**ORIGINAL RESEARCH**

**The incidence of post-endotracheal intubation hypotension among patients in the recovery room: impact of definitions**

Marie-Claire Lévesque, MD\*,†; Marcel Émond, MD, MSc\*,†,‡; Natalie Le Sage,MD, PhD\*,†; Simon Berthelot, MD, MSc\*,†; Valérie Boucher, BSc\*; Éric Mercier, MD\*,†

From the \*Centre de recherche du CHU de Québec, Axe Santé des populations et pratiques optimales en santé, QC; †Département de médecine familiale et médecine d’urgence, Université Laval; and the ‡Centre d’Excellence du Vieillissement de Québec, CIUSSS de la Capitale Nationale.

**Correspondence to:** Marcel Émond, Unité de recherche en traumatologie - urgence - soins intensifs, CHU de Québec, Hôpital de l'Enfant-Jésus 1401, 18e rue, Québec (Québec) G1J 1Z4; Email: marcelemond1@me.com

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**Introduction**

Endotracheal intubation (ETI) is a technique frequently used in resuscitation room emergencies and that can be potentially life-saving for patients in critical situations.1-3 In fact, emergency physicians are routinely involved in the recognition of respiratory failure and subsequently initiating ETI.[4](#_ENREF_4)ETI is an important technique that is becoming more significant in influencing the prognosis of patients who are subject to it.5 However, it is reported that, when compared to methods of non-invasive ventilation, ETI is associated with more adverse events.6-8 These side effects may be minor or major in nature, ranging from dental trauma to hemodynamic alterations such as bradycardia, hypotension, or even cardiopulmonary arrest. Unfortunately, death can also occur.9,10 Post-intubation hypotension (PIH) is one of the known adverse effects reported in the literature.11

The recognized risk factors of PIH are sepsis, the presence of chronic obstructive pulmonary disease (COPD),11,12 systolic blood pressure (SBP) of less than 140 mmHg before intubation,11 advanced age, and hemodynamic instability pre-intubation. Other factors that can increase risk of hypotension include weight under 55 kg,11 ahigh shock index before intubation, and the presence of kidney disease or a diagnosis of acute respiratory failure.13 The pathophysiology of PIH remains hypothetical, but several mechanisms have been proposed. The hypotensive effect of certain induction agents, the low sympathetic tone in patients with sepsis exacerbated by the hemodynamic effect of intubation, and mechanical ventilation which decreases venous return to the right ventricle are various proposed mechanisms of PIH.14-17

It is well documented that hypotension in a seriously ill population increases mortality and morbidity.18-20 However, conflicting data exists regarding a potential association between PIH and increased mortality. So far, two studies have examined the possibility of such an association: Green et al. evaluated potential increases in mortality and in hospital stays in the emergency room among patients with PIH and found no significant association between these variables.12 An association was observed by Heffner et al. in the same year.13 The latter had a larger sample of 336 patients in the ED (Emergency Department), through which they were able to identify PIH as a significant predictor of in-hospital increased mortality. However, each of the two studies used different PIH definitions, which may account for these opposing results.

The incidence of PIH varies, depending on which author you read7,12,21-24: some suggest that this is a rare complication,25 while others report this side effect to be relatively common.7,23,26,27 Its incidence varies from 0% to 44% according to the available studies on the subject.7,21-24 Inconsistencies in PIH definitions affect not only the evaluation of the impact on mortality or the estimate of its incidence, they also impact on the heterogeneity of results and weaken potential clinical conclusions or applications. A measurement of SBP (systolic blood pressure) of ≤ 90 mmHg is commonly used to determine the presence of hypotension, but this definition is not unanimous.16,17,25,28-31 Some authors have instead proposed that a decrease of ≥ 20% in SBP compared to baseline SPB,12,30 the use of a vasopressor,12,30 or a mean blood pressure of ≤ 65 mmHg as alternative definitions. In addition, the period during which the SPB is measured after intubation is variable, ranging from 5 to 60 minutes.11-13,32 We speculate that the time parameter in the definitions has an influence on the incidence of PIH.

The primary objective of this study is to assess the impact that the choice of the PIH definition has on its incidence. A secondary objective is to describe the incidence of PIH by comparing hypotensive patients (SBP ≤ 90 mmHg) to patients considered normotensive (SBP> 90 mmHg) before intubation, according to six definitions. Another objective is to determine the incidence of PIH (definition SPB≤ 90 mmHg) depending on the time interval during which the first hypotension occurred.

