

# A comparison of preoperative hypoalbuminaemia with the NNIS and SENIC risk scores for the prediction of surgical site infection in a South African setting

N Naidoo,<sup>1</sup> TE Madiba,<sup>1</sup> Y Moodley<sup>2</sup>

<sup>1</sup>Department of Surgery, University of KwaZulu-Natal, South Africa

<sup>2</sup>Faculty of Health and Environmental Sciences, Central University of Technology, South Africa

Corresponding author, email: drnnaidoo@outlook.com

**Introduction:** Preoperative hypoalbuminaemia is a risk factor for surgical site infection (SSI) in the South African (SA) setting. However, the predictive accuracy of preoperative hypoalbuminaemia has not been tested against established SSI risk stratification models in our setting, which could have important implications for SSI prevention strategies. With reference to SSI in SA settings, the study objective was to compare the overall predictive accuracy of preoperative hypoalbuminaemia with that obtained for the SENIC/NNIS risk scores.

**Method:** This was a sub-analysis of a pre-existing laparotomy patient registry ( $N = 439$ ). Variables collected as part of the registry included preoperative serum albumin measurements and all parameters of the SENIC/NNIS risk scores. Preoperative hypoalbuminaemia was defined as preoperative serum albumin of  $< 30$  g/L. The study outcome was SSI up to 30 days postoperatively. Overall predictive accuracy was determined through a receiver-operator-characteristic (ROC) curve analysis, with results presented as C-statistics (95% confidence intervals [CI]).

**Results:** The C-statistics obtained for preoperative hypoalbuminaemia, the SENIC risk score, and the NNIS risk score were 0.677 (CI: 0.609–0.746), 0.652 (CI: 0.582–0.721), and 0.634 (CI: 0.563–0.705).

**Conclusion:** All three methods display similar predictive accuracy for SSI. However, preoperative hypoalbuminaemia has several practical advantages over the SENIC/NNIS scores which must be considered.

**Keywords:** hypoalbuminaemia, surgical site infection, predictive accuracy, SENIC, NNIS, South Africa

## Introduction

Surgical site infection (SSI) is recognised as an important cause of morbidity, mortality, and increased healthcare resource utilisation amongst surgical populations across the world.<sup>1-3</sup> The identification of surgical patients at high-risk of developing SSI and implementation of preventative strategies in these patients therefore remains an important consideration for surgeons.<sup>4,5</sup> There are two commonly used risk stratification models for SSI: The Study on the Efficacy of Nosocomial Infection Control (SENIC) risk score and the National Nosocomial Infections Surveillance (NNIS) risk score.<sup>4,5</sup>

The SENIC risk score was developed by Hayley et al. using data collected during the 1970s for almost 59 000 American surgical patients.<sup>4</sup> It is a multivariate risk model consisting of four variables, including: abdominal operation, operation  $> 2$  hours in duration, contaminated-dirty wound, and having  $\geq 3$  discharge diagnoses. Each variable in the model, if present, is allocated a point score of "1". Cumulative scores, which could theoretically range between 0 and 4 points, are then determined for each patient. Hayley et al. reported that the incidence of SSI in individuals with a cumulative score of  $\geq 2$  points ranged between 10% and 30%.<sup>4</sup> Accordingly, the cumulative score of

$\geq 2$  points for the SENIC method was used as a threshold to define the "high-risk" group for SSI. From their study sample of almost 59 000 surgical patients, these authors determined that the high-risk group accounted for approximately 90% of all SSIs.<sup>4</sup>

The NNIS risk score was proposed during the early 1990s as an improvement on the SENIC risk stratification for SSI.<sup>5</sup> Using a cohort of almost 85 000 surgical patients, Culver and colleagues were able to develop a multivariate risk model consisting of three factors: surgical wound class, operation longer than T-time (where "T" is the usual duration of a surgical procedure), and American Society of Anesthesiologists (ASA) preoperative physical status classification of  $\geq 3$ . The inclusion of the ASA classification in the NNIS risk score was thought to have improved the predictive accuracy of the model by accounting for intrinsic risk. Similar to the SENIC risk score, all components in the NNIS risk score are allocated a single point. Cumulative scores for the NNIS risk score can range between 0 and 3 points. Culver et al. found that the incidence of SSI was much higher in patients with cumulative NNIS scores  $\geq 2$  points (6.8–13.0%) when compared with patients who had cumulative NNIS scores  $< 2$  (1.5–2.9%).<sup>5</sup>

