Incidence of and Risk Factors for Acute Respiratory Distress Syndrome in Patients Admitted to Surgical Intensive Care Units: The Multicenter Thai University-Based Surgical Intensive Care Unit (THAI-SICU) Study

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Objective: The incidence and outcomes of acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) are unclear. We evaluated the cumulative incidence of, risk factors for, and outcomes of ALI/ARDS in surgical ICUs (SICUs). **Material and Method:** The multicenter Thai University-based Surgical Intensive Care Unit (THAI-SICU) study was a prospective, observational cohort study including nine university-based SICUs throughout Thailand from April 2011 to January 2013. All >18-year-old surgical patients who were admitted to general SICUs were recruited. The primary outcome was the incidence of ALI/ARDS.

Results: In total, 4,652 patients were analyzed. ALI/ARDS new developed in 114 patients (2.5%). Patients with ALI/ARDS had higher APACHE II (20.0 vs. 11.4, respectively; p<0.001) and SOFA scores (7.3 vs. 3.1, respectively; p<0.001) and a higher incidence of past or current smoking (48% vs. 36%, respectively; p<0.001) than the non-ARDS patients. The 28-day mortality rate was significantly higher in patients with than without ALI/ARDS (50% vs. 12%; p<0.001). Higher APACHE II and SOFA scores and higher rates of current or past smoking were independent predictors of ALI/ARDS.

Conclusion: The incidence of ALI/ARDS in the THAI-SICU study was low, but the mortality rate was high. Higher severity scores and smoking were associated with ALI/ARDS.

Keywords: Acute lung injury, Acute respiratory distress syndrome, Incidence, Critically ill, Surgical

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The diagnoses of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) have several aspects, including a history of predisposing factors, the acute onset of hypoxemic respiratory failure, and bilateral pulmonary infiltrations on chest x-rays⁽¹⁾. Despite the use of formalized criteria for decades⁽¹⁾, the incidence of ALI/ARDS within the adult population has varied among studies. Major studies from European countries have reported an ARDS incidence ranging from 5.0 to 7.2 cases per 100,000

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population⁽²⁻⁴⁾, whereas studies from the United States have reported figures much greater than expected^(5,6). Variations in healthcare systems, demographics, socioeconomics, and population types might explain these remarkable differences.

Patients undergoing operative procedures comprise a subset of critically ill patients that have a tendency to develop postoperative ARDS associated with a higher mortality rate⁽⁷⁾. The insults from surgical procedures and perioperative treatment strategies (e.g., activation of the coagulation cascade, injury to the capillary endothelium, alterations in the immune system, and ventilator, fluid, and transfusion administration) can result in postoperative lung injury⁽⁸⁾. Moreover, patients' conditions, including comorbidities and environmental factors, play important contributory

roles in the development of postoperative pulmonary complications. Identification of predictive perioperative risk factors might help to prevent postoperative ARDS and help to establish early treatment strategies. Nevertheless, the incidence of and risk factors for ARDS in surgical patients have been evaluated in few previous studies⁽⁷⁻⁹⁾. These studies involved different subtypes of surgical populations ranging from high-risk patients who might require ICU admission to low-risk surgical patients. Kor et al⁽⁷⁾ reported an ARDS incidence of 7.5% in a multicenter cohort of 1,562 at-risk surgical patients. Variables considered major risk factors for ARDS included aspiration, pneumonia, sepsis, shock, pancreatitis, high-risk trauma, and high-risk surgery. The independent risk factors for ARDS in their study included sepsis, high-risk aortic vascular surgery, highrisk cardiac surgery, emergency surgery, cirrhosis, admission location other than home, increased respiratory rate (20-29 and >30 breaths/min), FIO of >35%, and SpO₂ of <5%. In another study, Kor et al⁽⁸⁾ reported a postoperative ALI incidence of 2.6% in patients who underwent elective surgery and required mechanical ventilation for >3 hours during general anesthesia. Independent predictors of postoperative ALI were high-risk cardiac, vascular, and thoracic surgery; diabetes mellitus; chronic obstructive pulmonary disease; gastroesophageal reflux disease; and alcohol abuse. In a different large retrospective cohort of low-risk patients undergoing general surgery such as non-cardiothoracic, vascular, and trauma surgery, the incidence of new postoperative ARDS was only 0.2% (9). Pre-operative risk factors for developing ARDS included an American Society of Anesthesiologists physical status of 3 to 5, emergent surgery, renal failure, chronic obstructive pulmonary disease, a higher number of anesthetics, and male sex. Because of the scarce reports on the incidence of and risk factors for ARDS in general surgical patients requiring admission to the SICU, the Thai Universitybased Surgical Intensive Care Unit (THAI-SICU) study, a large national multicenter study, aimed to determine prospectively the incidence of, outcomes of, and perioperative risk factors for ALI/ARDS in general surgical patients (excluding cardiac and neurological surgery) requiring admission to the SICU with or without operations.