**METHODS**

***Research Design and Population***

We conducted a consecutive prospective cohort study at the CHU de Québec – Université Laval (Hôpital de l’Enfant-Jésus), from June 2011 to July 2012. Patients in this study had to be 16 and over, and intubated in the emergency department due to a critical situation, without regard to the ETI method used (e.g. direct laryngoscopy, video-laryngoscopy, or other), by performing a rapid sequence intubation with the aid of a muscle relaxant.

Patients intubated before they arrived at the emergency, as in the case of a transfer between hospitals, were excluded. Note that the pre-hospital staff do not carry out ETI in Quebec. Other exclusion criteria were the need for surgical airway access, ETI failure, lack of use of muscle relaxants, and cardio-respiratory arrest before ETI. ETI was defined as passing an endotracheal tube through the glottis in a patient to keep the airway open. In our Center, intubation is done routinely by the certified emergency physician on site or by a resident under supervision by an emergency physician. Pre-oxygenation is used. The use of the laryngoscope or video-laryngoscope is left to the discretion of the emergency physician.

***Data Collection***

All patients were cared for using the *ReaScribe+* electronic clinical decision support (eCDS) from Logibec Inc., installed in each recovery room since June 2011, which gives a standardized and automated report on the vital signs of patients.

The information recorded by *ReaScribe+* served as an electronic medical record for episodes in the recovery room, as all the medical interventions were recorded by nurses via the touch screen interface. When a patient had more than one episode of intubation (e.g. during different visits to the emergency), only the first episode of intubation was considered. BP (blood pressure), measured with a cuff, was automatically recorded by the information system every two minutes to reliably and systematically determine the presence or absence of PIH. This data was exported directly to the real-time collection software. In addition, to validate the automatic measurements of the platform, the first BP measurement was taken manually by the nurse and also recorded manually using the platform touch screen interface. Other data collected via the platform was: demographics, the reason for consultation, and the medication used for the ETI.

***Different Definitions***

There is no standard definition for PIH. Following a review of the literature, an advisory committee (MCL, ME, NL) chose a value of PIH which has the advantage of being easily applicable and often used by clinicians in emergency situations, i.e. the presence of at least one SPB measurement of 90 mmHg or less.[11-13](#_ENREF_11), [16](#_ENREF_16), [17](#_ENREF_17), [25](#_ENREF_25), [28-33](#_ENREF_28) The detailed definitions forming the subgroups of our main objective were also preset (Table 1). The first definition tested reflected the SPB measurements up to 5 minutes post-ETI. The second definition tested reflected the SPB measurements up to 15 minutes. The third definition tested reflected the SPB measurements up to 30 minutes. The fourth and final definition tested took into account all the SPB measurements taken after intubation during the stay in the recovery room. Two other definitions of PIH, which did not take into account the moment of the BP measurement, were examined: an MBP (mean blood pressure) of ≤ 65 mmHg and the use of vasopressors. Similarly, pre-intubation hypotension was defined as the presence of at least one SPB measurement of 90 mmHg or less. Blood pressure measurements up to 15 minutes before intubation were considered for all patients. The time intervals of the second sub-objective were: 0-5 minutes, 6-15 minutes, 16-30 minutes, and 31 minutes and more.

**Table 1: Key Definitions**

|  |  |
| --- | --- |
| **Definition** | **Time of BP measurement post-intubation** |
| 1 | SBP ≤ 90 mm Hg  Up to 5 minutes |
| 2 | SBP ≤ 90 mm Hg  Up to 15 minutes |
| 3 | SBP ≤ 90 mm Hg  Up to 30 minutes |
| 4 | SBP ≤ 90 mm Hg  at all times |
| 5 | Use of vasopressors at any time |
| 6 | MAP ≤ 65 mmHg at all times |

The results are presented as proportions with confidence intervals set at 95%. A GEE model was used. The comparison of the incidence obtained was performed using a Wald chi-square test. A subsequent power calculation compared to our main objective was performed using a McNemar test (Appendix 1).

 All analyses were performed using the *SAS software 9.4*, Canada. The study was approved by the research ethics board of the CHU of Québec.

