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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^{-1}) before surgery, 8538 (23.8%) had hyponatraemia (serum sodium ≤137 mmol litre^{-1}) and 5335 (14.9%) had hypernatraemia (serum sodium ≥143 mmol litre^{-1}). After adjustment for potential confounding factors, moderate to severe hypernatraemia (serum sodium concentration ≥150 mmol litre^{-1}) 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.[1–3] 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.[4–6] A number of tests are routinely performed before surgery, but the predictive utility of most investigations is unclear.[7 8] 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^{-1}), 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)[9–14] and is associated with increased health-care costs.[15] However, there are few published data exploring the association between preoperative dysnatraemia and postoperative adverse outcomes. Recently, Leung and colleagues[16 17] 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.[18] 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)[19] 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.[19] 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^{-1}.

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^{-1}) 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 χ^2 tests.

Three sensitivity analyses were performed to assess the robustness of the results. Two multivariate generalized estimating equation regression models were developed using the categories of hyponatraemia, normal serum sodium, and hypernatraemia, where borderline dysnatraemia was included in either the normal or dysnatraemia groups. To adjust for multiple testing (comparison of the two dysnatraemia groups with reference) an adjusted two-sided significance level of $P<0.025$ (0.05/2) was applied. A number of sensitivity analyses were performed. These included the following: (i) a multiple imputation methodology that was performed to account for the influence of selection bias through preoperative sodium measurements; and (ii) a propensity score analysis that was performed to account further for this factor. The propensity score-matched analysis was performed for the multivariate model for hospital mortality, adjusting it based on the propensity score for serum sodium measurement. The propensity score was calculated using logistic regression on the full data set, including patients with no available data describing serum sodium, and then introduced into the multivariate model.

Results

Cohort description and prevalence of dysnatraemias

From the full EuSOS cohort of 46 539 patients, a total of 35 816 patients were included in this analysis (Table 1 and Supplementary data Table S1). The mean (SD) age was 59 (18) yr, and 17 683 patients (49%) were male. Of the total number of patients, 26 282 (73%) were presenting for elective surgery. For 21 943 (61.3%) patients, the serum sodium measurement was within the 138–142 mmol litre^{-1} interval, whereas 8538 (23.8%) patients were hyponatraemic (serum sodium ≤137 mmol litre^{-1}) and 5335 (14.9%) were hypernatraemic (serum sodium concentrations ≥143 mmol litre^{-1}). Patients presenting with dysnatraemia were more likely to undergo emergency surgery (Table 1) and to present with co-morbid disease (Table 2). Hyponatraemia and hypernatraemia were twice as frequent in patients with cirrhosis, congestive heart failure, or coronary artery disease as in those who did not have these diseases. Hyponatraemia was also more prevalent in patients with chronic obstructive pulmonary disease (Table 2).

Association of dysnatraemias with mortality

In the univariate analysis, both hyponatraemia and moderate to severe hypernatraemia were associated with increased mortality (Table 3). In the logistic regression model, after correcting for age, gender, ASA score, co-morbid disease, surgical procedure category, severity, grade, and urgency of surgery, only moderate and severe hypernatraemia were significantly associated with increased mortality [OR 3.4 (95% CI 2.0–6.0), $P<0.001$]. The association between mortality and serum sodium concentration is

Table 1 Basic patient characteristics of cohort split by preoperative serum sodium measurement. COPD, chronic obstructive pulmonary disease

