EMERGENCY NURSES ASSOCIATION

Clinical Practice Guideline

Clinical Assessment of Acute Hypovolemia

In adult and pediatric emergency department patients, which non-invasive bedside procedure is best of identification of acute hypovolemia?

930 E. Woodfield Road, Schaumburg, IL 60173 | 800.900.9659 | www.ena.org | Follow us

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Background and Significance

Determining whether a patient has suffered a significant acute loss of fluid, blood or otherwise, is a high priority and guides initial resuscitative measures. Standard vital signs such as blood pressure, heart rate, and respiratory rate are influenced by factors other than volume loss and may not reflect fluid volume accurately. Researchers have evaluated other indices and technologies for use at the bedside for this purpose. These include orthostatic vital signs (OVS), pulse pressure (PP), shock index (SI), variations of SI, peripheral perfusion index (PPI), passive leg raising (PLR), heart rate over pulse pressure (ROPE), stroke volume variation, and ultrasound. Of these, OVS, PP, SI and variations of SI have been studied extensively and are easily performed in the emergency department (ED) by emergency nurses with no special equipment; thus, they are the focus of this CPG. The clinical question addressed is: in adult and pediatric emergency department patients, which non-invasive bedside procedure is best of identification of acute hypovolemia?

ORTHOSTATIC VITAL SIGNS

Orthostatic or postural vital signs historically were used to evaluate the body's response to position changes when volume loss is suspected. Under normal conditions, blood pooling in the lower extremities during position change is directed back to the upper body through the vasoconstriction of blood vessels (Winslow et al., 1995). This vasoconstriction is accomplished through the unloading of the arterial baroreceptors to enhance sympathetic outflow, which increases systemic vascular resistance, venous return, and cardiac output (Arnold & Shibao, 2013). Baroreceptors are mechanoreceptor sensory neurons that are excited by stretching of the corresponding blood vessel.

The most common reason for performing OVS in the ED is to evaluate fluid volume status. However, studies have demonstrated that OVS are not reliably sensitive to volume losses in adult patients (Barraf & Schriger, 1992; Knopp et al. 1980). Wide variations in response to orthostatic challenge have been demonstrated in healthy adults and adolescents (Horam & Roscelli, 1992; Koziol-McLain et al., 1991; Levitt et al., 1992). In addition, the procedure for measurement of OVS is not standardized, as evidenced by literature reflecting significant variations in practice. The duration of position change differs between studies as do the position changes (i.e., lying to standing, lying to sitting to standing), and there is lack of agreement about the clinical indicators of orthostatic hypotension and the cut-points for vital sign changes.

PULSE PRESSURE

Pulse pressure, defined as the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP), is another physiological variable that has been evaluated for utility in detecting acute hypovolemia. Multiple studies have determined that a narrowed PP is an early indicator of acute bleeding (Priestley et al., 2019; Warren et al., 2019; El-Menyar et al., 2018; Yadav et al., 2016; Morrison et al., 2012).

SHOCK INDEX

Shock index is another non-invasive, objective, bedside tool that may be used to identify acute hypovolemia Isolated vital signs including heart rate (HR) and blood pressure (BP) are poor predictors of volume loss (Mutschler et al., 2013; Vandromme et al., 2011), but SI uses HR and SBP to calculate an index that correlates with other indicators of impaired cellular perfusion such as lactic acidosis and decreased venous oxygen levels (King et al., 1996; Mutschler et al., 2013; Vandromme et al., 2011). Shock index was first defined in 1967 by Allgower and Buri (Linnaus et al., 2017; Van Sickle et al., 2013) as the ratio of HR divided by SBP, and correlates inversely with left ventricular stroke volume and cardiac output (Borovac-Pinheiro et al., 2017; Mutschler et al., 2013). Several studies have demonstrated that an SI ≥ 0.9 is associated with acute hypovolemia in adults (Rappaport et al., 2013; Van Sickle et al., 2013; Day et al., 2016; McNab et al., 2012; Vandromme et al., 2011; Wang et al., 2019).

Methods

This CPG is based on a thorough review and critical analysis of the literature, following ENA's CPG Development Manual (ENA, 2019). Via a comprehensive literature search, all articles relevant to the topic were identified. The following databases were searched: PubMed, Google Scholar, CINAHL, Cochrane Library, BioMed Central-Open Access, and Agency for Healthcare Research and Quality. The articles reviewed to formulate the recommendations in this CPG are described in Appendix 1. Various terms appear in the literature relating to vital sign changes with position changes. These terms are tilt test (which may involve passive

versus active position change), postural vital signs, and orthostatic vital signs. Searches were conducted using the keywords and subject headings: blood pressure, hypotension, orthostatics, orthostatic hypotension, orthostatic vital signs, orthostatic, and vital signs. The search term of "hypovolemic" was added to identify orthostatic vital sign research related to volume status rather than pharmacological treatment. Searches in previous versions of this CPG were limited to the English language from 1940 to June 2015. This timeframe went back to the 1940s to include the seminal orthostatic vital sign studies. In addition, the reference lists in the selected articles were scanned for pertinent research findings. For this revision, an additional literature search was performed from June 2015 to May 2020 with a paucity of new research found regarding OVS (Appendix 2). Thus, the CPG question was broadened to include other clinical indicators of acute hypovolemia, and the following search terms were added: shock index, modified shock index, pulse pressure, *and* hypovolemia. Research articles from ED settings, non-ED settings, position statements, and guidelines from other sources were also reviewed. For this revision, all studies on the Evidence Table were reviewed and graded based on a standardized and rigorous scoring method, which includes approval by a research ethics body. This review resulted in the exclusion of many studies that were previously included as evidence. Clinical findings and levels of recommendations regarding patient management are made by the CPG Committee according to ENA's classification of levels of recommendation for practice (Table 1).

Table 1. Levels of Recommendation for Practice

Level A Recommendations: High
• Reflects a high degree of clinical certainty • Based on availability of high-quality level I, II and/or III evidence available using Melnyk & Fineout-Overholt grading system (Melnyk & Fineout-Overholt, 2019) • Based on consistent and good quality evidence; has relevance and applicability to emergency nursing practice • Is beneficial
Level B Recommendations: Moderate
• Reflects moderate clinical certainty • Based on availability of Level III and/or Level IV and V evidence using Melnyk & Fineout-Overholt grading system (Melnyk & Fineout-Overholt, 2019) • There are some minor or inconsistencies in quality evidence; has relevance and applicability to emergency nursing practice • Is likely to be beneficial
Level C Recommendations: Weak
• Level V, VI and/or VII evidence available using Melnyk & Fineout-Overholt grading system (Melnyk & Fineout-Overholt, 2019) - Based on consensus, usual practice, evidence, case series for studies of treatment or screening, anecdotal evidence and/or opinion • There is limited or low-quality patient-oriented evidence; has relevance and applicability to emergency nursing practice • Has limited or unknown effectiveness
Not Recommended for Practice
• No objective evidence or only anecdotal evidence available, or the supportive evidence is from poorly controlled or uncontrolled studies • Other indications for not recommending evidence for practice may include: ◦ Conflicting evidence ◦ Harmfulness has been demonstrated ◦ Cost or burden necessary for intervention exceeds anticipated benefit ◦ Does not have relevance or applicability to emergency nursing practice • There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. For example: ◦ Heterogeneity of results ◦ Uncertainty about effect magnitude and consequences ◦ Strength of prior beliefs ◦ Publication bias
Insufficient Evidence (I/E) and No Evidence (N/E)
I/E: There is insufficient evidence upon which to make a recommendation N/E: There is no evidence upon which to make a recommendation

Summary of Literature Review

ORTHOSTATIC VITAL SIGNS

The most common variables measured to assess OVS include BP and HR, measured with the patient in different positions (i.e., supine, sitting, standing). Much of the OVS literature addresses orthostatic hypotension as a result of autonomic dysfunction. For the purposes of this document, positive OVS are defined as a change in vital signs or onset of symptoms after position change in patients with a decrease in intravascular volume. There is a lack of quality research specific to the utility of OVS in diagnosing intravascular hypovolemia.

Sensitivity to Hypovolemia

Orthostatic vital changes are not a reliable or sensitive method to detect volume losses of 450 ml or less in adults (Barraf & Schriger, 1992; Witting et al., 1994). Barraf and Schriger (1992) determined that an increase in HR by 20 bpm in combination with a greater than 10 mmHg drop in diastolic BP was the most sensitive vital sign combination to detect a 450 ml blood loss, but this combination was only 17% sensitive (98% specificity). Witting et al. (1994) studied healthy blood donors and found that HR performed better than other criteria. However, in the cohort under 65 years old, a HR increase of 20 or more had a sensitivity of 43% with a specificity of 91%. The same criteria in the group 65 years and older, resulted in a sensitivity of 25% with a specificity of 100% (Witting et al., 1994).

Body Positioning and Timing

In the OVS literature, the period of rest before the supine measurement varies from one minute to 30 minutes (Barraf & Schriger, 1992; Lance et al., 2009) but there is little evidence upon which to base practice, and some studies do not specify the time interval used. Lance et al. (2009), in a small study of young, healthy euvolemic subjects, found that 10 minutes of rest prior to the supine measurement was required to assess orthostatic vital signs accurately.

There are also inconsistencies in the process of measuring vital signs after standing with some studies measuring vital signs immediately and some studies measuring at intervals up to 10 minutes (Lance et al., 2009). Lance et al. (2009) found significant changes in SBP ($F=8.36$, $p = 0.01$) and dizziness ($F = 7.15$, $p < 0.10$) between the zero- and two-minute measurements but not at five minutes. Witting et al. (1994) found no difference in results between measurements taken at one and two minutes after standing following blood donation. Using continuous vital signs monitoring on blood donors, Yadav et al. (2016) demonstrated the time between maximal vital signs changes and recovery to baseline changed after blood donation, but the total time to recovery was only 11-16 seconds. Again, there is scant evidence on which to base practice because most studies use their usual time intervals and do not attempt to investigate the appropriateness of these intervals.

Most studies evaluate lying-to-standing OVS. One study of heathy, euvolemic adults found that OVS changes were less extreme with siting-to-standing measurements than they were with lying-to-standing measurements (Witting & Gallagher, 2003) and thus would require different positivity criteria.

Syncope Symptoms

Witting et al. (1994) determined that mild lightheadedness did not have the discriminative power to detect a 450 ml blood loss. They concluded that lightheadedness significant enough to require leaning or lying down should indicate a positive tilt test.

PULSE PRESSURE

Pulse pressure changes may be useful for detecting even mild hypovolemia when the systolic and diastolic blood pressure is unchanged (Yadav et al., 2016). In the study, 56 healthy volunteers donated 450 ml of blood and had vital signs monitored pre- and post-donation. The decrease in PP post-donation was statistically significant but not clinically significant (61.80 mmHg ± 8.79 to 58.19 mmHg ± 11.4, $p = 0.005$). There were no statistically significant post-donation changes in systolic, diastolic, or mean arterial pressure (Yadav et al., 2016). While the generalizability of findings from the Yadav study was limited by the use of healthy volunteers, other research evaluated PP response in a variety of patients with traumatic injuries and hemorrhage.

In a 2019 study, researchers sought to determine whether a narrowed PP could detect active hemorrhage in patients with traumatic injuries who were normotensive (Priestley et al., 2019). The study of 283 patients with clinically significant hemorrhage,

demonstrated that a narrowed PP was an early independent predictor of clinically significant hemorrhage in patients with blunt and penetrating trauma (Adjusted odds ratio 0.975, p < 0.0001; Priestley et al., 2019). Active hemorrhage was defined as receiving three units of red blood cells in any 60-minute period within 24 hours of admission and either interventional radiology or surgery for hemorrhage control (Priestley et al., 2019). The ability of shock index (SI) to predict massive transfusion was evaluated as a primary endpoint in another study assessing patients with blunt and penetrating trauma who received blood transfusions in the ED (El-Menyar et al., 2018). El-Menyar and colleagues (2018) studied the correlation between SI and PP in over 8,600 trauma patients. A high SI was an independent predictor for blood transfusion and that there was good correlation between SI and PP (r = -0.51, p = 0.001).

