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Discovering associations between radiological features and COVID-19 patients' deterioration

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Abstract

Background and Aims: Data mining methods are effective and well-known tools for developing predictive models and extracting useful information from various data of patients. The present study aimed to predict the severity of patients with COVID-19 by applying the rule mining method using characteristics of medical images.

Methods: This retrospective study has analyzed the radiological data from 104 COVID-19 hospitalized patients diagnosed with COVID-19 in a hospital in Iran. A data set containing 75 binary features was generated. Apriori method is utilized for association rule mining on this data set. Only rules with confidence equal to one were generated. The performance of rules is calculated by support, coverage, and lift indexes.

Results: Ten rules were extracted with only X-ray-related features on cases referred to ICU. The Support and Coverage index of all of these rules was 0.087, and the Lift index of them was 1.58. Thirteen rules were extracted from only CT scan-related features on cases referred to ICU. The CXR_Pleural effusion feature has appeared in all the rules. The CXR_Left upper zone feature appears in 9 rules out of 10. The Support and Coverage index of all rules was 0.15, and the Lift index of all rules was 1.63. the CT_Adjacent pleura thickening feature has appeared in all rules, and the CT_Right middle lobe appeared in 9 rules out of 13.

Conclusion: This study could reveal the application and efficacy of CXR and CT scan imaging modalities in predicting ICU admission to a major COVID-19 infection via data mining methods. The findings of this study could help data scientists, radiologists, and clinicians in the future development and implementation of these methods in similar conditions and timely and appropriately save patients from adverse disease outcomes.

KEYWORDS
association rule mining, COVID-19, chest images, data mining, frequent patterns

1 | INTRODUCTION

According to the World health organization (WHO) statistics, due to the COVID-19 outbreak, about 528,816,317 confirmed cases and 6,294,969 deaths have been reported.[1] Many studies were conducted regarding diagnosis,[2,3] treatment,[4,5] prevention,[6] prognosis,[7] and vaccine production[4,8] of COVID-19 disease. Various diagnostic methods have been introduced to control the disease, and also many studies have been conducted to evaluate the effectiveness of these methods. Reverse transcription-polymerase chain reaction (RT-PCR) test,[9] chest CT scan and chest X-ray (CXR)[10] were used to diagnose the COVID-19 disease. However, due to the importance of pulmonary manifestations[11] as well as the appearance of false positive and false negative results in RT-PCR tests, the use of medical images has received more attention.[12] Also,[13] has shown that many research have used X-ray and CT scan methods to diagnose and predict the severity of the disease of Covid-19 to calculate the severity score of the disease based on the lung involvement.

According to studies, the COVID-19 disease in patients may be asymptomatic or symptomatic.[14] Also, COVID-19 severity could be in the range of mild to severe, and in some cases, it might progress from mild to severe and even lead to the patient's death. This requires different approaches to care and treatment depending on the disease severity[15–18] showed that about 20% of patients enter a severe stage after a mild course of the disease and experience symptoms such as pulmonary edema, septic shock, and acute respiratory distress. Therefore, determining and predicting the severity of the disease is vital. In[14] pointed out the importance of predicting the COVID-19 severity and considered it an essential way to prioritize patients and provide timely and appropriate services to those patients whose condition is likely to worsen. Incorrect diagnosis of the disease severity could lead to either inadequate medical services for patients in need, and their condition worsens, or provide unnecessary interventions for those patients whose disease is not severe.[19] On the other hand, due to the lack of resources and beds in intensive care units (ICU) and hospitals, predicting the severity of the disease could be effective in better managing and allocating hospital resources.[14,20]

Artificial intelligence (AI), machine learning (ML), and data mining (DM) methods have played an important role in coronavirus research.[16,21,22] According to studies, these methods are effective and well-known tools for developing predictive and data analysis models and extracting useful information from the available data set[23,24] applied the Support Vector Machine (SVM) technique to demographic, clinical, and laboratory data of patients with COVID-19 to predict their ICU admission, mortality rate, and length of hospital stay. Also,[25] used laboratory data sets to predict the intensity of COVID-19 using data mining techniques.

Association rule mining is one of the major data mining technique used to find the most frequent items appearing together in a data set.[26] In medicine this technique could be used to identify the association between diseases.[27] This technique is used to discover symptom patterns of COVID-19.[27]

These studies provided characteristics to predict the condition of patients and compare these characteristics in severe and non-severe groups. Moreover,[23] used data mining techniques to predict the mortality of COVID-19 patients based on predetermined factors and patients' records.