Baseline characteristics	Total	≤130 mmol litre^{-1}	131–135 mmol litre^{-1}	136–137 mmol litre^{-1}	138–142 mmol litre^{-1}	143–144 mmol litre^{-1}	145–149 mmol litre^{-1}	≥150 mmol litre^{-1}	P-value
Number of patients [n (%)]	35 816 (100)	602 (1.7)	3338 (9.3)	4598 (12.8)	21 943 (61.3)	3805 (10.6)	1422 (4.0)	108 (0.3)	
Age (yr)	58.5 (18.2)	67.2 (16.2)	63.0 (17.9)	58.5 (18.9)	57.3 (18.1)	59.2 (17.1)	60.4 (17.5)	62.8 (18.9)	<0.0001
Male sex [n (%)]	17 683 (49)	303 (50.3)	1686 (50.5)	2322 (50.5)	10 740 (49.0)	1861 (48.9)	712 (50.1)	59 (54.6)	0.26
Urgency of surgery [n (%)]									
Elective	26 282 (73.4)	252 (41.9)	1732 (51.9)	2998 (65.2)	16 988 (77.4)	3129 (82.2)	1130 (79.5)	53 (49.1)	<0.0001
Urgent	7394 (20.6)	257 (42.7)	1189 (35.6)	1228 (26.7)	3932 (17.9)	532 (14)	223 (15.7)	33 (30.6)	<0.0001
Emergency	2140 (6)	93 (15.5)	417 (12.5)	372 (8.1)	1023 (4.7)	144 (3.8)	69 (4.9)	22 (20.4)	<0.0001
General anaesthesia	27 804 (77.6)	463 (76.9)	2557 (76.6)	3605 (78.4)	17 111 (78.0)	2908 (76.4)	1073 (75.5)	87 (80.6)	0.05
ASA score [n (%)]									
I	7732 (21.6)	40 (6.7)	389 (11.7)	943 (20.6)	5246 (24.0)	823 (21.7)	277 (19.6)	14 (13.0)	<0.0001
II	16 619 (46.5)	178 (29.8)	1263 (37.9)	1956 (42.6)	10 625 (48.5)	1901 (50)	666 (47)	30 (27.8)	<0.0001
III	9929 (27.8)	297 (49.7)	1368 (41.0)	1423 (31.0)	5426 (24.8)	978 (25.7)	402 (28.4)	35 (32.4)	<0.0001
IV	1389 (3.9)	77 (12.9)	299 (9.0)	248 (5.4)	570 (2.6)	100 (2.6)	69 (4.9)	26 (24.1)	<0.0001
V	78 (0.2)	6 (1)	14 (0.4)	19 (0.4)	33 (0.2)	0 (0)	3 (0.2)	3 (2.8)	<0.0001

Table 2 Co-morbidities by preoperative serum sodium measurement. COPD, chronic obstructive pulmonary disease; ID, insulin dependent; NID, non-insulin dependent

Co-morbidities	Total	≤130 mmol litre^{-1}	131–135 mmol litre^{-1}	136–137 mmol litre^{-1}	138–142 mmol litre^{-1}	143–144 mmol litre^{-1}	145–149 mmol litre^{-1}	≥150 mmol litre^{-1}	P-value
Cirrhosis	427 (1.2%)	26 (4.3%)	81 (2.4%)	61 (1.3%)	194 (0.9%)	38 (1%)	22 (1.6%)	5 (4.6%)	<0.0001
Congestive heart failure	1830 (5.1%)	72 (11.9%)	271 (8.1%)	275 (6.0%)	939 (4.3%)	174 (4.6%)	86 (6.1%)	13 (12.0%)	<0.0001
COPD	4220 (12.0%)	104 (17.2%)	515 (15.5%)	569 (12.4%)	2423 (11.1%)	412 (10.8%)	186 (13.1%)	11 (10.2%)	<0.0001
Coronary artery disease	5289 (15%)	147 (24.4%)	709 (21.3%)	754 (16.4%)	2900 (13.2%)	532 (14%)	225 (15.8%)	22 (20.4%)	<0.0001
Diabetes mellitus ID	1786 (5%)	70 (11.6%)	326 (9.8%)	304 (6.6%)	884 (4.0%)	136 (3.6%)	59 (4.2%)	7 (6.5%)	<0.0001
Diabetes mellitus NID	2919 (8.2%)	71 (11.8%)	373 (11.2%)	428 (9.3%)	1637 (7.5%)	283 (7.4%)	116 (8.2%)	11 (10.2%)	<0.0001
Metastatic cancer	1898 (5.3)	61 (10.1%)	265 (8.0%)	272 (5.9%)	1026 (4.7%)	196 (5.2%)	66 (4.7%)	12 (11.1%)	<0.0001
Stroke	1748 (4.9%)	53 (8.8%)	236 (7.1%)	260 (5.7%)	953 (4.4%)	163 (4.3%)	74 (5.2%)	9 (8.3%)	<0.0001

