The shock index predicts acute mortality outcomes in stroke

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Abbreviations:

AOR: Adjusted odds ratio

ASCNES: Anglia Stroke Clinical Network Evaluation Study

COPD: Chronic obstructive pulmonary disease

CT: Computed tomography

HR: Heart rate

LACS: Lacunar Stroke

MRI: Magnetic resonance imaging

mRS: Modified Rankin scale

NIHSS: National Institute of Health Stroke Scale

OCSP: Oxfordshire Community Stroke Project

PACS: Partial Anterior Circulation Stroke

POCS: Posterior Circulation Stroke

PVD: Peripheral vascular disease

ROC: Receiver operating characteristic curve

SBP: Systolic blood pressure

SD: Standard Deviation

SI: Shock Index

TACS: Total Anterior Circulation Stroke

TIA: Transient ischemic attacks

Highlights:

- Both the Shock Index and Systolic BP are good at predicting acute stroke mortality
- SI and SBP are easily available in a clinical setting, and thus useful prognostic markers.
- Shock index is particularly associated with 3-day morality in stroke.

Abstract

Background : Shock index (SI) (ratio between heart rate and systolic blood pressure) has been shown to be associated with poor mortality outcomes in trauma and pneumonia; however it has yet to be examined in stroke. We aimed to examine the relationship between SI and acute outcomes of inpatient, 3-day and 7-day mortality in stroke. Secondly, we aimed to compare SI and systolic blood pressure (SBP) alone in predicting above outcomes.

Methods: Data from a multicentre prospective cohort study conducted between October 2009 and September 2012 in eight NHS trusts in East of England were analysed. The relationships between SI, SBP and study outcomes were assessed using multivariable logistic regression models using mid-quintile groups as the reference category. Receiver operating characteristic (ROC) curves assessed the discriminating ability between the SI and SBP models.

Results: A total of 2121 stroke patients were included (47.4%men; mean age 77.10 (sd) 12.40) years. The lowest quintile of the SI, had an increased odds of 3-day and 7-day mortality, adjusted odds ratio (AOR) 2.45(95%CI:1.16-5.17) and 1.88(1.01-3.49), respectively. Patients with the highest quintile of SI also had increased odds of in-patient, 3-day and 7-day mortality, AORs 1.85(1.17-2.92), 2.18(1.03-4.63) and 2.45(1.34-4.49), respectively. Similarly, SBP had a U-shape relationship with mortality. All measures had an ROC area under the curve >0.8 but there was no difference in the discriminating ability between SI and SBP.

Conclusions: SI at extremely high and low values appeared to predict stroke mortality and appears to be particularly useful in predicting very early (3-day) mortality.

1.1 Introduction

Stroke mortality is highest within first 30 days and both low and high blood pressure during acute stroke phase are associated with poor mortality outcomes. [1-3] Approximately 80% of patients have raised blood pressure immediately after a stroke and recent trials have shown that blood pressure lowering has benefits immediately after a stroke. Thus, much effort has been made in examining the association between blood pressure and outcomes following a stroke, while there is a lack of research examining the effects of other physiological parameters of hemodynamics. For example, heart rate is a relatively understudied physiological factor that may be associated with stroke outcome; shown by the contrasting results from two observational studies. [4,5]

The Shock Index (SI) (the ratio between HR and SBP), was used initially to detect hypovolemia in patients with septic or hemorrhagic shock, indicated by a SI value of greater than 0.7. [6,7] In both these instances it has been a useful prognostic measure and has shown to be associated with poor clinical outcomes. . Whilst a lower SI may have prognostic significance in stroke serving as an indicator for severe neurological stress associated with a high systolic BP and reduced heart rate, large strokes with dysphagia or posterior circulation stroke presenting with vomiting are at high risk of aspiration pneumonia and may be associated with a higher SI as the result of sepsis and/or hypovolemia.

The usefulness of shock index (SI) in predicting acute mortality outcomes in stroke has not been previously examined. In this paper, we examine the relationship between SI at the time of admission and acute outcomes of inpatient, 3 day and 7 day mortality, independently of other prognostic factors. We also examined the relationship between SBP and acute outcomes in stroke. We finally assessed the discriminating ability of both SI and SBP in predicting above outcomes.

