

# Shock index in the emergency department: utility and limitations

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Erica Koch<sup>1</sup>  
Shannon Lovett<sup>2</sup>  
Trac Nghiem<sup>2</sup>  
Robert A Riggs<sup>2</sup>  
Megan A Rech<sup>2,3</sup>

<sup>1</sup>Stritch School of Medicine, Loyola University Chicago, Maywood, IL 60153, USA; <sup>2</sup>Department of Emergency Medicine, Loyola University Medical Center, Maywood, IL 60153, USA; <sup>3</sup>Department of Pharmacy, Loyola University Medical Center, Maywood, IL 60153, USA

**Abstract:** Shock index (SI) is defined as the heart rate (HR) divided by systolic blood pressure (SBP). It has been studied in patients either at risk of or experiencing shock from a variety of causes: trauma, hemorrhage, myocardial infarction, pulmonary embolism, sepsis, and ruptured ectopic pregnancy. While HR and SBP have traditionally been used to characterize shock in these patients, they often appear normal in the compensatory phase of shock and can be confounded by factors such as medications (eg, antihypertensives, beta-agonists). SI >1.0 has been widely found to predict increased risk of mortality and other markers of morbidity, such as need for massive transfusion protocol activation and admission to intensive care units. Recent research has aimed to study the use of SI in patients immediately on arrival to the emergency department (ED). In this review, we summarize the literature pertaining to use of SI across a variety of settings in the management of ED patients, in order to provide context for use of this measure in the triage and management of critically ill patients.

**Keywords:** shock index, emergency, trauma, hemorrhage, myocardial infarction, pulmonary embolism, sepsis, obstetrics, ectopic pregnancy, pediatrics

## Introduction

Prediction tools and risk stratification algorithms play an important role in the evaluation and management of acutely ill and injured patients. In the compensatory phase of shock, vital signs are often initially within normal ranges. Shock index (SI), defined as the ratio of heart rate (HR) to systolic blood pressure (SBP), is one such measure that has been studied in multiple patient populations.<sup>1</sup> First described in 1967, SI provided an approximation of hemodynamic status in addition to traditional vital signs.<sup>1</sup> The normal range for this unitless measure is currently accepted as 0.5–0.7, though some evidence suggests that up to 0.9 is acceptable.<sup>2–5</sup> Values approaching 1.0 are indicative of worsening hemodynamic status and shock.<sup>1</sup> Elevation in SI has been correlated with reduced left ventricular end-diastolic pressure and circulatory volume, even when HR and SBP are within normal limits.<sup>5,6</sup>

In addition to SI, modified SI (MSI) [HR/mean arterial pressure (MAP)] and age SI (age × SI) have been proposed in continued efforts to improve the prognostic value (Table 1). MSI was developed to incorporate the MAP rather than only SBP, as DBP is also used to determine clinical severity of illness.<sup>7</sup> Age × SI has been shown to be more indicative of mortality in geriatric patients.<sup>6</sup> The pediatric adjusted shock index (SIPA) was developed for pediatric populations and has

Correspondence: Megan A Rech  
Department of Emergency Medicine,  
Stritch School of Medicine, Loyola  
University Chicago, Loyola University  
Medical Center, 2160 S 1st Ave,  
Maywood, IL 60513, USA  
Tel +1 708 327 2567  
Email mrech@lumc.edu

**Table 1** Variations of shock index

Shock index (SI) name variation	Equation	Notes
SI	HR/SBP	
Modified SI (MSI)	HR/MAP	<ul style="list-style-type: none"> <li>• MAP substituted for SBP</li> </ul>
Age SI	Age × (HR/SBP)	<ul style="list-style-type: none"> <li>• SI multiplied by patient's age</li> </ul>
Shock Index Pediatric Adjusted (SIPA)	(HR/SBP)	<ul style="list-style-type: none"> <li>• Formula for SI is the same. Cutoffs are different for each age group:               <ul style="list-style-type: none"> <li>○ Ages 4–6: &gt;1.22</li> <li>○ Ages 7–12: &gt;1.0</li> <li>○ Ages 13–16: &gt;0.9</li> </ul> </li> </ul>

**Abbreviations:** HR, heart rate; MAP, mean arterial pressure; SBP, systolic blood pressure.

proven to be more reliable than the standard adult cutoffs.<sup>2,3,8</sup> Despite these advances, there is no consensus on when, where, and if SI has a role in the emergency department (ED). The purpose of this review was to summarize and evaluate the role of SI in the ED in order to provide context for use of this measure in the triage and management of critically ill patients.

## Methods

This review of therapeutics was undertaken to describe the utility of SI in emergency medicine. Articles were selected from PubMed using the following search terms: shock index in combination with trauma, hemorrhage, myocardial infarction, pulmonary embolism, sepsis, obstetrics, ectopic pregnancy, or pediatrics. Articles were reviewed for inclusion by at least two independent reviewers and selected for inclusion based on the consensus of the authors.

## Triage

Traditionally, HR and SBP, among other vital signs, have been used to assess the hemodynamic status on arrival to the ED. However, these parameters can be normal, even in critically ill patients. This may lead to delayed intervention, increased need for intensive care, and morbidity and mortality.<sup>9,10</sup> For example, patients with advanced age and chronic hypertension may not initially show signs of hemodynamic compromise, such as tachycardia and hypotension.<sup>11</sup> Furthermore, hemorrhaging patients may have a HR and SBP within normal limits even after losing up to 450 mL of blood.<sup>12</sup> Due to these findings, SI has been studied to identify a population at risk for decompensation and poor outcomes.

In a retrospective cohort of 1285 patients with an Emergency Severity Index (ESI) of 2 (corresponding to high risk), SI, MSI, and age SI were found to be better

predictors of inpatient mortality than SBP (Table 2). However, these parameters were not predictive of intensive care unit (ICU) admission.<sup>13</sup> A similar study included 3375 patients with ESI of 3 (stable vital signs but significant discomfort or sickness) found that all types of SI were associated with increased mortality, but only age SI predicted ICU admission.<sup>7</sup> In an adjusted multivariable logistic regression analysis, male sex, SBP, and age SI were predictive of mortality. While this model did not account for multicollinearity, it demonstrates that age SI may be a useful tool to predict mortality. It should be noted that these two studies only included adult patients who were triaged for general medicine complaints; thus, these results may not be applicable to a surgical population.

More recently, a retrospective cohort study included 58,336 adult ED encounters for any chief complaint over a 1-year period to determine the probability of admission and mortality based on the SI at presentation.<sup>14</sup> SI values between 0.5 and 0.7 (normal) had the lowest likelihood of admission and inpatient mortality, whereas SI >1.2 conferred nearly 12 times more likelihood of being admitted compared to normal SI (Table 2).

As SI is calculated from data routinely collected in triage and can be incorporated automatically into the electronic medical record (EMR), it may help with resource allocation and patient flow. It can serve as another data point in addition to traditional vital signs. No prospective studies have examined the impact of triage SI on time to treatment, length of stay (LOS), and mortality.

## Traumatic injury

SI has been studied most extensively in traumatic injury. Hemorrhagic shock (HS) is one of the leading causes of death during initial trauma treatment, and early recognition of shock can be challenging as normal vital signs may be

