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Risk factors affecting post-traumatic acute respiratory distress syndrome development in thoracic trauma patients

Torasik travma hastalarında post-travmatik akut solunum sıkıntısı sendromu gelişimini etkileyen risk faktörleri

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ABSTRACT

Background: This study aims to investigate the risk factors affecting post-traumatic acute respiratory distress syndrome development in thoracic trauma patients.

Methods: This two-centered, retrospective study included 3,080 thoracic trauma patients (2,562 males, 518 females; mean age 33.9±19.4 years; range, 2 months to 91 years) treated between January 2005 and January 2019. Demographic characteristics, mechanisms of injury, traumatic injuries, injury severity score and new injury severity score results, treatments, comorbidities, complications, morbidity and mortality rates, and durations of hospital stay were collected. Data were used to predict the risk factors for development of post-traumatic acute respiratory distress syndrome by univariate and multivariate statistical analysis.

Results: Acute respiratory distress syndrome was detected in 81 patients. In multivariate logistic regression analysis; age, pulmonary contusion, intracranial hemorrhage, rib fracture (unilateral and four-five pieces), femur and tibia fracture, diabetes mellitus, chronic obstructive pulmonary disease, blood transfusion (≥3 units), high white blood cell count at admission, sepsis, and hepatic injury were detected as independent risk factors ($p<0.05$). Optimal cutoff points (sensitivity/specificity ratios) for acute respiratory distress syndrome development risk were ≥16 (79%/68%) for injury severity score, ≥27 (90%/68.7%) for new injury severity score, and ≥16,000 (75.3%/71.6%) for admission white blood cell count. New injury severity score was superior than injury severity score to predict the development of acute respiratory distress syndrome.

Conclusion: Acute respiratory distress syndrome causes significant mortality and morbidity in trauma patients. In addition to the well-known risk factors, diabetes mellitus and chronic obstructive pulmonary disease were independent risk factors. We defined a cutoff value for new injury severity score to predict post-traumatic acute respiratory distress syndrome.

Keywords: Acute respiratory distress syndrome, risk, thoracic, trauma.

ÖZ

Amaç: Bu çalışmada torasik travma hastalarında post-travmatik akut solunum sıkıntısı sendromu gelişimini etkileyen risk faktörleri araştırıldı.

Çalışma planı: Bu iki merkezli, retrospektif çalışmaya Ocak 2005-Ocak 2019 tarihleri arasında tedavi edilen 3,080 torasik travma hastası (2,562 erkek, 518 kadın; ort. yaş 33.9±19.4 yıl; dağılım, 2 ay-91 yıl) dahil edildi. Demografik özellikler, yaralanma mekanizmaları, travmatik yaralanmalar, yaralanma şiddeti skoru ve yeni yaralanma şiddeti skoru sonuçları, tedaviler, eşlik eden hastalıklar, komplikasyonlar, morbidite ve mortalite oranları ve hastane yatış süreleri toplandı. Veriler tek değişkenli ve çok değişkenli istatistiksel analiz yoluyla post-travmatik akut solunum sıkıntısı sendromu gelişimi için risk faktörlerini öngörmek üzere kullanıldı.

Bulgular: Akut solunum sıkıntısı sendromu 81 hastada saptandı. Çok değişkenli lojistik regresyon analizinde yaş, pulmoner kontüzyon, kafa içi kanama, kaburga kırığı (tek taraflı ve dört-beş parça), femur ve tibia kırığı, diabetes mellitus, kronik obstrüktif akciğer hastalığı, kan transfüzyonu (≥3 ünite), başvuru anı yüksek beyaz küre sayımı, sepsis ve karaciğer yaralanması bağımsız risk faktörleri olarak saptandı ($p<0.05$). Akut solunum sıkıntısı sendromu gelişimi riski için optimal kestirim noktaları (duyarlılık/özgüllük oranları) yaralanma şiddeti skoru için ≥16 (%79/%68), yeni yaralanma şiddeti skoru için ≥27 (%90/%68.7) ve başvuru anı beyaz küre sayımı için ≥16000 (%75.3/%71.6) idi. Akut solunum sıkıntısı sendromu gelişimini öngörmede yeni yaralanma şiddeti skoru, yaralanma şiddeti skorundan daha üstün idi.

