Crit Care Shock (2020) 23:136-141

Lung injury prediction score as a predictor of acute respiratory distress syndrome in intensive care unit

Tjokorda Gde Agung Senapathi, Made Wiryana, I Made Gede Widnyana, Christopher Ryalino, Budi Hartono

Abstract

***Background*: Acute respiratory distress syndrome (ARDS) is a clinical syndrome characterized by acute hypoxemia and bilateral infiltrates in the lung after a triggered injury. A major obstacle in ARDS prevention is the identification of patients at risk of ARDS. The goal of this study was to assess the validity of lung injury prediction score (LIPS) as a predictor of ARDS in the intensive care unit (ICU).**

***Patients and methods*: This is a retrospective observational study conducted in the ICU of Sanglah General Hospital (Bali, Indonesia) in 2019 with 451 subjects were eligible after a systematic random sampling method. Receiver operating characteristics (ROC) analysis was used to assess the ability of LIPS to predict ARDS and determine the best cutoff point for LIPS in predicting ARDS.**

***Results*: The area under ROC curve (AUC) value was 0.86 (95% CI 0.81-0.91). The best cutoff point was at LIPS ≥5 (sensitivity 85.71%, specificity 80.77%). From a cross tabulation calculation, we obtained a relative risk of 18.6 (95% CI 7.4-46.77). A logistic regression analysis obtained an odds ratio of 1.71 (95% CI 1.45-2.03).**

***Conclusion*: LIPS is valid for predicting the incidence of ARDS in ICU patients. It can be used as a screening tool to identify those with a high risk of developing ARDS.**

Key words: LIPS, ARDS, validity, prediction, ICU.

Introduction

Acute respiratory distress syndrome (ARDS) is a clinical syndrome characterized by acute hypoxemia and bilateral infiltrates in the lung after a triggered injury. The main characteristic of this syndrome is an increase in pulmonary capillary permeability. Damage to the capillary endothelium and alveoli epithelium cause the accumulation of protein-rich fluids into the alveoli. This triggers cytokine release, causing diffuse alveoli damage. (1) This syndrome is a form of pulmonary edema without cardiogenic causes that can be induced by pulmonary or systemic inflammation. (2,3)

Since described by Ashbaugh in 1967, ARDS has been known as a serious clinical problem throughout the world with high economic burdens, morbidity, and mortality. (4,5) The incidence of ARDS varies from 1.5 cases per 100,000 to 79 cases per 100,000 population. (5) The Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure (LUNGSAFE) study in 2014 reported that the incidence of ARDS in the intensive care unit (ICU) was 10.4% of the total patients treated in ICU, and 23.4% of patients requiring mechanical ventilation. (6)

A major obstacle in ARDS prevention is the identification of patients at risk of ARDS. (7,8) Trillo-Alvarez designed an acute lung injury prediction scoring system, namely lung injury prediction score (LIPS), to identify patients at risk of developing acute lung injury (ALI). (8,9) This scoring system has been reviewed in several studies to i-

From Department of Anesthesiology and Intensive Care, Faculty of Medicine, Udayana University, Bali, Indonesia (Tjokorda Gde Agung Senapathi, Made Wiryana, I Made Gede Widnyana, Christopher Ryalino, Budi Hartono).

Address for correspondence:
Tjokorda Gde Agung Senapathi
Department of Anesthesiology and Intensive Care
Faculty of Medicine, Udayana University
Jl. PB Sudirman, Denpasar 80232, Bali, Indonesia
Email: tjoksenapathi@unud.ac.id

dentify patients at risk of ARDS in the emergency department and is relatively acceptable as a good prediction method. (7,9,10) Other studies also support the validity of LIPS as a predictor of ARDS and a predictor of death in critically surgical patients. (11)

Soto, et al (12) assessed the use of LIPS for the prediction of patients at risk of ARDS in the treatment room. This study showed that LIPS was less convincing, with an area under the ROC curve (AUC) of 0.7. LIPS ≥4 had a sensitivity of 90%, a specificity of 31%, a positive predictive value (PPV) of 17%, and a negative predictive value (NPV) of 95%. This study was designed to assess the validity of LIPS as a predictor of ARDS in the ICU.

