



The Role Of Computed Tomography In The Evaluation Of Thoracic Complications In Rib Fractures According To Their Sites And Types

Kot Kırıklarının Yerleşim Yerlerine ve Tiplerine Göre İntrapulmoner Komplikasyonların Değerlendirilmesinde Bilgisayarlı Tomografinin Rolü

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Abstract

Aim: To evaluate the complication risks by different locations and types of rib fractures and to emphasize the role of computed tomography (CT).

Material and Method: Patients' findings undergoing thoracic CT due to blunt chest trauma in the emergency department of our hospital between 1st September 2021 and 31st December 2023 were retrospectively evaluated, and 560 patients with rib fractures were included in the study. Such factors as age, gender, axial (anterior, posterior, lateral, and multiple) and coronal plane (upper, middle, and lower) fracture status, and the incidence of intrapulmonary complications of all patients were evaluated through CT. It was investigated whether there were statistical differences between the study findings.

Results: In the Mann-Whitney U test, the mean age of females was seen to be significantly higher than in males ($p<0.001$). It was also found that the frequency of displaced fractures was significantly higher in those with advanced age ($p=0.022$), and the frequency of intrapulmonary complications was significantly higher ($p<0.001$). Rib fractures were most commonly localized in the posterior region on the axial plane and in the middle segment (5th–8th ribs) on the coronal plane. However, in the Kruskal-Wallis test, the development of complications was found to be significantly higher in these localizations, compared to other regions ($p<0.001$).

Conclusion: CT plays a critical role in those with rib fractures, both in determining the location of the fracture and in detecting fracture-related complications. Our study findings reveal that CT should be included in clinical decision-making processes in the management of rib fractures.

Keywords: Computed tomography, fracture, intrapulmonary complication, rib

Öz

Amaç: Kot kırıklarının farklı yerleşim yerleri ve tiplerine göre komplikasyon risklerini değerlendirmek ve bilgisayarlı tomografinin (BT) rolünü vurgulamak.

Gereç ve Yöntem: 1 Eylül 2021 ile 31 Aralık 2023 tarihleri arasında hastanemiz acil servisinde künt toraks travması nedeniyle toraks BT'si yapılan hastaların verileri geriye dönük olarak değerlendirildi ve kot kırığı saptanan 560 hasta çalışmaya dahil edildi. Hastaların yaşı, cinsiyeti, aksiyel (anterior, posterior, lateral ve çoklu) ve koronal düzlemdeki (üst, orta ve alt) kırık durumları ile intrapulmoner komplikasyon görülme sıklıkları BT ile değerlendirildi. Elde edilen bulgular arasında istatistiksel fark olup olmadığı araştırıldı.

Bulgular: Mann-Whitney U testi sonucunda kadınların yaş ortalamasının erkeklerle göre anlamlı derecede yüksek olduğu görüldü ($p<0.001$). Ayrıca, ileri yaş grubunda deplase kırık sıklığı ($p=0.022$) ve intrapulmoner komplikasyon sıklığı ($p<0.001$) anlamlı derecede yüksek bulundu. Kot kırıkları aksiyel planda en sık posterior, koronal planda ise en sık orta düzeyde görüldü. Kruskal-Wallis testi ile bu lokalizasyonlarda komplikasyon gelişiminin diğer bölgelere kıyasla anlamlı derecede yüksek olduğu saptandı ($p<0.001$).

Sonuç: BT, kot kırığı olan hastalarda hem kırık lokalizasyonunun belirlenmesinde hem de kırığa bağlı komplikasyonların saptanmasında kritik bir rol oynamaktadır. Çalışma bulgularımız, BT'nin kot kırığı yönetiminde klinik karar verme sürecine dahil edilmesi gerektiğini ortaya koymaktadır.

