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ORIGINAL RESEARCH

Are lower preoperative serum sodium levels associated with postoperative surgical site infection? Results from a propensity matched case-control study

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Background: We previously reported a statistical trend toward a harmful association between lower preoperative serum sodium levels and surgical site infection (SSI) in South African (SA) laparotomy patients. Serum sodium tests are widely available and could serve as a cost-effective method for preoperatively identifying patients at risk for SSI who might benefit from additional preventative strategies. We sought to investigate the possible association between lower serum sodium levels and SSI further, in a larger sample of SA patients undergoing various surgical procedures.

Objective: To determine if lower preoperative serum sodium levels are associated with SSI in SA surgical patients.

Method: This was a propensity matched case-control study involving data from 729 surgical patients who attended a quaternary SA hospital between 01 January 2012 and 31 July 2016. Cases were defined as patients who developed SSI. Controls were defined as patients who did not develop SSI. Multivariate logistic regression was used to investigate the association between preoperative serum sodium levels (in mmol/L) and SSI.

Results: Lower preoperative serum sodium levels were associated with a higher risk of SSI (odds ratio per 1.0 mmol/L decrease in serum sodium: 1.051, 95% confidence interval: 1.007–1.097; $p = 0.026$).

Conclusion: Although we report a statistically significant association between lower preoperative serum sodium levels and a higher risk of SSI, the magnitude of this effect size (odds ratio) is minimal and clinically insignificant. Preoperative serum sodium levels are unlikely to be useful for SSI risk stratification in our setting.

Keywords: preoperative period, sodium, surgical wound infection, surgical site infection

Introduction

Surgical site infection (SSI) is an important postoperative complication in African settings, where it is associated with increased morbidity, mortality, and healthcare resource utilisation.[1,2] Preoperative identification of high-risk patients in these settings would allow for a full range of preventative strategies to be implemented throughout the perioperative period.[3] We recently demonstrated the pitfalls of using conventional SSI risk stratification methods, namely the National Nosocomial Infections Surveillance (NNIS) score and the Study of the Efficacy of Nosocomial Infection Control (SENIC) score, in South African (SA) patients undergoing abdominal surgery.[4] A major limitation is that intraoperative variables are required to compute these scores. Accordingly, these scoring systems cannot be used preoperatively to estimate postoperative SSI risk.[4] On the other hand, our previous research also suggests that routinely measured analytes, such as serum albumin, can be used during the preoperative period to provide postoperative estimates of SSI risk that are comparable to those provided by the NNIS and SENIC scores.[4] In another of our prior studies, involving 439 SA laparotomy patients, we found a statistical trend toward a harmful association between lower preoperative serum sodium and SSI.[5] Serum sodium measurements are widely available, cost-effective tests that are usually ordered as part of the urea and electrolyte panel.[6] The panel is used to screen for renal impairment during the preoperative and postoperative period.[7] We sought to investigate the possible association between lower serum sodium levels and SSI further, in a larger sample of patients undergoing various surgical procedures.

Materials and methods

Study design

This was a propensity matched case-control study.

Study setting

The study setting was the Inkosi Albert Luthuli Central Hospital (IALCH) in Durban, South Africa. This public-sector, quaternary level hospital provides surgical and medical services to residents of the eastern seaboard of South Africa.

Study sample

The study sample consisted of adult patients (aged ≥ 18 years old) who underwent surgical procedures at IALCH between 01 January 2012 and 31 July 2016. Additional eligibility criteria

used to derive the study sample are provided in Table I. Our decision to include only patients who had orthopaedic, vascular, general, or gynaecology surgeries in this study was based on the findings of our prior research involving procedure rates and SSI at IALCH.[2]

Table I: Additional eligibility criteria for this study

Inclusion criteria	Exclusion criteria
Patients who underwent orthopaedic, vascular, general, or gynaecology surgery	Patients with missing data required for matching or missing preoperative sodium measurement
	Patients with complete datasets but who could not be matched