**RESULTS**

***Demographic Data***

During the study period, 2275 patients were evaluated in the resuscitation area. A total of 219 intubated patients were identified and, of these, 155 patients were intubated in the ED. Of these 155 patients, 81 patients met inclusion criteria while 74 patients were excluded, mostly for technical reasons related to the staff's varying degrees of comfort in the use of the platform during the implementation period and the absence of muscle relaxants (Appendix 2: n = 5, since <16 years, n = 30 for missing SBP or only values of SPB before or after intubation, n = 5 recording error, n = 34 for absence of neuromuscular blocking agent). Demographic and clinical characteristics of the patients included are reported in Table 2. The average age was 54 years (s.d.: +/- 19) and 64% were men. The most frequent presentations were altered state of consciousness (53.1%), followed by trauma (29.6%). The most frequently used induction agent was etomidate (58.0%), followed by propofol (33.3%). A level 1 triage rating (P1 - immediate), according to the Canadian Triage and Acuity Scale (CTAS),34 was allocated to 58 of the 81 patients, while 17 patients received a level 2 priority (P2 - very urgent), and a small proportion of patients received a P3 priority level (urgent) and P4 priority level (less urgent) (n=1 and n=2 respectively). No patient received a P5 priority level (non-urgent). The median number of BP collected per patient was 14 (IQR (interquartile range: 9-19). Intubation due to trauma or an altered state of consciousness was more common in hemodynamically stable patients than in patients with PIH. PIH patients received more fentanyl and midazolam during rapid sequence intubation compared to patients showing no PIH; the latter group received propofol and etomidate more frequently.

**Table 2**. Clinical and demographic characteristics of patients

|  |  |  |  |
| --- | --- | --- | --- |
| **Cohorte**  | **All, n=81** | **PIH +, n=23** | **PIH -, n=58** |
| **Characteristics** |
| Age (years), mean **±** s.d.\* | 54±19 | 59±18 | 52±19 |
| Age (years), median (Q1-Q3) | 56 (39-69) | 63 (49-74) | 53 (36-64) |
| Sex (male), n (%) | 51 (63.8) | 14 (60.9) | 37 (64.9) |
| Time spent in resuscitation room (min) median (Q1-Q3)) † | 51 (40-70) | 61 (45-103) | 49 (39-64) |
| Available SBP measurements (median (Q1-Q3)) | 14 (9-19) | 18 (15-24) | 13 (8-18) |
| TAS measurement available post-EIT (median (Q1-Q3)) ‡ | 10 (7-15) | 14 (10-22) | 8 (6-13) |
| **Reason for consultation, n (%)** |
| Trauma | 24 (29.6) | 5 (21.7) | 19 (32.8) |
| Retrosternal pain | 2 (2.5) | 4 (4.4) | 1 (1.7) |
| Dyspnea | 7 (8.6) | 5 (21.7) | 2 (3.5) |
| Altered state of consciousness | 43 (53.1) | 10 (43.5) | 33 (56.9) |
| Other | 5 (6.2) | 2 (8.7) | 3 (5.2) |
| **Medication used for intubation, n (%)**§ |
| Fentanyl induction | 27 (33.3) | 10 (43.5) | 17 (29.3) |
| Fentanyl perfusion | 3 (3.7) | 1 (4.3) | 2 (3.4) |
| Etomidate induction | 47 (58.0) | 11 (47.8) | 36 (62.1) |
| Etomidate perfusion | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Ketamine | 3 (3.7) | 3 (13.0) | 0 (0.0) |
| Propofol induction | 4 (4.9) | 1 (4.3) | 3 (5.2) |
| Propofol perfusion | 39 (48.2) | 7 (30.4) | 32 (55.2) |
| Midazolam induction | 14 (17.3) | 6 (26.1) | 8 (13.8) |
| Midazolam perfusion | 6 (7.41) | 2 (8.7) | 4 (8.7) |
| Vasopressor | 4 (4.9) | 4 (17.4) | 0 (0.0) |

\* s.d.: standard deviation

† Q1 is the 25th percentile; Q3 is the 75th percentile

‡EIT = endotracheal intubation

§The categories are not mutually exclusive; more medication has occasionally been administered to the same patient.