Anahtar Kelimeler: Bilgisayarlı tomografi, kırık, intrapulmoner komplikasyon, kot



INTRODUCTION

Rib fractures are among the most common injuries in thoracic trauma, and take place especially as a result of motor vehicle-induced accidents, falls from heights, and direct impacts.^[1] Such fractures can lead to serious complications such as lung contusion, hemothorax, and pneumothorax, which increase the length of hospital stay and the rate of mortality.^[2] Various imaging methods such as clinical examination, chest roentgenography, and computed tomography (CT) are used in the evaluation of rib fractures.^[3] Chest radiographs are known to have markedly lower sensitivity, particularly in detecting non-displaced or posteriorly localized rib fractures. In addition, plain radiographs are insufficient for reliably assessing the number of multiple fractures and their associated complications. These limitations further justify the use of CT as the preferred modality for accurate and early diagnosis in trauma patients. However, CT is considered the gold standard in the diagnosis of rib fractures and the evaluation of complications due to its high sensitivity and detailed anatomical imaging ability.^[4] Rib fractures can develop in different locations such as anterior, posterior, and lateral planes, and in the form of multiple fractures with different locations. While anterior rib fractures generally lead to less serious complications, posterior and lateral fractures can bring about serious problems such as lung injuries and vascular damage. Even so, multiple rib fractures can lead to serious deteriorations in respiratory functions, especially by disrupting the stability of the thoracic wall, which can increase the need for mechanical ventilation.^[2,4,5] Therefore, the accurate evaluation of the complications associated with the locations and types of rib fractures is of critical importance for the prognosis of the patients. Parallel to our study findings, studies in the literature evaluating the complications associated with anterior, posterior, lateral, and multiple rib fractures also emphasize the role of CT within the process.^[6]

Thus, our study aimed to evaluate the complication risks based on different locations and types of rib fractures and emphasize the role of CT within this context.

MATERIAL AND METHOD

This retrospective study was carried out with the permission of the Necmettin Erbakan University Non-pharmaceutical and Non-medical Device Research Ethics Committee (Date: 20.12.2024, Decision No: 2024/5415). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population

Undergoing thoracic CT due to blunt chest trauma in the emergency department of our hospital between 1st September 2021 and 31st December 2023, 6198 patients were retrospectively evaluated through the radiology information

system (RIS). Of 6198 patients, 678 were detected to have rib fractures. The patients with rib fractures due to penetrating trauma (n=12), those not undergoing CT within 24 hours after chest trauma (n=29), those under the age of 18 (n=33), those with rib fractures due to cardiovascular resuscitation (n=4), and those with motion artifacts on CT images (n=40) were not included in the study. Therefore, a total of 560 patients (153 females and 407 males) were included in the study (**Figure 1**). Only rib fractures were included in the study, while other thoracic bone fractures (such as sternum, clavicle, scapula, etc.) were excluded.

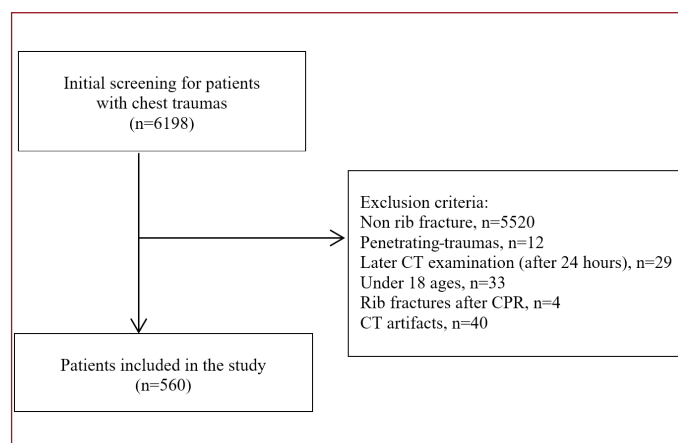


Figure 1. Flow chart of the study.

Imaging Protocols

To evaluate the data, thoracic imaging was performed with 128-slice dual-source CT (MSCT, SOMATOM Flash Definition, Siemens, Forchheim, Germany) by using the automatic dose modulation software with the acquisition parameters 200 mAS, 120 kV, 200 mm FOV (CARE Dose4D™, Siemens, Forchheim, Germany). The slice thickness was 1 mm, and the increment was 0.5 mm; the images were taken in the supine position without contrast and were evaluated axially and coronally in the bone, soft tissue, and lung parenchyma window at the workstation. In terms of the evaluation criteria, the localization of the rib fracture was evaluated as anterior, posterior, lateral, and multiple in the axial plane, and as upper (between 1st and 4th ribs), middle (between 5th and 8th ribs), and lower (between 9th and 12th ribs) in the coronal plane. This dual classification was added because different localizations may be associated with different types of complications, and axial plane assessment provides additional clinically relevant information beyond the rib level itself.