The correlation between PP and hemorrhage in patients with penetrating trauma was examined in two other studies. In one study, Warren et al. (2019) aimed to determine whether a narrowed PP was associated with the need for both massive transfusion (defined as > 10 units of PRBCs within the first 24 hours of admission) and emergent surgical intervention to control hemorrhage. The 178 patients who presented with a narrowed PP were more likely to receive massive transfusion (11% vs. 2%, p < 0.001) (Warren et al., 2019). A military study in 2012 demonstrated the utility of PP for detecting hemorrhage. In this study, Morrison and colleagues (2012) compared physiologic variables of patients with ballistic battlefield torso trauma who had life-threatening torso hemorrhage (LTTH) versus those with non-life-threatening torso hemorrhage (non-LTTH). An SI > 0.9 was identified as the most predictive of torso hemorrhage, but PP values between the LTTH group and non-LTTH group were also statistically significant (LTTH 44 ± 17; non-LTTH 56 ± 13, p < 0.001; Morrison et al., 2012).

The cutoff value for a narrowed PP identifying hemorrhage varies among studies. In recent research by Priestley et al. (2019), a PP cutoff of 55 mmHg for patients 61 years or older (AOR 3.44, p = 0.005, AUC 0.955) versus 40 mmHg for patients 16 to 60 years old (AOR 2.73, p < 0.0001, AUC 0.940) indicated a significantly higher risk of active hemorrhage and the probability increased as the pulse pressure narrowed. Warren and colleagues (2019) used a PP of less than 30 mmHg to define a narrowed PP.

Table 2. Tools to Predict Hypovolemia

Name of Tool	Abbreviation	Calculation
Shock Index	SI	HR / SBP
Modified Shock Index	MSI	MAP / HR
Age SI	--	Age multiplied by SI
Reverse Shock Index	RSI	SBP / HR
Respiratory Rate Adjusted Shock Index	RASI	(HR / SBP) multiplied by (RR / 10)
Pediatric Age-Adjusted Shock Index	SIPA	maximum normal HR for age / minimum normal SBP for age
Delta Shock Index	Δ SI	Difference between SI values at selected times
Revised Assessment of Bleeding and Transfusion Score	RABT	4-point score (one point for each element): • Positive focused assessment with sonography in trauma (FAST) • SI > 1.0 • Pelvic fracture • Penetrating mechanism of injury
Assessment of Blood Consumption Score	ABC	4-point score (one point for each element): • Positive focused assessment with sonography in trauma (FAST) • ED SBP ≤ 90mmHg • ED HR ≥ 120 bpm • Penetrating mechanism of injury
Legend: HR = heart rate; SBP = systolic blood pressure; MAP = mean arterial pressure; RR = respiratory rate		

SHOCK INDEX

Shock index was first defined in 1967 by Allgower and Buri (Linnaus et al., 2017; VanSickle et al., 2013) as the ratio of HR divided by SBP (HR/SBP), and correlates inversely with left ventricular stroke volume and cardiac output (Borovac-Pinheiro et al., 2017; Mutschler et al., 2013). Other literature describes variations of SI (Table 2). The cut-off value for an elevated SI in most research is defined as an SI ≥ 0.9 (Rappaport et al., 2013; Van Sickle et al., 2013).

Adults with Blood Donation

In a single study evaluating SI with 483 adults who donated blood (mean = 473mls), Pasquier et al. (2019) found a significant difference between pre- and post-blood donations (0.54 vs. 0.57, p = 0.002), which represented a 10.4% change. However, the multivariate analysis failed to show any significance between SI and blood donation volume (p=0.91) (Pasquier et al., 2019).

Adults with Injuries in the Pre-Hospital Environment

An SI ≥ 0.9 in the pre-hospital environment correlates with acute blood loss and the need for transfusion, as evidenced by several retrospective trauma database studies (Day et al., 2016; McNab et al., 2012; Vandromme et al., 2011; Wang et al., 2019). Vandromme et al. (2011) evaluated the association of SI with massive transfusion (MT; ≥ 10 units in 24 hours) in patients with blunt traumatic injuries, and in a review of 20,095 patients, 3.4% patients receiving MT had an SI > 0.9 indicating an increased risk for MT. The authors also found that as SI increased, so did the need for MT (Vandromme et al., 2011). Additionally, Vandromme et al. (2011) found that patients with an SI between 0.7 - 0.9 had a two-fold risk for MT, while an SI > 1.3, indicated a 20-fold increased risk. Wang et al. (2019) evaluated MSI and SI as tools to predict the need for MT. This study reported significant elevations in both indices for those who received MT (p < 0.001), and established cut-off values for both: SI = 0.91(65% sensitivity; 77% specificity); MSI = 1.28 (60% sensitivity; 82% specificity) (Wang et al., 2019).

Three retrospective studies evaluated pre-hospital SI and the need for blood transfusion. Day et al. (2016) performed an analysis of 116 patients who received blood in the first 6 hours after ED arrival and noted that in transfused patients, a significantly higher mean pre-hospital SI value was present (0.98 ± 0.28; p = 0.006). Even though the sample size was small, and MT was not required. Day et al. (2019) also reported that a pre-hospital SI = 1.0 was significantly associated with multiple transfusions (p = 0.02). The McNab et al. study (2012) evaluated the correlation of SI with increased resource use, which included blood administration, but not necessarily MT. They found that both pre-hospital and ED SI values correlated with blood product administration (p < 0.001), although the volumes transfused were small (average of 0.68 units) (McNab et al., 2012). A pre-hospital study by Wu et al. in 2019, conflicts with the conclusions previously described. Wu et al. (2019) found that, as an independent factor, pre-hospital SI was not associated with risk for MT (MT: pre-hospital SI = 0.7 ± 0.2; No MT: pre-hospital SI = 0.6 ± 0.3; p = 0.271). The authors also evaluated Δ SI and reported that a Δ SI of 0.06 was associated with MT (41.5% sensitivity, 84.1% specificity), and any Δ SI (≥ 0.00) was significant for MT (p = 0.01) (Wu et al., 2019).

Adults with Injuries in the Emergency Department

Shock Index derived from the first set of ED vital signs has been studied in ED patients with injuries to determine the need for transfusion or MT. In three retrospective studies, the researchers were able to correlate a SI ≥ 0.9 with acute blood loss and need for transfusion (DeMuro et al., 2013; Morrison et al., 2012; Rau et al., 2016). A study by DeMuro et al. in 2013 evaluated SI values for patients with blunt or penetrating trauma. Using trauma registry data for 4,277 patients, DeMuro et al. (2013) found an overall sensitivity of 54.5% and specificity of 93.6% (PPV 15.2%) for an SI ≥ 0.9 to determine bleeding, but when the SI cut-off was lowered to ≥ 0.8, the overall sensitivity and specificity improved (76.1% & 87.4%; PPV 11.3%). When comparing blunt vs. penetrating trauma, no significant sensitivity difference was noted in SI = 0.9 (58.8% vs. 47.2%, p = 0.05) (DeMuro et al., 2013). The Morrison et al. (2012) study evaluated adults with penetrating trauma only (N = 122); 44 had life-threatening injuries and underwent immediate surgery while 59 were not considered to have life-threatening injuries and did not require immediate surgery. Using a cut-off value for SI > 0.9 correlated with need for surgery to control bleeding (p < 0.05; PPV 81%) but all patients with non-life-threatening conditions had a SI < 0.9 (Morrison et al., 2012). In the Rau et al. (2016) study, the authors evaluated SI, MSI, and Age SI as markers for MT. Patients with blunt or penetrating trauma (N = 2,509) were evaluated, and results indicated that patients undergoing MT had elevated SI, MSI, and Age SI values (p < 0.0001). An SI of 0.95 was the cut-off value for MT (AUROC 0.76; sensitivity 56.3%; specificity 87.6%), the MSI cut-off for MT was 1.15 (AUROC 0.716; sensitivity 72.5%; specificity 63.6%), and the Age SI cut-off was 36.95 (AUROC 0.627; sensitivity 54.2%; specificity 72.3%) (Rau et al., 2016). In a separate study by Paladino et al. (2011), SI > 0.9 was examined for the ability to differentiate between major and minor injury in blunt and penetrating trauma patients ≥ 13 years of age. Major trauma patients were those who received blood transfusion, had a greater than 10-point drop in hematocrit in the first 24 hours, or had an Injury Severity Score of greater than 15 (Paladino et al., 2011). In this study, Paladino et al. (2011) found an inability of SI to differentiate between major and minor injuries in trauma patients arriving to the ED (SI = 0.79; 95% CI: 0.75-0.83 vs. SI = 0.67; 95% CI: 0.66-0.68), and while the mean SIs for minor trauma and major trauma were different(p < 0.01), the SIs for both categories were below the cutoff of 0.9.

Alternatively, some studies reported an SI value ≥ 1.0 indicated acute blood loss and need for transfusion. These studies also evaluated patients with blunt or penetrating trauma in the ED. In 2017, Joseph et al. evaluated 380 patients using the Revised Assessment of Bleeding and Transfusion (RABT) score and the Assessment of Blood Consumption (ABC) score (Table 2) to determine the need for MT. The study reported that a SI > 1 was an independent predictor for MT administration with an odds ratio of 8.9 (7.50-11.3) and in fact, was the strongest independent variable of the RABT score (Joseph et al., 2017). Mutschler et al. (2013) reviewed 21,853 subjects with traumatic injury and found SI must be ≥ 1.0 to identify the 52% of patients receiving ≥ 1 unit of blood, but when the SI was ≥ 1.4, 79% of patients received blood. In the MT group, an SI ≥ 1.0 was associated with a 31% MT rate, while SI ≥ 1.4 had a 57% MT rate (Mutschler et al., 2013). Another article supporting an SI cut off ≥ 1.0 for transfusion is Schroll et al. (2017). This study also compared the ABC score to SI to determine the best predictor for MT by analyzing 664 patients with blunt or penetrating trauma (Schroll et al., 2017). Unfortunately, only 34 patients received MT, but in patients with an SI ≥ 1.0, 17% received MT compared to 2% who did not ($p < 0.001$; Schroll et al., 2017). Overall, in the Schroll et al. (2017) study, an SI ≥ 1.0 had a sensitivity and specificity of 67.7% and 81.3%, respectively, and an AUROC of 0.83 for MT.

Four other retrospective studies evaluated different SI cutoff values to determine acute blood loss and need for transfusion. Two of these evaluated an SI < 0.9 with the first study by El-Menyar et al. in 2018. In a sample of 8,710 patients with blunt or penetrating injuries, patients that underwent transfusion had higher mean SI values (0.85 ± 0.35; $p = 0.001$), and a multivariable regression analysis of SI ≥ 0.8 gave an odds ratio of 3.57 (95% CI; 3.012 - 4.239) when predicting transfusion (El-Menyar et al., 2018). An SI cut-off value for MT was determined by AUROC at 0.82 (95% CI; 0.772 - 0.863) (El-Menyar et al., 2018). King et al. (1974) also evaluated SI to evaluate for hemorrhage in blunt or penetrating trauma. Just over 1,000 patient records were reviewed, and SI was compared to several outcome variables, including blood administration ≥ 2 units (King et al., 1974). In this sample, 134 patients received ≥ 2 units of blood, and an SI = 0.85 was indicative of transfusion with a sensitivity of 54%, a specificity of 80%, and a PPV 29% (King et al., 1974). In 2019, El-Menyar et al. re-examined SI in patients with solid organ injury using a cut-off of 0.8 to predict the need for blood transfusion and MTP. In this study, 50.5% of the study population had an SI ≥ 0.8 on arrival. Of those with a high SI, 60.2% underwent transfusion compared to 22.6% of the group with a lower SI ($p=0.001$), and 21.8% with an SI > 0.8 underwent MTP vs. 3.9% for those with an SI < 0.8 ($p=0.001$) (El-Menyar et al., 2019). They also noted the SI was higher in those with blunt abdominal trauma vs. penetrating abdominal trauma (0.89 ± 0.36 vs. 0.79 ⍰0.30) (El-Menyar et al., 2019).