Also, some studies have used CXR and chest CT scan images to predict the deterioration of COVID-19 disease using machine learning methods. Irmak[28] used the convolutional neural networks (CNN) to assess the severity of COVID-19 disease based on CXR images. Also, some studies,[17,29,30] have been used chest CT images to identify and predict the deterioration of COVID-19 using various deep learning techniques.

However, these studies considered only one group of images or made their predictions based on images and not the interpretation of experts extracted from them. On the other hand, most studies that have predicted the severity of COVID-19 by data mining methods used clinical and laboratory data. Some studies[14,17] suggested that medical images are more accurate and sensitive than laboratory methods and can show the severity of the disease more accurately. Chest CT is used in China as an essential tool to assess the severity of COVID-19.[30] Therefore, proposing a model that uses radiological characteristics extracted from CXR and chest CT images by utilizing data mining and rule mining methods for predicting the disease severity and recognizing the need to refer to ICU could be helpful. This study aimed to predict the severity of patients with COVID-19 by applying the rule mining method using radiological characteristics of CXR and chest CT scan images.

2 | METHODS

2.1 | Data set

This retrospective study has analyzed the radiological data from COVID-19 patients. Data were extracted from the CXR reports and chest CT scans of the patients admitted to the Imam Khomeini hospital, Tehran, Iran, from March 2020 to July 2020. Imam Khomeini hospital's institutional ethics committee review boards, Tehran University of Medical Sciences, approved the study.

Overall, 104 hospitalized patients were diagnosed with COVID-19 in Imam Khomeini Hospital Complex, Tehran, Iran. More than half of the patients were male (Male:61, Female:43) and the mean age of patients was 55.84 years (range 20–93). The diagnosis of COVID-19 was confirmed by polymerase chain reaction (PCR) test. All 104 patients underwent CXR, and 78 of them also took chest CT scans at the time of admission to the hospital or during hospitalization. Two expert radiologists thoroughly assessed all chest images to confirm signs and patterns of COVID-19 in the imaging of patients. Then, the radiological features were reported, and a data set containing 75 binary features was gathered. The radiological features are listed in Table 1.

TABLE 1 Radiological features.

Feature	Values frequency
Chest CT scan features	
CT_Left upper lobe	True:67, False:11
CT_Left lower lobe	True:68, False:10
CT_Right upper lobe	True:69, False:9
CT_Right middle lobe	True:62, False:16
CT_Right lower lobe	True:72, False:6
CT_Central and peripheral	True:61, False:17
CT_Peripheral	True:72, False:6
CT_Peribronchovascular	True:26, False:52
CT_Central	True:63, False:15
CT_Subpleural pairing	True:0, False:78
CT_Anterior	True:70, False:4, Missing:4
CT_Posterior	True:71, False:3, Missing:4
CT_Patchy to confluent	True:74, False:1, Missing:3
CT_Nodular	True:14, False:61, Missing:3
CT_Reticular	True:9, False:65, Missing:4
CT_Elongated	True:40, False:38
CT_Round	True:20, False:58
CT_Wedged	True:51, False:27
CT_Confluent	True:44, False:34
CT_Mixed ground glass and consolidation	True:58, False:20
CT_Ground glass opacification	True:73, False:5
CT_Consolidation	True:60, False:18
CT_Crazy paving pattern	True:20, False:58
CT_Reverse halo	True:2, False:76
CT_Margin	True:76, False:0, Missing:2
CT_Interlobular septal thickening	True:15, False:63
CT_Air bronchogram sign	True:47, False:31
CT_Linear opacities combined	True:4, False:74
CT_Tree in bud	True:4, False:74
CT_Pentorex	True:2, False:76
CT_Other signs lesion	True:5, False:73
CT_Adjacent pleura thickening	True:14, False:64
CT_Pleural effusion	True:20, False:58
CT_Lymphadenopathy	True:3, False:75
CT_Pulmonary emphysema	True:1, False:77
CT_Pneumothorax pneumoperitoneum	True:1, False:77

TABLE 1 (Continued)