Although the SENIC and NNIS risk stratification methods represent an important move forward in the prediction of SSI,

the ability of these models to discriminate between patients with and without SSI has been questioned in recent years. Some experts have suggested that future methods aimed at SSI prediction should be based on biomarkers, as this approach might demonstrate an improved ability to discriminate between patients with and without SSI.<sup>6</sup> Albumin is one biomarker which has been proposed for the prediction of SSI. This small, globular protein is produced in the liver and accounts for 50% of the total serum protein content in healthy individuals.<sup>7</sup> Hypoalbuminaemia, or a serum albumin measurement below the lower limit of the normal reference range, is often used as a marker for malnutrition.<sup>8</sup> It is proposed that malnutrition increases an individual's susceptibility to postoperative infection in two ways. Firstly, malnutrition impairs wound healing by diminishing fibroblast proliferation and collagen synthesis.<sup>6</sup> Secondly, albumin deficiency is linked to lymphocytopenia and immune dysfunction.<sup>6</sup> It is not surprising that much of the global literature has reported preoperative hypoalbuminaemia to be associated with an increased risk of SSI.<sup>9-11</sup> Our recent study in South African (SA) surgical patients also identified preoperative hypoalbuminaemia as a risk factor for SSI.<sup>12</sup>

With reference to SSI prediction in SA patients undergoing open abdominal surgery, the objective of the current study was to compare the overall predictive accuracy for preoperative hypoalbuminaemia with that obtained for the SENIC and NNIS methods. As this has not been previously investigated in the SA setting, the current study also sought to address an important gap in the literature.

## Materials and methods

### Study design and setting

This was a sub-analysis of patient data from our prior study of SSI risk factors in a SA setting.<sup>12</sup> The study setting was the Inkosi Albert Luthuli Central Hospital (IALCH) located in Durban, SA. IALCH is a public sector facility which provides quaternary-level healthcare services to the populace of the KwaZulu-Natal Province, located on the east coast of SA.

### Study sample

We included all 439 patients from our prior study<sup>12</sup> in the current sub-analysis. All patients were adults, and had undergone laparotomy procedures at IALCH between 01 January 2006 and 31 December 2010.

### Data collection

Data for our prior study were collected via a retrospective chart review. We had collected the following variables for each patient: demographic information, comorbidities, medication use, pre-operative laboratory test results (including serum albumin measurements), surgery-related variables, and all parameters of the SENIC/NNIS risk scores. Cumulative SENIC/NNIS scores were computed for each patient. SENIC and NNIS scores were complete for all patients in this study. The study outcome was SSI up to 30 days postoperatively. This outcome was based on the widely used definition proposed by the Centers for Disease

Control (CDC).<sup>13</sup> This definition incorporates clinical signs and symptoms of infection and is not solely based on microbiological evidence of infection. Preoperative hypoalbuminaemia was defined as a preoperative serum albumin measurement < 30 g/L. This threshold for preoperative hypoalbuminaemia has been proposed in recent perioperative nutrition guidelines.<sup>14</sup> All preoperative serum albumin measurements were taken at least one month prior to surgery, which is in keeping with the current preoperative work-up practices at IALCH. All serum albumin measurements were performed by a SANAS-accredited chemical pathology laboratory located on the hospital premises.

### Data analysis

Descriptive statistics were used to summarise the characteristics of the study sample. Descriptive results for categorical variables are presented as frequencies (%). We analysed all the continuous variables in the study for normality using the Kolmogorov-Smirnov (KS) test. All KS test results were found to be statistically significant ( $p < 0.05$ ), indicating that the data for all continuous variables did not demonstrate a normal distribution. Therefore, summary data for the continuous variables in this study are presented as medians with interquartile range (IQR). The overall predictive accuracy of hypoalbuminaemia, the SENIC risk score, and the NNIS risk score were assessed using receiver-operator-characteristic (ROC) curves. The resulting C-statistic was used to classify overall predictive accuracy as follows: < 0.500 = not any better than chance, 0.600–0.699 = fair, > 0.700 = good. Standard 2 x 2 epidemiological tables and equations were used to determine the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for each risk stratification method. For this aspect of the analysis, conventional SENIC/NNIS thresholds for high-risk individuals were adopted from the published literature.<sup>4,5</sup> In addition, 95% confidence intervals (CIs) are provided for all estimates of predictive accuracy. When comparing the three risk stratification methods, estimates of predictive accuracy with discreet confidence intervals were considered to be statistically different (i.e.  $p < 0.05$ ).