Other tools evaluating acute blood loss and need for transfusion include the Reverse Shock Index (RSI) and the Respiratory Rate Adjusted Shock Index (RASI) (Caputo et al., 2018; Lai et al., 2016). Lai et al. (2016) evaluated the RSI upon ED arrival and departure, comparing the values to transfusion as an outcome. Group I had arrival and departure RSI ≥ 1; Group II had an RSI ≥ 1 on arrival but < 1 on departure; Group III had an RSI < 1 on arrival and ≥ 1 on departure; Group IV had an RSI < 1 on arrival and departure (Lai et al., 2016). In 10,234 patients with blunt or penetrating trauma, Groups II, III, & IV received more transfusions than those having a consistent RSI ≥ 1 ($p < 0.001$). Overall, for Groups, II, III, and IV, which had either an arrival or departure RSI less than one there was a significant correlation with transfusion need (Lai et al., 2016). Caputo et al. (2017) attempted to determine if the SI, coupled with RR, would improve early shock identification with the RASI. In this retrospective pilot study, the RASI was calculated for 3,093 patients with blunt and penetrating trauma (Caputo et al., 2017). The authors concluded that RASI was a better indicator of shock (AUROC = 0.94; 95% CI; 92.8 - 95.4; $p < 0.001$) and the need for transfusion than SI (AUROC = 0.58; 95% CI; 55.8 - 60.9; $p < 0.0001$) (Caputo et al., 2017).

Adults with Traumatic Brain Injuries

Three retrospective studies evaluated SI in patients with traumatic brain injury (TBI). El-Menyar et al. (2018) evaluated SI in 8,710 patients, 3,026 of whom had a TBI. In patients with a Glasgow Coma Score (GCS) ≤ 12, an SI ≥ 0.8 was associated with a higher transfusion rate than patients with an SI < 0.8 (32% vs. 15%; $p = 0.001$; El-Menyar et al., 2018). Fröhlich et al. (2016) looked specifically at patients with TBI to determine if SI predicted the need for MT. In a review of trauma registry data, they identified 16,760 patients with a TBI as defined by an Abbreviated Injury Scale-Head (AIS_{head}) ≥ 3 and found that an SI ≥ 1.4 was associated with a lower GCS score (3.9 ± 0.2; Fröhlich et al., 2016). The authors also noted as SI increased (SI ≥ 1 to ≤ 1.4), the need for transfusion increased but was not statistically significant between those with or without TBI (non-TBI group received 8.1 ± 0.9 blood products vs. TBI group received 8.3 ± 0.9 blood products; Fröhlich et al., 2016). Fröhlich et al. (2016) also reported that while 3% of TBI patients with an SI < 0.6 received MT, 46% with an SI ≥ 1.4 received MT. Finally, the authors noted no significant difference in the ability of SI to predict the need for transfusion for patients with or without TBI (AUROC 0.706 with TBI; 0.718 without TBI) (Fröhlich et al., 2016). As discussed previously, Joseph et al. (2018) compared RABT to ABC scores with SI as an

independent variable and noted that SI ≥ 1.0 was the strongest predictor for MT. In the Joseph et al. (2018) study, patients with TBI who underwent MT had lower GCS scores than those without TBI (11 vs. 14; p = 0.019), but no specific link was reported between SI, transfusion, and TBI.

Older Adults with Injuries

DeMuro et al. (2013) looked at SI values for adults with blunt and penetrating trauma and evaluated the SI cut-off ≥ 0.9 in a group of patients 65 years and older (n = 2,093). In the entire study population (N = 4,277), sensitivity was 54.5%, and specificity was 93.6% (PPV = 15.2) for an SI ≥ 0.9, but when evaluating the patients ≥ 65 years of age, they noted an increased specificity (95.7%), a decreased sensitivity (41.2%), and a reduced PPV (7.3) (DeMuro et al., 2013).

Children with Injuries

Normal vital sign parameters vary with age and some research in injured children incorporates age-adjusted versions of SI to predict the need for blood transfusion. In a study by Strutt et al. (2019) using trauma registry data from 2010, the authors calculated age-adjusted SI from the highest normal HR values and the lowest normal SBP values from the 9th edition *Advanced Trauma Life Support* manual. Five age groups and corresponding SI values were calculated in injured children less than 1 year of age up to 15 years, and the SI values were used as a predictor of mortality and other negative outcomes, including blood transfusion (Strutt et al., 2019). Examining a sample of 28,741, 9.9% of patients with an elevated-for-age SI received blood transfusion versus 1.2% with a normal SI (p<0.001) with a median SI of 0.86 (Strutt et al., 2019). A retrospective study by Acker et al. (2015) examined children (≥ 4 years) with blunt trauma using the standard SI > 0.9 cut-off, and the Age Adjusted Shock Index (SIPA) (Acker et al., 2015). The researchers created cut-offs for three age groups: SI > 1.22 for ages 4-6 years; SI > 1.0 for ages 7-12 years; SI > 0.9 for ages 13-16 years (Acker et al., 2015). In the SI-only data, an SI > 0.9 was found in 49% of the 543 patients, and in those patients receiving transfusions, 19.9% had an SI > 0.9 (p < 0.001) (Acker et al., 2015). In the SIPA-only data, elevation was noted in 27.6% of the children receiving transfusions (27.3%; p < 0.001) (Acker et al., 2015). Based on this data, the researchers concluded that SIPA performed better than SI when predicting the need for transfusion.

Linnaus et al. (2017) re-evaluated the Acker study data to confirm validity of the SIPA tool and were able to confirm Acker et al.'s findings and they reported that both an SI > 0.9 and an elevated SIPA identified patients requiring transfusion (SI: 29%, p < 0.001; elevated SIPA: 33%, p < 0.001). They further reported that while both tools have good sensitivity for transfusion (SI = 95.9% & SIPA = 94.8%), SIPA had better specificity (35.1% vs. 21.5%; Linnaus et al., 2017). Nordin et al. (2018) also retrospectively evaluated SI and SIPA in 22,957 children (≥ 1 year) with either blunt or penetrating injury (penetrating n = 613, blunt n = 22,334). For children with blunt trauma, an SI > 0.9 identified 2.0% of patients (p < 0.0001) requiring transfusion while elevated SIPA identified 4% (p < 0.001) (Nordin et al., 2018). In children with penetrating trauma, an SI > 0.9 identified 15.5% (p = 0.0017) requiring transfusion while SIPA identified 25.2% (p > 0.001) (Nordin et al., 2018). Overall SIPA was found to be a better indicator than SI in both blunt and penetrating trauma: SI > 0.9, sensitivity 69.66%, specificity 59.07% (p < 0.0001) and elevated SIPA, sensitivity 52.43%, specificity 84.85% (p < 0.0001) (Nordin et al., 2018). All four pediatric studies included patients with TBI, but no correlations were made between SI, SIPA, and transfusion in the presence or absence of TBI (Acker et al., 2015; Linnaus et al., 2017; Nordin et al., 2018; Strutt et al., 2019).

Women with Postpartum Hemorrhage

Multiple studies have examined SI as a marker for acute blood loss in women with post-partum hemorrhage (PPH). In a study by Borovac-Pinheiro et al. (2017), researchers attempted to determine if SI values varied significantly for women with PPH who required transfusion versus those who did not require transfusion. Using a retrospective case-control design, the sample included 105 patients who were transfused and 129 patients who were not transfused (Borovac-Pinheiro et al., 2017). Shock Index values were calculated at time of delivery and 10-, 30-, and 120-minutes following delivery with findings showing that the SI was higher for those undergoing transfusion (10 minutes, p = 0.012; 30 minutes, p < 0.001; 120 minutes, p = 0.32) (Borovac-Pinheiro et al., 2017). The sensitivity and specificity of SI ≥ 0.83 (95% CI) to predict transfusion was calculated at delivery (30%; 74%; PPV=1.16), 10 minutes after delivery (40%; 77%; PPV=1.76), and 30 minutes after delivery (47%; 79%; PPV=2.21) (Borovac-Pinheiro et al., 2017). Overall, Borovac-Pinheiro et al. (2017), found that patients with an SI ≥ 0.8 thirty minutes following delivery were five times more likely to have received a transfusion. The first of two studies by Nathan et al. (2015) reviewed data from 233 post-partum women and found for women with > 1500 ml estimated blood loss, the median SI was 0.95, and that value had an AUROC of 0.67 for women undergoing transfusion ≥ 4 units (Nathan et al., 2015). Cut-off values were determined, and an SI ≥ 0.9 for women

receiving transfusion had an 80% sensitivity, but only a 45% specificity (PPV 23.5%, 95% CI) (Nathan et al., 2015). If the SI cutoff was increased to ≥ 1.7, the PPV reached 57.1% with a specificity of 98.4%, but only 10% sensitivity (Nathan et al., 2015). In an attempt to evaluate the normal SI ranges for women without PPH, the second study by Nathan et al. (2016) examined SI and vital signs of women in the immediate postpartum period to determine if SI could be used to develop an early warning score. In a sample of 316 women, the authors identified that the normal range for SI was 0.52 - 0.89 in the first hour after delivery, for either a vaginal or surgical delivery (Nathan et al., 2016). The findings from this study also identified a normal threshold SI as ≥ 0.9 for post-partum women without hemorrhage (Nathan et al., 2016).

Two other studies used higher cut-off values of SI when evaluating postpartum hemorrhage patients. In a study evaluating 302 patients, Sohn et al., (2018) evaluated the need for transfusion in the first 24 hours following delivery. Patients undergoing MT (≥ 10 units) and those without MT were compared, and those receiving MT had higher SI values (> 1.1; $p < 0.01$) compared to those who did not undergo MT (> 0.8; $p < 0.01$) (Sohn et al., 2018). Shock Index was found to have a positive association with MT (OR 10.26; 95% CI; $p < 0.01$), and SI > 1.0 was 78.7% specific, 59.2% sensitive, with a 58.7% PPV for undergoing MT (Sohn et al., 2018). Kohn et al. (2019) also evaluated SI in women with PPH undergoing transfusion. In this study, they used the 5^{th} and 95^{th} percentile values from controls (admission: 0.437-0.870; just prior to delivery: 0.497-1.096; and peak: 0.775-1.140) and determined that an SI ≤ 1.1 may be considered normal in pregnant patients (Sohn et al., 2018). For those who were transfused for PPH, a peak SI ≥ 1.412 had a sensitivity of 21% and specificity of 100%, a peak SI ≥ 1.143 had a sensitivity of 53% and specificity of 84%, and an SI ≥ 0.9 only had a 24% specificity (Kohn et al., 2019). Additional outcomes included peak SI (highest value during hospitalization) and Δ SI (peak SI - SI at last antenatal visit or upon presentation for admission). They found a Δ SI ≥ 0.332 was the best indicator of PPH (sensitivity 68%, specificity 76%), and a Δ SI ≥ 0.559 was the best indicator for transfusion (sensitivity 37%, specificity 95%) (Kohn et al., 2019).