Patients and methods

This was a retrospective observational study conducted in the ICU of Sanglah General Hospital (Bali, Indonesia) in 2019. Inclusion criteria include patients of 18-65 years old who were treated in the ICU of Sanglah General Hospital in 2018. Exclusion criteria include incomplete data in the medical records, those who were diagnosed with ARDS or pulmonary illnesses upon ICU admission, cardiac pathologies, history of bone marrow transplantation, severe burns, drug overdose, and history of lung transplantation and embolectomy.

This study used systematic random sampling to achieve the minimum sample size based on the standard sample size formula. In eligible subjects, LIPS variables and other factors were assessed on the day of ICU admission. The medical record was used to assess if the patient developed ARDS based on the Berlin criteria. The study protocol was approved by the institutional review boards of the Faculty of Medicine, Udayana University and Sanglah General Hospital to ensure that this study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All subjects provided their informed consent prior to their inclusion in the study.

Data were analyzed using SPSS 24.0 software. Descriptive analysis was used to describe the characteristics of the subject. Variables with a numerical data scale were presented in the form of a mean and standard deviation. Data in categorical scale were presented in proportions. Receiver operating characteristics (ROC) analysis was used to assess the ability of LIPS to predict ARDS and determined the best cutoff point for LIPS in predicting ARDS. A p value <0.05 was considered significant.

Results

Out of 1,227 patients who were admitted to ICU in 2018, we collected the data of 451 subjects to be included in this study. From these, 241 (53.4%) were male subjects, and 210 (46.6%) were female. The mean age of the subjects was 43.92±13.46 years, as presented in **Table 1**.

The LIPS was assessed on the first day of treatment in ICU. The medical record was used to obtain the data to assess the incidence of ARDS based on Berlin criteria. In the LIPS, the lowest score was zero and the highest was 11.5 (**Table 2**). Amongst the LIPS components, the three most frequently occurring components were oxygen inspiration fractions (FiO2) of >0.35 in 343 subjects (76.05%), hypoalbuminemia in 197 subjects (43.68%), and acidosis in 73 subjects (16.19%).

To assess the validity of LIPS as a predictor of ARDS, an analysis was performed using the ROC curve. From the analysis using this curve, an area under the ROC curve (AUC) value was 0.86 (95% CI 0.81-0.91). This score had an AUC value in the range of 0.80 to 0.90, which meant it was included in both categories as a diagnostic tool. Based on the analysis, the best cutoff point was at LIPS≥5 (sensitivity 85.71%, specificity 80.77%, PPV 27.3%, and NPV 98.5%). Subjects were then grouped into two groups based on LIPS: LIPS<5 and LIPS≥5 (**Table 3**). From a cross tabulation calculation, we obtained a relative risk of 18.6 (95% CI 7.4-46.77). This meant patients with LIPS≥5 had an ARDS risk of 18.6 times higher than patients with LIPS<5. Based on ARDS frequency data for each LIPS, a logistic regression analysis was performed and we obtained an OR of 1.71 (95% CI 1.45-2.03). This showed that each increase in LIPS was associated with an increase in ARDS incidence of 1.7 times.

Discussion

The subjects in this study was never planned to undergo a LIPS assessment. However, because this scoring system was easily done using routine available clinical data, this score could be applied without significant difficulty. This is consistent with one of the advantages of the LIPS. (7)

In this study, we obtained varied LIPS from 0 to 11.5. The mean LIPS was 3.4. The three most frequent LIPS components present were oxygen inspirational fractions (FiO2) >0.35, hypoalbuminemia, and acidosis. Based on the LIPS component, subjects with peripheral saturation <95% amounted to 0.67%, but oxygen consumption of more than 0.35 reached 76.05%. This can illustrate

the use of excessive oxygen therapy in ICU.

We obtained an AUC value of 0.86 (95% CI 0.81-0.91). This shows that the LIPS is a good diagnostic tool to predict the incidence of ARDS. Based on the ROC analysis, it is known that the best cutoff point LIPS was ≥5. When compared with the results of previous studies, this study is in accordance with the research of Trillo-Alvares, et al (9) who reported that LIPS distinguished well from ICU patients who developed ALI (AUC 0.84, 95% CI 0.80–0.89). In the prospective cohort, LIPS performed almost similar (AUC 0.84, 95% CI 0.77-0.91).