Sonuç: Akut solunum sıkıntısı sendromu travma hastalarında ciddi mortalite ve morbiditeye neden olur. İyi bilinen risk faktörlerine ek olarak, diabetes mellitus ve kronik obstrüktif akciğer hastalığı bağımsız risk faktörleri idi. Post-travmatik akut solunum sıkıntısı sendromunu öngörmede yeni yaralanma şiddeti skoru için kestirim değeri tanımlandı.

Anahtar sözcükler: Akut solunum sıkıntısı sendromu, risk, torasik, travma.

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Trauma represents one of the most common causes of morbidity and mortality.[1] The acute respiratory distress syndrome (ARDS) remains a significant contributing factor to mortality and morbidity in the traumatically injured patients.[2] Both direct and indirect causes of pulmonary injury are associated with the development of disease.[3] Post-traumatic ARDS has quite different properties from ARDS related to other causes. Patients with post-traumatic ARDS tend to be younger and have fewer comorbid medical conditions.[4] However, the treatment and rehabilitation of ARDS carries a great cost with increased intensive care and duration of hospital stay, prolonged mechanical ventilation and thus it remains an important health problem. Despite ongoing efforts to improve therapy in trauma patients, mortality related to ARDS has traditionally been high, and represents one of the most common complications during hospitalization with a rate of 6.3%.[5] National Trauma Databank shows the incidence of trauma related ARDS to be 6.5%.[6] However, it is difficult to predict patients at risk of ARDS development.

Well-known independent risk factors for development of post-traumatic ARDS are those aged >65 years, high injury severity score (ISS), pulmonary contusion, a large volume of transfusion requirement, hypotension on admission, pneumonia, sepsis, severe traumatic brain injury (TBI), urgent thoracotomy and long bone fractures.[7] Additionally, there are a number of other possible risk factors such as injury mechanism (blunt, penetrant), white blood cell (WBC) count on admission, comorbidities, mechanical ventilation requirement, coagulopathy, late operations, or other post-traumatic complications stated in several reports.[1-8] However, these are not widely accepted factors according to large cohorts and meta-analyses. In this study, we aimed to investigate the risk factors affecting post-traumatic ARDS development in thoracic trauma patients.

PATIENTS AND METHODS

This study was conducted between January 2005 and January 2019 in two tertiary University Hospitals, which are the major healthcare resources in their regions, with coverage of about five million people around the south and southeast of the country. This retrospective observational cohort study included all hospitalized thoracic trauma patients. The patients discharged home from emergency department (ED) and hospitalized into other clinics were excluded. Thoracic trauma denoted radiologically confirmed chest wall bone fractures and injuries of lungs and other intrathoracic organs and structures. In polytraumatized patients, other injuries were noted as extrathoracic trauma. All patients were scored by the injury severity score (ISS) and new injury severity score (NISS) on admission. The study protocol was approved by the Çukurova University Faculty of Medicine Ethics Committee (No: 2019/85). A written informed consent was obtained from each patient or his/her legal guardians. The study was conducted in accordance with the principles of the Declaration of Helsinki.

We performed a 15-year (2005-2019) retrospective review of 3,080 thoracic trauma patients (2,562 males, 518 females; mean age 33.9±19.4 years; range, 2 months to 91 years). The following prospectively collected variables were evaluated to determine the risk factors of post-traumatic ARDS: demographic characteristics (age, gender), mechanism of injury (penetrant; knife, sharp devices, hand gun, hunting rifle, military rifle, bomb and blunt; road accident, fall, assault), thoracic trauma (pneumothorax, hematothorax, pulmonary contusion, rib fractures, chest wall injuries, diaphragmatic injuries, tracheoesophageal injuries, sternal fractures, heart injury, major vascular injuries, parenchymal foreign bodies), extrathoracic trauma (skull fracture, brain injury, cervical injury, clavicle fracture, scapula fracture, upper extremity bone fractures, pelvic fracture, lower extremity bone fractures, intraabdominal solid organ injury including spleen, liver, and kidney; intestine injuries, urinary system injury), ISS-NISS, WBC counting at admission, all comorbidities (endocrinological, cardiovascular, pulmonary), admitting time interval, duration of intensive care unit (ICU) stay, transfusion, requirement of mechanical ventilation, chest tube inserting and drainage, operations performed (emergency, late), in-hospital complications, i.e. atelectasis, pneumonia, ARDS, prolonged air leak, pleural empyema, pleural hematoma, wound infection, sepsis; and the mortality rate.