CONCLUSIONS

This CPG evaluates the effectiveness of various non-invasive, objective, bedside procedures in detecting acute hypovolemia in patients in the ED. There is limited evidence supporting the utility of orthostatic vital signs in determining acute volume loss. There is substantial evidence of the usefulness of PP and SI in evaluating acute fluid loss. Levels of recommendation follow.

Description of Decision Options/Interventions and the Level of Recommendation

Note that the references listed after each recommendation represent the evidence considered when making the recommendation. This does not mean that the evidence in each individual reference supports the recommendation.

Description of Decision Options/Interventions and the Level of Recommendation		
Orthostatic Vital Signs		
Procedure	After the patient assumes a standing position, measure orthostatic vital signs after one minute. (Witting et al., 1994; Yadav et al., 2016)	**C**
	There is insufficient evidence to make a recommendation about how long the patient should rest in a supine position prior to measuring orthostatic vital signs. (Lance et al., 2009)	**IE**
Interpretation	Orthostatic vital signs lack the sensitivity to reliably detect volume losses of 450 ml or less. (Barraf & Schriger, 1992; Witting et al., 1994)	**C**
	When measuring lying-to-standing orthostatic vital signs, one or more of the following findings may indicate intravascular volume loss: • Decrease in diastolic blood pressure greater than 10 mmHg • Increase in heart rate greater than 20 beats per minute (Baraff & Schriger, 1992; Witting et al., 1994)	**C**
	There is insufficient evidence as to whether moderate to severe lightheadedness (requiring leaning or lying down) may constitute a positive test. (Witting et al., 1994)	**IE**
	There is insufficient evidence to determine whether sitting-to-standing tests require different positivity criteria from lying-to-standing tests. (Witting & Gallagher, 2003)	**IE**
Pediatric and Adolescent Population	There is insufficient evidence appears in the literature to make recommendations about orthostatic vital signs in the pediatric and adolescent population with fluid volume alteration	**IE**
Pulse Pressure		
A narrowed pulse pressure correlates with acute blood loss requiring transfusion in trauma patients. (Priestley et al., 2019; Warren et al., 2019; El-Menyar et al., 2018; Morrison et al., 2012)		**B**
A narrowed pulse pressure is an early indicator of acute blood loss. (Priestley et al., 2019; Warren et al., 2019; Yadav et al., 2016)		**B**
There is insufficient evidence to define pulse pressure cutoff values that indicate a high risk of active hemorrhage. (Priestley et al., 2019)		**IE**
There is no evidence regarding the utility of pulse pressure assessment in children.		**NE**
Shock Index		
Adults with Injuries	A pre-hospital Shock Index ≥ 0.9 correlates with acute blood loss requiring transfusion (Day et al., 2016; McNab et al., 2012; Vandromme et al., 2011; Wang et al., 2019)	**B**
	A Shock Index ≥ 0.8 or ≥ 1.0 correlates with acute blood loss requiring transfusion in the presence of blunt or penetrating trauma. (DeMuro et al., 2013; ; El-Menyar et al., 2019; Joseph et al., 2018; Morrison et al., 2012; Mutschler et al., 2013; Rau et al., 2016; Schroll et al., 2018)	**B**
	A Shock Index > 0.8 correlates with acute blood loss requiring transfusion regardless of co-existing traumatic brain injury. (El-Menyar et al., 2018; Fröhlich et al., 2016; Joseph et al., 2018)	**C**
	There is insufficient evidence for the Respiratory Rate Adjusted Shock Index (RASI) as an indicator for acute blood loss requiring transfusion with blunt or penetrating trauma. (Caputo et al., 2017)	**IE**
	There is insufficient evidence for the Reverse Shock Index (RSI) as an indicator of acute blood loss requiring transfusion with blunt or penetrating trauma. (Lai et al., 2016)	**IE**
	There is insufficient evidence about the ability of SI to differentiate between minor and major injury. (Paladino et al., 2011)	**IE**
Older Adult with Injuries	There is insufficient evidence to specify a Shock Index cut-off indicating acute blood loss requiring transfusion. (DeMuro et al., 2013; El-Menyar et al., 2018)	**IE**

Description of Decision Options/Interventions and the Level of Recommendation		
Shock Index (cont.)		
Children with Injuries	A Shock Index > 0.9 correlates with acute blood loss requiring transfusion in children > 1 year old with *blunt trauma.* (Acker et al., 2015; Linnaus et al., 2017; Nordin et al., 2018)	**B**
	An elevated age-adjusted Shock Index correlates with and outperforms Shock Index in detecting acute blood loss requiring transfusion in children with *blunt trauma.* (Acker et al., 2015; Linnaus et al., 2017; Nordin et al., 2018; Strutt, et al., 2019)	**B**
	There is insufficient evidence that a Shock Index > 0.9 is an indicator for acute blood loss requiring transfusion in children > 1 year old with *penetrating trauma.* (Nordin et al., 2018)	**IE**
	There is no evidence to specify a Shock Index cut-off as an indicator for acute blood loss in children with co-existing *traumatic brain injury.* (Acker et al., 2015; Nordin et al., 2018)	**NE**
Healthy Young Adults	There is insufficient evidence for Shock Index as an indicator of acute blood loss. (Pasquier et al., 2019)	**IE**
Women in Postpartum	A Shock Index ≥ 0.8 correlates with acute blood loss requiring transfusion in women with postpartum hemorrhage. (Borovac-Pinheiro et al., 2017; Kohn et al., 2019; Nathan et al., 2015; Nathan et al., 2016; Sohn et al., 2018)	**B**

A	Level A (High)	Based on consistent and good quality of evidence; has relevance and applicability to emergency nursing practice.
B	Level B (Moderate):	There are some minor inconsistencies in quality of evidence; has relevance and applicability to emergency nursing practice.
C	Level C (Weak)	There is limited or low-quality patient-oriented evidence; has relevance and applicability to emergency nursing practice.
NR	Not Recommended	Based upon current evidence.
IE	Insufficient Evidence	Insufficient evidence upon which to make a recommendation.
NE	No Evidence	No evidence upon which to make a recommendation.

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Authors

2020 ENA Clinical Practice Guideline Committee

Jean A. Proehl, MN, RN, CEN, CPEN, TCRN, FAEN, FAAN
Lisa Gilmore, DNP, ACCNS-AG, ACCNS-P, FNP-C, NREMT-P, CEN, CPEN
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Methodologist

Jessica Bishop-Royse, PhD, MS

Staff Liaison

Altair Delao, MPH, Senior Associate ENR

Administrative Staff

Leslie Gates, Sr. Administrative Assistant ENR

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Kathleen E. Zavotsky, PhD, RN, ACNS-BC, CEN, CCRN, FAEN, Chairperson
Kathy Baker, PhD, RN, NE-BC
Paul R. Clark, PhD, MA, RN
Courtney Edwards, DNP, MPH, RN, CEN, CCRN, TCRN
Warren Frankenberger, PhD, MSN, RN, CCNS
Kimberly Johnson, PhD, RN, CEN
Lisa Wolf, RN, PhD, FAEN, CEN, Director ENR

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Appendix 1: Evidence Table

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Acker et al., 2015	To determine if age adjusted shock index (SIPA) could more accurately predict outcomes in injured children.	Design: Retrospective review of trauma registry data with review of the electronic health record for missing data. Sample: N = 534 (4-6 yo: n = 128; 7-12 yo: n = 237; 13-16 yo: n = 194) Inclusion criteria - age 4-16 yr, with ISS > 15 admitted with blunt trauma Setting: 2 Urban academic trauma centers, 1 pediatric and 1 general hospital	Variables related to fluid volume: Independent - Blood transfusion within 24 hr; spleen or liver laceration requiring transfusion Dependent – SI; age-adjusted shock index (SIPA) Measures: HR, SBP at time of ED arrival Maximum normal SIPA defined as maximum normal HR by age divided by minimum normal SBP by age. SIPA cutoffs were SI > 1.22 (age 4–6 yr), > 1.0 (7–12 yr), and > 0.9 (13–16) yr Analysis: Descriptive stats for demographics/clinical characteristics. Chi-square for age group comparisons. multiple logistic regression for relations. between binary outcomes; AUROC to identify cut-offs; general linear modals for continuous outcomes	Pediatric normal VS vary by age and may result in an elevated SI as defined for adults (> 0.9) in the absence of sig injury. SIPA was more accurate than SI in identifying: -Blood transfusion within 24 hr (27% v. 20%, p < 0.0001) - Intraabdominal injury requiring transfusion (41% v. 26%, p < 0.001) SIPA cutoff for blood transfusion within 24 hr (regardless of age group) - 1.22	2 - IV
Barraf & Schriger, 1992	Purposes: 1) To assess variation with age on orthostatic vital signs. 2) To determine the sensitivity and specificity of various definitions of abnormal with regard to orthostatic vital signs with a 450ml blood loss.	Design: Prospective Sample: Convenience, N = 200 (100 healthy blood donors and 100 ambulatory senior citizens) Setting: blood donation center & senior citizen center	Variables: heart rate, diastolic BP, systolic BP Measures: Manual blood pressure measurements were taken after 1 minute in a supine position and 30 seconds in a standing position. Blood donors served as their own controls, and the measurements were repeated immediately after phlebotomy. Analysis: Vital sign changes were tested for normality using chi-square; linear regression was used for changes associated with age; differences between age groups determined with t-test. McNemar's test was used to compare differences in sensitivities with identical specificities.	1) There were no clinically significant orthostatic BP changes associated with age. 2) The pulse rate was the most sensitive single orthostatic vital sign to detect acute blood loss. A pulse increase > 20 bpm had a 9% sensitivity and 98% specificity. Adding a diastolic BP decrease > 10 mmHg to an increase in HR > 20 bpm improved the sensitivity to 17% and with no decrease in specificity (98%). Including systolic BP change did not improve sensitivity for a given specificity. No combination of vital signs with a specificity > 95% was sensitive enough to detect a 450 ml blood loss.	3 - IV
Borovac-Pinheiro et al., 2018	To evaluate if shock index (SI) varies between women undergoing postpartum blood transfusion, and those women who do not undergo transfusion.	Design: Retrospective case-control study with data from the medical record. Sample: N=105 women were transfused; N=129 women not transfused (controls) Power analysis—180 with 90 controls and 90 cases needed. Setting: Women's Hospital in Brazil	Variables: Patient demographics, type of delivery (vaginal or section), gestation at time of delivery, and SI calculations. at delivery. Measures: SI calculations made at delivery time and 10-, 30-, and 120-minutes following delivery. Compared between groups. Analysis: Variables compared between control and case groups with ?2, Student t, and Fisher exact tests. Mean SI calculations compared across groups with Mann-Whitney U test. SI of 0.83 cutoff used and p < 0.05 was significant.	SI significantly higher in women receiving transfusion at 10, 30, and 120 minutes after delivery vs. women not receiving transfusion (p = 0.012; p < 0.001; p = 0.032). This included vaginal and c-section deliveries. There was a weak correlation between SI values and number of blood units needed. At all measurement intervals, the mean SI for control group was 0.8 and for study group, 0.9. Postpartum women with an SI > 0.83 at 30 minutes following delivery were 5 times more likely to be transfused.	3 - IV
Caputo et al., 2018	To determine if Shock Index (SI) coupled with Respiratory Rate (RR) will improve diagnosis of early shock in trauma patients.	Design: Retrospective observational cohort pilot study using chart review data. Sample: All presenting trauma patients admitted with lactate level were included. Excluded cardiac arrest, intubated, overt shock. No power analysis. N=3093 Setting: Level I trauma center in New York City	Variables: Respiratory Adjusted Shock Index (RASI) calculated as HR/SBP*(RR/10). Lactate >2mmol/L indicated hypoperfusion. Positive RASI > 1.3. Positive SI > 0.7. Measures: Triage trauma bay vital signs used, data collection for HR, BP, RR from the electronic medical record. Lactate level obtained within 30 minutes of arrival. Analysis: Youden indices calculated for RASI and SI. Student's t was used for comparison. Receiver Operator characteristics curves (ROC).	Average age of 47 with no range provided. Areas under Curve (AUC) for SI to determine shock—0.58 (95% CI, 55.8 - 60.9, p < 0.0001). AUC for RASI for shock—0.94 (95% CI, 92.8-95.4, p < 0.001). Youden J index for SI = 0.11 and RASI = 0.28. RASI improves capacity of SI to determine occult shock.	2 - VI