Displaced and non-displaced fractures were also evaluated as a separate parameter, and their associations with complications were statistically analyzed. Additionally, the localizations and types of rib fractures (displaced-nondisplaced) and so the presence of accompanying complications were also evaluated. All evaluations were carried out by two experienced radiologists to reach a consensus.

In this study, traumatic pulmonary pseudocysts, pulmonary contusions, and pneumomediastinum were evaluated as associated complications only when they were detected concurrently with rib fractures. These findings were not regarded as isolated thoracic trauma findings but only in the context of coexisting rib fractures.

Statistical Analysis

Statistical analyses of the study findings were evaluated with the Statistical Package for the Social Sciences statistical software, version 25.0 (SPSS Inc., Chicago, IL, USA). The numerical variables were expressed as mean±standard deviation (SD) or numbers (percentage) under the appropriateness. The appropriateness of the variables for normal distribution, however, was examined visually (histogram and probability graphs) and analytically using the Kolmogorov-Smirnov tests. The descriptive variables were given using means and SDs for not normally distributed variables. Since the age of the patients showed no normal distribution, the comparisons were performed using the Mann-Whitney U test between the groups created according to the parameter of age in terms of gender, displaced fractures, non-costal fractures, subcutaneous emphysema, pneumothorax, hemothorax, post-traumatic cysts, contusion and whether there was pneumomediastinum or not.

The chi-square test was carried out to determine whether there was statistical significance between the gender and complications of displaced fracture, non-costal fracture,

subcutaneous emphysema, pneumothorax, hemothorax, post-traumatic cyst, contusion, and pneumomediastinum.

The Kruskal-Wallis test was conducted to find whether there was a significant relationship between age, showing no normal distribution, the localization of rib fractures in the axial and coronal planes, the presence of complications, and whether the complications were unilateral or bilateral. The paired comparisons were implemented using the Mann-Whitney U test and evaluated using the Bonferroni correction. A p-value below 0.05 was considered statistically significant.

RESULTS

The mean age of the patients was found as 51.66±0.79 (ranging between 18-96 years). In terms of female and male gender differences, the distributions of rib fractures in the axial and coronal planes concerning their locations are shown in **Tables 1** and **2**. The number of those with displaced rib fractures was detected to be a total of 423 (116 females and 307 males). No complications developed as well as the rib fractures in 48 female patients and 97 male patients.

While unilateral and bilateral complications were observed in 100 female patients, 305 and five male patients were found to have unilateral and bilateral complications, respectively. The distribution of complications observed as well as the rib fractures by the male and female gender is presented in **Table 3**.

Table 1. Distribution of rib fractures under their locations in the axial plane

Gender	Anterior	Lateral	Posterior	Multiple	Total
F	42 (27.5%)	36 (23.5%)	49 (32.0%)	26 (17.0%)	153
M	82 (20.2%)	101 (24.8%)	142 (34.9%)	82 (20.2%)	407
Total	124 (22.1%)	137 (24.5%)	191 (34.1%)	108 (19.3%)	560

F: Female, M: Male

Table 2. Distribution of rib fractures under their locations in the coronal plane

Gender	Upper (1-4)	Middle (5-8)	Lower (9-12)	Multiple	Total
F	33 (21.6%)	42 (27.5%)	23 (15.0%)	55 (35.9%)	153
M	74 (18.2%)	137 (33.7%)	72 (17.7%)	124 (30.5%)	407
Total	107 (19.1%)	179 (32.0%)	95 (17.0%)	179 (32.0%)	560

F: Female, M: Male

Table 3. Distribution of complications observed in addition to rib fractures under both genders

Gender	Other bone fractures associated with rib fractures. (n)	Subcutaneous Emphysema(n)	Pneumothorax (n)	Hemothorax (n)	Posttraumatic Cysts (n)	Contusion (n)	Pneumo-Mediastinum (n)	Total (n)
F	30	27	45	54	6	87	1	250
M	79	112	133	162	33	279	7	805
Total	109	139	178	216	39	366	8	1055

F: Female, M: Male

In the Mann-Whitney U test, the mean age of female patients was figured out to be significantly higher than in men ($p<0.001$). It also turned out that the frequency of displaced fracture, pneumomediastinum, pneumothorax, and post-traumatic cyst increased significantly with advanced ages ($p=0.002$, $p=0.022$, $p=0.013$, and $p<0.001$, respectively). In the chi-square test, the frequency of subcutaneous emphysema and contusion was found to be significantly higher among males than in females ($p=0.018$ and $p=0.010$).

