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The Potential Factors and the Outcomes of Hypotensive Patients after Emergent Endotracheal Intubation

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Purpose: Hypotension after emergency endotracheal intubation (ETI) is one of the major complications from emergency airway management. The aim of this study was to determine the possible risk factors that may predict postintubation hypotension (PIH) and its impact on in-hospital mortality.

Methods: We conducted a retrospective, standardized chart review of consecutive emergency department patients that required intubation between January 2011 and December 2014. Patients were divided into 2 groups according to the presence or absence of PIH. PIH was defined as any recorded systolic blood pressure with less than 90 mmHg or mean arterial pressure with less than 65 mmHg within the 60-minute period after intubation. The outcome measures were in-hospital mortality, as well as intensive care unit and hospital length of stay.

Results: The incidence of PIH was 23% (80 of 352 patients). Patients in the PIH group were slightly older and had more comorbid diseases than those in the non-PIH group. PIH patients had a significantly higher mortality rate (54% vs. 30%, p<0.01). PIH was a strong predictor for in-hospital mortality of intubated patients (hazard ratio, 2.3; 95% confidence interval, 1.3 to 3.4).

Conclusion: Older age, lack of skill, history of hypertension, low albumin and pH, and elevated were risk factors for the occurrence of hypotension after ETI. Patients with PIH show increased risk of in-hospital mortality.

Key Words: Emergency service, Hospital, Hypotension, Intubation, Mortality, Risk factors

Introduction

Hypotension after emergency endotracheal intubation (ETI) is one of major complications during emergency airway management. Comparing to elective intubations performed in the operating room, emergent ETI can be considered risky and challenging. Several studies focused on postintubation hypotension (PIH) have shown poor outcomes including mortality, length of stay, and other outcomes of patients with PIH[1-5].

In a systematic review of PIH associated with emergent intubation in emergency department (ED) and intensive care unit (ICU) patients, the incidence of PIH ranged from 0.5% to 44% with a pooled estimate of 11%[6]. Despite of considering the study design and inhospital location, PIH is a common event after ETI. Variable factors such as positive pressure ventilation, anesthetic agents, and preexisting comorbidities may contribute to hemodynamic alterations after ETI[7]. Based on literatures, there were few studies describing of PIH as their primary objective with focusing prediction as well as its outcomes in the ED settings[8,9]. For emergency medicine practitioners, predicting and evaluating outcomes of the hemodynamic complication after rapid sequence intubation (RSI) can be helpful for safe performance.

The aim of this study was to determine the risk factors predicting of PIH and the impact of PIH on in-hospital mortality.

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Article Summary

What is already known in the previous study

Hypotension after emergency endotracheal intubation (ETI) is one of major complications during emergency airway management. Several studies focused on postintubation hypotension (PIH) have shown poor outcomes including mortality, length of stay, and other outcomes of patients with PIH.

What is new in the current study

Variable factors such as positive pressure ventilation, anesthetic agents, and preexisting comorbidities may contribute to hemodynamic alterations after ETI.

Materials and Methods

1. Study setting and population

We conducted a retrospective, standardized chart review of consecutive ED patients requiring intubation at an urban, tertiary-care teaching hospital, from January 2011 to December 2014. We included all adult patients (≥18 years) who required ETI. ETI was defined as the passage of an endotracheal tube through a patient's glottis in any patient intubated in the ED. Training in emergency airway management is done in the emergency airway course by the emergency airway committee as core curriculum.

Patients with the following conditions were excluded from the study: 1) systolic blood pressure (SBP) measurements less than 90 mmHg or mean arterial pressure (MAP) less than 65 mmHg before intubation; 2) received inotropic agents; 3) had cardiac arrest (Fig. 1).

2. Study protocol and data collection

This study was approved by the institutional review board before implementation. For analyzing risk factors of hemodynamic instability, patients were divided into 2 groups according to the presence or absence of PIH. PIH was defined as any recorded SBP less than 90 mmHg or MAP less than 65 mmHg within the 60-minute period after intubation. The outcome measures were in-hospital mortality as well as ICU and hospital length of stay. A structural telephone follow-up was performed for patients who were transferred to other hospital before completion of management.

