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Use of biomarkers in the prediction of culture-proven infection in the surgical intensive care unit

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ABSTRACT

Purpose: The purpose of this study was to prospectively analyze the predictive role of classic predictors for suspected infection (temperature, WBC and derivatives) with two biomarkers, procalcitonin and lactate, on the incidence of culture-proven infection in the surgical intensive care unit (SICU).
Materials and methods: One hundred forty-six consecutive patients admitted for suspected infection had admission and 12-h procalcitonin values, admission and every 6-h lactate values for 24 h, and admission temperature, leukocyte count, lymphocyte count and percentage measured and analyzed in this study.
Results: Peak (highest measured value ≤24-h of admission) procalcitonin values were not predictive for culture-proven infection. However, a culture-negative subset was identified when peak procalcitonin values were < 2.9 ng/mL and when peak lactate values were < 1.3 mmol/L with a probability of 98.3% ($P < .001$). No other admission predictor was statistically associated with culture-proven infection. Following boosted-tree partitioning, a C-index of 0.85 was calculated with a misclassification rate of 23.3%.
Conclusions: The ability to utilize procalcitonin values in the diagnosis of culture-proven infection was not realized in this study. However, the association of admission peak procalcitonin values with admission peak lactate values identified a group of patients who were culture-negative for suspected infection. No other admission predictor was associated with culture-proven infection.

1. Introduction

The development of sepsis following surgery is associated with increased rates of morbidity, mortality, and healthcare costs [1-4]. Although previous studies have shown improved outcomes following implementation of goal-directed fluid resuscitation protocols guided by serial lactate clearances [3-9], analysis of procalcitonin values could provide an additional decision tool regarding appropriate antibiotic therapy in surgical patients [10-21]. A recent study in the emergency department examined the predictive roles of elevated procalcitonin and lactate levels in patients with suspected infection [22]. The purpose of this prospective observational study was to analyze admission procalcitonin values in concert with admission lactate values in patients admitted to the surgical intensive care unit (SICU) with suspected infection.

2. Materials and methods

Following approval of the institutional review board, this study was conducted within the SICU of Ochsner Medical Center from May 2016 through February 2018. All consecutive SICU adult patients admitted with suspected infection were enrolled into the study with the exception of surgical patients who received organ transplantation, cardiac surgery, or current immunosuppressive treatments.

The following data were recorded for each patient: demographics, comorbidities, anatomical site of operation, etiology of clinical presentation, admission and 12-h procalcitonin values, admission and every 6-h lactate values for 24 h, admission temperature, admission leukocyte counts, admission lymphocyte count and percentage [18], and the presence of distributive shock requiring vasopressor or mechanical ventilation support. The peak or higher measured value for the two measured procalcitonin levels and peak or highest measured value for the four measured lactates obtained during the first 24 h following SICU admission were used in the development of this model, as these biomarkers

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are frequently measured during the early stages of injury to establish trends in direction [16,21]. Outcome events of culture-proven infection (blood, pulmonary, abdominal, wound, urinary) and hospital mortality were recorded. The SICU and hospital length of stays were also recorded.

Diagnosis of suspected infection was based upon clinical presentation (respiratory, abdominal, wound, or urinary tract symptoms); pyosis during clinical examination; isolation of pathogen(s) from specimens of blood, urine, wound, or sputum; and imaging examination(s): chest x-ray, abdominal ultrasound, and computed tomography [CT] scanning. Classic measures for infection included admission temperature > 100.4 °F or < 96.8 °F, heart rate > 90/min, respiratory rate > 20/min, WBC >12,000/mm^3 or < 4000/mm^3. Severe sepsis was defined as known or suspected infection with evidence of organ dysfunction, and septic shock was defined as severe sepsis with persistent hypotension or requiring vasopressors, despite fluid resuscitation [2].