The American-European Consensus Conference definition was used since the data collection was started in 2005 in this study.[3] Accordingly, diagnosis was established by acute onset, ratio of arterial oxygen partial pressure to fractional inspired oxygen less than 200 mmHg regardless of the level of positive end-expiratory pressure, bilateral infiltrates on chest radiography, pulmonary artery occlusion pressure less than 18 mmHg (if measured) or no clear evidence of left atrial hypertension. To concretize the diagnosis, consecutive arterial blood gas measurements, plain chest

graphies, electrocardiographies and echocardiography were applied if necessary.

Statistical analysis

All analyses were performed using the IBM SPSS Statistics version 20.0 statistical software package (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation. Chi-square test was used to compare categorical variables between the ARDS and non-ARDS groups. For comparison of continuous variables between the ARDS and non-ARDS groups, the Student's t-test was used. Logistic regression analysis was performed to determine significant predictors of ARDS development. In univariate analysis, variables significant at the $p<0.25$ level were entered in logistic regression analysis. A receiver operator characteristic (ROC) curve analysis was performed in order to identify the optimal cutoff point of ISS, NISS and WBC for predicting ARDS development. The statistical level of significance for all tests was considered to be 0.05.

RESULTS

The cohort comprised of 3,080 trauma patients with a mean age of 33.9±19.4 years (median 30 years; 2 months to 91 years) who were treated in thoracic surgery clinics. Polytraumatized patients hospitalized in other clinics and discharged home from ED were excluded. Vast majority of the patients were male (83.2%). Trauma mechanisms were blunt in 60.4% and penetrant in the remaining. Trauma mechanism was detailed as traffic accident (36.7%), cutting or drilling tool injury (29.3%), fall (18.4%), gun injury (6.4%),

Table 1. Baseline characteristics of patients

	n	%	Mean±SD
Age (year)			33.9±19.4
Gender			
Male	2562	83.2	
Female	518	16.8	
Trauma mechanism			
Blunt	1860	60	
Penetrant	1220	40	
Admission WBC counting (10^3/μL)			13.5±4.7
Admission ISS score			13.4±6.9
NISS score			19.5±9.9
Thoracic injury			
Pleural (pneumothorax, hemothorax, mixed)	2337	75.8	
Rib fracture	1188	38.5	
Pulmonary contusion	1041	33.7	
Others	425		
Extrathoracic injury			
Head and cervical injury	208	6.7	
Orthopedic injury	881	28.6	
Intraabdominal injury	230	7.4	
Chest tube inserting	1964	63.7	
Surgical operation (emergency/elective)			
Thoracic	214/116		
Abdominal	79/7		
Orthopedic	28/61		
Other	10/1		
Blood transfusion (unit)			0.7±1.5
ICU stay time (days)			2.6±3.2
Duration of hospital stay (days)			7.5±5.4

SD: Standard deviation; WBC: White blood cell; ISS: Injury severity score; NISS: New injury severity score; ICU: Intensive care unit.