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Day, 2016	To evaluate the association between prehospital SI and the need for multiple transfusions of RBC in the trauma patient while in the ED.	Design: Case series retrospective review Sample: N=116 Convenience sample of all activated trauma patients who were transfused one or more RBCs during the first 6 hrs after arrival Setting: Level II academic trauma center in US	Variables: Demographics, injury data, vital sign data, laboratory work, transfusion data, and outcome at 24 hrs. Measures: Prehospital SI was calculated from initial prehospital heart rate, divided by initial prehospital systolic blood pressure Analysis: Means and standard deviations. Descriptive statistics and a regression model used to determine association of prehospital SI, RBC transfusion, and MULT. Pearson correlation coefficient. Statistical significance $p < 0.05$.	Patients who received uncrossmatched RBCs in the trauma bay had significantly higher mean prehospital SI (mean = 0.98 ± 0.28) than those who did not (mean = 0.82± 0.33), p = 0.006. A prehospital shock index of 1 was significantly associated with multiple transfusions (p = 0.02).	3 - VI
DeMuro et al., 2013	To determine if the cutoff SI of 0.9 is too high for the older adults and whether the SI cutoff should be different in blunt versus penetrating trauma.	Design: Retrospective, observational study Sample: N= 4277 convenience sample of patients from 2000-2010. Setting: Academic trauma center in US	Variables: Age, gender, initial vital signs at presentation to the ED, injuries, mechanism of trauma, procedures, transfusions, and disposition Measures: SI of ≤ 0.9 evaluated for false positives and negatives, then divided into subcategories of 65 years and older, younger than 65, blunt wounds, and penetrating wounds. For each group, the cutoff SI is varied from 0.1 to 2.0 in increments of 0.1. Analysis: Sensitivity, specificity, and positive and negative predictive values calculated for each case. Student t test.	Using SI ≥ 0.9 as a threshold for bleeding, the sensitivity was 54.5% and specificity 93.6% for all patients. No statistically significant difference in sensitivity between geriatric age subgroups, but SI more specific in the older patients. No difference in sensitivity using SI in blunt versus penetrating trauma. Lowering the SI to ≥ 0.8 increases the sensitivity to 76.1%, with a specificity of 87.4%.	2 - VI
El-Menyar et al., 2018	Purpose: To determine the ability of shock index (SI) to predict the need for transfusion and predict outcomes in trauma	Design: Retrospective descriptive study Sample: Convenience, N=8710 from trauma registry database 2012-2016 Setting: Level 1 trauma center in US	Variables: Patient demographics, vitals, pulse pressure, injury mechanism, ISS, NISS, TRISS, need for blood, MTP, ex lap, HLOS, mortality. Measures: First set of VS on admission used to calculate SI and PP. Analysis: Chi square and student t. Correlation coefficients and regression analysis.95% CI, and AUC curves, p<0.05	Patients that received transfusion (n=976) had higher mean SI values. SI ≥ 0.8 was an indicator for transfusion (OR, 3.57; 95% CI: 1.604-4.062). Need for transfusion was also significantly correlated with pulse pressure (r = -0.51, p = 0.001), base deficit, and amount of blood transfused. There was a negative correlation for older adults. SI ≥ 0.8 is associated with worse outcomes.	2 - VI
El-Menyar et al., 2019	Purpose: Assess Shock Index (SI) in trauma patients with solid organ injury to predict MTP need, transfusion need, and need for exploratory laparotomy.	Design: Retrospective trauma registry review Sample: Adult trauma patients presenting to ER with abdominal trauma between June 2011 and June 2014. N=572 Setting: Level I trauma Center at Hamad General Hospital in Qatar	Variables: demographics, mechanism of injury, admission vitals, labs, GCS, ISS, AIS, TRISS, ABC score, site of injury, FAST results. Procedures, number of PRBCs, MT, ICU stay, mortality Measures: vitals on admission to calculate SI. Used SI of > 0.8 as indicator for MTP. Analysis: proportions, medians, means, Chi Square and Student's t. Pearson correlation coefficient used for linear relationships and multivariable regression analysis performed.	50.5% of study population had elevated SI on arrival (≥ 0.8). Same population had elevated lactate (p = 0.001). Higher SI was noted in blunt trauma vs. penetrating abdominal trauma (0.89±0.36 vs. 0.79±0.30). 60.2% with elevated SI were transfused (vs. 22.6%; p=0.001) and MTP with elevated SI was 21.8% vs 3.9% without MTP (p=0.001). Using ROC curves, SI cut -off for SI ≥ 0.70 = 0.62 (0.56-0.69) and with a SI ≥ 0.8 AUC was 0.71) 0.66-0.77; p= 0.001 for both). SI ≥ 0.8 was independent predictor for MTP (OR 2.81; 95% CI).	2 - IV
Fröhlich et al., 2016	In the presence of head injury in adult patients with trauma, does Shock Index predict the need for massive transfusion.	Design: Retrospective review of trauma registry data Sample: From 2001-2013, all adult (≥ 16 years) with primary admission, ICU admission, and complete data sets. N = 40,888 Setting: German Trauma Society registry	Variables: Patient demographics, admission info, SBP, HR, GCS, injury pattern, blood product administration, INR and AIS_{head} scores. Measures: Initial vitals in ED used to calculate SI. MTP defined as ≥10 units in 24 hrs. Four classes of shock defined: Class I: SI < 0.6 Class II: SI ≥ 0.6 to < 1.0 Class III: SI ≥ 1.0 to < 1.4 Class IV: SI ≥ 1.4 Analysis: 95% CI for continuous or percentage for categorical items. To compare SI with and without brain injury, AUROC used.	Severe head injury occurred in 41%. SI ≥ 1.4 had lower GCS scores. Hgb and platelets were lower with worsening SI scores. As SI worsened, blood volume and vasopressor use increased significantly. AUROC showed SI for TBI 0.706 and without TBI of 0.718. The presence or absence of TBI did not affect the ability of SI to determine hypovolemia.	2 - VI

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Joseph et al., 2018	Evaluate the Revised Assessment of Bleeding and Transfusion score (RABT) and compare to the Assessment of Blood Consumption Score (ABC) for determination of need for MTP in adult trauma patients.	Design: Retrospective analysis of data abstracted from trauma registry Sample: N=380 Inclusion: high level trauma activation, > 18 yr; 26.8% received MT Setting: Urban, level one trauma center	Variables: Independent – received MT, defined as > 10 units of PRBCs within 24 hr of admission Dependent – ABC score calculated with mechanism of injury (MOI), SBP, HR, & focused assessment by sonography for trauma [FAST] result. RABT score calculated with shock index, the presence of pelvic fracture or penetrating MOI, and FAST result. Measures: HR & SBP on ED arrival, FAST result, presence of pelvic fracture, mechanism of injury. Analysis: Descriptive statistics, logistic regression model for independent predictors, multivariate analysis to assess association b/w variable and outcomes. Predictive capacity assessed with AUROC; cutoff determined with Youden Index	RABT more sensitive than ABC in predicting need for MT. RABT: AUROC = 0.828, 95% CI =0.782-0.873, p < 0.001 ABC: 0.617, 95% CI = 0.551, p <0.001 Optimal cutoff for RABT score > 2 to predict need for MT (sensitivity -84%, specificity -77%). All four of RABT components independently predicted MT (including SI; odds ratio 8.9 for S I >1). SI was the strongest independent predictor for MT.	2 - VI
King et al., 1996	To determine if shock index (SI) is a useful marker for significant injury and hemorrhage in trauma patients in comparison to tachycardia or hypotension.	Design: Retrospective review of trauma registry data Sample: N = 1,004 patients >14 yr meeting criteria for a full or partial trauma alert and with complete data Setting: Inner city community teaching hospital	Variables related to fluid volume: Independent – blood transfusion > 2 units (BT) Dependent - SI Measures: HR, & SBP within 5 minutes of ED arrival Analysis: Descriptive statistics, PPV & NPV (95% CI), AUROC for optimal cut-off values	Abnormal SI, HR, or SBP are not accurate predictors of significant injury or hemorrhage (sensitivity <54% for SI, NR, or SBP) 0.85 was the optimal SI for predicting BT -Sensitivity 54% -Specificity 80% -PPV -29% -NPV -92% -Accuracy -77%	3 - IV
Kohn et al., 2019	Evaluate shock index (SI) vs HR or SBP to best predict post-partum hemorrhage, need for transfusion, or need for surgical intervention. Additionally, identify useful thresholds for patients requiring further intervention.	Design: Retrospective case control study using database Sample: Controls (n = 41): < 500 ml loss for vaginal delivery and < 1000 ml loss for C-section. Study population (n = 41): >500 ml loss for vaginal delivery and > 1000 ml loss for C- section. Setting: Academic tertiary hospital.	Variables: Patient demographics, mode of delivery, estimated blood loss, change in Hgb and Hct, transfusion and number of units, surgical intervention. HR, SBP, SI. Measures: Vitals measured at last antenatal visit, on admission, immediately post-delivery and at peak SI. Also measured delta SI (peak SI-SI at last antenatal visit). Analysis: Compared characteristics and outcomes with Student's t, Mann-Whitney-U, Pearson's chi-square. ROC curves used to assess performance of variables to determine transfusion and other variables.	Controls: Blood loss median for vaginal = 350 ml. Blood loss median for C-section = 750 ml. PPH cases: Vaginal median was 750 ml and C- section median was 1800ml. SI < 1.1 normal in gravid patient (5th and 95th percentile VS used to determine normal range). SI ≥ 1.143 correctly classified 67–77% all adverse outcomes. SI ≥1.412 predicted PPH and need for transfusion with 100% specificity and predicted surgical intervention with 97% specificity. Peak SI and Δ SI are superior to proposed maternal early warning criteria as predictors of PPH, transfusion, and surgical intervention	3 – IV

