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Original article

Serum osmolarity as an outcome predictor in hospital emergency medical admissions

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ABSTRACT

Background: To determine whether the serum osmolarity, calculated at the time of an emergency medical presentation, alone or combined with other predictors, could identify patients at low and high risks of an inpatient death by day 30.

Methods: A retrospective analysis of all emergency medical patients admitted to St. James's Hospital (SJH), Dublin between the 1st of January 2002 and the 31st of December 2009, using the hospital in-patient enquiry (HIPE) system, linked to the patient administration system, and laboratory datasets. Hospital inpatient mortality (30 days) was obtained from a database of deaths over the same period. Multivariate logistic regression was used to derive the best predictive model, with goodness of fit and Area Under the Receiver Operator Curves (AUROC) assessing the predictive accuracy.

Results: Univariate analysis identified two quantiles of <10% and >75% of the osmolarity distribution as being at an increased mortality risk. Their respective mortality rates were 13.7% and 15.7% respectively, with unadjusted odds rate that were 1.66 (1.47, 1.88): p<0.0001 and 3.14 (2.87, 3.43): p<0.0001. After adjustment for other outcome predictors, a significant association with increased mortality remained, with OR = 1.82 (1.61, 2.06), p<0.0001. Although the calculated osmolarity alone was not sufficiently predictive with AUROC = 0.74 (95% CI: 0.73, 0.76), when combined with other predictors, the AUROC increased to 0.86 (95% CI: 0.84, 0.88).

Conclusion: Admission osmolarity, a simple calculation, is associated with the risk of mortality in acutely ill medical patients; deviations outside the normal range are relevant. A useful clinical predictive algorithm requires the incorporation of additional predictors.

1. Introduction

Factors that are associated with increased mortality among medical patients admitted to hospital as emergencies include age, altered mental status and the presence of co-morbidities such as ischaemic heart disease, diabetes mellitus, and stroke [1]. Many of these factors, together with various clinical findings such as the presence or severity of haemodynamic instability, hypoxia, pyrexia and coma or altered mental status, have been incorporated into various risk-stratification clinical scoring systems such as the Modified Early Warning Score (MEWS) [2], the Rapid Acute Physiology Score (RAPS) [3] and the Rapid Emergency Medicine Score (REMS) [4].

Mortality may be predicted based on the specific derangement of certain laboratory parameters at time of emergency presentation; these include disturbance of sodium balance [5–8], altered albumin levels [9,10] and hyperglycaemia [11–14]. Elevated serum urea carries prognostic significance [7,15,16]. These changes reflect significant physiological derangement, the prediction is usually considered in ‘aggregate’ [17]. It is unclear what influence derangement of osmolar homeostasis may have on mortality in acute medical admissions, and although sodium and glucose homeostasis are accepted as significant factors affecting mortality, serum osmolarity has not been specifically reported in these studies.

In normal circumstances, sodium, glucose and urea all contribute to the serum osmolarity, whereas albumin contributes very little. Hyperosmolarity has been associated with higher mortality among specific patient subgroups such as trauma patients [18] and intensive care patients [19]. The relationship between osmolar imbalance and mortality has not previously been studied among acute medical patients, a more heterogenous group than trauma or ICU patients; moreover whilst individual derangements of sodium, urea or glucose may be quantitated, their interactions in relation to state of body water deficit may be complex [20].

Risk prognostic models may be developed with methods such as logistic regression (LR) or Cox proportional analyses. Despite the

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widespread use of these methods, clinicians often find the application of such prognostic information into clinical practice problematic. We have therefore, using multivariate regression methods, investigated whether the calculated serum osmolarity (at time of an emergency medical admission), either alone or in combination with other predictor variables, could usefully estimate subsequent mortality in a group of over 24,000 patients, presenting to a large university teaching hospital over an eight-year period.

2. Materials and methods

2.1. Background

St. James' Hospital (SJH) is a tertiary referral centre for various specialties, but is on continuous call for emergency medical admissions in its local Dublin catchment area. All such patients requiring hospitalisation, apart from cases admitted directly to the coronary care or intensive care units, are admitted to the Acute Medical Admission Unit (AMAU), essentially a medical unit dedicated to acute care. The 59 bed capacity of the AMAU is sufficient, that with an average of 20 admissions each day, up to 70% of all medical admissions receive their entire hospital care within this environment.