Material and Method

The THAI-SICU study was a multicenter, prospective, observational cohort study including nine university-based SICUs covering all regions across the

country from April 2011 to January 2013 of total cohort time. The basic objectives of the THAI-SICU study were to identify the adverse events and mortality in SICUs. The study proposals and all case record forms were approved by the Thailand Joint Research Ethics Committees (No. 001/2011) or by the ethics committee or institutional review board of each individual institution prior to data collection. All patients or relatives provided informed consent before information was gathered. The Trial.gov identification number for this study is NCT01354197.

All adult surgical patients aged >18 years who were admitted to general SICUs during the study period were recruited. The investigators excluded moribund patients, those who required an ICU stay of <6 hours, nonsurgical patients, cardiac surgery and neurosurgery patients, and foreign nationals. All methodological details are described in a previous publication(10). The study was primarily designed to identify the incidence and outcomes of ALI/ARDS in critically ill surgical patients. The primary outcomes were the incidence of ALI/ARDS at any time after ICU admission and allcause, 28-day mortality. Secondary outcomes were the independent risk factors associated with ALI/ARDS. Collected data were divided into three categories: "on admission", "daily recording data", and "at discharge". Information on the patients' characteristics, risk factors, ventilator data, adverse events, and outcomes were initially collected at the time of admission and throughout the ICU stay or up to 28 days of ICU admission. The patients were followed until 28 days after ICU admission even discharge from SICU or death.

The American-European Consensus Conference definition(11) of ALI/ARDS was used in the present study because this study was performed before implementation of the Berlin definition of ARDS⁽¹²⁾, a newer definition in which ARDS is categorized as mild, moderate, or severe. The American-European Consensus Conference criteria include the presence of acute hypoxemia with a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO₂/FiO₂) of \leq 300 mmHg (for ALI) or \leq 200 mmHg (for ARDS); bilateral infiltrates on a frontal chest radiograph; and no clinical evidence of left atrial hypertension or, if measured, a pulmonary artery occlusion pressure of ≤18 mmHg. Formal training was performed to understand accurately the definitions for each variable prior to data collection.

Data analysis

The incidence of ALI/ARDS is reported in

percentages. Mean and standard deviation or median and interquartile range were used to present continuous data with a parametric or nonparametric distribution, respectively. Categorical data are reported as counts and percentages. Univariable analysis was used to detect the differences between patients with and without ALI/ARDS. Student's t-test and analysis of variance test were used for continuous variables with a normal distribution. The Mann-Whitney U test and the Kruskal-Wallis were used for non-parametric data. The chi-square test or Fisher's exact probability test was used for categorical data. Less than 3% of patients had missing data. We performed multiple imputations for missing values. Correlations between predictors and outcomes were analyzed by regression analysis with multivariable controls. To determine which characteristics were independently associated with ALI/ARDS, all of the covariates that were statistically significant at a p-value of ≤ 0.2 in the unadjusted analyses were entered simultaneously into the adjusted logistic regression model. The multicollinearity association was checked on the regression model. The adjusted model contained only statistically significant variables. The adjusted odds ratios of ALI/ ARDS are reported along with their 95% confidence intervals. Statistically significant differences are defined as p<0.05. STATA, version 11.0 (STATA Inc., College Station, TX) was used for statistical analysis.

Results

In total, 6,548 SICU patients were enrolled; 1,807 of these patients were excluded. The reasons for exclusion were previously described⁽¹⁰⁾. A total of 89 patients (1.9%) had incomplete or missing data. Consequently, 4,652 patients were included in the analysis. Of these, 238 patients (5.2%) were diagnosed with ALI/ARDS and 124 had met the ALI/ARDS criteria since the day of admission. Consequently, 114 patients (2.5%) developed ALI/ARDS during their ICU stay. The median onset of ALI/ARDS occurred on day 1 (interquartile range, 1-3). On the day of admission, the average PaO₂/FiO₂ ratio in patients with ALI/ARDS was 224.67±132.57, the average positive end-expiratory pressure was 8.28±4.48 cmH₂O, and the average tidal volume per predicted body weight was 8.08±3.02 ml/kg.

The baseline characteristics of patients with and without ALI/ARDS are shown in Table 1. Patients with ALI/ARDS were primarily men, had a higher body mass index, and had significantly higher severity scores on either the Acute Physiology and Chronic Health

Evaluation II (APACHE II) (20.0 vs. 11.4, *p*<0.001) or Sequential Organ Failure Assessment (SOFA) (7.3 vs. 3.1, p < 0.001) on admission. The indications for admission of patients with ALI/ARDS were mainly associated with unstable and severe underlying diseases (priority 3), whereas a requirement for invasive monitoring was the major indication for admission of patients without ALI/ARDS (priority 2). Significantly more patients with than without ALI/ARDS had a past or current smoking habit (48% vs. 36%, respectively; p<0.001); however, there was no significant difference in the number of pack-years among smoking patients. No significant differences in major comorbid diseases, including cardiovascular and respiratory disease, chronic renal failure, diabetic mellitus, and a history of stroke, were noted between the two groups. The hemoglobin and albumin concentrations on admission were slightly but significantly lower in patients with than without ALI/ARDS; in both groups, the hemoglobin concentration was around 10 g/dl and the albumin concentration was <3 g/dl. Significantly more patients with than without ALI/ARDS had sepsis on admission.