Patients were identified through an electronic chart review after sorting all potential subjects with our proce-

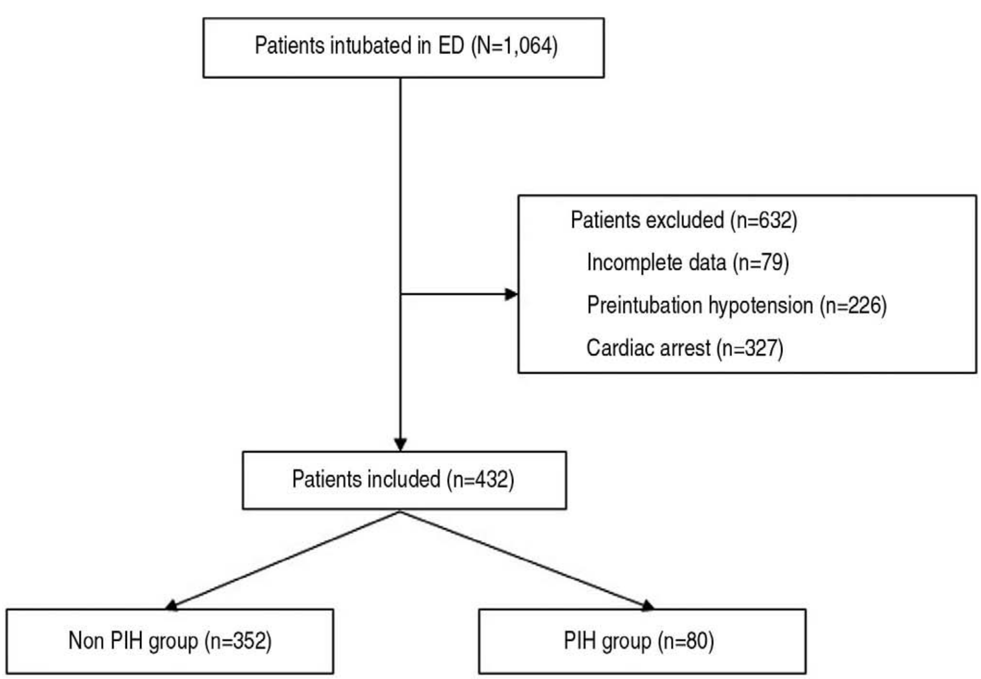

Fig. 1. Algorithm of the selection of patients.
ED: emergency department, PIH: postintubation hypotension

dure code of endotracheal tube. Record review and data collection were performed by two independent researchers. The data were collected as follows: demographic data, patient comorbidities, ED clinical variables, biochemistry tests of blood, and medications prescribed upon intubation.

3. Statistical analyses

Continuous variables were expressed as mean±standard deviation or median and interquartile ranges (IQR) and, when appropriate, were compared for statistical differences using independent t tests or Mann-Whitney U-tests. Categorical variables are reported as numbers and percentages using chi-square test or Fisher exact test. For all statistical tests, $p<0.05$ was considered significant.

Variables found to be statistically significant in the univariate analysis were selected as candidates for the subsequent multivariate analysis using PIH as the dependent variable. This model was refined using forward stepwise elimination with Hosmer-Lemeshow goodness-of-fit test.

Table 1. Characteristics of the patients

Variables	Total Group (N=432)	Non PIH Group (N=352)	PIH Group (N=80)	*p*-value
Male sex	266 (62)	216 (61)	50 (63)	0.85
Age (yr)	64±17	63±18	71±14	<0.01
Body weight (kg)	61±13	61±13	60±11	0.64
Comorbidities				
Hypertension	210 (49)	156 (44)	54 (68)	<0.01
Heart failure	34 (8)	21 (6)	13 (16)	<0.01
COPD	23 (5)	15 (4)	8 (10)	0.04
Liver disease	15 (4)	11 (3)	4 (5)	0.49
Diabetes mellitus	109 (25)	91 (26)	18 (23)	0.53
End stage renal disease	24 (6)	15 (4)	9 (11)	0.01
Case (non-trauma)	300 (69)	242 (69)	58 (73)	0.51
GCS before intubation	9.4±4.3	9.4±4.3	9.6±4.7	0.81
Vital status, before intubation				
SBP (mmHg)	160±42	162±41	149±45	0.01
DBP (mmHg)	88±22	89±22	84±24	0.03
Heart rate (rate/min)	104±29	103±29	108±31	0.18
Shock index*	0.70±27	0.68±0.25	0.79±0.33	<0.01
Laboratory value before RSI				
WBC ($\times 10^3$ cells/μL)	13.4±6.0	13.4±6.0	13.4±6.2	0.97
Hemoglobin (g/dl)	12.8±2.6	12.9±2.6	12.6±2.5	0.40
Platelet ($\times 10^3$ cells/μL)	241±92	240±90	246±101	0.65
Total bilirubin (mg/dL)	0.8±1.4	0.9±1.5	0.8±0.6	0.63
Albumin (g/dL)	3.9±0.7	4.0±0.6	3.6±0.9	<0.01
Blood urea nitrogen (mg/dL)	22.0±19.5	20.1±16.0	27.0±30.1	0.08
Creatinine (mg/dL)	1.6±1.8	1.6±1.9	1.7±1.5	0.67
Sodium (mmol/L)	139±6.4	139±5.9	137±8.0	0.03
Potassium (mmol/L)	4.3±6.6	4.3±7.3	4.1±0.9	0.77
pH	7.3±0.1	7.3±0.1	7.3±0.2	<0.01
PCO_2 (mmHg)	42±17	41±16	47±21	0.03
PaO_2 (mmHg)	110±95	116±101	84±55	<0.01
O_2 saturation (%)	88±17	89±16	83±21	0.02
Bicarbonate (mmol/L)	21±6	21±5	21±7	0.86

