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Simple clinical predictors of brain lesions in patients with impaired consciousness: a cross sectional study from a rural, tertiary hospital in central India☆

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Abstract

Objective: To evaluate the diagnostic accuracy of vital signs for detecting brain lesions in patients with impaired consciousness in a rural setting.
Methods: We enrolled patients older than 12 years who presented with impaired consciousness of non-traumatic origin to the intensive care unit of a rural teaching hospital. The design was a cross sectional analysis of a hospital-based case series, independently comparing vital signs on admission (temperature, pulse, systolic and diastolic blood pressure) against a reference standard (final diagnosis). Diagnostic accuracy was measured by computing multi-level likelihood ratios, and area under the receiver operating characteristic (ROC) curve.
Results: We studied 386 patients of whom 242 (62.7%) were men. A total of 178 patients (46%) had a brain lesion. None of the clinical predictors could accurately distinguish between those with and without a brain lesion. The area under the ROC curve for pulse was 0.61 (S.E. 0.02); that for the systolic and diastolic blood pressure 0.70 (S.E. 0.02) each. Systolic BP provided informative test results in 29.7%, diastolic BP in 37.2% and pulse rate in 19.9% patients.
Conclusion: Our findings suggest that the vital signs lack accuracy for ruling in or ruling out brain lesion in patients with impaired consciousness.

Keywords: Brain lesion; Impaired consciousness; Diagnosis; Predictors; Accuracy; Sensitivity; Specificity; Likelihood ratio

1. Introduction

The diagnostic workup of patients presenting with impaired consciousness is difficult, particularly in resource-limited settings. Some patients with impaired consciousness have underlying brain lesions, whereas others do not [1]. It is inappropriate and prohibitively expensive to routinely perform neurological imaging studies on every single patient presenting with impaired consciousness. Computed tomography (CT) scans are expensive and generally not available in most rural hospitals in developing countries such as India [2]. Even in settings where CT is available, time delays in obtaining a scan to rule out a brain lesion can compromise care of patients admitted with impaired consciousness. We, there-

Abbreviations: CT, computed tomography; ICU, intensive care unit; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; LR, likelihood ratio; 95% CI, 95% confidence interval; ROC, receiver operating characteristic; S.D., standard deviation; S.E., standard error

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fore, need a simpler diagnostic strategy that can help identify those patients with impaired consciousness that have an underlying brain lesion. This strategy, ideally, should be easy to perform, inexpensive and available at the bedside. Such a test can be extremely helpful in rural hospitals with limited resources.

Patients with impaired consciousness and increased intracranial pressure may have bradycardia and hypertension—the Cushing's response [3]. By contrast, patients without a brain lesion, such as those with sepsis and metabolic coma may present with hypotension and tachycardia. A study from Japan [4] that evaluated the accuracy of vital signs in the diagnosis of impaired consciousness concluded that systolic blood pressure (SBP) could discriminate patients with impaired consciousness who were at high risk from those who were at low risk of an organic brain lesion, and argued that use of SBP in the diagnosis of impaired consciousness can improve the efficient use of technology and reduce the healthcare costs.

We conducted this study in our rural hospital to determine if we could use vital signs (temperature, pulse rate, systolic and diastolic blood pressures) to identify the presence of brain lesions in patients presenting with impaired consciousness.

2. Materials and methods

2.1. Setting and study design

The Mahatma Gandhi Institute of Medical Sciences, Sevagram, is a rural medical school located in a small town in central India. It is a 648-bed, teaching institution with over 325,000 patient visits and about 5500 patient admissions to the internal medicine wards, each year. Impaired consciousness is a fairly common reason for admission to the medical intensive care unit (ICU) in our hospital. Residents, supervised by the internal medicine faculty, evaluate all patients admitted to the ICU. For a period of 10 months, beginning in March 2003, we prospectively recruited consecutive patients, aged 13 and above, who presented with impaired consciousness to our ICU. Potential study participants were identified by the ICU residents or by the study coordinator (Y.G.). To be eligible for the study, patients had to be at least 12 years old and had to have been admitted to the medical ICU with impaired consciousness—defined as a Glasgow Coma Scale (GCS) score of 14 or less [5]. We excluded patients presenting 24 h after the onset of impaired consciousness; patients with head injury; those patients whose complete clinical data were not available; patients who had already been investigated or treated before they were admitted to our hospital; and patients who died before a final diagnosis was established. The institutional review board concurred with our suggestion that because we were collecting data that is routinely obtained from all patients in the ICU, an informed consent was not necessary.