Within the first week after admission, patients with ALI/ARDS received a larger volume of fluids and red blood cell transfusions than did patients without ALI/ARDS. With respect to ventilatory data, the maximum tidal volume was not different between patients with and without ALI/ARDS; however, patients with ALI/ARDS had a significantly higher positive end-expiratory pressure and received a significantly higher amount of neuromuscular blocking agents, especially cisatracurium, during the first 7 days (Table 1). With respect to types of surgery, the numbers of emergency and intra-abdominal surgeries were significantly higher in patients with than without ALI/ARDS. Only 7% of the patients in this cohort were trauma patients; there was a significantly higher percentage of trauma patients among those with than without ALI/ARDS. Patients with ALI/ARDS received significantly higher red cell transfusion volumes in the operating room than did patients without ALI/ARDS.

Patients with ALI/ARDS also developed a significantly higher number of complications during their ICU stay, including pneumonia, shock, sepsis, and acute kidney injury, than did patients without ALI/ARDS. However, there were no significant differences in the rates of reintubation, symptomatic deep vein thrombosis, or gastrointestinal bleeding between patients with and without ALI/ARDS. Regarding clinical outcomes, patients with ALI/ARDS demonstrated a

Table 1. Comparison of characteristics between patients with and without ALI/ARDS

| | No ALI/ARDS $n = 4,414$ | ALI/ARDS n = 238 | <i>p</i> -value |
|-------------------------------------------------------|-------------------------|---------------------|-----------------|
| Patient data | | | |
| Age in years (SD) | 61.73 (17.34) | 62.11 (17.13) | 0.763 |
| BMI in kg/m ² (SD) | 22.98 (5.69) | 23.43 (4.71) | 0.014 |
| Male (%) | 2,559 (58.11) | 165 (69.33) | 0.001 |
| Priority of admission#(%) | , , , | , | |
| Priority 1: Unstable patients | 935 (21.33) | 121 (51.05) | |
| Priority 2: Require invasive monitoring | 3,301 (75.30) | 97 (41.00) | |
| Priority 3: Unstable with severe underlying diseases | 117 (2.70) | 16 (68.00) | < 0.001 |
| Severity of diseases (%) | (, | (| |
| ASA physical status more than II (III-V) | 2,101 (47.60) | 93 (39.08) | 0.010 |
| APACHE II score on admission (IQR) | 11.40 (6.74) | 20.14 (9.13) | < 0.001 |
| SOFA score on admission (IQR) | 3.09 (3.25) | 7.29 (4.56) | < 0.001 |
| Smoking status (%) | (, , , | | |
| Current smoking | 519 (11.76) | 38 (15.97) | 0.002 |
| History of smoking | 1,073 (24.31) | 75 (31.51) | |
| Number of pack-years in smoking patients (IQR) | 30 (17.67-40) | 30 (20-40) | 0.753 |
| Comorbid diseases (%) | 2 (2.1.2. 1.0) | () | |
| Cardiovascular disease | 740 (16.76) | 39 (16.39) | 0.879 |
| Vascular disease | 248 (5.62) | 20 (8.40) | 0.072 |
| Respiratory disease | 131 (2.97) | 3 (1.26) | 0.125 |
| Chronic renal failure | 413 (9.36) | 29 (12.18) | 0.147 |
| Diabetic mellitus | 976 (22.11) | 42 (17.65) | 0.105 |
| Stroke | 265 (6.00) | 11 (4.62) | 0.379 |
| Sepsis | 538 (12.25) | 70 (29.41) | < 0.001 |
| Laboratory results, fluid and transfusion | (-=.=) | (=>) | |
| Hemoglobin on admission in g/dl (SD) | 10.63 (2.17) | 10.01 (2.18) | < 0.001 |
| Albumin on admission in g/dl (SD) | 2.77 (0.81) | 2.60 (0.78) | 0.002 |
| Balance fluid at 7 days in ml (IQR) | 1,251 (0-3,490) | 4,903 (840-10,232) | < 0.001 |
| Red blood cell transfusion average 7 days in ml (IQR) | 0 (0-520) | 586.5 (196-1,595) | < 0.001 |
| Surgical data (%) | 0 (0 320) | 300.3 (170 1,373) | (0.001 |
| Elective surgery | 2,271 (67.77) | 40 (37.04) | < 0.001 |
| Emergency surgery | 1,080 (32.23) | 68 (62.96) | < 0.001 |
| Trauma patients | 302 (6.84) | 25 (10.50) | 0.031 |
| Intra-abdominal surgery | 2,109 (47.78) | 64 (26.89) | < 0.001 |
| Vascular surgery | 397 (8.99) | 18 (7.56) | 0.451 |
| Thoracic surgery | 173 (3.92) | 15 (6.30) | 0.069 |
| Other site surgery | 257 (5.82) | 16 (6.72) | 0.565 |
| Duration of surgery in min (IQR) | 21.84 (18.03) | 22.69 (19.56) | 0.766 |
| Fluid balance in OR in ml (IQR) | 1,700 (787.5-2847.5) | | 0.725 |
| PRC in OR in ml (IQR) | 0 (0-519) | 251.5 (0-817) | 0.723 |
| Ventilator data (average first 7 days) (%) | 0 (0 31)) | 231.3 (0 017) | 0.017 |
| CMV mode (PCV + VCV) | 2,152 (49.01) | 230 (96.64) | < 0.001 |
| SIMV mode | 546 (12.43) | 21 (8.82) | 0.098 |
| Maximum tidal volume | 500 (450-574.86) | 520 (473-600) | 0.048 |
| Maximum PEEP | 5 (5-5) | 5.79 (5-7.43) | < 0.048 |
| Tidal volume/predicted body weight | 9.51 (2.08) | 9.56 (2.16) | 0.69 |
| ridar volume, predicted body weight | 7.51 (2.00) | 7.50 (2.10) | 0.07 |

