



Shock Index as a Predictor of Post-Intubation Hypotension and Cardiac Arrest; A Review of the Current Evidence

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Received: August 23, 2018

Revised: November 23, 2018

Accepted: December 7, 2018

ABSTRACT

Endotracheal intubation is a lifesaving procedure that is performed in various settings within the hospital or even in the pre-hospital field. However, it can result in serious hemodynamic complications, such as post-intubation hypotension (PIH) and cardiac arrest. The most promising predictor of such complications is the shock index (SI), which holds great prognostic value for multiple disorders. On the other hand, most of the studies that have assessed the predictability of the pre-intubation SI have been small and were limited to a particular setting of a single center; thus, the results were not generalizable, and the predictive value vary according to the setting. This review comprehensively assessed the utility of the pre-intubation SI for predicting PIH and post-intubation cardiac arrest by classifying and comparing evidence compiled from various settings, such as pre-hospital settings, emergency departments (EDs), intensive care units (ICUs), and operating rooms (ORs). The vast majority of these studies, conducted in ED and ICU settings, which revealed a significant correlation between an elevated SI and PIH or post-intubation cardiac arrest. The reliability and simplicity of obtaining a pre-intubation SI value are important considerations that encourage the extension of its use to all in-hospital intubations. Further studies are required to assess the predictive value of the SI in the pre-hospital setting.

Keywords: Shock index; Intubation; Post-intubation hypotension; Cardiac arrest; Complication.

Please cite this paper as:

Althunayyan SM. Shock Index as a Predictor of Post-Intubation Hypotension and Cardiac Arrest; A Review of the Current Evidence. *Bull Emerg Trauma*. 2019;7(1):21-27. doi: 10.29252/beat-070103.

Introduction

One of the complications of intubation is post-intubation hypotension (PIH). There are several definitions describing PIH in the literature. A clinically relevant definition describes it as a decrease in systolic blood pressure (SBP) to ≤ 90 mmHg, a decrease in SBP of $\geq 20\%$ from a baseline, a decrease in mean arterial pressure (MAB) to ≤ 65 mmHg, or the initiation of vasopressors within the 30-min

following intubation [1]. Although all the definitions of PIH agree on the concept of a reduction in blood pressure after intubation, they may disagree either on the expression of the decline or in its duration after the intubation. The causes and mechanisms of PIH are probably multifactorial due to several physiological changes during intubation. Potential mechanisms include the abrupt loss of adrenergic tone due to the sedative or the paralytic drugs that decrease vascular resistance, also the increase in intrathoracic pressure

due to positive-pressure ventilation, which negatively affects venous return to the heart (preload), and moreover the direct side effects of induction agents on the cardiovascular system. Pre-existing volume depletion or severe acidosis which are transiently worsened by pCO₂ during the apnea might also contribute to the development of PIH and cardiac arrest if not managed appropriately.

A large multicenter prospective surveillance study of 17,583 ED intubations was conducted to identify peri-intubation adverse events [2]. The most common adverse events of endotracheal intubation are hypotension (1.6%) and cardiac arrest (1.5%). The incidence outside the ED varies according to the setting, patient clinical characteristics and the cause of intubation, but generally ranges from 5%-45% of intubated patients. However, because hypotension affects organs perfusion, the evidence confirms that even a brief episode of hypotension is a contributing factor to patient mortality and morbidity [3-5]. As PIH recognized to be a common complication with worse outcomes, it is critical to identify susceptible patients to prevent it and reduce the associated consequences.

The shock index (SI) is defined as heart rate divided by the systolic blood pressure (SBP), with a normal range from 0.5 to 0.7. It was first introduced by Allgöwer and Burri in 1967 as a simple tool assessing the intensity of hypoperfusion states [6]. Subsequently, an elevated SI value was correlated with numerous disease severity and adverse outcomes [7]. Three systematic reviews, two of which were meta-analyses, confirmed the value of the SI in predicting adverse outcomes in trauma, myocardial infarction, and hemorrhagic shock [8-10]. However, in the context of intubation complications, the reliability of the predictive value of the SI is different. Because intubation complications can occur in various settings, patient's clinical conditions and intubation circumstances or even methods may vary among the settings. Thus, the predictive capability and numerical cut-off value may vary accordingly. Moreover, most studies that assessed the relationship between the pre-intubation SI value and PIH were small and limited to the setting of a single center; therefore, the results cannot be generalized to larger populations. The purpose of this review is to summarize the evidence from which the pre-intubation SI can be assessed as being predictive of PIH and post-intubation cardiac arrest in different settings, such as pre-hospital settings, emergency departments (EDs), intensive care units (ICUs), and operating rooms (ORs). To the best of our knowledge, this is the first review to evaluate the relationship between the pre-intubation SI value and intubation complications.

