Original Article

Prediction of ipsilateral and contralateral pneumothorax using a simple chest X-ray

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Background: Accurate prediction is essential for the effective management of spontaneous pneumothorax (SP). To improve prediction, this study primarily focuses on using simple chest X-rays to predict ipsilateral recurrence and contralateral occurrence of SP.

Methods: All consecutive subjects diagnosed with SP from July 2017 to June 2023 were retrospectively reviewed. Ipsilateral recurrence and contralateral occurrence of SP within two years of completing treatment were analyzed. Using simple chest X-rays and clinical parameters such as age, sex, smoking, chronic obstructive pulmonary disease (COPD) and surgery, machine learning algorithms were applied to predict SP development. Gradient-weighted Class Activation Mapping (Grad-CAM) was used to highlight the X-ray regions associated with SP development.

Results: The study included 1,086 cases of SP, with 546 right-side and 540 left-side developments. Surgeries were performed in 243 right and 204 left cases. Ipsilateral recurrence occurred in 93 cases total, while contralateral occurrence occurred in 60 right and 34 left cases. For predicting ipsilateral recurrence in the young group, gradient boosting (GB) [area under curve (AUC) of 0.686, accuracy of 0.769, F1 score of 0.733, precision of 0.706, and recall of 0.769] for the right side and logistic regression (AUC of 0.628, accuracy of 0.781, F1 score of 0.753, precision of 0.737, and recall of 0.781) for the left side were the top-performing models. In the older group, K-nearest neighbors (KNN) (AUC of 0.615, accuracy of 0.801, F1 score of 0.760, precision of 0.735, and recall of 0.801) for the right side and logistic regression (AUC of 0.623, accuracy of 0.824, F1 score of 0.804, precision of 0.794, and recall of 0.824) for the left side were the best models. For predicting contralateral occurrence in the young group, random forest (RF) (AUC of 0.597, accuracy of 0.774, F1 score of 0.741, precision of 0.709, and recall of 0.774) for the right side and KNN (AUC of 0.650, accuracy of 0.893, F1 score of 0.849, precision of 0.809, and recall of 0.893) for the left side were the most effective models. In the older group, logistic regression (AUC of 0.630, accuracy of 0.935, F1 score of 0.914, precision of 0.894, and recall of 0.935) for the right side and neural network (NN) (AUC of 0.765, accuracy of 0.961, F1 score of 0.948, precision of 0.936, and recall of 0.961) for the left side were the top performers. Grad-CAM analysis revealed that apical lung portions were strongly associated with both ipsilateral recurrence and contralateral occurrence of SP.

Conclusions: The results of this study suggest that machine learning algorithms using simple X-rays and basic clinical data can predict SP development with fair performance. The apical regions of the lung were strongly associated with SP development, consistent with clinical knowledge.

Keywords: Prediction; machine learning; spontaneous pneumothorax (SP); chest X-ray

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Introduction

Pneumothorax refers to the presence of air in the pleural cavity (1). This air accumulation causes the lung on the affected side to collapse, leading to chest pain and dyspnea (1,2). Spontaneous pneumothorax (SP) can be classified into primary and secondary types, each with varying causes and treatment approaches (1,2). Key issues in the management of SP include ipsilateral recurrence and contralateral occurrence (3,4). SP recurrence rate varies widely based on the type and patient characteristics (1,5). In primary SP, the recurrence rate is reportedly between 20% and 50% within the first year after the initial incident (6,7). In secondary SP, which affects individuals with preexisting lung conditions such as chronic obstructive pulmonary disease (COPD), a higher recurrence rate is reported, often ranging from 40% to 80% (1,6). The risks of recurrence have been investigated in previous studies that mostly included similar variables and surgical outcomes (8,9); however, few novel predictive factors or tools have been proposed (6,10). The most significant independent predictive factor for SP recurrence is failure to identify and resect blebs or bullae during the surgical procedure, with a recurrence rate of 5% after surgery (5,6,11-13). In addition, contralateral recurrence of SP after unilateral surgery has been reported in several studies, with recurrence rates ranging from 18% to 50% (4,6,14). This variation highlights the need for more accurate prediction methods and strategies to effectively manage both ipsilateral recurrence and contralateral occurrences in clinical practice (4,12). The clinical features of SP and the risk factors associated with ipsilateral recurrence have been described (9,11). However, the prevention and prediction of contralateral occurrence in patients with SP has not been specifically discussed (4,14-17). The risk factors associated with contralateral occurrence of SP also remain unclear (11,15-18). Historically, chest computed tomography (CT) scans have been the primary tool for studying the development of SP (5,7,11). However, despite being fundamental to SP diagnosis, chest X-rays have not been widely utilized for research in this area (7,10,12,19). Therefore, we aimed to investigate the efficacy of a simple chest X-ray in predicting the ipsilateral recurrence and contralateral occurrence of SP for the first time. We present this article in accordance with the TRIPOD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1729/rc).