Values are presented as mean±standard deviation or number (%).
PIH: postintubation hypotension, COPD: chronic obstructive lung disease, GCS: Glasgow Coma Scale, SBP: systolic blood pressure, DBP: diastolic blood pressure, RSI: rapid sequence intubation, WBC: white blood cell
* Shock index: heart rate/systolic blood pressure.

The cumulative survival rates between groups were assessed using Kaplan-Meier survival curves and the log-rank test. To determine the independent factors of inhospital mortality, we performed univariate Cox proportional hazards analysis and variables with $p<0.1$ were entered in multivariate full model. The results are expressed as hazard ratio and 95% confidence interval (CI). All analyses were performed using SPSS ver. 15.0 (SPSS Inc., Chicago, IL, USA) and Microsoft Excel (Microsoft Corp., Redmond, WA, USA).

Results

A total of 432 patients were enrolled to the study. The mean age of patients was 64±17 years, and 62% of them was male. The median time to intubation after RSI was 2 minutes (IQR, 1 to 3 minutes). Of 80 patients with PIH, 64 patients (80%) received intravenous fluids and inotropics for hemodynamic support. Sixteen 0f 80 patients (20%) received intravenous fluids only. There were 2 patients (3%) with PIH who were still in shock state regardless of the aggressive management before admission to the ICU. Baseline demographics and clinical characteristics of the study subjects are outlined in Table 1. Table 2 documents medications prior to ETI and ventilator parameters in the ED. The incidence of PIH was 18%. The median time to hypotension after ETI was 25 minutes (IQR, 12 to 48 minutes). Of 432 patients, 388 (90%) patients received etomidate for sedation. Neuromuscular blocking agents were used for 88% of patients for ETI. There were no significant differences of the use of the medications and ventilator parameters between the groups (Table 2).

Table 2. RSI medications and ventilator parameters

Variables	Total Group (N=432)	Non PIH Group (N=352)	PIH Group (N=80)	*p*-value
More than 2 consecutive attempts for intubation	19 (4)	11 (3)	8 (10)	<0.01
Sedatives	399 (92)	327 (93)	72 (90)	0.63
Etomidate	388 (90)	318 (90)	70 (88)	
Midazolam	8 (2)	6 (2)	2 (3)	
Ketamine	3 (1)	3 (1)	0 (0)	
Etomidate dose/kg (mg/kg)	0.29±0.09	0.29±0.09	0.27±0.10	0.12
Neuromuscular blocking agents	382 (88)	313 (89)	69 (86)	0.03
Rocuronium	335 (78)	269 (76)	66 (83)	
Vecuronium	47 (11)	44 (13)	3 (4)	
Dose of rocuronium (mg/kg)	0.71±0.22	0.72±0.22	0.69±0.24	0.38
Dose of vecuronium (mg/kg)	0.11±0.17	0.10±0.17	0.17±0.22	0.51
Ventilator parameters				
PEEP (cmH_2O)	5.7±2.2	5.6±2.3	6.0±2.0	0.17
Tidal volume (ml/kg)	7.3±1.6	7.3±1.7	7.3±1.2	0.95

Values are presented as mean±standard deviation or number (%).
RSI: rapid sequence intubation, PIH: postintubation hypotension, PEEP: positive end expiratory pressure

Table 3. Logistic regression analysis for predicting postintubation hypotension

Variables	OR	95% CI	*p*-value
Age (yr)	1.02	1.00-1.04	0.034
No. of intubation attempts	3.15	1.11-8.92	0.031
Hypertension	2.59	1.44-4.68	0.002
Albumin (g/dL)	0.64	0.43-0.96	0.030
pH	0.15	0.03-0.78	0.025
Shock index	3.24	1.24-8.46	0.016

OR: odds ratio, CI: confidence interval, Hosmer-lemeshow test χ^2, p=0.16.
* Number of intubation attempts: ≥2 consecutive attempts of intubation.