Feature	Values frequency
Chest X-ray features	
CXR_Left upper zone	True:41, False:59, Missing:4
CXR_Left lower zone	True:87, False:13, Missing:4
CXR_Right upper zone	True:57, False:43, Missing:4
CXR_Right lower zone	True:86, False:14, Missing:4
CXR_Central	True:79, False:21, Missing:4
CXR_Peripheral	True:92, False:8, Missing:4
CXR_Reticular	True:4, False:93, Missing:7
CXR_Nodular	True:7, False:90, Missing:7
CXR_Patchy to confluent	True:90, False:8, Missing:6
CXR_Wedged	True:11, False:79, Missing:14
CXR_Elongated	True:7, False:82, Missing:15
CXR_Confluent	True:53, False:37, Missing:14
CXR_Round	True:11, False:79, Missing:14
CXR_Mixed ground glass and consolidation	True:62, False:33, Missing:9
CXR_Consolidation	True:68, False:27, Missing:9
CXR_Ground glass opacification	True:85, False:10, Missing:9
CXR_Margin	True:98, False:0, Missing:6
CXR_Air bronchogram sign	True:57, False:47
CXR_Linear opacities combined	True:3, False:101
CXR_Other signs in the lesion	True:3, False:101
CXR_Pleural effusion	True:14, False:90
CXR_Cardiomegaly	True:4, False:100
Target feature	
ICU	True:66 in X-ray data set, 48 in CT data set, False:38 in X-ray data set, 30 in CT data set

Abbreviations: CXR, chest X-ray; ICU, intensive care unit.

2.2 | Association rule mining

we used association rule mining technique to find the factors related to a disease or condition. For example, in our data set, we used this technique to find factors associated with *referral to ICU*. We used this technique to create *if* → *then* rules representing the antecedent (if) and consequent (then). In our case, the latter shows *referral to ICU*, and the former shows the conditions examined from X-ray and CT scan images. Apriori is an implementation method for Association rule mining. We have used RStudio 2021.09.2 Build 382 (R version

4.1.2) to apply the Apriori algorithm to the data set to extract rules related to ICU referral. We conducted the experiment in two phases listed below:

- Association rule mining with only X-ray-related features on cases referred to ICU
- Association rule mining with only CT scan-related features on cases referred to ICU

Multiple measures could be used for the evaluation of these rules. Support, Confidence, and Lift are the most used indexes for evaluating these rules. They are defined as below in our context:

$$\text{Support (X}\rightarrow\text{Referral to ICU)} = \frac{\text{Cases having X and referred to ICU}}{\text{Total number of cases}}.$$

$$\text{Confidence (X}\rightarrow\text{Referral to ICU)} = \frac{\text{Cases having X and referred to ICU}}{\text{Cases having X}}.$$

$$\text{Lift (X}\rightarrow\text{Referral to ICU)} = \frac{\text{(Cases having X and referred to ICU)/(Cases having X)}}{\text{Total number of cases}}.$$

Value of Lift represents the correlation between X and Referral to ICU. If the Lift of a rule equals one, X is independent of referral to ICU. If its value is greater than one, it shows a positive relationship between X and ICU referral. And if its value is lower than one, it shows a negative relation between X and the referral to ICU.

Also, the Coverage index represents the relative frequency of cases that have the antecedent part is defined as below:

$$\text{Coverage (X}\rightarrow\text{Referral to ICU)} = \frac{\text{Cases having X}}{\text{Total number of cases}}.$$

The possible rules generated are enormous. Thus, we limited the rules with the following conditions:

1. Rules with confidence equal to one (showing rules that are always true for cases referred to ICU).
2. The items in the antecedent part of the rules are less than four (this value is chosen because of including only valuable factors in generated rules).
3. The rules having maximum support value.

3 | RESULTS

3.1 | Association rule mining with only X-ray-related features on cases referred to ICU

The rules extracted on cases with only X-ray-related features in cases referred to ICU are tabulated in Table 2. The Support and Coverage index of all rules is equal to 0.087, and the Lift index of all rules is equal to 1.58. The CXR_Pleural effusion feature has appeared in all the rules. The CXR_Left upper zone feature appears in 9 rules out of 10.

3.2 | Association rule mining with only CT scan-related features on cases referred to ICU

The rules extracted on cases with only CT scan-related features in cases referred to ICU are tabulated in Table 3. The Support and Coverage index of all rules is equal to 0.15, and the Lift index of all rules is equal to 1.63. the CT_Adjacent pleura thickening feature has appeared in all rules, and the CT_Right middle lobe appeared in 9 rules out of 13.

