Shock Index Predicts up to 90-day Mortality Risk after Intracerebral Haemorrhage

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ABSTRACT

Background: Shock index (SI - heart rate/systolic blood pressure) has been studied as a measure of haemodynamic status. We aimed to determine whether SI measures within 72 hours of admission were associated with adverse outcomes in intracerebral haemorrhage (ICH).

Methods: Patients were drawn from the Virtual International Stroke Trials Archive-Intracerebral Haemorrhage (VISTA-ICH). Multivariable Cox regressions modelled the relationship between SI (on admission, 24, 48, 72 hours) and mortality (at 3-, 7-, and 90-days), 90-day incident pneumonia and cardiovascular events (MACE). Ordinal logistic regressions modelled the relationship between SI and 90-day modified Rankin Scale (mRS).

Results: 979 patients were included. Baseline SI was not associated with mortality. 24h SI >0.7 was associated with 7-day mortality (hazard ratio (95% confidence interval) = 3.14 (1.37-7.19)). 48h and 72h SI >0.7 were associated with 7-day (4.23 (2.07-8.66) and 3.24 (1.41-7.42) respectively) and 90-day mortality (2.97 (1.82-4.85) and 2.05 (1.26-3.61) respectivley). SI <0.5 at baseline, 48h and 72h was associated with decreased pneumonia risk. 24h and 48h SI >0.7was associated with increased MACE risk. 48h and 72h SI >0.7 was associated with increased odds of higher 90-day mRS.

Conclusion: Higher-than-normal SI subsequent to initial encounter was associated with higher post-ICH mortality at 3, 7, and 90 days. Lower-than-normal SI was associated with a decreased risk of incident pneumonia.

INTRODUCTION

In the acute setting, consistent and reliable predictors of poor outcomes are useful tools to inform rapid decisions and aid communication with patients and their families. The ICH score was developed for the stratification by mortality risk[1]. However, this score is complex, requires neuroimaging and is not amenable serial measurements. Simpler predictors, such as systolic blood pressure (SBP) and heart rate (HR), have also been proposed as individual indicators of early mortality in a variety of settings. Nevertheless, these simple measurements may be unreliable on their own, especially at the extremes of age[2].

The shock index (SI) is defined as the ratio between heart rate and systolic blood pressure (SBP) and has been studied as a surrogate measure of haemodynamic status which may improve the prognostic value of either heart rate or SBP alone. SI was initially proposed as a measure of severity in hypovolaemic shock[3]. It has since been demonstrated that SI is a useful point-of-care indicator of early sepsis[4], predictor of mortality in community-acquired pneumonia[5,6] and pulmonary embolism[7]. The normal range for SI is 0.5-0.7, with values >0.7 indicating worsening haemodynamic status[4]. It has been previously shown that SI >0.7 is associated with increased stroke in-hospital mortality[8]. SI also predicted length-of-stay and discharge status after ischaemic stroke or intracerebral haemorrhage (ICH)[9]. Nevertheless, it remains unknown whether SI is associated with longer-term ICH adverse outcomes. Furthermore, serial assessment of SI may also represent an easy measurement that could be used to identify patients more likely to suffer adverse short- and medium-term outcomes[1]. In this study, we aimed to delineate the relationship between longitudinal SI measurements and post-ICH outcomes.

METHODS

This study was conducted in accordance with the Declaration of Helsinki (1964). The individual clinical trials included in this study were approved by their respective ethics committees. The VISTA-ICH steering committee approved the conduct of this study. The data supporting the study findings are available from the VISTA database after approval of the VISTA-ICH steering committee upon reasonable request.

Data source and inclusion criteria

Patients were drawn from the intracerebral haemorrhage section of the Virtual International Stroke Trials Archive (VISTA-ICH), a collection of anonymised patient-level data from completed ICH clinical trials[10,11]. Figure 1 details the patient population flowchart. For the baseline analysis, 86 patients were excluded from a total of 1062 initially extracted from the VISTA-ICH archive with available systolic blood pressure and heart rate data on admission, yielding 979 eligible patients for this analysis. Patients with missing systolic blood pressure/heart rate data at 24, 48 or 72 hours after admission, as well as those dying before 24, 48 and 72 hours after admission, were sequentially excluded from the 24-, 48- and 72-hours analyses, respectively. A total of 927, 901 and 883 patients were included in the 24-, 48- and 72-hour analyses, respectively.

Definition of exposure, confounders and outcomes

Exposures

SI was calculated at baseline, 24h, 48h and 72h after admission by dividing the heart rate by the systolic blood pressure. Patients were divided into three mutually exclusive groups: those with SI <0.5, those with SI 0.5-0.7 (reference category) and those with SI >0.7 at each timepoint.

Confounders

Pre-existing cardiac co-morbidities were defined as: myocardial infarction, hypertension, diabetes mellitus, congestive heart failure, coronary heart disease, atrial fibrillation, transient ischaemic attack or stroke. Supplementary Table 1 details the Anatomical therapeutic chemical (ATC) classification codes used to identify anticoagulant, antiplatelets and antihypertensive medications as well as fluid and inotropes administered during the clinical trials. Supplementary Tables 2 and 3 detail the clinical trial manual entries used to classify surgical procedures undertaken during the trials as well as the causes of death.