Patients of the PIH group were slightly older, had more comorbid disease than the no PIH group. Comparing the vital signs before ETI, blood pressure (BP) of the hypotensive patients tend to be lower along with higher in shock index (the quotient of heart rate divided by SBP) than the patients having normal BP after ETI. Meanwhile, there were no differences found in laboratory variables except the value of albumin and sodium. On arterial blood analysis, the hypotensive patients were found to have hypercabia (47±21 vs. 41±

Table 4. Hospital mortality and intensive care unit and hospital length of stay

Variables	Non PIH Group (N=352)	PIH Group (N=80)	*p*-value
Hospital mortality	105 (30)	43 (54)	<0.01
Hospital stay (day)	29.3±35.5	25.6±34.6	0.41
ICU stay (day)	15.3±16.8	15.8±19.2	0.80

Values are presented as mean±standard deviation or number (%).
ICU: intensive care unit, PIH: postintubation hypotension

Table 5. Cox proportional hazard for inhospital mortality regression analysis

Variables	Hazard ratio	95% CI	*p*-value
PIH	2.32	1.31-3.35	<0.001
Age (yr)	1.02	1.01-1.04	<0.001
Glasgow coma scale	0.92	0.88-0.95	<0.001
pCO_2 (mmHg)	0.98	0.97-0.99	<0.001

CI: confidence interval, PIH: postintubation hypotension

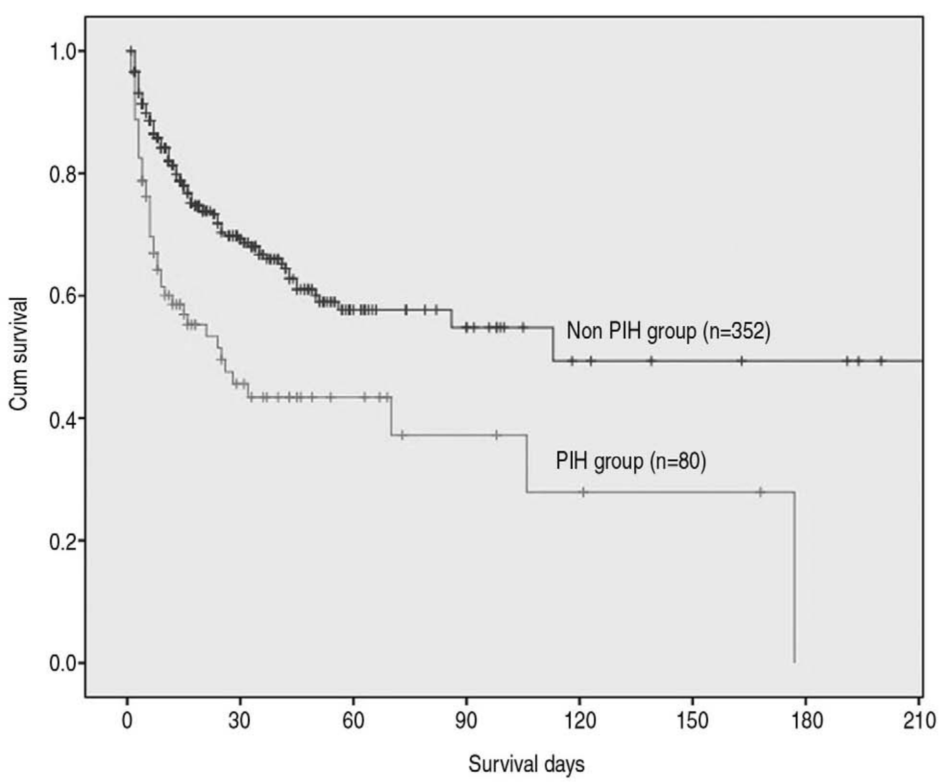

Fig. 2. Kaplan Meier analysis.
PIH: postintubation hypotension

16, p=0.03) and hypoxemia (84±55 vs. 116±101, p<0.01) (Table 1).