2.1 Material and Methods

2.2 Study Population and design

The study population was drawn from the Anglia Stroke Clinical Network Evaluation Study (ASCNES). ASCNES's aims, rationale, and study methods have already been previously described. [8,9] This was a multi-centre prospective cohort study using routinely collected stroke data from eight acute NHS trusts in East of England of all acute stroke admissions during between October 2009 and September 2011, with one year follow up. Only confirmed cases of ischemic and hemorrhagic strokes were eligible to be included in the study thus transient ischemic attacks (TIAs) and other neurological deficits were specifically excluded. Case ascertainment was verified by the patient's medical history, clinical examination and evidence of ischemia or haemorrhage by neuroimaging (computed tomography (CT) or magnetic resonance imaging (MRI)). The study followed the ethical guidelines set out in the Declaration of Helsinki. [10] Ethical approval was obtained from the Norfolk Research Ethics Committee. The study was funded by the UK National Institute of Health Research, Research for Patient Benefit Programme (PB-PG1208-18240).

We selected variables which have been previously shown to predict mortality outcome and other potential confounders for this outcome in stroke. The three mortality outcomes were death within 3 or 7 days of admission, or at any time during the admission. The prognostic variables used were age, sex, stroke type (ischemic or hemorrhagic), Oxfordshire Community Stroke Project (OCSP) classification based on clinical syndrome regardless of stroke subtype of ischemia or haemorrhage (total anterior stroke (TACS), lacunar stroke (LACS), posterior circulation stroke (POCS) and partial anterior circulation stroke (PACS)), pre-stroke modified Rankin scale (mRS), [11,12] thrombolysis therapy, heart rate, systolic blood pressure on admission, dates of admission and discharge, and co-morbidities (hypertension, myocardial infarction, diabetes mellitus, hypercholesterolemia, chronic obstructive

pulmonary disease (COPD), peripheral vascular disease (PVD)) and use of antihypertensive medications on admission (yes/no).

2.3 Outcomes

Our primary endpoint was the inpatient mortality and the secondary endpoints were 3-day and 7-day mortality. The 3-day and 7-day mortality outcomes were derived using the date of admission and date of discharge data, thus any patient transferred to another hospital was excluded from the study.

2.4 Exposures

The primary predictor variable was the SI at presentation to a secondary care centre, calculated by dividing the heart rate by the systolic blood pressure (SBP). Both SBP and heart rate were measured on the admission by clinical teams from 8 NHS stroke services using the validated BP machines. For the primary analysis the continuous SI was divided into quintiles to better understand the relationship between different level of SI and chosen outcomes. In a secondary analysis we categorized the SI into three categories defined by clinical cut off points, as follows. For clinical cut points we used the normal SI range (0.5-0.7) as the reference category with a SI <0.5 as having a low SI score and those with >0.7 classed as those with hemodynamic sign of shock. The secondary predictor variable was SBP.

2.5 Statistical analysis

Data were analysed using SPSS version 21.0 (Chicago, Illinois, USA). Descriptive statistics such as the Kruskal-Wallis and Chi square tests for trend were used to assess the difference between patient characteristics among the quintiles of the SI and SBP independently. Multiple logistic regression models were constructed for each outcome with the arithmetic quintile groups of SI as the primary exposure variable. For each outcome, model A adjusted for age and sex, model B adjusted for age, sex and pre-stroke mRS, model C adjusted for age,

sex, pre-stroke mRS , OCSP classification and stroke type and model D additionally adjusted for previous co-morbidities, antihypertensive use, and whether the patient was treated for thrombolysis or not. When examining the relationship with SBP only fully adjusted model (Model D) was used for each mortality outcomes. The stratified analysis used the traditionally defined normal values of SI as the exposure for each outcome. We used model D to examine the usefulness of SI stratified by age groups (<65, ≥65), sex (male and female), OCSP classification (Other than TACS and TACS), prestroke mRS categories (no to moderate disability (mRS <3) and severe prestroke disability (mRS ≥3)) and for ischemic stroke type (due to low numbers for hemorrhagic stroke). The variable of interest was excluded from the each of the respective stratified analyses (e.g. age was not included in the model in age stratified analysis). In all analyses, missing data were excluded from the individual analyses.