Outcomes

The primary outcome was mortality, while secondary outcomes were incident major adverse cardiovascular events (MACE) and pneumonia as well as functional status (modified Rankin Scale - mRS) at 90 days post-ICH. Mortality was ascertained based on vital status information from the individual trials and was considered as the number of days from randomisation when death occured. Incident pneumonia and MACE (within 90-days) were determined based on reported complications. Supplementary Table 4 details the reported complications used to define incident pneumonia and MACE. Disability at 90 days post-ICH was quantified as a 1-point increase on the 90-day modified Rankin Scale (mRS).

Statistical Analysis

All analyses were performed using Stata 12.1SE, Stata Statistical Software. P <0.05 was considered significant for all analyses.

Descriptive Statistics

Patient characteristics were compared between the three categories of SI (<0.5, 0.5-0.7, >0.7) using either the χ^2, ANOVA or Kruskal-Wallis test, as appropriate.

Handling of Missing Data

There were ten variables collected at baseline with missing data: race, smoking status, ICH volume, NIHSS, intraventricular haemorrhage (IVH) at baseline, ICH location (infratentorial, lobar) and pre-existing co-morbidities (transient ischaemic attack, diabetes, hypertension) (Supplementary Table 6). A further three variables measured after baseline contained missing data (mRS at 7 and 90 days; NIHSS at 90 days). Supplementary Table 6 details the number of patients with missing data for the thirteen variables at each timepoint. Supplementary Tables 7-19 detail the patient characteristics of the included sample stratified by whether the data for each variable from Supplementary Table 5 were missing.

Having explored the differences between patients with and without missing data for each variable (Supplementary Tables 7-19), we have observed that patients with missing data were more likely to have suffered more severe strokes (higher ICH volumes, NIHSS scores, mRS levels, lower Glasgow Coma Scale (GCS) values, IVH at baseline), lower blood pressure measurements, have higher incidence of adverse outcomes, and more likely to have pre-existing co-morbidities. The data were thus deemed likely to be missing-at-random[12]. Multiple imputation by chained equation algorithm with 20 iterations was implemented to impute the missing data[12]. All variables were imputed using predictive mean matching drawing from five nearest neighbours. Age, sex, pre-existing co-morbidities (myocardial infarction, atrial fibrillation, coronary heart disease, congestive heart failure, stroke), in-hospital medication (antithrombotics, antihypertensives) and three different Nelson-Aalen cumulative hazard functions (90-day mortality, incident pneumonia and incident MACE) were used as predictors.

Association between shock index and outcomes

Given that the following outcomes were provided as time-to-event data (mortality, incident MACE and incident pneumonia), multivariable Cox regressions were employed to assess the relationship between shock index categories (<0.5; 0.5-0.7 – reference; >0.7) and these outcomes. In order to provide meaningful and clinically useful estimates of 3-, 7- and 90-day mortality, the follow-up time for the time-to-event analyses considering the mortality outcome was truncated at 3, 7 and 90 days, respectively. An ordinal logistic regression model was employed to assess the relationship between SI categories and 1-point increase on the mRS scale at 90 days. In order to account for multiple testing, the calculated *P* values were false discovery rate-adjusted[13].

Adjusting co-variates

All models were adjusted for potential confounders selected based on clinical judgement and previous reports[8,9]: age, sex, race, ICH volume at baseline, ICH location (lobar, infratentorial), NIHSS at baseline, IVH at baseline, body mass index, serum creatinine, pre-existing cardiac co-morbidities, incident complications during hospitalisation (pneumonia, MACE), antihypertensive medications, inotrope agents or fluids administered during hospitalisation and ICH-related surgical procedures.

Receiver operating characteristic (ROC) analysis

Receiver operating characteristic (ROC) analyses for SI and SBP (each measured at baseline, 24h, 48h and 72h) predicting 3-, 7- and 90-day mortality were performed. The areas under the ROC curve (AUROC) of each SI-SBP pair were compared using the Stata command *roccomp*.

RESULTS

Descriptive Statistics

Table 1 and Supplementary Table 5 summarise patient characteristics at baseline. A total of 979 ICH patients were included in the baseline analysis. The mean (standard deviation - SD) age of the patient population was 65.79 (12.44). There were 621 (63.43%) males. The mean (SD) SI of the entire patient population at baseline was 0.46 (0.11). At baseline, there were 659 (67.3%) patients with an SI < 0.5, 283 (28.9%) with SI 0.5-0.7 and 37 (3.8%) with an SI > 0.7. There were no statistically significant differences between SI groups in age, sex or race. Patients with SI > 0.7 had higher rates of prevalent congestive heart failure and diabetes than patients with SI 0.5-0.7 or < 0.5. The 3-, 7- and 90-day mortality rates amongst the entire patient cohort were 5.41%, 9.91% and 20.53%, respectively. There were no significant differences in mortality at 3-, 7- or 90-days between different SI groups. All patients were followed up until either death or 90 days after ICH. Median folllow-up (95% confidence interval) was 90 (90-90) days while maximum follow-up was also 90 days.