Table 2. Demographic characteristics and their comparison variables between acute respiratory distress syndrome and non-acute respiratory distress syndrome groups

	ARDS (+) (n=81)			ARDS (-) (n=2,999)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			45.1±19.4			33.6±19.4	<0.001
Gender							<0.001
Male	70	86.5		2492	83		
Female	11	13.5		507	17		
Comorbidities							
Cardiovascular comorbidity	22	27.1		223	7.4		<0.001
Endocrinological: Diabetes mellitus	7	8.6		60	2		0.002
Pulmonary: COPD	7	8.6		49	1.6		0.001
Injury severity score			22.4±9.1			13.2±6	<0.001
New injury severity score			32.7±8.9			19.2±10	<0.001
Admission hematocrit (%)			30.9±5.8			35.4±5.4	<0.001
Admission WBC count (10^3/μL)			18.7±6			13.3±4.6	<0.001
Trauma-admission time interval (min)			178.4±140.7			183.4±146.3	0.763
Trauma mechanism							<0.001
Blunt	69	85.2		1791	59.7		
Penetrant	12	14.8		1208	40.3		
Thoracic injuries							
Unilateral pneumothorax	10	12.3		881	29.4		0.784
Unilateral hemothorax	18	22.2		643	21.4		0.891
Bilateral pneumothorax	2	2.4		70	2.3		0.714
Bilateral hemothorax	3	3.7		44	1.4		0.125
Pulmonary contusion	73	90.1		968	32.2		<0.001
Contusion: Unilateral, unique lobe	14	17.2		458	15.2		0.638
Contusion: Bilateral, lobar	12	14.8		205	6.8		0.013
Contusion: Unilateral, widespread	36	44.4		252	8.4		<0.001
Contusion: Bilateral, widespread	11	13.5		54	1.8		<0.001
Rib fracture	61	75.3		1127	37.6		<0.001
Rib fracture: Unilateral, 1-3	8	9.8		492	16.4		0.128
Rib fracture: Unilateral, 4-5	13	16		258	8.6		0.027
Rib fracture: Unilateral, >5	18	22.2		234	7.8		<0.001
Rib fracture: Bilateral, 1-3	0	0		2	0.06		1.000
Rib fracture: Bilateral, 4-5	4	4.9		31	1		0.013
Rib fracture: Bilateral, >5	18	22.2		112	3.7		<0.001
Flail chest	8	9.8		15	0.5		<0.001
Chest wall damage	2	2.4		84	2.8		1.000
Diaphragmatic injury	8	9.8		54	1.8		<0.001
Esophageal injury	1	1.2		16	0.5		0.365
Tracheobronchial injury	1	1.2		10	0.3		0.454
Heart injury	1	1.2		24	0.8		0.488
Intercostal vessel injury	1	1.2		34	1.1		0.609
Internal mammary vessel injury	1	1.2		25	0.8		0.501
Paravertebral vessel injury	0	0		6	0.2		1.000
Other vessel injury	1	1.2		13	0.4		0.312
Hemopneumothorax: Unilateral	21	25.9		572	19		0.152
Hemopneumothorax: Bilateral	9	11.1		64	2.1		<0.001
Parenchymal tear (operative finding)	11	13.5		100	3.3		<0.001
Sternal fracture	0	0		103	3.4		1.000

Table 2. Continued

	ARDS (+) (n=81)			ARDS (-) (n=2,999)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Extrathoracic injuries							
Brain edema	10	12.3		51	1.7		<0.001
Intracranial hemorrhage	19	23.4		44	1.4		<0.001
Cranium bone fracture	9	11.1		65	2.1		<0.001
Cervical injury	1	1.2		9	0.3		0.234
Clavicle fracture	12	14.8		156	5.2		0.001
Scapula fracture	11	13.5		143	4.7		0.002
Hepatic injury	15	18.5		99	3.3		<0.001
Splenic injury	9	11.1		67	2.2		<0.001
Intraabdominal free liquid	21	25.9		192	6.4		<0.001
Urinary injury	6	7.4		34	1.1		0.001
Humerus fracture	7	8.6		70	2.3		0.004
Radius-ulna fracture	3	3.7		58	1.9		0.215
Vertebral fracture	9	11.1		234	7.8		0.292
Pelvic fracture	9	11.1		106	3.4		0.003
Femur fracture	13	16		74	2.4		<0.001
Tibia fracture	8	9.8		46	1.5		<0.001
Hypotension on admission	44	54.3		251	8.3		<0.001
Surgical operations	25	30.9		479	16		0.001
Thoracic operation	9	11.1		312	10.4		0.853
Abdominal operation	9	11.1		77	2.5		<0.001
Orthopedic operation	6	7.4		83	2.7		0.028
Operation, emergency surgery	21	25.9		308	10.2		<0.001
Chest tube							
Chest tube inserting	63	77.7		1889	63		0.007
Chest tube drainage (mL), initial			461.4±364.7			263.1±325.9	<0.001
Chest tube drainage (mL), total			1486±911			531±544	<0.001
Blood transfusion							
Blood transfusion (unit)			4.46±5.4			0.6±1.3	<0.001
Blood transfusion (≥3 units)	66	81.4		249	8.3		<0.001