Highlight box

Key findings

- Machine learning models using chest X-rays showed fair performance in predicting both ipsilateral recurrence and contralateral development of spontaneous pneumothorax (SP), although further validation is needed.

What is known and what is new?

- The apical portions of the lung are strongly associated with the development of SP, based on clinical observations.
- This is the first study to utilize machine learning algorithms with chest X-rays to provide a potential tool for predicting both ipsilateral recurrence and contralateral occurrence of SP, offering a new approach for clinical decision-making in SP management.

What is the implication, and what should change now?

- Machine learning tools may assist in surgical decision-making and improve patient care by providing more accurate predictions.

Methods

All consecutive subjects who underwent treatment for SP at Uijeongbu Saint Mary's Hospital from July 2017 to June 2023 were retrospectively reviewed. SP was managed by oxygen therapy, closed thoracostomy drainage with or without pleurodesis, or thoracoscopic surgery (1,7). Subjects included in the present study had to have either primary or secondary SP without concurrent bilateral SP. In addition, participants could not have any underlying lung conditions such as primary or metastatic lung cancer, catamenial pneumothorax, tuberculous-destroyed lung, coronavirus disease 2019 (COVID-19) infection or traumatic pneumothorax (1). A simple posteroanterior chest X-ray was obtained and documented during the last outpatient follow-up visit after completing treatment for the initial SP episode. Chest CT scans were routinely performed during hospitalization to assist in selecting appropriate management options (7). Recurrence, defined as the reappearance of SP after completing treatment, was specifically identified as the development of ipsilateral SP following the initial episode (20). Contralateral pneumothorax was defined as the occurrence of SP on the opposite side after the completion of treatment for SP (4). The follow-up period was limited to two years after the completion of treatment for ipsilateral SP to reduce time-relative effects (1,3). Examining the peri-management data for SP, the parameters assumed to be associated with development of SP after completion of treatment of pneumothorax were age at the first episode, sex, COPD, smoking, and management options (non-surgical *vs.* surgical) (2,8,9). Current or history of smoking was regarded as a risk factor for development of SP. We collected and analyzed data for these clinical parameters during SP treatment. Surgical indications for SP typically include the presence of clearly visible bullae on imaging studies, persistent air leaks lasting more than 5 days, massive air leaks, recurrent SP, clinically significant hemopneumothorax, tension pneumothorax, high-risk occupations, and simultaneous bilateral SP (7,11,12). All surgeries were performed via thoracoscopic methods.

There are currently no definitive tools available for predicting recurrent or contralateral SP despite the identification of certain risk factors and the reporting of overall recurrence rates (6,10). In this study, we addressed the issues first by analyzing statistics associated with ipsilateral recurrence and contralateral occurrence of SP. Next, we applied machine learning algorithms using simple chest X-ray images to predict such developments, conducting all analyses according to age (teenagers *vs.* adults) of young and older groups. Finally, we investigated specific portions of the X-rays associated with SP development.

Statistical analysis

All data were expressed as mean ± standard deviation (SD). Group comparisons were conducted using Student's *t*-test. Chi-square tests were used to evaluate the independence of categorical variables. To identify independent influencing factors, binary logistic regression (LR) with a backward stepwise method was applied. Statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA), and a P value <0.05 was considered statistically significant.

