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THE CORRELATION OF BLOOD PRESSURE AND ICH SCORE WITH THE OUTCOME AT 90 DAYS IN CASES OF SPONTANEOUS HYPERTENSIVE INTRACEREBRAL HEMORRHAGE

Neurology

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ABSTRACT

Aims: To correlate the Blood pressure and the ICH score with the functional outcome at 90 days in cases of spontaneous hypertensive intracerebral hemorrhage.

Settings and Design: An Observational study where a total of 50 consecutive cases of Hypertensive Intracranial hemorrhage were studied from a tertiary hospital of Command Hospital of Command Hospital.

Methods and Materials: The admission Blood pressure was measured along with the calculation of ICH score. This was correlated with the functional score at 90 days.

Statistical analysis: Analysis of Variance (ANOVA).

Results: A total of 50 patients were studied. There was a strong correlation of the MAP at 72hrs with the outcome at 90 days in the subjects who were undertaken MAP lowering therapy as compared to those in whom MAP was not lowered. This study showed that the ICH score had a significant effect on outcome the higher the score, the worse was the outcome..

Conclusions: It was observed that admission BP and BP at 72 hours post symptom onset and the ICH score had a bearing on the functional outcome at 90 days.

KEYWORDS

Intracerebral hemorrhage, Mean arterial pressure (MAP), Hematoma

Introduction

Intracerebral hemorrhage (ICH) is the second most common cause of stroke and accounts for 8% to 15% of strokes in the world with an estimated incidence of 10 to 25 per 100 000 persons. (1–3) Despite advances in the field of stroke and neurocritical care,(4) the 30-day mortality has not changed significantly over the past 20 years.(3) Indeed, ICH has the highest rates of dependence or death among stroke types and proven treatments are lacking. Hematoma expansion in the early phase of the illness contributes to the morbidity and mortality.

One of the major determinants of hematoma expansion is uncontrolled hypertension. Lowering blood pressure (BP) is commonly practiced to prevent hematoma enlargement in patients with intracerebral hemorrhage (ICH). Besides hematoma growth, other pathophysiological processes occur in the setting of ICH and may serve as potential therapeutic targets. In the acute period after ICH, a rapid rise in intracranial pressure (ICP) from an expanding hematoma may reduce cerebral perfusion pressure. Adequacy of the perfusion of the brain is represented by a normal cerebral perfusion pressure (CPP). This is derived from Mean arterial pressure (MAP) minus ICP. Hence if raised ICP is managed by standard means then CPP is dependent on MAP. Current guidelines for managing blood pressure state that the MAP should be treated if it crosses 130 mm of Hg. This higher MAP has been fixed due to the fear of a drop in CPP if MAP is lowered drastically leading to worsening of deficits. There is scope for lowering the BP even further as shown in some studies which improved outcome with lower BP. Current guidelines for the acute management of ICH provide an indication of perceived harm associated with “very high” BP levels but also highlight ongoing uncertainty over what is the optimal BP in this condition. (10) Definitive evidence to support such a low-cost and widely applicable treatment is urgently required for ICH, because the only currently proven management strategy is stroke unit-based supportive care and rehabilitation.

Since phase III clinical trial data are lacking, recent guidelines do not have Class I recommendations for blood pressure reduction in ICH. (12) The European Stroke Initiative Guidelines recommend a target mean arterial pressure (MAP) of 125 mmHg in patients with a history of hypertension and 110 mmHg in those without a history of hypertension. The American Heart Association Guidelines recommend keeping MAP at less than 130 mmHg while maintaining cerebral perfusion pressure at more than 60 mmHg in patients with elevated intracranial pressure. A goal MAP of 110 mmHg is recommended for patients without elevated intracranial pressure. There has therefore been considerable controversy regarding the initial control of BP after the onset of ICH.

This study has been designed to test the correlation of Blood pressure on admission and ICH score and outcome measure at 90 days in cases of intracerebral haemorrhage. The study intends to evaluate the factors which has an effect on the functional outcome at 90 days and also to evaluate the contribution of the mean arterial pressure (MAP) both on admission and at 72 hrs on the outcome.

