached with questionnaires that helps in deciphering patient's current functional status 6) Patients who were hospitalized in another institute but subsequently brought to our hospital within 6 hours of ictus was included.

Exclusion criteria: 1) Patient with mRS score  $>2$  prior to ICH 2) Patients with traumatic ICH 3) No previous adverse intracranial events (e.g. stroke, moderate to severe traumatic brain injury and brain surgery for any pathology)

4) ICH related to intracranial tumors, vascular malformation (cerebral aneurysm, arteriovenous malformation, cavernoma etc.) and cerebral venous sinus thrombosis 5) Patients who are taking blood thinners despite meeting the eligibility criteria as they are identifiable compounding factor 6) Patients with isolated intraventricular hemorrhage 8) Incomplete medical records or data collection sheet 8) Patient lost to follow up.

## Baseline Recordings

Patients who had clinical symptoms of stroke with known chronic arterial hypertension with presence of parenchymal hemorrhage typical of hypertensive bleed on a cerebral CT (cCT) scan were the patients selected for the study. In case of doubt that the bleed is not clear cut hypertensive cerebral hemorrhage, CT scan of the brain with contrast and CT angiogram was performed to rule out other pathology. Demographic data, comorbidities, clinical and radiological data, and information about surgical intervention were all collected using a set data collection sheet. All the patient's medical records were stored in hard copy format (we lack electronic record keeping system).

The Charlson comorbidity index was used to estimate comorbidity, a scoring system predicting 10 years survival in patients with multiple comorbidities [19]. A baseline cCT scan was available for all patients, including the ones referred from other hospitals. The two authors of this study, blinded to patient's characteristics, examined all cCTs. Hematoma location was classified as supratentorial (subcortical white matter, thalamus and basal ganglia) or infratentorial (brainstem, or cerebellum). Hematoma volume was calculated manually with the modified ellipsoid formula  $(A \times B \times C)/2 \text{ cm}^3$  [20]. The patients with intraventricular hemorrhage (IVH) was evaluated using modified Graeb score (mGS) [21]. Hematoma expansion was determined based on sequential repeat brain imaging during hospital stay, and defined as relative parenchymal volume increase of more than 33% from initial to follow-up imaging within 3 to 72 hours [22]. If several sequential repeat cCT were performed, the one closest to the 24 hour time was chosen. Patients with hematoma evacuation before any follow-up imaging were excluded from the hematoma expansion analysis.

## Outcome assessment

Patient's Glasgow Coma Scale (GCS) at presentation was taken the actual GCS in this study, the most commonly used scale to determine the level of consciousness. It is an integral component of neurological examination performed on all admitted patients. All the patients were followed up for a period of 12 months. They had follow up outpatient visit as an outpatient at 3, 6 and 12 months after ICH. Functional outcome was determined using the modified Ranking Scale (mRS) score before the ICH and the 3, 6 and 12 months after ICH. The mRS score is as follows: 0-No symptoms, 1-No significant disability, 2-Slight disability, 3-Moderate disability, 4- Moderate/ Severe disability, 5- Severe disability and 6- Dead [23].

The mRS score of each patient during outpatient visit at specified time periods were noted by the author examining him/her. Patients who were lost to follow-up or could not attend outpatient clinic, their next of kin were phoned personally by the authors to assess their current clinical and functional status. In such case, mRS was estimated by the consensus of both the authors of this study. As an additional indicator for clinical outcome, cohabitation before and after the ICH was assessed.

## Statistics

Statistical Package for Social Sciences (SPSS) 24.0 was used for statistical analysis. Descriptive statistics were computed for baseline characteristics. Student's t test and Chi-square test were used for continuous and categorical variables respectively. Cox regression analysis was employed to determine predictors of severe disability or death (mRS 5 and 6) at 3 months after ICH. Variables from the univariate analyses with a p-value <0.01 were included in the multivariate model. Effect sizes were present as relative risk in this prospective cohort study with 95% confidence interval. If the p-value is less than 0.05, it was considered statistically significant.