Machine learning algorithms

Machine learning is particularly effective in image analysis, excelling at classification and prediction tasks (21,22). When using advanced algorithms, machine learning can recognize patterns, extract key features, and accurately categorize images (21,22). This capability allows machine learning models to make informed predictions from visual data, enhancing efficiency and precision in fields such as medical imaging and object recognition (21,22). Therefore, we used machine learning analyses to predict ipsilateral recurrence and contralateral occurrence of SP using simple chest X-ray images. Machine learning analyses were performed using Orange® data mining program (version 3.37), an open-source toolkit designed for data mining and machine learning, developed by the Bioinformatics Lab at the University of Ljubljana (22). The program offers a user-friendly visual programming interface as well as Python scripting for more advanced users (22). In the present study, the model learning process utilized both training and validation sets, with 10-fold stratified cross-validation applied for the training and validation phases. Inception v3 was used by the image embedder as a deep learning model within the Inception family of architectures, designed for image classification and feature extraction (21,22). In the context of Orange® data mining, Inception v3 can be utilized as a pre-trained convolutional neural network (NN) to analyze and interpret image data for various applications (22). The performance of each model was assessed and evaluated using several metrics, including the area under the curve (AUC), accuracy, precision, F1 score, and recall. The model that demonstrated the best performance was chosen based on AUC, a metric used to evaluate how well a model distinguishes between classes.

Five machine learning algorithms were utilized for prediction: gradient boosting (GB), LR, K-nearest neighbors (KNN), random forest (RF), and NN. The GB model used 100 trees, a 0.100 learning rate, a max tree depth of three, and two samples per split. The LR model applied Ridge (L2) regularization with C=1. The KNN model had five neighbors and used Euclidean distance and uniform weights. The RF model used 10 trees with a minimum split size of five. The NN model had hidden layers of 100, 50, and 20 neurons with rectified linear unit activation and Adam optimization (α=0.0001, 200 iterations).

In addition, we employed Gradient-weighted Class Activation Mapping (Grad-CAM) to visualize the decision-making process of a deep learning model predicting SP development from chest X-ray images. We fine-tuned a pre-trained ResNet50 model for binary classification. By applying Grad-CAM, we generated heatmaps that highlighted the regions in the images most influential to the model's predictions. This visualization demonstrated that

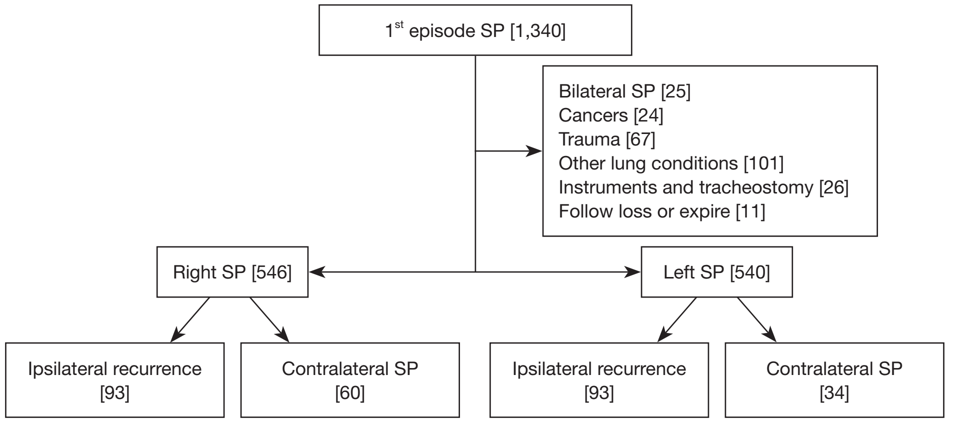

Figure 1 The flowchart represents a breakdown of patients experiencing their first episode of SP. SP, spontaneous pneumothorax.

the model focused on clinically relevant areas of the lungs, enhancing the interpretability and potential clinical utility of our predictive model (21-23). Google Colab® was used to implement Grad-CAM in the present study. Google Colab® is a cloud-based platform that allows users to write and execute Python code within a browser-based notebook and is commonly utilized for data science and machine learning tasks due to its free access to high-performance resources such as graphics processing units and tensor processing units (24).

Ethical statement

The requirement for informed consent was waived due to the retrospective design of the study, which did not disclose patient information. The study was reviewed and approved by the Ethics Committee of Uijeongbu Saint Mary's Hospital (No. UC24RISI0106). We affirm that this study adhered to the ethical principles outlined in the Declaration of Helsinki (as revised in 2013).