Emergency Department (ED)

PIH occurs in up to one-quarter of ED intubations and associated with high mortality and extended ICU

care [11, 12]. Heffner *et al.* conducted a retrospective cohort study on 300 patients who underwent ED intubation to identify the risk factors associated with PIH [13]. The study revealed that PIH occurred in 22% of patients and was associated with higher in-hospital mortality. Multiple logistic regression analysis for the predictors of PIH showed that the SI was the strongest predictive factor (OR, 55; 95% CI, 13-232) followed by chronic renal failure, acute respiratory failure, and age. Receiver operating characteristic curves revealed the optimal SI value of 0.8 or higher predicted PIH with a sensitivity of 67% and specificity of 80%.

A small retrospective cohort study assessed 240 intubated patients in the ED to quantify the relationship between SI with PIH and mortality [14]. The authors found that patients with a pre-intubation SI value of 0.8 or more were at higher risk of PIH (OR, 2.28; 95% CI, 1.18-4.43), but this value was not associated with a longer duration of intubation or higher in-hospital mortality.

Kim *et al.* conducted a retrospective study of 352 patients intubated in the ED to determine the risk factors for PIH [15]. The SI value was 0.68 for non-PIH patients and 0.79 for patients who developed PIH ($p < 0.01$). The authors concluded that high SI values, increased age, a lack of skill, a history of hypertension, low albumin and pH levels were risk factors for PIH and found that PIH patients were at increased risk of in-hospital mortality.

An additional retrospective cohort study of 417 patients underwent intubation in the ED examined the ability of the SI value and the modified shock index (MSI) in prediction of PIH [16]. The authors defined MSI as heart rate divided by mean arterial pressure (MAP) and hypothesized that MSI would be a more accurate predictor for PIH and mortality as it provides a better estimate of perfusion. Both the MSI and SI had a similar predictive ability as the area under the curve of their respective receiver operating characteristic curves was similar (0.646 and 0.650, respectively).

Regarding post-intubation cardiac arrest, a retrospective study revealed that intubation-related cardiac arrest represents 23.3% of all non-traumatic arrests in the ED, and the authors concluded that post-intubation cardiac arrest occurred more frequently than was commonly recognized [17]. Accordingly, the study emphasized the importance of understanding the predictive factors.

A retrospective cohort study expanded the perception of the problem by assessing the incidence and the factors associated with post-intubation cardiac arrest (defined as an arrest within 60 min of intubation) [18]. After analyzing 410 intubated patients in the ED the authors found that post-intubation cardiac arrest accrued in 4.2% of ED intubations and a 14-fold increase in the odds of hospital mortality. The study also found that the average SI value of the cardiac arrested patients

was 0.9, which was significantly higher than the average SI value of the non-arrested intubated patients (0.71) ($p < 0.01$). The authors concluded that a pre-intubation SI value > 0.9 and weight were independent predictors of post-intubation cardiac arrest. Their data confirmed previous evidence demonstrating that ED intubation was associated with higher mortality, especially when compared with intubation in the OR as the cardiac arrest considered as rare complication [19-21].

An additional retrospective case-control study evaluated the incidence of and risk factors for post-intubation cardiac arrest [22]. Of 2,403 patients who underwent intubation, there were 41 cardiac arrests that occurred within ten min after intubation; a case-control group of patients intubated without cardiac arrest was three times larger. The arrested group had a significantly higher SI value than did the control group (1.1 and 0.9, respectively) ($p = 0.03$).

Another retrospective descriptive study confirms the correlation between the pre-intubation SI value and post-intubation cardiac arrest in all inpatient intubations, including those in the ED [23]. The study analyzed peri-arrest clinical data for these

patients and found that the average SI value for the cardiac arrested patients was 0.95.

The ED results are summarized in Table 1. There is a clear consensus among the studies that the pre-intubation SI has strong predictive power for post-intubation complications. Luckily, the slight discrepancies between the studies methodologies did not affect the results; the studies demonstrated that a pre-intubation SI value of approximately 0.8 or more predicts the risk of PIH and the SI value of approximately 0.9 or more predicts the risk of post-intubation cardiac arrest.