Association between shock index and outcomes

Figure 2 summarises the associations between shock index measured at different time points and the pre-specified outcomes, after full multivariable adjustment.

Primary Outcomes

There were no statistically significant associations between baseline SI and any of the mortality outcomes. SI >0.7 measured at 24h was significantly associated with increased 3-day (5.59 (1.42-22.09), FDR-adjusted *P* value = 0.045), 7-day mortality (3.14 (1.37-7.19)), FDR-adjusted *P* value = 0.027). SI >0.7 measured at 48h was significantly associated with increased 7-day (4.23 (2.07-8.66), FDR-adjusted *P* = 0.002) and 90-day mortality (2.97 (1.82-4.85), FDR-adjusted *P* = 0.001). Similarly, SI >0.7 measured at 72h was significantly associated with increased 7-day (3.24 (1.41-7.42), FDR-adjusted *P* = 0.025) and 90-day mortality (2.05 (1.16-

3.61), FDR-adjusted P = 0.045). There were no statistically significant associations between SI <0.5 measured at any timepoint and any of the mortality outcomes.

Secondary Outcomes

SI <0.5 measured at baseline (0.53 (0.37-0.76), FDR-adjusted P = 0.006), 48h (0.49 (0.33-0.72), FDR-adjusted P = 0.004) and 72h (0.44 (0.30-0.66), FDR-adjusted P = 0.002) was associated with decreased risk of incident pneumonia in the first 90-days post-ICH. Whilst there were no significant associations between baseline, 24h or 48h SI and incident MACE, both SI >0.7 at 72h was associated with increased risk of incident MACE in the first 90 days post-ICH: 2.32 (1.38-3.92), FDR-adjusted P = 0.010. SI >0.7 at 48h and 72h was associated with increased odds of higher mRS at 90 days: odds ratio (95% confidence interval) = 2.68 (1.44-4.98), FDR-adjusted P = 0.010 and 2.85 (1.53-5.28), FDR-adjusted P =0.007, respectively.

Receiver operating characteristic (ROC) analysis

Supplementary Figure 1 displays the results of the ROC analyses comparing the predictive value of SI against systolic blood pressure at all timepoints. SI at baseline had only a poor [14] (area under ROC (AUROC) <60%) predictive power for all mortality outcomes. SI at 48h and 72h had a fair-to-good (AUROC ≥70%) predictive power for 3- and 7-day mortality which was significantly better than SBP. SI at 48h and 72h had only a poor (60-70%) predictive power for 90-day mortality which was nevertheless significantly better than SBP.

DISCUSSION

In this analysis of over 900 ICH patients, we found that SI was an independent predictor of important post-ICH adverse outcomes. While SI was not associated with mortality when measured at baseline, an elevated SI at 24h, 48h or 72h was associated with 2-4-fold increases in mortality risk up to 90 days. SI may be an easily measured, useful predictor of mortality in

clinical practice. Furthermore, SI was superior to SBP alone in predicting 3-, 7-, and 90-day mortality when measured after 48 or 72 hours after initial patient encounter. Patients with a lower-than-normal SI at any timepoint were less likely to develop incident pneumonia. Higher-than-normal SI values at 72h were significantly associated with increased risk of incident MACE, whilst increased 48h and 72h SI was associated with increased odds of higher mRS at 90 days.

The SI has been studied as a prediction tool of poor outcomes in a large variety of conditions, especially in those where hypovolaemia or sepsis plays a major role[4,15–17]. It has been previously shown that SI predicts adverse outcomes in stroke[8,9]. More specifically, baseline SI exhibited a U-shaped relationship with 72-hour mortality, with both high and low baseline SI values being associated with an increased mortality risk. Nevertheless, these previous studies analysed patient samples consisting of mostly ischaemic stroke patients and assessed only short-term in-hospital outcomes[8]. In the present study, we found that, as opposed to baseline SI, a high SI measured at 24, 48 and 72h can predict mortality in the days following SI measurement in patients with ICH. Given that all our models were adjusted for in-hospital antihypertensive medication, these findings likely support the hypothesis that SI becomes a useful predictor of mortality risk in ICH patients once they are haemodynamically stabilised after admission.

A possible explanation for the delayed predictive value of SI in the context of ICH could be the development of an acute hypertensive response. The acute hypertensive response of stroke is a well-established, transient, and self-limiting post-stroke phenomenon, present in up to 80% of ICH patients and approximately 75% of those with an ischaemic stroke[18,19]. Transient increases in SBP in the first 24 hours after ICH may thus confound the calculation of SI in the hyperacute ‘baseline’ period. As SBP normalises after the initial hypertensive response, SI may start reflecting the ‘true’ haemodynamic status and become a useful predictor

of outcomes. This may also explain why SBP and HR in isolation may be unreliable outcome predictors in the very early stages of assessment. Nevertheless, we have found that SI is superior to SBP at predicting mortality in ICH patients after the initial 24h period, suggesting that SI is a significantly better as a prognostic tool than SBP or HR alone even after this period.