2.1. Statistics

Categorical variables were presented as counts and percentages with 95% confidence intervals (CI) with differences between the groups (culture-positive or culture-negative) assessed using Chi-square (χ^2) tests. Continuous variables with skewed distributions were presented as medians with 25%–75% interquartile range [IQR] with differences between groups assessed by the Wilcoxon rank sum test. The statistical technique, recursive partitioning or decision-tree analysis with 5-fold cross-validation was used to group patients into different levels of risk for culture-proven infection based upon the six admission suspected infection parameters [23-29]. A calculated LogWorth value of ≥2.0 for the G^2 statistic (the χ^2 statistic for this model) was considered statistically significant at the <0.01 value [24,28]. The recursive partitioning model underwent boosted-trees to optimize the predictive performance of the model, to minimize overfitting [30,31], and to develop a confusion matrix to measure discriminative ability with C-statistics [32,33]. Misclassification rates and other predictor calculations were also developed from the confusion matrix [34,35]. *P* values for the test statistics were set for statistical significance at <0.01 to minimize the risk of false discovery rates or in declaring associations significant by chance alone [36,37]. The statistical program JMP (version 13.2, SAS Inc., Cary, SC) was used for analyses.

2.2. Sample size calculations

We estimated a 30 ± 7.5% incidence of culture-proven infection in the SICU for analyzing the six admission parameters in patients with suspected infection [18,38-40]. Based upon this estimated incidence with a total width range of 15%, 143 consecutive medical records were calculated as an appropriate sample size for this prospective, descriptive study [41].

3. Results

In this study of 146 consecutive surgical patients admitted for suspected infection, the incidence of culture-proven infection was 41.8% CI 34.1–49.9% with the suspected site of infection at SICU admission being abdominal (64.3%), thoracic (17.1%), urinary (8.2%), blood (4.1%), and wound (2%). This incidence was comparable to reported observations in other surgical studies (23–87%) utilizing biomarkers for suspected infection [16,18,38-40].

The associations of admission demographics, type of surgery, comorbidities, etiologies of SICU admission, and initial supportive therapies of patients with suspected infection are shown in Table 1. The timing interval of broad-spectrum antibiotics once ordered to patient administration was 58 [29–104] minutes in all 146 patients. There were no statistical differences in the demographics, site of surgery, comorbidities, etiologies of SICU admission, and initial supportive therapies in the culture-positive group when compared to the culture-negative group (Table 1).

Table 1
Patient demographics, anatomical site of surgery, comorbidities, etiology of admission and initial supportive therapy in 146 consecutive patients with suspected infection during admission into the surgical intensive care unit.

Variables	Culture-Positive $n = 61$	Culture-Negative $n = 85$	P value
Demographics			
Age, yrs. median [IQR]	62 [54–72]	63 [54–71]	0.7002
Gender, female n, %	30 (49)	47 (55)	0.4655
Site of Surgery n, (%)			
Abdominal	47 (77.1)	64 (75.3)	
Thoracic	4 (6.6)	6 (7.1)	0.9704
Other	10 (16.4)	15 (17.7)	
Co-morbidities n, (%)			
Diabetes mellitus	28 (46)	22 (26)	0.0119
Reactive airway disease	8 (13)	17 (20)	0.2761
Chronic renal disease	8 (13)	10 (12)	0.8067
Chronic liver disease	4 (7)	8 (9)	0.5311
History of cancer	19 (31)	24 (28)	0.7038
Etiology of SICU Admission n, (%)			
Respiratory failure	10 (16)	17 (20)	0.2102
Suspected sepsis	29 (48)	26 (30)	
Distributive shock	11 (18)	19 (22)	
Other	11 (18)	23 (27)	
Initial Supportive Therapy n, (%)			
Mechanical ventilation	40 (66)	49 (58)	0.3316
Vasopressor support	34 (58)	36 (42)	0.0709

IQR: 25–75% interquartile range; n = number of patients; SICU: Surgical intensive care unit; P values <.01 are statistically significant.

Infection parameters used during admission to the SICU with suspected infection are shown in Table 2. Admission infection markers for patient temperature, leukocyte count and peak lactate values were not statistically significant between the two groups (Table 2). In contrast, admission absolute lymphocyte counts, absolute lymphocyte percentage, and peak procalcitonin values were statistically different between the two groups (Table 2).

Recursive partitioning with 5-fold cross-validation was performed to determine the role of the six admission parameters used for the workup of suspected infection on the prediction of culture-proven infection and the results of that analysis are shown in Fig. 1. The incidence of culture-proven infection in this study was 41.8% CI 34.1–49.9% (Node 1, Fig. 1). The admission predictor with the greatest statistical importance on the incidence of culture-proven infection was peak procalcitonin values with a cut-point of 2.9 ng/mL (Nodes 2 & 3, Fig. 1) with a G^2 test statistic of 198 and an associated $P < .0001$ calculated between the two groups. In the 69 patients with a peak procalcitonin value <2.9 ng/mL (Node 2, Fig. 1), 20.3% of patients had culture-proven infection (Probability 20.6%). In the group of patients with peak procalcitonin values ≥2.9 ng/mL (Node 3, Fig. 1), 61% of patients had

Table 2
Infection parameters in 146 consecutive patients with suspected infection during admission into the surgical intensive care unit.