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Lai et al., 2016	To assess complications in trauma pts with reverse shock index (RSI) < 1 on arrival (A) or departure(L) from the ED.	Design: Retrospective review of trauma registry data. Sample: N = 10, 234 > 20 yr Group I: (A & L) RSI > 1, n = 9827 (stable throughout) Group II: (A) RSI > 1 & (L) RSI < 1, n = 76 (decompensating) Group III: (A) RSI < 1 & (L) RSI > 1, n = 251 (improving) Group IV: (A & L) RSI < 1, n = 80 (unstable throughout) Setting: Level 1 trauma center, urban	Variables pertinent to fluid volume: Independent – blood transfusion in the ED Dependent - RSI (SBP divided by HR) Measures: HR & SBP arrival and departure from ED RSI=SBP/HR Analysis: Odds rations, logistic regression Pearson's $\chi 2$ test, Fisher's exact test, or independent Student's t-test to compare Group I with Groups II, II, & IV	RSI < 1 either on arrival or departure from ED indicated poor outcome even without hypotension. Groups II, III, & IV received more blood transfusions than Group I ($p < 0.001$) and had higher values for all other outcome measures as well. Group II: OR 11.8 (CI 6.5-21.5) Group III: OR 11.4 (CI 8.0-16.3) Group IV: OR 34.9 (CI 21.8-55.9)	3 - IV
Lance et al., 2009	Purpose: To compare procedures for measuring orthostatic vitals (5 v. 10 minutes lying and 0 – 2 minutes while standing).	Design: Randomized crossover Sample: Convenience, N=34 normotensive young adults (average - 21.6 years). Power 90% for DPB change of 6mmHg = 35 subjects. Sleep, activity, and food intake was standardized. Setting: inpatient research hospital	Variables: Independent – lying and standing procedure Dependent - blood pressure, heart rate, dizziness intensity Measures: BP & HR – Dinemap (1846 SX) vital signs monitor on dominant arm VAS for dizziness: 10 cm visual analog scale Measurements were obtained after 5 and 10 minutes in a supine position, immediately upon standing and again after 2 and 5 minutes. Subjects served as their own controls. Analysis: Descriptive statistics, ANOVA for repeated measures, $p < 0.25$	Lying BP differed between 5 & 10 minutes ($F=21.33$, $p < 0.001$) Mean BP differed between 5 & 10 minutes ($F=5.23$, $p < 0.03$) Standing BP and dizziness differed between 0 & 2 minutes ($F=8.36$, $p = 0.01$) & ($F=7.15$, $p< 0.10$). There were no significant changes at any other time points. For normotensive individuals, vitals while lying stabilized by 10 min. Standing vitals can be measured immediately upon standing and again at 2 min.	2 - IV
Linnaus et al., 2017	In a prospective, multi-institutional setting, the aim is to determine the validity of the pediatric age adjusted shock index (SIPA).	Design: Secondary analysis of data from a prospective observational study by Acker et al., 2015. Sample: N = 386 children > 4 years, but ≤ 17, presenting to ED with blunt liver or spleen injury (BLSI). ISS greater or equal to 15. Setting: Ten Level 1 Pediatric Trauma Centers in Arizona, Texas, Oklahoma, Arkansas, Tennessee, Wisconsin, Ohio, Missouri, and Georgia.	Variables: Trauma bay vital signs including SBP and HR. SIPA and SI. Hemoglobin levels, transfusion requirements, ISS score, type of injury, operative management, ICU stay. Patient demographics. Measures: Vitals collected in the trauma bay with max HR and minimum SBP used for SIPA calculations. SIPA > 1.22 for 4 - 6.9 years SIPA > 1.0 for 7-12.9 years SIPA > 0.9 for 13 - 16.9 years Elevated SI > 0.9 Analysis: Medians for continuous data. Comparisons between categorical and continuous variables included Chi Square and Kruskal-Wallis. Compared SI > 0.9 to SIPA based on age, to predict need for blood transfusion (sensitivity and specificity with 95% CI.	83% of BLSI had elevated SI and 73% had elevated SIPA. Both tools able to determine those who needed blood transfusions. SIPA better than SI in determining adverse outcomes and identifying the need for blood transfusion (34% vs 30%). Both SI and SIPA sensitive for blood transfusion (95.9 and 94.8; 95% CI) with SIPA improving specificity (21.5% for SI and 35.1% for SIPA).	2 - IV
McNab et al., 2012	An investigation of trauma center and pre-hospital shock index (SI) to determine multiple outcomes including the need for blood transfusion.	Design: A retrospective analysis of trauma center registry data. Sample: All trauma patients over 16 ears transported by EMS. N = 16,269 Setting: Level 1 Trauma Center in Florida.	Variables: SI, HR, SBP, disposition, hospital stay, vent days, blood transfusion. Patient demographics. Measures: First available vital signs in prehospital system and trauma center. 3 Groups used related to SI: SI < 0.7, SI 0.71 to 0.89, and SI > 0.9. Analysis: Pearson correlation coefficients used to evaluate SI as compared to other variables including transfusion need. Chi Square evaluated relationship to other variables.	Mean Pre-Hospital SI = 0.64. Mean SI in the ED was 0.71. Prehospital SI Values & Blood Received: SI ≤ 0.7 - 0.07 units; SI 0.7-0.89 - 0.16 units; SI ≥ 0.9 - 0.68 units Both EMS and ED SI positively correlated with blood use (and other outcomes), $p < 0.001$. Pearson coefficient for blood admin (0.113 for EMS SI & 0.108 for ED SI)	3 - VI

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Morrison et al., 2012	Purpose: Evaluate usefulness of admission physiological parameters (HR, SBP, PP, SI, and base excess) in determining hemodynamic stability and surgical triage in patients with ballistic torso trauma.	Design: Retrospective cohort analysis comparing life-threatening torso hemorrhage (LTTH) patients with non-life-threatening hemorrhage (non-LTTH) patients Sample: Convenience. N-122 (n=44 LTTH; n=59 non- LTTH) Setting: Military surgical facility in Afghanistan	Variables: HR, BP, BE from ABG analysis, CT scan findings, operative intervention, injury pattern, transfusion requirement, and 28-day mortality Measures: First recorded vital signs used to calculate SI and PP Analysis: Parameters compared using two sample t tests, Mann–Whitney, Fisher's exact, and Chi-square tests. ROC curves used to identify significant parameters and determine optimum cut-off values. $p < 0.05$ considered significant.	SI correlated best with the need for surgical torso hemorrhage control, ($p < 0.05$) and SI of > 0.9 was most predictive of torso hemorrhage (positive and negative predictive value of 81% and 82% respectively). Pulse pressure values between the LTTH group and non-LTTH group were also statistically significant (PP ± SD LTTH group 44 ± 17; non- LTTH group 56 ± 13, $p < 0.001$)	3 - IV
Mutschler et al., 2013	To correlate 4 levels of SI classification to fluid resuscitation, massive transfusion, base deficit, demographics, outcomes, & ISS.	Design: Retrospective review of trauma registry data. Sample: N=21,853 > 16 yr Setting: 600 hospitals in Germany	Variables pertinent to fluid volume: Independent – massive transfusion (MT; units of blood products from ED arrival until ICU admission), intravenous fluid (IVF) administration, use of vasopressors. Dependent – SI Measures: HR & SBP upon ED admission; SI Strata: I: < 0.6; II: < 0.6 to < 1.0; III: > 1.0 to < 1.4; IV: > 1.4 Analysis: Difference between groups evaluated by Kruskal-Wallis test; Chi square for categorical variables, AUROC for comparison of SI in prediction of need for MT	SI is a clinical indicator of hypovolemic shock. Increasing SI category correlated with increasing transfusion requirements, IVF administered, & use of vasopressors. Strata of SI equaled differentiation by base deficit so SI can be used to classify shock when point of care testing is not available.	2 - VI
Nathan et al., 2015	To determine the vital sign (SI, HR, SBP DBP, MAP, PP) that is most effective at prediction for adverse outcomes (including blood transfusion) for post-partum hemorrhage (PPH). They also sought to develop identification criteria for referral and to identify patients who need urgent action.	Design: Secondary analysis of data from a prospective observational study of women with PPH using chart review. Sample: N=233 Women with blood loss > 1,500 ml with PPH. Setting: UK tertiary referral center	Variables: Patient demographics. Vitals including BP, HR, SI, MAP, PP. Adverse outcomes included ICU admission, transfusion, hemoglobin < 7 g/dl, and surgical intervention. Measures: Vitals obtained in the first hour following PPH recognition. Analysis: AUROC values and 95% CI used for each outcome. The highest SI calculation were the vitals used for analysis.	Median SI value was 0.95. SI was the best indicator for transfusion (AUROC 0.67). SI ≥ 0.7 had 92.5% sensitivity but only 15.2% specificity for transfusion ≥ 4units. SI ≥ 0.9 had 80% sensitivity and 45% specificity. SI ≥ 0.09 indicated need for referral and SI > 1.7 needed for urgent intervention.	3 - VI
Nathan et al., 2016	To determine normal ranges of vital signs including SI in immediate post-partum (PP) period to help develop an obstetrical early warning score.	Design: Secondary analysis of data from a prospective cohort study Sample: N=316 Setting: maternity units at urban hospitals	Variables: Independent – estimated blood loss < 500 ml in the first hour PP Dependent - BP, HR, MAP, & SI Measures: HR, BP Analysis: Simple & multilinear regression to associate demographic & obstetrical factors with SI. Median, lower, & upper quartiles & 90% reference ranges calculated	Identified normal ranges in the first hour after obstetrical delivery (vaginal or surgical): -HR 61-102 bpm; -SBP 100-145 mmHg; -DBP 58-90 mmHg; -MAP 73-108 mmHg; -SI 0.52 – 0.89. There was a significant association between SI and 3rd stage use of syntometrine & epidural, primarily due to increased HR. -SI decreased by 0.03 with synometrine use -SI increased by 0.05 with epidural These changes did not move SI out of usual normal range and are clinically unimportant.	3 – IV

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Nordin et al., 2018	Attempt to validate the SIPA (shock index, pediatric age adjusted) using pediatric trauma data from a national trauma database. Also attempted to generate cutoff values for patients < 4 years and determine if elevations in SIPA are associated with outcomes in children with penetrating injuries.	Design: Retrospective review of 2014 Pediatric Trauma Quality Improvement Program (TQIP) database patient information. Sample: Children aged 1-16 years with blunt and penetrating trauma and Abbreviated Injury Scale ≥ 2. Penetrating trauma n = 613, blunt trauma n = 22,334 Setting: Children's hospital in Columbus, Ohio	Variables: Patient demographics, injury mechanism, ISS, head abbreviated injury scale (hAIS), vitals on emergency department arrival, ICU length of stay, ventilator use, transfusion requirement, and disposition. Measures: SI and SIPA calculations. Application of SIPA cutoff values: Creation of a SIPA cutoff value for 1-3 years. Analysis: Separate data evaluation for blunt and penetrating trauma. Patients with ISS > 15 also evaluated separately as a subgroup of each. Chi- square used to compare SI and SIPA. Student's t used for continuous variables. Sensitivity, specificity, and positive predictive value also calculated for SI and SIPA.	Blunt Trauma: 41.3% with elevated SI and 15.6% with elevated SIPA. Elevated values of both were associated with increased need for transfusion. For transfusion, SI had higher sensitivity (69.6 vs 52.4%; p < 0.0001) while SIPA had higher specificity (59.0 vs 84.8%; p < 0.0001). SIPA also had double the positive predictive value (2.02 vs 4.02%; p < 0.001). Penetrating Trauma: 40.0% had elevated SI and 19.4% had elevated SIPA. Both were associated with increased need for transfusion. In transfused patients, sensitivity was higher in SI (56.9 vs. 46.1%; p =0.0082) while SIPA was greater in specificity (83.7 vs. 63.1%; p < 0.001).	2 - IV
Paladino et al., 2011	Examine the ability of SI to differentiate between major and minor trauma in trauma patients ≥ 13 years of age.	Design: Retrospective review of a prospective trauma cohort. Sample: Trauma patients ≥ 13 years with blunt or penetrating trauma. N = 1435 Setting: Level I Trauma Center Emergency Department, New York, NY	Variables: HR, SBP, DSP, base deficit, lactate, and SI. Minor or Major trauma classification, transfusions, injury severity score. Measures: Initial vital signs and arterial blood gas obtained in the ED on arrival. Analysis: Means and SD, counts and percentages with 95% CI. Student's t or X2. Sensitivity and specificity along with receiver operator characteristic curves.	Minor Trauma (n = 1193): Mean SI 0.67 (95% CI: 0.66-0.68; p < 0.01). Major Trauma (n = 242): Mean SI 0.79 (95% CI: 0.75-0.83; p < 0.01). SI of 0.9 sensitivity 24% (19-30%); specificity 92% (90-93%). Differences between groups was significant (p < 0.01) but both were below the cutoff of 0.9.	3 - IV
Pasquier et al., 2019	To evaluate HR, SBP, and SI and measure changes during blood donation.	Design: Prospective observational study with active-duty soldiers donating blood. Sample: Healthy military volunteers. Power analysis with 80% power required 378 subjects. N = 483 Setting: Multiple military bases in France.	Variables: HR, BP, temperature, patient demographics. Medical hx, hemoglobin, blood bas volume. Measures: HR and BP measured after 2-minute rest in sitting position. Blood removed via 16- gauge catheter. Two minutes after phlebotomy, HR and BP obtained in sitting position. Analysis: Mean and SD for continuous variables. Chi-square test for categorical. Associations between SI and blood donation volume with multivariate analysis.	Mean donation volume = 473 mls. Mean pre- and pos-donation SI were significantly different (0.54 vs 0.57; p = 0.002). While the 0.03 difference is statistically significant, it is not clinically significant.	3 - IV
Priestley et al., 2019	Purpose: To determine if narrow pulse pressure (PP) in non-hypotensive pts predict active hemorrhage (AH; defined as requiring intervention [operative or radiologic] and 3 units of PRBCs within any 60 min period in the 1st 24 hr after admission)	Design: Retrospective cohort analysis comparing AH patients to non-AH patients Sample: N = 18,015 (n= 283 with AH) from trauma registry data 1/10 to 10/14. Setting: Urban trauma center in US	Variables: Field and admission vital signs (GCS, HR, BP), blood products received in 24 hours, IR findings and procedure completed, surgical intervention, intraoperative findings, ventilator days, hospital length of stay, ICU length of stay, and mortality. Measures: Admission systolic and diastolic blood pressure used to calculate pulse pressure Analysis: Univariate analysis for demographics, hospital outcomes, and clinical interventions. Multivariate analysis for variables with p < 0.2, AOR with 95% CI derived from logistic regression. Stepwise logistic regression to identify independent predictors of AH. p < 0.05	In non-hypotensive patients, narrowed PP is an independent predictor of hemorrhage requiring operative or radiological intervention and transfusion. Higher risk of AH with PP cutoff >61 yr: 55 mmHg (AOR 3.44, p <0.005, AUC 0.955)) 16- 60 yr: 40 mmHg (AOR 2.73, p <0.0001, AUC 0.940)	2 - IV