BMI = body mass index; ASA = American Society of Anesthesiologists; APACHE = Acute Physiology and Chronic Health Evaluation; SOFA = Sequential Organ Failure Assessment; PRC = packed red cell; FFP = fresh frozen plasma; OR = operating room; CMV = controlled mechanical ventilation; SIMV = synchronized intermittent mandatory ventilation; PEEP = positive end-expiratory pressure; NMBA = neuromuscular blocking agent

[#] Guidelines for ICU admission, discharge, and triage. Crit Care Med 1999;27:633–8.

Table 1. Cont.

| | No ALI/ARDS $n = 4,414$ | $\begin{array}{c} ALI/ARDS \\ n=238 \end{array}$ | <i>p</i> -value |
|-----------------------------------|-------------------------|--------------------------------------------------|-----------------|
| Neuromuscular blocking agents (%) | | | |
| No | 4,239 (96.54) | 179 (75.21) | < 0.001 |
| Atracurium | 25 (0.57) | 4 (1.68) | |
| Cisatracurium | 99 (2.25) | 43 (18.07) | |
| Pancuronium | 12 (0.27) | 4 (1.68) | |
| Vecuronium | 15 (0.34) | 8 (3.36) | |

significantly higher number of ventilator days and ICU length of stay. The 28-day mortality rate was 50% in patients with ALI/ARDS and only 12% in those without ALI/ARDS (p<0.001). Similarly, the hospital mortality rate was significantly higher in patients with ALI/ARDS (Table 2).

Table 3 shows the clinical predictors for ALI/ARDS in the final logistic regression model. Higher APACHE II and SOFA scores and a current or past smoking habit were independent predictors of ALI/ARDS. A pre-operative American Society of Anesthesiologists physical status of >2 was nearly an independent risk factor for ALI/ARDS (p=0.07) (Table 3).

Discussion

ARDS is considered a serious complication that contributes to high mortality rates among critically ill patients. In this multicenter, prospective, observational cohort study including nine university-based SICUs, the overall incidence of new-onset ALI/ARDS in SICUs was approximately 2.5%. The other main results of this study are as follows⁽¹⁾. The onset of ALI/ARDS was early (day 1)⁽²⁾. Patients with ALI/ARDS developed a significantly higher number of complications during their ICU stay, including pneumonia, shock, sepsis, and acute kidney injury, than did patients without ALI/ARDS was high at 50%⁽⁴⁾. Higher severity scores and smoking were associated with ALI/ARDS in this cohort.

The population in this cohort comprised general surgical patients requiring SICU admission; neurologic and post cardiac surgery patients were excluded. The investigators decided to focus only on general surgical patients because neurologic and post cardiac surgery patients were admitted to other specific ICUs in most of the institutions involved in this study. Although previous studies^(1,7-9) have reported the

incidence of ALI/ARDS in surgical patients, their study populations differed from that in the present study. The incidence of ALI/ARDS in our study was higher than that reported in general surgical patients $(0.2\%)^{(9)}$, lower than that reported in high-risk surgical patients $(7.5\%)^{(7)}$, and comparable to that reported in elective surgical patients involving all procedures (2.6%)⁽⁸⁾. Although our general surgical population was admitted to SICUs, the patients had a low incidence of ALI/ ARDS⁽⁹⁾ because almost half of the population comprised abdominal surgical patients and there were low proportions of trauma patients (7%) and vascular patients (9%). Previous studies have demonstrated a high incidence of ALI/ARDS in trauma patients (12-25%)^(5,13,14). Similarly, in high-risk surgical patients including cardiac and vascular patients, the incidence of ARDS was approximately 7.5%⁽⁷⁾.

