

# Hyponatremia in the Prognosis of Acute Ischemic Stroke

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*Background:* Hyponatremia is a risk factor for stroke and cardiovascular disease. Even mild hyponatremia is associated with increased 30-day mortality after myocardial infarction, and it has recently shown to increase the 3-year mortality after a stroke. In this work, we investigated both acute and chronic clinical outcomes after a stroke in hyponatremic patients. *Methods:* We reviewed all patients admitted between 2004 and 2011 with the diagnosis of acute ischemic stroke. Hyponatremia was defined as serum sodium level less than 135 mmol/L and recorded on admission. All hemorrhagic strokes were excluded. Data were analyzed using multivariate logistic regression. *Results:* A total of 3585 patients with stroke were identified. Hyponatremia was observed in 565 (16%) patients. Baseline characteristics were similar between groups except heart failure ( $P = .015$ ), cancer ( $P = .038$ ), diabetes ( $P < .001$ ), and dementia ( $P = .015$ ). Hyponatremic patients had higher National Institutes of Health Stroke Scale (NIHSS) score on admission ( $P = .032$ ) and at discharge ( $P = .02$ ). Despite similar modified Barthel Index (mBI) preadmission, patients with hyponatremia had worse mBI on admission ( $P = .049$ ). Hyponatremia was associated with higher mortality in hospital ( $P = .039$ ) and at 3-month ( $P = .001$ ) and 12-month follow-ups ( $P = .001$ ). A poorer discharge disposition was seen in the hyponatremia group ( $P = .004$ ). Complications during admission were similar between groups except for urinary infection ( $P = .008$ ). Patients with hyponatremia had worse NIHSS and mBI values on admission, and their deficits worsened during their hospitalization. *Conclusions:* This is the first study to demonstrate that hyponatremia is associated with acute mortality and poorer discharge dispositions and to confirm that higher mortality occurs in these patients, even after 12 months after a stroke. **Key Words:** Hyponatremia—prognosis—acute ischemic stroke—epidemiology—mortality—disposition.

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## Introduction

Acute ischemic stroke (AIS) affects 795,000 people every year, is the fourth leading cause of death, and the most common cause of long-term disability in the United States.<sup>1</sup> Hyponatremia has long been described as a risk factor for stroke and cardiovascular disease.<sup>2-4</sup> Low

serum sodium levels are also seen as a complication of cerebrovascular disease, especially after subarachnoid hemorrhage.<sup>5,6</sup> The proposed mechanisms are related to cerebral salt-wasting syndrome or inappropriate secretion of antidiuretic hormone.<sup>7</sup> Hypertonic saline is one of the main therapies used to decrease intracranial pressure (ICP) and optimize cerebral blood perfusion after brain injury.<sup>8</sup> Even mild hyponatremia is a factor for poor prognosis in the general population, and low sodium levels on admission were associated with increased 30-day mortality after a myocardial infarction.<sup>9,10</sup> A recent study demonstrated higher 3-year mortality in hyponatremic patients with first-ever ischemic stroke.<sup>11</sup> The relationship between hyponatremia and early clinical outcomes after an AIS is unknown. The prognosis of AIS in patients with hyponatremia remains unclear. In this

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study, the data of patients with AIS admitted to a major stroke center found to have hyponatremia on admission were assessed to evaluate risk factors, comorbidities, short-term and long-term mortality, disability rates, and disposition.