Data sources and definitions

The hospital electronic admissions system was used to identify surgical patients, establish the surgical speciality involved, determine patient age and gender, determine the nature of the surgery and its indication, as well as calculate the duration of surgery in minutes. This information, along with the patient hospital number, was directly extracted from the electronic admissions system and saved as a Microsoft Excel spreadsheet. The duration of surgery was calculated as the time in minutes between skin incision and closure of the surgical wound. Surgical wounds were classified as clean, clean/contaminated, contaminated, or dirty/infected.[8] Serum sodium measurements and microbiological culture tests were performed by a National Health Laboratory Service (NHLS) facility located on IALCH premises. We received approval from the NHLS to access preoperative serum sodium test results and microbiological culture results during the study period. We used the patient hospital number to link patients in the Microsoft Excel spreadsheet with preoperative serum sodium and postoperative microbiology results on the NHLS system. The closest preoperative serum sodium measurement was used. Although the preoperative sodium is usually measured by surgeons and anaesthetists within four weeks prior to surgery, measurements outside this period are acceptable for patients who are clinically stable (i.e. those patients without significant comorbidity or those considered very low risk for perioperative complications) in our setting. It is common practice at IALCH for surgeons to collect pus swabs for microbiological culture from surgical wounds which appear infected on clinical examination. For the purpose of this research, all pus swabs were treated as SSIs (irrespective of the final culture result). This is in keeping with the definition of SSI proposed by the Centers for Disease Control, which does not necessarily require a positive microbiological culture result when establishing the presence of a SSI.[9] We extended our review of microbiological culture orders for each patient up to 30 days postoperatively. Cases were defined as patients who experienced SSI within 30 days postoperatively. Controls were defined as patients who did not experience SSI within 30 days postoperatively. The Microsoft Excel spreadsheet was imported into R version 3.6.2 (R Foundation, Vienna, Austria) for the matching process and the subsequent statistical analysis.

Matching

Patients were matched on surgical speciality, surgical wound class, and duration of surgery using "nearest neighbour" propensity matching.[10] This approach involves deriving a propensity score based on an initial binary logistic regression model in which all the matching variables are entered. Cases are then matched with controls that share similar propensity score values. A case:control ratio of 1:2 was used as this ratio has been demonstrated to add optimal statistical power to a case-control study.[11] The matching process was qualitatively evaluated using a jitter plot.

Statistical analysis

Descriptive statistics were used to summarise the characteristics of the entire study sample. This involved calculating means with standard deviations (SD) for continuous variables, and frequency distributions with percentages for categorical variables. We compared characteristics between case and control groups using univariate binary logistic regression. We then tested for a possible relationship between preoperative serum sodium levels and SSI using a conditional multivariate binary logistic regression model which was adjusted for patient age, gender, and time in weeks between the sodium measurement and surgery. For conditional regression models, only those variables which did not form part of the matching process are entered into the regression equation. Results of the univariate and multivariate binary logistic regression analyses are presented as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was set at $p < 0.050$.

Results

Figure 1 shows how the final study sample was derived. The final study sample consisted of 729 patients (243 cases matched with 486 controls). The jitter plot shows a fairly similar distribution of propensity scores in matched case and control groups (Figure 2), indicating that the matching process was satisfactory.

The characteristics of the study sample are described in Table II. The mean age of the study sample was 54.4 years old, and just over half of the study population were male. The most common procedures were vascular surgery procedures, which comprised 52.9% of the study sample. While most surgical wounds were categorised as clean wounds (57.6%), there was still a substantial proportion of surgical wounds which were categorised as dirty/infected wounds (28.4%). The mean duration of the surgical procedure was 102.7 minutes. The mean preoperative sodium level in the study sample was 138.7 mmol/L.