The pathophysiological mechanisms underlying the relationship between abnormal SI values and adverse post-ICH outcomes remain mostly unclear. It has been previously proposed[8,9] that the development of the Cushing triad, involving an increase in blood pressure aimed at counteracting the increasing intracranial pressure and accompanied by a reflex decrease in heart rate and respiratory depression, may explain the relationship between SI and adverse post-stroke outcomes. However, the mechanisms behind the association between SI post-ICH mortality are complex and likely not explained by single phenomena. As well as the acute hypertensive response seen in stroke and the Cushing triad, there are other factors affecting heart rate and blood pressure, such as sympathetic activation due to stress, hydration status, anxiety, and pre-existing conditions, like chronic hypertension and atrial fibrillation. Furthermore, the pathophysiological mechanisms behind the association between lower-than-normal SI and the decreased risk of incident pneumonia require further investigation.

The present study benefits from several strengths. Firstly, this is the first study to analyse the relationship between SI and medium-term post-ICH outcomes, not only as a single measurement, but also in a longitudinal fashion. This is also the first study to analyse the relationship between SI and 90-day incident post-stroke complications and medium-term disability. Furthermore, we were able to perform robust statistical analyses which included multivariable models adjusting for important confounders, such as baseline NIHSS and the use of antihypertensive medication during the study period. Finally, a major advantage of the SI is that it is easy to calculate, in contrast to other prognostic models.

We acknowledge some limitations. As a retrospective analysis of clinical trial data, our study sample may not be reflective of the general population, particularly in relation to clinical demographics, in which more elderly, co-morbid and frailer patients may be excluded from clinical trials. The results of our study may, therefore, not be generalisable to patient groups with different demographics. Furthermore, we were unable to differentiate between different pneumonia types, such as community-, hospital- or ventilator-acquired, and therefore further research is required to ascertain the association between SI and these specific types of pneumonia. Given that only ~20% of patient records included in VISTA-ICH had available information on length of hospitalisation, we were not able to perform analyses evaluation the relationship between SI and length of ICH-related hospitalisation.

The shock index can help in identifying the patients at higher risk of death and can, therefore, aid in making informed decisions about their care. SI is a straightforward measurement that can be easily derived at the point of care using heart rate and blood pressure, two routinely collected parameters. Displaying SI along with other parameters on patient monitors and charts in settings such as neurocritical care units may allow healthcare staff to very rapidly determine when and which patients may require further assessment or intervention. Finally, SI assessment can be particularly useful in low-resource settings, where more advanced methods of assessing a patient's haemodynamic state may not be available.

Further research should focus on confirming our results on other patient cohorts, to ensure generalisability of the findings. Furthermore, future studies should also assess whether the routine use of SI in clinical care of ICH patients may improve the identification of patients that are likely to deteriorate in a short period of time.

CONCLUSIONS

In conclusion, higher-than-normal SI values measured after the initial stabilisation of ICH patients upon admission predicted post-ICH mortality up to 90 days. Conversely, lower-than-normal SI values were associated with a decreased risk of incident pneumonia. Higher-than-normal SI measured after 48h predicted higher odds of disability at 90 days. SI is an extremely simple measurement which could be incorporated into routine care of ICH patients to determine which patients are more likely to die as well as which patients are more likely to have a higher burden of disability at 90 days.

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AUTHOR CONTRIBUTIONS

TJQ and PKM conceived the study. Data were analysed by TAP, JAP-L and WAS. under the supervision of PKM. TAP, JAP-L and WAS drafted the article, and all the authors contributed to writing the article. PKM is the guarantor.

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CONFLICTS OF INTEREST

None.

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TABLES

Table 1. Descriptive Statistics at baseline, unless otherwise stated. Also see *Supplementary Table 5*.