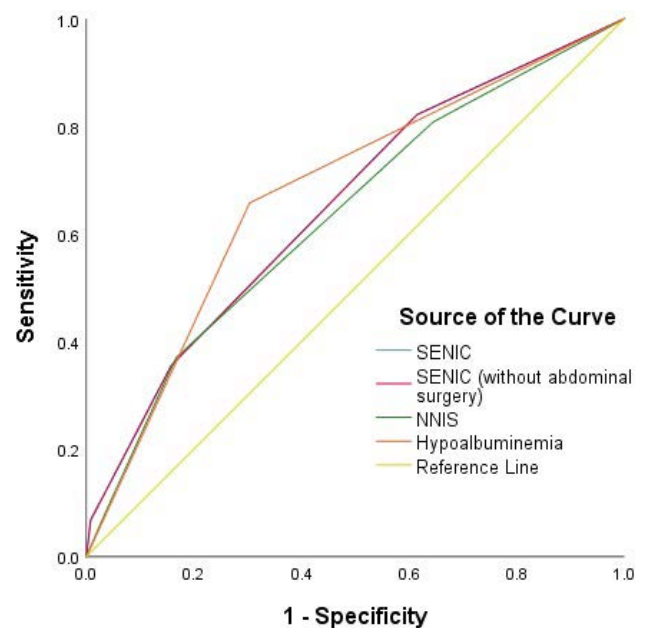


Figure 1: Results of the ROC curve analysis

## Results

The characteristics of the study sample are presented in Table I.

Figure 1 shows the results of the ROC curve analysis. The performance of each risk stratification method is presented as a separate line (four lines). In keeping with the general format of ROC curve analyses, a reference line (fifth line) indicating the

**Table I:** Description of the study sample (N = 439)

Characteristic	Median (IQR) or n (% N)
Age in years	42.0 (30.0–56.0)
Male gender	145 (33.0)
Obesity	152 (34.6)
Indication for surgery	
Bleed	12 (2.7)
Cancer	183 (41.7)
Infection	36 (8.2)
Other	151 (34.4)
Trauma	57 (13.0)
ASA preoperative classification ≥ 3	207 (47.2)
Preoperative nonsteroidal anti-inflammatory use	62 (14.1)
Preoperative statin use	25 (5.7)
Hypertension	140 (31.9)
Diabetes	57 (13.0)
Cardiovascular disease	50 (11.4)
HIV	30 (6.8)
Metastatic cancer	86 (19.6)
Obstructive airway disease	25 (5.7)
Gastric ulcers	17 (3.9)
Current smoker	44 (10.0)
Preoperative leukocyte count, x10 <sup>9</sup> cells/L	8.0 (5.9–10.6)
Preoperative platelets count, x10 <sup>9</sup> /L	263.0 (187.0–351.0)
Preoperative serum creatinine, μmol/L	75.0 (65.0–108.0)
Preoperative haemoglobin, g/dL	10.9 (9.2–12.4)
Preoperative sodium, mEq/L	139.0 (137.0–142.0)
Preoperative serum albumin, g/L	35.0 (22.0–42.0)
Preoperative hypoalbuminaemia	159 (36.2)
Abdominal procedure	439 (100.0)
Emergency procedure	150 (34.2)
Contaminated-dirty procedure	88 (20.0)
Surgery duration > T-time (2 hours)	153 (34.9)
Bogota bag	70 (15.9)
Antibiotic prophylaxis	366 (83.4)
Perioperative blood transfusion	157 (35.8)
Patient-controlled analgesia postoperatively	33 (7.5)
≥ 3 discharge diagnoses	136 (31.0)
SSI within 30 days postoperatively	73 (16.6)
SENIC score ≥ 2	285 (64.9)
NNIS score ≥ 2	88 (20.0)