Table 2 Shock index literature

Study design	Population	Primary end point	Findings
<b>Emergency department triage</b>			
Retrospective cohort <sup>7</sup>	3375 patients who presented to ED and were triaged to ESI level 3 over 1-year period	Association of SI calculated using triage vital signs with mortality and ICU admission	<ul style="list-style-type: none"> <li>● SI was associated with increased odds of mortality (OR 1.31, 95% CI 1.14–1.50)</li> <li>● SI did not predict ICU admission</li> <li>● In multivariable logistic regression, SI was not associated with mortality or ICU admission</li> </ul>
Retrospective cohort <sup>13</sup>	1285 patients who presented to the ED and were triaged to ESI level 2 over 1-year period	Association of SI calculated using triage vital signs with mortality and ICU admission	<ul style="list-style-type: none"> <li>● SI was associated with increased odds of mortality (OR 1.09, 95% CI 1.04–1.14) and ICU admission (1.01 95% CI 1.00–1.01)</li> <li>● SI, MSI, and age SI were found independently associated with mortality after multivariable analysis</li> </ul>
Retrospective cohort <sup>14</sup>	58,336 patients who presented to the ED over a 1-year period	Probability of admission and mortality based upon SI calculated using triage vital signs	<ul style="list-style-type: none"> <li>● SI:                             <ul style="list-style-type: none"> <li>○ 0.5–0.7: positive LR of 0.74 (0.73–0.76) for inpatient admission and 0.58 (0.46–0.74) for inpatient mortality</li> <li>○ &gt;0.7: positive LR of 1.4 (1.37–1.43) for inpatient admission and 1.49 (1.36–1.63) for inpatient mortality</li> <li>○ &gt;1.0: positive LR 5.63 (5.15–6.16) for inpatient admission and 3.31 (2.70–4.05) for inpatient mortality</li> <li>○ &gt;1.2: positive LR of 11.69 (9.50–14.39) for inpatient admission and 5.82 (4.31–7.85) of inpatient mortality</li> </ul> </li> </ul>
<b>Traumatic Injury</b>			
Prospective cohort <sup>12</sup>	46 healthy blood donors	Change in SI and vital signs after 450 mL blood donation	<ul style="list-style-type: none"> <li>● Baseline sitting SI 0.61 increased to 0.65 after donation (<math>p=0.005</math>).</li> <li>● 1- and 5 mins standing mean SI was 0.76 and 0.75 (<math>p&lt;0.001</math>), respectively</li> </ul>
Retrospective cohort <sup>16</sup>	8111 patients admitted to a level I trauma center over an 8-year period with a blunt trauma and pre-hospital SBP >90 mmHg	Risk for MTP activation based on SI calculated from pre-hospital vital signs	<ul style="list-style-type: none"> <li>● MTP activation according to SI:                             <ul style="list-style-type: none"> <li>○ &lt;0.5= RR 1.41 (95% CI 0.90–2.21)</li> <li>○ &gt;0.7–0.9= RR 1.06 (95% CI 0.77–1.45)</li> <li>○ &gt;0.9–1.1= RR 1.61 (95% CI 1.13–2.31)</li> <li>○ &gt;1.1–1.3= RR 5.57 (95% CI 3.74–8.30)</li> <li>○ &gt;1.3= RR 8.13 (95% CI 4.60–14.36)</li> </ul> </li> <li>● 276 received massive transfusion</li> </ul>

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Table 2 (Continued).

Study design	Population	Primary end point	Findings
Retrospective cohort <sup>17</sup>	4292 trauma patients over 11 years divided into bleeding vs non-bleeding groups	Sensitivity and specificity of SI cutoffs for predicting bleeding (defined as $\geq 2$ units PRBC in 24 hrs)	<ul style="list-style-type: none"> <li>● SI cutoff for all ages:               <ul style="list-style-type: none"> <li>○ <math>&gt;0.7</math>: sensitivity 87.5% and specificity 73.8%</li> <li>○ <math>&gt;0.8</math>: sensitivity 76.4% and specificity 87.4%</li> <li>○ <math>&gt;0.9</math>: sensitivity 54.5% and specificity 93.6%</li> <li>○ <math>&gt;1.2</math>: sensitivity 15.9% and specificity 99%</li> </ul> </li> <li>● SI cutoff for patients 65 y/o and older:               <ul style="list-style-type: none"> <li>○ <math>&gt;0.7</math>: sensitivity 82.4% and specificity 83.0%</li> <li>○ <math>&gt;0.8</math>: sensitivity 58.8% and specificity 91.9%</li> <li>○ <math>&gt;0.9</math>: sensitivity 41.2% and specificity 95.7%</li> <li>○ <math>&gt;1.2</math>: sensitivity 23.5% and specificity 99.4%</li> </ul> </li> </ul>
Retrospective cohort <sup>19</sup>	505,296 adult patients from National Trauma Databank	SBP $<90$ mmHg vs SI $\geq 1.0$ to predict trauma center need defined by ISS $> 15$ , need for emergent operation, death in ED, or $>24$ hrs in ICU	<ul style="list-style-type: none"> <li>● Model using SBP <math>&lt;90</math> mmHg: sensitivity 41.67%, specificity 82.41%, NPV 65.37%, PPV 63.95%               <ul style="list-style-type: none"> <li>○ AUC: 0.62 (0.619–0.622)</li> </ul> </li> <li>● Model using SI <math>&gt; 1.0</math>: sensitivity 44.39%, specificity 80.19%, NPV 65.84%, PPV 62.64%               <ul style="list-style-type: none"> <li>○ AUC: 0.623 (0.622–0.625)</li> </ul> </li> </ul>

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Study design	Population	Primary end point	Findings																				
Retrospective <sup>21</sup>	1101 trauma patients over 14 years old presenting to a level I trauma center over a 2-year period	ROC curves used to find the value of SI that maximized sensitivity and specificity for predicting death within 24 hrs, ISS > 16, ICU stay ≥ 1 day, and amount of blood transfused ≥ 2 units	<ul style="list-style-type: none"> <li>ROC optimal SI values:                             <ul style="list-style-type: none"> <li>Death &lt;24 hrs: 1.10</li> <li>ISS &gt;16: 0.71</li> <li>ICU stay ≥ 1 day: 0.77</li> <li>Transfusion ≥ 2 units: 0.85</li> </ul> </li> <li>Optimal SI values for above measures: 0.83                             <ul style="list-style-type: none"> <li>Sensitivity: 37% (95% CI 32–42%)</li> <li>HR &gt; SI &gt; SBP</li> <li>Specificity: 83% (95% CI 80–87%)</li> <li>SI &gt; SBP &gt; HR</li> </ul> </li> <li>Prediction of death in &lt;24 hrs:                             <table border="1"> <thead> <tr> <th>Parameter</th> <th>Sensitivity</th> <th>Specificity</th> <th>PPV</th> <th>NPV</th> </tr> </thead> <tbody> <tr> <td>SI 1.1</td> <td>57% (95% CI 20–94)</td> <td>94% (95% CI 92–95)</td> <td>5% (95% CI 0–10)</td> <td>99% (95% CI 99–100)</td> </tr> <tr> <td>HR 112 bpm</td> <td>43% (95% CI 6–80)</td> <td>82% (95% CI 80–84)</td> <td>2% (95% CI 0–3)</td> <td>99% (95% CI 99–100)</td> </tr> <tr> <td>SBP 104 mm Hg</td> <td>100% (95% CI 100–100)</td> <td>91% (95% CI 89–92)</td> <td>6% (95% CI 2–11)</td> <td>100% (95% CI 100–100)</td> </tr> </tbody> </table> </li> </ul>	Parameter	Sensitivity	Specificity	PPV	NPV	SI 1.1	57% (95% CI 20–94)	94% (95% CI 92–95)	5% (95% CI 0–10)	99% (95% CI 99–100)	HR 112 bpm	43% (95% CI 6–80)	82% (95% CI 80–84)	2% (95% CI 0–3)	99% (95% CI 99–100)	SBP 104 mm Hg	100% (95% CI 100–100)	91% (95% CI 89–92)	6% (95% CI 2–11)	100% (95% CI 100–100)
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Prospective longitudinal study <sup>22</sup>	9860 adult trauma patients presenting to the ED over a 1-year period	Correlation of HR, SBP, SI, and MSI with hospital stay, ICU stay, and in-hospital mortality	<ul style="list-style-type: none"> <li>Mortality:                             <ul style="list-style-type: none"> <li>HR &gt; 120 bpm: OR 2.5 (95% CI 1.7–3.3)</li> <li>SBP &lt;90 mmHg: OR 2.6 (95% CI 1.9–3.4)</li> <li>DBP &lt;60 mmHg: OR 1.9 (95% CI 1.4–2.3)</li> <li>SI &lt;0.5: OR 1.3 (95% CI 0.8–1.6)</li> <li>SI &gt;0.9: OR 1.1 (95% CI 0.7–1.7)</li> <li>MSI &lt;0.7: OR 3.5 (95% CI 2.1–6.9)</li> <li>MSI &gt;1.3: OR 4.5 (95% CI 2.9–6.6)</li> </ul> </li> </ul>																				

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Table 2 (Continued).