Admission Parameters [IQR]	Culture-Positive n = 61	Culture-Negative n = 85	P value
Temperature, °F	99.5 [96.7–100.5]	99.0 [97.4–100]	0.2622
Leukocyte Count, mm^3	14.7 [8.7–23.4]	14.2 [9.6–19.9]	0.6227
Absolute Lymphocyte Count, mm^3	0.7 [0.4–1.3]	1.0 [0.6–1.6]	0.0077
Absolute Lymphocyte Percentage	5.2 [2.7–8.6]	7.3 [4.1–12.8]	0.0075
Peak Procalcitonin, ng/mL	6.5 [3.0–38.5]	2.5 [0.9–8.6]	<0.0001
Peak Lactate, mmol/L	2.6 [1.7–4.6]	1.9 [1.1–5.1]	0.1154

IQR: 25–75% interquartile range; Peak: Maximum measured value ≤24-h of admission; n = number of patients; P values <.01 are statistically significant.

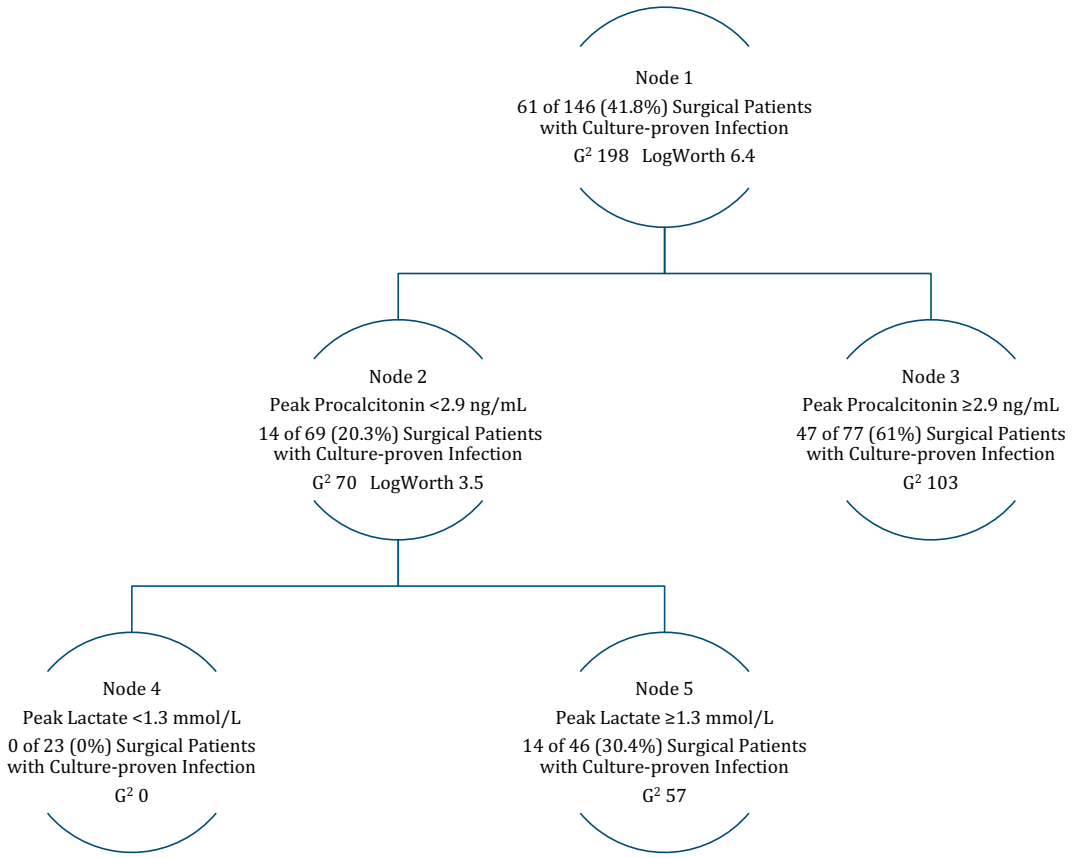

Fig. 1. Recursive partitioning graph of the role of infectious markers for culture-proven infection in patients admitted to the surgical intensive care unit for suspected infection. Peak values are defined as the highest biomarker value measured ≤24 h of admission. G^2: G-square statistic (equivalent to Chi-square statistic for this model); LogWorth values >2.0 are statistically significant at the <0.01 value.