Aims

To correlate the admission Blood pressure and the ICH score with the functional outcome at 90 days in cases of spontaneous hypertensive intracerebral hemorrhage

Objectives

This single centre observational study in patients with spontaneous hypertensive intracerebral hemorrhage have the following objectives

a) To measure the MAP on admission in the patients.
b) To evaluate the MAP at 72hrs after admission & treatment initiation
c) To calculate the ICH score on admission
d) To compare late outcome at 90 days as assessed by modified rankin scale & clinically.

Materials and Methods

The study has been conducted at tertiary hospital Command Hospital (Eastern Command) Kolkata. A total of **Fifty (50)** consecutive subjects

of hypertensive intracerebral hemorrhage have been study subjects

Inclusion criteria
a) Spontaneous hypertensive intracerebral hemorrhage
b) Duration <72 hrs from time of onset
Informed written consent taken from the subject/NOK

Exclusion criteria
Brain death on admission

MAP measurement at initiation of therapy:
MAP measurement to be confirmed by three consecutive readings 5 minutes apart. The standard manual mercury sphygmomanometer was used & all the recordings were done by either the Physician or the treating Neurologist. It was ensured that the average of 3 readings of MAP taken were from the same physician to prevent any variability.

BP lowering protocol: The drug administered to lower the BP would be any of the standard recommended drugs used for treating hypertensive related emergencies. The subsequent switch to oral drug would be at the discretion of the treating neurologist and will be any one of the standard drugs used. The aim would be to maintain the MAP at or below 130 mm Hg.

Monitoring: Monitoring at the end of 72 hours would be done by firstly, a repeat CT scan to document any increase in hematoma size if indicated due to clinical deterioration and secondly by clinical examination to document any worsening.

Calculation of ICH volume:- The volume of hematoma was calculated using the software available on-line which uses the parameters of maximum length, breadth & the number of slices of the 10mm cuts on which the hemorrhage was visible on the plain CT scan.

Evaluation of mass effect & midline shift on CT scan:- The CT mass effect was calculated by the amount of midline shift in millimeters as observed on the plain CT head.

Calculation of ICH score:- The ICH score was calculated on admission based on the five parameters given below & tabulated accordingly. The maximum score is 6 & the minimum score is 0. The ICH score predicts 30-day mortatlity & the higher the score, higher the mortality.

Component	Points
GCS score	
3-4	2
5-12	1
13-15	0
ICH volume (cm^3)	
>30	1
<30	0
IVH	
Yes	1
No	0
Infratentorial origin of ICH	
Yes	1
No	0
Age (y)	
>80	1
<80	0

Protocol for raised ICP: During this period raised intracranial pressure (ICP), defined by mass effect or any midline shift on a plain CT brain, was be treated as appropriate using standard therapy which included a) Head end elevation to atleast 30 degree b) Hyperventilation with target PCo2 = 30 – 35 mmHg & either Mannitol 20% dose 0.25 – 1Gm/kg or Hypertonic saline (3%) in appropriate doses as deemed necessary by treating neurologist. The subjects who had intra-ventricular extension underwent External ventriculostomy device (EVD) when indicated. In cases where there was infra-tentorial hemorrhage was present, hematoma evacuation was undertaken whwnever feasible as per the discretion of the Neurosurgeon.

Outcome at 90 days: All patients were followed up at 90 days when outcome was assessed using modified Rankin Scale. Analysis was by intention to treat. A statistical analysis was be done and the correlation of the level of MAP with the outcome at 90 days was assessed. Statistical analysis of outcome assessment was done at CHEC Kolkata by the approved biostatistician.

Results

Table 1 – Baseline characteristics of variables

Variables	Mean	Median	SD	Min.	Max.
Age (years)	66.5	66	6.6	54	80
GCS on admission	9.0	9	3.3	4	13
MAP on admission (mm Hg)	128.7	128	7.3	112	148
MAP at 72 hrs (mm Hg)	120.7	118	6.4	112	131
CT hematoma volume (cmm)	47.9	45	17.9	15	90
CT mass effect shift (mm)	5.8	6	4.0	0	15

- The baseline characteristics of the study population has been shown as above. The mean age was 66.5 yrs with a SD of 6.6 & the median age was 66 yrs. The mean & median values of GCS were 9 with a SD of 3.3 with a minimum score of 4/15 & maximum of 13/15.
- The mean & median MAP on admission were 128 mmHg with a SD of 7.3 with a minimum of 112 mmHg & maximum 148 mmHg. The MAP at 72hrs was a median of 118 mmHg with a SD of 6.4. The minimum & maximum MAP were 112 & 131 mmHg.

