

## Preoperative abnormalities in serum sodium concentrations are associated with higher in-hospital mortality in patients undergoing major surgery

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### Abstract

**Background:** Abnormal serum sodium concentrations are common in patients presenting for surgery. It remains unclear whether these abnormalities are independent risk factors for postoperative mortality.

**Methods:** This is a secondary analysis of the European Surgical Outcome Study (EuSOS) that provided data describing 46 539 patients undergoing inpatient non-cardiac surgery. Patients were included in this study if they had a recorded value of preoperative serum sodium within the 28 days immediately before surgery. Data describing preoperative risk factors and serum sodium concentrations were analysed to investigate the relationship with in-hospital mortality using univariate and multivariate logistic regression techniques.

**Results:** Of 35 816 (77.0%) patients from the EuSOS database, 21 943 (61.3%) had normal values of serum sodium (138–142 mmol litre<sup>-1</sup>) before surgery, 8538 (23.8%) had hyponatraemia (serum sodium  $\leq$ 137 mmol litre<sup>-1</sup>) and 5335 (14.9%) had hypernatraemia (serum sodium  $\geq$ 143 mmol litre<sup>-1</sup>). After adjustment for potential confounding factors, moderate to severe hypernatraemia (serum sodium concentration  $\geq$ 150 mmol litre<sup>-1</sup>) was independently associated with mortality [odds ratio 3.4 (95% confidence interval 2.0–6.0),  $P < 0.0001$ ]. Hyponatraemia was not associated with mortality.

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**Conclusions:** Preoperative abnormalities in serum sodium concentrations are common, and hypernatraemia is associated with increased mortality after surgery. Abnormalities of serum sodium concentration may be an important biomarker of perioperative risk resulting from co-morbid disease.

**Key words:** high-risk surgery; hypernatraemia; hyponatraemia; perioperative medicine

#### Editor's key points

- Abnormalities of serum sodium (dysnatraemia) are likely to be associated with increased perioperative risk.
- Dysnatraemias are more common in those with co-morbidity or undergoing emergency surgery.
- Dysnatraemia could be a useful biomarker of perioperative risk and warrant further investigation before surgery.

Postoperative mortality and morbidity are significant problems for health-care systems.<sup>1–3</sup> A better understanding of the preoperative factors associated with postoperative complications could lead to improved methods of risk stratification. This could allow more effective allocation of perioperative care resources in order to maximize the benefit to the greatest number of patients.<sup>4–6</sup> A number of tests are routinely performed before surgery, but the predictive utility of most investigations is unclear.<sup>7,8</sup> The UK National Institute for Health and Care Excellence (NICE) has confirmed the paucity of information regarding the clinical value of preoperative electrolyte testing.

Serum sodium concentrations are commonly measured before major surgery. Sodium, chloride, and bicarbonate ions contribute ~90% of the extracellular osmolality. In normal homeostatic conditions, serum sodium concentrations are maintained within a very tight range (138–142 mmol litre<sup>-1</sup>), although values slightly outside this range are often considered normal. Previous studies suggest that dysnatraemia, defined as either hyponatraemia or hypernatraemia, is associated with worse outcomes in medical and surgical patients in both hospital wards and intensive care units (ICUs)<sup>9–14</sup> and is associated with increased health-care costs.<sup>15</sup> However, there are few published data exploring the association between preoperative dysnatraemia and postoperative adverse outcomes. Recently, Leung and colleagues<sup>16,17</sup> reported that both preoperative hypo- and hypernatraemia are independently associated with increased hospital mortality, length of hospital stay, and complications in surgical patients. Similar associations have been found in postsurgical ICUs.<sup>18</sup> Given that derangements of serum sodium are detected using routine preoperative blood tests and are potentially treatable, understanding the implications of dysnatraemia for perioperative outcomes is of great importance.

We therefore performed a secondary analysis of data collected during the European Surgical Outcomes Study (EuSOS)<sup>19</sup> to describe the relationship between preoperative serum sodium concentration and postoperative mortality, in order to evaluate whether dysnatraemia is independently associated with death after surgery.

## Methods

This study is a secondary analysis of data collected during a major prospective observational study of non-cardiac surgery (EuSOS). The investigators collected data on all patients undergoing surgery in participating hospitals within a 1 week period in April 2011. Full methodological details can be found in the original publication.<sup>19</sup>

All surgical patients were enrolled unless they were <16 yr of age or were having outpatient, obstetric, cardiac, or neurosurgical procedures.

### Cohort description

Patients were included in this analysis if there were complete data describing preoperative serum sodium measurements and postoperative hospital mortality in the database. For the purposes of the present study, a preoperative serum sodium measurement was the most recent measurement performed within the 28 days before surgery. Patients were excluded if they were recruited in a hospital that provided data describing 10 patients or fewer in the study week, or in hospitals above the 95th centile for mortality.

### Definitions

For the analyses, seven intervals were defined from severe hyponatraemia to severe hypernatraemia, with the reference serum sodium interval defined as being between 138 and 142 mmol litre<sup>-1</sup>.

### Statistical analysis

The primary outcome measure was in-hospital mortality, censored at 30 days. Statistical analyses were performed with SAS (version 9.2, produced by Statistical Analytical Software, North Carolina State University, USA) and R (version 2.13.0 produced by R Development Core Team). Categorical variables are presented as *n* (%) and continuous variables as mean (SD). Results of statistical models are reported as adjusted odds ratios (ORs) with 95% confidence intervals (CIs).

General estimating equations were used to assess the association between preoperative serum concentration and subsequent postoperative in-hospital mortality. First, the association between the risk factors and in-hospital mortality was explored using logistic regression analysis, including the dysnatraemia groups as fixed factors only. All factors significantly associated with mortality (*P*<0.05) were then entered as covariables into a general estimating equation regression model, accounting for clustering of patients within sites. Patients were excluded if their data were missing values for any of the covariates. Patients with serum sodium concentrations within the normal range (138–142 mmol litre<sup>-1</sup>) were used as the reference group. To account for multiple comparisons, an adjusted two-sided significance level of *P*<0.008 (0.05/6) was applied.

In order to illustrate graphically the association between preoperative serum sodium concentration and mortality, a logistic regression function was estimated using splines. We expected the association between mortality and extreme values for serum sodium concentrations to be unreliable because of low patient numbers. Patients with serum sodium values from the lowest and highest 0.25% of values were therefore excluded from the analysis. In a secondary analysis, resource utilization variables were compared across the sodium categories in univariate analysis using the analysis of variance (ANOVA) and  $\chi^2$  tests.

Three sensitivity analyses were performed to assess the robustness of the results. Two multivariate generalized estimating

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