Study design	Population	Primary end point	Findings
Retrospective cohort <sup>26</sup>	645 adult trauma patients who presented to the ED over 4-year period	Ability of ABC score and SI to predict MTP use (>10 units PRBC transfusion within 24 hrs of presentation)	<ul style="list-style-type: none"> <li>● SI <math>\geq</math> 1:                             <ul style="list-style-type: none"> <li>○ Sensitivity: 67.7% (95% CI 49.5–82.6%)</li> <li>○ Specificity: 81.3% (95% CI 78.0–84.3%)</li> <li>○ AUROC: 0.83</li> </ul> </li> <li>● ABC Score <math>\geq</math> 2:                             <ul style="list-style-type: none"> <li>○ Sensitivity: 47.0% (95% CI 29.8–64.9%)</li> <li>○ Specificity: 89.8% (95% CI 87.2–92.1%)</li> <li>○ AUROC: 0.74</li> </ul> </li> </ul>
Retrospective cohort <sup>27</sup>	21,853 adult trauma patients between 2002 and 2011	Impact of increasing SI on transfusion needs, mortality, and ISS	<ul style="list-style-type: none"> <li>● PRBC needs: mean (<math>\pm</math>SD)                             <ul style="list-style-type: none"> <li>○ SI &lt;0.6=1.0 (4.8)</li> <li>○ SI 0.6–0.99=2.8 (9.0)</li> <li>○ SI 1.0–1.39=9.9 (17.60)</li> <li>○ SI <math>\geq</math> 1.4=10.7 (12.7)</li> </ul> </li> <li>● Mortality:                             <ul style="list-style-type: none"> <li>○ SI &lt;0.6=10.9%</li> <li>○ SI 0.6–0.99=9.7%</li> <li>○ SI 1.0–1.39=22.9%</li> <li>○ SI <math>\geq</math> 1.4=39.8%</li> </ul> </li> <li>● ICU Days: mean (<math>\pm</math>SD)                             <ul style="list-style-type: none"> <li>○ SI &lt;0.6=7.5 (10.6)</li> <li>○ SI 0.6–0.99=9.3 (12.1)</li> <li>○ SI 1.0–1.39=14.0 (16.0)</li> <li>○ SI <math>\geq</math> 1.4=15.5 (18.9)</li> </ul> </li> </ul>
Retrospective cohort <sup>23</sup>	10,420 adult trauma patients from 2000 to 2012	In-hospital mortality in high- and low-SI groups compared to reference group of SI 0.5 –0.7	<ul style="list-style-type: none"> <li>● In-hospital mortality:                             <ul style="list-style-type: none"> <li>○ SI &lt;0.3: OR 2.2 (95% CI 1.2–4.1)</li> <li>○ SI &gt; 1.3: OR 3.3 (95% CI 1.6–5.9)</li> </ul> </li> </ul>
Retrospective cohort <sup>30</sup>	3680 adult trauma patients admitted to hospital over 4-year period	In-hospital mortality	<ul style="list-style-type: none"> <li>● In-hospital mortality (area under the curve <math>\pm</math>SD):                             <ul style="list-style-type: none"> <li>○ REMS: 0.91 (<math>\pm</math>0.02)</li> <li>○ RTS: 0.89 (<math>\pm</math>0.04)</li> <li>○ ISS: 0.87 (<math>\pm</math>0.01)</li> <li>○ SI: 0.55 (<math>\pm</math>0.31)</li> </ul> </li> </ul>

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Study design	Population	Primary end point	Findings																				
<b>Obstetrics</b>																							
Prospective cohort <sup>40</sup>	65 patients presenting to the ED with ectopic pregnancy managed surgically	SI in patients with ruptured vs unruptured ectopic pregnancy	<ul style="list-style-type: none"> <li>● SI in ruptured ectopic pregnancy (0.74±0.16) was significantly higher than unruptured ectopic pregnancy (0.67±0.14; <math>p=0.04</math>)</li> <li>● SI &gt;0.81: RR 1.84 for ruptured ectopic pregnancy                             <ul style="list-style-type: none"> <li>○ PPV 94%, sensitivity 35%, specificity 95%</li> </ul> </li> </ul>																				
Retrospective cohort <sup>41</sup>	52 patients presenting to the ED ectopic pregnancy managed surgically	SI and SBP in ruptured vs unruptured ectopic pregnancy	<ul style="list-style-type: none"> <li>● Triage SI was statistically higher in ruptured vs unruptured ectopic pregnancy (0.84±0.6 vs 0.65±0.3, <math>p&lt;0.001</math>)                             <ul style="list-style-type: none"> <li>○ SI &gt;0.7: Sensitivity 72% (95% CI 51–88%), specificity 67% (95% CI 58–91%), PPV 75%</li> </ul> </li> <li>● Sensitivity of HR &gt;100 and SBP &lt;100 mmHg for ruptured ectopic pregnancy was 28% (95% CI 12–49%) and 36% (95% CI 18–58%) with specificities of 96% (95% CI 81–99%) for both</li> </ul>																				
Prospective cohort <sup>28</sup>	280 patients presenting to the ED in first trimester of pregnancy	SI in patients with ruptured ectopic pregnancy, unruptured ectopic pregnancy, and nonectopic pregnancy Ability of SI to predict ruptured ectopic pregnancy	<ul style="list-style-type: none"> <li>● SI median (IQR):                             <ul style="list-style-type: none"> <li>○ Unruptured ectopic: 0.65 (0.59–0.68)</li> <li>○ Ruptured ectopic: 0.80 (0.70–0.98)</li> <li>○ Non-ectopic pregnancy: 0.66 (0.6–0.74)</li> </ul> </li> <li>● Parameters for detecting ruptured ectopic pregnancy:                             <table border="1" data-bbox="954 138 1315 966"> <thead> <tr> <th>Parameter</th> <th>Sensitivity</th> <th>Specificity</th> <th>Positive LR</th> </tr> </thead> <tbody> <tr> <td>SBP &lt;100 mmHg</td> <td>16% (95% CI 5–36%)</td> <td>98% (95% CI 95–100%)</td> <td>22.6</td> </tr> <tr> <td>HR &gt;100bpm</td> <td>28% (95% CI 12–49%)</td> <td>92% (95% CI 86–95%)</td> <td>3.29</td> </tr> <tr> <td>SI &gt;0.7</td> <td>76% (95% CI 55–91%)</td> <td>70% (95% CI 63–77%)</td> <td>2.26</td> </tr> <tr> <td>SI &gt;0.85</td> <td>40% (95% CI 21–61%)</td> <td>97% (95% CI 94–99%)</td> <td>15.0</td> </tr> </tbody> </table> </li> </ul>	Parameter	Sensitivity	Specificity	Positive LR	SBP <100 mmHg	16% (95% CI 5–36%)	98% (95% CI 95–100%)	22.6	HR >100bpm	28% (95% CI 12–49%)	92% (95% CI 86–95%)	3.29	SI >0.7	76% (95% CI 55–91%)	70% (95% CI 63–77%)	2.26	SI >0.85	40% (95% CI 21–61%)	97% (95% CI 94–99%)	15.0
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<b>Sepsis</b>																																																					
Retrospective cohort <sup>29</sup>	2524 adult patients with suspicion of sepsis over 15-month period	PPV, NPV, sensitivity, and specificity of SI and SIRS for hyperlactatemia and 28-day mortality	<ul style="list-style-type: none"> <li>● Hyperlactatemia:                             <table border="1"> <thead> <tr> <th>Parameter</th> <th>Sensitivity</th> <th>Specificity</th> <th>PPV</th> <th>NPV</th> </tr> </thead> <tbody> <tr> <td>SI ≥1.0</td> <td>0.48</td> <td>0.81</td> <td>0.24</td> <td>0.92</td> </tr> <tr> <td>SI ≥0.7</td> <td>0.83</td> <td>0.42</td> <td>0.16</td> <td>0.95</td> </tr> <tr> <td>SIRS</td> <td>0.78</td> <td>0.52</td> <td>0.18</td> <td>0.95</td> </tr> <tr> <td>SIRS without WBC</td> <td>0.63</td> <td>0.54</td> <td>0.15</td> <td>0.92</td> </tr> </tbody> </table> </li> <li>● 28-day mortality:                             <table border="1"> <thead> <tr> <th>Parameter</th> <th>Sensitivity</th> <th>Specificity</th> <th>PPV</th> <th>NPV</th> </tr> </thead> <tbody> <tr> <td>SI ≥1.0</td> <td>0.37</td> <td>0.8</td> <td>0.23</td> <td>0.88</td> </tr> <tr> <td>SI ≥0.7</td> <td>0.71</td> <td>0.41</td> <td>0.17</td> <td>0.89</td> </tr> <tr> <td>SIRS</td> <td>0.64</td> <td>0.51</td> <td>0.18</td> <td>0.89</td> </tr> <tr> <td>SIRS without WBC</td> <td>0.47</td> <td>0.52</td> <td>0.14</td> <td>0.86</td> </tr> </tbody> </table> </li> </ul>	Parameter	Sensitivity	Specificity	PPV	NPV	SI ≥1.0	0.48	0.81	0.24	0.92	SI ≥0.7	0.83	0.42	0.16	0.95	SIRS	0.78	0.52	0.18	0.95	SIRS without WBC	0.63	0.54	0.15	0.92	Parameter	Sensitivity	Specificity	PPV	NPV	SI ≥1.0	0.37	0.8	0.23	0.88	SI ≥0.7	0.71	0.41	0.17	0.89	SIRS	0.64	0.51	0.18	0.89	SIRS without WBC	0.47	0.52	0.14	0.86
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SI ≥1.0	0.37	0.8	0.23	0.88																																																	
SI ≥0.7	0.71	0.41	0.17	0.89																																																	
SIRS	0.64	0.51	0.18	0.89																																																	
SIRS without WBC	0.47	0.52	0.14	0.86																																																	
Retrospective cohort <sup>32</sup>	295 adults in ED with severe sepsis over 2-year period	SI as a predictor of vasopressor use	<ul style="list-style-type: none"> <li>● n=140 sustained SI elevation (SI &gt;0.8 at least 80% of vital sign measurements)</li> <li>● Vasopressors required within 72 hrs:                             <ul style="list-style-type: none"> <li>○ Sustained elevation 38.6% vs no sustained elevation 11.6% (p&lt;0.001)</li> <li>○ Sustained elevation for vasopressor requirements OR 4.42 (95% CI 2.28–8.55)</li> </ul> </li> </ul>																																																		

(Continued)



Table 2 (Continued).