Gajic, et al (7) concluded that LIPS was able to distinguish patients with ALI (AUC 0.80, 95% CI 0.76-0.83). They also reported that the positive likelihood ratios and negative likelihood ratios values for the occurrence of ALI were 3.1 (95% CI 2.9-3.4) and 0.4 (95% CI 0.3-0.5), with a sensitivity of 0.69 (0.64-0.74) and specificity 0.78 (0.77-0.79).

Another cohort study by Levitt, et al (13) found that LIPS had an AUC of 0.82 (95% CI 0.76-0.88). A score of more than four has a sensitivity of 97%, a specificity of 37%, a positive predictive value of 33%, and a negative predictive value of 97%. Another study obtained LIPS having an AUC of 0.883 (95% CI 0.78-0.98). A LIPS of ≥3.5 predicted ALI with a sensitivity of 73% and specificity of 95%. (14)

Soto, et al (12) reported that the LIPS could be used to predict ARDS and had an AUC of 0.7. A LIPS of four or more had a PPV of 17%, sensitivity of 90%, specificity of 31%, and associated with a fourfold increase in the incidence of ARDS (OR 4.17, 95% CI 2.26-7.72; AUC=0.60, 95% CI 0.57-0.63).

Bauman, et al (11) study in postoperative ICU patients obtained an AUC of 0.79 (95% CI 0.74-0.84) with a cutoff point of LIPS 7 to predict ARDS. Xu, et al (15) reported that they obtained LIPS value of 5.25 with AUC 0.704 (95% CI 0.618-0.789), sensitivity 62%, specificity 68%, PPV 0.4375, and NPV 0.8191. Xie, et al (16) reported that in ICU patients, they found that the predictive value of LIPS was also low with an AUC of 0.77(95% CI 0.73-0.81). Using 4 as the cutoff point of LIPS, the sensitivity and specificity were 0.72 and 0.59, with PPV and NPV of 0.37 and 0.87, respectively.

These varied results may be influenced by geographical or demographic factors. As we observed, research carried out in the United States yields a similar AUC value, an average of 0.8. Different results were obtained in a study by Soto, et al (12) who received an AUC of 0.7. Two other studies in China produced an average AUC value of 0.74. (15,16)

Logistic regression analysis with the incidence of ARDS on various LIPS showed an OR of 1.7 (95% CI 1.45-2.03). This shows that each increase in LIPS is associated with an increase in the incidence of ARDS by 1.7 times. This is supported by the results of previous studies by two other studies. Bauman, et al (11) found that with every increase in LIPS there was an increase in ARDS tendency (OR 1.5, 95%C, 1.34-1.67). Soto, et al (12) reported that LIPS were associated with an increased tendency for ARDS to occur (OR 1.31, 95% CI 1.21-1.42).

The major limitation of this study was that the subjects of our study were heterogenous ICU-admitted patients. Other limitation includes the retrospective nature of this study. Future studies with a larger number and more homogenous subjects are needed in order to understand its exact role in predicting ARDS.

Conclusion

LIPS is valid for predicting the incidence of ARDS with AUC of 0.86 in ICU patients. The best cutoff point is ≥5 with sensitivity 85.71% and specificity 80.77%. It can be used as a screening tool to identify those with high risk of developing ARDS.

Acknowledgment

The authors report no conflict of interest.

Table 1. Subjects' characteristics

Variables	n=451
Age (years), mean±SD	43.92 (12.46)
Sex - Male, n (%) - Female, n (%)	 241 (53.44) 210 (46.56)
Patient group - Surgical, n (%) - Non surgical, n (%)	 396 (87.8) 55 (12.2)

Legend: SD:=standard deviation.