Receiver operating characteristic (ROC) curves were used to evaluate the discriminating ability for both SI and SBP for each morality outcomes. The ROC curves used the predicted values from each logistic regression model and a combined analysis tested for equality between each of the curves. We used Stata V.13 (STATA Corp, Texas, USA) for this analysis.

3.1 Results

The sample consisted of 2,625 patients admitted to stroke services of the participating hospitals during the study months; 266 patients were transferred out or did not meet the study inclusion criteria detailed in the methods and therefore were excluded. A further 238 patients were excluded due to missing heart rate or systolic blood pressure data, thus a total of 2,121 patients were eligible. Of them 47.4% were male, the mean age was 77.10 (sd, 12.40) years, 87.5% had an ischemic stroke and 42.8% had a pre-stroke mRS of 0. PACS was the most common OCSP classification (35.2%) and over half (59.2%) of the patients had previous history of hypertension. In this study, inpatient mortality was 19.8% and acute mortality figures were 7.4% and 11.6% for 3-day and 7-day mortality, respectively.

Table 1 shows the distribution of sample characteristics across the quintiles of the shock index. There was a higher proportion of ischemic strokes in the fifth quintile in comparison to the first quintile (91.3% vs. 85.6, $p < 0.03$). The inpatient mortality was the highest in the fifth quintile at 30.1% while the other quintiles have a lower proportion of inpatient morality at around 17%. For both the 3-day and 7-day mortality there appears to be a U/J-shaped relationship according to SI quintiles. In these outcomes the mortality rate appears to be higher at the fifth and first quintiles while the lowest at the third quintile.

Supplementary Table 1 highlights the sample characteristics across the quintiles of SBP. There was a higher proportion of ischemic strokes in the first quintile in comparison to the fifth quintile (90.9% vs. 80.2%). Similar to SI, SBP exhibits a U/J shape relationship with the mortality outcomes.

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Table 2 shows the logistic regression analysis that presents the likelihood of inpatient mortality, 3-day mortality or 7-day mortality. After adjusting for all the covariates, stroke patients who were in the highest SI quintile on admission were at an increased likelihood of inpatient mortality, 3-day mortality and 7-day morality in comparison to stroke patients in the third quintile of the SI (reference category) with the strongest association for inpatient mortality. Patients in the first quintile did not appear to have an increased likelihood of inpatient morality, however these patients had an increased likelihood of 3-day morality with an odds ratio (OR) of 2.45 (95% CI 1.16-5.17) compared to the third quintile. Similarly stroke patients with low SI had an increased likelihood of a 7-day mortality with an OR of 1.88 (95% 1.01-3.49) compared to the third quintile.

Table 2 also describes the association between SBP and the mortality outcomes using the fully adjusted model (Model D). Higher and lower quintiles of SBP pressure are associated with an increased likelihood of in-patient and 7 day mortality. Unlike SI only high quintiles of SBP are associated with 3 day mortality (OR 2.58 (95% CI:1.15-5.79)).

Supplementary Table 2 shows the relationship between SI categories defined using lower and upper limit of clinical normal range of SI as the cut off points and the likelihood of in-patient mortality, 3-day mortality and 7-day mortality stratified by age groups (<65 and ≥65 years), sex (males and females), binary OCSP classification (TACS and others) and pre-stroke mRS categories (no to moderate disability (mRs<3)and ≥3)).

Table 3 demonstrates that both SI and SBP are very good predictors of mortality outcomes with excellent area under the curves (AUC) for all of outcomes assessed. SI and SBP had the same AUC for both inpatient mortality and 3-day mortality with an AUC of 0.87 (95%CI:

0.85-0.89) and 0.91 (95% CI: 0.89-0.94), respectively. Both SI and SBP had a similarly high AUC for 7 day mortality. However, there was no significant difference between SI and SBP in any of the mortality outcomes with a p value of > 0.05 for each combined ROC curve analysis.