threshold for a test/risk method performing better than pure chance is also included (C-statistic for reference line = 0.500). We had some concerns related to overestimation of SSI when applying SENIC to our study sample, which was comprised solely of abdominal surgery patients (abdominal surgery is a component of the original SENIC score). We tested an adapted SENIC score (with abdominal surgery omitted) against the original score and did not find any difference in the predictive accuracy between the two variations of the SENIC score (C-statistic, CI for both = 0.652, 0.582–0.721). This explains why the two lines overlap with each other on the ROC curve graph. A decision was made to continue with the use of the original SENIC score for the subsequent aspects of the statistical analysis. The C-statistic obtained for the NNIS score was 0.634 (CI: 0.563–0.705). The C-statistic obtained for preoperative hypoalbuminaemia was 0.677 (CI: 0.609–0.746). Based on the observed C-statistics, all methods were found to demonstrate “fair” predictive accuracy for SSI. The CIs for all estimates were found to overlap, suggesting no statistically significant difference ( $p > 0.05$ ) in the overall predictive accuracy between all three risk stratification methods.

The sensitivity, specificity, PPV, and NPV for all three risk stratification methods are presented in Table II. Comparison of the CIs for sensitivity and specificity between the three methods revealed several statistically significant ( $p < 0.05$ ) differences. Preoperative hypoalbuminaemia and the SENIC score were found to have a higher sensitivity for SSI than the NNIS score. Based on the overlapping CIs for the sensitivity estimates obtained for hypoalbuminaemia and SENIC, there was no difference in overall sensitivity between the two tests. The NNIS score had a higher specificity when compared with preoperative hypoalbuminaemia and SENIC. Preoperative hypoalbuminaemia had a higher specificity when compared with SENIC. Comparison of the CIs obtained for PPV/NPV estimates did not reveal any statistically significant differences between the three risk stratification methods for these parameters.

## Discussion

Preoperative hypoalbuminaemia, the SENIC score, and the NNIS score displayed similar overall predictive accuracy for SSI. A more in-depth comparison of predictive parameters (sensitivity, specificity, PPV, NPV) between the three risk stratification methods revealed that the similar performance was due to either high sensitivity being offset by low specificity (preoperative hypoalbuminaemia and the SENIC score) or high specificity being offset by low sensitivity (the NNIS score).

Notwithstanding the similar predictive performance for SSI, preoperative hypoalbuminaemia has several practical advantages over the SENIC and NNIS risk scores. Serum albumin measurements are a particularly important assessment in

**Table II:** Sensitivity, specificity, PPV, and NPV for each risk stratification method

Method	Sensitivity % (CI)	Specificity % (CI)	PPV % (CI)	NPV % (CI)
Hypoalbuminaemia	65.8 (53.7–76.5)	69.7 (64.7–74.3)	30.2 (23.2–38.0)	91.1 (87.1–94.1)
SENIC risk score	82.2 (71.5–90.2)	38.5 (33.5–43.7)	21.1 (16.5–26.3)	91.6 (86.0–95.4)
NNIS risk score	37.0 (26.0–49.1)	83.3 (79.1–87.0)	30.7 (21.3–41.4)	86.9 (82.9–90.2)

patients with abdominal pathologies, such as our study sample of laparotomy patients, where it is often used as a measure of liver function.<sup>15</sup> Serum albumin measurements are included as part of the preoperative work-up in patients undergoing surgery for abdominal pathologies. Therefore, an assessment of SSI risk can be made for almost all patients awaiting abdominal surgery procedures. The serum albumin test is also widely available, and can be performed by a laboratory or as a point-of-care assay.<sup>16,17</sup> Serum albumin measurements are also cost-effective, with current costs per test invoiced at approximately US\$ 3 in our setting. This cost is negligible when compared to the excessive costs required to treat SSI.<sup>3</sup> The process of risk score computation, such as that in the SENIC and NNIS methods,<sup>4,5</sup> might be viewed as a tedious process by the often inundated surgeon in the SA public healthcare sector. In comparison, identifying high-risk patients through evaluation of preoperative serum albumin measurements is a simpler process. While the SENIC/NNIS were complete for each patient in this study, there also exists a potential drawback in the SENIC/NNIS risk scores when a component of the score is missing or inaccurately recorded for a patient. For example, the ASA preoperative classification is a component of the NNIS risk score,<sup>5</sup> but evidence from a SA setting suggests that this score is inconsistently recorded or missing from the preoperative assessments completed by anaesthetists.<sup>18</sup> In such situations, it becomes impossible to compute a cumulative risk score, and subsequently estimate SSI risk in a patient using the NNIS score.