	Shock Index			Total	P value
	<0.5	**0.5-0.7**	**>0.7**		
N, (% of total)	659 (67.31)	283 (28.91)	37 (3.78)	979	
Age, N (%)	66.26 (12.46)	64.84 (12.21)	64.86 (13.60)	65.79 (12.44)	0.247
Sex, N (%)					0.873
M	415 (62.97)	183 (64.66)	23 (62.16)	621 (63.43)	
F	244 (37.03)	100 (35.34)	14 (37.84)	358 (36.57)	
Ethnicity, N (%)					0.287
White	500 (75.87)	236 (83.39)	33 (89.19)	769 (78.55)	
Black	42 (6.37)	12 (4.24)	0 (0)	54 (5.52)	
Asian	103 (15.63)	28 (9.89)	3 (8.11)	134 (13.69)	
Hispanic	2 (0.30)	1 (0.35)	0 (0)	3 (0.31)	
Other	10 (1.52)	5 (1.77)	1 (2.7)	15 (1.63)	
Missing	2 (0.30)	1 (0.35)	0 (0)	3 (0.31)	
Shock index, N (%)					
Baseline	0.40 (0.06)	0.57 (0.05)	0.77 (0.07)	0.46 (0.11)	**<0.001**
24 hours	0.48 (0.11)	0.53 (0.11)	0.56 (0.14)	0.50 (0.11)	**<0.001**
48 hours	0.49 (0.13)	0.54 (0.11)	0.58 (0.15)	0.50 (0.13)	**<0.001**
72 hours	0.49 (0.14)	0.53 (0.11)	0.57 (0.16)	0.50 (0.14)	**<0.001**
Systolic Blood Pressure, mean (SD)					
Baseline	183.70 (26.96)	158.52 (14.02)	132.16 (22.51)	174.47 (29.54)	**<0.001**
24 hours	159.14 (23.72)	153.31 (22.00)	143.72 (23.98)	156.95 (23.51)	**<0.001**
48 hours	157.67 (23.57)	151.88 (22.03)	143.34 (25.41)	155.50 (23.44)	**<0.001**
72 hours	156.01 (23.45)	150.55 (21.43)	141.42 (20.37)	153.90 (23.02)	**<0.001**
Heart Rate, mean (SD)					
Baseline	72.55 (11.52)	89.44 (13.63)	101.89 (16.69)	78.54 (15.24)	**<0.001**
24 hours	74.53 (13.90)	80.70 (14.34)	78.44 (13.60)	76.42 (14.21)	**<0.001**
48 hours	75.07 (14.72)	80.33 (15.49)	80.16 (14.35)	76.75 (15.11)	**<0.001**
72 hours	73.97 (14.42)	78.31 (14.22)	79.09 (18.86)	75.41 (14.68)	**<0.001**
Co-morbidities, N (%)					
Previous MI	21 (3.19)	9 (3.18)	2 (5.41)	32 (3.27)	0.758
Previous Stroke	76 (11.53)	37 (13.07)	5 (13.51)	118 (12.05)	0.771
AF	43 (6.53)	19 (6.71)	4 (10.81)	66 (6.74)	0.599
CHD	72 (10.93)	41 (14.49)	5 (13.51)	118 (12.05)	0.294
CHF	14 (2.12)	7 (2.47)	4 (10.81)	25 (2.55)	**0.005**

TIA	28 (4.25)	14 (4.95)	0 (0)	42 (4.29)	-
missing	10 (1.52)	2 (0.71)	1 (2.70)	13 (1.33)	
Diabetes	65 (9.86)	43 (15.19)	11 (29.73)	119 (12.16)	**0.002**
missing	84 (12.75)	31 (10.95)	2 (5.41)	117 (11.95)	
Hypertension	386 (58.57)	155 (54.77)	17 (45.95)	558 (57.00)	0.059
missing	84 (12.75)	31 (10.75)	2 (5.41)	117 (11.95)	
Surgical treatment, N(%)					
ICH evacuation	14 (2.12)	7 (2.47)	1 (2.70)	22 (2.25)	0.775
ICP reduction procedures	37 (5.61)	6 (2.12)	3 (8.11)	46 (4.70)	0.020
Treatments affecting blood pressure, N(%)					
Antihypertensive agents, N (%)	57 (8.65)	35 (12.37)	3 (8.11)	95 (9.70)	0.210
Fluids, N(%)	113 (17.15)	35 (12.37)	4 (10.81)	152 (15.53)	0.143
Inotropes, N(%)	43 (6.53)	15 (5.30)	5 (13.51)	63 (6.44)	0.149
Outcomes					
Mortality, N (%)					
3 days	33 (5.01)	19 (6.71)	1 (2.70)	53 (5.41)	0.432
7 days	63 (9.56)	30 (10.60)	4 (10.81)	91 (9.91)	0.871
90 days	135 (20.49)	61 (21.55)	5 (13.51)	201 (20.53)	0.522
Cause of death at 90 days, N (% of deaths)					0.696
Direct complications of ICH	90 (66.67)	38 (62.30)	3 (60.00)	131 (65.17)	
Cardiorespiratory causes	32 (23.70)	21 (34.43)	2 (40.00)	55 (27.36)	
Infection/Sepsis	5 (3.70)	1 (1.64)	0 (0.00)	6 (2.99)	
Renal Failure	2 (1.48)	0 (0.00)	0 (0.00)	2 (1.00)	
Other/Unknown	6 (4.44)	1 (1.64)	0 (0.00)	7 (3.48)	
NIHSS, median (IQR)					
Baseline	14 (10-18)	13 (9-17)	12 (8-17)	13.5 (9-18)	**0.04**
90 days	5 (2-10)	3.5 (2-8)	3 (1-5)	5 (2-10)	**<0.001**
mRS, median (IQR)					
7-15 days	4 (4-5)	4 (4-5)	5 (4-5)	4 (4-5)	**0.014**
90 days	3 (2-4)	3 (2-4)	3 (2-4)	3 (2-4)	**0.001**
Incident complications (up to 90 days), N (%)					
MACE	167 (25.34)	58 (20.49)	11 (29.73)	236 (24.11)	0.201
Pneumonia	86 (13.05)	50 (17.67)	5 (13.51)	141 (14.40)	0.178