4.1 Discussion

To our knowledge, this is the first study to examine the association between the shock index and acute mortality outcomes in stroke. We have found that both low and high values of the SI are associated with increased risk of 3-day and 7-day mortality, while only high values of the SI are associated with inpatient mortality. We have further shown that low and high levels of SBP are associated with inpatient and 7-day mortality. Both SI and SBP are very good predictors of morality outcomes, however there is little differentiation between the discriminating ability. Only low levels of SI are associated with 3-day mortality. Thus SI may be a useful indicator of very early mortality outcome in acute stroke.

4.2 Context of findings

A high SI has been reported to have a prognostic significance in conditions such as sepsis and severe volume depletion. [6,13,14] Previous research has shown that stroke patients with pneumonia and stroke associated infection are at an increased risk of mortality. [15,16] Thus, an explanation for a higher likelihood of mortality in the high SI group may be due to stroke associated infections. To our knowledge, this is the first study to show the predictive value of the higher shock index in stroke patients.

Previous studies have used the SI to assess outcomes in patients with community acquired pneumonia, acute circulatory failure and predicting patients that require immediate intensive therapy. [13,14,17,18] Moreover, a recent study that used prospectively collected audit data showed that a SI of >1.0 was predictive of inpatient mortality in individuals age 90 years and over. [19] In this report, for the first time we have shown that low values of the SI were associated with very acute stroke outcomes; this indicates that mortality was higher among patients with signs of a low SI than those with a normal SI. A possible explanation for this is

that a low SI is only apparent in severe stroke injuries indicating severe insult to the brain. One possible explanation for this is the Cushing's reflex, this is where there is a sharp rise in intracranial pressure (ICP) which attempts to maintain cerebral perfusion with resultant reflex bradycardia. Kalmer et al. [20] showed the Cushing reflex indicated by hypertension and bradycardia predicted poor intracranial perfusion and high ICP even during the neurological endoscopy, a minimally invasive procedure used in the management of brain tumors and tumor related hydrocephalus. Another study highlighted that mortality after a subarachnoid hemorrhage was predicted by high ICP, which demonstrated poor intracranial perfusion. [21]However, further work is required to assess whether there is a biologically plausible relationship between the Cushing's reflex and acute stroke mortality. This will however require serial measurements of both heart rate and blood pressure.

Previous research has shown that both high and low SBP measurements after stroke are associated with morality. [2,22,23] These studies showed that there was a U-shape relationship between systolic blood pressure and acute mortality outcome. The high levels of mortality in the fifth quintile could be explained by the high proportion of hemorrhagic strokes and previous history of hypertension seen in this sample. Previous research has suggested this association may be due an increased likelihood of a fatal cerebral edema in high SBP patients. [24,25] The association between low SBP (first quintile) and mortality may be due to inadequacy of cerebral perfusion due to low mean arterial pressure and subsequent reduce cerebral blood flow. [2]

4.3 Strengths of the study
Our study is likely to be representative of the stroke population of the UK and western populations as it used a systematic sampling strategy over an adequately long time period

from eight different NHS trusts. As this is an observational study thus causation between the SI and poor stroke outcomes cannot be drawn. Nevertheless, the SI may be useful in providing prognostic information as well as in identifying those patients with stroke who are at highest risk of mortality outcomes.

4.4 Limitations

Our study has a few limitations. Although the study population is generalizable to the UK it may not reflect the case mix of other world regions due to the lack of ethnic diversity in this study population; the study population is mainly Caucasians (>95%). However, there is no reason to believe that other ethnic populations would have different physiological responses in stroke with regard to BP and HR. In the UK setting, NIHSS (National Institute of Health Stroke Scale) which is an acute stroke severity marker was not assessed routinely for all strokes. Therefore, we have NIHSS data available only in those who were assessed for thrombolysis treatment. However, we were able to control for OCSP classification which usually reflects the NIHSS. As with all quantitative studies missing values are an issue, missing values in the pre-stroke mRS reduced the size of the final model. Nevertheless, this may only have reduced the study power and only likely to attenuate the results. Whilst assessment of multiple outcomes may increase the risk of Type 1 errors, arguably prognostic information on very early mortality in stroke is very important clinically as this information can potentially guide the clinicians in making treatment decisions including appropriate level and place of care.