The CT hematoma volume values were such that, mean was 47.9 cmm & a median of 45 cmm. The maximum volume was 90 & minimum 15 cmm. The median CT mass effect was 6 mm shift with a maximum of 15 mm & minimum of zero

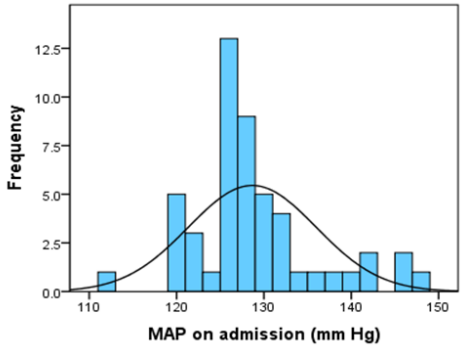

Figure 1 – Distribution of MAP on admission

- The MAP on admission had the maximum frequency scattered between the range of 120 – 145 mmHg. The maximum distribution were in the range of 125 mmHg with the next highest being at 128 mmHg. There were about 5 subjects with an MAP of 120 mmHg and one had a value of around 110 mmHg. There were five subjects with a MAP of more than 140 mmHg.

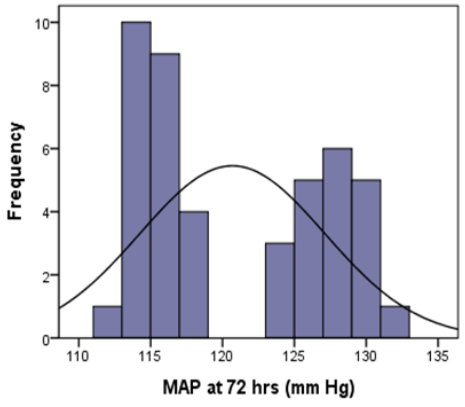

Figure 2 – Distribution of MAP at 72 hrs

- The plotting of the values of MAP at 72hrs revealed that the distribution was at both extremes of higher & lower values. There were about 24 subjects in the range of MAP between 112 – 118

mmHg with about 10 of them having MAP around 115 mmHg. There were 23 subjects whose MAP ranged between 122 – 132 mmHg with one (1) subject having MAP more than 130 mmHg. The lowest MAP recorded was 112 mmHg in one subject.

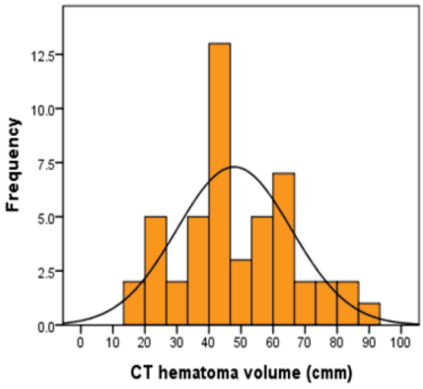

Figure 3 – Distribution of CT Hematoma volume

- The distribution of CT hematoma had a peak at a value of 45 cmm with 12 subjects having the same. There were seven patients with a volume of less than 30 cmm. There were thirteen (13) subjects with a volume of more than 60 cmm.

Table 2 – MAP lowering used

Use of MAP lowering	n	%
No	24	48.0
Yes	26	52.0
Total	50	100.0

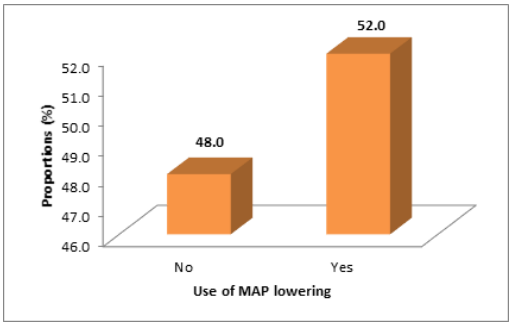

Figure 4 – MAP lowering used

- There were twenty six (26) subjects in whom MAP lowering therapy was used which was about 52 %. In twenty four (24) subjects, the MAP lowering was not done which was about 48 %.

