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Elevated blood urea nitrogen/creatinine ratio is associated with poor outcome in patients with ischemic stroke

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ABSTRACT

Objective: Dehydration may impair cerebral oxygen delivery and worsen clinical outcome in patients with acute ischemic stroke (AIS). We evaluated if elevated blood urea nitrogen to creatinine ratio (BUN/Cr) as a marker of dehydration was associated with poor clinical outcome in emergency department (ED) patients presenting with AIS.
Methods: We conducted a prospective cohort study using a stroke registry enrolling all ED patients with AIS from 10/2007 through 6/2009. Poor clinical outcome was defined as death, placement in a nursing home for purposes other than rehabilitation, or hospice within 30 days of ED presentation. A BUN/Cr ratio of ≥15 was considered elevated. (IQR). Logistic regression was performed adjusted for age >64 years, NIHSS >8, diabetes, prior CVA, and coma at presentation reporting odds ratios with 95% confidence intervals.
Results: 324 patients had a final diagnosis of AIS. 163 (50%) were female, 19 (6%) died, 44 (14%) received t-PA, and 89 (27%) had a poor clinical outcome. The median NIHSS, BUN and Cr were 4 (IQR 1–9), 14 mg/dL (IQR 11–21), and 1.02 mg/dL (IQR 0.87–1.27) respectively. The median BUN/Cr was 13.9 (IQR 10.6–18.5). The variables associated with a poor clinical outcome were: high NIHSS OR 6.5 (3.6–11.8), age >64 years OR 2.7 (1.5–5.0), and BUN/Cr ratio of ≥15 OR 2.2 (1.2–4.0).
Conclusion: An elevated BUN/Cr ratio in patients with AIS is associated with poor outcome at 30 days. Further study is needed to see if acutely addressing hydration status in ED patients with AIS can alter outcome.

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1. Introduction

Adequate hydration status is important to maintain physiologic homeostasis in humans. Hydration is maintained by osmoregulation which can be controlled by the intake of fluid and adjustments in the concentration of urinary excretion. The desire to drink, thirst, has been shown to be driven by increased plasma osmolarity and to a lesser degree by a decrease in extracellular fluid volume [2].

Appropriate euvolemia is important for adequate blood flow to ensure oxygen delivery and proper organ function. It has been shown that blood flow to organs including muscle and kidney is significantly reduced in states of dehydration [3,4]. Cardiac output will also decrease as dehydration increases [5]. The human body has several mechanisms to reduce water loss in states of dehydration including the release of hormones renin and vasopressin to stimulate renal water reabsorption.

The brain is able to control cerebral blood flow through autoregulation allowing constant cerebral perfusion pressure despite moderate variations of blood pressure. Dehydration has been shown to blunt cerebral autoregulatory response to orthostatic positioning but did not lower cerebral perfusion overall [6].

Dehydration is not an uncommon finding of patients presenting to an emergency department with an overall prevalence of 7% [7]. It is more common in elderly patients with one estimate suggesting 1.5% of independent elderly patients will be admitted for dehydration annually and evidence of chronic dehydration can be seen in almost half of geriatric patients presenting to emergency departments for care [8,9]. Dehydration in the elderly is often associated with other diseases such as pneumonia, influenza, chronic obstructive pulmonary disease and gastroenteritis which contribute to the overall severity of illness. Elderly patients are more susceptible to dehydration as they are more likely to have physical barriers to self hydration, are more likely to be on medications that promote dehydration such as diuretics, have diseases

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that increase water loss such as diabetes and show decrease thirst sensation [10].

The role of dehydration in cerebral infarction is thought to be multifactorial. Dehydration increases blood viscosity and is felt to diminish cerebral blood flow due to lower intravascular volume. Elevated hematocrit has been shown to be associated with a larger infarct volume in patients with cerebral infarction [11]. Dehydration also has been shown to be associated with recurrent embolic stroke and thrombotic events including venous thromboembolism after an acute stroke [12,13].

Unfortunately, the clinical assessment of dehydration by physicians is not always accurate. Physicians managing geriatric patients tend to overestimate dehydration by one-third [14].

The effect of dehydration at presentation on the risk and outcome of ischemic stroke has been evaluated using plasma osmolality both measured directly and calculated from serum sodium, glucose, and blood urea nitrogen (BUN). One study found an increased risk of mortality with elevated osmolality for all patients while another found an increased risk of ischemic stroke only for patients with elevated osmolality who were aged 65 or older [15,16]. The absolute differences in serum osmolality between the study groups were small ranging from 3.1 to 4.6 mOsm/kg. Serum osmolality is not routinely ordered in the evaluation of cerebral infarction and is not recommended as a diagnostic test in the early management of cerebral infarction [17].