In the Kruskal-Wallis test, the localized in the middle and bilateral rib fractures were found to be more common than those localized in the upper part at advanced age level ($p=0.002$ and $p<0.001$). In the Kruskal-Wallis test, the non-costal bone fractures, subcutaneous emphysema, pneumothorax, post-traumatic pseudocysts, hemothorax and contusion (**Figure 2**) were observed to be significantly higher in the laterally localized rib fractures in axial

plane than in bilaterally localized rib fractures ($p=0.003$, $p=0.006$, $p<0.001$, $p<0.001$, and $p<0.001$, respectively). It was also seen that pneumothorax and hemothorax were significantly higher in rib fractures localized anteriorly and posteriorly in the axial plane than in rib fractures localized on both sides in the axial plane ($p<0.001$ and $p<0.001$). The contusion in rib fractures localized posteriorly in the axial plane was observed to be significantly higher than that localized anteriorly and on both sides in the axial plane ($p=0.003$ and $p=.002$). The contusion in rib fractures localized anteriorly in the axial plane was also seen to be significantly higher than that localized in both sides in the axial plane ($p<0.001$).

In the Kruskal-Wallis test, the displaced fractures in rib fractures localized superiorly in the coronal plane were significantly higher than those in the rib fractures localized inferiorly in the coronal plane ($p=0.01$). However, the displaced fractures, subcutaneous emphysema, pneumothorax, hemothorax,