ARDS: Acute respiratory distress syndrome; SD: Standard deviation; COPD: Chronic obstructive pulmonary disease; WBC: White blood cell.

crushing and jamming injury (3.1%), military rifle injury (2.1%), hunting rifle injury (1.9%), assault (1.7%), and bomb injury (0.2%).

Baseline and detailed characteristics of the patients were presented in Tables 1 and 2. Acute respiratory distress syndrome was diagnosed in 81 patients (2.6%). The majority of ARDS developed within first four days (82.7%). Acute respiratory distress syndrome developed earlier at the penetrant group (mean 2.1±0.7 vs. 4.2±2.2 days, median 2 (1-3) vs. 4 (1-12), respectively). Acute respiratory distress syndrome development days were given in Figure 1.

According to univariate analysis, male gender, blunt trauma, older age, higher ISS and NISS levels, lower hematocrit and higher WBC levels at admission, higher volume of chest tube drainage, larger amount of blood transfusion, pulmonary contusion, rib fractures,

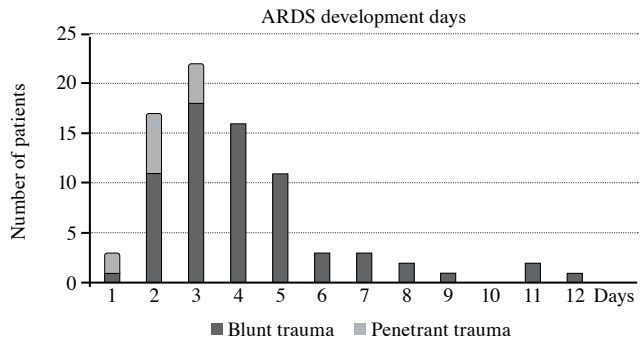

Figure 1. Acute respiratory distress syndrome development days according to trauma mechanism.
ARDS: Acute respiratory distress syndrome.

Table 3. Logistic regression analysis results

	p	OR	95% CI for OR*
Pulmonary contusion	<0.001	10.69	4.50-25.40
Intracranial hemorrhage	<0.001	17.80	6.76-46.92
Rib fracture: unilateral, 4-5	0.014	3.35	1.27-8.83
Femur fracture	0.026	3.12	1.15-8.47
Tibia fracture	0.044	3.48	0.93-13.05
Age	0.029	1.02	1.01- 1.03
Diabetes mellitus	0.014	5.78	1.42-23.43
Chronic obstructive pulmonary disease	0.006	7.22	1.77-29.48
Transfusion requirement ≥3 units	<0.001	31.59	13.71-72.77
Admission white blood cell count	<0.001	1.11	1.05-1.17
Sepsis	<0.001	22.30	6.99-71.10
Hepatic injury	0.013	3.01	1.26-7.18
Emergency operation	0.189	1.68	0.77-3.67

OR: Odds ratio; CI: Confidence interval; * Age and emergency operation adjusted odds ratios were given.

bilateral hemopneumothorax, chest tube inserting, diaphragmatic injury, and emergency thoracic operation were predictors for ARDS development. Concomitant injuries, such as head, solid organ, urinary tract injuries, fractures of clavicle, scapula, pelvis and long bones were also related with ARDS development. Hypotension on admission, extrathoracic surgical operation, comorbidities including diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), and need of blood transfusion were other risk factors ($p<0.05$). The comparison of several variables in terms of ARDS was shown in Table 2.