The independent risk factors for ARDS in this cohort were high severity scores and a current or past smoking habit. Unlike some previous studies^(8,9,15), we did not demonstrate that packed red cell transfusion, the type of surgery, or some underlying diseases were predictors of ARDS. Packed red cell transfusion was shown to be a risk factor for ARDS in several groups of critically ill patients^(9,14,15); in those studies, immunosuppression and interactions among nonspecific systemic inflammatory mediators might have contributed to this association. Despite the higher PRC transfusion rate in both the operating room and in the ICU for patients with ALI/ARDS, packed red cell transfusion was not demonstrated to be a significant predictor of ALI/ARDS in this cohort. As mentioned above, this study focused on the low-risk surgical population, mainly those undergoing intra-abdominal surgery; thus, the risk factors might differ from those of previous studies. Additionally, the disease severity in patients in this study was mild to moderate as indicated by the average APACHE II score of only 12. Moreover, the severity of ARDS was categorized as

Table 2. Complications and outcomes between patients with and without ALI/ARDS

| | No ALI/ARDS $n = 4,414$ | $\begin{array}{l} ALI/ARDS \\ n = 238 \end{array}$ | <i>p</i> -value |
|---------------------------|-------------------------|----------------------------------------------------|-----------------|
| Complications | | | |
| Reintubation | 131 (2.97) | 10 (4.20) | 0.279 |
| Symptomatic DVT | 13 (0.29) | 1 (0.42) | 0.730 |
| Pneumonia | 262 (5.94) | 50 (21.00) | < 0.001 |
| Shock | 801 (18.15) | 163 (68.50) | < 0.001 |
| Sepsis | 729 (16.60) | 93 (39.08) | < 0.001 |
| Gastrointestinal bleeding | 27 (0.61) | 4 (1.68) | 0.050 |
| Acute kidney injury | 596 (13.57) | 92 (38.66) | < 0.001 |
| Outcomes | | | |
| Ventilator days | 2 (1-4) | 5 (5-13) | < 0.001 |
| ICU LOS | 2 (1-4) | 6 (3-13) | < 0.001 |
| 28-day mortality | 523 (11.85) | 119 (50.00) | < 0.001 |
| Hospital mortality | 340 (7.70) | 107 (44.96) | < 0.001 |

Data are presented as n (%) or median (interquartile range).

DVT = deep vein thrombosis; ICU = intensive care unit; LOS = length of stay

Table 3. Independent risk factors for ALI/ARDS

| | Odds ratio | <i>p</i> -value | 95% confidence interval |
|-------------------------------|------------|-----------------|-------------------------|
| APACHE II score | 1.08 | < 0.001 | 1.05-1.10 |
| SOFA score | 1.12 | < 0.001 | 1.08-1.17 |
| Current or past smoking habit | 1.24 | 0.008 | 1.05-1.44 |
| ASA physical status of >2 | 1.35 | 0.070 | 0.97-1.88 |

ASA = American Society of Anesthesiologists; APACHE = Acute Physiology and Chronic Health Evaluation; SOFA = Sequential Organ Failure Assessment

mild to moderate according to the Berlin definition, and ALI/ARDS developed quite early in the ICU (day 1). This may explain why we did not demonstrate the same risk factors as shown in previous reports.

We found that smoking was associated with the development of ALI/ARDS. In previous studies, current cigarette smoking was reported as an independent risk factor for the development of ARDS⁽¹⁶⁻¹⁸⁾. Additionally, active and passive cigarette smoking were associated with an increased risk of developing ARDS⁽¹⁹⁾, transfusion-related ARDS⁽²⁰⁾, and primary graft dysfunction after lung transplantation^(21,22). Smoking prevention strategies might play an important role both in an active and passive cigarette smoking. Iribarren et al⁽¹⁶⁾ reported a clear dose-response association between ARDS and cigarette smoking (heavy smoking of >20 cigarettes per day was associated with a 5.7-fold increased risk of ARDS) and a borderline association between ARDS

and a history of cigarette smoking. In the present study, however, the amount of smoking in terms of the number of pack-years was not associated with ALI/ARDS. The history and amount of smoking might be underestimated because of the difficulty in obtaining a history, both from the relatives and from the patients, at the time of ICU admission⁽²³⁾. Only two institutions that participated in our study performed formal preoperative examinations that provided accurate data on smoking history. Nevertheless, heavy smoking can contribute to alveolar damage and directly cause respiratory insufficiency and ARDS. Moreover, precipitating factors for ALI/ARDS, including pneumonia, vascular disease, sepsis, and gastrointestinal tract or cardiopulmonary surgery, are more likely to develop in smokers (18,24,25). High concentrations of reactive oxygen species, which result in membrane peroxidation and increased inflammation⁽²⁶⁾, can contribute to the development of

ALI/ARDS in smokers.