A distribution of characteristics between case-control groups and the results of the univariate statistical analysis is shown in Table III. As expected, the matching process produced no statistical differences in surgical speciality, wound class, or duration of surgery between case and control groups. For the unmatched variables, there was no statistically significant difference observed for age, gender, or number of weeks between sodium measurement and surgery. However, there was a

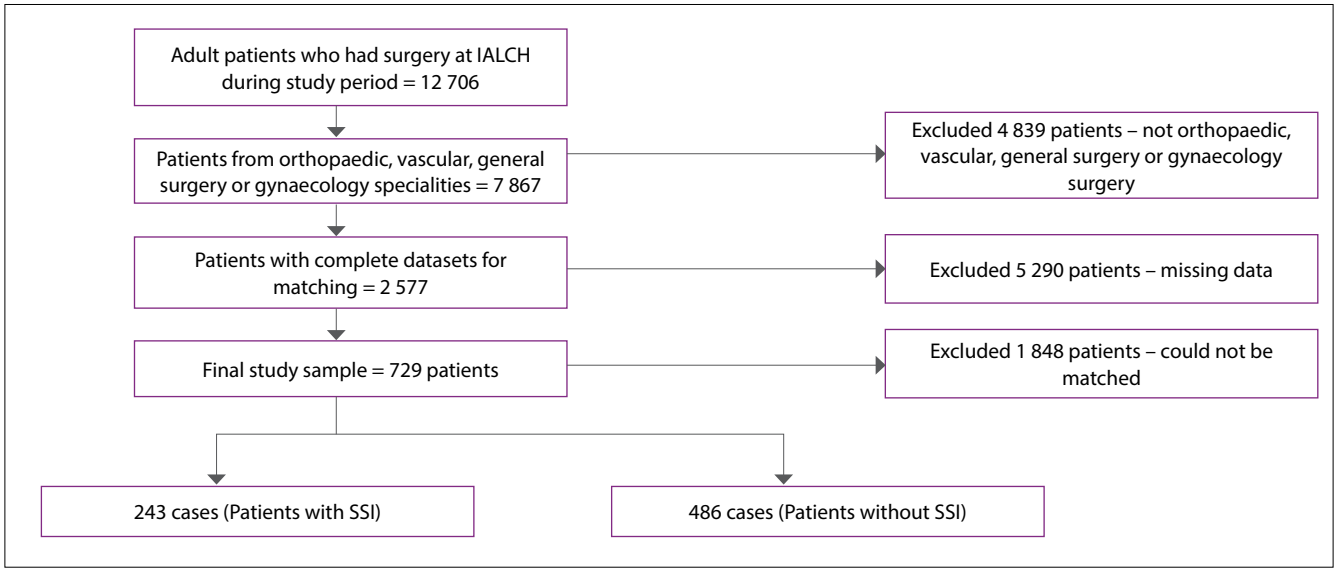

Figure 1: Derivation of the study sample

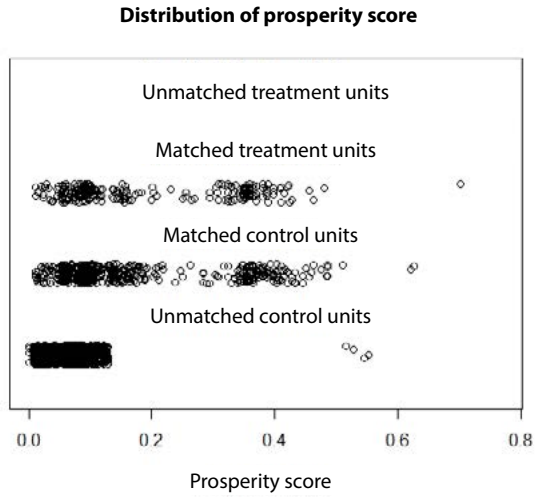

Figure 2: Jitter plot showing distribution of propensity scores in matched cases (treatment units) and controls.