The logistic regression model to the end point of PIH has demonstrated that shock index, age, multiple attempts of intubation, and the medical history of hypertension were significant prognostic factors for hypotension after ETI. Whereas ongoing DM, relatively normal albumin, and pH were less likely factors associated with the occurrence of hypotension after ETI (Table 3).

Of the 432 patients, 148 died in the hospital for an overall mortality rate of 34%. The PIH patients had significantly higher mortality rate (54% vs. 30%, p<0.01) than the non PIH group. However, there were no statistical differences in hospital and ICU stay between the groups (Table 4). Among the independent variables in cox-proportional hazard analysis for inhospital mortality, PIH was the strong predictor for inhospital mortality of intubated patients (hazard ratio, 2.3; 95% CI, 1.3 to 3.4) (Table 5). In Kaplan Meier survival curves, the mean survival time of the PIH patients was significantly shorter than the counterpart (101±11 vs. 145±5, Log-rank test p=0.000) (Fig. 2).

Discussion

In this study, we observed an occurrence of 18% of PIH within one hour after emergent tracheal intubation in hemodynamically stable patients before intubation in the ED. Increasing age, multiple attempts of intubation, hypertension, and high shock index (SI) were independently associated with the development of PIH. When controlling other factors, PIH was the strong predictor of inhospital mortality. Prediction of potential factors for developing postintubation hypotension and evaluation of its impact on mortality could be helpful for emergency physician to guide the emergent tracheal intubation in the ED.

ETI can be cardinal lifesaving procedure in critically ill patients[10,11]. Patients who need this procedure may result in suboptimal condition[11]. Complications related to ETI include both mechanical adverse events (dental trauma, malpositions) and broader life-threatening events (hypotension, dysrhythmia, and hypotension)[1-7,9,12-15]. Despite the fact that hypotension after ETI is a common complication in the ED, there are little information about predicting the associating factors and its significance.

PIH may be based on multiple factors, including comorbidities and hemodynamic alterations[7]. Besides, PIH may be related to other factors such as skills of physicians, medications to facilitate ETI, baseline conditions of patients in the ED[6,14]. Our study showed that, multiple attempts of intubation was significantly correlated with the development of PIH. If a difficult intubation is anticipated, more experienced physician should be allocated for the task, and alternative airway techniques and accessory device should be considered[16]. Etomidate is considered as a safe and effective agent for use in a range of patients undergoing rapid sequence intubation in the ED[17,18]. We also found no clear association with the use of etomidate as an induction agent and the development of hypotension after ETI. The use of neuromuscular blockers have protective effect for the development of PIH in studies based on ED settings[8,9]. However, we did not find any statistically significant difference with the use of these agents.

Although heart rate did not show the difference between the groups, SI before ETI was independently associated with PIH in this study. Similarities were observed in other study that SI was confirmed for a predictor of PIH in the ED and ICU[8,19]. Elevated SI was a useful marker to evaluate acute critical illness in the ED where patients had apparently stable vital signs at triage[20]. Heffner et al[8] evaluated predictors of the complication of PIH during emergency airway management in 300 patients in the ED, and they concluded that the elevated SI was a strong predictor of systolic hypotension after ETI. A similar association between preintubation SI and postintubation systolic hypotension was found in the study of ICU patients[19]. We also found that elevated SI significantly predicts the development of PIH. In patents who are in high-risk, hemodynamic support, such as empiric volume loading, blood transfusion, and peri-RSI catecholamine support is necessary. The RSI medication of these patients should be selected according to clinical condition using hemodynamically stable agents and its dose[8].

PIH is one of an adverse events that may occur during ETI, however, few studies described the impact of the event on patient mortality[2,5,9]. Despite of confounding results about the association between the PIH and hospital mortality, emergency physicians cannot oversight the development of PIH in terms of its impact on patient morbidity and mortality[2,9]. We did observe increased inhospital mortality associated with PIH and may insist of its importance to outcome in intubated patients. The results of this study can be the foundation of further investigation into an area of safe lifesaving ETI. Emergency physicians should consider therapeutic options to reduce PIH and its adverse outcomes.

There are several limitations to this study. First, there are potential biases because of a retrospective analysis. Second, our chart review was done at a single center, as so a multi-center cohort study should be followed to address PIH. Third, we only used noninvasive blood pressure measurements, therefore, discrete hemodynamic changes may have undetected.