2.2. Ascertainment of clinical predictors

The study design employed was cross-sectional. We recorded four clinical variables (pulse rate, systolic blood pressure, diastolic blood pressure and temperature) on an enrolment data form, within 30 min of the patient's admission to the medical ICU. The study coordinator (Y.G.) either collected data from the patients herself or abstracted the information from the medical records.

2.3. Ascertainment of the reference standard

Patients were assessed by their attending physicians who ordered pertinent investigations to diagnose the underlying cause of impaired consciousness. Two investigators (R.J. and S.P.K.) reviewed the discharge summaries and the information available on the enrolment data form and assigned confirmed diagnoses according to the *International Classification of Diseases, 10th version* (ICD-10) classification [6]. Any discrepancies in assigning ICD codes were resolved by consensus. We considered the final diagnosis as the reference standard. The codes were then used to create a binary variable representing the presence or absence of brain lesion in the study population. The reference diagnosis was categorized as "brain lesion" and "no brain lesion". The group categorized as having "brain lesions" included patients with strokes, brain tumours, meningo-encephalitis, cerebral malaria and degenerative diseases of nervous system (e.g., Parkinson's disease). The group categorized as having "no brain lesions" comprised of patients with pesticide poisoning, hepatic coma, diabetic coma, hypoxic-ischaemic encephalopathy, snakebites and hypovolemia. The reference diagnosis was considered definite when the final diagnosis could be confirmed (e.g., evidence of stroke on CT scan), probable when the investigations were inadequate (example, suspected stroke not confirmed by CT scan) and uncertain when a clear diagnosis could not be made. Of the total 555 eligible patients, definite diagnosis could not be reached in 117, and these were excluded from the analysis. Another 52 patients were excluded as they either presented after 24 h of symptom onset, or had received treatment before admission. Hence a total of 386 patients were included; 274 of them (70.9%) had CT scans as part of their diagnostic work-up.

2.4. Statistical analysis

Diagnostic accuracy was measured by computing point estimates of the following test properties using standard methods: multi-level likelihood ratios (LR), and area under the receiver operating characteristic (ROC) curve. The precision of these estimates was evaluated using 95% confidence intervals. The likelihood ratio is the probability of a given test result when the disease is present, divided by the probability of the same test result when the disease is absent. LRs indicate by how much a given test result will raise or lower the pre-test probability of the target disease. A likelihood ratio

Table 1
Admission characteristics and distribution of clinical predictors among study patients with impaired consciousness, with and without a brain lesion

	With brain lesion ($n = 178$)	Without brain lesion ($n = 208$)	p value
Mean age (S.D.) years	53.73 (17.0)	45.88 (18.3)	<0.001†
Number (%) of women	62 (34.3)	82 (39.9)	0.68‡
Glasgow Coma Scale score (S.D.)	9.24 (3.3)	9.72 (3.2)	0.14†
Pulse (beats per minute) (S.D.)	91.5 (22.3)	102.2 (27.2)	0.26†
Systolic blood pressure (mmHg) (S.D.)	144.5 (41.5)	110.2 (36.5)	<0.001†
Diastolic blood pressure (mmHg) (S.D.)	85.6 (24.2)	64.0 (27.4)	<0.001†
Temperature (°C) (S.D.)	37.4 (0.58)	37.4 (0.53)	0.32

S.D.: standard deviation.
† Student's t-test.
‡ χ^2 test.

of 1 indicates that the post-test probability is the same as the pre-test probability (poor accuracy). Likelihood ratios >1.0 increase the probability that the target disorder is present. On the other hand, LRs <1.0 decreases the probability of the target disorder [7]. We considered that LR value of >2.0 and <0.5 would lead to a meaningful shift in the probability of brain lesion.