In addition, the most crucial difference between evaluating preoperative serum albumin measurements and the SENIC/NNIS methods for SSI prediction is that the SENIC/NNIS methods require certain information which is only available intraoperatively or postoperatively. This information includes the surgical incision wound classification, the duration of surgery, and the number of discharge diagnoses.<sup>4,5</sup> The World Health Organization (WHO) has proposed multiple preventative interventions for SSI, some of which can be considered for implementation in high-risk patients during the preoperative period.<sup>19</sup> It would be more resource-efficient to target high-risk patients for these interventions, rather than targeting all patients. Therefore, the added advantage of using preoperative hypoalbuminaemia to predict SSI is that it would allow for a full range of SSI preventative measures (pre-, intra-, and postoperatively) to be implemented in high-risk patients, whereas the SENIC/NNIS risk scores would only allow for postoperative interventions (i.e. once the cumulative SENIC/NNIS score is computed) to be implemented.

Along with the SSI preventative interventions proposed by the WHO, possible consideration must be given to optimising preoperative serum albumin as a risk reduction strategy for SSI in our setting. Optimisation of preoperative serum albumin can be achieved through the provision of comprehensive preoperative nutrition to patients awaiting surgery.<sup>20,21</sup> The appropriate time-point in the preoperative period when it would be best to initiate such a strategy in our patient population is unknown, but it is inevitable that the duration of the nutritional intervention would have a direct impact on expenditure within health departments.

The costs incurred by health departments in ensuring appropriate perioperative nutrition in patients awaiting surgery will likely be far lower than the costs which would be incurred if these patients were to develop SSI. Therefore, new research studies should be conducted in our setting to evaluate the impact of preoperative serum albumin optimisation on SSI risk.

There were limitations to this research, some of which have been declared in our previous manuscript involving the same laparotomy patient registry.<sup>12</sup> Amongst these previously declared limitations was a possible lack of generalisability in our findings as the patient registry was compiled at a single, quaternary-level institution which might not necessarily reflect the patient population in other SA settings. Another previously declared study limitation was that there might have been some patients who had developed SSI outside of the 30 day period proposed by the CDC definition.<sup>13</sup> There is also the possibility that some patients with minor forms of SSI might have self-managed their condition or presented for treatment at lower level healthcare facilities. These patients would have been considered as not having SSI in our statistical analysis. A limitation unique to our current sub-analysis is that we did not investigate other predictive biomarkers for SSI proposed in the literature, such as C-reactive protein,<sup>22</sup> due to the inconsistency in which the tests were ordered preoperatively at our institution. Another limitation unique to our current study is that we did not stratify our results by age and gender. We believe that a more in-depth investigation of this nature would require a larger sample size far beyond the scope of our pre-existing laparotomy patient registry.

## Conclusion

In conclusion, preoperative hypoalbuminaemia and the SENIC/NNIS scores demonstrated a similar predictive accuracy for SSI. There are however, several practical advantages to using preoperative hypoalbuminaemia over the SENIC/NNIS risk scores for SSI prediction. The most important of these advantages is that evaluating serum albumin levels allows for the preoperative calculation of SSI risk and the implementation of SSI preventative strategies in high-risk patients when compared with those which can be only be implemented postoperatively following calculation of SENIC/NNIS scores. Further research in our setting is recommended which seeks to investigate the impact of preoperative serum albumin optimisation on SSI risk.

## Conflicts of interest/Commercial interests

The authors declare no conflict of interest.

## Funding source

No funding was required.

## Ethical approval

This study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, South Africa (Protocol number: BCA208/18).



## ORCID

N Naidoo  <https://orcid.org/0000-0002-8551-9455>

TE Madiba  <https://orcid.org/0000-0002-0155-9143>

Y Moodley  <https://orcid.org/0000-0002-4119-1734>

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