Conclusion

This study suggested that variable factors induce postintubation hypotension. Older age, lack of skill, history of hypertension, low albumin and pH, and elevated SI were risk factors for occurrence of hypotension after ETI. Apparently, patients with PIH show increased risk of inhospital mortality. Further studies are needed to investigate therapeutic strategies to reduce PIH in high risk populations.

REFERENCES

1. Franklin C, Samuel J, Hu TC. Life-threatening hypotension associated with emergency intubation and the initiation of mechanical ventilation. Am J Emerg Med. 1994;12:425-8.
2. Heffner AC, Swords D, Kline JA, Jones AE. The frequency and significance of postintubation hypotension during emergency airway management. J Crit Care. 2012;27:417.e9-13.
3. Kim WY, Kwak MK, Ko BS, Yoon JC, Sohn CH, Lim KS, et al. Factors associated with the occurrence of cardiac arrest after emergency tracheal intubation in the emergency department. PLoS One. 2014;9:e112779.
4. Perbet S, De Jong A, Delmas J, Futier E, Pereira B, Jaber S, et al. Incidence of and risk factors for severe cardiovascular collapse after endotracheal intubation in the ICU: a multicenter observational study. Crit Care. 2015;19:257.
5. Green RS, Turgeon AF, McIntyre LA, Fox-Robichaud AE, Fergusson DA, Doucette S, et al. Postintubation hypotension in intensive care unit patients: A multicenter cohort study. J Crit Care. 2015;30:1055-60.
6. Green R, Hutton B, Lorette J, Bleskie D, McIntyre L, Fergusson D. Incidence of postintubation hemodynamic instability associated with emergent intubations performed outside the operating room: a systematic review. CJEM. 2014;16:69-79.
7. Mort TC. Complications of emergency tracheal intubation: hemodynamic alterations. part I. J Intensive Care Med. 2007;22:157-65.
8. Heffner AC, Swords DS, Nussbaum ML, Kline JA, Jones AE. Predictors of the complication of postintubation hypotension during emergency airway management. J Crit Care. 2012;27:587-93.
9. Green RS, Edwards J, Sabri E, Fergusson D. Evaluation of the incidence, risk factors, and impact on patient outcomes of postintubation hemodynamic instability. CJEM. 2012;14:74-82.
10. Dorges V. Airway management in emergency situations. Best Pract Res Clin Anaesthesiol. 2005;19:699-715.
11. Shuster M, Lim SH, Deakin CD, Kleinman ME, Koster RW, Morrison LJ, et al. Part 7: CPR techniques and devices: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation. 2010;122 (16 Suppl 2):S338-44.
12. Hagberg C, Georgi R, Krier C. Complications of managing the airway. Best Pract Res Clin Anaesthesiol. 2005;19:641-59.
13. Jaber S, Amraoui J, Lefrant JY, Arich C, Cohendy R, Landreau L, et al. Clinical practice and risk factors for immediate complications of endotracheal intubation in the intensive care unit: a prospective, multiple-center study. Crit Care Med. 2006;34:2355-61.
14. Lin CC, Chen KF, Shih CP, Seak CJ, Hsu KH. The prognostic factors of hypotension after rapid sequence intubation. Am J Emerg Med. 2008;26:845-51.
15. Mort TC. Complications of emergency tracheal intubation: immediate airway-related consequences: part II. J Intensive Care Med. 2007;22:208-15.
16. Lundstrøm LH, Møller AM, Rosenstock C, Astrup G, Gätke MR, Wetterslev J, et al. Avoidance of neuromuscular blocking agents may increase the risk of difficult tracheal intubation: a cohort study of 103,812 consecutive adult patients recorded in the Danish Anaesthesia Database. Br J Anaesth. 2009;103:283-90.
17. Smith DC, Bergen JM, Smithline H, Kirschner R. A trial of etomidate for rapid sequence intubation in the emergency department. J Emerg Med. 2000;18:13-6.
18. Zed PJ1, Abu-Laban RB, Harrison DW. Intubating condi-

tions and hemodynamic effects of etomidate for rapid sequence intubation in the emergency department: an observational cohort study. Acad Emerg Med. 2006;13: 378-83.
19. Trivedi S, Demirci O, Arteaga G, Kashyap R, Smischney NJ. Evaluation of preintubation shock index and modified shock index as predictors of postintubation hypotension and other short-term outcomes. J Crit Care. 2015;30: 861.e1-7.
20. Rady MY, Smithline HA, Blake H, Nowak R, Rivers E. A comparison of the shock index and conventional vital signs to identify acute, critical illness in the emergency department. Ann Emerg Med. 1994;24:685-90.