

The predictive ability of a weighted systemic inflammatory response syndrome score for microbiologically confirmed infection in hospitalised patients with suspected sepsis

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The 1992 American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) Consensus Conference Committee proposed a set of definitions that could be applied to patients with sepsis and its sequelae.¹ The main aims of the consensus conference were to give clinicians a conceptual and practical framework for the diagnosis and management of sepsis, and to facilitate sepsis research.

In particular, the concept of a systemic inflammatory response syndrome (SIRS) was put forward. SIRS is defined as a host response phenomenon characterised by two or more of the following clinical findings: body temperature $>38^{\circ}\text{C}$, or $<36^{\circ}\text{C}$; heart rate >90 beats/min; hyperventilation evidenced by respiratory rate >20 breaths/min or $\text{Paco}_2 <32$ mmHg; and a white cell count of $>12 \times 10^9/\text{L}$, $<4 \times 10^9/\text{L}$ or $>10\%$ immature (band) forms. Infection is defined as a microbial phenomenon characterised by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms. Sepsis is present when SIRS is the result of a confirmed or suspected infectious process.¹

The diagnostic criteria for SIRS were selected through a process of consensus among experts, rather than an empirical process based on laboratory and trial data.² Nevertheless, several studies have assessed the value of each physiological parameter in the diagnosis of infection. Bossink and colleagues studied the clinical host response to infection among 300 medical patients and found that peak body temperature and peak white cell count predicted infections, whereas tachypnoea and tachycardia were of no predictive value.³ Another study found inconsistent association of tachypnoea and tachycardia with infection, although they were useful in predicting morbidity and mortality associated with critical illness.⁴ It is widely believed that deranged temperature and white cell count are more predictive measures of infection compared with tachypnoea and tachycardia.

SIRS has been criticised for its lack of specificity.⁵⁻⁷ When used to define sepsis, it identifies a heterogeneous group of patients with different aetiologies and host responses. Many non-infective conditions, such as burns, pancreatitis and trauma, can also produce SIRS.^{1,8} Despite concerns regarding its limitations, the concept of SIRS has gained widespread acceptance among clinicians and researchers

ABSTRACT

Background: The systemic inflammatory response syndrome (SIRS) concept lacks sensitivity and specificity for guiding clinical practice and sepsis research.

Objective: To assess the performance of a weighted SIRS score, with emphasis on white cell count and temperature criteria in predicting microbiologically confirmed infection.

Design and setting: Prospective cohort study at Princess Alexandra Hospital, a tertiary teaching hospital in Queensland, Australia.

Participants: Patients aged 18 years or older who were hospitalised with suspected infection and started on antimicrobial therapy.

Main outcome measures: The utility of each SIRS criterion, the 1992 consensus conference recommendation (≥ 2 SIRS criteria) and a weighted SIRS score in predicting microbiologically confirmed infection were compared.

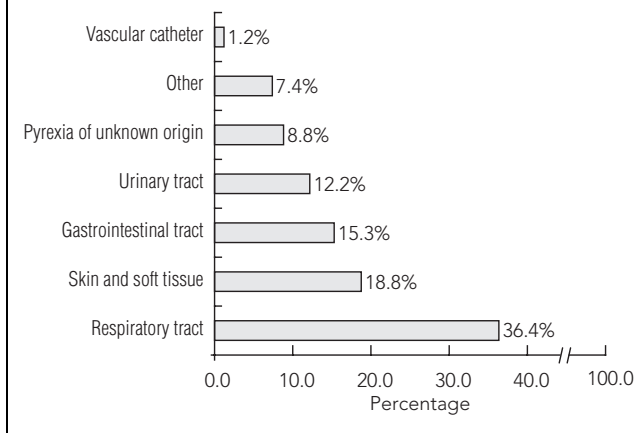
Results: 2085 patients were included in the analysis. All criteria performed poorly, with low sensitivities (27.3%–70.6%), low specificities (37.5%–77.5%), low positive predictive values (61.5%–65.3%), low negative predictive values (39.8%–45.1%), and likelihood ratios close to 1.0. Both SIRS and weighted SIRS scores did not perform better than clinicians' suspicion for infection.

Conclusions: Both SIRS and weighted SIRS score had low predictive ability for microbiologically confirmed infection. A more robust conceptual framework incorporating clinical, biochemical and immunological markers must be formulated and validated to better guide clinical practice and research. Clinicians' suspicions may be as good as any scoring system at identifying patients with infection and sepsis.