A patient database, established in 2002 to support developments in Acute Medicine, is linked from the patient administration system (PAS) to the Hospital In-Patient Enquiry Scheme (HIPE). HIPE is a national database of coded discharge summaries from acute public hospitals in Ireland. Ireland uses the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; ICD-10 from 2005) for both diagnosis and procedure coding since 1990, with updates every five years [21]. Sixty hospitals nationally participate in the system; it may be useful in investigation patterns of disease and outcome in routinely collected clinical data [22]. Additional biochemical and haematological data were downloaded from other hospital systems; this information can be integrated for other purposes such as score predictions for prognostication [16]. Data related to all emergency medical patients admitted to SJH between the 1st of January 2002 and the 31st of December 2009. For the purposes of prediction, although all patients were assessed, we used each patient once only in the derivation (80% random selection) and validation (20% random sample). Where patients had multiple admissions, for consistency the last episode was selected; approximately 60% of patients had a single admission only. Mortality data was any hospital death recorded within 30 days of the index acute hospital admission. Serum osmolarity was calculated using serum values for sodium, urea and glucose, and using the following formula: 2(sodium) + urea + glucose. Where there was no glucose value requested during the hospital stay, an interpolated normally distributed value was used to maximise the utilisation of the dataset. All laboratory blood test results used were on admission to hospital. No interpolation of urea or sodium was performed.

2.2. Statistical methods

Descriptive statistics for baseline demographic data included as appropriate, means/standard deviations (SD), medians/inter-quartile ranges (IQR) or percentages. Quantile analysis, based on the frequency distribution divided patients into five groups; Q1 $\leq$ 10%, Q2 > 10% and $\leq$25%, Q3 > 25 and $\leq$75%, Q4 > 75 and $\leq$90%, Q5 > 90%. Comparisons between categorical variables and mortality were with Chi-square tests. We used multivariate logistic regression, taking significant ($p<0.1$) predictors identified by the univariate analyses to examine the association between 30-day mortality and the following predictor variables: age, number of admissions, Major Disease Category (MDC), an ICU admission, the Emergency Department Triage Category and time delay to medical referral, troponin status (no request, negative, positive), any blood transfusion, the Charlson co-morbidity index [23] and a time variable related to the introduction of the Acute Medical Admission Unit [24]. For the logistic regression, we used backward and forward stepwise methods to determine whether the AUROC could be usefully increased, by adding or subtracting candidate predictors, whilst testing the ensuing goodness-of-fit using the Hosmer and Lemeshow's test [25]. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated for those predictors that significantly entered the model ($p<0.10$). Statistical significance was at $p<0.05$ throughout. The analysis software was JMP (version 7: SAS Institute Inc.) and Stata (versions 10/11). We calculated the probability of death for each individual from the regression equation above using standard methods [25]. We used the Hanley approach to estimate AUROC statistics [26], and compared the area under the receiver operator curves as previously described.

3. Results

3.1. Patient characteristics (Table 1)

There were twenty four thousand and two hundred and thirty two patients admitted acutely via the ED in the 8 years between Jan 1st 2002–Dec 31st 2009, whose hospital episode had been completed or who died within 30 days. From these medical admissions, 11,040 patients had a glucose determination in the Emergency Department or during the hospital admission. The median length of stay was 4.9 days (IQR 2.0, 9.7); the 90% limit of the length of stay was 19.4 days. Their median age was 59.1 years (IQR 38.3, 76.1) with the upper 10% boundary at 84.1 years respectively; 48.1% were male.

3.2. Logistic regression of osmolarity (unadjusted odds ratios)

The median osmolarity was 292.2 mOsm/kg (IQR 286.4, 297.6); the 90% and 99% values were 303.3 and 340.4 mOsm/kg respectively. Unadjusted odds ratios were calculated from logistic regression of the

Table 1
Details of 24,232 emergency admissions — 2002–09.

Admission characteristics	
Gender n (%)	
Male	11,657 (48.1%)
Female	12,575 (51.9%)
Age (years)	
Median (IQ range)	59.1 (38.3, 76.1)
Length of stay (days)	
Median (IQ range)	4.9 (2.0, 9.7)
Charlson co-morbidity index	
>0	10,539 (43.5%)
>1	4526 (18.7%)
Admission osmolarity (mOsm/kg)	
Median (IQ range)	292.2 (286.4, 297.6)
Mortality by osmolarity quantile[a]	
Q1 (<280)	336/2098 = 3.80%
Q2 (<286)	265/3361 = 7.31%
Q3 (<298)	621/11,493 = 5.13%
Q4 (<303)	353/3282 = 9.71%
Q5 (≥303)	649/1774 = 26.78%
Length of stay (days)	Mean (SD)
Q1 (< 280)	8.8 (7.2)
Q2 (<286)	7.2 (6.8)
Q3 (<298)	6.5 (6.4)
Q4 (<303)	6.7 (6.6)
Q5 (≥303)	8.2 (7.3)

Patient characteristics on admission to hospital.
[a] Number of patients who died/survived, %.