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FIGURES

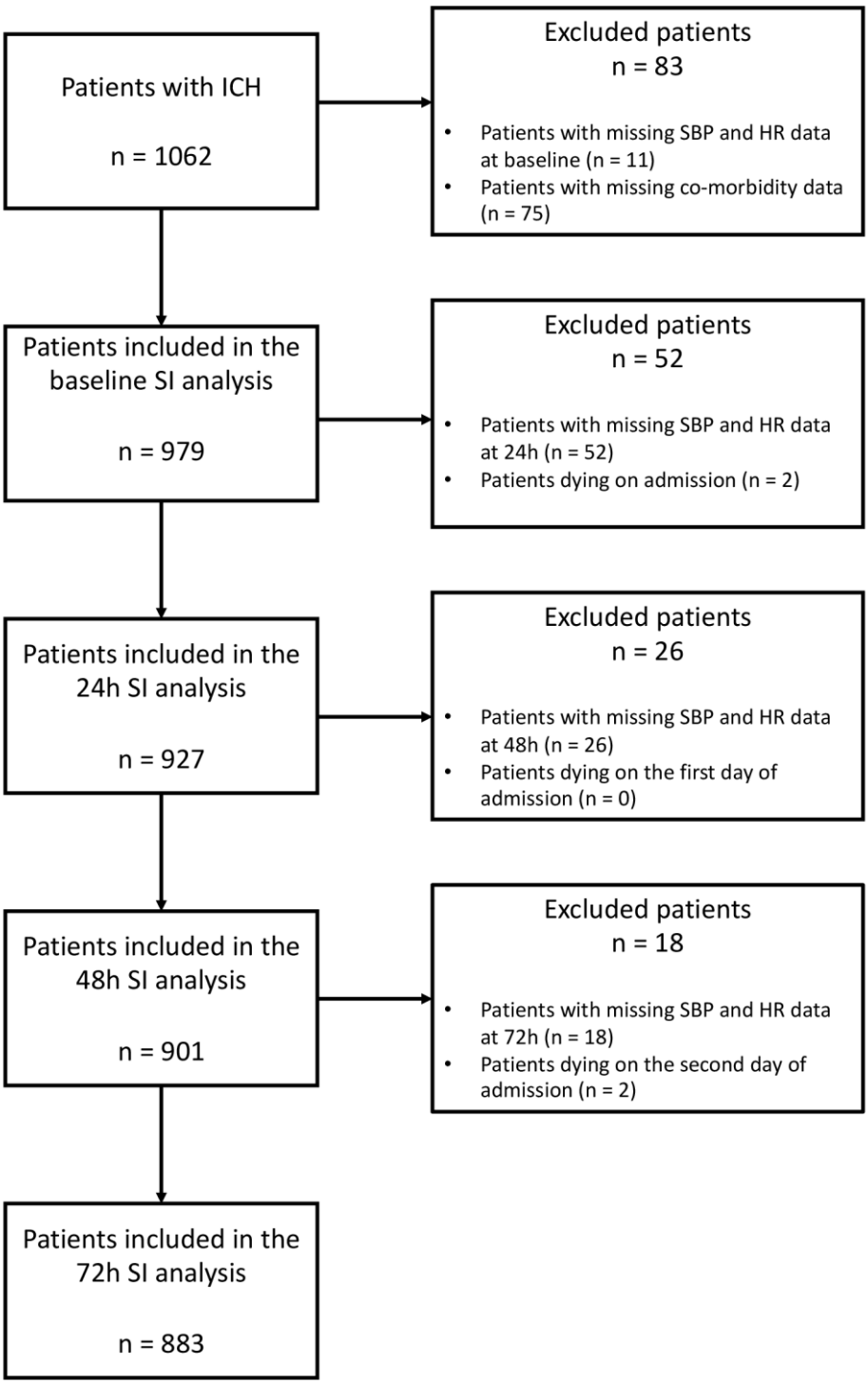
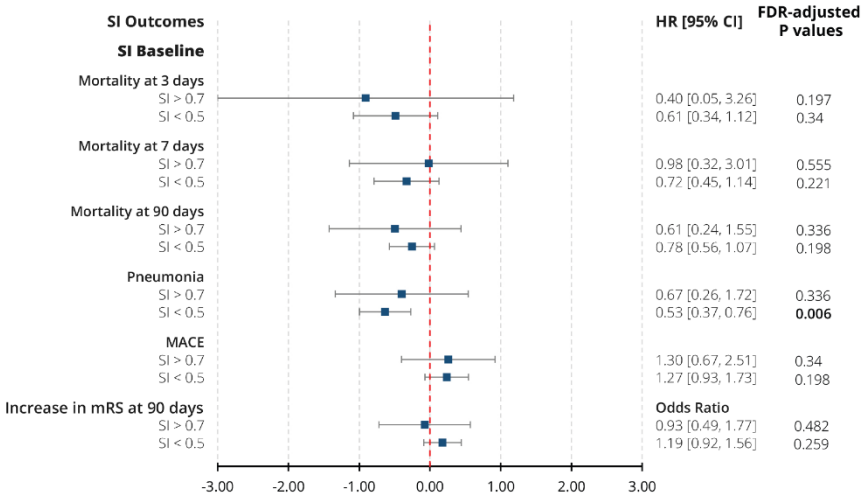
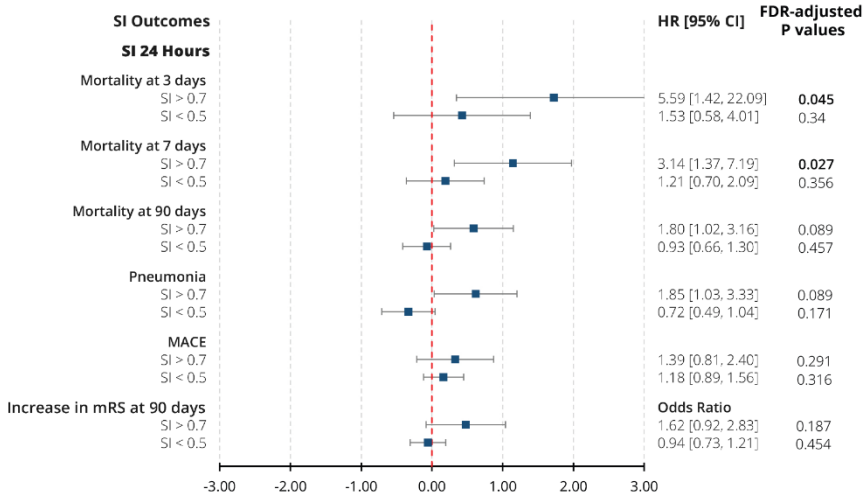
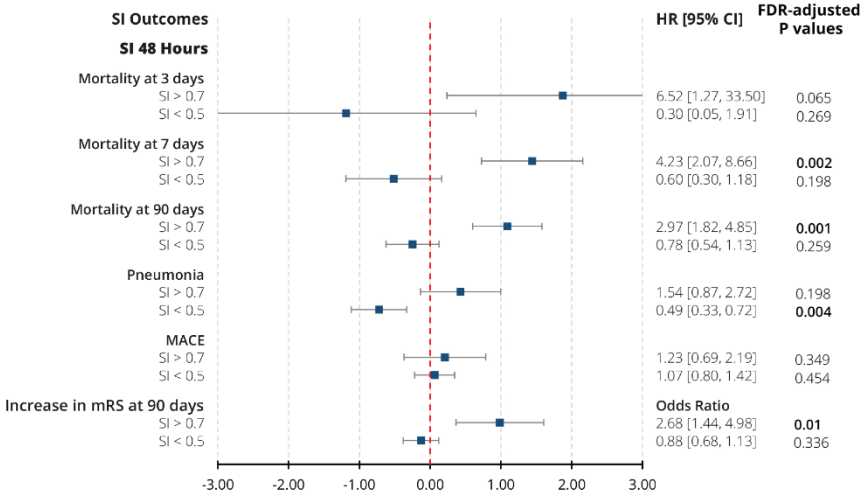