Even with the low incidence and mild to moderate severity of ALI/ARDS, the 28-day mortality rate reached 50% in the patients with ALI/ARDS in this study. Similarly, the number of ventilator days, ICU length of stay, and hospital mortality rate were significantly higher in patients with than without ALI/ARDS. The mortality rate was slightly higher than that reported in the study conducted in the same population⁽⁹⁾. The development of ARDS in this cohort was associated with high mortality. It is clinically beneficial to establish a strategy with which to prevent post operative pulmonary complications and early treatment of ALI/ARDS in the surgical population.

This study had several limitations. First, ALI/ ARDS developed very early in this cohort; some potential risk factors for the development of ALI/ARDS might have been present or occurred in the operating room. However, information regarding ventilator management in the operating room and choices of volatile anesthetic agents was not available. A previous experimental study reported that a specific volatile anesthetic agent was able to attenuate lung damage⁽²⁷⁾. A recent study reported lower major pulmonary and extrapulmonary complications occurring within the first 7 days after surgery in patients assigned to lungprotective ventilation during anesthesia in major abdominal surgery(28). Atelectasis and pneumonia occurring within 7 days were significantly lower in the patients who underwent lung-protective ventilation. However, the development of ALI/ARDS within 7 days was not significantly different between patients with and without lung-protective ventilation during anesthesia. Likewise, some of the potential risk factors such as amount of fluid, red blood cell transfusion, tidal volume, PEEP and neuromuscular blocking agents might be the consequences of ALI/ARDS because ALI/ARDS developed earlier than we expected. Second, the limited number of patients with ALI/ARDS (n = 238) as well as the low frequency or lack of some potential risk factors in this cohort might have masked the significant associations with ALI/ARDS. Examples of relevant risk factors include obesity, alcohol consumption, and cancer. Obesity can affect either the respiratory mechanics or ALI/ARDS pathophysiology through alterations in circulating inflammatory mediators⁽²⁹⁾. However, no causal relationship has been established between the effect of obesity and the pathogenesis of lung injury in obese patients⁽³⁰⁾. In one study, critically ill or septic patients with a history of alcohol abuse showed a significantly higher

incidence of ARDS than did patients without a history of alcohol abuse(31). Likewise, another study showed a higher incidence of lung injury in patients with than without cancer⁽³²⁾. Third, our study demonstrated the same limitation present in other clinical studies of ARDS in terms of the reproducibility of the ARDS diagnosis. Atelectasis and ventilatory management in postoperative patients may confound the diagnosis of ALI/ARDS. However, structured training in ARDS assessment was mandatory for primary investigators in each institution before commencing the study, and the data were collected prospectively, ensuring the monitoring of ALI/ARDS development. Finally, this study was performed in tertiary-care, university-based hospitals. The patient population may not represent the typical patients seen in other locations in Thailand.

In conclusion, this investigation provides information on the incidence of ALI/ARDS in low-risk general surgical patients admitted to SICUs, which is a poorly studied population. We demonstrated a low incidence but high mortality rate of ALI/ARDS. Higher severity scores and smoking were the only two independent risk factors associated with ALI/ARDS in this cohort. The information from this study offers clinicians opportunities to monitor and reduce the risk of ALI/ARDS in general surgical patients, particularly in abdominal surgical patients. Nevertheless, further studies are required before establishing the causation of ALI/ARDS in this population.

What is already known on this topic?

The incidence of ALI/ARDS in low-risk general surgical patients was low. The onset of ALI/ARDS was early during ICU admission and the mortality was high.

What this study adds?

Higher severity scores and smoking were the only two independent risk factors associated with ALI/ARDS in this cohort. Smoking prevention strategies might play an important role in general surgical patients admitted to SICU.

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Potential conflict of interest

None.

References

- Villar J, Sulemanji D, Kacmarek RM. The acute respiratory distress syndrome: incidence and mortality, has it changed? Curr Opin Crit Care 2014; 20: 3-9.
- Linko R, Okkonen M, Pettila V, Perttila J, Parviainen I, Ruokonen E, et al. Acute respiratory failure in intensive care units. FINNALI: a prospective cohort study. Intensive Care Med 2009; 35: 1352-61.
- 3. Villar J, Blanco J, Anon JM, Santos-Bouza A, Blanch L, Ambros A, et al. The ALIEN study: incidence and outcome of acute respiratory distress syndrome in the era of lung protective ventilation. Intensive Care Med 2011; 37: 1932-41.
- Sigurdsson MI, Sigvaldason K, Gunnarsson TS, Moller A, Sigurdsson GH. Acute respiratory distress syndrome: nationwide changes in incidence, treatment and mortality over 23 years. Acta Anaesthesiol Scand 2013; 57: 37-45.
- 5. Rubenfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M, et al. Incidence and outcomes