Because all clinical predictors were continuous measures, we also constructed the ROC curve by plotting the true positive rate against the false positive rate to evaluate how well vital signs discriminate patients with brain lesion from those without. ROC curve is a graphic means of assessing the extent to which a diagnostic test can be used to discriminate between persons with and without disease. The area under the curve provides some measure of how well the test performs. We classified accuracy of the area under ROC as low if the area was between 0.5 and 0.7; as moderate, if between 0.7 and 0.9; and as high if greater than 0.9 [8].

We used the t test for continuous variables and the χ^2 test for categorical variables to determine the association of age, gender and clinical predictors with brain lesion. All analyses were performed using Stata software (Version 8, Stata Corporation, College Station, TX).

3. Results

3.1. Study patients

During the period March–December, 2003, a total of 386 patients were included in the study, consisting of 242 men and 144 women, between 12 and 95 years of age [mean (S.D.) age 49.5 (18.1) years]. Table 1 shows the characteristics of the patients according to the presence ($n = 178$) or absence ($n = 208$) of a brain lesion. The clinical characteristics of the two groups at admission (sex and score on the GCS) were similar, except that patients with a brain lesion were significantly older ($p = <0.001$) than those without a brain lesion.

3.2. Clinical predictors

Table 1 and Fig. 1 show that compared with those patients without a brain lesion, patients with a brain lesion tended

Table 2
Cause of impaired consciousness and distribution of clinical predictors among patients with and without brain lesion

Disease	Glasgow Coma Scale score, mean (S.D.)	Systolic blood pressure (mmHg), mean (S.D.)	Diastolic blood pressure (mmHg), mean (S.D.)	Pulse rate (beats per minute), mean (S.D.)	Temperature (°C), mean (S.D.)
With brain lesion					
Intra-cerebral haemorrhage ($n = 48$)	7.9 (3.5)	176.0 (37.2)	103.1 (23.6)	85.7 (19.6)	37.3 (0.4)
Cerebral infarction ($n = 71$)	10.2 (2.9)	146.1 (36.1)	84.7 (21.3)	91.4 (24.5)	37.5 (0.7)
Brain tumour ($n = 5$)	10.6 (2.4)	123.6 (39.7)	77.6 (13.4)	98.4 (22.0)	37.2 (0.1)
Meningo-encephalitis ($n = 29$)	9.0 (3.1)	112.7 (30.5)	69.8 (18.3)	91.9 (24.1)	37.5 (0.5)
Cerebral malaria ($n = 20$)	9.9 (3.4)	115.4 (27.4)	70.2 (19.7)	100.7 (15.2)	37.7 (0.5)
Other brain lesions ($n = 5$)	6.4 (3.8)	140.4 (38.1)	92.0 (17.9)	105.0 (13.6)	37.7 (0.3)
Without brain lesion					
Pesticide poisoning ($n = 33$)	8.8 (3.6)	117.8 (28.4)	75.0 (18.0)	109.6 (28.6)	37.6 (0.5)
Hepatic coma ($n = 33$)	9.9 (3.1)	110.7 (23.0)	65.5 (19.3)	95.0 (20.5)	37.4 (0.4)
Diabetic coma ($n = 12$)	8.4 (3.8)	126.5 (22.3)	74.3 (15.9)	95.1 (19.6)	37.1 (0.3)
Renal failure ($n = 11$)	10.2 (3.5)	115.3 (54.2)	71.8 (31.6)	97.3 (32.4)	37.3 (0.3)
Alcohol intoxication ($n = 12$)	11.1 (3.3)	125.2 (14.6)	74.3 (10.6)	93.5 (22.1)	37.2 (0.2)
Hypoxia ($n = 71$)	10.3 (2.8)	105.8 (45.2)	56.9 (33.8)	106.5 (30.8)	37.4 (0.7)
Snakebite ($n = 7$)	8.6 (4.0)	82.3 (39.4)	47.4 (26.5)	82.3 (29.2)	37.3 (0.2)
Malignancy ($n = 10$)	9.1 (2.7)	117.6 (20.4)	71.6 (13.3)	101.4 (21.9)	37.4 (0.4)
Gastroenteritis ($n = 15$)	10.1 (2.8)	94.1 (35.9)	56.1 (26.0)	104.7 (22.4)	37.6 (0.4)
Other non-brain lesions ($n = 4$)	7.3 (2.6)	106.0 (28.0)	44.5 (51.4)	114.8 (19.7)	37.3 (0.3)