Table 3 Odds ratios for in-hospital mortality according to preoperative serum sodium, patient characteristics, and type of surgery. Odds ratios [OR (95% confidence intervals)] are presented for the univariate and multivariate analysis (adjusted in a two-level analysis with patient at the first level and site at the second level)

Serum sodium intervals	OR (univariate model)	*P*-value	OR (multivariate analysis)	*P*-value
Normal range (138–142 mmol litre^{-1})	Reference		Reference	Reference
Severe hyponatraemia (Na ≤130 mmol litre^{-1})	3.5 (2.6–4.6)	<0.0001	1.4 (1.0–2.0)	0.061
Moderate hyponatraemia (Na 131–135 mmol litre^{-1})	2.3 (1.9–2.7)	<0.0001	1.3 (1.0–1.6)	0.033
136–137 mmol litre^{-1} Na range	1.4 (1.1–1.6)	0.0007	1.0 (0.8–1.2)	0.94
143–144 mmol litre^{-1} Na range	1.1 (0.9–1.3)	0.55	1.1 (0.9–1.3)	0.48
Moderate hypernatraemia (Na 145–149 mmol litre^{-1})	1.8 (1.4–2.3)	<0.0001	1.3 (1.0–1.8)	0.074
Severe hypernatraemia (Na ≥ 150 mmol litre^{-1})	10.1 (6.3–16.1)	<0.0001	3.4 (2.0–5.9)	<0.0001

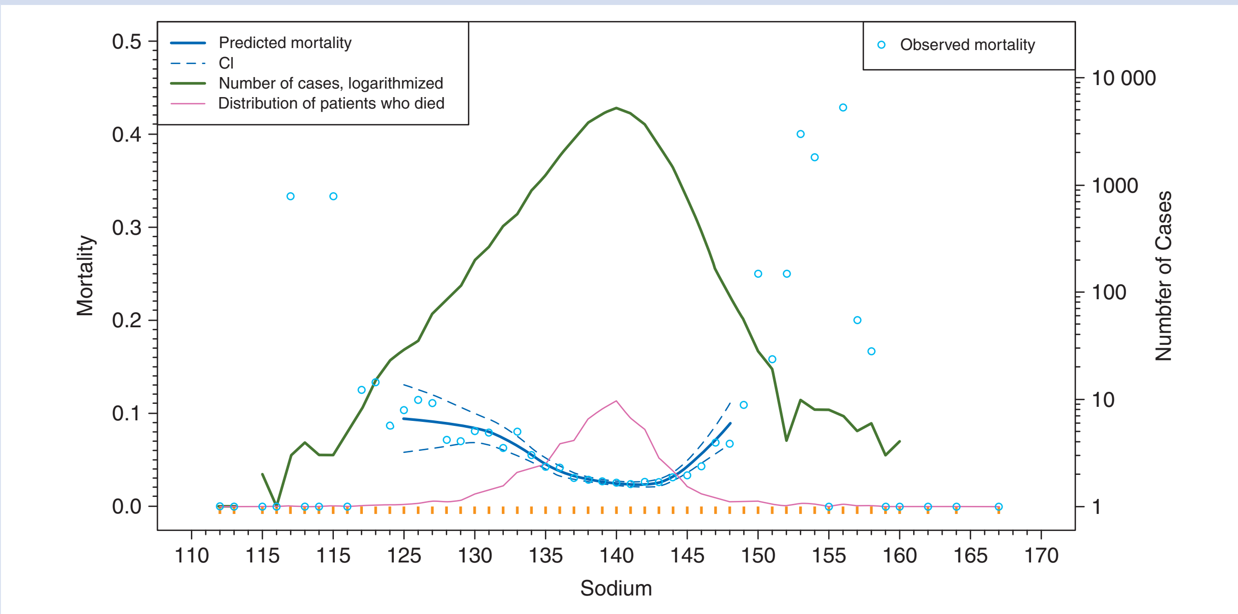

Fig 1 Distribution of sodium concentration-predicted mortality and contribution to total mortality according to sodium concentration (in millimoles per litre) in the total study population. CI, confidence interval.