Study design	Population	Primary end point	Findings															
Prospective cohort <sup>33</sup>	25 patients $\geq 14$ years admitted to ICU with septic shock over an 18-month period	Effect of SI and CVP on hemodynamic response to volume expansion	<ul style="list-style-type: none"> <li>Hemodynamic response to volume expansion:                             <table border="1"> <thead> <tr> <th>Parameter</th> <th>PPV</th> <th>NPV</th> </tr> </thead> <tbody> <tr> <td>SI <math>\geq 1</math></td> <td>44% (22–69%)</td> <td>88% (60–98%)</td> </tr> <tr> <td>CVP <math>\geq 8</math> mmHg</td> <td>60% (27–86%)</td> <td>83% (62–95%)</td> </tr> <tr> <td>SI <math>\geq 1</math> and CVP <math>\geq 8</math> mmHg</td> <td>45% (30–50%)</td> <td>93% (71–100%)</td> </tr> </tbody> </table> </li> </ul>	Parameter	PPV	NPV	SI $\geq 1$	44% (22–69%)	88% (60–98%)	CVP $\geq 8$ mmHg	60% (27–86%)	83% (62–95%)	SI $\geq 1$ and CVP $\geq 8$ mmHg	45% (30–50%)	93% (71–100%)			
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<b>Cardiovascular disease</b>																		
Retrospective cohort <sup>34</sup>	644 patients diagnosed with STEMI	Correlation with SI and mortality	<ul style="list-style-type: none"> <li>Mortality:                             <ul style="list-style-type: none"> <li>SI <math>\geq 0.8</math> 20.3% vs SI <math>&lt; 0.8</math> 4% (OR 81.2, 95% CI 9.76–676.51)</li> <li>SI <math>\geq 0.8</math>: sensitivity: 75%, specificity: 61%</li> </ul> </li> </ul>															
Retrospective cohort <sup>35</sup>	1206 patients with objectively confirmed pulmonary emboli	Association of sPESI and SI with predicting all-cause 30 day mortality	<ul style="list-style-type: none"> <li>Test characteristics for 30-day mortality:                             <table border="1"> <thead> <tr> <th>Parameter</th> <th>Sensitivity</th> <th>Specificity</th> <th>PPV</th> <th>NPV</th> </tr> </thead> <tbody> <tr> <td>sPESI</td> <td>95% (95% CI 91.0–98.9)</td> <td>33.4% (95% CI 30.6–36.2)</td> <td>13.5% (95% CI 11.2–15.8)</td> <td>98.4% (95% CI 97.1–99.7)</td> </tr> <tr> <td>SI</td> <td>28.6% (95% CI 20.4–36.7)</td> <td>86.4% (95% CI 84.3–88.4)</td> <td>18.7% (95% CI 13–24.3)</td> <td>91.7% (95% CI 90–93.4)</td> </tr> </tbody> </table> </li> <li>The net reclassification improvement with the sPESI was 13.4% (<math>p=0.07</math>).</li> </ul>	Parameter	Sensitivity	Specificity	PPV	NPV	sPESI	95% (95% CI 91.0–98.9)	33.4% (95% CI 30.6–36.2)	13.5% (95% CI 11.2–15.8)	98.4% (95% CI 97.1–99.7)	SI	28.6% (95% CI 20.4–36.7)	86.4% (95% CI 84.3–88.4)	18.7% (95% CI 13–24.3)	91.7% (95% CI 90–93.4)
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Retrospective cohort <sup>36</sup>	159 patients with objectively identified acute pulmonary embolism	Association of SI and echocardiographic findings with in-hospital mortality	<ul style="list-style-type: none"> <li>SI <math>\geq 1.0</math> associated with increased hospital mortality (<math>p=0.005</math>)</li> </ul>															
<b>Pediatrics</b>																		
Retrospective cohort <sup>2</sup>	543 children (ages 4–16 years) admitted to trauma centers with blunt injury with ISS $\geq 15$	Ability of SI $> 0.9$ vs SIPA to predict severe injury (ISS $> 24$ ) and in-hospital mortality	<ul style="list-style-type: none"> <li>ISS <math>&gt; 24</math>: 54% elevated SIPA vs 44% SI <math>&gt; 0.9</math></li> <li>Transfusion with 24 hrs: 27% of elevated SIPA vs 20% SI <math>&gt; 0.9</math></li> <li>In-hospital mortality: 11% with elevated SIPA vs 7% SI <math>&gt; 0.9</math></li> <li>Grade III liver/spleen laceration: 27% elevated SIPA vs 20% SI <math>&gt; 0.9</math></li> </ul>															

(Continued)

Table 2 (Continued).

Study design	Population	Primary end point	Findings					
Retrospective cohort <sup>8</sup>	559 children (age 4–16) admitted with an ISS $\geq$ 15 after blunt trauma	Ability of SIPA vs age-adjusted hypotension to identify injured children requiring emergency operation, intubation, or transfusion	● Outcomes by tool:					
			Outcome	Overall cohort	Elevated SIPA	Age-adjusted hypotension		
			Operation	21%	30%	13%		
			Intubation	37%	40%	17%		
			Transfusion	22%	53%	22%		
Sensitivity	–	58%	89%					
Prospective cohort <sup>3</sup>	386 patients (age 4–16) presenting to the ED with blunt liver/spleen injury and an ISS $\leq$ 15	Ability of SIPA and SI >0.9 to predict need for blood transfusion within 24 hrs, ISS >24, having a grade 3 or greater BLSI requiring transfusion, in-hospital mortality, need for surgery, need for ICU admission	● Outcomes by tool:					
			Outcome	SI >0.9		SIPA		
				Sensitivity	Specificity	Sensitivity	Specificity	
			Transfusion	95.9% (95% CI 89.8–98.9)	21.5% (95% CI 16.8–26.8)	94.8% (88.4–98.3)	35.1 (29.5–44.1)	
			ISS >24	88.1% (95% CI 82.2–92.6)	20.6% (95% CI 15.5–26.6)	78.6% (71.6–84.5)	31.2% (25.1–37.8)	
			BLSI needing transfusion	94.8% (95% CI 88.3–93.8)	20.7% (95% CI 16.2–25.8)	94.8% (88.3–98.3)	34.1% (28.7–39.9)	
			Operation	97.9% (95% CI 88.7–99.9)	18.9% (95% CI 14.9–23.5)	97.9% (88.7–99.9)	30.4% (25.5–35.6)	
			ICU admission	92.4% (95% CI 88.1–95.5)	29.5% (95% CI 22.7–37.3)	84.8% (79.4–89.3)	43.2% (35.5–51.2)	
			In-hospital mortality	100% (95% CI 78.2–100)	17.6 (95% CI 13.8–21.8)	93.3% (68.1–99.8)	27.8% (23.3–32.7)	
			Any outcome	89.0% (95% CI 84.8–92.4)	33.0% (95% CI 24.1–43.0)	79.5% (74.3–84.1)	44.7% (34.9–54.8)	

(Continued)