Table II: Description of the study sample

Characteristic	Summary statistic
Mean age, years (SD)	54.4 (16.0)
Female gender, *n* (% of *n* = 729)	352 (48.3)
Male gender, *n* (% of *n* = 729)	377 (51.7)
Orthopaedic surgery, *n* (% of *n* = 729)	202 (27.7)
Vascular surgery, *n* (% of *n* = 729)	386 (52.9)
General surgery, *n* (% of *n* = 729)	120 (16.5)
Gynaecology surgery, *n* (% of *n* = 729)	21 (2.9)
Clean wound, *n* (% of *n* = 729)	420 (57.6)
Clean-contaminated wound, *n* (% of *n* = 729)	86 (11.8)
Contaminated wound, *n* (% of *n* = 729)	16 (2.2)
Dirty/infected wound, *n* (% of *n* = 729)	207 (28.4)
Mean duration of surgery, minutes (SD)	102.7 (79.3)
Mean time between sodium test and surgery, weeks (SD)	3.5 (10.2)
Mean preoperative serum sodium, mmol/L (SD)	138.7 (3.6)

Table III: Results of the univariate statistical analysis

Characteristic	Cases (*n* = 243)	Controls (*n* = 486)	OR (CI)*	*p*
Mean age, years (SD)	54.8 (15.1)	54.2 (16.4)	1.002 (0.993–1.102)	0.656
Female gender, n (% of *n*)	125 (51.4)	226 (46.7)	Reference category	–
Male gender, n (% of *n*)	118 (48.6)	259 (53.3)	0.827 (0.608–1.126)	0.228
Orthopaedic surgery, n (% of *n*)	78 (32.1)	124 (25.5)	Reference category	–
Vascular surgery, n (% of *n*)	118 (48.6)	268 (55.1)	0.700 (0.490–1.000)	0.050
General surgery, n (% of *n*)	39 (16.0)	81 (16.7)	0.765 (0.476–1.232)	0.271
Gynaecology surgery, n (% of *n*)	8 (3.3)	13 (2.7)	0.978 (0.388–2.468)	0.963
Clean wound, n (% of *n*)	126 (51.9)	294 (60.5)	Reference category	–
Clean-contaminated wound, n (% of *n*)	31 (12.8)	55 (11.3)	1.315 (0.808–2.141)	0.270
Contaminated wound, n (% of *n*)	8 (3.3)	8 (1.7)	2.333 (0.857–6.355)	0.097
Dirty/infected wound, n (% of *n*)	78 (32.0)	129 (26.5)	1.411 (0.994–2.002)	0.054
Mean duration of surgery, minutes (SD)	95.7 (77.9)	106.2 (79.9)	0.998 (0.996–1.000)	0.094
Mean time between sodium test and surgery, weeks (SD)	4.0 (14.5)	2.6 (8.2)	1.011 (0.997–1.026)	0.119
Mean preoperative serum sodium, mmol/L (SD)	138.3 (4.0)	138.9 (3.4)	1.051 (1.007–1.097)	0.022

*Risk estimate for age and surgery duration based on per unit increase. Risk estimate for mean preoperative serum sodium based on per unit decrease. Reference category for male gender = "Female".

Table IV: Results of the multivariate statistical analyses

Characteristic	OR (CI)*	*p*
Age in years, per unit increase	0.999 (0.989–1.009)	0.840
Male gender	0.820 (0.599–1.122)	0.215
Time between sodium test and surgery, per week increase	1.011 (0.996–1.026)	0.147
Preoperative serum sodium in mmol/L, per unit decrease	1.051 (1.007–1.097)	0.026

*Reference category for male gender = "Female".

statistically significant difference in preoperative serum sodium levels between case and control groups.

The results of the conditional binary logistic regression analyses are shown in Table IV. When the analysis was adjusted for age, gender, and time between the sodium measurement and surgery, lower preoperative serum sodium levels (per 1.0 mmol/L decrease) were found to be associated with a higher likelihood of developing SSI (OR: 1.051, CI: 1.007–1.097; $p = 0.026$).