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globally. In particular, SIRS has been used to define populations of patients for interventional clinical trials.^{8,9} There is a need for a better system that enables us to accurately identify patients with sepsis earlier, in order to commence antimicrobial therapy or to investigate novel therapies that target the body's responses to infection.

Figure 1. Suspected sources of infection among 2085 hospitalised patients



We aimed to determine whether a weighted SIRS score (with temperature and white cell count given more points, based on the findings of Bossink et al's study³) better predicts microbiologically confirmed infection than the 1991 consensus conference SIRS definition ("traditional SIRS").¹

Methods

Data collection and definitions

Data collection was approved by the Princess Alexandra Hospital Research Ethics Committee (approval no. 2005/224) and conducted from May 2006 to October 2008 as part of a screening process to recruit eligible patients for an interventional sepsis study.¹⁰ A daily computer-generated report identified all patients admitted to hospital with any of 97 potential sepsis-related diagnoses (International Classification of Diseases, ninth revision [ICD-9] diagnostic database). Patients aged 18 years and older and specifically fulfilling the definition for presumed infection as per standard United States Centers for Disease Control and Prevention criteria¹¹ and for whom antibiotic therapy had been commenced were included in the database. Basic demographic data were collected and the worst value in the first 48 hours following hospital admission for each of the SIRS criteria was recorded for each patient. Date of admission, date of discharge and hospital outcome were also recorded for each patient.

A weighted SIRS score was calculated for each patient by allocating 2 points each for body temperature ($>38^{\circ}\text{C}$, or $<36^{\circ}\text{C}$) and white cell count ($>12 \times 10^9/\text{L}$, $<4 \times 10^9/\text{L}$) and 1 point each for tachycardia (heart rate >90 beats/min) and tachypnoea (respiratory rate >20 breaths/min). A total score of 3 or more was deemed to indicate significant systemic inflammation.

Details of microbiological investigations performed for each patient within 72 hours of index admission were

recorded. It was specifically noted whether any specimens were collected and whether there were positive culture results. Based on available clinical and laboratory data, culture results that were deemed to reflect colonisation or contamination were not considered positive clinically relevant microbiology results.

Data management and statistical analysis

Microsoft Excel (Microsoft Corporation, Redmond, Wash, USA) was used for data management and statistical analysis. Sensitivities, specificities, positive predictive values, negative predictive values and likelihood ratios were calculated using Bayes's theorem¹² for each SIRS criterion, traditional SIRS and the weighted SIRS score in relation to microbiologically confirmed infection. Continuous variables were compared using the Student *t* test or the Mann-Whitney *U* test, and categorical variables were compared using the χ^2 test or the Fisher exact test.¹² We made no assumption regarding missing data, and all proportions were calculated as percentages of the patients with available data.

Results

Patient characteristics

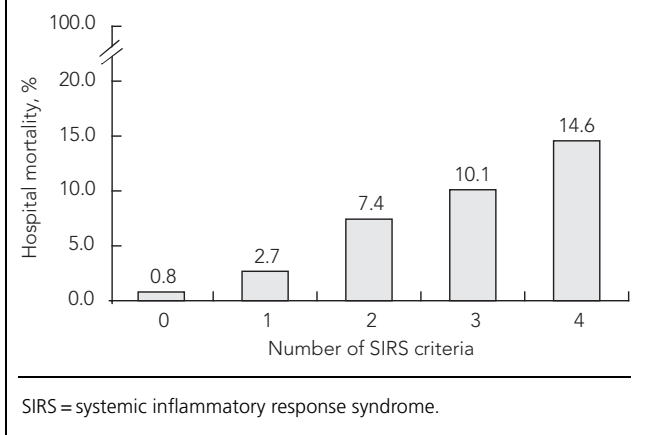
Of the 2279 patients identified by the computer-generated report and screened, 194 patients were excluded due to incomplete SIRS or microbiological data. In total, 2085 patients had complete SIRS and microbiological data and were included in the final analysis.

The mean age of the study population was 62 years (SD, 17 years), and 1207 patients were men (57.9%). Intensive care unit admission was required for 388 patients (18.6%). Hospital discharge date and outcome data were available for 2050 patients (98.3%). Their median length of stay was 6 days (interquartile range, 3–14 days) with a hospital mortality of 7.3% ($n = 149$).