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Rau et al., 2016,	Purpose is to investigate SI, MSI, and Age SI as predictors for massive transfusion in trauma patients.	Design: Retrospective trauma registry data review. Sample: Patients at who received transfusion in first 24 hours. N = 2,509 Setting: Level I regional trauma center from January 2009 to December 2014	Variables: Patient demographics. SBP and HR on arrival to ED and calculated SI, MSI, and Age SI. Measures: SI, MSI (HR/MAP), Age SI (Age*SI), Base Deficit (BD) Analysis: Odds ratio for associated conditions calculated with 95% CI. Categorical variables evaluated with Fisher or Pearson chi square. Unpaired Student t used for continuous data. Cut-off points evaluated for SI, MSI, and Age SI to predict transfusion needed with ROC curves.	Those who received MT had significantly higher HR, lower SBP & BD, and increased SI, MSI, and Age SI. (1.1, 1.4, and 43.1 respectively; $p < 0.0001$). SI of 0.95 and MSI of 1.15 were identified as cut-off values for massive transfusion with an AUC of 0.760, sensitivity: 56.3% and specificity: 87.6%) and 75.6% (sensitivity: 61.5% and specificity: 82.3%). SI is moderately accurate in predicting the need for MT. Predictive power may be compromised in patients with HTN, DM or CAD. MSI and Age SI failed to provide better discriminating power than the SI.	2 - IV
Schroll et al. 2018	Evaluate ABC (Assessment of Blood Consumption) vs Shock Index (SI) to determine best predictor for early activation of massive transfusion.	Design: Retrospective cohort study from trauma registry data Sample: Adult (≥18) trauma patient activations between Jan 2009-Dec 2013 without TBI. N = 664 Setting: Level I trauma center	Variables: Patient demographics, HR, SBP, FAST, GCS, ISS, blood units given. Measures: ABC Score from 0-4: 1 point each for: penetrating trauma, positive FAST, SBP ≤ 90 in ED, HR ≥ 120 in ED. ABC ≥ 2 was cutoff to predict MTP. MTP > 10 units in 24 hrs. Analysis: T-testing and 2 proportion chi square analysis. McNemar Chi square test used for sensitivities and specificities of ABC and SI. AUROC used to evaluate accuracy and discriminative ability of ABC and SI.	Of 644 patients included, only 34 got MTP. MTP was used in 17% of those with SI ≥ 1 and ($p < 0.001$) and 21% of those with ABC ≥ 2 ($p < 0.001$). SI ≥ 1 had sensitivity of 67.7% and specificity of 81.3% for predicting MTP. ABC had 47% and 89.8% sensitivity and specificity for MTP. McNemar's showed SI with greater sensitivity ($p = 0.035$) but weak specificity ($p < 0.001$). SI ≥ 1 was stronger with AUROC (0.83).	3 - IV
Sohn et al., 2018.	Determine if initial lactate is associated with need for massive transfusion following post-partum hemorrhage PPH) and then compare lactate combined with SI to see if there is improved prediction for transfusion.	Design: Retrospective observational study Sample: all PPH patients referred to the ED with lactate test between Jan 2004-Dec 2015. PPH = required blood in first 24 hours following delivery. N = 302 Setting: Emergency department of university tertiary referral center in South Korea	Variables: Initial vitals, temperature, SI, patient demographics. Measures: On arrival blood lactate obtained. Two groups evaluated: massive transfusion (> 10 units) and non-massive transfusion. Analysis: Medians and interquartile ranges for continuous and frequencies for categorical. Comparisons evaluated with Person's X2 or Fishers exact. Multivariate logistic regression used for factors associated with transfusion, reported as odds rations, and confirmed with ROC curves.	101 required MT. Those requiring MT had significantly lower BP and higher HR on arrival with higher SI noted (1.1; $p < 0.01$). Patients with MT had higher lactate levels. SI was associated with MT (Odds ratio of 10.26 with 95% CI; $p < 0.01$). Lactate was also associated with MT (Odds ratio 1.56; $p < 0.01$). SI elevation > 1.0 was 78.7% specific with a 58.7% positive predictive value for MT. Lactate > 4 was 86.1% specific and 67.8% noted for positive predictive value. When both were combined, positive predictive value increased to 82.4% and specificity of 95.5%.	2 - IV

Appendix 1: Evidence Table

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Strutt et al., 2019	Evaluate shock index in pediatric trauma patients for prediction of negative outcomes including mortality blood transfusion need, ventilation need, procedures, and ICU stay.	Design: Retrospective review of trauma registry data Sample: N=28,741. Pediatric trauma patients in national registry Setting: Over 900 trauma centers in the United States	Variables: Age, GCS, ISS, SI, mortality, transfusion (ICD Code), ventilation, OR/IR procedure, ICU stay, general demographics. Measures: SI cutoff calculated from highest normal HR and lowest normal SBP per ATLS <12 months - SI <2.7 1 to <2 years - SI <2.1 2 to <5 years - SI <1.9 5 to <12 years - SI <1.5 12-14 years - SI <1.1 Analysis: Means for continuous variables, medians for ordinal variables, Mann-Whitney U and Student's t to examine differences. Multivariate regression analysis used to assess factors in mortality.	Median SI = 0.86 with 1.7% having elevated SI on arrival. Patients with elevated SI for age were more likely to be transfused (p<0.001). 9.9% with an elevated SI received blood transfusions (p <0.001) while 1.2% with normal SI received blood. In those receiving blood, an elevated SI had a 12.6% sensitivity and 98.4% specificity. Elevated SI was the strongest predictor of mortality (OR-22; 95% CI)	3 - IV
Vandromme et al., 2011	Assess association between prehospital SI and risk of massive transfusion (MT) in relatively normotensive patients who had blunt trauma.	Design: Retrospective review of trauma registry data Sample: N = 20,095 pts, (3.4%) received MT Setting: Level 1 trauma center, urban	Variables: Independent - SBP > 90, MT (> 10 units RBCs/1st 24hrs) Dependent – SI Measures – HR & SBP prehospital Normal SI defined as > 0.5 to 0.7 Analysis: Demographics, injury, clinical characteristics compared with $\chi 2$, ANOVA for categorial & continuous variables, proportional hazards regression for risk ratio (95% CI)	Prehospital SI > 0.9 in relatively normotensive patients is associated with incrementally increased risk of MT. No increased risk for SI < 0.5 (RR 1.41, CI 0.90-2.21) >0.7-0.9 (RR1.06, CI 0.77-1.45) Significantly increased risk: SI > 0.9-1.1: RR 1.61, CI 1.13-2.31 SI > 1.1-1.3: RR 5.57, CI 3.74-8.30 SI > 1.3: RR 8.13, CI 4.60-14.36 SI from ED vitals showed a similar but more exaggerated trend. SI > 0.7-0.9 had two-fold risk for MTP while SI > 1.3 had 20-fold risk.	2 - IV
Warren et al. 2019	Purpose: To determine if narrowed pulse pressure is associated with the need for both a massive transfusion and emergent surgical intervention to control hemorrhage in patients with penetrating trauma.	Design: Retrospective cohort analysis comparing patients with initial ED PP < 30 mmHg to patients with a normal PP. Sample: N=957 penetrating trauma patients from trauma registry data 11/14 to 4/17. Setting: Level 1 trauma center in US	Variables: Demographics, mechanism of injury, Injury Severity Score, vital signs including the shock index, transfusion requirements (MTP defined as a transfusion of >10 units of packed red blood cells within the first 24 h of admission), and need for emergent surgery Measures: Initial VS on ED admission used to calculate SI and PP Analysis: Student's t-test, Mann-Whitney U test, Chi-square, Fisher's exact test. p < 0.05	178 patients (18.7%) presented with a narrowed PP (< 30 mmHg). Patients with narrowed PP were more likely to receive a massive transfusion (11% vs. 2%, p < 0.001). Pts who had massive transfusion had an elevated SI (> 0.7) (70% vs. 46%, p = 0.004), and narrowed PP (53% vs. 17%, p < 0.001).	2 - IV
Wang et al., 2019	Evaluate ability of prehospital MSI (modified shock index) to predict massive transfusion in trauma patients. Additionally, compare predictive ability of prehospital SI and prehospital MSI for massive transfusion.	Design: Retrospective observational study from Korean Trauma Data base. Sample: Adult (>18) patients with blunt or penetrating trauma presenting between Jan 2016-Dec 2017. N=1007 Setting: single center trauma center tertiary facility in Korea	Variables: Prehospital HR, SBP, DBP values. Patient demographics. Transfusion in first 24 hrs, and 24 hr mortality Measures: BP measured in prehospital phase. Prehospital SI (HR/SBP) and MSI (HR/MAP) calculated. Lower BP of 1 or 2 readings used. MT = >10 units in first 24 hrs. Analysis: Continuous with mean and SD or median with IQR. Categorical with percentages. ROC curves used to determine cut-off values for prehospital SI and MSI. Predictive ability assessed by ROC with high accuracy >0 .9, moderate of 0.7-0.9 and low < 0.7	Median values of prehospital SI and MSI 0.73 and 0.94. 30.2% received blood administration in 4 hours and 37.4% within 24 hrs. 7.7% had MT Prehospital SI and MSI in the massive transfusion group was higher than non-massive transfusion group significantly (p < 0.001). Cut-off values for MT prediction for pre-SI ≥ 0.91 (sensitivity of 65% and specificity of 77%) and for pre MSI- 1.28 (sensitivity of 60% and 82% for specificity).	2 - IV