Table 3 ICH Score

ICH score	n	%
0	1	2.1
1	7	14.6
2	22	45.8
3	9	18.8
4	6	12.5
5	3	6.3
Total	48	100

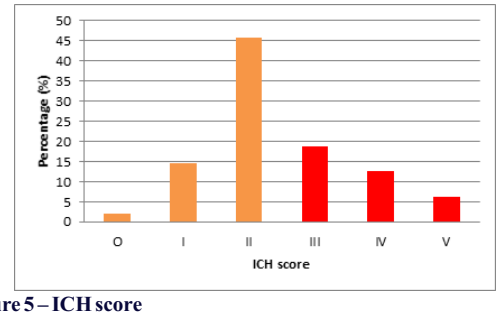

Figure 5 – ICH score

- There were twenty two subjects with an ICH score of 2, while three had a score of 5. One subject had a score of zero while seven had a score of 1. There were a total of fifteen subjects with a score range 3 and 4.

Table 4 – ICP lowering therapy used

Type of ICP lowering therapy	n	%
EVD & Hypertonic saline	2	4
EVD & Mannitol	5	10
Hematoma evacuation & Mannitol	2	4
Hypertonic saline	6	12
Mannitol	35	70
Total	50	100

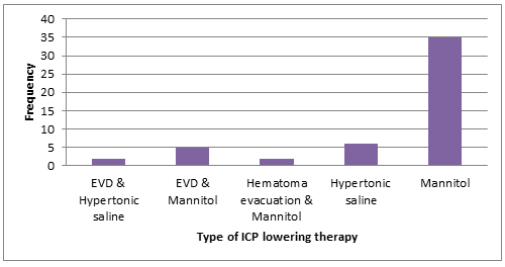

Figure 6 – ICP lowering therapy used

- The commonest ICP lowering therapy used was Mannitol which was used in thirty five subjects. The agent Hypertonic saline alone was used in six subjects, while EVD was used along with the same in two subjects. The agent mannitol was combined with EVD in five subjects, while hematoma evacuation was done in two subjects.

Table 5 – Modified Rankin scale at 90 days

Modified Rankin scale at 90 days	n	%
1	5	11.4
2	12	27.3
3	10	22.7
4	2	4.5
5	3	6.8
6	12	27.3
Total	44	100.0

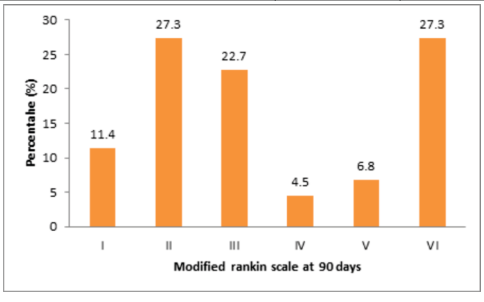

Figure 7 – Modified Rankin scale at 90 days

- There were five subjects with a mRs of 1, while twelve subjects had an mRs of 2. There were a total of ten subjects who had mRs of 3, while two had a score of 4.There were twelve subjects who did not survive, which resulted in an mRs of 6.

Table 6 – Modified Rankin scale at 90 days with MAP lowering

Modified Rankin scale at 90 days	Use of MAP lowering				Total		p value
	No		Yes				
	n	%	n	%	n	%	
1	0	0	5	21.7	5	11.4	0.030
2	6	28.6	6	26.1	12	27.3	
3	3	14.3	7	30.4	10	22.7	
4	2	9.5	0	0	2	4.5	
5	3	14.3	0	0	3	6.8	
6	7	33.3	5	21.7	12	27.3	
Total	21	100	23	100	44	100	

- The use of MAP lowering was compared with mRs for each value from 1 – 6 with variables of yes or no.
- It was found that the correlation of the same was statistically significant in that, out of a total of fifteen (15) subjects who had a worse mRs of 5 – 6, there were 10 subjects in the group when MAP

was not lowered while it was only five (5) in the other group.
- Similarly, out of a total of nineteen (19) subjects with a good mRs of 1 – 2, there were only six (6) in the group without MAP lowereing while the other group had eleven (11) subjects
- The probability value P = 0. 030.