**Table 2** (Continued).

Study design	Population	Primary end point	Findings
Retrospective cohort <sup>4</sup>	286 children (age 4–16) admitted with ISS $\geq$ 15 after a blunt trauma	Trends in SIPA at 0, 12, 24, 36, and 48 hrs predicting death, ICU LOS, and other markers of morbidity	<ul style="list-style-type: none"> <li>● 81.6% of patients with an elevated SIPA at 12 hrs and 100% elevated at 24 hrs died                             <ul style="list-style-type: none"> <li>○ 2.4% of patients with normal SI throughout died (<math>p&lt;0.001</math>)</li> </ul> </li> <li>● 18.4% of patients who developed an elevated SIPA at 12 hrs after admission died</li> <li>● Hospital LOS increased from 5 days (normalized by 12 hrs) to 15 days (normalized by 48 hrs)</li> <li>● ICU LOS increased from 2 days (normalized by 12 hrs) to 10.5 days (normalized after 48 hrs) in patients with increasing time of elevation in SIPA (<math>p=0.032</math>)</li> </ul>
Retrospective cohort <sup>5</sup>	146 children admitted to the PICU with septic shock	Correlation between abnormal SIPA and risk of death	<ul style="list-style-type: none"> <li>● Median SI at admission : non-survivors 1.86 (IQR 1.56–2.55) vs survivors 1.67 (IQR 1.46–2.01, <math>p=0.02</math>)</li> <li>● Median SI at 4 hrs: non-survivors 1.77 (IQR 1.52–2.16) vs survivors 1.63 (IQR 1.33–1.93; <math>p=0.03</math>)</li> <li>● Median SI at 6 hrs: non-survivors: 1.87 (IQR 1.52–2.26) vs survivors: 1.60 (IQR 1.28–1.94; <math>p&lt;0.01</math>)</li> <li>● Relative Risk of Death with abnormal SIPA:                             <ul style="list-style-type: none"> <li>○ Admission: 1.85 (95% CI 1.04–3.26)</li> <li>○ Hour 1: 1.59 (95% CI 0.96–2.65)</li> <li>○ Hour 2: 1.33 (95% CI 0.80–2.22)</li> <li>○ Hour 4: 1.63 (95% CI 0.92–2.87)</li> <li>○ Hour 6: 2.17 (95% CI 1.18–3.96)</li> </ul> </li> </ul>

(Continued)

Table 2 (Continued).

Study design	Population	Primary end point	Findings						
			Time	Age	Cutoff	Sensitivity	Specificity	PPV	NPV
Prospective cohort <sup>37</sup>	120 children <14 years admitted with diagnosis of severe sepsis or septic shock	Correlation between SIPA and death within 48 hrs of admission – established cutoff values at 0 and 6 hrs for increased risk	<ul style="list-style-type: none"> <li>SIPA test characteristics according to time:</li> </ul>						
			0 hrs	1 month -<1 year	1.98	77%	75%	67%	83%
			6 hrs	1–6 years	1.5	65%	65%	68%	63%
			6–12 years	1.25	90%	67%	77%	83%	
			1 month -<1 year	1.66	85%	80%	73%	89%	
			1–6 years	1.36	73%	70%	73%	70%	
			6–12 years	1.3	74%	73%	78%	69%	
<b>Geriatrics</b>									
Retrospective cohort <sup>6</sup>	16,077 patients admitted to Level I trauma center aged 18–84 years with blunt injury	Ability of HR, SBP, SI, and age x SI to predict of 48-hr mortality	<ul style="list-style-type: none"> <li>AUC for patients ≥55 years for 48-hr mortality:                             <ul style="list-style-type: none"> <li>HR: 0.66 (95% CI 0.59–0.73)</li> <li>SBP: 0.76 (95% CI 0.95–0.83)</li> <li>SI: 0.79 (95% CI 0.73–0.85)</li> <li>Age x SI: 0.83 (95% CI 0.78–0.88)</li> </ul> </li> </ul>						
Retrospective cohort <sup>24</sup>	189,574 patients aged 18–81 years admitted with blunt, non-neurologic trauma	HR, SBP, SI, and age x SI as predictors of 48-hr mortality	<ul style="list-style-type: none"> <li>AUC for patients ≥55 years for 48-hr mortality:                             <ul style="list-style-type: none"> <li>HR: 0.63 (95% CI 0.6–0.65)</li> <li>SBP: 0.66 (95% CI 0.63–0.68)</li> <li>SI: 0.68 (95% CI 0.66–0.71)</li> <li>Age x SI: 0.69 (95% CI 0.67–0.72)</li> </ul> </li> <li>Proposed cutoff for age x SI for patients &gt;55 years old: 48.8                             <ul style="list-style-type: none"> <li>Sensitivity 55%, specificity 80%</li> </ul> </li> <li>Proposed cutoff for SI for patients &gt;55 years old: 0.73                             <ul style="list-style-type: none"> <li>Sensitivity 53%, specificity 82%</li> </ul> </li> </ul>						

(Continued)

Table 2 (Continued).

Study design	Population	Primary end point	Findings																																
Retrospective cohort <sup>25</sup>	45,880 patients older than 65 years admitted with traumatic injuries	Predictive ability of SI, age SI, and MSI on in-hospital and ED mortality	<ul style="list-style-type: none"> <li>AUC for in-hospital mortality:                             <ul style="list-style-type: none"> <li>SI: 0.674 (95% CI 0.65–0.7)</li> <li>MSI: 0.682 (0.66–0.7)</li> <li>Age SI: 0.74 (0.72–0.76)</li> </ul> </li> <li>SI vs age SI: <math>p &lt; 0.001</math></li> <li>SI vs MSI: <math>p = 0.514</math></li> </ul>																																
Retrospective cohort <sup>39</sup>	409 geriatric patients $\geq 65$ -years-old visiting the ED diagnosed with influenza	Association between SI and 30-day mortality	<ul style="list-style-type: none"> <li>SI <math>\geq 1</math> predicting 30-day mortality:                             <ul style="list-style-type: none"> <li>OR 6.8 (95% CI 2.39–19.39)</li> </ul> </li> <li>AUC 0.62, sensitivity, 30% specificity 94.1%</li> <li>PPV 20%, NPV 96.4%</li> </ul>																																
Retrospective cohort <sup>11</sup>	111,019 first-time ED visits	Association between age $\geq 65$ , diabetes, hypertension, and use of BB or CCB and effect on SI prediction of 30-day mortality	<ul style="list-style-type: none"> <li>Test characteristics for SI <math>\geq 1.0</math> for 30-day mortality:</li> </ul> <table border="1"> <thead> <tr> <th>Parameter</th> <th>OR</th> <th>Sensitivity</th> <th>Specificity</th> </tr> </thead> <tbody> <tr> <td rowspan="2">Age</td> <td>&lt;65 years</td> <td>18.9 (95% CI 15.6–23)</td> <td>98% (95% CI 98–98)</td> </tr> <tr> <td><math>\geq 65</math> years</td> <td>8.2 (95% CI 7.2–9.4)</td> <td>98% (95% CI 98–98)</td> </tr> <tr> <td rowspan="2">CCB/BB</td> <td>No</td> <td>12.3 (95% CI 11–13.8)</td> <td>98% (95% CI 98–98)</td> </tr> <tr> <td>Yes</td> <td>6.4 (95% CI 4.9–8.3)</td> <td>98% (95% CI 98–98)</td> </tr> <tr> <td rowspan="2">HTN</td> <td>No</td> <td>12.9 (95% CI 11.1–14.9)</td> <td>98% (95% CI 98–98)</td> </tr> <tr> <td>Yes</td> <td>8 (95% CI 6.6–9.4)</td> <td>97% (95% CI 97–98)</td> </tr> <tr> <td rowspan="2">Diabetes</td> <td>No</td> <td>10.8 (95% CI 9.6–12)</td> <td>98% (95% CI 98–98)</td> </tr> <tr> <td>Yes</td> <td>9.3 (95% CI 6.7–12.9)</td> <td>97% (95% CI 97–98)</td> </tr> </tbody> </table>	Parameter	OR	Sensitivity	Specificity	Age	<65 years	18.9 (95% CI 15.6–23)	98% (95% CI 98–98)	$\geq 65$ years	8.2 (95% CI 7.2–9.4)	98% (95% CI 98–98)	CCB/BB	No	12.3 (95% CI 11–13.8)	98% (95% CI 98–98)	Yes	6.4 (95% CI 4.9–8.3)	98% (95% CI 98–98)	HTN	No	12.9 (95% CI 11.1–14.9)	98% (95% CI 98–98)	Yes	8 (95% CI 6.6–9.4)	97% (95% CI 97–98)	Diabetes	No	10.8 (95% CI 9.6–12)	98% (95% CI 98–98)	Yes	9.3 (95% CI 6.7–12.9)	97% (95% CI 97–98)
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**Abbreviations:** ABC, Assessment of Blood Consumption; AUC, area under the curve; BB, beta-blockers; BLSI, blunt liver and/or spleen injury; CCB, calcium channel blockers; CVP, central venous pressure; ED, Emergency Department; ESI, Emergency Severity Index; HR, heart rate; HTN, hypertension; ICU, intensive care unit; IQR, interquartile range; ISS, injury severity scale; LOS, length of stay; LR, likelihood ratio; MSI, modified shock index; MTP, massive transfusion protocol; NPV, negative predictive value; OR, odds ratio; PICU, Pediatric Intensive Care Unit; PPV, positive predictive value; PRBC, packed red blood cells; REMS, Rapid Emergency Medicine Score; ROC, receiver operating characteristics; RTS, Revised Trauma Score; SI, shock index; SIPI, shock index pediatric adjusted; SIRS, systemic inflammatory response syndrome; sPESI, simplified pulmonary embolism severity index; STEMI, ST elevation myocardial infarction; VS, vital signs; WBC, white blood cells; SBP, systolic blood pressure.

present in the compensatory phase of shock.<sup>15</sup> Over the last few decades, “late deaths”, such as that from sepsis or multi-organ failure, have decreased, while “early deaths”, such as that from HS, have remained constant.<sup>15</sup> Much of the literature relating to SI in the ED is aimed at identifying a reliable and early tool for predicting HS, need for massive transfusion, and mortality (Table 2).