Results

Cases of right pneumothorax [546] and left pneumothorax [540] among 1,086 consecutive patients were included in the present study (*Figure 1*). The mean age at the first episode of subjects with right SP was 36.6±20.5 years, and that of those with left SP was 32.1±20.0 years. The mean intervals of ipsilateral recurrence and contralateral occurrence and mean period of observation were 8.0±7.7, 12.4±5.66, and 15.66±10.28 months for the right side and 8.8±6.5, 7.9±7.0, and 16.1±9.9 months for the left side, respectively. The study included 983 males and 103 females. Surgeries at the first episode consisted of 243 cases on the right side and 204 cases on the left side. Ipsilateral recurrence occurred in 93 cases on each side, and contralateral occurrence developed in 60 cases on the right side and 34 cases on the left side. The general clinical profiles of the study participants are presented in *Table 1*.

Risk factors for ipsilateral recurrence and contralateral occurrence

Previously reported parameters associated with development of pneumothorax include age at the first episode, sex, COPD, smoking, and management options (non-surgical *vs.* surgical) (1,5,8). In the present study, univariate analysis with these factors showed that surgery was the only independent influencing factor for ipsilateral recurrence (*Table 1*). In addition, univariate analysis showed that age, surgery, and COPD were associated with contralateral occurrence of pneumothorax (*Table 1*). Multivariate analysis showed that age, surgery, and COPD were also associated with contralateral occurrence of pneumothorax (*Table 2*).

Prediction of ipsilateral recurrence and contralateral occurrence of SP using machine learning models

Age at the first episode, sex, smoking history, COPD, and surgery were regarded as covariates in the machine learning algorithms. In Orange®, the data from these parameters were merged with X-ray image data, and the five machine learning algorithms were used to predict ipsilateral recurrence and contralateral occurrence of SP. The best model was that with the highest AUC. All predictions were conducted based on age groups, with separate models tailored to younger and older cohorts to ensure age-specific

Table 1 The general clinical profiles of the study participants

Variables	Ipsilateral recurrence			Contralateral occurrence		
	NRG (n=900)	RG (n=186)	P value	NOG (n=992)	OG (n=94)	P value
Age (years)	34.2±20.0	35.0±22.3	0.66	35.4±20.6	23.7±14.1	<0.001
Sex (male)	818	165	0.41	897	86	0.86
Smoking	643	128	0.48	712	59	0.07
Surgery	419	28	<0.001	387	60	<0.001
COPD	214	50	0.40	258	8	<0.001

Values are presented as mean ± standard deviation for continuous variables and as numbers for categorical variables. NRG, non-recurrent group; RG, recurrent group; NOG, non-occurrent group; OG, occurrent group; COPD, chronic obstructive pulmonary disease.

Table 2 Multivariate analysis of risk factors for contralateral occurrence

Variables	Relative risk	P value	95% confidence interval
Age	0.937	<0.001	0.909–0.968
Surgery	2.502	<0.001	1.601–3.908
Chronic obstructive pulmonary disease	4.049	0.06	0.923–17.658

Table 3 Prediction of ipsilateral recurrence

Models	Age group	Side	AUC	Accuracy	F1 score	Precision	Recall
Gradient boosting	Young	Right	0.686	0.769	0.733	0.706	0.769
Logistic regression	Young	Left	0.628	0.781	0.753	0.737	0.781
K-nearest neighbors	Old	Right	0.615	0.801	0.760	0.735	0.801
Logistic regression	Old	Left	0.623	0.824	0.804	0.794	0.824

AUC, area under curve.

accuracy and relevance in the outcomes.

For predicting ipsilateral recurrence in the young group, GB for the right side and LR for the left side were the top-performing models. GB achieved an AUC of 0.686, accuracy of 0.769, F1 score of 0.733, precision of 0.706, and recall of 0.769. LR scored an AUC of 0.628, accuracy of 0.781, F1 score of 0.753, precision of 0.737, and recall of 0.781. In the older group, KNN for the right side and LR for the left side were the best models. KNN had an AUC of 0.615, accuracy of 0.801, F1 score of 0.760, precision of 0.735, and recall of 0.801. LR achieved an AUC of 0.623, accuracy of 0.824, F1 score of 0.804, precision of 0.794, and recall of 0.824 (*Table 3*).

