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A deep learning-based system capable of detecting pneumothorax via electrocardiogram

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Abstract

Purpose To determine if an electrocardiogram-based artificial intelligence system can identify pneumothorax prior to radiological examination.

Methods This is a single-center, retrospective, electrocardiogram-based artificial intelligence (AI) system study that included 107 ECGs from 98 pneumothorax patients. Seven patients received needle decompression due to tension pneumothorax, and the others received thoracostomy due to instability (respiratory rate ≥ 24 breaths/min; heart rate, < 60 beats/min or > 120 beats/min; hypotension; room air O₂ saturation, < 90%; and patient could not speak in whole sentences between breaths). Traumatic pneumothorax and bilateral pneumothorax were excluded. The ECGs of 132,127 patients presenting to the emergency department without pneumothorax were used as the control group. The development cohort included approximately 80% of the ECGs for training the deep learning model (DLM), and the other 20% of ECGs were used to validate the performance. A human–machine competition involving three physicians was conducted to assess the model performance.

Results The areas under the receiver operating characteristic (ROC) curves (AUCs) of the DLM in the validation cohort and competition set were 0.947 and 0.957, respectively. The sensitivity and specificity of our DLM were 94.7% and 88.1% in the validation cohort, respectively, which were significantly higher than those of all physicians. Our DLM could also recognize the location of pneumothorax with 100% accuracy. Lead-specific analysis showed that lead I ECG made a major contribution, achieving an AUC of 0.930 (94.7% sensitivity, 86.0% specificity). The inclusion of the patient characteristics allowed our AI system to achieve an AUC of 0.994.

Conclusion The present AI system may assist the medical system in the early identification of pneumothorax through 12-lead ECG, and it performs as well with lead I ECG alone as with 12-lead ECG.

Keywords Artificial intelligence · Electrocardiogram · Deep learning · ECG12Net · Pneumothorax · Out-of-hospital

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Abbreviations

ECG Electrocardiogram
AI Artificial intelligence
DLM Deep learning model

ROC Receiver operating characteristic

AUC Areas under the receiver operating characteristic

curves

ED Emergency department BMI Body mass index

Introduction

Chest pain is one of the most common complaints that calls for emergency medical services or admission to the emergency department (ED) [1, 2]. Pneumothorax, the presence of air in the pleural space, is a possible cause of chest pain and needs proper management even in prehospital situations. Therefore, early detection of pneumothorax is an important issue.

The incidence of spontaneous pneumothorax is approximately 17–24/100,000 in males and 1–6/100,000 in females, and it shows a bimodal age distribution with a peak at 15–34 years and another peak at ages older than 55 years. [3–5] The overall in-hospital mortality rate of spontaneous pneumothorax is approximately 1.7–3%, and it shows an obvious age-dependent trend that can rise up to 15.93% in the > 90-year-old group [5, 6]. However, up to 31.04% of patients with spontaneous pneumothorax are misdiagnosed in prehospital care and undergo delayed adequate management [6].

Clinical presentations of pneumothorax include dyspnea, chest pain and tachycardia. Physically, asymmetrical expansion of the chest wall, diminished or absent breathing sounds, hyperresonance upon percussion, and decreased tactile fremitus are often seen [7, 8]. The definite diagnosis is based on imaging examinations, including chest plain film, ultrasonography, or computer tomography [9, 10]. Tools to screen for pneumothorax before imaging may assist in early decision-making for patients with chest pain or dyspnea.

Electrocardiography is the first modality that is used to manage patients with acute chest pain. There are significant electrocardiogram (ECG) changes in patients with pneumothorax, including axis deviation, reduced voltage and poor R wave progression in precordial leads, and T wave inversion, occurring in only approximately 20% of patients with spontaneous pneumothorax [11–15]. There are no studies regarding physicians' capacities to identify pneumothorax by ECG. Such evidence supports the difficulties for physicians in detecting pneumothorax by ECG alone. Moreover, utilizing ECG to determine pneumothorax is not a standard in many parts of the world, leading to the low performance of physicians in detecting pneumothorax by ECG. Importantly,

ECG presentations in pneumothorax may exhibit a similar pattern to those of myocardial infarction or pulmonary embolism [16, 17]. All the results indicate that ECG may provide important information for the differential diagnosis in patients with acute chest pain.