***Hemodynamic Parameters***

 Hemodynamic parameters of the patients, such as the mean average of SBP and DBP (diastolic blood pressure), the average saturation, and the average heart rate are presented according to the time elapsed since intubation (Figure 1). The period of 15 minutes before intubation was included. A decrease was observed in mean SBP and mean DBP during the post-intubation period, while the other parameters were stable.

**Figure 1: Distribution of the hemodynamic parameters**

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In addition, the same parameters are shown, firstly, in PIH patients and, secondly, in hemodynamically stable patients (Figure 2). Mean SBP, mean DBP, and average saturation is lower in PIH patients, regardless of the time elapsed since intubation. Moreover, mean SBP and DBP for the PIH group tend to decrease over time. This decrease begins from the pre-intubation period. Among non PIH patients, a downward trend was also noted, but only in the post-intubation period. In fact, a slight increase in blood pressure was observed during pre-intubation in this non PIH group.

**Figure 2: Distribution of the hemodynamic parameters: based on the presence of PIH**

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***Incidence of Post-Intubation Hypotension***

PIH was observed in 23 (28.4%; 95% CI 20.1-40.1) of the 81 patients at all times following the intubation (Table 3) (definition 4). The incidence of PIH increases gradually along with increases in the BP measurement time: the incidence of PIH was 9.9%, 18.5%, and 24.7%, respectively, for definitions 1, 2, and 3. In a comparison between the observed incidence proportions (definition 1 to 4), statistically significant differences were observed between the definitions *(p* <0.05) for each comparison (Table 4), with the exception of the comparison between definitions 3 and 4. The incidence of PIH determined by the presence of vasopressors (definition 5) and a lowered MBP (definition 6) is 4.9% and 28.4%, respectively. The median time in the occurrence of the first PIH was 13 minutes (IQR 2.5-18.0).

**Table 3**. Main objective: Cumulative incidence of post-intubation hypotension (PIH)

|  |  |  |
| --- | --- | --- |
| **Definition** | **Intervals of post-intubation SBP measurements** | **Cumulative incidence of PIH (%; CI 95%)** |
| 1 | SBP ≤ 90 mm Hg : 0-5 minutes | 8/81 (9.9; 5.1-19.1) |
| 2 | SBP ≤ 90 mm Hg : 0-15 minutes | 15/81 (18.5; 11.7-29.2) |
| 3 | SBP ≤ 90 mm Hg : 0-30 minutes | 20/81 (24.7; 16.9-36.1) |
| 4 | SBP ≤ 90 mm Hg : At any time following intubation (≥0 minutes) | 23/81 (28.4; 20.1-40.1) |
| 5 | Need for vasopressors | 4/81 (4.9; 1.9-12.0) |
| 6 | MAP ≤ 65 mmHg | 23/81 (28.4; 19.7-39.0) |

**Table 4**. Statistical comparison of the incidence of PIH based on different definitions.

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| --- | --- | --- | --- |
| **Definitions** | **Comparison** | ***Z-Value*** | ***p Value*** |
| 1 vs 2 | 0-5 min vs 0-15 min | 2.60 | 0.0092 |
| 1 vs 3 | 0-5 min vs 0-30 min | 3.35 | 0.0008 |
| 2 vs 3 | 0-15 min vs 0-30 min | 2.23 | 0.0259 |
| 1 vs 4 | 0-5 min vs at any time | 3.70 | 0.0002 |
| 2 vs 4 | 0-15 min vs at any time | 2.81 | 0.0050 |
| 3 vs 4 | 0-30 min vs at any time | 1.73 | 0.0835 |

In total, the cumulative incidence of PIH at any time following the intubation in patients with pre-intubation hypotension was 62.5% (95% CI 28.5-87.5) (Table 5). Adversely, the cumulative incidence of PIH at any time following the intubation in patients with no pre-intubation hypotension was 24.7% (95% CI 16.1-35.8). Regardless of the definition used, the incidence of PIH is always significantly higher in the presence of pre-intubation hypotension (Table 5).