3.3 | Limitations

This study had some limitations. One of the limitations was the small number of samples used to draw features to import into the rule

TABLE 2 Extracted rules with only X-ray-related features on cases referred to ICU.

	Rules
1	CXR_Left upper zone, CXR_Pleural effusion => ICU
2	CXR_Left upper zone, CXR_Pleural effusion, CXR_Central => ICU
3	CXR_Left upper zone, CXR_Pleural effusion, CXR_Ground glass opacification => ICU
4	CXR_Left upper zone, CXR_Pleural effusion, CXR_Left lower zone => ICU
5	CXR_Left upper zone, CXR_Pleural effusion, CXR_Right lower zone => ICU
6	CXR_Left upper zone, CXR_Pleural effusion, CXR_Patchy to confluent => ICU
7	CXR_Left upper zone, CXR_Pleural effusion, CXR_Peripheral => ICU
8	CXR_Left upper zone, CXR_Pleural effusion, CXR_Margin => ICU
9	CXR_Central, CXR_Pleural effusion, CXR_Peripheral => ICU
10	CXR_Left lower zone, CXR_Pleural effusion, CXR_Peripheral => ICU

Abbreviations: CXR, chest X-ray; ICU, intensive care unit.

TABLE 3 Extracted rules with only CT scan-related features on cases referred to ICU.

	Rules
1	CT_Right middle lobe, CT_Adjacent pleura thickening => ICU
2	CT_Right middle lobe, CT_Adjacent pleura thickening, CT_Peripheral => ICU
3	CT_Right middle lobe, CT_Adjacent pleura thickening, CT_Right lower lobe => ICU
4	CT_Right middle lobe, CT_Adjacent pleura thickening, CT_Ground glass opacification => ICU
5	CT_Right middle lobe, CT_Adjacent pleura thickening, CT_Patchy to confluent => ICU
6	CT_Right middle lobe, CT_Adjacent pleura thickening, CT_Margin => ICU
7	CT_Right middle lobe, CT_Adjacent pleura thickening, CT_Right upper lobe => ICU
8	CT_Right middle lobe, CT_Adjacent pleura thickening, CT_Left upper lobe => ICU
9	CT_Right middle lobe, CT_Adjacent pleura thickening, CT_Left lower lobe => ICU
10	CT_Right upper lobe, CT_Adjacent pleura thickening, CT_Left lower lobe => ICU
11	CT_Right lower lobe, CT_Adjacent pleura thickening, CT_Left lower lobe => ICU
12	CT_Left lower lobe, CT_Adjacent pleura thickening, CT_Left upper lobe => ICU
13	CT_Left lower lobe, CT_Adjacent pleura thickening, CT_Patchy to confluent => ICU

Abbreviation: ICU, intensive care unit.

mining analysis. The other limitation of this study was the limitations of the association rule mining method and the absence of more robust AI features and tools in generating study results. Also, including only one disease outcome was the other limitation of this study. Despite these limitations, this study successfully showed the role of data-driven form imaging modalities in predicting COVID-19 outcomes and provided evidence on the utilization of association rule mining in interpreting imaging data.

4 | DISCUSSION

This study aimed to investigate the role of radiological features extracted and reported from CXR and chest CT scan in predicting ICU admission by association rule mining. The main findings of this study were the efficacy of imaging markers in the prediction of worse clinical conditions in terms of ICU admission and the better function of data derived by CT scan in this investigation.

Digital imaging modalities and artificial intelligence applications have been extensively used in the COVID-19 diagnosis in the past 2 years.[31] A systematic review found that digital intervention during the recent pandemic enhanced the response to the disease, highlighted the role of medical imaging, and provided the healthcare force to handle the patients with lesser contact and more accurate diagnosis.[31] Regarding the medical image processing in the process of COVID-19 diagnosis, four main steps are required, including image preprocessing and augmentation, feature extraction, feature selection, and classification of the findings.[32] Therefore, each step needs to be correctly implemented to make the proper use of digital and imaging techniques in the diagnosis of this disease.

Association rule mining is one of the AI-powered data mining approaches vastly used in the analysis of medical data sets and imaging in the past two decades.[33] During the COVID-19 pandemic, this method was mainly used to analyze the text data in various studies and explorations. One study utilized association rule mining to discover frequent word sets and generate rules and inferences through Twitter data.[34] Another study used this approach to perform descriptive data mining to understand the impacts of various nonpharmaceutical interventions in controlling the COVID-19 infection rate in the United States.[35] One study could implement COVID-19 diagnosis and treatment data mining via association rules on infected patients' various demographic, clinical, and laboratory data.[36] A previous study could discover symptom patterns in COVID-19 patients using the association rule mining, and it was successful in reporting the most frequent symptoms of this disease.[27] Although this method is widely used on the COVID-19 data, its application on radiological data is rare, making the comparison of the current study results with similar evidence difficult.