Intensive Care Units (ICUs)

The incidence of PIH in ICUs is between 20 and 46% for intubated patients and is associated with poor outcomes [24, 25]. A large multicenter prospective observational ICU study was performed to evaluate the immediate complications of intubation and found that hypotension occurred in 25% of intubations and cardiac arrest occurred in 2% of intubations [26].

The first ICU study that assessed the utility of the pre-intubation SI was performed by Trivedi

Table 1. Summary of ED studies.

Author (year)	Study population	Purposes and measured outcome	Related findings
Heffner <i>et al.</i> , (2012) [13]	300 patients underwent intubation	To identify factors associated with PIH	-SI ≥ 0.8 was the most strongly associated factor with 67% sensitivity and 80% specificity
Koby <i>et al.</i> , (2015) [14]	240 patients underwent intubation	To quantify the relationship between the pre-intubation SI value and PIH and mortality	-SI ≥ 0.8 indicated a higher risk of PIH but was not associated with a longer duration of intubation or higher in-hospital mortality
Kim <i>et al.</i> , (2016) [15]	352 patients underwent intubation	To determine the possible risk factors that predict PIH	-SI was 0.68 for non-PIH and 0.79 for PIH cases ($P < 0.01$) - PIH patients had higher in-hospital mortality
Corey <i>et al.</i> , (2017) [16]	417 patients underwent intubation	To compare the predictive ability of the pre-intubation SI value and the (MSI) for PIH; the areas under the curves of receiver operating characteristic curves were compared between the two groups in terms of the outcomes of PIH and in-hospital mortality	-MSI and SI had a similar predictive ability for PIH; the areas under the curves were 0.646 and 0.650, respectively
Heffner <i>et al.</i> , (2013) [18]	410 patients who underwent intubation	To study the incidence of and the risk factors associated with post-intubation cardiac arrest in comparison to a control group of patients intubated without arrest	-17 patients with post-intubation cardiac arrest (4.2%) -the pre-intubation SI mean of the arrested group was 0.9; this value was higher than that for a non-arrested group (0.71) ($P < 0.01$)
KIM <i>et al.</i> , (2014) [22]	2,403 patients underwent intubation	To study the incidence and the risk factors associated with cardiac arrest in comparison to a case-control group of patients intubated without arrest	-47 patients with post-intubation cardiac arrest (1.7%) - SI was 1.1 for the arrested group and 0.9 for the control group ($P = 0.03$)
Vyas <i>et al.</i> , (2015) [23]	Analyzed 30 patients who underwent cardiac arrest within 10 min of intubation	To identify risk factors of post-intubation cardiac arrests.	-The average shock index value was 0.95 in the arrested group

et al., [27]. This retrospective cohort study of 140 intubations in hemodynamically stable patients compared short-term outcomes between patients with pre-intubation SI values of less than 0.9 and those with pre-intubation SI values of 0.9 or more. Pre-intubation SI values ≥ 0.90 were significantly associated with PIH and ICU mortality according to univariate and multivariate analyses, and the authors advocated using the pre-intubation SI value as a predictor of such complications.

An additional retrospective study determined the incidence and risk factors of PIH and its effect on 147 patients that were intubated in the ICU [24]. The definition of PIH was restricted to the requirement of a vasopressor within 60 min after intubation. PIH developed in 20% of the patients and was associated with higher mortality and longer stays. The study illustrated that the risk factors are decreased MAB, the administration of neuromuscular blockers, intubation complications, and age. The results were inconsistent with other studies, which showed that pre-intubation SI value was not significantly associated with PIH because the pre-intubation SI value was 0.92 for stable patients and 0.99 for patients who developed PIH ($p=0.36$). Nevertheless, this restricted definition might be biased by the non-standard practices of physicians managing hemodynamics after intubation. This finding could be interpreted as showing that the administration of vasopressor after intubation was associated with a higher mortality and longer stay if the other hemodynamic variables were similar among the two groups. However, no hemodynamic variables were reported after intubation, and blood pressure was stable before intubation in all groups.

Wardi *et al.*, [28] conducted a five-year retrospective case-control study investigating patient clinical characteristics, and the suspected interventions that might predict or associated with post-intubation cardiac arrest in the ICU or the ward. Twenty-nine patients who suffered cardiac arrests within 20 min after intubation were compared to intubated patients who did not suffer cardiac arrest in the same setting. The pre-intubation SI value was 0.98 in the arrested group and 0.86 in the control group ($p=0.036$). A pre-intubation SI value of 1 was associated with post-intubation cardiac arrest with a sensitivity of 0.52 and a specificity of 0.75; these findings illustrate that a pre-intubation SI value ≥ 1 is an independent predictor of post-intubation cardiac arrest (OR 3.4, 95% CI 1.23, 9.35; $p=0.018$).