- of acute lung injury. N Engl J Med 2005; 353: 1685-93.
- Li G, Malinchoc M, Cartin-Ceba R, Venkata CV, Kor DJ, Peters SG, et al. Eight-year trend of acute respiratory distress syndrome: a population-based study in Olmsted County, Minnesota. Am J Respir Crit Care Med 2011; 183: 59-66.
- 7. Kor DJ, Lingineni RK, Gajic O, Park PK, Blum JM, Hou PC, et al. Predicting risk of postoperative lung injury in high-risk surgical patients: a multicenter cohort study. Anesthesiology 2014; 120:1168-81.
- Kor DJ, Warner DO, Alsara A, Fernandez-Perez ER, Malinchoc M, Kashyap R, et al. Derivation and diagnostic accuracy of the surgical lung injury prediction model. Anesthesiology 2011; 115: 117-28.
- Blum JM, Stentz MJ, Dechert R, Jewell E, Engoren M, Rosenberg AL, et al. Preoperative and intraoperative predictors of postoperative acute respiratory distress syndrome in a general surgical population. Anesthesiology 2013; 118: 19-29.
- 10. Chittawatanarat K, Chaiwat O, Morakul S, Pipanmekaporn T, Thawitsri T, Wacharasint P, et al. A multi-center Thai university-based surgical intensive care units study (THAI-SICU study): methodology and ICU characteristics. J Med Assoc Thai 2014; 97 (Suppl 1): S45-54.
- Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 1994; 149: 818-24.
- 12. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA 2012; 307: 2526-33.
- 13. Treggiari MM, Hudson LD, Martin DP, Weiss NS, Caldwell E, Rubenfeld G. Effect of acute lung injury and acute respiratory distress syndrome on outcome in critically ill trauma patients. Crit Care Med 2004; 32: 327-31.
- Watkins TR, Nathens AB, Cooke CR, Psaty BM, Maier RV, Cuschieri J, et al. Acute respiratory distress syndrome after trauma: development and validation of a predictive model. Crit Care Med 2012; 40: 2295-303.
- Chaiwat O, Lang JD, Vavilala MS, Wang J, MacKenzie EJ, Jurkovich GJ, et al. Early packed red blood cell transfusion and acute respiratory

- distress syndrome after trauma. Anesthesiology 2009; 110: 351-60.
- Iribarren C, Jacobs DR Jr, Sidney S, Gross MD, Eisner MD. Cigarette smoking, alcohol consumption, and risk of ARDS: a 15-year cohort study in a managed care setting. Chest 2000; 117: 163-8.
- Hsieh SJ, Zhuo H, Benowitz NL, Thompson BT, Liu KD, Matthay MA, et al. Prevalence and impact of active and passive cigarette smoking in acute respiratory distress syndrome. Crit Care Med 2014; 42: 2058-68.
- 18. Calfee CS, Matthay MA, Kangelaris KN, Siew ED, Janz DR, Bernard GR, et al. Cigarette Smoke Exposure and the Acute Respiratory Distress Syndrome. Crit Care Med 2015; 43: 1790-7.
- Calfee CS, Matthay MA, Eisner MD, Benowitz N, Call M, Pittet JF, et al. Active and passive cigarette smoking and acute lung injury after severe blunt trauma. Am J Respir Crit Care Med 2011; 183: 1660-5.
- 20. Toy P, Gajic O, Bacchetti P, Looney MR, Gropper MA, Hubmayr R, et al. Transfusion-related acute lung injury: incidence and risk factors. Blood 2012; 119: 1757-67.
- Bonser RS, Taylor R, Collett D, Thomas HL, Dark JH, Neuberger J. Effect of donor smoking on survival after lung transplantation: a cohort study of a prospective registry. Lancet 2012; 380: 747-55.
- 22. Diamond JM, Lee JC, Kawut SM, Shah RJ, Localio AR, Bellamy SL, et al. Clinical risk factors for primary graft dysfunction after lung transplantation. Am J Respir Crit Care Med 2013; 187: 527-34.
- 23. Van Rompaey B, Elseviers MM, Schuurmans MJ, Shortridge-Baggett LM, Truijen S, Bossaert L. Risk factors for delirium in intensive care patients: a prospective cohort study. Crit Care 2009; 13: R77.