One of the strengths of this study was the comparison of the association rule mining analyses on two imaging modalities to make a deeper evaluation of these methods possible. Various studies implemented AI approaches on imaging findings to improve the diagnosis of COVID-19.[37,38] CXR was extensively used in the literature due to its wide availability and application in the detection of COVID-19.[39] Texture feature analysis by machine learning classification methods was one of the methods that could accurately classify the levels of COVID-19 infection.[40] In a further expansion of these methods, deep learning was the dominant method in the exploration of X-ray imaging obtained from suspected patients with this disease.[21,41–43] However, one study used a combination of deep and machine learning models for COVID-19 diagnosis in CXR images, and a higher classification accuracy and effective diagnostic performance by this combination.[44]

This study was successful in proposing overall 10 rules for chest X-ray and 13 rules for prediction of ICU admission among patients diagnosed with COVID-19. The patterns of pulmonary parenchyma involvement summarized in these rules were much more comprehensive and robust than other studies in the field, since the current study benefits a strong methodology utilizing the association rule mining. Some previous studies tried to investigate the radiologic markers predicting severe COVID-19 course and ICU admission. One study developed a CT severity score based on a logistic regression model and showed that patients with scores >8 had more than three-fold risk of ICU admission, intubation, and mortality.[45] Another study found that lung involvement >50% was associated with early death or ICU admission.[46] Similar study also was done on findings of chest X-ray and higher extent of alveolar opacities was correlated with mortality and hospitalization rates.[47] Finally, one study compared the features of X-ray and CT for outcome prediction in hospitalized patients with COVID-19 and found that at admission, the prognostic value of CT was not superior to the value of X-ray.[48]

Considering the lower sensitivity of X-ray images, further evaluation with a chest CT scan was proposed for COVID-19 diagnosis.[49] This pattern also happened in the application of AI methods in the investigation of COVID-19 related imaging data, and CT generated data was available for machine and deep learning models.[50] One study using CT scan imaging for machine learning techniques in the detection of COVID-19 found an accuracy of 91% for the classification of this disease. It proved the efficacy of this modality in the management of COVID-19.[51]

Although the AI-powered tools were helpful in the diagnosis and management of COVID-19 patients and they had high application value in disease diagnosis, especially through the imaging and big data collections,[5,52] some questions and challenges were also raised in the application of these methods for scientists.[37] One of these concerns was the clinical relevance of AI solutions and the discrepancy between the findings and methods of these approaches with real-world patient data.[53] One recent systematic review of numerous studies conducted by the use of machine learning for the diagnosis of COVID-19 found many methodological flaws and underlying biases in these studies that compromise the clinical validity and implication of these methods. It recommended some ideas to develop higher-quality AI models in clinical investigations like the COVID-19 situation.

5 | CONCLUSION

This study could reveal the application and efficacy of CXR and CT scan imaging modalities in predicting ICU admission to a major COVID-19 infection via data mining methods. The findings of this study could help data scientists, radiologists, and clinicians in future development and implementation of these methods in similar conditions and timely and appropriately save patients from adverse disease outcomes.

AUTHOR CONTRIBUTIONS

Nasrin Ahmadinejad: Conceptualization; data curation; investigation; methodology; project administration; resources; supervision; validation; writing—review & editing. **Seyed Mohammad Ayyoubzadeh**: Data curation; formal analysis; investigation; methodology; software; validation; visualization; writing—original draft; writing—review & editing. **Fahimeh Zeinalkhani**: Data curation; investigation; project administration; validation; writing—review & editing. **Sina Delazar**: Investigation; writing—original draft; writing—review & editing. **Zohreh Javanmard**: Investigation; writing—original draft; writing—review & editing. **Zahra Ahmadinejad**: Data curation; investigation; validation; writing—review & editing. **Amirhassan Mohajeri**: Investigation; validation; writing—review & editing. **Marzieh Esmaeili**: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; software; supervision; validation; writing—original draft; writing—review & editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

TRANSPARENCY STATEMENT

The lead author Marzieh Esmaeili affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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