shown in Figure 1. Overall, patients with serum sodium concentrations <136 mmol litre^{-1} represented 11% of the overall population and accounted for 243 deaths (6.2% mortality in this category), which represented 20.1% of all deaths. Patients with a serum sodium >144 mmol litre^{-1} represented 4.3% of the overall population. They accounted for 87 deaths (5.7% mortality in this category) and 7.4% of all deaths. Both hypo- and hypernatraemia were associated with a three-fold greater use of central venous catheters during surgery. Patients with serum sodium <130 or >150 mmol litre^{-1} were, respectively, three and five times more likely to be admitted to critical care after surgery. The use of both mechanical ventilation and inotropic support in the immediate postoperative period was also greater for patients with dysnatraemia (Table 4). Graphical representation of mortality in the overall, the elective, and the non-elective population is present in Figure 2.

Sensitivity analyses

Owing to the proportion of patients with missing serum sodium values in the initial cohort (21%), a multiple imputation analysis was performed, which confirmed the original multivariate analysis. A propensity analysis with probability of having serum sodium measured being the outcome was conducted to validate the association between preoperative serum sodium and mortality. The effect of serum sodium on mortality was significant even after this adjustment, meaning that the association between serum sodium and mortality were maintained even after correcting for this factor (see Supplementary data Table S4).

Discussion

The principal findings of this study were that dysnatraemia was common in patients presenting for non-cardiac surgery, and was significantly associated with mortality. However, after correction for confounding factors, only severe hypernatraemia was independently associated with mortality. Our results suggest that although abnormal serum sodium concentrations may be associated with adverse postoperative outcomes, it is likely that the underlying cause of the abnormality has much greater prognostic significance. Preoperative serum sodium abnormalities

Table 4 Perioperative outcomes according to preoperative serum sodium values

Outcomes	Total	≤130 mmol litre^{-1}	131–135 mmol litre^{-1}	136–137 mmol litre^{-1}	138–142 mmol litre^{-1}	143–144 mmol litre^{-1}	145–149 mmol litre^{-1}	≥150 mmol litre^{-1}	P-value
In-hospital mortality [n (%)]	1172 (3.3)	51 (8.5)	192 (5.8)	162 (3.5)	574 (2.6)	106 (2.8)	64 (4.5)	23 (21.3)	<0.0001
Length of stay in hospital [days; median (IQR)]	4.0 (2.0–7.0)	7.0 (3.0–15.0)	6.0 (2.0–11.0)	4.0 (2.0–8.0)	3.0 (1.0–7.0)	3.0 (1.0–6.0)	3.0 (2.0–7.0)	7.0 (2.0–16.0)	<0.0001
Admitted to critical care [n (%)]	3028 (8.5)	112 (18.6)	469 (14.1)	454 (9.9)	1532 (7.0)	275 (7.2)	149 (10.5)	37 (34.2)	<0.0001
Non-invasive ventilation within 24 h [n (%)]	368 (1.0)	8 (1.3)	43 (1.3)	52 (1.1)	211 (1.0)	35 (0.9)	18 (1.3)	1 (1.0)	0.63
Mechanical ventilation within 24 h [n (%)]	1307 (3.7)	62 (10.3)	237 (7.1)	203 (4.4)	590 (2.7)	109 (2.9)	78 (5.5)	28 (26.0)	<0.0001
Inotrope or vasopressor [n (%)]	1079 (3.0)	59 (9.8)	219 (6.6)	162 (3.5)	481 (2.2)	72 (1.9)	64 (4.5)	22 (20.4)	<0.0001
Central venous catheter inserted [n (%)]	2766 (7.7)	99 (16.6)	436 (13.1)	416 (9.1)	1386 (6.3)	255 (6.7)	145 (10.2)	29 (26.90)	<0.0001

therefore remain an important biomarker of postoperative mortality risk.