Figure 1. Patient Population Flowchart.

ICH – intracerebral haemorrhage, SI – shock index, SBP – systolic blood pressure, HR – heart rate


SI Outcomes
SI Baseline
HR [95% CI]
FDR-adjusted P values
Mortality at 3 days
SI > 0.7 0.40 [0.05, 3.26] 0.197
SI < 0.5 0.61 [0.34, 1.12] 0.34
Mortality at 7 days
SI > 0.7 0.98 [0.32, 3.01] 0.555
SI < 0.5 0.72 [0.45, 1.14] 0.221
Mortality at 90 days
SI > 0.7 0.61 [0.24, 1.55] 0.336
SI < 0.5 0.78 [0.56, 1.07] 0.198
Pneumonia
SI > 0.7 0.67 [0.26, 1.72] 0.336
SI < 0.5 0.53 [0.37, 0.76] 0.006
MACE
SI > 0.7 1.30 [0.67, 2.51] 0.34
SI < 0.5 1.27 [0.93, 1.73] 0.198
Increase in mRS at 90 days
Odds Ratio
SI > 0.7 0.93 [0.49, 1.77] 0.482
SI < 0.5 1.19 [0.92, 1.56] 0.259
-3.00 -2.00 -1.00 0.00 1.00 2.00 3.00