Suspected sources of infection are shown in Figure 1. The respiratory tract was most commonly implicated, followed by skin and soft tissue, gastrointestinal tract and urinary tract. There were 327 patients (15.7%) with positive blood cultures. In all, 1826 patients fulfilled at least one SIRS criteria (87.6%), and 1406 (67.4%) developed two or more SIRS criteria within 48 hours of admission. The most frequently encountered SIRS criterion was tachycardia (62.8%), followed by abnormal white cell count (50.5%), tachypnoea (48.9%) and deranged temperature (44.4%).

Positive microbiological investigations were seen in 1460 patients (70.0%) of the study population. Of these, 192 patients had samples that were deemed to represent colonisation or contamination based on available clinical and laboratory data. As a result, 1268 patients (60.8%) were deemed to have clinically significant microbiologically

Figure 2. Number of SIRS criteria and hospital mortality



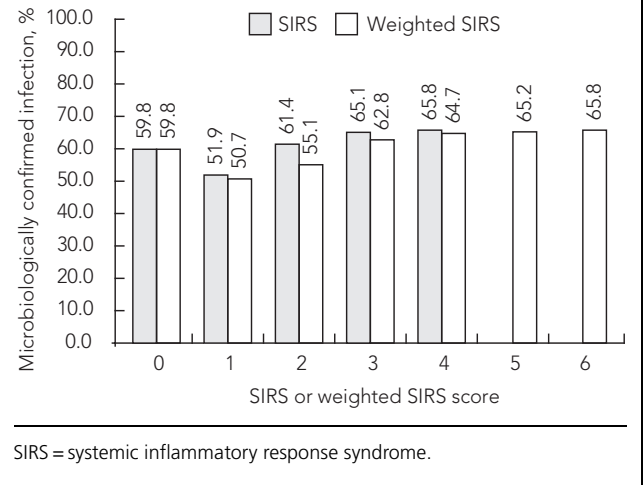
confirmed infection. Patients with microbiologically confirmed infection had higher hospital mortality (9.3%) compared with patients with negative microbiological cultures (4.0%) ($P < 0.001$).

Using measures of systemic inflammatory response syndrome to predict microbiologically confirmed infection

In this population of hospitalised patients with presumed infection, increased hospital mortality was seen with increasing number of SIRS criteria (Figure 2). Patients with no SIRS criteria had a hospital mortality below 1.0% compared with 14.6% for patients with all four SIRS criteria (Figure 2). The number of SIRS criteria present and the weighted SIRS score were both associated with a marginal increase in the likelihood of microbiologically confirmed infection (Figure 3). In this respect, the weighted SIRS score did not perform better than traditional SIRS.

Sensitivities, specificities, positive predictive values, negative predictive values and likelihood ratios for each SIRS

Figure 3. Number of SIRS or weighted SIRS score and percentage microbiologically confirmed infection



criterion, traditional SIRS and weighted SIRS score in predicting microbiologically confirmed infection are shown in Table 1. All parameters performed poorly, with low sensitivities (27.3%–70.6%), low specificities (37.5%–77.5%), low positive predictive values (61.5%–65.3%), low negative predictive values (39.8%–45.1%), and likelihood ratios close to 1.0. The weighted SIRS score had marginally higher specificity and lower sensitivity than traditional SIRS. Mandating the presence of both temperature and white cell criteria increased specificity to 77.5% and decreased sensitivity to 27.3% (Table 1).

Discussion

Since the ACCP/SCCM consensus conference, several cohort studies have examined the epidemiology of SIRS, its relationship with infection and progression to severe sepsis.¹³⁻¹⁵ Our study is the first to examine the utility of a

Table 1. SIRS criteria and weighted SIRS scores in predicting microbiologically confirmed infection

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio
WCC	52.5%	52.8%	63.3%	41.7%	1.11	0.90
Temperature	46.6%	59.0%	63.8%	41.6%	1.13	0.90
Tachycardia	65.2%	41.0%	63.2%	43.2%	1.11	0.85
Tachypnoea	49.4%	51.9%	61.5%	39.8%	1.03	0.97
Traditional (≥ 2) SIRS	70.6%	37.5%	63.7%	45.1%	1.13	0.79
Weighted SIRS ≥ 3	63.5%	45.7%	64.5%	44.6%	1.17	0.80
Both temp and WCC present	27.3%	77.5%	65.3%	40.7%	1.21	0.94

SIRS = systemic inflammatory response syndrome. WCC = white cell count.

weighted SIRS score in the prediction of microbiologically confirmed infection. We also evaluated the performance of each SIRS criterion in relation to microbiologically confirmed infection.