Since 2012, deep learning models (DLMs) have been used in numerous applications for ECG recognition. Initially, artificial intelligence (AI) was trained to detect well-known ECG changes, such as arrhythmia, hyperkalemia, and hypokalemia, and it showed noninferior performance compared with experienced physicians [18–20]. Furthermore, using the associated database, AIs can screen for cardiac contractile dysfunction, recognize aortic stenosis, predict atrial fibrillation, and estimate age or sex through ECG, which are difficult for physicians [21–24]. These results highlight the critical role of AI in classifying ECGs for medical applications.

Since ECG changes in pneumothorax have been well reported, we hypothesized that there would be specific ECG changes in patients with pneumothorax that could be detected by DLM. Our study aimed to train a DLM to distinguish pneumothorax and non-pneumothorax through a 12-lead ECG. Using an AI might help clinicians to take pneumothorax into account and thereby shorten the diagnostic process and optimized management.

Methods

Data source

This was a single-center retrospective study in which all the data were collected from Tri-Service General Hospital, Taipei, Taiwan. The pneumothorax cases were collected from January 2016 to May 2019 in our ED with the following inclusion criteria: (1) at least one chest plain film to confirm pneumothorax, (2) needle decompression (clinically suspicious tension pneumothorax), tube thoracostomy, or catheter thoracostomy due to instability (respiratory rate ≥ 24 breaths/min; heart rate, < 60 beats/min or > 120 beats/min; hypotension; room air O₂ saturation, < 90%; and patient couldn't speak in whole sentences between breaths) [25], and 3) at least one ECG before intervention. Minimal pneumothorax (<20%), bilateral pneumothorax, traumatic pneumothorax, combined hemothorax and pneumothorax, or other indications of tube or catheter thoracostomy were excluded. All patients with pneumothorax underwent ECG examination due to the presentations of chest tightness, chest pain, or dyspnea. Seven patients received needle decompression due to tension pneumothorax, and all the patients received a thoracostomy. All ECG recordings were collected by a Philips 12-lead ECG machine (PH080A) in digital format, and the sampling frequency was 500 Hz, with 10 s recorded



in each lead. The study was given ethics approval by the institutional review board (IRB NO. C202005055).

Development cohort and validation cohort

There were 107 pneumothorax ECGs from 98 patients enrolled in this study. Non-pneumothorax ECGs were collected from patients in the ED during the same period. Those with history of pneumothorax were excluded. A total of 132,020 ECGs from 66,485 patients were defined as non-pneumothorax ECGs in this study. The corresponding patient characteristics and laboratory data were also collected and assigned for each ECG record. The data were divided into a development cohort (80%) and a validation cohort (20%), and there were no overlapping patients between the two groups.

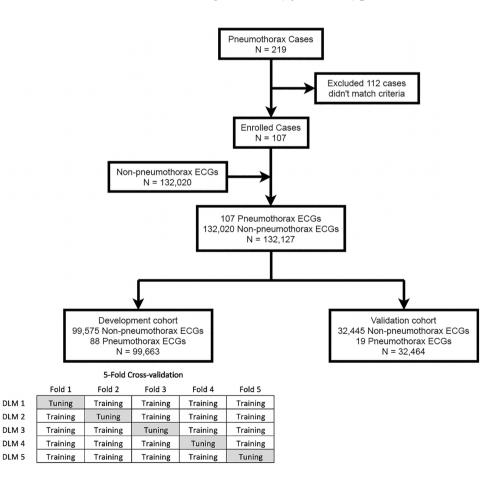
The development cohort comprised 99,575 non-pneumothorax ECGs and 88 pneumothorax ECGs. All the data were divided into five subgroups for fivefold cross-validation, which used four subgroups for the training set and the other one subgroup for the tuning set in each fold. There were no overlapping data between these five subgroups. The validation cohort included 32,445 non-pneumothorax ECGs and 19 pneumothorax ECGs from different patients. The algorithm is displayed in Fig. 1.