- 24. Benson RA, Poole R, Murray S, Moxey P, Loftus IM. Screening results from a large United Kingdom abdominal aortic aneurysm screening center in the context of optimizing United Kingdom National Abdominal Aortic Aneurysm Screening Programme protocols. J Vasc Surg 2016; 63: 301-4.
- Walter V, Jansen L, Hoffmeister M, Ulrich A, Chang-Claude J, Brenner H. Smoking and survival of colorectal cancer patients: population-based study from Germany. Int J Cancer 2015; 137: 1433-45.
- Milara J, Cortijo J. Tobacco, inflammation, and respiratory tract cancer. Curr Pharm Des 2012; 18: 3901-38.
- Voigtsberger S, Lachmann RA, Leutert AC, Schlapfer M, Booy C, Reyes L, et al. Sevoflurane ameliorates gas exchange and attenuates lung damage in experimental lipopolysaccharideinduced lung injury. Anesthesiology 2009; 111: 1238-48.
- Futier E, Constantin JM, Paugam-Burtz C, Pascal J, Eurin M, Neuschwander A, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. N Engl J Med 2013; 369: 428-37
- 29. Hibbert K, Rice M, Malhotra A. Obesity and ARDS. Chest 2012; 142: 785-90.
- 30. Konter JM, Parker JL, Baez E, Li SZ, Ranscht B, Denzel M, et al. Adiponectin attenuates lipopolysaccharide-induced acute lung injury through suppression of endothelial cell activation. J Immunol 2012; 188: 854-63.
- 31. Liang Y, Yeligar SM, Brown LA. Chronic-alcoholabuse-induced oxidative stress in the development of acute respiratory distress syndrome. ScientificWorldJournal 2012; 2012: 740308.
- 32. Soubani AO, Shehada E, Chen W, Smith D. The outcome of cancer patients with acute respiratory distress syndrome. J Crit Care 2014; 29: 183.

อุบัติการณ์และปัจจัยเสี่ยงของการเกิดภาวะปอดอักเสบเฉียบพลันในผู้ป่วยที่เขารับการรักษาในหอผู้ป่วยหนักศัลยกรรม การศึกษาสหสถาบันในหออภิบาลผู้ป่วยหนักทางศัลยกรรมของโรงพยาบาลมหาวิทยาลัยในประเทศไทย (THAI-SICU) study

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วัตลุประสงค์: การรายงานอุบัติการณ์ของภาวะปอดอักเสบเฉียบพลันยังมีความแตกต่างกันมาก การศึกษานี้มีจุดประสงค์ในการศึกษาหาอุบัติการณ์ ปัจจัยเสี่ยงและผลลัพท์ของภาวะปอดอักเสบเฉียบพลันในหออภิบาลผู้ป่วยหนักทางศัลยกรรม

วัสดุและวิธีการ: การศึกษาสหสถาบันในหออภิบาลผู้ป่วยหนักทางศัลยกรรมของครงพยาบาลมหาวิทยาลัยในประเทศไทย (THAI-SICU) study เป็นการศึกษาแบบไปข้างหน้าในโรงเรียนแพทย์ 9 สถาบัน ตั้งแต่เคือนเมษายน พ.ศ. 2554 ถึงเคือนมกราคม พ.ศ. 2556 ประชากรที่เข้าการศึกษา คือผู้ป่วยศัลยกรรมอายุมากกว่า 18 ปีที่เข้ารับการรักษาในหออภิบาลผู้ป่วยหนักทางศัลยกรรม ผลการศึกษาหลักคืออุบัติการณ์ของภาวะ ปอดอักเสบเฉียบพลัน

ผลการศึกษา: ผู้ป่วยที่เข้าเกณฑ์การศึกษาทั้งหมด 4,652 คน ผู้ป่วย 114 คน (ร้อยละ 2.5) เกิดภาวะปอดอักเสบเฉียบพลัน ผู้ป่วยที่เกิดภาวะ ปอดอักเสบเฉียบพลันมีความรุนแรงของโรควัดโดย APACHE II และ SOFA scores สูงกว่า (20.0 vs. 11.4; p<0.001 และ 7.3 vs. 3.1; p<0.001 ตามลำดับ) ผู้ป่วยที่ในมีภาวะปอดอักเสบเฉียบพลัน ผู้ป่วยที่เกิดภาวะปอดอักเสบเฉียบพลันยังมีอุบัติการณ์ของการสูบบุหรี่สูงกว่า (ร้อยละ 48 vs. 36, p<0.001) อัตราการตายที่ 28 วัน สูงกว่าอยางมีนัยสำคัญในผู้ป่วยที่เกิดภาวะปอดอักเสบเฉียบพลัน (ร้อยละ 50 vs. 12; p<0.001) ความรุนแรงของโรคและการสูบบุหรี่เป็นปัจจัยเสี่ยงของการเกิดภาวะปอดอักเสบเฉียบพลันในผู้ป่วยหนักทางสัลยกรรม

สรุป: อุบัติการณ์การเกิดภาวะปอดอักเสบเฉียบพลันในการศึกษาสหสถาบันในหออภิบาลผู้ป่วยหนัก ทางศัลยกรรมของโรงพยาบาลมหาวิทยาลัย ในประเทศไทย (THAI-SICU) study ค่อนข้างต่ำแต่มีอัตราตายสูง ความรุนแรงของโรคและการสูบบุหรี่เป็นปัจจัยเสี่ยงของการเกิดภาวะปอดอักเสบ เฉียบพลัน