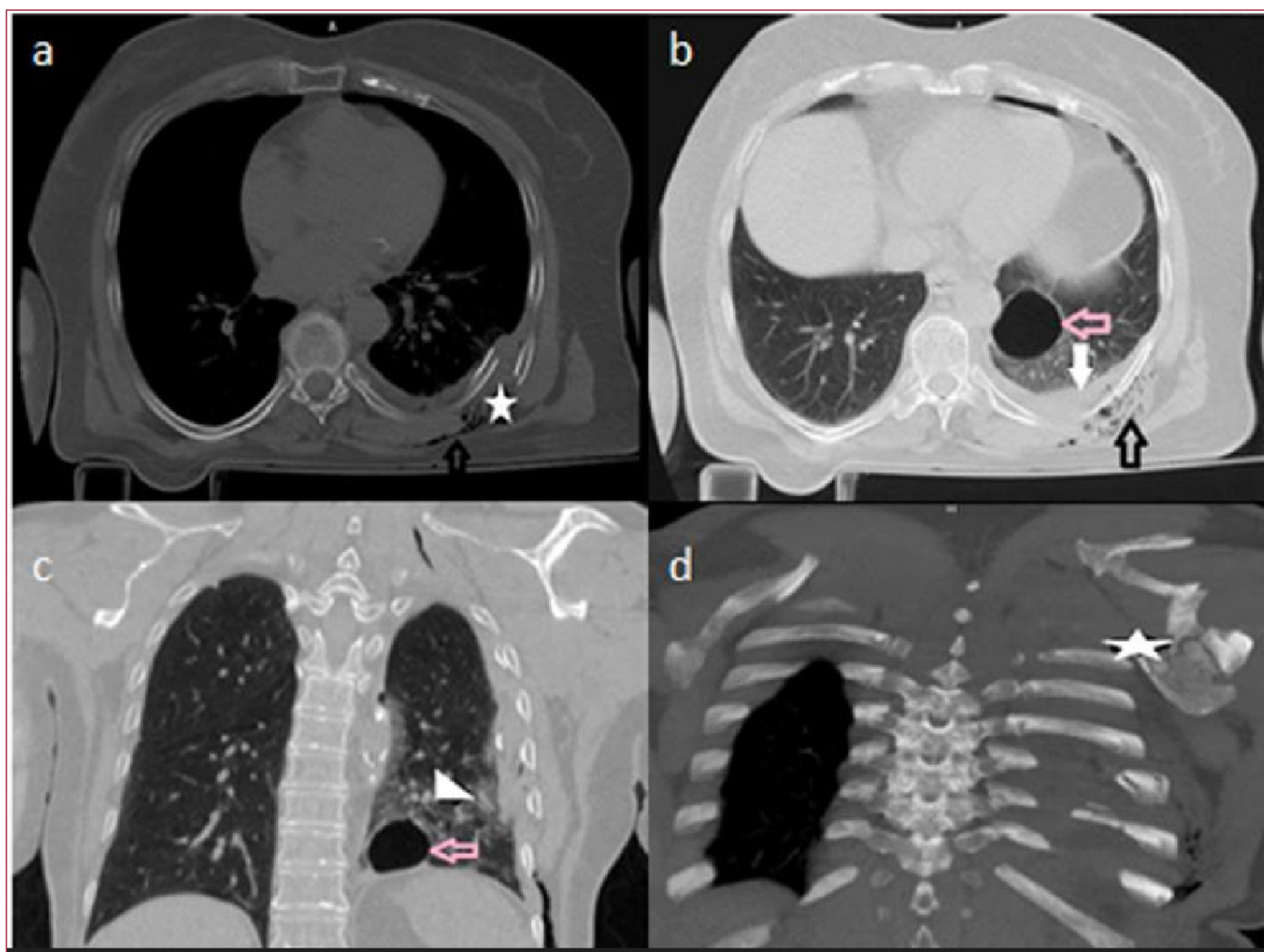


Figure 2. Sixty-seven advanced-age female patients with chest trauma. Multiple fracture (white asterisks) lines with displacement in the posterolateral ribs of the left hemithorax and accompanying hemothorax in the bone window in the axial plane: Hemothorax (white arrow), subcutaneous emphysema (black arrow), contusion (white triangle), and post-traumatic cyst (pink arrow) in (a) the axial and (b) the coronal planes, and (c) in the parenchymal window. Multiple displaced fracture (white asterisks) lines in the scapula on the bone window in the coronal plane (d).

and contusion in rib fractures localized on both sides in the coronal plane were significantly higher than those in rib fractures localized superiorly in the coronal plane ($p<0.001$, $p=0.001$, $p<0.001$, $p<0.001$, and $p<0.001$, respectively). These complications were recorded in association with rib fractures, although they may also arise from the overall thoracic trauma. The non-costal fractures in the rib fractures localized in the middle section in the coronal plane were observed to be significantly higher than those in the superiorly localized rib fractures in the coronal plane ($p<0.001$). The subcutaneous emphysema, pneumothorax, hemothorax, and contusion in the rib fractures localized on both sides in the coronal plane were also observed to be significantly higher than those in the inferiorly localized rib fractures in the coronal plane ($p<0.001$, $p<0.001$, $p<0.001$, and $p<0.001$, respectively).

The detailed statistical comparisons are summarized in

Table 4.

DISCUSSION

Rib fractures are one of the serious injuries, especially developing after traumas, and should be carefully evaluated in terms of their complications and outcomes. CT is already well established as the gold standard imaging modality for detecting rib fractures and their complications.^[6] Therefore, the main aim of our study was not to re-confirm the diagnostic superiority of CT, but rather to investigate the relationship between different fracture localizations (anterior, posterior, lateral, multiple) and fracture types (displaced and non-displaced) with their associated complications. Chest traumas are usually not isolated organ injuries, and systemic injuries can also be accompanied by chest traumas. For this reason, both the traumas and the symptoms led by the traumas should be carefully evaluated in patients presenting with traumas without focusing only on the systems.^[7] In our study, rib fractures were most frequently detected posteriorly in the axial plane, and such complications as contusion and

pneumothorax were most frequently seen in the fractures of this region. Direct force applied to the ribs leads to fractures and also damages adjacent tissues.^[8] As in our study, posteriorly localized fractures may be an important factor in intrathoracic injuries (**Figure 3**).