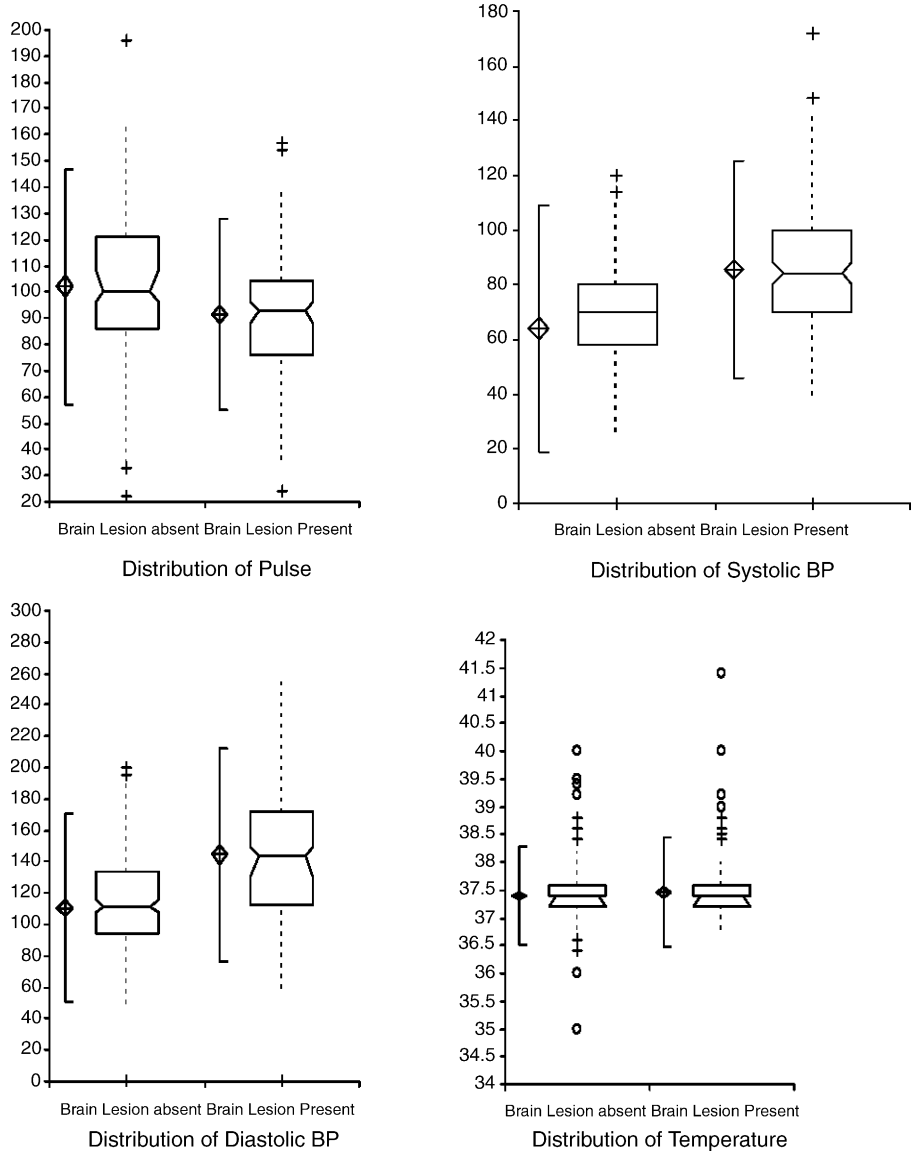

Fig. 1. Distribution of pulse, SBP, DBP and temperature in patients with impaired consciousness.

to have higher systolic BP (144 mmHg versus 111 mmHg; $p = 0.001$), higher diastolic BP (85 mmHg versus 64 mmHg; $p = 0.001$) and lower pulse rate (91 beats per minute versus 102 beats per minute; $p = 0.26$). Body temperature was similar in the two groups.