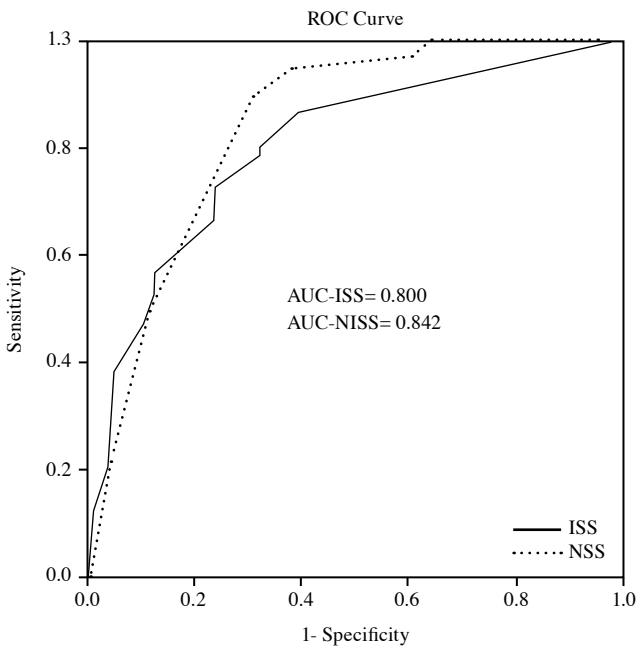

Figure 2. Sensitivity and specificity receiver operator characteristic curve and area under curve values of injury severity score and new injury severity score.

ROC: Receiver operator characteristic; AUC: Area under curve; ISS: Injury severity score; NISS: New injury severity score.

Multivariate logistic regression analysis showed age, pulmonary contusion, intracranial hemorrhage, rib fracture (unilateral and four-five pieces), femur fracture, tibia fracture, DM, COPD, blood transfusion (≥3 units), admission WBC count, sepsis, and hepatic injury as the independent risk factors for development of post-traumatic ARDS (Table 3).

Optimal cutoff points with sensitivity/specificity ratios for ARDS development risk were ≥16 (79%/68%) for ISS, ≥27 (90%/68.7%) for NISS, and ≥16,000 (75.3%/71.6%) for WBC. In our study, NISS was superior than ISS to predict development of ARDS in trauma patients. Sensitivity and specificity ROC curve and area under curve (AUC) values of ISS and NISS comparison were given in Figure 2.

As expected, ARDS resulted in increased morbidity and mortality in the study population. In ARDS group, the duration of mechanical ventilation, durations of ICU and hospital stays were significantly increased ($p<0.05$). The comparison of the outcome variables in the study group was given in Table 4.

DISCUSSION

In addition to the previously reported risk factors including pulmonary contusion, intracranial hemorrhage, unilateral multiple rib fractures, femur and tibia fractures, older age, blood transfusion requirement ≥3 units, high WBC count at admission,

Table 4. Comparison of outcomes between acute respiratory distress syndrome and non-acute respiratory distress syndrome groups in terms of mortality and morbidity

		ARDS (+) (n=81)			ARDS (-) (n=2,999)			
	n	n	%	Mean±SD	n	%	Mean±SD	*p*
Atelectasis	251	19	23.5		232	7.7		<0.001
Pneumonia	110	20	24.7		90	3		<0.001
Prolonged air leak	53	5	6.2		48	1.6		0.012
Pleural empyema	35	4	4.9		31	1		0.013
Pleural hematoma	50	2	2.5		48	1.6		0.381
Wound infection	48	5	6		43	1.4		0.008
Abdominal complication	4	1	1.2		3	0.1		0.101
Sepsis	30	22	27.3		8	0.3		<0.001
Paralysis	46	3	3.7		43	1.4		0.119
Acute renal failure	60	39	48.1		21	0.7		<0.001
Intensive care unit stay time (days)				13.3±6.9			2.4±3.3	<0.001
Mechanical ventilation (days)				8.56±5.2			0.2±1.2	<0.001
Hospital stay (days)				16.6±9.9			7.3±5.3	<0.001
Mortality	92	39	48.1		53	1.8		<0.001

ARDS: Acute respiratory distress syndrome; SD: Standard deviation; ICU: Intensive care unit.

sepsis and hepatic injury, we determined DM and COPD as unsuspected risk factors of post-traumatic ARDS development. In addition, to our knowledge for the first time, we reported a cutoff value for NISS for the prediction of post-traumatic ARDS. New injury severity score ≥27 predicted post-traumatic ARDS with a sensitivity and specificity of 90% and 68.7%, respectively. The mortality and the morbidity rates were significantly higher in patients with ARDS.