For predicting contralateral occurrence in the young group, RF for the right side and KNN for the left side were the most effective models. RF had an AUC of 0.597, accuracy of 0.774, F1 score of 0.741, precision of 0.709, and recall of 0.774. KNN performed better, with an AUC of 0.650, accuracy of 0.893, F1 score of 0.849, precision of 0.809, and recall of 0.893. In the older group, LR for the right side and NN for the left side were the top performing models. LR had an AUC of 0.630, accuracy of 0.935, F1 score of 0.914, precision of 0.894, and recall of 0.935. NN performed even better with an AUC of 0.765, accuracy of 0.961, F1 score of 0.948, precision of 0.936, and recall of 0.961 (*Table 4*). ROC curves for prediction of ipsilateral recurrence and contralateral occurrence of SP are shown in *Figures 2,3*, respectively.

Grad-CAM

The development of SP is generally associated with the presence of bullae or blebs in the lung apex (17). However, few studies have utilized chest X-ray images to confirm this

Table 4 Prediction of contralateral occurrence

Models	Age group	Side	AUC	Accuracy	F1 score	Precision	Recall
Random forest	Young	Right	0.597	0.774	0.741	0.709	0.774
K-nearest neighbors	Young	Left	0.650	0.893	0.849	0.809	0.893
Logistic regression	Old	Right	0.630	0.935	0.914	0.894	0.935
Neural network	Old	Left	0.765	0.961	0.948	0.936	0.961

AUC, area under curve.