## Results

Out of 100 patients who met the eligibility criteria for the study, 75 patients were included for further analyses. This resulted primarily from drop out in this longitudinal study intended for 1 year. Other reasons were incompletely filled data collection sheet, transfer of patient to other hospital prior to completion of treatment at our institute or inability to afford hospital care (we lack universal healthcare insurance).

## Patient characteristics

Patient and hematoma characteristics are presented in Table 1. The mean age was 60.4 years and 56% were male. 60% (n=45) of patients had documented history of chronic arterial hypertension, where as 40% (n=25) were unaware of it. Chronic renal failure was present in 25% (n=19) of patients. The mean Charlson comorbidity index score was 1.2 (SD 1.5). In total, 10 (13%) patients had surgical management. Seven (9%) underwent craniotomy and evacuation of ICH. Three (4%) patients had decompressive hemicraniectomy along with

**Table 1** Patient and hematoma Characteristics.

| Data Particulars   | Total, N, (%) N = 75 (100) |
|--|----------------------------|
| <b>Demographic</b>   |                            |
| Male sex, N (%)  | 42(56%)                    |
| Age, Mean, $\pm$ SD  | 52 $\pm$ 15.2              |
| Age, Median (IQR, range)                                     | 56(15, 30-80)              |
| Age $\geq$ 70 years  | 5(6.6%)                    |
| Current Alcohol consumption                                  | 50 (66%)                   |
| Current Smoking  | 25 (33%)                   |
| <b>Cohabitation</b>  |                            |
| Before ICH   |                            |
| Home   | 68 (91%)                   |
| Home with assistance   | 7 (9%)                     |
| After ICH  |                            |
| Home   | 20 (27%)                   |
| Home with assistance   | 25 (33%)                   |
| Assisted Facility  | 20 (27%)                   |
| Nursing Home   | 10 (13%)                   |
| <b>Comorbidities</b>   |                            |
| Hypertension   | 75 (100%)                  |
| Compliant to antihypertensive medications                    | 30 (40%)                   |
| Non-compliant to antihypertensive medications                | 45 (60%)                   |
| Regular blood pressure check-up#                             | 25 (33%)                   |
| Irregular blood pressure check-up#                           | 50 (66%)                   |
| BP<180/110 mm of Hg beyond 24 hours post ICH                 | 65 (90%)                   |
| BP $\geq$ 180/110 mm of Hg 24 beyond 24 hours post ICH       | 10 (13%)                   |
| Diabetes Mellitus  | 30 (40%)                   |
| Chronic renal failure (dialysis dependent)                   | 25 (33%)                   |
| Hyperlipidemia   | 20 (26%)                   |
| Ischemic heart disease                                       | 10 (13%)                   |
| Chronic Obstructive pulmonary disease                        | 10 (13%)                   |
| Congestive heart disease                                     | 5 (7%)                     |
| Peripheral vascular disease                                  | 4 (5%)                     |
| Chronic Liver disease  | 4 (5%)                     |
| Cancer (not originating or involving central nervous system) | 3 (4%)                     |
| <b>Charlson Comorbidity Index</b>                            |                            |
| Mean (SD)  | 1.2 (1.5)                  |
| <b>Surgical Management</b>                                   |                            |
| Craniotomy and evacuation of brain clot                      | 7 (9%)                     |
| External ventricular drainage along with clot evacuation     | 4 (5%)                     |
| Decompressive hemicraniectomy with clot evacuation           | 3 (4%)                     |
| <b>Hematoma Characteristics, initial CT</b>                  |                            |
| Location   |                            |
| Supratentorial   | 64 (75%)                   |
| Basal ganglia involvement only                               | 40 (53%)                   |
| Basal ganglia and thalamus both involved                     | 17 (22%)                   |
| Thalamus only  | 7 (9%)                     |
| Infratentorial   | 11(25%)                    |
| Cerebellum   | 6 (8%)                     |
| Brain stem   | 5 (7%)                     |
| Mean Volume (SD)   | 25 (40.2)                  |
| <30 ml   | 52 (70%)                   |
| 30-60 ml   | 13 (17%)                   |
| >60 ml   | 10(13%)                    |
| <b>Intraventricular hemorrhage</b>                           |                            |
| Graeb Score  |                            |
| Mean (SD)  | 8.2 (6.4)                  |
| Median (IQR, range)  | 8 (11,0-28)                |
| <b>Hematoma Characteristics, follow-up CT</b>                |                            |
| Expansion  | 8 (10%)                    |
| Modified Graeb Score   |                            |
| Mean (SD)  | 7.4 (7.2)                  |
| Median (IQR)   | 6 (14, 0-22)               |