## Methods

### Population

We reviewed all consecutive patients admitted to Hartford Hospital Stroke Center Database between 2004 and 2011, with AIS and over 18 years of age. All patients were evaluated by a neurology attending, and the diagnosis of an AIS was made according to the World Health Organization criteria and confirmed by head computed tomography and/or by brain magnetic resonance imaging.<sup>12</sup> All patients with hemorrhagic stroke (subarachnoid, subdural, epidural, intraparenchymal, and intraventricular hemorrhages) were excluded from this review. Initial serum sodium level on admission was recorded and hyponatremia was defined as Na less than 135 mmol/L.<sup>11</sup> Baseline characteristics were checked for homogeneity between groups. Patient characteristics recorded were age, gender, living situation, history of comorbidities, premorbid functioning, and subtype of acute stroke (Trial of Org 10175 in Acute Stroke Treatment).<sup>13</sup> Primary outcome was assessed by the National Institutes of Health Stroke Scale (NIHSS) score on admission, modified Barthel Index (mBI), inpatient mortality, and disposition after discharge. The mBI is an ordinal scale that measures performance in activities of daily living with 10 questions and scores ranging from 0 to 20.<sup>14</sup> A higher mBI is associated with a greater likelihood of living independently after discharge from the hospital. Data were compared at discharge and at 3-month and 12-month follow-ups. Follow-up data including the mBI were obtained through hospital records for visits, subsequent admissions, and by follow-up phone calls performed by a trained stroke center nurse. Univariate statistical analyses were performed using SPSSv14 (SPSS, Inc, Chicago, Illinois, USA) and included chi-square/Fisher exact test for categorical variables and *t* test for continuous variables (Wilcoxon ranked sum test was used for variables not following a normal distribution). Multivariate logistic regressions were conducted using variables identified as having some relationship with hyponatremia and variables preidentified by review of literature. Confidence intervals were established at 95%. This study was approved by our local Institutional Review Board and conducted in accordance to the Declaration of Helsinki.

## Results

A total of 3585 patients with AIS were identified, of whom 3541 had sodium levels documented on admission. Hyponatremia was observed in 565 (16%) patients. Baseline clinical characteristics and risk factors for stroke

were similar between groups except for higher prevalence of congestive heart failure ( $P = .015$ ), history of cancer ( $P = .038$ ), diabetes ( $P < .001$ ), and dementia ( $P = .015$ ) in the hyponatremic cohort (Table 1).

Patients with hyponatremia had worse NIHSS scores at admission. The comparison of ranked scores shows a trend for this effect ( $P = .056$ ) with significant differences found when the scores are classified into 4 severity groups ( $P = .032$ ) (Table 2).

Worse NIHSS score at discharge was observed in 12.1% of the hyponatremia group patients compared with 7.7% in the patients with normal sodium levels ( $P = .02$ ).

Patients with hyponatremia on admission have significantly higher rates of short-term mortality defined as either expiring during the initial hospital stay or a composite of in-hospital death or discharge to hospice. Chronic mortality rates are also higher for patients with hyponatremia on cumulative comparisons of known death at 3-month and 12-month follow-ups. A "discharge to worse disposition" defined as death, hospice, or new extended care facility placement was also seen in the hyponatremia group ( $P = .004$ ). Fewer patients were discharged to home in the hyponatremia group compared

**Table 1.** Baseline characteristics and risk factors for stroke among patients with and without hyponatremia

Characteristics	Hyponatremia (%)	Normal (%)	<i>P</i>
Gender (F)	299 (52.9)	1517 (51)	.40
Age	71 ± 14.9	70.9 ± 15.2	.643
Living situation			.701
Home	138 (25.3)	660 (22.7)	
VNA	348 (63.7)	1933 (66.4)	
Homeless	0	4 (.10)	
ECF	40 (7.3)	196 (6.7)	
ALF	17 (3.1)	98 (3.4)	
Other	3 (.50)	19 (.70)	
Diuretics	76 (13.5)	420 (14.1)	.741
CHF	88 (15.9)	351 (12)	.015
Heart disease	230 (40.7)	1153 (38.7)	.397
Hyperlipidemia	262 (46.4)	1436 (48.3)	.435
Stroke	128 (22.7)	764 (25.7)	.139
Smoking	109 (21.5)	588 (21.6)	1
Blood clots	29 (5.1)	114 (3.8)	.161
Seizures	25 (4.4)	100 (3.4)	.214
Head injury	2 (.40)	1 (0)	.068
Cancer	99 (17.5)	420 (14.1)	.038
Angina	13 (2.3)	54 (1.8)	.403
Lung disease	70 (12.4)	342 (11.5)	.567
Asthma	28 (5)	151 (5.1)	1
Depression	73 (12.9)	369 (12.4)	.729
Dementia	38 (6.7)	298 (10)	.015
Atrial fibrillation	162 (28.7)	832 (28)	.80
Diabetes	217 (38.4)	847 (28.5)	<.001

Abbreviations: ALF, assisted living facility; CHF, Congestive heart failure; ECF, extended care facility; VNA, visiting nurse services.

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