Therefore, thoracic CT may be required to evaluate lung injuries in patients with posterior fractures. In the present study, the most common complications after the contusions were detected as hemothorax and pneumothorax. Considering all rib fractures, similar to the findings reported in other studies, hemothorax and pneumothorax were most frequently detected in multiple fractures, upper and middle ribs, and displaced fractures, respectively.^[4] On the other hand, such complications are less common in lower rib fractures, and the accompanying complications with hemothorax and pneumothorax are rarely encountered. As in other studies, it was also considered in our study that the lower incidence of pneumothorax in lower rib fractures could be due to the anatomical structure of the lower ribs being more stable and that the significantly higher incidence of pneumothorax in displaced fractures might be due to the rupture of the pleural structure through the displaced rib.^[9] In our study, rib fractures were most frequently detected in the middle segment (5th-8th ribs) in the coronal plane in all age groups and both genders. In addition, the complication rate was also found to be high in this plane.^[10] Traumatic pulmonary pseudocysts (TPPs) are rarely encountered complications and the frequency of TPPs increases among males with advanced age. Blunt chest trauma and accompanying lung injuries are the most severe complications resulting from TTP. As in our study, TPPs are seen in most cases together with contusion and rib fractures.^[11,12] While the rate of TTP was detected to be approximately 7% among the patients presenting with blunt chest trauma in our study, the rate was reported as 8.3% in another study.^[13] However, in other studies, the rate of TTP was stated as 2 and 3%.^[14,15] TPP is a self-limiting condition not requiring specific treatment modalities.

Table 4. Statistical comparisons of rib fracture localizations, complications, and demographic parameters

Variable / Comparison	Test Used	Key Finding	p-value
Mean age (female vs. male)	Mann-Whitney U	Female patients significantly older than males	$p<0.001$
Age vs. displaced fracture	Mann-Whitney U	Displaced fractures increased with advanced age	$p=0.022$
Age vs. pneumomediastinum	Mann-Whitney U	Frequency increased with age	$p=0.013$
Age vs. post-traumatic cysts	Mann-Whitney U	Post-traumatic cysts increased with age	$p<0.001$
Gender vs. subcutaneous emphysema	Chi-square	More frequent in males	$p=0.018$
Gender vs. contusion	Chi-square	More frequent in males	$p=0.010$
Age vs. fracture localization (middle, bilateral ribs)	Kruskal-Wallis	More common at advanced ages	$p=0.002$, $p<0.001$
Lateral rib fractures vs. complications	Kruskal-Wallis	Higher complication rates vs. bilateral fractures	$p=0.003$ – <0.001
Anterior/posterior vs. bilateral fractures	Kruskal-Wallis	Higher pneumothorax & hemothorax	$p<0.001$
Posterior vs. anterior/bilateral fractures	Kruskal-Wallis	Higher contusion rate	$p=0.003$, $p=0.002$
Anterior vs. bilateral fractures	Kruskal-Wallis	Higher contusion rate	$p<0.001$
Superior vs. inferior rib fractures	Kruskal-Wallis	More displaced fractures in superior ribs	$p=0.01$
Bilateral fractures (coronal plane) vs. superior	Kruskal-Wallis	Higher displacement, emphysema, pneumothorax, hemothorax, contusion	$p<0.001$
Middle vs. superior rib fractures	Kruskal-Wallis	More non-costal fractures	$p<0.001$
Inferior vs. bilateral fractures (coronal)	Kruskal-Wallis	Bilateral fractures higher complications	$p<0.001$

Although the rate of TTP increased with advanced age in our study, another study reported that the rate was higher, and there were fewer fractured ribs in younger patients.^[13] In the study by Cho et al., the condition was referred to by asserting that intraparenchymal TPP is related to younger age and high-energy impact in the mid-rib region. We consider that the difference between our findings and those reported by Cho et al. was due to age-related parameters. In cases of intraparenchymal TPP, concomitant injuries should be evaluated and managed more meticulously. In our study, an increase in all complications was observed due to the increase in the incidence of rib fractures and the rate of non-displaced fractures with increasing age. Since the chest

wall is more elastic, and rib fractures occur only in higher energy situations in young patients than in the elderly, rib fractures may occur more easily in lower energy traumas in older patients due to osteoporosis.^[16] In our study, the mean age of female patients was significantly higher than that of male patients. This may be explained by the higher frequency of low-energy falls in elderly women and the role of postmenopausal osteoporosis and decreased bone mineral density, which increase susceptibility to fractures even after minor trauma. In contrast, rib fractures in younger males are more commonly associated with high-energy mechanisms such as traffic accidents, which they experience more frequently.