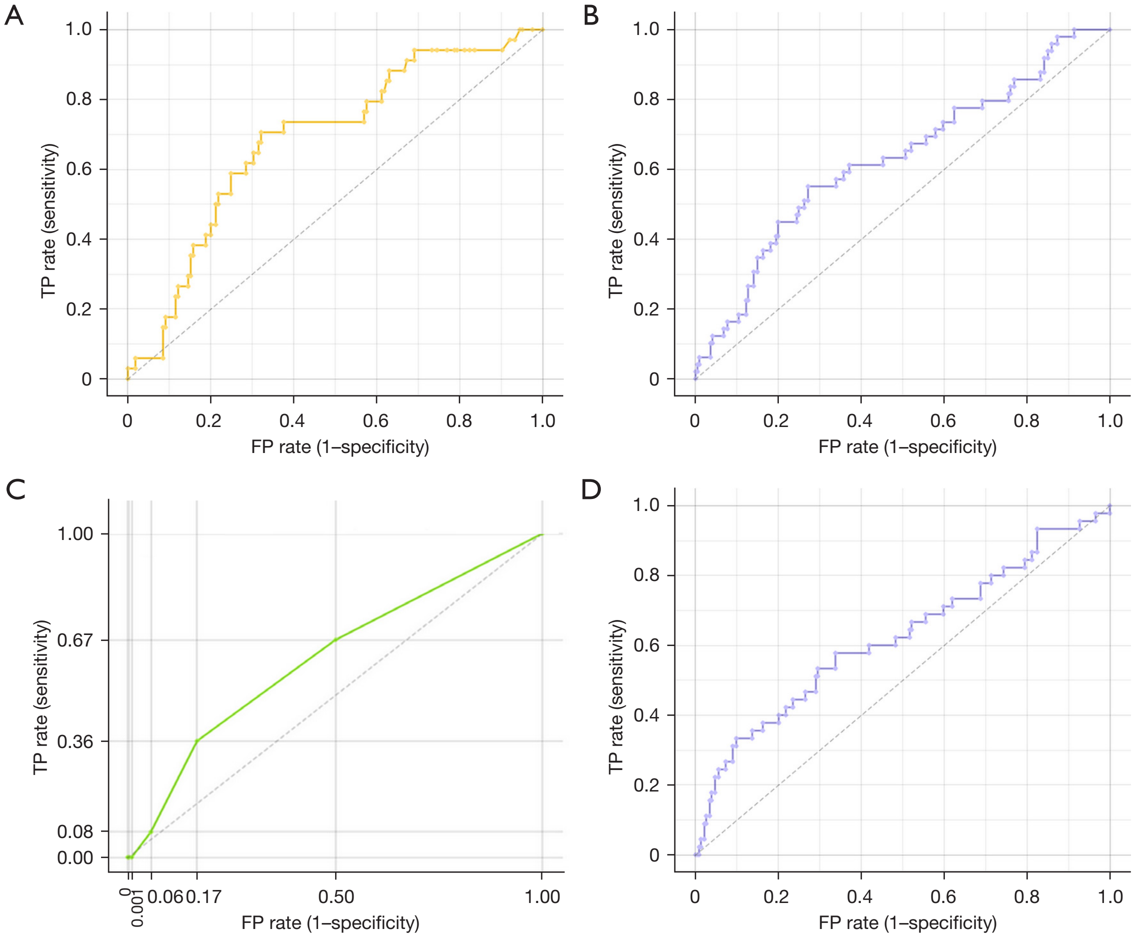

Figure 2 Receiver-operating characteristic curves for predicting ipsilateral recurrence of spontaneous pneumothorax. (A) Right side, young group. (B) Left side, young group. (C) Right side, older group. (D) Left side, older group. TP, true positive; FP, false positive.

finding (6,19,21). In this study, we employed Grad-CAM analysis to examine chest X-rays and highlight the portions of the images most closely associated with the development of SP. In the present study, Grad-CAM analysis indicated the apical portions of the lung to be strongly associated with the development of both ipsilateral and contralateral SP. Therefore, these regions may play a critical role in the development of pneumothorax on both the affected side and the opposite side (*Figure 4*).

Discussion

Although the management of SP is generally well-established, the high recurrence rate, particularly in cases