SI may be more valuable in predicting HS or bleeding requiring the activation of massive transfusion protocol (MTP) compared to traditional measures of HS such as tachycardia or hypotension.<sup>16</sup> A prospective study in 46 healthy blood donors found that after 450 mL of blood loss, SI was persistently elevated at 1 and 5 mins, though HR and SBP were still within normal limits.<sup>12</sup> A retrospective cohort study including 8111 patients with blunt trauma aimed to identify those at risk of requiring activation of the MTP despite relatively stable SBP (>90 mm Hg).<sup>16</sup> In patients with SI >0.9, the risk of MTP rose substantially, despite being relatively normotensive. SI >0.9 has been the most commonly accepted value for predicting need for MTP, but more work is needed to further evaluate the best threshold, particularly in the geriatric population.<sup>17</sup>

The National Trauma Triage Protocol algorithm is comprised of four steps used to evaluate trauma patients in the field to determine treatment and transport needs.<sup>18</sup> Step 1 involves evaluation of the following physiologic criteria that would mandate immediate transport to a trauma center: Glasgow Coma Scale <14, SBP <90 mm Hg, or respiratory rate <10 or >29 breaths per minute.<sup>18</sup> A retrospective study of 505,296 patients substituted SI >1.0 instead of SBP <90 mm Hg to determine if SI lends additional benefit in identifying patients in need of referral to a trauma center.<sup>19</sup> Trauma center need was defined according to the following: Injury Severity Score (ISS)  $\geq 16$  (corresponding to severe injury involving multiple systems with a chance of death >10%), need for emergent surgery, ICU LOS >24 hrs, or death in the ED.<sup>20</sup> Substituting SI for SBP resulted in a significant reduction in under-triage rates without causing a large increase in over-triage, suggesting that SI may be more useful than SBP in determining where patients should be transferred. Future studies should evaluate longer-term outcomes like LOS beyond 24 hrs and mortality.<sup>6</sup>

Other studies have yielded equivocal results when comparing SI to HR and BP indices.<sup>21,22</sup> SI has been directly compared to HR and SBP in a retrospective cohort of 1101 trauma patients to predict severity measures.<sup>21</sup>

The severity measures included the following: death within 24 hrs, ISS  $\geq 16$ , ICU LOS >24 hrs, and need for  $\geq 2$  units of blood. According to receiver operating curve characteristics, the optimal SI thresholds were as follows:  $\geq 1.1$  for death within 24 hrs,  $\geq 0.71$  for ISS  $\geq 16$ ,  $\geq 0.77$  for ICU stay  $\geq 1$  day, and  $\geq 0.85$  for transfusion  $\geq 2$  units. SI  $\geq 0.83$  was the best cutoff for predicting any of the severity measures.

A subsequent prospective longitudinal study of 9860 adult trauma patients compared the predictive value of SI and MSI for hospital mortality. MSI <0.7 and >1.3 had higher odds of mortality compared to HR, SBP, DBP, and SI.<sup>22</sup> A low MSI is common in head injury patients or patients with significant hyperperfusion, whereas a high MSI is more suggestive of hypoperfusion. A retrospective study including 10,480 patients similarly found a bimodal relationship with SI and mortality; however, only high SI predicted mortality in trauma patients without head injury.

SI has been compared to other tools, including the Rapid Emergency Medicine Score (REMS). A retrospective cohort compared the discriminatory power of REMS, Revised Trauma Score (RTS), ISS, and SI. All of these scores except ISS allow for prompt calculation at the bedside, although SI is simplest and fastest. Although REMS was originally validated in nonsurgical patients, it performed similarly to RTS and superior to both ISS and SI in predicting mortality in trauma patients.<sup>23</sup>

In a retrospective study of 16,077 patients, the predictive ability of HR, SBP, SI, and age  $\times$  SI on 48-hr mortality in patients admitted to a level 1 trauma center with blunt injury was evaluated.<sup>6</sup> In patients  $\geq 55$  years, SI and age SI were 0.79 (95% CI 0.73–0.85) and 0.83 (95% CI 0.78–0.88), respectively,  $p=0.0005$ . Both SI and age  $\times$  SI performed better than HR and SBP alone. These findings were corroborated by similar studies.<sup>24,25</sup>

SI has also been used in comparison to the Assessment of Blood Consumption (ABC) score, which is comprised of the following: penetrating mechanism,  $\leq$ SBP of 90 mmHg, HR  $\geq 120$  bpm, and positive Focused Assessment with Sonography in Trauma exam.<sup>26</sup> Presence of at least two criteria predicts activation of the MTP. SI was the strongest predictor followed by ABC score and had significantly greater sensitivity ( $p=0.04$ ), but a significantly weaker specificity ( $p<0.001$ ) compared to ABC score (Table 2). A similar study using the German Trauma Society registry found that SI was associated with increasing ISS, increased transfusion requirements, and increased mortality.<sup>27</sup>

SI has been used to predict mortality and MTP activation in trauma patients, especially values exceeding 1.0. Results comparing SI to HR and SBP in trauma patients are mixed, suggesting the need for further studies. Additional data are needed to determine if SI should be a component of the National Trauma Triage Protocol. MSI should also be further examined in trauma to determine if it is more efficacious than SI. It is unclear if any trauma centers are utilizing SI in real time and the implications thereof as all research to date in this population is retrospective. More prospective studies using SI in trauma and directly comparing SI to other predictive scores such as RTS and REMS are needed to determine if widespread utilization in trauma patients could improve outcomes.

## Obstetrics

In an obstetric population, SI has been used in ectopic pregnancy as a diagnostic tool and predictor of rupture (Table 2). In a prospective cohort study of 65 ED patients who presented in need of surgical management for ectopic pregnancy, a significant difference in SI was observed between ruptured and unruptured pregnancies ( $0.74 \pm 0.16$  vs  $0.67 \pm 0.14$ , respectively;  $p=0.04$ ); however, this absolute difference of 0.07 has questionable clinical relevance.<sup>27</sup> Nevertheless, this study found that  $SI \geq 0.81$  corresponded with increased risk for ruptured ectopic pregnancy (Table 2). A retrospective case-control study of 52 patients found that patients with ruptured ectopic pregnancy had a significant elevation in triage HR and SI, but not SBP.<sup>28</sup> Finally, a subsequent prospective cohort of 280 patients presenting to the ED in the first trimester of pregnancy determined the optimal cutoff for SI in the prediction of ruptured ectopic pregnancy (Table 2).<sup>28</sup> An SI cutoff value of 0.7 had 76% sensitivity and 70% specificity in detecting ruptured ectopic pregnancy. Increasing this value to  $SI \geq 0.85$  lowered the sensitivity to 40% while increasing the specificity to 97%. Based on these results, marked elevation in SI ( $>0.85$ ) may be useful for identifying patients at increased risk of ruptured ectopic pregnancy. Since SI appears more sensitive in this setting than HR or SBP, it may be useful as a screening tool. Considering its lack of specificity, transvaginal ultrasound remains the standard of care. Further prospective studies could examine the utility of SI in predicting which patients require immediate intervention through urgent obstetrics consultation and bedside ultrasound in preparation for emergent surgical intervention.

## Sepsis

Systemic Inflammatory Response (SIRS) criteria have traditionally been used to screen for sepsis in patients presenting to the ED.<sup>29</sup> SIRS criteria were used to define sepsis until the 2016 Third International Consensus Definitions Task Force changed the definition to a life-threatening organ dysfunction due to a dysregulated host response to infection, as quantified by the use of Sequential Organ Failure Assessment (SOFA) and qSOFA ("quick" SOFA;  $\geq 2$  of the following: respiratory rate  $\geq 22$ /minute, SBP  $\leq 100$  mm Hg or altered mentation) were recommended to identify sepsis in the hospital and ED settings, respectively.<sup>30,31</sup> While SI has been investigated as an additional measure to identify patients meeting SIRS criteria in need of immediate intervention, it has not been compared or added to SOFA or qSOFA.