a) At least twice weekly BP check-up using automatic BP measuring machine at home or b) Doctor visit at least once a month for manual BP check using sphygmomanometer.

ICH evacuation. Four (5%) patients had external ventricular drainage placement for IVH along with clot evacuation. Ten (13%) patients had persistently elevated systolic BP>180 and/or diastolic BP>110 mm of Hg for >24 hours, out of which 7 (9.9%) patients had chronic renal failure.

**Radiological characteristics**

The most common location of the hemorrhage was deep (basal ganglia and thalamus) 75% (n=56), cerebellar 10% (n=8), and brainstem 15% (n=11) (Table 1). Hence, out of the total 75 patients with ICH, 75% (n=64) had a supratentorial and 25% (n=11) infratentorial location. Among all the locations, hemorrhage in the putamen was the most common which accounted for 53% (n=40). Overall, the mean baseline hematoma volume was 25 ml (SD 40.2), intraventricular hemorrhage was observed in 28% (n=21) and hematoma expansion in 10% (n=8).

**Functional outcome**

Clinical presentation and functional outcome are presented in Table

2. Median mRS score before ICH was 1 (interquartile range [IQR] 1); all the patients had mRS score  $\leq$ 2 prior to stroke. For the survivors at 3, 6 and 12 months, it was 5(IQR 3), 4(IQR 3) and 3(IQR 2) respectively. The proportion of fatal outcome was 20% at 1 week, 34% at 3 months, 38% at 6 months, and 42% at 12 months. Patients who survived ICH at 3 months were younger than the ones who died (46.2 versus 57.2 years, mean difference 7.1 years, 95% CI 1.5-4.4, p=0.002) Median mRS score before ICH was 1 (interquartile range [IQR] 2); for survivors at 3, 6 and 12 months, it was 5(IQR 3), 4(IQR 3) and 3(IQR 2) respectively. Among survivors at 3 months (66%, n=49), 51% (n=38) were severe disabled (mRS 5), at 6 months 30% (n=22), and at 12 months 15% (n=11). Functional outcome status before ICH, and 3, 6 and 12 months after the event is presented in detail in Table 2.

The univariate analyses (Table 3) showed the following variables as significant predictors of severe disability or death within 3 month: age> 70 years, increasing Charlson comorbidity index score, high mRS score before stroke, GCS< 9 on admission, hematoma volume> 60 mL, infratentorial location of ICH, intraventricular hemorrhage, hydrocephalus and persistently