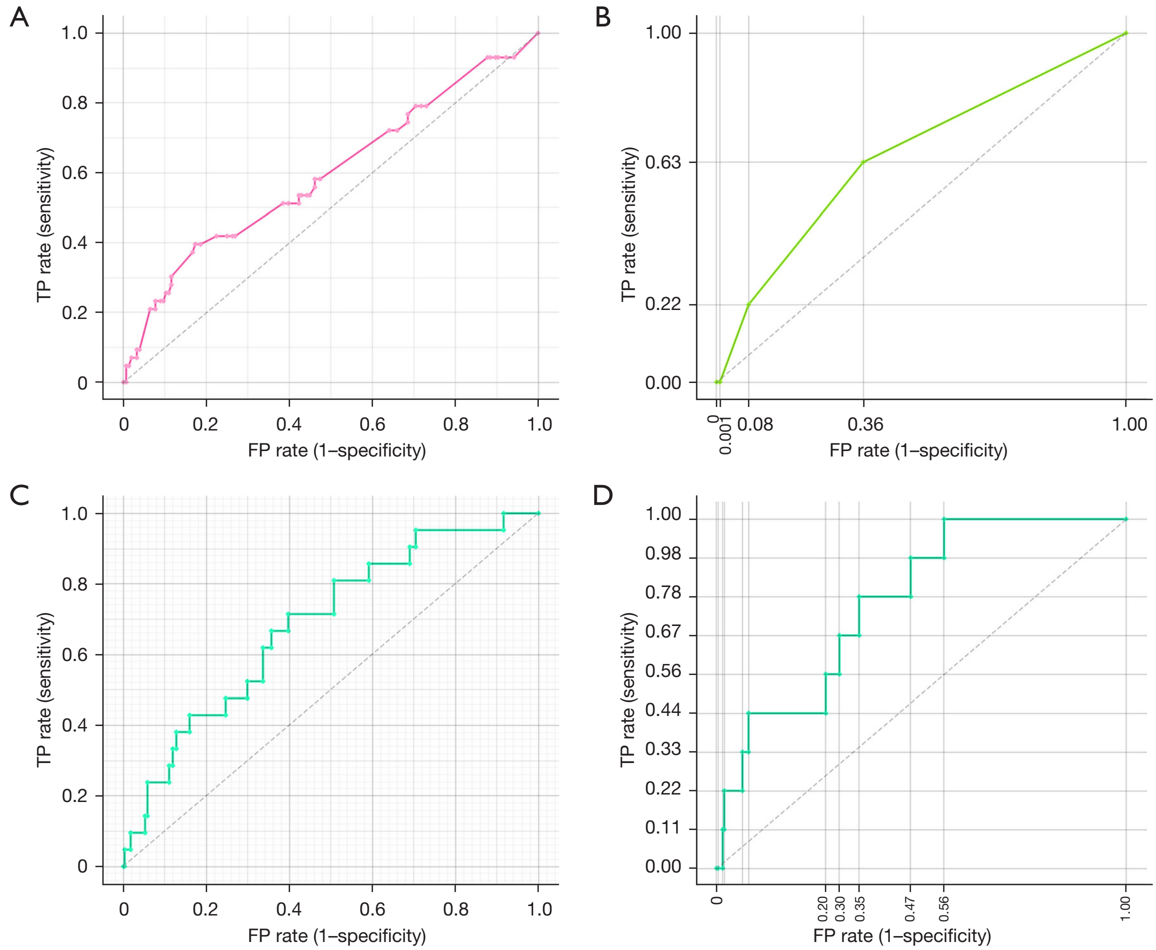

Figure 3 Receiver-operating characteristic curves for predicting contralateral occurrence of spontaneous pneumothorax. (A) Right side, young group. (B) Left side, young group. (C) Right side, older group. (D) Left side, older group. TP, true positive; FP, false positive.

not treated surgically, remains a significant challenge (1,3,25). Addressing this issue is crucial to improve long-term outcomes for patients who experience SP. Despite extensive research identifying various factors associated with the recurrence of SP, a definitive tool has not been developed to clinically predict recurrence (10-12). In addition, information regarding contralateral occurrence of SP is limited (4,11,14,15). Furthermore, it remains uncertain whether adolescents and adults experience ipsilateral recurrence or contralateral occurrence differently after completing treatment for the first episode of SP (1,2,7). This gap in understanding highlights the need for further research to determine the recurrence patterns in different age groups following initial treatment.

The prediction of SP development is influenced by multiple factors and evolves over time (1). Understanding the interplay of these variables is essential for accurately forecasting the likelihood of SP contralateral occurrence and ipsilateral recurrence. As in previous studies, the present research showed that recurrence of SP is significant, and contralateral SP does occur, although the incidence rate is relatively low (4,14). Thus, although recurrence is a notable concern, the occurrence of SP on the opposite side, though possible, remains less common (16,26). The incidence of SP varied between the age groups, while the recurrence rate did not (6,7). Notably, the younger group exhibited a significantly higher rate of contralateral occurrence compared with the older group. This indicates that, although age influences the initial occurrence of SP, the risk of recurrence is relatively similar across age groups, with younger patients being more prone to pneumothorax on the opposite side (4,14).

To investigate the risk factors for SP, a multivariate analysis was conducted. We hypothesized that factors of age

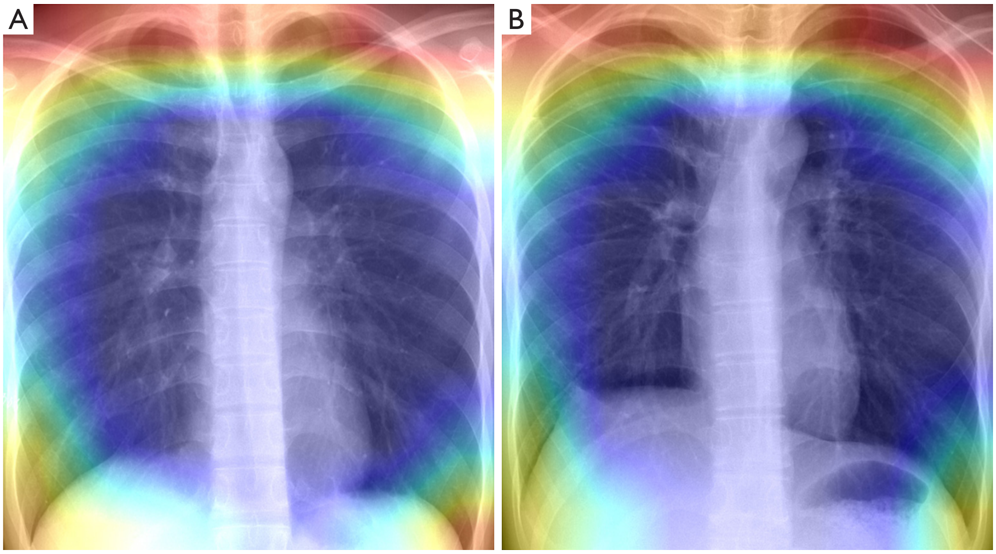

Figure 4 Gradient-weighted Class Activation Mapping analysis indicates that the apical portions of the lung are associated with the occurrence of both ipsilateral and contralateral spontaneous pneumothorax. (A) Ipsilateral recurrence. (B) Contralateral occurrence.