An additional retrospective study determined the incidence and risk factors of PIH in immunocompromised, critically ill patients [29]. Two hundred and sixty-nine intubated patients were studied, and a PIH incidence of 52% was reported, which was associated with higher ICU and hospital mortality. In addition, multivariate analyses of the data showed that there was a pre-intubation SI value of 1 in the PIH group and a pre-intubation SI value

of 0.84 in the non-PIH group ($p<0.01$); therefore, the authors concluded that high pre-intubation SI value is a significant risk factor for PIH.

The most comprehensive study was performed by Smischney *et al.*, [30] who conducted a case-control study of 420 intubated patients in ICUs to identify the predictors of hemodynamic derangement. Hemodynamic derangement was defined as the occurrence of cardiac arrest or hypotension evident as an SBP below 90 mmHg and/or MAP below 65 mmHg after the intubation. The study demonstrated that age, the non-invasive ventilation, and SI values are associated with the hemodynamic derangement. The mean pre-intubation SI value was 0.96 in the hemodynamic derangement group and 0.81 in the patients without derangement ($p=0.001$).

These ICU studies are summarized in Table 2. Notably, the majority of the studies revealed that high SI values were predictive for PIH and post-intubation cardiac arrest. The differences in the methodologies and definitions used might have affected the predictive power of the cut-off values among the studies. In addition, no ROC curve was constructed to compare the sensitivity and specificity of particular cut-off values in any ICU study. Therefore, it is difficult to determine the optimal cut-off value; however, the reported range of high SI values that were considered predictive was equal to or greater than 0.9-1. The minor variation in cut-off values between ER and ICU pre-intubation SI values might be attributed to several factors, such as volume state, the cause of intubation, the progress of deterioration, and the method of intubation.

Operating Room (OR)

PIH occurred in 10% of patients intubated for elective surgery [31]. Based on the patient's condition, the occurrence can increase to 60% for vascular surgery and can be associated with worse outcomes [32]. Several of the studies assessed the risk factors of PIH in the OR, but none reported a relationship between the pre-intubation SI value and the outcome of interest.

Pre-Hospital Field

In the pre-hospital setting, PIH incidence ranged from 7% to 36% [33-37]. No study primarily assessed the relationship between the pre-intubation SI value and PIH in the pre-hospital setting. However, two studies reported that the shock index was related to blood pressure after intubation. The first study was a prospective observational study that investigated the hemodynamic response of out-of-hospital intubation to ketamine [36]. The authors enrolled 112 patients and the patients' heart rates and SBPs were compared between the pre-intubation and post-intubation periods up to 9 minutes. The authors noted that the patients with high shock index values (≥ 0.9) were

Table 2. Summary of ICU studies.

Author (year)	Study population	Purposes and measured outcomes	Related findings
Trivedi <i>et al.</i> , 2015 [27]	A total of 140 patients who underwent intubation	To compare short-term outcomes between patients with a pre-intubation SI value ≥ 0.9 and those with a pre-intubation SI value < 0.9	A pre-intubation SI value ≥ 0.90 was significantly associated with PIH and ICU mortality
Smischney <i>et al.</i> , 2016 [24]	A total of 147 patients who underwent intubation	To determine the incidence and risk factors of PIH	- PIH occurred in 20% of intubations and was associated with higher mortality and longer hospital stays -The pre-intubation SI value was not associated with PIH because the SI value was 0.92 for stable patients and 0.99 for patients who developed PIH (P = 0.36)
Wardi <i>et al.</i> , 2017 [28]	Twenty-nine patients who underwent cardiac arrest within 20 min after intubation were compared with 116 patients who were intubated without cardiac arrest	The authors examined patient characteristics, interventions, that may predict post-intubation cardiac arrest	- A pre-intubation SI value ≥ 1 was an independent predictor of post-intubation cardiac arrest
Smischney <i>et al.</i> , (2017) [29]	A total of 269 immunocompromised patients who underwent intubation	To identify the incidence and risk factors of PIH in immunocompromised critically ill patients	A pre-intubation SI value of 1 was found in the PIH group and a pre-intubation SI value of 0.84 was found in the non-PIH group (P < .01)
Smischney <i>et al.</i> , 2018 [30]	A total of 420 patients who underwent intubation	To identify the predictors of hemodynamic derangement	- The mean pre-intubation SI value was 0.96 in the hemodynamic derangement group and 0.81 in the patients without complications (P = 0.001)

more hypotensive after intubation (26%) than were those with low shock index values (< 0.9) (2%). Unfortunately, the researchers did not extend the investigation to measure the effect of SI values on patient's mortality and morbidity.