**Table 2 Clinical Characteristics.**

| Clinical Presentation                 | Number (%)  |
|---------------------------------------|-------------|
| Before ICH                            |             |
| Median mRS score (IQR, range)         | 1 (1, 0-2)  |
| On admission                          |             |
| GCS score on admission                |             |
| Median GCS (IQR, range)               | 13(7, 3-15) |
| 13-15                                 | 40          |
| 9-12                                  | 25          |
| 3-8                                   | 10          |
| Follow-up                             |             |
| 1 week                                |             |
| Mortality rate at 1 week              | 15(20%)     |
| 3 months                              |             |
| Overall median mRS (IQR, range)       | 5(3, 0-6)   |
| Severe Disability (mRS 5)             | 20 (27%)    |
| Dead (mRS 6)                          | 26 (34%)    |
| Good functional outcome (mRS 0-2)     | 20 (26%)    |
| Median mRS (IQR, range) for survivors | 4 (2, 0-5)  |
| 6 months                              |             |
| Overall median mRS (IQR, range)       | 4(3, 0-6)   |
| Severe Disability (mRS 5)             | 17 (23%)    |
| Dead (mRS 6)                          | 29(38%)     |
| Good functional outcome (mRS 0-2)     | 18 (24%)    |
| Median mRS (IQR, range) for survivors | 3(2, 0-5)   |
| 12 months                             |             |
| Overall median mRS (IQR, range)       | 3(2, 0-6)   |
| Severe Disability (mRS 5)             | 14(18%)     |
| Dead (mRS 6)                          | 32(42%)     |
| Good functional outcome (mRS 0-2)     | 15(20%)     |
| Median mRS (IQR, range) for survivors | 3(2, 0-5)   |

**Table 3 Factors associated with severe disability or death (mRS score 5-6) at 3- month follow-up.**

| Variable                                  | Univariable regression RR (95% CI) p - value | Multivariable regression RI (95% CI) p - value |
|---|--|--|
| Age $\geq$ 70 years                       | 2.4 (1.8-3.6) < 0.001                        | 0.6 (0.2-1.3) 0.02                             |
| Male sex                                  | 1.2 (0.8-1.9) 0.320                          | - -  |
| Charlson Comorbidity index <sup>a</sup>   | 1.4 (1.1-1.7) < 0.001                        | 1.2 (0.7-1.5) 0.250                            |
| mRS score before ICH <sup>b</sup>         | 2.3 (0.6-2.4) < 0.001                        | 2.1 (1.3-3.8) 0.01                             |
| GCS < 9 on admission                      | 18.4 (9.0-38.2) < 0.001                      | 4.3 (2.1-6.6) <0.001                           |
| GCS $\geq$ 13 on admission                | 2.1 (0.7-2.9) < 0.001                        | 0.3 (0.1-1.1) <0.001                           |
| Infratentorial location                   | 2.6 (0.9-3.4) < 0.001                        | 2.2 (1.3-5.5) 0.03                             |
| Persistent BP $\geq$ 180/110 <sup>c</sup> | 5.2 (3.1-8.7) < 0.001                        | 3.2 (1.3-4.5), 0.002                           |
| Hematoma volume > 60 mL                   | 6.8 (3.6-12.4) < 0.001                       | 3.2 (1.8-6.2) 0.005                            |
| Intraventricular hemorrhage               | 5.6 (3.8-9.7) < 0.001                        | 3.4 (2.4-6.8) <0.001                           |
| Hydrocephalus                             | 7.2 (5.1-13.4) < 0.001                       | 1.3 (0.7-4.1) 0.113                            |

<sup>a</sup>Per Increment.

<sup>b</sup>Score range from mRS 0 (no symptoms) to 6 (death) (per increment).

<sup>c</sup>Persistently elevated blood pressure  $\geq$  180 and/or 110 millimeter of mercury lasting beyond 24 hours after ICH despite best medical management.

raised BP > 180/110 mm of Hg for over 24 hours despite best medical management. In the multivariable analysis, independent predictors of severe disability (mRS of 5) or death (mRS of 6) at 3 months after ICH were mRS score before the ICH (RR 2.1, 95% CI 1.3-3.8,  $p=0.01$ ), Glasgow Coma Scale (GCS) on admission (RR 4.3, CI 2.1-6.6,  $p<0.001$ ), hematoma volume > 60ml (RR 3.2, CI 1.8-6.2,  $p=0.005$ ), infra-tentorial location of ICH (RR 2.2, CI 1.3-5.5,  $p=0.03$ ), intraventricular hematoma expansion (RR 3.4, CI 2.4-6.8,  $p<0.001$ ) and persistently raised BP > 180/110 mm of Hg for > 24 hours after ictus (RR 3.2, CI 1.3-4.5,  $p=0.002$ ).