Other markers exist for the assessment of dehydration although none have been considered a gold standard. A common marker used for the assessment of dehydration is the blood urea nitrogen to creatinine ratio (BUN/Cr). This marker has been used in multiple studies evaluating hydration status for differing disease processes [18–21]. BUN and creatinine are both used in the assessment of renal function and are frequently ordered as part of an electrolyte panel in patients presenting with cerebral infarction. The calculation of the BUN/Cr ratio is rather simple and can be performed quickly without a calculator. It would be useful if, when used as a marker for dehydration, the BUN/Cr ratio would be predictive of poor outcomes in patients with cerebral infarction. The goal of this study was to evaluate if an elevated BUN/Cr ratio was predictive of poor outcomes in patients presenting with acute cerebral infarction.

2. Methods

We conducted a prospective cohort study of all patients presenting with acute ischemic stroke to our institution from October 2007 to June 2009. The registry was approved by our local IRB with a waiver of informed consent. Inclusion criteria included an ED diagnosis of acute ischemic stroke. Exclusion criteria included ED transfer to another in patient facility, hemorrhagic stroke, and a non-ischemic stroke diagnosis given by a neurologist later in the hospitalization. All patients with an ED diagnosis of acute stroke are entered into a registry with data collected from their ED visits including demographic laboratory and clinical information. Data were collected using a structured instrument by trained investigators, (MG, KD, JWS). All laboratory values were primary ED collections that occurred upon their arrival to the ED. Along with BUN and creatinine, hemoglobin, hematocrit, and glucose values at presentation were collected as well. The BUN/Cr ratio of greater than 15/1 was selected a priori to represent dehydration in patients at presentation. This ratio has been used in other studies and medical textbooks as a marker of dehydration [22–25]. The National Institutes of Health Stroke Scale Score (NIHSS), a previously validated score of stroke severity, was recorded at the time of ED presentation [26,27]. The NIHSS was performed upon arrival to the ED by trained physicians with over 80% of our ED physician staff certified in the NIHSS. Other data recorded included the presence of comatose state at presentation, disposition at discharge, and hospital length of stay. Clinical outcomes defined as a poor outcome for this study included death, placement in hospice, or placement in a nursing home for purposes other than rehabilitation within 30 days of ED presentation.

To evaluate the odds of an elevated BUN/Cr ratio on poor outcome we performed multivariate logistic regression adjusting for male gender, age >64 year, NIHSS >8, presence of diabetes, prior CVA and coma at presentation. Other data are presented as percentages and medians with interquartile ranges (IQR) where appropriate.

Table 1
Subject demographics.

Demographic	No. (%)	No. (%) with elevated BUN/Cr ratio
Female	163 (50)	83 (51)
Male	161 (50)	55 (34)
Caucasian	202 (62)	109 (54)
African American	100 (31)	17 (17)
Hispanic	21 (6)	12 (57)
Prior CVA	102 (31)	39 (38)
Prior TIA	26 (8)	14 (54)
Hypertension	244 (75)	109 (45)
Hyperlipidemia	147 (45)	59 (40)
Atrial fibrillation	44 (14)	30 (68)
Coronary artery disease	87 (27)	37 (43)
Diabetes	106 (33)	48 (54)
Current smoker	135 (34)	36 (27)

Table 2
Presenting vital signs and serum levels.

Blood urea nitrogen (BUN)	14.5 mg/dL (IRQ 11–21.5)
Creatinine	1.02 mg/dL (IQR 0.87–1.27)
Hemoglobin	13.6 (IQR 12.4–15)
Hematocrit	41.4 (IQR 38.2–45.2)
Glucose	120 (IQR 103–160)
Systolic blood pressure	150 mm/Hg (IQR 131–173)
Diastolic blood pressure	75 mm/Hg (IQR 61–87)
Heart rate	78 bpm (IQR 69–88)

3. Results

We evaluated 398 subjects of whom 324 (81%) had a final diagnosis of acute cerebral infarction. In the final cohort, 163 (50%) were female, 19 (6%) died, and 89 (27%) had a poor clinical outcome. The median time from symptom onset to presentation was 4.5 h (IQR 1–23.8). Baseline demographic data for the whole population and those with an elevated BUN/Cr ratio are listed in Table 1. The median BUN and Cr levels were 14.5 mg/dL (IQR 11–21.5) and 1.02 mg/dL (IQR 0.87–1.27) respectively. Presenting vital signs and serum levels of electrolytes and blood counts can be seen in Table 2. The most common cardiac rhythm upon presentation was normal sinus rhythm 236 (74%) followed by sinus bradycardia 38 (12%) and atrial fibrillation 32 (10%). A total of 44 (14%) of patients received tissue plasminogen activator (tPA). The results of the logistic regression model, seen in Table 3, shows that an elevated BUN/Cr

Table 3
Logistic regression for poor outcome after cerebral infarction.

Variable	Odds ratio	95% Confidence intervals
Diabetes	1.19	0.63–2.2
Age 65 or older*	2.8	1.5–5.1
Male	1.3	0.7–2.3
NIHSS >8*	6.5	3.6–11.9
Prior CVA	1.1	0.61–2.1
Elevated BUN/Cr ratio*	2.2	1.2–4.0

* $P < 0.05$.