culture-proven infection (Probability 60.8%). In the peak procalcitonin patient group with values <2.9ng/mL (Node 2, Fig. 1), recursive partitioning identified peak lactates as the next important predictor for culture-proven infection with a G^2 test statistic of 70, $P < .001$ when comparing differences between the two groups. In this group of patients (Node 2, Fig. 1), those patients with peak lactates <1.3 mmol/L had a zero incidence of culture-proven infection (Probability 98.3%) (Node 4, Fig. 1), whereas those patients with associated peak lactate values ≥1.3mmol/L had a 30.4% incidence (Probability 30.6%) of culture-proven infection (Node 5, Fig. 1). Although no other infectious admission predictor was statistically associated with culture-proven infection in this study, the admission temperature was clinically interesting as the decision-tree model identified a sub-group of patients within Node 5, Fig. 1 in that six patients were culture-negative for suspected infection when admission temperature was <95.8 °F ($G^2 = 57$, LogWorth = 0.6 or $P > .1$).

In the group of 23 patients (Node 4 group) with peak procalcitonin values <2.9 ng/mL and with peak lactates <1.3 mmol/L (Node 4, Fig. 1), the duration of antibiotic therapy in the Node 4 group was 6.0 [4.4–7.7] days and was 8.8 [5.0–15.6] days for patients in the rest of the study ($\chi^2 = 3.1$, $P = .0804$). In the Node 4 group the SICU length of stay was 2.6 [1.6–5.0] days versus 5.0 [2.1–11.3] days for patients in the rest of the study ($\chi^2 = 7.5$, $P = .0062$). The hospital length of stay for the Node 4 group was 9.7 [7.8–23] days versus 16.8 [8.2–25] days for patients in the rest of the study ($\chi^2 = 1.6$, $P = .2078$). Finally, a mortality rate of 13% CI 4.5–32% observed in the Node 4 group versus 24.4% CI 17.6–32.7% observed for patients in the rest of the study ($\chi^2 = 1.6$, $P = .2087$). Although these observations in the Node 4 group when compared to patients in the rest of the study were not all statistically significant, there are real gains in clinical outcomes observed in this interest group.

The decision-tree model underwent boosted-trees regression to reduce overfitting of the model and to generate a confusion matrix with the results of the prediction calculations shown in Table 3. The accuracy of the model was 76.7% CI 68.6–83.2%. The misclassification rate observed in this study was 0.233 (23.3%) CI 0.168–0.314 with the number needed to misdiagnose of 1 in 4.289 CI 3.188–5.968 (Table 3). Additional test statistics and their formula are grouped according to dependence on prevalence (Table 3).

There was a tendency for increased crystalloid administration within 24 h in the culture-positive group, 8.3 L [4.3–11.5 L], when compared to the culture-negative group, 5.6 L [3.6–8.8 L], ($\chi^2 = 2.7$, $P = .1020$). Culture-proven infection increased SICU length of stay from 3.7 [2.0–6.8] days to 6.9 [2.1–6.8] days ($\chi^2 = 4.8$, $P = .0289$) and increased hospital length of stay from 14.5 [7.4–22.9] days to 20.0 [10.8–27.3] days ($\chi^2 = 7.1$, $P = .0076$). The duration of antibiotic therapy in the culture-positive group was 11.5 [7.9–19] days and was 6.2 [3.7–11.4] days in the culture-negative group of ($\chi^2 = 19.3$, $P < .0001$). The duration of antibiotic therapy in both groups was not associated with statistical differences in 28-day mortality rates (Culture-positive group, 48.1% CI 30.7–66.0%; Culture-negative group, 55.9% CI 39.4–71.1%; $\chi^2 = 0.36$, $P = .5479$).