In a similar multivariate analysis, only age  $\leq 70$  years (RR 0.6, 95% CI 0.2-1.3,  $p=0.002$ ) and GCS  $\geq 13$  (RR 0.3, 95% CI 0.1-1.1,  $p<0.001$ ) were found to be independent predictor of favorable outcome defined as mRS 0-2 at three months after ICH.

Before the event, 91% (n= 68) patients lived at home without assistance and remainder 9% (n=7) stayed at home with assistance from the family members. At 3 months after ICH, about 60% (n=45) patients continued to live at home despite high rate of poor functional outcome (median mRS score at 3 months was 5).

## Discussion

This prospective single centered study in a high resource setting was designed specifically for patients with spontaneous ICH from long standing hypertension. This study had stringent selection criteria. We purposefully excluded patients who had poor functional status and were dependent of care prior to stroke. The same applies for patients who had significant intracranial adverse events prior to enrollment in the study. This was aimed to minimize the variables that could directly or indirectly lead to overestimation of the poor functional outcome and mortality in this study.

Our study revealed spICH associated with chronic arterial hypertension is associated with high mortality, and the majority of survivors become dependent of care. This is unfortunate considering significant stride has been made in recent times in understanding the disease process, better diagnostic tools, easily accessible stroke centers and improved armamentarium to treat the disease.

Despite our effort to exclude patients with poor medical condition in this study, we had modest number of patient's significant pre-morbid medical conditions (most notable is chronic renal disease). Albeit in this study, the Charlson comorbidity index as a measure of the severity of pre-existing medical condition, had its median at 1.2 which is close to its lowest value of 1. All the patient's in present study were living at home (with or without assistance from the loved ones) prior to stroke and were independent in carrying out activities of daily living.

Independent predictors of severe disability (mRS of 5) or death (mRS of 6) were mRS score before the ICH Glasgow Coma Scale (GCS) on admission, hematoma volume > 60mL, infra-tentorial location of bleed, intraventricular hematoma expansion and persistently raised BP > 180/110 mm of Hg for > 24 hours after stroke (Table 3). In a similar multivariate analysis, only age  $\leq 70$  years and GCS  $\geq 13$  were found to be independent predictor of favorable outcome defined as mRS 0-2 at three months after ICH.

The mortality rate in the current study was 20% at 1 week, 34% at 3 months, 38% at 6 months, and 42% at 12 months. This is in concordance with the previous studies reporting mortality rate ranging from 25-50% [24-26]. Following stroke, patients with good functional outcome (mRS 0-2) were low and showed a declining trend over time. Favorable outcome (mRS < 2) was 26%, 24% and 20% at 3, 6 and 12 months respectively, in line with previous studies exhibiting independent functional status rates from 12% to 39% after ICH [27]. Prior to ICH, 100% patients lived at home. At 3 months after the event, only 60% patients continued to live at home despite high rate of poor functional outcome (median mRS score at three months was 5). Financial constraints and social norms probably dictated this anomaly, despite the need for assisted facility or nursing home for patients who were dependent of care.

Chronic hypertension is present in 50-70% of patients who develop ICH. Sturgeon et al. revealed patients with systolic BP  $\geq 160$  mm of Hg or a diastolic BP  $\geq 110$  mm Hg have a 5.5 (95% CI 3.0-10.0) times increased risk rate of ICH, compared to normotensive patients with ICH. The authors employ strict BP control < 140/90 mm Hg for patients presenting with ICH at all times. Intermittent use of injection Labetalol 10-20 mg is used to keep the BP in the normal range. Failure of this protocol leads to continuous intravenous infusion of Labetalol, Nicardipine or Sodium Nitroprusside, titrate to keep patient normotensive.