The second study was a large retrospective study of 1,516 patients that evaluated the effect of ketamine on vital signs and intubation complications [37]. A high mean shock index value of $1.35 \pm .57$ was associated with a 36% incidence of hypotension during intubation. However, when the variables associated with hypotension were evaluated, patients who experienced hypotension had lower baseline values of SBP, DBP, MAP, and SI. Surprisingly, the SI value in the hypotensive group was 1.12, whereas the SI value in patients without hypotension was 1.49 (P<0.001). Clinically both groups had very high SI values, and the authors did not find a decrease in the SI values after intubation and did not exclude hypotensive patients to meet the criteria for defining PIH.

Notably, the previous studies show that elevated pre-intubation SI values are common in pre-hospital settings, but further studies required to assess the SI for predicting PIH and post-intubation cardiac arrest.

Recommendations for Intubating Patients at Risk of PIH and Associated Cardiac Arrest

Although this review does not aim to provide a

specific approach to prevent or manage PIH but rather to discuss practical clinical aspects of PIH, some preventive measures are worth mentioning. The standard interventions have been recommended to reduce the risk of PIH, including loading the patient with a bolus of fluid before intubation and restricting the induction choice to hemodynamically stable drugs, such as ketamine or etomidate at a reduced dose. Few studies assessed the efficacy of vasopressors as a preventive measure during intubation. Vasopressor use shows promising results in improving hemodynamics, but the benefits were not extended to evaluate patient-oriented outcomes [38, 39]. Although one study shows no superiority of vasopressor use over the administration of a bolus of fluid, some experts advocate the use of vasopressors as an adjunct intervention before or during the intubation [13, 40, 41]. Others recommend avoiding pretreatment drugs that blunt sympathetic tone, such as fentanyl and lidocaine [42, 43]. Additionally, attention should be paid to sit a small tidal volume of 6-8 ml/kg with low PEEP (Positive end-expiratory pressure) to decrease intrathoracic pressure. Lastly, according to the clinical context, a nasogastric tube should be inserted to decompress the distended stomach that affecting intrathoracic or abdominal compartment pressure. When a patient develops PIH, the immediate action along with resuscitation efforts should be to ruling out other causes of hypotension,

such as tension pneumothorax, tamponade, pulmonary embolism, cardiogenic or distributive shock.

Recommendations for Future Studies

Although most of the studies did not exclude patients on beta or calcium channel blockers in their samples, we were unable to find a study that compared the predictive power of the SI value in patients using or not using those drugs. Furthermore, we did not find any study that compared the effectiveness of different vasopressors in preventing or treating PIH. Further prospective studies are required to establish a comprehensive approach to optimize the intubation conditions of hemodynamically unstable patients.

Further studies are also required to assess the predictive power of the pre-intubation SI in pre-hospital settings. Conducting a systematic review with a meta-analysis for the predictors of PIH in each setting is encouraged.

Conclusion

Most of the studies that assessed the pre-intubation SI with PIH and cardiac arrest were from the ED and ICU literature. There is a remarkable consensus among ED studies demonstrating the reliability of

the SI with a cut-off of approximately 0.8 or higher for predicting the risk of PIH and the cut-off of approximately 0.9 or higher, for predicting the risk of post-intubation cardiac arrest. In ICU studies, elevated SI values (≥ 0.9 -1) are found to predict PIH and post-intubation cardiac arrest. The great predictive power revealed from ED and ICU studies and the simplicity of obtaining pre-intubation SI values are important considerations that encourage the extension of this measurement to all in-hospital intubations. Further studies are required to assess the predictive power of pre-intubation SI values in the pre-hospital setting.

Acknowledgments

This article was supported by the College of Prince Sultan Bin Abdulaziz for Emergency Medical Services, Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia. I would like to express my appreciation to the Deanship of Scientific Research at King Saud University. Furthermore, I would like to thank the librarians at the University of California, Davis, Medical Center, who participated in searching the literature.

Conflicts of Interest: None declared.

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