Fig. 1 Summary of the study datasets and development/ validation cohort generation. The study datasets comprised 107 pneumothorax ECGs and 132,020 non-pneumothorax ECGs, which were randomly divided into a development cohort (80%) and a validation cohort (20%). Fivefold cross-validation was used for training the DLM and selecting hyperparameters in the development cohort. *N* number of records, *ECG* electrocardiogram

The implementation of the deep learning model

We have developed an 82-convolutional-layer attention DLM called ECG12Net. Its technological details, including model architecture, data augmentation, and model visualization, were described in a previous publication [18]. Based on the same architecture, we developed two new DLMs for detecting pneumothorax and recognizing the lesion side (left or right). All the data input for the first DLM were divided into two categories, pneumothorax and non-pneumothorax, and the output of the model was a 2-class softmax output. The second DLM was trained by pneumothorax ECGs labeled left or right pneumothorax, and the output of the model was a 2-class softmax output for pneumothorax side recognition.

The signal length of our original 12-lead ECG was 5000, but the length of the standard input format to ECG12Net has a length of 1024. To complete the training process, we randomly cropped a signal with a length of 1024 as input. For the inference stage, the 9 overlapping signals of length 1024 based on interval sampling were used to generate predictions and were averaged as the final prediction. The oversampling process was used in the training step because of the rare proportion of pneumothorax in our dataset. The settings for the training model were as follows: (1) Adam optimizer with standard parameters ($\beta_1 = 0.9$ and $\beta_2 = 0.999$) and a batch





size of 36 for optimization; (2) learning rate of 0.001; and (3) a weight decay of 10^{-4} . The 100th epoch model was used as the final model, whose performance in the validation cohort was only evaluated once.

Human-machine competition

The human-machine competition was performed by using a validation database to verify the capacities of our DLM in detecting pneumothorax by ECG. The database has 100 ECGs, including 81 non-pneumothorax, 11 left-side pneumothorax and 8 right-side pneumothorax. Three doctors participated in the competition (two emergency physicians and one cardiologist), and the tests were conducted through an online standardized data entry program without patient information except the 12-lead ECGs. All the physicians participating in the study read the provided knowledge describing ECG changes in pneumothorax before the human-machine competition. The sensitivity, specificity, and kappa value were calculated for comparison with our DLM.

Statistical analysis and model performance assessment

All the analyses were based on ECGs. We analyzed the characteristics and laboratory results of the pneumothorax and non-pneumothorax groups. The results were presented as the means and standard deviations for continuous variables and as numbers and percentages for categorical variables. We used Student's t test or the Chi /square test to compare the results between two groups, as appropriate, and p values < 0.05 were considered to be statistically significant. The statistical analysis was performed with R version 3.4.4, and the package MXNet version 1.3.0 was used to implement our DLM.

In the primary analysis, we focused on the performance of our DLM compared with human experts. Receiver operating characteristic (ROC) curves and areas under the curve (AUCs) were applied to evaluate the performance of pneumothorax recognition between DLMs and human experts. The human-machine competition was displayed by global performance rankings that are based on the 3-class (nonpneumothorax, right-side pneumothorax, and left-side pneumothorax) kappa values. In the secondary analysis, we evaluated the validation cohort. ROCs and AUCs were also applied to analyze the lead-specific performance on pneumothorax cases. Subgroup analysis and matched analysis for pneumothorax diagnosis in the validation cohort were performed based on the significant differences in characteristics. The matched analysis used a proportion of 1:20 to match a control with the same gender, similar age (difference < 5 years old) and BMI (difference $< 3 \text{ kg/m}^2$). We also applied the patient characteristics and clinical information to our DLM, and the results of univariable and multivariable logistic regression analyses were displayed.

Results

The patient characteristics corresponding to pneumothorax and non-pneumothorax ECGs are shown in Table 1. Figure 2 shows the performance comparison of the DLM and human experts in pneumothorax recognition. We presented the ROC curves for the predictions of the DLM in the validation cohort (AI-all), involving all ECGs, and the competition set (AI-sub), involving 100 ECGs. The AUCs were 0.9469 and 0.9565, respectively. The sensitivity and specificity of our DLM were 94.7% and 88.1%, respectively, using an optimal cutoff point in the validation cohort, which is better than those of the physicians participating in the study.