We categorised patients into two subgroups according to the presence or absence of a brain lesion. Table 2 shows the causes of impaired consciousness and the distribution of vital signs among different categories. Of the 178 (46%) patients with a brain lesion, 119 (66%) had a confirmed diagnosis of stroke; 5 (2%) had brain tumour; 29 (16%) had meningo-encephalitis; 20 (11%) had cerebral malaria; and 5 (2%) patients had other diseases. Of the 208 patients without a brain lesion, 33 (16%) had pesticide poisoning; 33 (16%) had hepatic coma; 71 (35%) had hypoxia due to cardiac or pulmonary causes; 15 (7%) had gastroenteritis; 12 (5%) had diabetic coma; 12 (5%) had alcohol intoxication; 11 (5%) had renal failure; 10 (5%) had malignancies; 7 (3%) had snake bite and 4 (2%) patients had other diseases.

Fig. 2 shows the ROC curve for each vital sign. The area under the ROC curve for pulse was 0.61 (S.E. 0.02); that for the systolic and diastolic blood pressure 0.70 (S.E. 0.02) each. These values indicate that if we draw two patients randomly from the group with brain lesion and the group without, and use SBP or DBP to guess which of the two is a patient with a brain lesion, we shall be correct 70% of the time.

As shown in Table 3, we divided the systolic BP, diastolic BP and pulse rate into five strata. We calculated multi-level likelihood ratios to assess the discriminatory power of each stratum of the diagnostic test result. We used LRs to determine which values led to a meaningful shift in the probability of brain lesion. We divided LRs into three categories: those that gave a reasonable evidence of brain lesion (LR > 2); those that gave reasonable evidence against brain lesion (LR < 0.5)

Table 3
Accuracy of clinical predictors for diagnosing brain lesion in patients with impaired consciousness

	With brain lesion ($n = 178$)[a]	Without brain lesion ($n = 208$)[a]	All ($n = 386$)[a]	Likelihood ratio (95% CI[b])	Post-test probability (%)
Systolic BP (mmHg)					
≤80	5 (2.8)	29 (13.9)	34 (8.8)	0.20 (0.18, 0.22)	9
80–119	52 (29.2)	96 (46.1%)	148 (38.3)	0.63 (0.59, 0.68)	29
120–159	55 (30.9)	68 (32.7)	123 (31.9)	0.95 (0.90, 0.99)	44
160–199	50 (28.1)	14 (6.7)	64 (16.6)	4.17 (2.39, 7.29)	78
≥200	16 (9)	1 (0.5)	17 (4.4)	18.70 (2.52, 140.27)	94
Diastolic BP (mmHg)					
≤60	18 (10.1)	68 (32.7)	86 (22.3)	0.31 (0.28, 0.34)	14
60–79	52 (29.2)	72 (34.6)	124 (32.1)	0.84 (0.80, 0.89)	39
80–99	59 (33.1)	59 (28.4)	118 (30.6)	1.17 (0.87, 1.58)	49
100–119	35 (19.7)	8 (3.8)	43 (11.1)	5.11 (2.44, 10.73)	81
≥120	14 (7.9)	1 (0.5)	15 (3.9)	16.36 (2.17, 123.19)	93
Pulse rate (beats per minute)					
≤60	12 (6.7)	12 (5.8)	24 (6.2)	1.17 (0.54, 2.54)	49
60–79	44 (24.7)	26 (12.5)	70 (18.1)	1.98 (1.27, 3.08)	62
80–99	55 (30.9)	60 (28.8)	115 (29.8)	1.07 (0.79, 1.46)	47
100–119	46 (25.8)	54 (25.9)	100 (25.9)	1.0 (0.95, 1.04)	46
≥120	21 (11.8)	56 (26.9)	77 (19.9)	0.44 (0.41, 0.47)	20