Table 7 – Modified Rankin scale at 90 days with ICH score

MRS score	ICH score				Total		p value
	0-2		>2				
	n	%	n	%	n	%	
1-2	14	51.9	3	18.8	17	39.5	0.002
3-4	9	33.3	2	12.5	11	25.6	
5-6	4	14.8	11	68.8	15	34.9	
Total	27	100.0	16	100.0	43	100.0	

- The ICH score was compared with mRs for each value after sub-grouping from 1-2, 3-4 & 5-6 with values from 0-2 and 2 or more.
- It was found that the correlation of the same was statistically significant in that, out of a total of fifteen (15) subjects who had a worse mRs of 5 – 6, there were eleven (11) subjects in the group which had ICH score of >2 while it was only four (4) in the other group.
- The probability value P = 0. 002

Table 8 – Modified Rankin scale at 90 days with all parameters

Analysis of variance (ANOVA) to compare between modified Rankin scale at 90 days and other scale parameter						
Scale variables		Sum of Squares	df	Mean Square	F	P value
Age (years)	Between Groups	824.0	5	164.8	5.69	0.001
	Within Groups	1101.2	38	29.0		
	Total	1925.2	43			
GCS on admission	Between Groups	223.3	5	44.7	7.18	0.0001
	Within Groups	236.3	38	6.2		
	Total	459.6	43			
MAP on admission (mm Hg)	Between Groups	224.9	5	45.0	0.73	0.602
	Within Groups	2327.0	38	61.2		
	Total	2551.9	43			
MAP at 72 hrs (mm Hg)	Between Groups	463.0	5	92.6	2.75	0.035
	Within Groups	1076.1	32	33.6		
	Total	1539.1	37			
CT hematoma volume	Between Groups	4999.2	5	999.8	3.74	0.008
	Within Groups	9884.8	37	267.2		
	Total	14884.0	42			
CT mass effect shift (mm)	Between Groups	150.3	5	30.1	2.02	0.098
	Within Groups	566.5	38	14.9		
	Total	716.8	43			

- The analysis of variance done by ANOVA revealed that the variables which were not significant statistically were MAP on admission with a probability value P = 0.602 and CT mass effect with a Probability value P = 0.098.
- The variables which were statistically significant were the following Age, GCS on admission, MAP at 72hrs and CT hematoma volume.
- The GCS on admission had the most significant effect on the mRs at 90 days followed by age and CT hematoma volume.

Discussion

This single centre observational study was done to correlate the admission blood pressure with the functional outcome at 90 days (Modified rankin Scale) and evaluate the variables in the outcome.

It was observed that age was a significant variable in the outcome and that higher the age, the worse was outcome at 90 days as seen in the higher mRs score. The independent analysis by ANOVA also confirmed that age had a significant impact on the outcome at 90 days.

The Glasgow coma score (GCS) on admission had a significant bearing on the outcome at 90 days as was found in this study that the lower GCS, which portends a lower sensorium was strongly associated with higher mRs at 90 days which meant that the functional outcome was poor.

The evaluation of MAP on admission had shown that the higher MAP was associated with a higher mRs which means a poorer functional outcome eventhough this contribution by MAP on mRs was not statistically significant.

There was a strong correlation of the MAP at 72hrs with the outcome at 90 days in that the subjects who were undertaken MAP lowering therapy to achieve a target below 130 mmHg and in whom it was achieved had better outcomes at 90 days as shown in the lower mRs scores as compared to those in whom MAP was not lowered.

This difference was statistically significant eventhough the exact range of the MAP for which the better outcome in mRs started could not be ascertained.

The reason for the admission MAP being not significantly affecting the outcome can be that the MAP on arrival to the hospital is affected to some extent by the reactionary elevation or reactionary hypertension and would have caused some degree of elevation if not entirely.

This study also demonstrated that the factors like hematoma volume, mass effect or presence of infra-tentorial hemorrhage had a significant effect on the outcome at 90 days in that the higher the hematoma volume or mass effect or presence of infra-tentorial bleed had higher mRs score correlating with a poor outcome. This effect was also very significant statistically.

This study showed hence that the ICH score which incorporates the variables given above had a significant effect on outcome in that, the higher the score, the worse was the outcome.

There was no difference in the outcome in the usage of different means of reducing the ICP whether it was Mannitol, Hypertonic saline or EVD with or without these two agents when given in appropriate circumstances.

This study demonstrates that the factors which has a significant bearing on the outcome at 90 days are the following
a) Age
b) Sensorium on admission – GCS
c) MAP at 72 hrs when MAP was lowered
d) The volume of hematoma
e) Infra-tentorial hemorrhage
f) CT mass effect
g) ICH score

The present study has shown that one of the important factors determining the functional outcome is the MAP after 72 hrs and any measures to lower the MAP if undertaken to bring it in the range of 130 mmHg. This is apart from the fact that there are other determinants in the form of age, GCS on admission, ICH score & hematoma volume which has a significant effect on the outcome at 90 days.