The global performance of discriminating among non-pneumothorax ECGs, left-side-pneumothorax ECGs and right-side-pneumothorax ECGs by our DLM and human experts are displayed in Fig. 3. The DLM achieved the best performance, with a 3-class kappa value of 0.806, while the

Table 1 Corresponding patient characteristics of pneumothorax and normal ECGs

normal ECGs			
	Pneumothorax $(n=107)$	Normal $(n = 132,020)$	p value
Dataset			0.101
Development cohort	88 (82.2%)	99,575 (75.4%)	
Validation cohort	19 (17.8%)	32,445 (24.6%)	
Gender (Male)	78 (79.6%)	68,801 (52.1%)	< 0.001
Age (years)	40.9 ± 24.2	63.2 ± 19.3	< 0.001
Height (cm)	168.5 ± 7.4	162.0 ± 19.2	0.012
Weight (kg)	57.3 ± 10.2	64.0 ± 14.2	< 0.001
BMI (kg/m ²)	20.2 ± 3.4	24.6 ± 8.3	< 0.001
Disease history			
AMI	0 (0.0%)	4988 (3.8%)	0.055
Stroke	1 (1.0%)	25,664 (19.4%)	< 0.001
CAD	10 (10.2%)	35,760 (27.1%)	< 0.001
HF	0 (0.0%)	14,798 (11.2%)	< 0.001
AF	1 (1.0%)	9225 (7.0%)	< 0.001
DM	6 (6.1%)	35,151 (26.6%)	< 0.001
HTN	11 (11.2%)	57,045 (43.2%)	< 0.001
CKD	1 (1.0%)	18,114 (13.7%)	< 0.001
Lipidemia	8 (8.2%)	40,169 (30.4%)	< 0.001
COPD	12 (12.2%)	27,688 (21.0%)	< 0.001

BMI body mass index, AMI acute myocardial infarction, CAD coronary artery disease, HF heart failure, AF: atrial fibrillation, DM diabetes mellitus, HTN hypertension, CKD chronic kidney disease, COPD chronic obstructive pulmonary disease



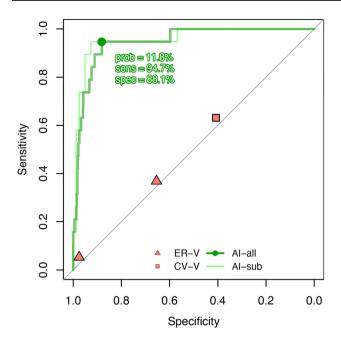


Fig. 2 Performance comparison of the deep learning model and human experts in pneumothorax recognition. The ROC curves were made by the predictions of the deep learning model in the validation cohort (AI-all) and competition set (AI-sub). The red and blue points represent visiting staff and residents, respectively. The triangle and square marks represent the emergency physicians and cardiologists, respectively. The AUCs were 0.9469 and 0.9565 in the validation cohort and competition set, respectively

human experts presented values of 0.110, 0.067, and 0.052. The DLM only mistook one left-side-pneumothorax ECG for non-pneumothorax ECG. Lead-specific performance on pneumothorax was analyzed in the validation cohort, and the results are shown in Fig. 4. Lead I made a major contribution, achieving 94.7% sensitivity and 86.0% specificity, with an AUC of 0.930, followed by lead aVR and lead V5. The worst performance was displayed by lead V2, with an AUC of 0.624.

In Supplemental Fig. 1, we shared four representative ECGs in our validation cohort, and we found that our DLM presented more focus on the precordial lead. Case A ECG was a left-side-pneumothorax ECG with low voltage and poor R wave progression in the lateral precordial lead (V4-V6). Case B was a right-side-pneumothorax ECG with the characteristics of counterclockwise rotation and a negative or isoelectric QRS wave with low voltage in the lead aVL. Case C and case D were non-pneumothorax ECGs that were misdiagnosed as left-side and right-side pneumothorax, respectively. Negative lead aVL with a left ventricular hypertrophy pattern was noted in case C, while counterclockwise rotation and low voltage in lead aVL were noted in case D.

The subgroup analysis and matched analysis for pneumothorax diagnosis in the validation cohort are shown in Fig. 5.