4. Discussion

Procalcitonin as a biomarker for infection has been studied in other clinical environments. The incidence of culture-proven infection in this study was 41.8% CI 34.1–49.9%. This incidence of culture-proven infection was comparable to reported observations (23–87%) in other surgical studies utilizing biomarkers for suspected infection [16,18,38-40]. However, these reported observations were obtained in either small groups of surgical patients [16,38-40] or in larger mixed medical/

Table 3
Confusion matrix for boosted-tree model.

		Actual Infection		
Predicted Infection		Culture-Positive	Culture-Negative	Totals
	Culture-Positive	41 (a or TP)	14 (b or FP)	55 (r1)
	Culture-Negative	20 (c or FN)	71 (d or TN)	91 (r2)
	Totals	61 (c1)	85 (c2)	146 (t)

TP: True positive; TN: FP: False positive; FN: False negative; True negative; CI: 95% Confidence Intervals.
Prevalence = *Culture-positive incidence* [c1/t] = 61/146 = 0.418 (41.8%) CI 0.341–0.499, *Culture-negative incidence* [c2/t] = 85/146 = 0.582 (58.2%) CI 0.501–0.659; Kappa = 0.515 CI 0.347–0.651.
Test statistics not dependent upon prevalence.
Sensitivity = a/c1 = 45/61 = 0.672 CI 0.576–0.750;
Specificity = d/c2 = 71/85 = 0.835 CI 0.766–0.891;
Positive Predictive Value = a/r1 = 45/55 = 0.745 CI 0.638–0.832;
Negative Predictive Value = d/r2 = 67/83 = 0.780 CI 0.715–0.833;
Positive Likelihood Ratio = Sensitivity/(1-Specificity) = 0.672/(1–0.835) = 4.073 CI 2.458–6.906;
Negative Likelihood Ratio = (1-Sensitivity)/Specificity = (1–0.672)/0.835 = 0.393 CI 0.280–0.554;
Odds Ratio = (a/b)/(c/d) = (41/14)/(20/71) = 10.368 CI 4.435–24.667;
Relative Risk = (a/r1)/(c/r2) = (41/55)/(20/91) = 3.387 CI 2.242–4.971;
Diagnostic Odds Ratio = (Sensitivity/(1-Sensitivity))/((1-Specificity)/Specificity) = (0.672/(1–0.672))/(0.835/(1–0.835)) = 10.368 CI 4.435–24.667;
Error Odds Ratio = (Sensitivity/(1-Sensitivity))/(Specificity/(1-Specificity)) = (0.672/(1–0.672))/(0.835/(1–0.835)) = 0.405 CI 0.415–0.367;
Difference in Proportions (DP) = [(a/r1)-(c/r2)] = [(41/55)-(20/91)] = 0.525 CI 0.354–0.665;
Absolute Risk Reduction (ARR) = [(c/r2)-(a/r1)] = [(20/91)-(41/55)] = which is equal to -DP = −0.525 CI -0.665 to −0.354;
Number Needed to Treat = (1/absolute value of DP) which is equal to (1/absolute value of ARR) = 1/0.525 = 1.904 CI 1.504–2.827;
Relative Risk Reduction = [ARR/(c/r2)] = [−0.525/(20/91)] = −2.387 CI -3.971 to −1.242;
Youden's J = (Sensitivity+Specificity-1) = (0.672 + 0.835–1) = 0.507 CI 0.341–0.642;
Number Needed to Diagnose = (1/(Sensitivity-(1-Specificity)) = (1/(0.672-(1–0.835)) which is equal to (1/Youden's J) = (1/0.507) = 1.972 CI 1.558–2.929.
Test statistics dependent upon prevalence.
Accuracy = (a + d)/t) = (41 + 71)/146 = 0.767 (77%) CI 0.686–0.832;
Misclassification rate = [(c + b)/t] = (20 + 14)/146 = 0.233 (23%) CI 0.168–0.314;
Number Needed to Misdiagnose = [1/(1-Accuracy)] = [1/(1–0.767)] = 4.289 CI 3.188–5.968.