[a] Values are expressed in number (percentage) unless otherwise indicated.
[b] CI denotes confidence intervals.

and an intermediate class for uninformative test results. Systolic BP provided informative test results in 29.7%, diastolic BP in 37.2% and pulse rate in 19.9% patients. Our data show that systolic BP was 160 mmHg or more in 81 (21%) patients, and pulse was less than 60 in 24 (6%) patients. However, only five (1.3%) patients had both hypertension and bradycardia (SBP > 160, pulse < 60); all of them had a brain lesion.

4. Discussion

Impaired consciousness, caused by structural brain lesions, metabolic, toxic and psychiatric causes, is a common clinical problem [1]. Clinical history, general physical and detailed neurological examination, used to determine the presence or absence of a structural lesion, provide a baseline for future evaluations and quickly differentiate the general categories to determine which further diagnostic tests are needed or if immediate intervention is necessary [9]. We conducted this study to evaluate if determination of vital signs, such as pulse and blood pressure, could accurately diagnose the presence of structural brain lesions in patients with impaired consciousness.

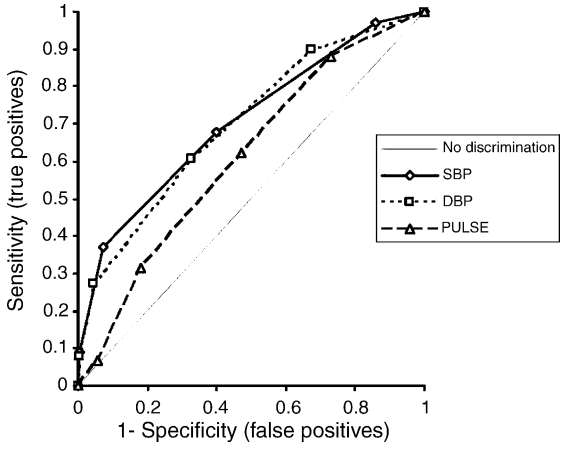

Fig. 2. Receiver operating characteristic curve for systolic BP, diastolic BP, and pulse in diagnosing brain lesion in patients with impaired consciousness. For each cut point of the SBP, DBP and pulse, the probability of finding a higher value in brain lesion (sensitivity) and in non-brain lesion (1-specificity) is plotted (the area under the ROC curve: SBP = 0.70; DBP = 0.70; pulse = 0.61).

Of the total 386 patients, 178 (46%) patients had brain lesion that accounted for impaired consciousness (pre-test probability of brain lesion in our setting). Our data show that most categories of systolic BP, diastolic BP and pulse rate generated likelihood ratios between 0.5 and 2.0, too insignificant to be clinically useful. Systolic and diastolic BP generated likelihood ratios that could significantly alter probability of brain lesion in approximately one-third study patients; pulse rate did so in only one-fifth of them. The discriminating power of systolic and diastolic BP resided mostly with extreme readings. For example, a patient with a systolic BP > 200 mmHg or a diastolic BP of >120 mmHg had >90% post-test probability of having a brain lesion. By contrast, systolic BP < 80 mmHg, or diastolic BP < 60 mmHg reduced the post-test probability of brain lesion to <15%. These values look impressive, and concur well with the findings from a study from Japan [4] that showed that systolic BP > 180 mmHg argued strongly for a brain lesion (LR = 26.4), whereas systolic BP < 90 mmHg argued convincingly against it (LR = 0.03). However, wide confidence intervals around the point estimates indicate that few patients belonged to the highest or lower categories of blood pressure—the very categories that could help one confidently

rule in or rule out a brain lesion. The area under the receiver operating curve for systolic BP, diastolic BP and pulse rate (0.70, 0.70 and 0.63, respectively) also suggest that these clinical predictors are incapable of making large and clinically meaningful shifts between pre-test and post-test probabilities.