Our results refute a common belief among clinicians that deranged temperature and white cell count are more sensitive and specific for infection than tachypnoea and tachycardia. Importantly, our study showed that with low negative predictive values and negative likelihood ratios that were close to 1.0, the absence of either a deranged white cell count or a deranged temperature could not be used to rule out infection.

In our cohort, the weighted SIRS score did not perform better than traditional SIRS (≥ 2 SIRS criteria) in predicting microbiologically confirmed infection. Both scores performed poorly, with low sensitivities, specificities, positive predictive values and negative predictive values. They did not perform better than the clinicians' assessment, which had a positive predictive value of 60.8%. We make this statement based on the fact that clinicians' suspicion for infection was the entry criterion for our study and 60.8% of our study population had microbiologically confirmed infection. In contrast to the study by Bossink et al,³ our data showed that specificities of deranged temperature and white cell count for microbiologically confirmed infection were similar to those of tachypnoea and tachycardia. Therefore, allocation of more points for the temperature and white cell criteria would not be expected to and did not improve the predictive ability of SIRS for microbiologically confirmed infection.

In our study, both traditional SIRS criteria and weighted SIRS scores produced high rates of false positives and false negatives when used to predict infection. There are a number of possible reasons to account for these. The positive criterion of ≥ 2 SIRS criteria or weighted SIRS score ≥ 3 when associated with a negative microbiological result was deemed a false-positive result in our study. Non-infective aetiologies of SIRS could account for some of the false-positive results, although patients only entered the study when the clinician suspected a diagnosis of infection and initiated treatment with antibiotics. Another possible explanation of a false-positive result was true infection with negative results from microbiological investigations. This could be associated with viral infection or infection caused by atypical or fastidious organisms. Inadequate sampling and prior antimicrobial therapy could also contribute to negative microbiological results among patients with infection. In our study, 39% of patients had negative results from microbiological investigations, consistent with other studies, which have reported that up to 50% of patients with suspected infection had negative results.^{13,14} The high false-positive rate observed in our study confirmed the lack

of specificity of the SIRS concept and weighting of abnormal white cell count and temperature only increased its specificity marginally.

Negative SIRS or weighted SIRS in association with a positive microbiological result were considered a false-negative result in our study. Several possible reasons exist for the observed high false-negative rate. These include mild or local infection with no systemic response, or the organisms cultured representing colonisation rather than infection. We attempted to identify all possible colonisation using available laboratory and clinical data, and in our final analysis these were not considered microbiologically confirmed infection. Analyses done without excluding possible colonisation did not change the results significantly (data not presented). False negatives may also occur as some patients may be unable to mount a systemic response to infection, or the intermittent measurement of clinical observations may miss transient derangements in SIRS parameters. Our study showed that a weighted SIRS score increased the false-negative rate and lowered sensitivity in predicting microbiologically confirmed infection compared with traditional SIRS. Thus, relying on white cell count and temperature may cause clinicians and researchers to miss a significant proportion of patients with positive microbiology.

Our study had several limitations. First, it was an observational cohort study. Presumptive diagnoses of infection were made by the admitting clinicians, and patients' physiological parameters were recorded by nursing staff as part of routine clinical management. Although there were subjective elements in clinicians' diagnoses and the measurements of physiological parameters, we believe this reflects real-world Australasian hospital conditions. Our study was a single-centre study with the associated limitations, but the demographics of our study population were similar to two previous multicentre cohort studies that examined the natural history and utility of SIRS.^{13,14}

Our results highlighted the limitations of the SIRS concept in predicting microbiologically confirmed infection in patients hospitalised with suspected infection. Due to the non-specific nature of each of the SIRS criteria, a weighted SIRS score with emphasis on temperature and white cell count did not perform better than the traditional SIRS in predicting microbiologically confirmed infection. Clinicians and researchers should be aware of these limitations when applying the concept of SIRS in their practice.

Conclusion

Our study demonstrated the lack of utility of individual SIRS criteria, traditional SIRS criteria and a weighted SIRS score in predicting microbiologically confirmed infection in a large cohort of patients admitted to a tertiary hospital with suspected infection. We also showed that the absence of

deranged temperature or white cell count could not be used to rule out infection. Neither the traditional nor the weighted SIRS score added to the predictive value over clinicians' suspicion of infection, which is based on complex clinical reasoning, pattern recognition and sometimes "gut feeling". Refinement of current criteria or development and validation of new criteria are needed to guide clinical practice and facilitate future sepsis research.

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Competing interests

None declared.

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