surgical populations [10-20]. The development of sepsis following surgery is associated with increased rates of morbidity, mortality, and healthcare costs [1-4]. Although previous studies have shown improved outcomes following implementation of goal-directed resuscitation protocols including intravenous fluid administration and timely administration of broad-spectrum antibiotics [5], analysis of procalcitonin values could provide an additional decision tool regarding appropriate antibiotic therapy in surgical patients [10-20]. Prior studies have shown that procalcitonin values ≥2.0 ng/mL are sensitive and specific for septic patients with values <0.5 ng/mL allowing for safe termination of antibiotic administration in medical ICUs [42]. However, an appropriate diagnostic cut-point value is unclear in surgical patients as most postoperative patients have elevated procalcitonin values due to presence of systemic inflammatory response syndrome (SIRS) [43,44]. In this study, the use of recursive partitioning or a decision-tree investigating measures for infection identified the two biomarkers, peak procalcitonin and lactate values when used in combination could provide an early clinical decision regarding antibiotic stewardship in a subset of patients. As procalcitonin kinetics have been shown to guide discontinuing antibiotic therapy [15,45], the use of recursive partitioning or decision trees for procalcitonin and lactate values could risk-stratify postoperative patients and guide antibiotic therapy to improve outcomes and reduce healthcare costs in the SICU [46].

4.1. Clinical studies

In the Clec'h, Fosse and colleagues' study of 67 surgical patients, they observed a postoperative infection incidence of 87% [16]. These results are not comparable to the observed incidence of culture-proven infection in this study. In their surgical population, the best diagnostic procalcitonin cut-point value for determining when to discontinue antibiotic therapy was 9.7 ng/mL with a reported 91.7% sensitivity and 74.2% specificity. In contrast, we observed a diagnostic cut-point value of 2.9 ng/mL with a 67.2% sensitivity and a 83.5% specificity. The observed differences in cut-point values and associated sensitivities and specificities between the two studies could be due to the sample size studied [16]. In agreement with the findings of Clec'h, Fosse and colleagues, we do find that procalcitonin values when used in concert with lactate values could provide important clinical guidance in antibiotic stewardship in surgical patients [16].

In the Svoboda, Kantorova and colleagues' study of 38 surgical patients, the authors observed a nonsignificant decrease in SICU days when trending procalcitonin values [10]. In agreement with these findings, we observed a non-statistically significant but clinically significant decrease in SICU length of stay in patients when culture-negative, and a statistically and clinically significant decrease in hospital length of stay in patients when culture-negative.

Nobre, Harbarth and colleagues observed in 31 mixed medical/surgical patients that procalcitonin-guided therapy reduced the duration of antibiotic therapy and shorter SICU stay [11]. In agreement with these findings, we observed a decrease in antibiotic duration in the culture-negative group– when compared to the culture-positive group– but our findings are in contrast with the findings reported by Shehabi, Sterba and colleagues who observed no reduction in duration of antibiotic therapy when utlizing a procalcitonin-guided protocol [19].

Hochreiter, Kohler and colleagues observed in 57 surgical patients and Schroeder, Hochreiter and colleagues observed in 14 surgical patients that procalcitonin-guided therapy resulted in shorter duration of antibiotic therapy without negative effects on clinical outcomes such as mortality [14,17]. In agreement with these findings, we observed no statistically significant assocation in the duration of antibiotic therapy with 28-day mortality with these results comparable to the reported observations in a large medical patient population [15], and with the findings of Hohn, Schroeder and colleagues [13], but are in contrast with the observations by Jensen, Hein and colleagues in a mixed medical/surgical unit [12]. Liu, Chen and colleagues in 320 surgical patients with suspected sepsis, analyzed three biomarkers including procalcitonin at admission and demonstrated a C-index statistic (0.85) for procalcitonin when analyzed alone [18]. We were unable to show predictive benefits with isolated procalcitonin in the diagnosis of culture-proven infection with the differences between this appropriate sample-sized study and our results are unknown [18,47].

Along with timely administration of broad-spectrum antibiotic therapy in the treatment of sepsis, another component of goal-directed therapy is early intravenous hydration [4-6] as guided by serial lactate clearances [7-9]. Nguyen, Loomba and colleagues demonstrated in

patients with severe sepsis and septic shock that early serial lactate clearance can reduce other serum biomarkers of inflammation and improve rates of organ dysfunction and mortality [21] and are in agreement with Otero, Nguyen and colleagues [3]. In culture-proven infection, patients did require greater amounts of intravenous fluids during the first 24 h following SICU admission when compared to culture-negative patients. These findings suggest that the presence of culture-proven infection increased the magnitude of cryptic shock requiring additional crystalloid resuscitation [3].