A retrospective cohort of 2524 adult patients compared SI with  $\geq 2$  SIRS criteria and modified SIRS (SIRS excluding white blood count) to predict serum lactate  $\geq 4$  mmol/L (Table 2).<sup>29</sup> When the SI was  $>0.7$ , subjects had a 3 times higher likelihood of hyperlactatemia when compared to those with  $SI < 0.7$ . Perhaps, the most useful finding from this study was that the negative predictive value (NPV) was 95% in patients with normal SI. Positive predictive value (PPV) was poor for predicting both hyperlactatemia and 28-day mortality for SI, SIRS, and modified SIRS. While it is unclear at this time how SI compares to SOFA or qSOFA as a predictor for the development of septic shock or outcomes like morbidity and mortality, it may prove useful at centers using SIRS-based assessments.

In 295 patients with severe sepsis, 38.6% of patients with sustained elevation in  $SI > 0.8$  for at least 80% of ED vital sign measurements required vasopressors within 72 hrs of admission, compared to only 11.6% of patients without a sustained elevation in SI.<sup>32</sup> Instead of using a single SI value (ie triage of vital signs), this study assessed trends over time. SI used at a single time point at the initiation of sepsis care did not predict vasopressor use or mortality. Similar to other vital signs, trending SI over time using the EMS may identify patients at of septic shock.

SI has also been evaluated in the context of predicting hemodynamic response to volume expansion. A prospective observational study of 25 patients with 34 volume expansions (10 mL/kg over  $<20$  mins) with septic shock examined central venous pressure (CVP), SI, and volume responsiveness.<sup>33</sup> The primary outcome was an increase of

cardiac index (CI) measured by echocardiography of  $\geq 15\%$  after expansion. Patients with a CVP  $\geq 8$  mm Hg and SI  $\leq 1$  were unlikely to respond to volume expansion (13 nonresponders and 1 responder), with a NPV of 93% (95% CI 71–100%). Patients with an SI  $>1$  were more likely to be fluid-responsive. This indicates that the combination of a high CVP and relatively low SI is better than either alone when assessing if a patient will respond to further fluid boluses, which may aid in avoiding fluid overload in critically ill patients.

While SI has been compared to SIRS for outcomes in sepsis, it is unclear how SI would compare to SOFA and qSOFA, which have improved test characteristics compared to SIRS. Furthermore, pairing the higher sensitivity of SIRS criteria with the improved specificity of SI  $>1$  may yield a more accurate way to identify septic patients needing immediate intervention. It appears that SI  $>1$  may be used to help guide fluid resuscitation and vasopressor use, though more studies are needed to determine populations that benefit most and specific cut points in SI that yield the best test characteristics.

## Cardiovascular disease

SI has been used across a variety of cardiovascular disorders (Table 2). In a retrospective study including 644 consecutive acute ST elevation myocardial infarction (MI) patients, SI was evaluated as a marker for patients at risk for cardiogenic shock (N=96).<sup>34</sup> SI  $\geq 0.8$  on admission to a percutaneous coronary intervention center was predictive of in-hospital mortality. Of those with SI  $\geq 0.8$ , 20.3% died compared to 4% with SI  $<0.8$ . Though these findings are impressive, replication is needed to explore SI's predictive ability in acute coronary syndromes.

A retrospective study of 1206 patients diagnosed with known or suspected PE compared the Simplified Pulmonary Embolism Severity Index (sPESI) and SI to predict 30-day mortality.<sup>35</sup> The sPESI variables include age  $\geq 80$ , history of cancer, chronic cardiopulmonary disease, HR  $>110$  bpm, SBP  $<100$  mmHg, and arterial oxygen saturation  $<90\%$ .<sup>35</sup> Presence of one or more variables deemed the patient high risk. The cutoff for high risk SI was 1. There were significantly more patients categorized as low risk via SI (85%) relative to low-risk sPESI (31%). More low-risk SI patients died compared to low-risk sPESI subjects (8.3% vs 1.6%). sPESI had better test characteristics compared to SI and thus SI cannot be reliably used to predict high-risk PE and mortality.

A similar retrospective study of 159 patients diagnosed with PE via spiral CT or high probability V/Q scanning found that an elevated SI  $\geq 1$ , independent of echocardiogram findings for evidence of right ventricular dysfunction (ie RV hypokinesis/RV dilation/pulmonary hypertension), was associated with increased in-hospital mortality ( $p<0.05$ ).<sup>36</sup> Furthermore, the mortality rate for patients with moderate-to-severe RV hypokinesis was higher regardless of SI ( $p<0.05$ ).

Though these studies are retrospective and limited in size, they suggest there may be a role for SI in the evaluation of patients presenting to the ED with cardiopulmonary disease. Prospective studies using a lower cutoff (perhaps 0.8) are needed to determine if a different SI threshold yields better test characteristics. More prospective studies overall are needed in the ED setting in patients with cardiopulmonary disease as initial retrospective data are promising that SI can be useful in predicting mortality.

## Pediatrics

Pediatric physiology and reserves differ from adults. In addition, normal pediatric vital signs vary by age, which can greatly influence SI values. Age-adjusted SI has been proposed by multiple studies to identify and predict outcomes in ill children.<sup>2</sup> Pediatric age-adjusted SI (SIPA) was defined by maximum normal HR and minimum normal SBP by age in a retrospective study of 543 children (Table 2).<sup>2-5,8,37</sup> SIPA more accurately identified children who were severely injured and at risk for in-hospital mortality when compared to SI. Unfortunately, there were no further analyses comparing the sensitivity and specificity of SIPA vs SI  $>0.9$ . However, a higher percentage of patients with elevated SIPA were found to have ISS  $>24$ , in-hospital mortality, and blood transfusion in the first 24 hrs. These findings suggest that SIPA may be more specific than vital signs or SI alone at predicting these outcomes. In a subsequent study of 559 children ages 5–16, SIPA better predicted the need for operation, endotracheal intubation, and blood transfusion when compared to age-adjusted hypotension at presentation (SBP  $<90$  mmHg in ages 4–6 and SBP  $<100$  mmHg in ages 7–16).<sup>8</sup>

SIPA has since been validated in a prospective pediatric study of 386 patients in blunt liver and spleen injury (BLSI).<sup>3</sup> Outcomes were blood transfusion in first 24 hrs, ISS  $>24$ , grade  $\geq 3$  BLSI requiring transfusion, need for operation, ICU admission, and in-hospital mortality. Sensitivity decreased slightly across all outcomes for SIPA compared to SI  $>0.9$ . However, specificity improved



for all parameters for SIPA compared to SI. This could lead to less over-triage in the initial phase of resuscitation.

A retrospective study of 286 pediatric patients investigated the utility of trending SIPA after admission.<sup>4</sup> Patients with a normal baseline SIPA that subsequently increased during the first 24 hrs of admission had an increased risk of mortality compared to those whose SIPA remained normal. Overall, 81.6% and 100% of patients with an abnormal SIPA after 12 and 24 hrs died. Similarly, time to normalize an elevated admission SIPA appeared to directly correlate with hospital LOS, ICU LOS, and other markers of morbidity. When time to normalize SIPA increased from 12 to 48 hrs, ICU LOS increased from 2 to 10 days, and hospital LOS increased from 5 to 15 days.

Finally, SIPA has also been used as a noninvasive marker of mortality risk in pediatric sepsis. A retrospective study of 146 children admitted to the pediatric ICU with septic shock showed that relative risk of mortality was higher in patients with persistently elevated SIPA if still elevated 6 h after admission.<sup>5</sup> A prospective study of 120 children <14 years old concluded that SIPA cutoff values may identify children at high risk of early mortality in severe sepsis/septic shock.<sup>37</sup> SIPA cutoff suggested upon arrival were 1.98 for 1 month to <1 year, 1.5 for 1–6 years, and 1.25 for 6–12 years. After 6 hrs, cutoffs were determined to be 1.66, 1.36, and 1.30, respectively.

These studies suggest that SIPA can be used in pediatric populations to assess patients at arrival, trend progress, and predict prognosis. However, prospective studies comparing SIPA to other resuscitative measures (eg, SBP, MAP, and lactate) are lacking. Additionally, there are no prospective studies incorporating SIPA with a treatment plan to determine if additional measures based on elevated SIPA can decrease mortality. To date, SIPA is not routinely accepted as standard practice in this population.