5.1 Conclusion

In summary, our study illustrated that SI and SBP are significant predictor of acute stoke morality. SI is a very simple index derived from two readily available vital signs at the time of stroke admission making it useful for the clinical setting. Given that the SI is an index, it is

likely to be more user friendly in clinical setting compared to continuous BP values. This paper uniquely highlights that patients at the extremes of the SI are at an increased likelihood of poor acute stroke mortality outcomes. Our results suggest that at low SI predicts very early mortality in stroke (3-day mortality) whilst high SI may be more useful beyond 3 days where complications and sepsis (e.g. post stroke pneumonia) are prevalent. While both high and low values of SBP were predictive of poor acute outcomes, SI has additional benefit of predicting 3-day mortality. Further work should be replicated to support the findings of this study and should also examine whether incorporating SI in prognostic scoring systems would improve the clinical prediction rules in stroke.

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Table 1: Sample characteristics of 2121 stroke patients in ASCNES (2009-2011) by quintiles of the Shock Index

		Quintiles of Shock Index					
		Q1	Q2	Q3	Q4	Q5	
Shock Index (SI)		0-0.396	0.397-0.467	0.468-0.542	0.543-0.643	0.645-1.5	
SI (n)		424	423	426	423	425	P-value
Age (Mean)		78	78	76	77	77	0.12
Sex (% Male)		208 (49.1)	217 (51.3)	197 (46.4)	201 (47.5)	182 (42.8)	0.03
Systolic Bp (Mean)		185	167	156	146	131	<0.0001
Length of stay in days (mean)		15	15	17	16	18	0.14
Heart rate (mean)		63	72	79	86	102	<0.0001
pre-stroke modified Rankin Scale (%)	0	196 (54.6)	198 (54.8)	181 (49.5)	182 (51.4)	151 (43.3)	<0.0001
	1	71 (19.8)	74 (20.5)	62 (16.9)	58 (16.4)	54 (15.5)	
	2	30 (8.4)	31 (8.6)	47 (12.8)	46 (13.0)	33 (9.5)	
	3	31 (8.6)	32 (8.9)	45 (12.3)	43 (12.1)	44 (12.6)	
	4	20 (5.6)	17 (4.7)	23 (6.3)	15 (4.2)	50 (14.3)	
	5	11 (3.1)	9 (2.5)	8 (2.2)	10 (2.8)	17 (4.9)	
Stroke type (%)	Ischemic	352 (85.6)	348 (84.5)	359 (87.3)	368 (88.7)	369 (91.3)	0.003
Oxford Stroke Project Classification (%)	LACS[a]	93 (21.9)	102(24.1)	95 (22.3)	94 (22.2)	84 (19.8)	0.08
	PACS[b]	151 (35.6)	148 (35.0)	147 (34.5)	160 (37.8)	140 (32.9)	

	POCS[c]	55 (13.0)	63 (14.9)	48 (11.3)	56 (13.2)	43 (10.1)	
	TACS[d]	87 (20.0)	63 (14.9)	94 (22.1)	68 (16.1)	109 (25.6)	
	Undetermined	40 (9.4)	47 (11.1)	42 (9.9)	45 (10.6)	49 (11.5)	
	Treat for thrombolysis - No (%)	402 (94.8)	403 (95.3)	403 (94.6)	403 (95.3)	408 (96.0)	0.47
Pre-co-morbidities (Yes %)	Myocardial Infarction	112 (26.4)	105 (24.8)	96 (22.5)	95 (22.5)	134 (31.5)	0.24
	Peripheral Vascular disease	13 (3.1)	21 (5.0)	13 (3.1)	15 (3.5)	21 (4.9)	0.43
	Diabetes Mellitus	75 (17.7)	72 (17.0)	66 (15.5)	70 (16.5)	85 (20.0)	0.50
	Hypertension	273 (64.4)	265 (62.6)	236 (55.4)	244 (57.7)	238 (56.0)	0.004
	Antihypertensive Rx	228 (53.8)	221 (52.2)	207 (48.6)	222 (52.5)	214 (50.4)	0.59
	Hypercholesterolemia	68 (16.0)	81 (19.1)	71 (16.7)	75 (17.7)	72 (16.9)	0.95
	COPD	12 (2.8)	23 (5.4)	27 (6.3)	30 (7.1)	37 (8.7)	<0.0001
Outcomes	In patient mortality n=419	73 (17.2)	70 (16.5)	74 (17.4)	74 (17.5)	128 (30.1)	<0.0001
	3 Day mortality n=158	35 (8.3)	22 (5.2)	25 (5.9)	29 (6.9)	47 (11.1)	0.07
	7 day mortality n=245	49 (11.6)	43 (10.2)	34 (8.0)	45 (10.6)	74 (17.4)	0.01