The incidence of post-traumatic ARDS varies between 0.5% and 32% in different studies.[8] The rate differences are possibly due to clinical heterogeneity (geographical region, type of trauma mechanism, versatile study populations and different subgroup analysis) of the study groups. In this large cohort study including all age groups, post-traumatic ARDS developed in 2.6% of the patients.

Everyone might be exposed to trauma in any time during lifetime. The mechanism and the severity of trauma may differ for each patient according to demographical characteristics; however, the inflammatory response may affect the outcome, which significantly changes with aging. In this study, we showed that the risk of post-traumatic ARDS increases with aging. Our study covered all age groups; pediatric (0-18 years, 25%), adult (19-64 years, 70.4%) and elderly (>65 years, 4.6%) and all hospitalized patients in thoracic surgery clinics. Among the 25% of the whole group, there was no post-traumatic ARDS in pediatric subgroup in this study. Likewise, de Roulet et al.[9] reported the incidence of post-traumatic ARDS in pediatric population as 0.5%.

Several scoring systems have been developed to predict the risk factors of post-traumatic ARDS. Although ISS is the most frequently used score among the trauma patients, it is criticized for missing multiple injuries to a single body region and evaluation of each body region equally.[10] Prior studies identified a large range of ISS cutoff points between 10 to 25 as a risk factor for ARDS development, probably due to the heterogeneous study groups; but failed to delineate the best cutoff point.[11] In the same report, Afshar et al.[11] pointed out that a cutoff point of ISS ≥16 provided good sensitivity and specificity and use of ISS ≥16 is a simple method to evaluate ARDS in trauma epidemiology and outcomes research. We found that an ISS ≥16 is the best cutoff point to determine the risk for ARDS development, with a sensitivity and specificity of 79% and 68%, respectively, and AUC of 0.8. NISS has been developed to overcome the disadvantages of ISS and reported as a more accurate score in predicting the outcomes (dependent variables), particularly in severe and specific trauma.[12] Abajas Bustillo et al.[13] reported that NISS is an index with higher predictive capability for in-hospital mortality and correlates better to duration of hospital stay and healthcare cost for trauma patients. For the first time in the literature, we determined a cutoff point for

NISS (≥27) with sensitivity and specificity of 90% and 68.7%, respectively, and with an AUC of 0.842 for post-traumatic ARDS development. We determined that NISS had higher predictive capability than ISS for ARDS development in trauma patients.

Acute respiratory distress syndrome risk also depends on the magnitude of the physiologic and systemic inflammatory response insults. Traumatic injury produces excessive proinflammatory mediators and subsequent activating or recruiting immune cells into the target organs and results in systemic inflammatory response.[14] Leukocytosis in trauma is due to neutrophilia, caused by neutrophil margination, and not due to increased marrow production or release of immature cells or bands. The phenomenon is short-lived, lasting only minutes to hours. Since the whole blood count is one of the first tests obtained from trauma patients in the ED, WBC level could serve as an easy-to-obtain marker for serious injury.[15] In our study, WBC count (≥16,000/mm^3) at admission was a risk factor for development of post-traumatic ARDS with a sensitivity and specificity of 75.3% and 71.6%, respectively.