4.2. Predictive Modeling

In predictive modeling, forecasting adverse events is desired when the prognosis is potentially severe, or if consequences increase with delayed diagnosis [48], hence the timely administration of broad-spectrum antibiotics along with implementation of goal-directed fluid resuscitation guided by serial lactate clearances [3-9]. However, many postsurgical patients manifest SIRS rather than postoperative infection [43,44] as shown in this study. The discriminative power of a predictive model to improve antibiotic stewardship can be calculated with several mathematical models to assess accuracy [48,49]. Boosted-trees was utilized to improve the predictive value of the recursive partitioning model, to reduce overfitting, and to generate a confusion matrix for predictive test statistics with their calculations [23-25,30,31]. The use of sensitivity and specificity calculations provide probability estimates of illness and the use of predictive values provide additional assessments that patients with a positive test do have the condition, or patients with a negative test do not have the condition. The use of odds ratios provide a measure of effect size, and the use of C-statistics provide a measure of discrimination [32,33,49-51]. However, these test statistics may not perform well in low prevalence conditions [52-54], and may overestimate their benefits or underestimate the costs of clinical resources [48,49,55]. Clinicians need a testing tool to limit the potential for negative consequences on patient health and on medical care expenditures [49]. Misclassification rates support that answer. Misclassification rates identify how often the model is wrong and account for the prevalence of the condition in guestion [34,35]. In our study, the misclassification rate for culture-proven infection following boosted-tree analysis was 23.3%, with the number needed to misdiagnose of 1 in 4.3. As both values are dependent upon the prevalence of the outcome, these calculations are reliable [52-54]. Although the model as a whole is not informative (kappa and Youden's values approach 0.5) due to the high percentages of false postives and false negatives, nevertheless a subgroup of patients could have an early decision regarding antibiotic stewardship [34,35].

4.3. Limitations and strengths

A limitation of clinical studies is missing data from incomplete medical records that require imputation strategies to utilize those records [56]. However, electronic medical records allow near 100% data collection as observed in this study (5.3% missing data). Another limitation of this study was the possibility of antibiotic administration prior to completion of culture acquisition or due to the residual effects of prior perioperative administration of prophylactic antibiotics. The development of protocols to improve antibiotic stewardship with emphasis in timely administration has long been a goal in critical care medicine [10-21,38-40]. The definitions of peak or maximum values used for the two biomarkers in the development of this model require external validation and these definitions are limitations but are based upon observations in clinical studies [16,21]. Strengths of the study include data that represent a consecutive set of patients who experienced a common diagnosis, suspected infection at SICU admission. The addition of admission lactates to this study provides an additional measured biomarker as clearance of this biomarker has been shown to reduce other known biomarkers such as procalcitonin [18]. However, this studied biomarker combination needs external validation and should not be used as the sole decision, but integrated with other clinical, laboratory and imaging data regarding antibiotic management.

An additional strength of this study is the use of recursive partitioning or decision-trees, an analytic that is resistant to the effects of outliers and of missing data. The application of boosted-trees combines a large number of simple decision-tree models that optimizes predictive performance [25,30,31]. Overall, the outcomes from this robust statistical technique are easy to understand with predictions expressed in percentages interpreted from decision-trees rather than from multivariable analyses tables containing beta coefficients, standard errors, and odds ratios, the latter statistic independent of prevalence. Additionally, recursive partitioning or decision-trees allows easy clinical interpretation of the results and does not require extensive knowledge about statistical mathematics [24-27,30,31]. With an increasing interest in minimizing adverse events for hospitalized patients following surgical care [27], the use of recursive partitioning provides a valuable statistical tool to help clinicians identify subgroups of patients who are at risk and direct appropriate healthcare resources to these subgroups [29], a technique difficult to explore with multivariable analysis.

5. Conclusions

The combination of biomarkers, procalcitonin and lactate observed during the first 24 h of SICU admission, lends strong predictive support for early antibiotic stewardship in surgical patients admitted for suspected infection. The classic measures of infection, temperature and WBC derivatives, did not demonstrate a statistical association with culture-proven infection in this model.

Conflict of interest and source of funding

The authors declare that they have no conflict of interest. This study was funded by an unrestricted grant provided by the King Abdulaziz University, Jeddah, Saudi Arabia.

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