[a]Lacunar Stroke; [b]Partial Anterior Circulation Stroke; [c]Posterior Circulation Stroke; [d]Total Anterior Circulation Stroke

Table 2: Odds ratios of in-patient mortality, 3-day mortality and 7 day mortality in each of the quintiles of the Shock Index in ASCNES: logistic regression models

	Q1		Q2		Q3	Q4		Q5	
Outcomes and models	**OR**	**95% CI**	**OR**	**95% CI**	**Reference**	**OR**	**95% CI**	**OR**	**95% CI**
In-hospital mortality[e]									
A[a]	0.94	(0.65-1.35)	0.93	(0.65-1.35)	1	1.01	(0.70-1.46)	2.1	(1.50-2.94)
B[b]	0.97	(0.64-1.46)	0.9	(0.59-1.36)	1	0.91	(0.60-1.38)	1.59	(1.08-2.35)
C[c]	1.02	(0.63-1.64)	1.1	(0.68-1.78)	1	1.25	(0.77-2.02)	1.89**	(1.20-2.97)
D[d]	1.02	(0.63-1.66)	1.09	(0.67-1.78)	1	1.25	(0.77-2.03)	1.85**	(1.17-2.92)
3-day mortality[e]									
A[a]	1.45	(0.85-2.49)	0.90	(0.50-1.63)	1	1.22	(0.70-2.14)	2.07**	(1.24-3.46)
B[b]	1.74*	(0.93-3.23)	0.84	(0.41-1.73)	1	1.21	(0.62-2.34)	1.67	(0.91-3.08)
C[c]	2.27*	(1.09-4.74)	1.04	(0.45-2.41)	1	1.89	(0.86-4.15)	2.32*	(0.86-4.15)
D[d]	**2.45***	**(1.16-5.17)**	1.1	(0.47-2.58)	1	1.9	(0.86-4.19)	2.18*	(1.03-4.63)
7-day mortality[e]									
A[a]	1.49*	(0.94-2.38)	1.33	(0.82-2.14)	1	1.41	(0.88-2.26)	2.5***	(1.61-3.88)
B[b]	1.56	(0.91-2.65)	1.33	(0.77-2.30)	1	1.38	(0.80-2.38)	1.86**	(1.11-3.11)

C[c]	1.84	(0.99-3.41)	1.75	(0.93-3.30)	1	2.14*	(1.14-4.03)	2.48**	(1.36-4.54)
D[d]	1.88*	(1.01-3.49)	1.76	(0.93-3.35)	1	2.11*	(1.12-3.99)	2.45**	(1.34-4.49)
Inpatient mortality[f,d]	1.97*	(1.19-3.26)	1.64	(0.99-2.73)	1	1.23	(0.73-2.06)	2.02***	(1.22-3.33)
3 Day mortality[f,d]	1.84	(0.79-4.28)	0.82	(0.32-2.09)	1	1.5	(0.65-3.48)	2.58*	(1.15-5.79)
7 Day mortality[f,d]	2.09*	(1.09-4.02)	1.00	(0.49-2.02)	1	1.63	(0.85-3.14)	2.23*	(1.18-4.24)

*<0.05 ** **≤0.01 ***≤0.001. [e]Shock Index quintiles (Q1 (<0.396), Q2 (0.397-0.467), Q3 (0.468-0.542), Q4 (0.543-0.6430 and Q5 (0.645-1.50)).