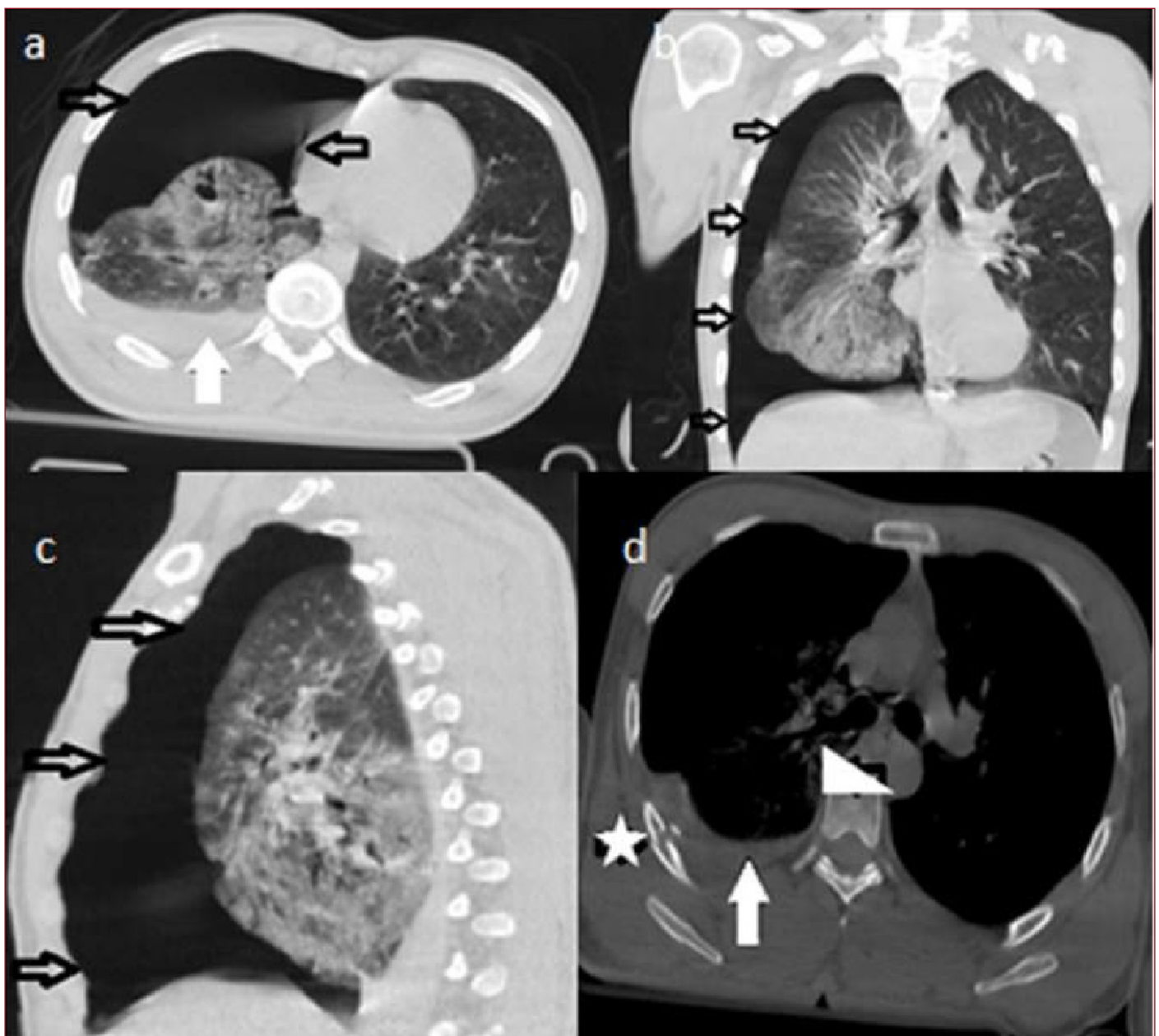


Figure 3. Twenty-five advanced-age male patients with chest trauma. Pneumothorax and hemothorax in the right hemithorax in the parenchymal window in the axial plane: (a) Pneumothorax (black arrow) in the right hemithorax in the parenchymal window in the coronal (b) and sagittal (c) planes. Displaced fracture line (white asteriks), hemothorax (white arrow), and contusion (white triangle) in the posterior rib in the right hemithorax in the bone window in the axial plane (d).