The outcome of chest trauma depends on many factors, one of which includes the comorbidities. More COPD patients are being admitted to hospitals as trauma victims. In a general surgical population study, COPD was one of the significant risk factors of postoperative ARDS development.[16] Risk factors for ARDS such as pneumonia, longer mechanical ventilation, sepsis, longer ICU and hospital stay are more commonly seen in COPD patients after chest trauma. Shoko et al.[17] showed a significant increase in mortality for trauma patients with COPD. In our study, previously diagnosed COPD was an independent risk factor for post-traumatic ARDS. Magni et al.[18] reported that inhaled corticosteroids (ICS) and inhaled beta-2 agonists (IBA) used for the treatment of COPD have definite role in the prevention of ARDS. Besides the direct delivery to the target organ, ICS and IBA are void of systemic adverse effects, and this makes them the prime candidates for the lung epithelial prevention. We did not observe similar effects in our study group. Further prospective researches are needed to clarify the potential effect of COPD and medications on post-traumatic ARDS.

There are contradictory reports about the effects of DM for ARDS development. Moss et al.[19] showed that the patients with DM have a lower incidence of ARDS. According to the report, decreased polymorphonuclear cell activity limits inflammatory lung injury. However, this study included only septic shock patients. In contrast, although not analyzing the specific reason, Ahmad et al.[20] suggests that ARDS was more common among diabetic patients with trauma. They performed a retrospective analysis of 12,489 patients and reported that trauma patients with diabetes may be attributed to changes in the immune system that are a consequence of the inciting injury. We showed that DM was an independent risk factor for the development of post-traumatic ARDS.

Altunkaya et al.[21] showed that pulmonary contusion was seen in 28.3% of thoracic trauma patients, and had an important role in mortality. We determined that pulmonary contusion was an independent risk factor for the development of post-traumatic ARDS correlated with its extending.

The vast majority of thoracic injuries were pleural pathologies in our study group. However, only bilateral hemopneumothorax was a significant risk factor for ARDS. A majority of pleural injuries had relationships with significant risk factors such as transfusion requirement, bleeding, parenchymal damage, pulmonary contusion, multiple rib fractures, and indications for emergency surgery in our trauma population. The second common thoracic injury in this study was the rib fracture. Although up to three rib fractures were not significant, the risk of ARDS increased with the number of fractured ribs. Multiple rib fractures were mostly seen in blunt trauma patients, and severe extrathoracic injuries generally accompanied them.

Patients with TBI frequently suffer from lung complications and ARDS. The association between TBI and ARDS in trauma patients is well recognized.[22] Holland et al.[23] reported ARDS in 31% of the isolated TBI patients. The possible underlying reasons have been proposed as neurogenic pulmonary edema due to release of catecholamines, frequent nosocomial pneumonia, and increased intracranial pressure. In our study, the presence of hemorrhagic TBI was another independent risk factor for development of post-traumatic ARDS. Long bone fractures were another significant risk factor for ARDS in our study. Although transfusion remains a crucial part of post-traumatic resuscitation, an increased use of packed blood red cells in the acute setting is associated with a higher risk for developing post-traumatic ARDS.[24] We determined that three units was the critical point for post-traumatic ARDS development. Interestingly, thoracic operations were not a significant risk factor for ARDS development in this study. We believe that this was due to the facts that this study was designed

in thoracic surgery clinics and 38.2% of thoracic operations were elective and ARDS developed in only two patients in late thoracic operation group.

Acute respiratory distress syndrome development was significantly related with increased mortality (2.9% vs. 48.1%, respectively) in this study group. Sepsis, atelectasis, pneumonia and acute renal failure were the most common reasons of morbidity. Causes and ARDS itself are the answerable reasons for this high mortality rate since mortality should not be attributed to a single risk factor or unique organ failure.

This study has some limitations. First, it was a retrospective cohort study. Second, it did not include all thoracic trauma patients. The patients discharged home from emergency department, and hospitalized into other clinics were excluded. Third, there was no standard tecnique in radiological studies particularly in the emegency department.

In conclusion, this study showed the importance of acute respiratory distress syndrome in trauma patients with significant mortality and morbidity. In addition to well-known risk factors, chronic obstructive pulmonary disease and diabetes mellitus were related with an increased risk of acute respiratory distress syndrome development. New injury severity score was found to be an index with higher predictive capability for predicting post-traumatic acute respiratory distress syndrome. Furthermore, to our knowledge for the first time, we defined a cutoff value for new injury severity score to predict acute respiratory distress syndrome development. Further prospective trials are required to define the high-risk patients to improve prognosis.

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