Table 2. Variables observed

Variables, n (%)	n=451	Developed ARDS	Not developed ARDS
LIPS, mean±SD	3.4±2.23	6±1.49	3.17±2.14
Shock	57 (12.64)	10	47
Aspiration	9 (2)	6	3
Sepsis	20 (4.43)	5	15
Pneumonia	29 (6.43)	11	18
Emergency surgery - Orthopedic spine surgery - Acute abdominal surgery - Cardiac surgery - Aortic vascular surgery	31 (6.87) 26 (5.67) 31 (6.87) 0 0	4 1 4 0 0	26 25 27 0 0
Traumatic brain injury	62 (13.75)	9	53
Smoke inhalation	0	0	0
Near drowning	0	0	0
Lung contusion	11 (2.44)	5	6
Multiple fractures	13 (2.88)	3	10
Alcohol abuse	0	0	0
Obesity	36 (7.98)	3	33
Hypoalbuminemia	197 (43.68)	19	178
Chemotherapy	22 (4.88)	1	21
Oxygen fraction given >0.35	343 (76.05)	35	308
Tachypnea	8 (1.77)	1	7
Peripheral oxygen saturation <95%	3 (0.67)	1	2
Acidosis	73 (16.19)	17	56
Diabetes mellitus in sepsis	6 (1.33)	3	3

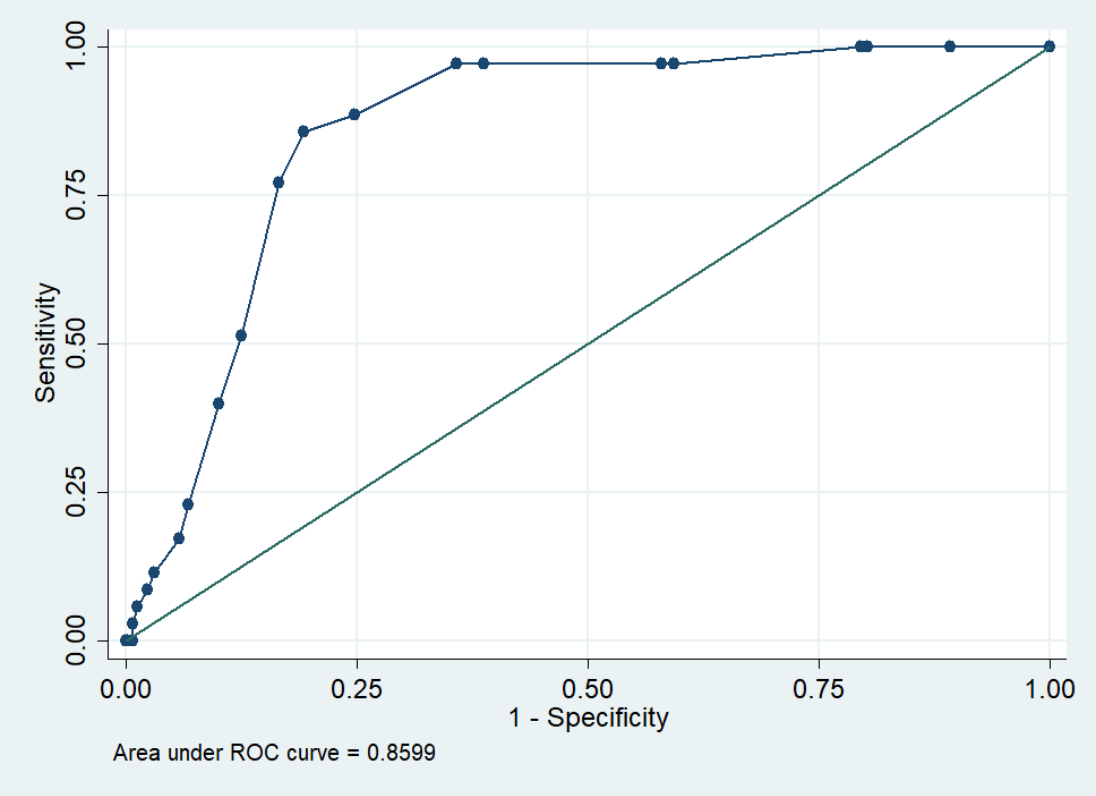
Legend: LIPS=lung injury prediction score; SD=standard deviation; ARDS=acute respiratory distress syndrome.