**Table 5**. Sub-objective: Cumulative effect of PIH (post-intubation hypotension) in the presence of pre-intubation hypotension

|  |  |  |
| --- | --- | --- |
| **Definition** | **Intervals of post-intubation SBP measurements** | **Cumulative incidence of PIH N (%; CI 95%)** |
| *Presence of hypotension prior to intubation N=8\** | *No hypotension prior to intubation N=73* | *p-value* |
| 1 | 0-5 min | 4 (50.0; 20.0-80.0) | 4 (5.5; 2.1-13.7) | 0.0011 |
| 2 | 0-15 min | 5 (62.5; 28.5-87.5) | 10 (13.7; 7.5-23.6) | 0.0035 |
| 3 | 0-30 min | 5 (62.5; 28.5-87.5) | 15 (20.6; 12.8-31.3) | 0.0177 |
| 4 | At any time following intubation (≥0 min) | 5 (62.5; 28.5-87.5) | 18 (24.7; 16.1-35.8) | 0.0367 |
| 5 | Need for vasopressors | 2 (25.0; 6.3-62.3) | 2 (2.7; 0.7-10.3) | 0.0467\*\* |
| 6 | MAP ≤ 65 mmHg (≥0 min) | 5 (62.5; 28.5-87.5) | 18 (24.7; 16.1-35.8) | 0.0334 |

\* The set of pre- intubation hypotension occurs within the first 15 minutes

The incidence of PIH (SPB ≤ 90 mm Hg) when hypotension first occurs, based on 0 to 5-minute, 6 to 15-minute, and 16 to 30-minute time intervals, is 9.9%, 8.6%, and 6.2%, respectively. The incidence of PIH for the 31-minute and more time interval is 3.7% (Table 6). Pre-intubation hypotension is present only in patients whose first PIH (SPB ≤ 90 mm Hg) was observed in the 0 to 5-minute and 6 to 15-minute intervals (Table 7). The incidence of PIH in the 0 to 5-minute range was significantly higher in patients with pre-intubation hypotension compared to hemodynamically stable patients during the pre-intubation period.

**Table 6**. Effect of PIH (post-intubation hypotension) according to time of occurrence of the first PIH

|  |  |  |
| --- | --- | --- |
| **Definition** | **Intervals of post-intubation SBP measurements** | **Incidence of PIH (%; IC1 95%)\*** |
| 1 | SBP ≤ 90 mm Hg : 0-5 min | 8/81 (9.9; 5.1-19.1) |
| 2 | SBP ≤ 90 mm Hg : 6-15 min | 7/81 (8.6; 4.3-17.5) |
| 3 | SBP ≤ 90 mm Hg : 16-30 min | 5/81 (6.2; 2.6-14.4) |
| 4 | SBP ≤ 90 mm Hg : (≥31 min) | 3/81 (3.7; 1.2-11.2) |

**Table 7**. Incidence of PIH (post-intubation hypotension) according to time of occurrence of the first PIH and the presence of pre-intubation hypotension

|  |  |  |
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| **Definition** | **Intervals of post-intubation SBP measurements** | **Incidence of PIH 1 N (%; IC2 95%)** |
| *Presence of hypotension prior to intubation N=8\** | *No hypotension prior to intubation N=73* | *p Value* |
| 1 | 0-5 minutes | 4 (50.0; 25.0-100.0) | 4 (5.5; 2.1-14.2) | 0.0002 |
| 2 | 6-15 minutes | 1 (12.5; 2.0-78.2) | 6 (8.2; 3.8-17.7) | n.s† |
| 3 | 16-30 minutes | 0 | 5 (6.9; 3.0-15.1)\*\* | n.a‡ |
| 4 | ≥ 31 minutes | 0 | 3 (4.1; 1.4-10.4)\*\* | n.a |

†n.s. (not significant)

‡n.a (not applicable)

**DISCUSSION**

The main purpose of this study was to evaluate the impact that the choice of the definition had on the incidence of PIH. To our knowledge, there is no specific data on this in the current literature. Our results demonstrate the incidence of PIH varies significantly depending on the definition used. It seems that the cumulative incidence increases with the time of BP measurements after an ETI. This new evidence is important in order to compare studies and also establish a working definition for clinical intervention and research. This length of time included in the post-intubation period has not been standardized in previous studies on the subject.

Hemodynamic data of our patient cohort shows that patients suffering from PIH have lower blood pressures during the pre-intubation period compared to non PIH patients. This may reveal a vulnerability that affects a certain population of patients which predisposes them to PIH.