at the first episode, sex, COPD, smoking, and management options would influence recurrence and occurrence (8,9,27). The results indicated that surgery was the only independent factor affecting ipsilateral recurrence. In addition, age, surgery, and COPD were associated with contralateral occurrence (16,26). Notably, ipsilateral surgery emerged as a risk factor, likely due to the more SP-prone lung conditions in surgical cases. The advancement of machine learning further enhances the accuracy of these predictions, enabling more precise identification of patients at risk for recurrence or contralateral SP. Based on the findings, the ipsilateral recurrence and contralateral occurrence of SP can be predicted using factors of age, COPD, and management options, along with simple chest X-rays (16,27). This integration of traditional clinical parameters with modern technology offers a promising approach for improving patient outcomes in SP management. Accurately predicting the recurrence and occurrence of SP is essential for preventing future episodes (16,17,26). An effective prediction model should identify the underlying risk factors contributing to SP development and highlight the likelihood of recurrence and contralateral occurrence (10). This dual approach helps clinicians better understand patient-specific risks, enabling more tailored and proactive management strategies to improve overall patient outcomes.

Historically, chest CT scans have been the primary tool for studying the development of SP. However, despite being fundamental to SP diagnosis, simple chest X-rays have not been widely utilized for research in this area (10,19). In the present study, we uniquely employed simple X-ray data within machine learning algorithms to predict the development of SP. To the best of our knowledge, this approach marks a novel use of basic imaging data in predicting SP outcomes, potentially expanding the tools available for managing this condition. In this study, the models utilizing simple chest X-rays demonstrated fair performance, providing potential predictions for the development of SP. However, refinement of these models could lead to more reliable and precise outcomes, potentially enhancing the role of simple X-rays as a valuable tool in predicting SP when combined with advanced machine learning techniques. In addition, the Grad-cam analysis results confirmed that the apical portions of the lung were strongly associated with the development of both ipsilateral and contralateral SP.

To the best of our knowledge, this is the first study in which ipsilateral recurrence and contralateral occurrence of SP were investigated using machine learning algorithms applied to simple chest X-rays. Although the initial results are promising, further research is needed to validate the findings. The integration of machine learning with readily available clinical data could be extended to develop other predictive models in the field of SP, potentially improving patient management and outcomes.

The clinical relevance of this study had certain limitations. First, the study was retrospectively conducted at a single institution, which may limit the generalizability of the findings. Second, if an air leak point exists in the lateral or basal portions of the lung, it is challenging to predict accurately with the current model. However, a more powerful model can be developed by including and training in more cases that involve such scenarios. This would enhance the model's ability to generalize and improve its predictive performance. Third, the simple X-rays used were influenced by various medical histories, potentially affecting the prediction accuracy for SP. To address this, strict eligibility criteria were applied, and the observation period was limited to two years to reduce time-related biases. Although the dataset was relatively small, the heterogeneity of the X-rays might more accurately reflect real-world conditions, rendering the machine learning model more applicable in clinical practice. Understanding SP is important because even a benign condition such as this can significantly affect patient quality of life.

Conclusions

The findings of this study indicate that machine learning algorithms using simple X-rays and basic clinical data can potentially predict ipsilateral recurrence and contralateral occurrence of SP with fair performance, although it is inconclusive for determining recurrence. In addition, consistent with clinical experience, the apical portions of the lung were strongly associated with both ipsilateral and contralateral SP. This machine learning approach could prove convenient and valuable in surgical decision-making. However, further large-scale studies and more advanced models are needed to validate these findings and develop comprehensive management guidelines for SP.

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None.

Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1729/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1729/dss

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The requirement for informed consent was waived due to the retrospective design of the study, which did not disclose patient information. The study was reviewed and approved by the Ethics Committee of Uijeongbu Saint Mary's Hospital (No. UC24RISI0106). We affirm that this study adhered to the ethical principles outlined in the Declaration of Helsinki (as revised in 2013).

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