Table 3. Cross tabulation between LIPS and ARDS

LIPS	ARDS, n (%)		Total, n
	No	Yes	
<5	336 (98.53%)	5 (1.47%)	341
≥5	80 (72.73%)	30 (27.27%)	110
Total	416	35	451

Legend: LIPS=lung injury prediction score; ARDS=acute respiratory distress syndrome.

Figure 1. ROC curve: LIPS as a predictor of ARDS



Legend: ROC=receiver operating characteristics; LIPS=lung injury prediction score; ARDS=acute respiratory distress syndrome.

References

1. Umbrello M, Formenti P, Bolgiaghi L, Chiumello D. Current concepts of ARDS: A narrative review. Int J Mol Sci 2016;18:64.
2. Luo J, Yu H, Hu Y-H, Liu D, Wang Y-W, Wang M-Y, et al. Early identification of patients at risk for acute respiratory distress syndrome among severe pneumonia: A retrospective cohort study. J Thorac Dis 2017;9:3979-95.
3. Senapathi TGA, Budiarta IG, Panji PAS, Aprilnita A. The significance of modified piro scoring with NLR biomarker on enhancing mortality prediction of patients with ventilators-associated pneumonia in intensive care unit. Bali J Anesthesiol 2018;2:80-5.
4. Herridge MS, Tansey CM, Matté A, Tomlinson G, Diaz-Granados N, Cooper A, et al. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med 2011;364:1293-304.
5. Confalonieri M, Salton F, Fabiano F. Acute Respiratory Distress Syndrome. Eur Respir Rev 2017;26:160116.
6. Bellani G, Laffey JG, Pham T, Fan E, LUNG SAFE Investigators and the ESICM Trials Group. The LUNG SAFE study: A presentation of the prevalence of ARDS according to the Berlin Definition! Crit Care 2016;20:1-2.
7. Gajic O, Dabbagh O, Park PK, Adesanya A, Chang SY, Hou P, et al. Early identification of patients at risk of acute lung injury: Evaluation of lung injury prediction score in a multicenter cohort study. Am J Respir Crit Care Med 2011;183:462-70.
8. de Haro C, Martin-Loeches I, Torrents E, Artigas A. Acute respiratory distress syndrome: Prevention and early recognition. Ann Intensive Care 2013;3:11.
9. Trillo-Alvarez C, Cartin-Ceba R, Kor DJ, Kojicic M, Kashyap R, Thakur S, et al. Acute lung injury prediction score: Derivation and validation in a population-based sample. Eur Respir J 2011;37:604-9.
10. Mikkelsen ME, Shah C V., Meyer NJ, Gaieski DF, Lyon S, Miltiades AN, et al. The epidemiology of acute respiratory distress syndrome in patients presenting to the emergency department with severe sepsis. Shock 2013;40:375-81.
11. Bauman ZM, Gassner MY, Coughlin MA, Mahan M, Watras J. Lung Injury Prediction Score Is Useful in Predicting Acute Respiratory Distress Syndrome and Mortality in Surgical Critical Care Patients. Crit Care Res Pract 2015;2015:157408.
12. Soto GJ, Kor DJ, Park PK, Hou PC, Kaufman DA, Kim M, et al. Lung Injury Prediction Score in Hospitalized Patients at Risk of Acute Respiratory Distress Syndrome. Crit Care Med 2016;44:2182-91.
13. Levitt JE, Calfee CS, Goldstein BA, Vojnik R, Matthay MA. Early acute lung injury: Criteria for identifying lung injury prior to the need for positive pressure ventilation. Crit Care Med 2013;41:1929-37.
14. Atta MS, Mahrous AAA, Hassanien AA. Developing prevention model of acute lung injury: Validity of lung injury prediction score and risk panel. Egypt J Chest Dis Tuberc 2013.
15. Xu Z, Wu G-M, Li Q, Ji F-Y, Shi Z, Guo H, et al. Predictive value of combined LIPS and ANG-2 level in critically ill patients with ARDS risk factors. Mediators Inflamm 2018;2018:1739615.
16. Xie J, Liu L, Yang Y, Yu W, Li M, Yu K, et al. A modified acute respiratory distress syndrome prediction score: A multicenter cohort study in China. J Thorac Dis 2018;10:5764-73.