## Geriatrics

As the population ages, more patients are diagnosed with chronic medical conditions, such as hypertension and diabetes. Although a normal SI is commonly considered 0.5–0.7, most studies did not take these confounding factors altering vital signs into account. In general, geriatric patients tend to have a slower HR response to physiologic stressors.<sup>11,38</sup> Hypertension alters baseline SBP, and medications, such as beta-blockers and calcium channel blockers, may blunt the tachycardia in response to hypovolemia.<sup>11</sup> Heart failure may limit the physiologic response to shock. In a retrospective

cohort study of 111,019 patients, beta or calcium channel blocker usage, hypertension, diabetes, and age >65 were recorded to determine if these factors weakened the association between SI and prediction of mortality (Table 2).<sup>11</sup> Patients >65 with an SI  $\geq 1$  had increased odds of 30-day mortality. Beta-blocker or calcium channel blocker use modified the odds of death. However, diabetes was not found to influence mortality. This study found that old age, hypertension, and beta-blocker or calcium channel blocker usage weaken the association between SI and mortality. However, SI >1 increased risk of 30-day mortality in all ED patients.

No study to date has examined SI in septic geriatric patients. One retrospective study including 409 patients  $\geq 65$  years with influenza found that SI  $\geq 1$  has a high specificity, NPV, and odds of 30-day mortality.<sup>39</sup> Although promising as a marker for those at risk for increased mortality, more research needs to be done to gain a better understanding of the utility of the SI, and perhaps age  $\times$  SI, in geriatric patients with infections.

For geriatric patients, SI and age  $\times$  SI may have better discrimination for mortality and other outcomes compared to HR and SBP alone. However, prospective studies are needed to determine if basing interventions on these measures has a widespread impact. Both measures can be automatically calculated in the EMR and included with the vital signs in the triage analysis of the patient. This may present a challenge as medical history and medications may not be immediately available upon patient arrival to the ED as it appears that antihypertensive use may blunt the association between SI and mortality.

## Limitations

While SI has proven useful in some settings, validation with prospective studies is limited. There is considerable heterogeneity across studies and disease states in terms of a specific threshold above which would be considered abnormal. Furthermore, utility of SI in the elderly, febrile patients, or those with chronic conditions that may alter baseline hemodynamics (eg, hypertension) may not have consistent changes in HR in response to hemodynamic stress. In addition, medications such as beta-blockers, beta-agonists, or other antihypertensives clearly affect vital signs and have been shown to alter the association of SI and mortality. Finally, there are many areas and populations that have yet to be studied, including burn injury and cardiogenic shock.

**Table 3** Shock index summary

Population	SI variation studied	SI value	Comparator	Outcomes studied	Comments and Limitations
Triage	<ul style="list-style-type: none"> <li>SI</li> <li>MSI</li> <li>Age SI</li> </ul>	<ul style="list-style-type: none"> <li>0.5-0.7</li> <li>&gt;0.7</li> <li>&gt;1.0</li> <li>&gt;1.2</li> </ul>	SBP	<ul style="list-style-type: none"> <li>Inpatient mortality</li> <li>ICU admission</li> <li>Hospital admission</li> </ul>	<ul style="list-style-type: none"> <li>SI, MSI, and age SI better at predicting inpatient mortality than SBP, but not ICU admission</li> <li>SI had poor sensitivity and specificity at predicting mortality</li> </ul>
Trauma	<ul style="list-style-type: none"> <li>SI</li> <li>MSI</li> <li>Age SI</li> </ul>	<ul style="list-style-type: none"> <li>&lt;0.7</li> <li>&gt;0.7</li> <li>&gt;0.9</li> <li>&gt;1.0</li> <li>≥1</li> <li>1.2</li> <li>&gt;1.3</li> </ul>	<ul style="list-style-type: none"> <li>ABC score</li> <li>DBP</li> <li>HR</li> <li>SBP</li> <li>RTS</li> <li>REMS</li> </ul>	<ul style="list-style-type: none"> <li>Death:                             <ul style="list-style-type: none"> <li>ED</li> <li>Within 24 hrs</li> <li>Hospital</li> </ul> </li> <li>Need for MTP</li> <li>Transfusion &gt;2 units PRBCs</li> <li>ISS:                             <ul style="list-style-type: none"> <li>&gt;15</li> <li>≥16</li> </ul> </li> <li>Emergent operation</li> <li>&gt;1-day ICU LOS</li> </ul>	<ul style="list-style-type: none"> <li>SI &gt;0.9 correlates with increased need for MTP</li> <li>SI ≥1 performs similarly to ABC Score in predicting need for MTP</li> <li>SI&gt;1.0 performed similarly to SBP&lt;90</li> <li>MSI may be more accurate predictor of mortality in trauma patients than SI, HR, SBP, or DBP alone</li> </ul>
Obstetrics	SI	<ul style="list-style-type: none"> <li>&gt;0.7</li> <li>&gt;0.85</li> </ul>	<ul style="list-style-type: none"> <li>HR</li> <li>SBP</li> </ul>	<ul style="list-style-type: none"> <li>Ruptured ectopic pregnancy</li> </ul>	<ul style="list-style-type: none"> <li>SI consistently higher in ruptured ectopic pregnancy compared to un-ruptured ectopic pregnancy</li> <li>SI &gt;0.7 was the most sensitive, SI &gt;0.85 most specific</li> <li>Only obstetrical condition studied was ectopic pregnancy</li> </ul>
Sepsis	SI	<ul style="list-style-type: none"> <li>&gt;0.7</li> <li>&gt;1</li> </ul>	<ul style="list-style-type: none"> <li>CVP</li> <li>SIRS</li> <li>SIRS without WBC</li> </ul>	<ul style="list-style-type: none"> <li>Hyperlactatemia</li> <li>28-day mortality</li> <li>Increase in CI as determined by ECHO</li> </ul>	<ul style="list-style-type: none"> <li>High NPV with normal SI for lactate &lt;4 mmol/L</li> <li>Poor PPV of hyperlactatemia and mortality for SI and SIRS</li> <li>Low SI and high CVP unlikely to improve CI with additional fluid boluses</li> </ul>
Cardiovascular Disease	SI	<ul style="list-style-type: none"> <li>&gt;0.8</li> <li>&gt;1</li> </ul>	<ul style="list-style-type: none"> <li>sPESI</li> <li>RV dysfunction on ECHO</li> </ul>	<ul style="list-style-type: none"> <li>In-hospital mortality in STEMI patients</li> <li>30-day mortality</li> <li>In-hospital mortality</li> </ul>	<ul style="list-style-type: none"> <li>PESI preferred to SI</li> <li>Low-quality studies</li> </ul>

(Continued)

**Table 3 (Continued).**

Population	SI variation studied	SI value	Comparator	Outcomes studied	Comments and Limitations
Pediatrics	SIPA	<ul style="list-style-type: none"> <li>Age-based cutoffs</li> </ul>	<ul style="list-style-type: none"> <li>SI</li> <li>HR</li> <li>SBP</li> <li>DBP</li> <li>Age-adjusted hypotension</li> </ul>	<ul style="list-style-type: none"> <li>Blunt liver/spleen injury</li> <li>ISS&gt;24</li> <li>Blood transfusion</li> <li>Operation</li> <li>ICU admission</li> <li>Death:                             <ul style="list-style-type: none"> <li>In-hospital mortality</li> <li>48-hr mortality</li> </ul> </li> <li>Mechanical ventilation</li> <li>ICU LOS</li> </ul>	<ul style="list-style-type: none"> <li>Higher sensitivities and specificities compared to other markers/indicators</li> </ul>
Geriatrics	SI	> 1	<ul style="list-style-type: none"> <li>Age SI</li> <li>MSI</li> <li>HR</li> <li>SBP</li> </ul>	<ul style="list-style-type: none"> <li>In-hospital mortality</li> <li>30-day mortality</li> </ul>	<ul style="list-style-type: none"> <li>Lower sensitivity and higher specificity</li> <li>Chronic conditions may limit applicability of SI in this population</li> </ul>

**Abbreviations:** CI, cardiac index; CVP, central venous pressure; HR, heart rate; ICU, Intensive Care Unit; MSI, modified shock index; NPY, negative predictive value; NPV, positive predictive value; PPV, positive predictive value; REMS, Rapid Emergency Medicine Score; RTS, Revised Trauma Score; RV, Right ventricle; SI, shock index; sPES], simplified pulmonary embolism severity index; SBP, systolic blood pressure.

## Conclusion

SI has been the subject of many studies in conditions including trauma, sepsis, ectopic pregnancy, MI, and pulmonary embolism (Table 3). As SI is based on factors immediately available on patient arrival, it can be automatically calculated in the EMR in triage in real time. Elevated SI (>0.7) has been shown to correlate with increased likelihood of inpatient admission, mortality, and other outcomes like MTP activation in trauma. Overall, SI carries poor sensitivity in predicting mortality. It should never be used to diagnose or rule out critical illness in isolation. Rather, it could be used in conjunction with vital signs and other markers in the clinical decision-making of patients at risk for outcomes like hospital or ICU admission, shock, and mortality.

## Disclosure

The authors report no conflicts of interest in this work.

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