[f]Systolic blood pressure quintiles (Q1 (<132mmHg), Q2 (132-148mmHg), Q3 (149-162mmHg), Q4 (163-182mmHg), Q5 (=>183mmHg)

[a]Model A age and sex adjusted (n=2116); [b]Model B= Model A + mRS (n=1787); [c]Model C= Model B + Oxford Stroke Project Classification +Stroke Type

(n=1752); [d]Model D =Model C + Previous Medical History +treated for thrombolysis (n=1752).

Table 3. The comparison of the receiver operating characteristic (ROC) curve analysis, examining the difference in the discriminating ability between quintiles

of the shock index and systolic blood pressure.

		Area under ROC curve	95% CI	P-value	χ^2 Value
Inpatient mortality	Shock Index model	0.87	(0.84-0.89)	0.85	0.04
	Systolic blood pressure model	0.87	(0.85-0.89)		
3-day mortality	Shock Index model	0.91	(0.89-0.94)	0.63	0.23
	Systolic blood pressure model	0.91	(0.89-0.94)		
7-day mortality	Shock Index model	0.86	(0.83-0.89)	0.26	0.61
	Systolic blood pressure model	0.87	(0.84-0.90)		

Supplementary Table 1: Sample characteristics of 2,121 stroke patients in ASCNES (2009-2011) by quintiles of the systolic blood pressure

		Quintiles of systolic blood pressure					
		Q1	Q2	Q3	Q4	Q5	
Quintiles (mmHg)		<131	132-148	149-162	163-182	≥163	
		425 (20.0)	449 (21.2)	416 (19.6)	419 (19.8)	412 (19.4)	P-value
Age (Mean)		76	76	78	78	78	0.122
Sex (% Male)		209 (49.2)	207 (46.2)	216 (51.9)	191 (45.6)	182 (44.2)	0.175
LOS (mean)		16	17	16	15	14	0.074
Heart rate (mean)		81	80	81	80	81	0.746
pre-stroke modified Rankin Score (%)	0	149 (42.8)	216 (56.5)	181 (50.8)	176 (49.3)	186 (53.8)	0.007
	1	58 (16.7)	58 (15.2)	76 (21.3)	64 (17.9)	63 (18.2)	
	2	38 (10.9)	38 (9.9)	33 (9.3)	48 (13.4)	30 (8.7)	
	3	47 (13.5)	39 (10.2)	39 (11.0)	38 (10.6)	32 (9.2)	
	4	39 (11.2)	21 (5.5)	22 (6.2)	20 (5.6)	23 (6.6)	
	5	17 (4.9)	10 (2.6)	5 (1.4)	11 (3.1)	12 (3.5)	
Stroke type (%)	Ischaemic	368 (90.9)	401 (91.8)	356 (88.6)	351 (85.6)	320 (80.2)	≤0.001
Oxford Stroke Project Classification (%)	LACS[a]	98 (23.1)	95 (21.2)	93 (22.4)	95 (22.7)	87 (21.1)	0.921
	PACS[b]	124 (29.2)	174 (38.8)	169 (40.6)	149 (35.6)	130 (31.6)	
	POCS[c]	56 (13.2)	50 (11.1)	54 (13.0)	52 (12.4)	53 (12.9)	

	TACS[d]	97 (22.8)	85 (18.9)	62 (14.9)	78 (18.6)	97 (23.5)	
	Undetermined	50 (11.8)	45 (10.0)	38 (9.1)	45 (10.7)	45 (10.9)	
	Treat for thrombolysis - Yes (%)	27 (6.4)	24 (5.3)	21 (5.0)	19 (4.5)	11 (2.7)	0.014
Pre-co-morbidities (Yes %)	Myocardial Infarction	138 (32.5)	110 (24.5)	107 (25.7)	107 (25.5)	80 (19.4)	≤0.001
	Peripheral Vascular disease	23 (5.4)	14 (3.1)	18 (4.3)	13 (3.1)	15 (3.6)	0.240
	Diabetes Mellitus	89 (20.9)	57 (12.7)	69 (16.6)	73 (17.4)	80 (19.4)	0.754
	Hypertension	242 (56.9)	248 (55.2)	228 (54.8)	277 (66.1)	261 (63.3)	0.002
	Antihypertensive Rx	221 (52.0)	226 (50.3)	205 (49.3)	235 (26.1)	205 (49.8)	0.857
	Hypercholesterolemia	70 (16.5)	91 (20.3)	70 (16.8)	69 (16.5)	67 (16.3)	0.471
	COPD	28 (6.6)	37 (8.2)	22 (5.3)	29 (6.9)	13 (3.2)	0.026
Outcomes	In patient mortality n=419	108 (25.4)	82 (18.3)	52 (12.5)	73 (17.4)	104 (25.2)	0.818
	3 Day mortality n=158	44 (10.4)	21 (4.7)	17 (4.1)	28 (6.7)	48 (11.7)	0.261
	7 day mortality n=245	69 (16.2)	35 (7.8)	25 (6.0)	47 (11.2)	69 (16.7)	0.374