Therefore, both age- and gender-related biological differences as well as the underlying trauma mechanism should be considered in the evaluation of rib fracture complications. It should be emphasized that findings such as traumatic pulmonary pseudocysts, pulmonary contusions, and pneumomediastinum can also occur without rib fractures. In our study, they were considered as associated complications only when present together with rib fractures. It should also be noted that not all complications, such as pneumothorax, hemothorax, or contusion, can be attributed solely to rib fractures; these findings may also reflect the overall impact of thoracic trauma. A stronger association can be assumed in cases with displaced or parenchyma-penetrating fractures, or when accompanied by subcutaneous emphysema. In addition, our findings demonstrated that complication rates were significantly higher in laterally and posteriorly localized rib fractures. Posterior fractures were more commonly associated with lung contusion and pneumothorax, while lateral fractures showed higher rates of hemothorax and other complications. This demonstrates the added value of axial classification in identifying risk patterns.

Furthermore, displaced fractures were strongly associated with pneumothorax and hemothorax compared with non-displaced fractures, underlining the clinical importance of this distinction. Based on this result, during the initial assessment in the emergency department, the presence of such fracture patterns should be regarded as a strong indication for early thoracic CT to proactively screen for associated intrathoracic injuries. This approach may allow earlier detection of complications and contribute to more effective treatment planning. Since chest traumas have high mortality and morbidity rates, it is extremely significant to rapidly detect traumatic pathologies and initiate the best regime during the diagnosis and treatment phase of such traumas.^[17] The findings obtained in our study revealed that age and gender are the determinants of traumatic pathologies and that these criteria should be taken into consideration in the evaluation of thoracic trauma patients.

Limitations

However, there were various limitations in our study. First, due to the retrospective design of our study, auxiliary variables may have been overlooked. Secondly, the study was conducted in a single center, and the characteristics of patients with rib fractures may differ from one hospital or trauma center to another; thus, further multicentric studies are needed. As another limitation, the initial thoracic CT findings of patients were evaluated in the study, and no late-stage CT findings could be performed; delayed organ injuries due to blunt traumas may have occurred in the later period. Moreover, long-term follow-up data (such as the development of pneumothorax or hemothorax during days 3–7 after trauma), as well as additional clinical parameters

including comorbidities, anticoagulant use, mobilization status, and length of hospital stay, could not be evaluated. In addition, not all complications can be attributed exclusively to rib fractures, since thoracic trauma should be considered as a whole; findings such as pneumothorax, contusion, or pulmonary pseudocyst may also result from the overall trauma mechanism. These limitations should be considered when interpreting our results. In addition, complications may occur in both the acute and delayed phases of trauma, making it difficult to establish a direct causal link with rib fractures. Finally, chest radiographs were not included in the evaluation; however, in routine clinical practice in evaluating trauma patients, the first imaging method is radiographs, and then, CT should be considered, if necessary. In the study by Soltanpour et al., it is reported that this practice does not always change the treatment protocol of those with polytraumas.^[18] Nevertheless, among the characteristics of blunt trauma-induced rib fractures, including posterior rib fractures, lateral rib fractures, ≥ 3 rib fractures or the number of rib fractures, and displaced fractures and the need for O₂ support, are the factors indicating the need for chest CT to identify intrathoracic and intraabdominal injuries in the emergency departments and may assist physicians in making early decisions to perform chest CT in rib fracture patients in the emergency settings.^[6]

CONCLUSION

Chest CT plays a critical role in patients with rib fractures, both in terms of accurately determining the location of fractures and in detecting trauma-related complications. Our study demonstrated that complication rates were significantly higher in posterior and lateral rib fractures, and that displaced fractures were strongly associated with pneumothorax and hemothorax. We also observed that complication frequency increased with advancing age, and that the mean age of female patients was significantly higher than that of male patients. These findings suggest that age- and gender-related differences may have an impact on the clinical course of rib fractures. The use of CT in such patients, especially due to the high risk of complications in multiple and displaced fractures, has a positive effect on the diagnosis and treatment process. The detailed anatomical information provided by CT helps clinicians determine appropriate treatment strategies and minimize potential complications. Based on our study findings, we recommend that CT be included in clinical decision-making processes in the treatment of rib fractures.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Necmettin Erbakan University Non-pharmaceutical and Non-medical Device Research Ethics Committee (Date: 20.12.2024, Decision No: 2024/5415).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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