In a previous study, Ikeda et al. [4] had suggested that systolic blood pressure is useful for diagnosing stroke-induced impaired consciousness and argued that meaningful use of systolic blood pressure in patients with impaired consciousness can reduce the necessity for computed tomography. Our study does not support this suggestion, probably due to a different distribution of competing conditions [10]. Our patient population differed significantly from the population described in previous studies [4,11]. A quarter of patients in the study by Plum and Posner [1] had drug poisoning; another quarter had stroke. By contrast, our study patients had problems peculiar to tropical, developing countries: meningitis, encephalitis, snakebites, pesticide poisoning, cerebral malaria and diarrhoea. Also, compared to the patients recruited by Ikeda et al. [4], our patients were younger (mean age 49 years versus 65 years) and were less likely to have had stroke (33% versus 49%).

The classic Cushing's response of systolic hypertension and bradycardia [9] was seen in only five patients (1.3%) in our study. This suggests that a combination of bradycardia and hypertension is an insensitive sign for the diagnosis of brain lesion in adults with impaired consciousness of non-traumatic origin in our setting. Pre-existing hypertension or systemic response to impaired auto regulation of cerebral blood flow, and not Cushing's response, may account for hypertension at admission in stroke patients in our setting, as about one-third patients with stroke who present with hypertension on admission, are not aware of their blood pressure status [2].

Our study had several strengths. Our patients represent a typical rural Indian population. By including a wide spectrum of patients with impaired consciousness, we avoided selection bias with respect to age, gender, disease severity and subtypes of patients. By including all patients with GCS score $\leq$14, we ensured an adequate spectrum of mild, moderate and severely impaired consciousness in our study population. We used the cross sectional design, the ideal design for studies of diagnostic test accuracy [10]. To avoid misclassification bias, two investigators, blind to the vital signs on admission, independently assigned ICD codes to the final diagnoses (the reference standard).

Our study had some limitations. Firstly, our study population represents only the hospitalised subgroups of patients with impaired consciousness in a rural area. Patients who died at home and those who did not get referred to the hospital were not included in our study. This might affect the predictive potential of the vital signs. Secondly, an appropriate history and neurological examination would be the best approach to assess the neurological deficits in a patient with impaired consciousness. The ability to perform a competent neurological examination and to be able to distinguish the normal from the abnormal is indeed important. Their importance in determining the diagnosis or at least their role in the localization of a neurological lesion is worth exploring particularly in settings where the hospitals may lack facilities for brain imaging [12]. We did not evaluate the predictive power of complete neurological examination in identifying brain lesion, however. Thirdly, temperature, pulse and blood pressure are influenced by several cardiac, pulmonary and infectious aetiologies of impaired consciousness as well. Fourthly, we used CT scan to discriminate patients with brain lesion from those without. Although a recent study has shown that immediate CT scanning of stroke patients is cost-effective and improves quality of life [13], many patients with mild stroke never show a visible infarct on CT scan, no matter when they are scanned [14]. CT scan may be negative in early brainstem lesions and structural white mater lesions and is not useful in ruling in metabolic or toxic causes of coma. Lastly, we could make accurate final diagnoses in some categories (e.g. CT scan-confirmed strokes or toxicological analysis in patients with pesticide poisoning), but not in other categories (e.g. undiagnosed fever syndromes). Several of our study participants had clinically unexplained fever and impaired consciousness possibly due to malaria or meningo-encephalitis. We found it difficult to discriminate cerebral malaria from meningo-encephalitis because their clinical profiles overlapped. These problems could have affected our final, gold standard diagnoses.

In conclusion, among patients with impaired consciousness presenting to a rural hospital in India, vital signs do not accurately distinguish between patients with brain lesion and those without. Patients with impaired consciousness need a detailed neurological evaluation, combined with relevant diagnostic tests to help physicians identify the presence of brain lesions.

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