One of our secondary outcomes was to describe the incidence of PIH, according to the six definitions, by comparing two groups of patients: in patients with pre-intubation hypotension and in patients hemodynamically stable before intubation. Our study demonstrated that the presence of hypotension before performing ETI increased nearly three-fold the risk of developing PIH. It has been described that pre-intubation hypotension is a predictor of PIH.11,12 The authors measured blood pressure up to 5 minutes and up to 30 minutes respectively after intubation. Our results suggest a similar outcome.

The incidence of PIH was also calculated according to the time of occurrence of the first hypotension. The first five minutes following intubation seems to correspond to the period during which patients are most at risk of presenting PIH for the first time. This result is in agreement with the proposed pathophysiology since the effect of induction drugs and the introduction of positive airway pressure occur in this interval.

As mentioned by Heffner et al., recent findings on PIH show that the next step would ideally be to develop a pre-ETI tool.35 Its purpose would be to properly identify patients at risk and apply hemodynamic optimization or vasopressor support during ETI to forestall hypotension and determine its effect on mortality. Another possibility for advancement in the field of PIH is to conduct a clinical trial using a vasopressor support to prevent PIH and determine the effect of this intervention on mortality.13 However, to this day, it is not clear that PIH in the emergency is a predictor of in-hospital mortality. If this association between PIH and mortality exists, it could be more or less important depending on the time of occurrence of hypotension after intubation.

This study is the first step in our project to establish a single definition for PIH. The next step will be to explore the consequences of PIH at different times after intubation. We plan to question more precisely the nature of PIH parameters that lead to an impact on in-hospital mortality. In our view, it is important to first achieve a consensus in the definition of PIH, and a better understanding of its consequences, in order to provide a preventative clinical tool. We believe that the definition to be used is connected to increased mortality and that a larger sample is needed in order to reach such a conclusion.

One strength of our study was the standardized and automated collection of patient data using an electronic clinical decision support (eCDS). An impressive superiority in capturing data via the *ReaScribe+* platform has previously been shown by a study funded by the FRQ-S. Indeed, the comparison between the hard copy records and the *ReaScribe+* electronic file showed that the eCDS contributed in reducing time spent in completing a report by 15 to 25% and in increasing time for bedside care. In addition, l00% of the data was available via the eCDS, while only 80% of data was available via the nurses' hard copy records. Vital signs were collected automatically by the informational system at a frequency of every 2 minutes, which is beneficial for detection of PIH and time of occurrence.

**LIMITATIONS**

We are aware that our study has certain limitations, such as the inclusion of only one academic tertiary trauma center. Indeed, the population under study is not necessarily representative of the customers in most emergency departments, due to the presence of a trauma centre at Hôpital de l’Enfant-Jésus. In our study, 29.6% of patients were intubated in the context of trauma.

Nearly a quarter of patients, for whom the code “intubation” was recorded on our platform, were excluded for technical and computing reasons, in the context of acquisition of automated data with a tool that was just being implemented. This element is probably the biggest limitation of our study because it is difficult to know if hypotension episodes were missed in these patients. However, SBP of less than 90 mmHg (pre- or post-intubation) was identified in only 4 of the 30 patients excluded (Appendix 2). This data led us to believe that such registration errors did not occur in these patients due to hemodynamic instability.

Note that etomidate was used in over half of the patients (58%), the most likely explanation being its alleged minimal effects on hemodynamics, unlike other inducing agents.

In addition, the large number of previously intubated patients being excluded from the study is explained by the high number of trauma patient transfers to our tertiary trauma center. Three patients were rated P3 or P4. This is explained by patients with less urgent initial conditions which experienced a deterioration requiring reassessment and, in their case, ETI.

Finally, the length of time spent resuscitating the patient was highly variable. Data up to 60 minutes was not available for all patients because of this variability. This technical limitation may have had a downward pull on our total PIH incidence and underestimated incidence deviations between the various definitions of PIH.

**CONCLUSION**

PIH is a frequent complication in the emergency department. Its incidence varies considerably from one study to another. Using varying definitions with one BP measurement time rather than another impacted the incidence of post-intubation hypotension considerably. It is possible that the differences in definition of the PIH partially explain the observed variation in incidence in the literature. In our opinion, it is necessary to reach a consensus on the definition of PIH in order to be able to explore its potential impacts and possibly create clinical tools to better predict its occurrence.

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