Our findings differ from those of previous studies in the sense that in our study only severe hypernatraemia was independently associated with increased mortality after surgery. These results are in contrast with the findings of Leung and colleagues[16 17] in the perioperative setting and studies in medical and critically ill patients.[9 11 20] In two separate studiess from a large American database, Leung and colleagues[16 17] found that both hyponatraemia and hypernatraemia were independently associated with increased mortality and incidence of postoperative complications. In a large cohort of patients from the Austrian Center for Documentation and Quality Assurance in Intensive Care, Funk and colleagues[11] found that mild degrees of dysnatraemia (hyponatraemia and hypernatraemia) were associated with worse outcome. This was confirmed recently by Darmond and colleagues[9] in another large multicentre study in French ICUs. From a physiological point of view, dysnatraemia originates from disturbances in water balance;[10 21] this is normally under the control of antidiuretic hormone.[14 21] Several preoperative conditions may predispose patients to a deranged water balance, such as volume depletion, pain, nausea, and preoperative co-morbid conditions, such as heart failure or cirrhosis. In the context of hyponatraemia, in patients requiring long-term renal replacement therapy, Waikar and colleagues[22] demonstrated that the association between mortality and hyponatraemia was independent of antidiuretic hormone activity. This association was also found in the SAPS II and APACHE II score[23 24] validations studies. In our study, we collected data for a wide range of co-morbidities. It is possible that our results differ from previous studies because we corrected better for preoperative co-morbidities. Another possible explanation for the difference between our results and previous literature is that we may have stratified hyponatraemia in more detail. It is possible that the classification used in our study allowed for a better stratification and therefore a more robust correction for confounding factors in the multivariate analysis. Nonetheless, the results regarding hypernatraemia are consistent with the published literature.[17] In the multivariate analysis, after adjusting for confounding factors we found a more than three-fold increase in mortality for patients presenting with serum sodium higher than 149 mmol litre^{-1} (OR 3.42). There are several possible explanations for this finding. First, it is possible that these patients were dehydrated, which was not a variable we collected in our data set, and were thus unable to correct for it; and secondly, it is possible that they were more exposed to significant fluid and electrolyte shifts during the perioperative period.[25 26] A further possible explanation could relate to other adverse effects of hypernatraemia, such as increased peripheral insulin resistance[27] and decreased cardiac contractility.[28] We also investigated the urgency of surgery as a possible confounding factor. In this sense, it is important to note that even if patients with hypernatraemia undergoing urgent and emergency surgery had a higher mortality than patients undergoing elective surgery (Fig. 2), the relationship between severe hypernatraemia and mortality was maintained after correcting for these factors.

These results have important implications in the perioperative setting. Although from our analysis it is difficult to justify serum sodium correction before surgery, dysnatraemia should be seen as a warning flag or a biomarker for risk of mortality and should prompt investigation for underlying disease processes that may warrant treatment before the commencement of surgery. In practice, our analysis suggests that preoperative serum sodium concentrations could be used to stratify perioperative mortality risk. It is a routine and cheap test, and in practice,