SI Outcomes
SI 24 Hours
HR [95% CI]
FDR-adjusted P values
Mortality at 3 days
SI > 0.7 5.59 [1.42, 22.09] 0.045
SI < 0.5 1.53 [0.58, 4.01] 0.34
Mortality at 7 days
SI > 0.7 3.14 [1.37, 7.19] 0.027
SI < 0.5 1.21 [0.70, 2.09] 0.356
Mortality at 90 days
SI > 0.7 1.80 [1.02, 3.16] 0.089
SI < 0.5 0.93 [0.66, 1.30] 0.457
Pneumonia
SI > 0.7 1.85 [1.03, 3.33] 0.089
SI < 0.5 0.72 [0.49, 1.04] 0.171
MACE
SI > 0.7 1.39 [0.81, 2.40] 0.291
SI < 0.5 1.18 [0.89, 1.56] 0.316
Increase in mRS at 90 days
Odds Ratio
SI > 0.7 1.62 [0.92, 2.83] 0.187
SI < 0.5 0.94 [0.73, 1.21] 0.454
-3.00 -2.00 -1.00 0.00 1.00 2.00 3.00


SI Outcomes
SI 48 Hours
HR [95% CI]
FDR-adjusted P values
Mortality at 3 days
SI > 0.7 6.52 [1.27, 33.50] 0.065
SI < 0.5 0.30 [0.05, 1.91] 0.269
Mortality at 7 days
SI > 0.7 4.23 [2.07, 8.66] 0.002
SI < 0.5 0.60 [0.30, 1.18] 0.198
Mortality at 90 days
SI > 0.7 2.97 [1.82, 4.85] 0.001
SI < 0.5 0.78 [0.54, 1.13] 0.259
Pneumonia
SI > 0.7 1.54 [0.87, 2.72] 0.198
SI < 0.5 0.49 [0.33, 0.72] 0.004
MACE
SI > 0.7 1.23 [0.69, 2.19] 0.349
SI < 0.5 1.07 [0.80, 1.42] 0.454
Increase in mRS at 90 days
Odds Ratio
SI > 0.7 2.68 [1.44, 4.98] 0.01
SI < 0.5 0.88 [0.68, 1.13] 0.336
-3.00 -2.00 -1.00 0.00 1.00 2.00 3.00

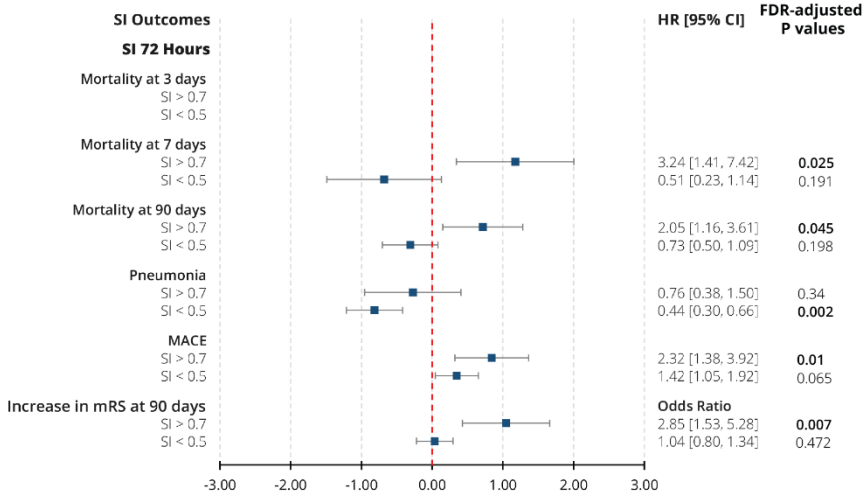

SI Outcomes
SI 72 Hours
HR [95% CI]
FDR-adjusted P values
Mortality at 3 days
SI > 0.7
SI < 0.5
Mortality at 7 days
SI > 0.7 3.24 [1.41, 7.42] 0.025
SI < 0.5 0.51 [0.23, 1.14] 0.191
Mortality at 90 days
SI > 0.7 2.05 [1.16, 3.61] 0.045
SI < 0.5 0.73 [0.50, 1.09] 0.198
Pneumonia
SI > 0.7 0.76 [0.38, 1.50] 0.34
SI < 0.5 0.44 [0.30, 0.66] 0.002
MACE
SI > 0.7 2.32 [1.38, 3.92] 0.01
SI < 0.5 1.42 [1.05, 1.92] 0.065
Increase in mRS at 90 days
Odds Ratio
SI > 0.7 2.85 [1.53, 5.28] 0.007
SI < 0.5 1.04 [0.80, 1.34] 0.472
-3.00 -2.00 -1.00 0.00 1.00 2.00 3.00

Figure 2. Results of Cox and ordinal logistic regressions assessing the associations between shock index and outcomes. All models were adjusted for age, sex, race, ICH volume at baseline, ICH location (lobar, infratentorial), NIHSS at baseline, IVH at baseline, body mass index, serum creatinine, pre-existing cardiac co-morbidities, incident complications during hospitalisation (pneumonia, MACE), antihypertensive medications, inotrope agents or fluids administered during hospitalisation and ICH-related surgical procedures.

SI – Shock Index, HR – Hazard Ratio, mRS – modified Rankin Scale, ICH – Intracerebral Haemorrhage, NIHSS – National Institute of Health Stroke Scale, IVH – Intraventricular Haemorrhage, MACE – Major Adverse Cardiac Events; FDR – False Discovery Ra