Since phase III clinical trial data are lacking, recent guidelines do not have Class I recommendations for blood pressure reduction in ICH. (62) The European Stroke Initiative Guidelines recommend a target mean arterial pressure (MAP) of 125 mmHg in patients with a history of hypertension and 110 mmHg in those without a history of hypertension.(11)

The American Heart Association Guidelines recommend keeping MAP at less than 130 mmHg while maintaining cerebral perfusion pressure at more than 60 mmHg in patients with elevated intracranial pressure. (11) A goal MAP of 110 mmHg is recommended for patients without elevated intracranial pressure.

Summary and Conclusions

This single centre observational study was done to correlate the admission blood pressure with the functional outcome at 90 days (Modified rankin Scale) and evaluate the variables in the outcome.

A total of fifty (50) subjects were studied for a period of about two years and a total of twelve (12) subjects could not complete the 90 days follow-up as they could not survive which resulted in the data available from the remaining thirty eight (38) at the end of 90 days.

The following conclusions can be drawn from this study.

1) Increasing age is an important adverse prognosticating factor in Hypertensive ICH, higher the age, the worse the functional outcome.
2) The sensorium on admission was also an important prognosticating factor with lower the GCS, the worse the outcome
3) The MAP at 72hrs on admission was one of the factors which had

an impact on the outcome with higher levels associated with poor outcome.

4) Other factors which were adversely affecting the outcome were ICH volume, Infra-tentorial bleed & CT mass effect which in combination would consist the formulation of ICH score.
5) The co-morbidities which were present did not affect the outcome significantly so also the sexual differences.
6) The intra-venticular hemorrhage did not affect the outcome significantly.