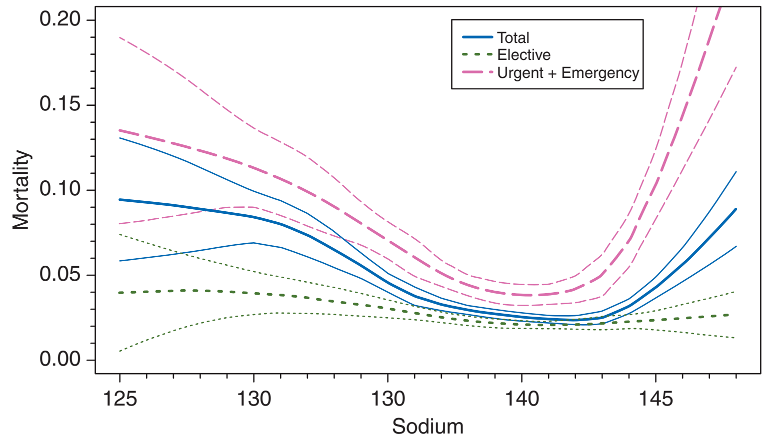

Fig 2 Predicted mortality according to sodium concentration in the total study population and in elective and non-elective (urgent plus emergency) surgery. On the y-axis, mortality rate (from 0 to 1). On the x-axis, sodium range (in millimoles per litre). Data are presented for the overall population (total; blue lines), for the elective population (elective; green lines) and for the non-elective population (urgent + emergency; pink lines). For each of the three groups, the central line represents the mean mortality for the sodium value and the top and bottom lines represent the 95% confidence interval.

behaves as a postoperative mortality biomarker related to the comorbidity status of surgical patients. Interestingly, although this may seem obvious, our data suggest that clinicians do not use serum sodium in this way. This is apparent when we look at resource utilization. In our study, dysnatraemia was also associated with different resource utilization in terms of ICU admission, use of ventilation, vasoactive drugs, central lines, and cardiac output monitors, but not all patients in the highest risk group used the same level of resources. Patients with moderate and severe hypernatraemia showed an in-hospital mortality in excess of 21%, but only <35% of this group were admitted to an ICU. It is difficult to interpret these results, because there may be many reasons for which high-risk surgical patients are not admitted to a critical care unit after surgery,[29] and can be explained partly by different resource availability and practice among the departments that took practice in the study; our results, however, suggest that risk was either not recognized or not acted upon, either for lack of resources or for clinical reasons.

Our study has several limitations. First, the original EuSOS database was not designed to investigate the effect of preoperative dysnatraemia on outcome. Second, we had no control on the timing of the blood test before surgery (we only knew that it was performed within 28 days before surgery). It is also not known whether some of the patients had already received specific treatment for dysnatraemia before or after the blood test and before or after surgery. It is also possible that severe hypernatraemia was still associated with mortality even in the multivariate analysis because other variables related to hypernatraemia were not collected in the EuSOS database; for instance, there was no descriptive description of volaemic status of these patients.

Conclusions

Dysnatraemia is a common finding in patients about to undergo surgery and is associated with increased mortality. However, after correction for other risk factors, this association with mortality is weakened, suggesting that other risk factors may be of greater importance, and only severe hypernatraemia was independently associated with increased mortality. Further research is needed to establish whether preoperative measurement of serum sodium has a valid role in assessment of mortality risk before surgery and whether treatment of dysnatraemia before surgery could improve outcome.

Ethics approval

This was a secondary analysis of the EuSOS database.[19] For the original publication, ethics requirements differed by country. In Denmark, centres were exempt from ethics; in all other nations, ethics approval was applied for and given. In Finland, written informed consent was obtained from individual patients. No additional research ethics committee approval was required for this publication.

Authors' contributions

Design of the study: M.Ce.
Participated in design of the study: P.M., R.P., A.R.
Supervised the statistical analysis: M.P.
Performed the statistical analysis: H.H., P.M.
Participated in analysis of the data: M.Ce., A.R.
Interpreted the data: H.H.
Interpreted the results: M.Ce.
Participated in interpretation of the data: M.Ch., M.G., A.H., E.H., I.J., M.P., P.M., P.P., R.M., R.P., J.-L.V., A.R.
Drafted the manuscript: M.Ch., M.G., A.H., E.H., I.J., M.P., P.M., P.P., R.M., R.P., J.-L.V., A.R.
Wrote the manuscript: M.Ce.
Participated in writing the manuscript: H.H.
Approved the final version of the manuscript: M.Ce., H.H., M.Ch., M.G., A.H., E.H., I.J., M.P., P.M., P.P., R.M., R.P., J.-L.V., A.R.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

Declaration of interest

R.P. has received honoraria or speaking fees from Edwards Lifesciences, Massimo, and Nestle Health Sciences, and a research

grant from Nestle Health Sciences. R.P. is a member of the Associate Editorial Board of the *British Journal of Anaesthesia*. Other authors: none declared.

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