Discussion

We found a statistically significant association between lower preoperative serum sodium levels and a higher risk of SSI. This finding is in general agreement with a study of a large American surgical registry by Leung et al., which also reported a higher rate of SSI amongst patients with lower preoperative serum levels.[12] There are two potential pathophysiological mechanisms which might explain our observation of a statistically significant association between lower preoperative serum sodium levels and SSI. The first mechanism relates to the role played by sodium during wound healing. Sodium is an important component of the exudate fluid. This fluid keeps wound surfaces moist and promotes wound healing.[13] Reduced sodium levels could impair wound healing by reducing the effectiveness of the exudate fluid, thereby making the surgical wound more susceptible to bacterial colonisation. The second mechanism relates to the role played by sodium during the immune response to infection. Phagocytes, particularly neutrophils, are involved during the initial immune response to bacteria that breach the upper epithelial layers of the skin.[14] Neutrophils eliminate bacteria via the combined processes of phagocytosis and reactive oxygen/nitrogen species production.[14] Although low sodium levels have little effect on the production of antimicrobial reactive oxygen/nitrogen species, low sodium levels can almost completely inhibit phagocytic activity in neutrophils.[15] The reduced killing activity of neutrophils can allow bacteria to survive and proliferate in the surgical wound.[15]

Although the observed association between lower preoperative serum sodium levels and a higher risk of SSI was statistically significant, this result is clinically insignificant. An odds ratio of 1.05 per unit decrease in serum sodium levels is indeed a small effect size. Such a trivial association might not be sufficient to impact surgeons' clinical decision-making and prompt them to institute additional interventions during the perioperative period in order to reduce SSI risk. Therefore, preoperative serum sodium levels are unlikely to have substantial clinical utility as a risk stratification tool for SSI in our setting. We do not believe that the findings of the current study should be seen as a barrier to investigating the potential association between levels of other analytes routinely that are measured during the preoperative period and SSI in our setting. Our prior work involving pre-operative albumin levels is testament to this, and we strongly recommend that associations between other analytes and SSI be investigated in future studies.

There were limitations to our study. Our study involved data from a single, quaternary level hospital. This has implications for the generalisability of our findings to other hospitals which may have different case-mixes, procedure rates, or SSI rates. Multicentre studies are recommended to address the limitation regarding the generalisability of our study findings.[16] The American Society of Anesthesiologists (ASA) score is noted as an important predictor of SSI,[17] but was not collected as part of the hospital administrative database. Patient age was used as a proxy for ASA score in this study, as both variables show a strong correlation.[18] This was a retrospective analysis and we did not have any information on pre-analytical variables such as patient preparation prior to the blood specimen being taken, whether the specimen was correctly taken (i.e. in the correct blood tube for the required test), and whether the specimen was correctly handled and processed on receipt at the laboratory. Therefore, we could not adjust our analysis for these variables. We adjusted our analysis, through matching and multivariate methods, for as many confounders as possible with the dataset that was available to us. This includes known risk factors for surgical site infection that are components of the NNIS score. However, we were limited by the number of variables and patient characteristics that are routinely collected as part of the hospital electronic admissions system from which the patient and surgery data was obtained. Owing to this, we could not adjust our analysis for other, lesser known risk factors associated with surgical site infection which were not captured by the hospital electronic admissions system. Future research investigating the association between various routine preoperative laboratory tests and SSI should seek to address these limitations.

Conclusion

Although we report a statistically significant association between lower preoperative serum sodium levels and a higher risk of SSI, this association lacks clinical significance. Preoperative serum sodium levels are unlikely to have value as a risk stratification tool for SSI in our setting. Nevertheless, the findings of the current study should not be seen as a barrier to investigating the association between other routinely performed preoperative laboratory tests and SSI in our setting for future risk stratification purposes.

Conflict of interest

The authors declare no conflict of interest.

Funding source

None.

Ethical approval

This research was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (Protocol number: BE595/16).

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