In the present study, continued high BP ( $\geq 180/110$  mm Hg) for over 24 hours despite best medical management (antihypertensive therapy) was found to be independent predictor of poor functional outcome (RR 3.2, CI 1.3-

4.5,  $p=0.002$ ). Out of 10 patients with BP  $\geq 180/110$  mm of Hg beyond 24 hours after ICH, 7 were dialysis dependent chronic renal failure patients (CRF). Six (60%) out of total 10 patients with CRF had hematoma expansion. Our institute is a major referral center for free of cost dialysis for CRF patients. It was a difficult task to normalize BP in CRF patients, requiring continuous infusion of combination of antihypertensive medications apart from scheduled dialysis on alternate days.

In line with the previous studies, we found that patient's initial level of consciousness, baseline hematoma volume, hematoma growth, infratentorial location and intraventricular hemorrhage were the independent predictors of outcome in patients with ICH [28]. Unlike the most widely used ICH score, which has been externally validated ICH grading scale, [29,30] present study did not find age as the prognostic factor of ICH. The same applies for gender, which is not a risk factor for poor functional outcome in the present study.

Hematoma expansion is a major determinant of early neurological deterioration, poor outcome, and death [31-33]. Current study validates the current literature on this matter. This is potentially a modifiable risk factor, and prevention of such expansion should be aggressively sought. It is important to identify accurate and reliable predictors of hematoma growth, so that appropriate measures can be taken to avert it. Prediction score for hematoma expansion has been published, [34-36] which includes common factors like shorter time from ICH onset to CT, anticoagulant use; and evidence of spot sign of CT angiogram (CTA). The spot sign observed on CTA was not part of the study, as spICH from chronic arterial hypertension were diagnosed on the basis of known hypertension and typical location of hypertensive bleed. Patients did not require CTA in this study. Notably, present study revealed patients with continued uncontrolled hypertension beyond 24 hours is a known determinant of hematoma expansion.

The widely used ICH score as the clinical grading scale for prognostication should not be used in isolation to limit intervention in the acute initial management of the patients with ICH. The pessimism related to poor prognosis surrounding high ICH scores should not preclude from deploying all the armamentarium available to treat the patient. This approach may positively impact functional outcome and survival in patients with spontaneous intracerebral hemorrhage.

In this prospective cohort study, patients who underwent neurosurgical intervention did not exhibit better outcome. At 3 months, more than one third of the patients receiving surgical management were dead (mRS 6) and another half had severe disability (mRS 5). The patients attributed to surgery had low GCS on admission, significant hematoma volume with mass effect and clinical features of raised ICP. Some had intraventricular hemorrhage which required external ventricular drainage apart from craniotomy for evacuation of brain clot.

It is evident that the surgical patients had poorer clinical status and significant hematoma size compared to non-surgical patients. This may account for their poor functional outcome considering more severely affected patients undergo surgery, and thus, selection bias exists. It is important to note that this study was not a treatment trial, was not designed to evaluate the effectiveness of various surgical treatment modalities for ICH. We employed traditional method of craniotomy and evacuation of clot. However, new exciting techniques like endoscopic evacuation of ICH with or without use of intra-hematoma thrombolytic and decompressive craniotomy without clot evacuation was not part of this study.

Despite present study being selective for patients with good functional outcome, independent of care and without significant past brain insult prior to ICH, the functional outcome and survival was not higher compared to other studies who did not have this stringent selection criteria. This suggests brain is a sensitive organ and the brain insult caused by ICH is sufficient onto itself to warrant poor clinical outlook.

## Conclusion

Despite advancement in the field of neurosurgery, this prospective study highlights persisting high morbidity and mortality in patient with spontaneous ICH. Majority of survivors become disable and dependent of care. The independent predictors of severe disability or death at 3 months were poor functional status prior to ICH, larger hematoma volume, infratentorial location of bleed, low GCS score on admission, intraventricular hemorrhage and persistently elevated high blood pressure.

## Acknowledgment

None

## Conflict of Interest

None



## Disclosure

None

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