[a]Lacunar Stroke; [b]Partial Anterior Circulation Stroke; [c]Posterior Circulation Stroke; [d]Total Anterior Circulation Stroke

Supplementary Table 2: Odds Ratios of in-patient mortality, 3-day mortality and 7-day mortality using normal range values of Shock Index as cut off points in stratified analyses by age categories, sex, stroke classification, prestroke disability and in ischemic stroke subtype.

			<0.5	95% CI	0.5-0.69	>0.7	95% CI
Age	In patient mortality	<65	0.26	0.04-1.85	1	5.52	(0.83-36.61)
		≥65	0.99	(0.70-1.39)	1	1.96***	(1.24-3.11)
	3 Day mortality	<65	0.75	(0.01-40.35)	1	0.27	(0.00-27.89)
		≥65	1.22	(0.70-2.12)	1	2.46**	(1.2-5.02)
	7 Day mortality	<65	.750	(0.08-7.42)	1	5.69	(0.26-126.56)
		≥65	1.05	(0.68-1.61)	1	1.74	(0.98-3.08)
Sex	In patient mortality	Female	1.1	(0.71-1.72	1	2.35**	(1.30-4.28)
		Male	0.76	(0.45-1.29)	1	2.14*	(1.09-4.19)
	3 Day mortality	Female	1.16	(0.58-2.33)	1	2.18	(0.84-5.63)
		Male	1.45	(0.60-3.52)	1	2.94	(1.00-8.68)
	7 Day mortality	Female	1.39	(0.80-2.43)	1	2.56*	(1.23-5.34)
		Male	0.78	(0.40-1.54)	1	1.48	(0.61-3.58)
Oxford Stroke Project Classification	In patient mortality	Other type	0.87	(0.57-1.34)	1	2.21**	(1.27-3.82)
		TACS	1.21	(0.70-2.07)	1	2.34*	(1.13-4.83)
	3 Day mortality	Other type	0.92	(0.41-2.06)	1	2.8	(0.98-8.02)
		TACS	1.66	(0.79-3.47)	1	2.46	(1.00-6.08)

	7 Day mortality	Other type	0.93	(0.51-1.69)	1	2.74*	(1.29-5.81)
		TACS	1.29	(0.71-2.32)	1	1.45	(0.68-3.10)
Pre-stroke mRS	In patient mortality	<3	1.06	(0.70-1.61)	1	3.27***	(1.85-5.78)
		≥**3**	0.75	(0.44-1.26)	1	1.4	(0.77-2.53)
	3 Day mortality	<3	1.81	(0.91-3.61)	1	2.73**	(1.01-7.38)
		≥**3**	0.6	(0.28-1.30)	1	1.39	(0.63-3.04)
	7 Day mortality	<3	1.18	(0.71-1.95)	1	1.92	(0.92-3.99)
		≥**3**	0.89	(0.47-1.71)	1	2.10*	(1.05-4.18)
Stroke Type – Ischemic[a]	In patient mortality		0.84	(0.57-1.23)	1	1.94**	(1.21-3.11)
	3 Day mortality		0.87	(0.41-1.84)	1	2.06	(0.92-4.58)
	7 Day mortality		0.77	(0.46-1.30)	1	1.58	(0.86-2.88)

*<0.05 **≤0.01 ***≤0.001. Models adjusted for age, sex, mRS, Oxford Stroke Project Classification, Stroke Type, previous co-morbidities, treated for thrombolysis. [a]Only included Ischemic strokes in analysis.