REFERENCES

1. Broderick JP, Brott T, Tomsick T, Miller R, Huster G. Intracerebral hemorrhage more than twice as common as subarachnoid hemorrhage. J Neurosurg. 1993;78:188 –191.
2. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol. 2009;8: 355–369.
3. Van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. Lancet Neurol. 2010;9:167–176.
4. Diringer MN, Edwards DF. Admission to a neurologic/neurosurgical intensive care unit is associated with reduced mortality rate after intracerebral hemorrhage. Crit Care Med. 2001;29:635– 640.
5. Mayer SA, Brun NC, Begtrup K, Broderick J, Davis S, Diringer MN, et al. Efficacy and safety of recombinant activated factor VII for acute intracerebral hemorrhage. N Engl J Med. 2008;358:2127–2137.
6. Mendelow AD, Gregson BA, Fernandes HM, Murray GD, Teasdale GM, Hope DT, et al. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the international surgical trial in intracerebral haemorrhage (STICH): a randomised trial. Lancet. 2005;365:387–397.
7. Morgenstern LB, Hemphill JC III, Anderson C, Becker K, Broderick JP, Connolly ES Jr, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2010;41:2108 –2129.
8. Anderson CS, Huang Y, Wang JG, Arima H, Neal B, Peng B, et al. Intensive blood pressure reduction in acute cerebral haemorrhage trial (INTERACT): a randomised pilot trial. Lancet Neurol. 2008;7:391–399.
9. Qureshi AI, Palesch YY, Martin R, Novitzke J, Cruz-Flores S, Ehtisham A, et al. Effect of systolic blood pressure reduction on hematoma expansion, perihematomal edema, and 3-month outcome among patients with intracerebral hemorrhage: results from the antihypertensive treatment of acute cerebral hemorrhage study. Arch Neurol. 2010;67:570–576.
10. Garg RK, Liebling SM, Maas MB, Nemeth AJ, Russell EJ, Naidech AM. Blood pressure reduction, decreased diffusion on MRI, and outcomes after intracerebral hemorrhage. Stroke. 2012;43:67–71.
11. Broderick J, Connolly S, Feldmann E., et al. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update: a guideline from the American Heart Association/American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Re-search Interdisciplinary Working group. Stroke. 2007; 38: 2001-23.
12. Kang BK, Na DG, Ryoo JW, Byun HS, Roh HG, Pyeun YS. Diffusion weighted MR imaging of intracerebral hemorrhage. Korean J Radiol. 2001;2:183–191.
13. Carhuapoma JR, Wang PY, Beauchamp NJ, Keyl PM, Hanley DF, Barker PB. Diffusion-weighted MRI and proton MR spectroscopic imaging in the study of secondary neuronal injury after intracerebral hemorrhage. Stroke. 2000;31:726 –732.
14. Herweh C, Juttler E, Schellinger PD, Klotz E, Jenetzky E, Orakcioglu B,et al. Evidence against a perihemorrhagic penumbra provided by perfusion computed tomography. Stroke. 2007;38:2941–2947.
15. Kidwell CS, Saver JL, Mattiello J, Warach S, Liebeskind DS, Starkman S, et al. Diffusion-perfusion MR evaluation of perihematomal injury in hyperacute intracerebral hemorrhage. Neurology. 2001;57:1611–1617.
16. Statistics Canada. (2011). Morality, Summary List of Causes 2008. Retrieved Feb¬ruary 2013, from the World Wide Web: http://www5.statcan.gc.ca/bsolc/olc-cel/ olc-cel?catno=84F0209X&CHROPG=1&lang=eng.
17. MacKay J, Mensah GA. Global Burden of Stroke. In: MacKay J, Mensah GA. The Atlas of Heart Disease and Stroke. Geneva: World Health Organization; 2004; p. 50-51.
18. Flaherty ML, Woo D, Haverbusch M., et al. Racial variations in location and risk of intracerebral hemorrhage. Stroke. 2005; 36: 934-7.
19. Mayer SA, Rincon F. Treatment of intracerebral haemorrhage. Lancet Neurol. 2005; 4: 662-72.
20. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statis¬tics--2012 update: a report from the American Heart Association. Circulation. Jan 3 2012; 125(1):e2-e220.
21. Heart and Stroke Foundation of Canada (2003). The Growing Burden of Heart Disease and Stroke in Canada. Retrieved April 7, 2013, from World Wide Web: http://www.cvdinfobase.ca/cvdbook/En/Index.htm.
22. Gebel JM, Broderick JP. Intracerebral hemorrhage. Neurol Clin. 2000; 18: 419-38.
23. Lovelock CE, Molyneux AJ, Rothwell PM, Oxford Vascular Study. Change in in-cidence and aetiology of intracerebral haemorrhage in Oxfordshire, UK, between 1981 and 2006: a population-based study. Lancet Neurol. 2007; 6: 487.
24. Viswanathan A, Greenberg SM. Cerebral amyloid angiopathy in the elderly. Ann Neurol. 2011; 70:871.
25. Ariesen MJ, Claus SP, Rinkel GJ, et al. Risk factors for intracerebral hemorrhage in the general population: a systematic review. Stroke. 2003; 34:2060.
26. Robert G. Hart, Bradley S. Boop, David C. Anderson. Oral Anticoagulants and Intracranial Hemorrhage. Stroke. 1995; 26: 1471-7.
27. Schievink WI. Intracranial aneurysms. N Engl J Med. 1997;336:28-40.