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Witting et al., 1994	Purpose: To determine which orthostatic vital signs have the best specificity and sensitivity to detect acute moderate blood loss. To standardize the tilt test.	Design: Prospective cross-sectional Sample: Convenience, N = 345 healthy, euvolemic adult blood donors Group 1: < 65 yr (n = 292) Group 2: > 65 yr (n = 44) Setting: Blood donation center	Variables: heart rate, blood pressure, lightheadedness Measures: BP & HR – Dinemap vital signs monitor & defined degrees of lightheadedness, before and after phlebotomy while reclined in blood donor chair and at 1 & 2 minutes after standing. Analysis: Paired comparison of pre-/post- vital signs to determine sensitivity and specificity used to generate receiver operating characteristics curves (ROC). Power calculations for proportions, p<0.05 Bonferroni adjustment used for multiple comparisons. Based on ROC curves, pulse alone was compared with published criteria for positive tilt test.	Only evaluated one-minute orthostatic vitals due to no significant difference in results from one to two minute. Pulse change performed better than other criteria (p<0.01) if pulse was >17, 18, and 25 for sensitivity in group 1 and in sensitivity in group 2 if pulse >18. Group 1: no other criteria was above pulse change ROC curve. Group 2: had criteria above pulse change ROC, but sensitivity and specificity were poor. Neither changes in tilt test vital signs nor mild lightheadedness have the discriminative power to detect 450-500 ml blood loss. Blood pressure measurement may be misleading.	2 - VI
Witting & Gallagher, 2003	Purpose: Determine normal vital signs changes associated with moving from sitting to standing (SS) versus lying to sitting (LS).	Design: Prospective cross-sectional Sample: Convenience, N = 176 healthy euvolemic adults (ED patients n = 79; healthcare providers n = 97). Power analysis – 160 subjects required Setting: Emergency department	Variables: Systolic BP, diastolic BP, heart rate, shock index (SI), orthostatic change in SI (OCSI), ratio of orthostatic Sis (ROSI) Measures: BP & HR – Dinemap vital signs monitor, after sitting for 5 minutes and one minute after standing. Analysis: Cutpoints selected for 95 percentile changes. Confidence intervals for means based on t-distribution; CI for proportions based on normal approximation of binomial distribution. Used data from a prior study for LS cutpoints.	Mean SS changes were less extreme than LS. HR increased 5.3 (95% CI: 4.3- 6.3 bpm) SBP decreased 1.2mmHg (95% CI: 0.3-2.6) SI increased 0.05 + 0.07 bpm/mmHg (95% CI:0.04-0.06) Cutpoints: HR > 20 bpm - 98 % specificity SBP decrease > 20 mmHg - 97% specificity OCSI increase > 0.2 - 99% Specificity ROSCI > 1.3 - 95% specificity. Vital sign changes are less extreme with sitting-to-standing tilt tests and therefore require different positivity criteria from lying-to-standing tilt tests.	3 - VI
Wu et al., 2019	Evaluate the ability of delta shock index (difference between EMS and ED SI) to predict massive transfusion need in trauma patients that present with stable blood pressures.	Design: Retrospective observational study with single center trauma database Sample: Adult (≥ 20 yr) trauma patients between Jan 2009-Dec 2016 who were admitted, transferred by EMS, with SBP ≥90mmHg on arrival to ED. N = 7,957 with n = 82 receiving MT Setting: Trauma database at Level 1 Trauma Center in Taiwan.	Variables: Patient demographics. Vitals, comorbids, ISS, units of blood transfused, in- hospital mortality. Measures: MT = > 10 units in 24rs of arrival to ED. Vitals from EMS and triage used for calculations of change in SI (ED SI- EMS SI). 2 groups evaluated: MT and no MT. Analysis: Unpaired student t and Mann-Whitney U used to evaluate normally and non-normally data (expressed as mean/SD and IQR. Odds ratio with 95% CI used to associate transfusion and change in SI. ROC curves used to determine cut- off values to predict need for MT. (.0.9 is high accuracy, 0.7-0.9 moderate, and <0.7 low). p < 0.05.	MT group had significantly higher EMS SI, ED SI, and delta SI. Only ISS was a significant independent risk for MT (OR 1.1; CI 95%; p < 0.001). SI in ED or EMS or delta SI was not significant independent risk for MT. Delta SI of 0.06 was determined as cut-off via ROC curve (sensitivity of 0.415 and specificity of 0.841) for MT. Delta SI ≥ 0.00 had significant need for MT vs those with delta SI < 0.00 (1.4% vs. 0.8%; p = 0.01). As delta SI increased, the need for MT increased significantly (p < 0.001).	3 - IV

Reference	Purpose	Design, Sample, Setting	Variables, Measures, Analyses	Findings, Implications	Quality – Level of Evidence
Yadav et al., 2016	Purpose: To evaluate the magnitude and time course of changes in HR and BP during change from reclining to standing, before and after 450 ml blood donation, to measure effect of mild hypovolemia on efficacy of reflex maintenance of BP.	Design: Prospective cross-sectional Sample: Convenience, N=51 healthy adults Setting: Blood bank, New Delhi, India	Variables: SBP, DBP, mean BP, pulse pressure, HR Measures: Baseline beat-to-beat BP and Lead II ECG (Finometer Model 2) measured after 10 min. in a semi-reclining position and continuously from 3 sec to 3 min after standing before and after a 450 ml blood donation. The patient remained reclining for 5 min after donation before standing. Change in BP & HR, and latency of response was calculated. Analysis: D'Agostino-Pearson omnibus normality test and Shapiro-Wilk tests. t test and Mann Whitney, $p < 0.05$.	BP did not change with blood donation in semi-reclining position, a clinically insignificant decrease in pulse pressure ($p = 0.005$) was noted in addition to an increase of approximately 10 bpm in HR ($p=0.002$). Standing after donation resulted in a statistically significant greater fall in SBP ($p = 0.0012$), DBP ($p = 0.0001$), mean BP ($p = 0.0035$), pulse pressure ($p = 0.0023$), and greater increase in HR ($p = 0.0002$). The largest vital sign changes were clinically significant for all values but returned to baseline in 11-16 seconds. Latency of response was significant but small in magnitude (2-3 sec). Baroreflex gain was not significant.	3 - VI

Grading the Quality of the Evidence

1. Acceptable Quality: No concerns
2. Limitations in Quality: Minor flaws or inconsistencies in the evidence
3. Major Limitations in Quality: Many flaws and inconsistencies in the evidence
4. Not Acceptable: Major flaws in the evidence

Grading the Levels of the Evidence (Melnyk & Fineout-Overholt, 2019)

I. Evidence from a systematic review or meta-analysis of all relevant, randomized, controlled trials or evidence-based clinical practice guidelines based on systematic reviews of RCTs
II. Evidence obtained from at least one properly designed, randomized, controlled trial
III. Evidence obtained from well-designed controlled trials without randomization
IV. Evidence obtained from well-designed case control and cohort studies.
V. Evidence from systematic reviews of descriptive and qualitative studies.
VI. Evidence from a single descriptive or qualitative study
VII. Evidence from opinion of authorities and/or reports of expert committees.

Clinical Practice Guideline:
Clinical Assessment of Acute Hypovolemia
Appendix 2: Study Selection Flowchart and Inclusion/Exclusion Criteria

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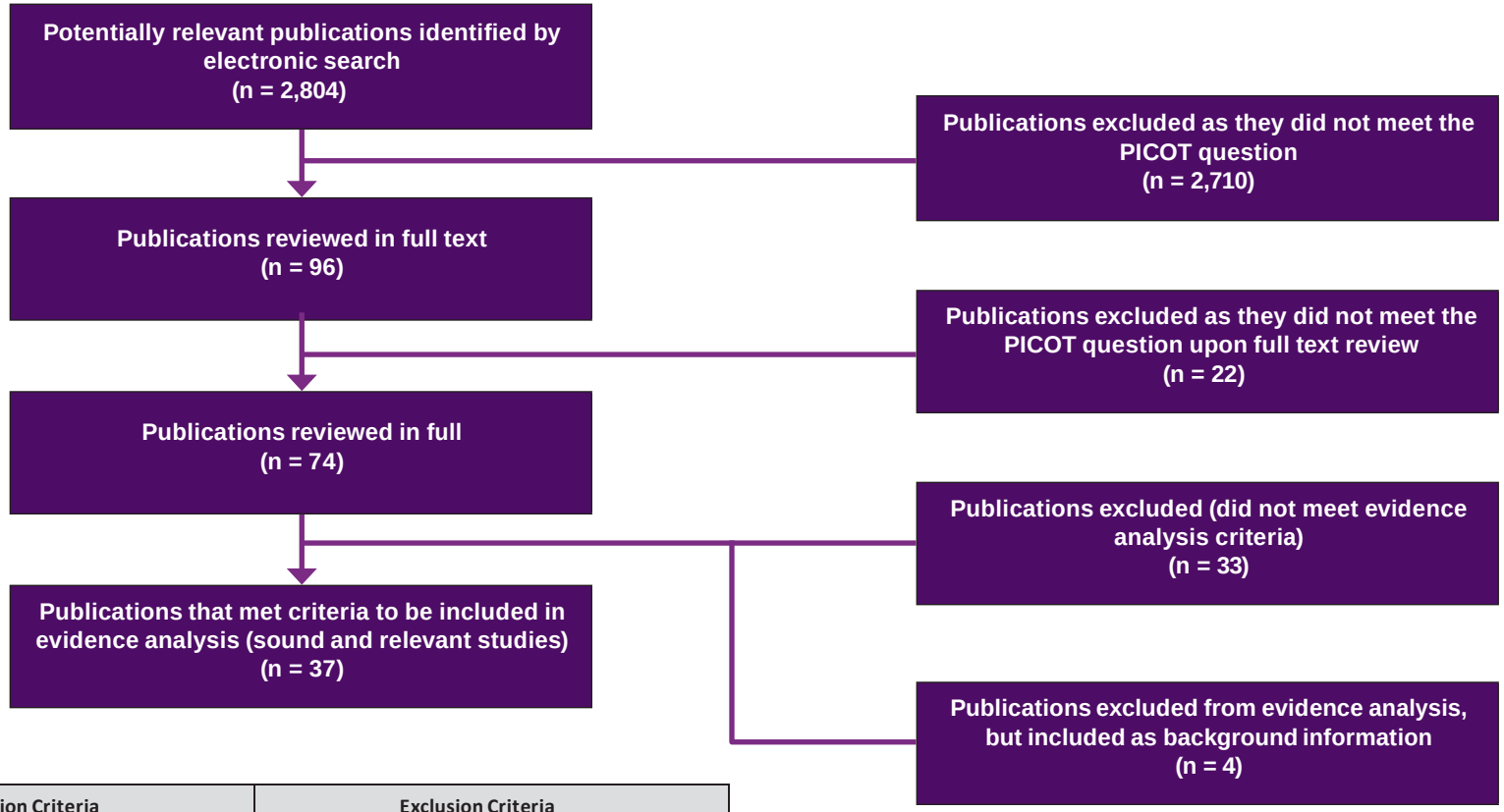

Inclusion Criteria	Exclusion Criteria
Studies published in English	Studies not published in English
Studies involving human subjects	Non-human studies
April 2011 – September 2020	Studies not in the timeframe listed
Studies addressing the PICOT question	Studies not addressing the PICOT questions

The following databases were searched: PubMed, Google Scholar, CINAHL, Cochrane Library, BioMed Central-Open Access, and Agency for Healthcare Research and Quality.
Search terms included: “tilt test,” “postural vital signs,” “orthostatic vital signs,” “blood pressure,” “hypotension,” “orthostatics,” and “hypovolemic,” using a variety of different search combinations.