28. Jonathan L. Brisman, Joon K. Song, David W. Newell. Cerebral aneurysms. N Engl J Med. 2006;355:928-39.
29. Brott T, Broderick J, Kothari R, Barsan W, Tomsick T, Sauerbeck L, Spilker J, Duldner J, Khoury J. Early hemorrhage growth in patients with intracerebral hemorrhage. Stroke. 1997;28:1–5.
30. Davis SM, Broderick J, Hennerici M, Brun NC, Diringer MN, Mayer SA, Begtrup K, Steiner T. Hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage. Neurology. 2006;66:1175–1181.
31. Mayer SA, Brun NC, Begtrup K, Broderick J, Davis S, Diringer MN, Skolnick BE, Steiner T; for the FAST Trial investigators. Efficacy and safety of recombinant activated factor VII for acute intracerebral hemorrhage.N Engl J Med. 2008;358:2127–2137.
32. Mayer SA, Davis SM, Skolnick BE, Brun NC, Begtrup K, Broderick JP, Diringer MN, Steiner T. Can a subset of intracerebral hemorrhage patients benefit from hemostatic therapy with recombinant activated Factor VII? Stroke. 2009;40:833– 840.
33. Mayer SA, Brun NC, Begtrup K, Broderick J, Davis S, Diringer MN, Skolnick BE, Steiner T; for the Recombinant Activated Factor VII Intracerebral Hemorrhage Trial Investigators. Recombinant activated factor VII for acute intracerebral hemorrhage. N Engl J Med. 2005;352:777–785.
34. Carhuapoma JR, Hanley DF, Banerjee M, Beauchamp NJ. Brain edema after human cerebral hemorrhage: a magnetic resonance imaging volumetric analysis. J Neurosurg Anesthesiol. 2003;15:230 –233.
35 Gould B, McCourt R, Asdaghi N, et al; on behalf of the ICH ADAPT investigators. Autoregulation of cerebral blood fl ow is preserved in primary intracerebral hemorrhage. Stroke 2013; 44: 1726–28.
36. Broderick JP, Brott TG, Duldner JE, et al. Volume of intracerebral hemorrhage. A powerful and easy-to- use predictor of 30-day mortality. Stroke. 1993; 24: 987–93.
37. Asia Pacific Cohort Studies Collaboration. Blood pressure indices and cardiovascular disease in the Asia Pacific region: a pooled analysis. Hypertension 2003; 42: 69–75.
38. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002; 360: 1903–13.
39. Ohwaki K, Yono E, Nagashima H, Hirata M, Nakagomi T, Tamura A. Blood pressure management in acute intracerebral hemorrhage: relationship between elevated blood pressure and hematoma enlargement. Stroke. 2004;35:1364 –1367.
40. Vemmos KN, Tsivgoulis G, Spengos K, Zakopoulos N, Synetos A, Manios E, Konstantopoulou P, Mavrikakis M. U-shaped relationship between mortality and admission blood pressure in patients with acute stroke. J Intern Med. 2004;255:257–265.
41. Krishnamurthi RV, Feigin VL, Forouzanfar MH, et al; on behalf of the Global Burden of Disease, Injuries and Risk Factors Study 2010 (GBD 2010) and the GBD Stroke Experts Group. Global and regional burden of fi rst-ever ischaemic and hemorrhagic stroke during 1990–2010: fi ndings from the Global Burden of Disease Study 2010. Lancet Glob Health 2013; 1: e259–81.
44. Fogelholm R, Murros K, Rissanen A, et al. Long term survival after primary intra¬cerebral hemorrhage: a retrospective population based study. J Neurol Neurosurg Psychiatry. 2005; 76: 1534-8.
43. Willmot M, Leonardi-Bee J, Bath PMW. High blood pressure in acute stroke and subsequent outcome: a systematic review. Hypertension 2004; 43: 18–24.
44. Ohwaki K, Yano E, Nagashima H, Hirata M, Nakagomi T, Tamura A. Blood pressure management in acute intracerebral hemorrhage: relationship between elevated blood pressure and hematoma enlargement. Stroke 2004; 35: 1364–67.
45. Powers WJ, Zazulia AR, Videen TO, Adams RE, Yundt KD, Aiyagari V, Grubb RL Jr, Diringer MN. Autoregulation of cerebral blood flow surrounding acute (6 to 22 hours) intracerebral hemorrhage. Neurology. 2001;57:18 –24.
46. Misra UK, Kalita J, Ranjan P, Mandal SK. Mannitol in intracerebral hemorrhage: a randomized controlled study. J Neurol Sci. 2005;234: 41–45.
47. Vespa P. What is the optimal threshold for cerebral perfusion pressure following traumatic brain injury? Neurosurg Focus. 2003;15:E4. Review.
48. Hemphill JC III, Bonovich DC, Besmertis L, et al. The ICH score: a simple, reli-able grading scale for intracerebral hemorrhage. Stroke. 2001; 32(4): 891-7.
49. Rost NS, Smith EE, Chang Y, et al. Prediction of functional outcome in patients with primary intracerebral hemorrhage: the FUNC score. Stroke 2008; 39(8): 2304-9.
50. Fernandes HM, Siddique S, Banister K, Chambers I, Wooldridge T, Gregson B, Mendelow AD. Continuous monitoring of ICP and CPP following ICH and its relationship to clinical, radiological and surgical parameters. Acta Neurochir Suppl. 2000;76:463– 466.
51. Qureshi AI, Tuhrim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral hemorrhage. N Engl J Med 2001; 344: 1450–60.a