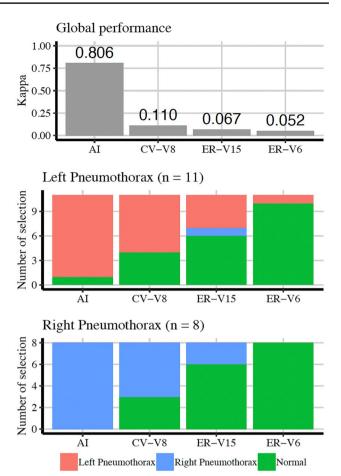


Fig. 3 Location analysis of pneumothorax in the human–machine competition. Global performance is ranked based on the 3-class kappa values. Only the performances of discrimination of pneumothorax location are presented

The forest plot presents the diagnostic odds ratio (OR) based on sensitivity and specificity. The overall diagnostic OR was 89.2 (95% conference interval 16.9–472.1), with 94.7% sensitivity and 88.1% specificity. Stratification by sex showed no significant change in diagnostic OR, but the diagnostic OR (29.1) was lower in young patients (age < 40). The major reason for this reduction was lower specificity, which was also present in the lean group (BMI < 20). Among the subgroup analyses, the subgroup of young, tall, lean males presented with the lowest specificity (46.8%) and diagnostic OR (12.3), which explained the importance of these three factors. The matched analysis revealed diagnostic ORs of 23.1 (95% conference interval: 4.3–123.7) and 19.4 (95% conference interval: 3.6-104.2) in gender/age-matched and gender/age/BMI-matched patients, respectively, and both sensitivities showed unchanged but lower specificities.

Supplemental Fig. 2 demonstrates the results of univariable and multivariable logistic regression analysis on pneumothorax in the development cohort. Male sex, young age,



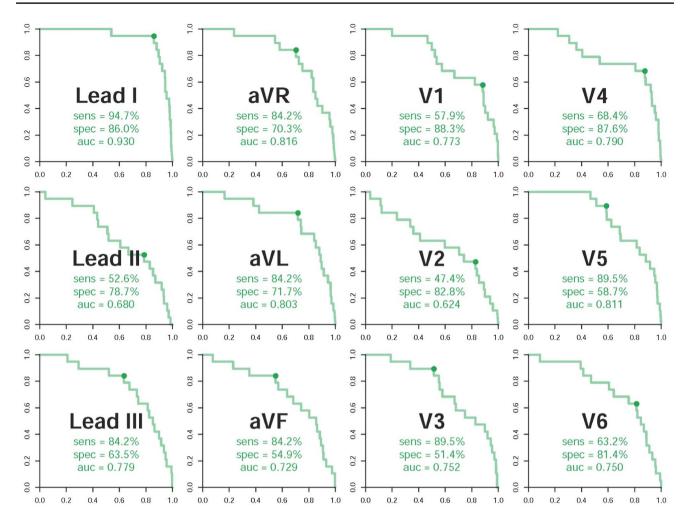


Fig. 4 Lead-specific performance analysis of pneumothorax in the validation cohort. These are ROC curves with the specificity of the x axis and the sensitivity of the y axis

and low BMI were independent risk factors for pneumothorax. We performed a multivariable analysis that involved patient characteristics and disease histories. Chronic kidney disease was correlated with a significantly lower risk of pneumothorax. We applied these results to our DLM in the validation cohort, and it revealed significantly better performance than analysis only with ECGs (Supplemental Table 1). The AUC rose from 0.9469 to 0.9944 (*p* value 0.0269) with model 1 risk factors (characteristics and disease histories).

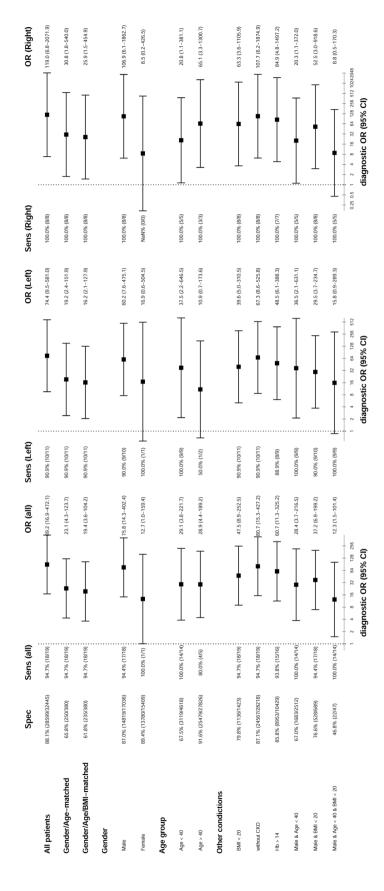
Discussion

Our DLM was trained by more than 130,000 ECGs, including 107 pneumothorax ECGs, and it shows outstanding discrimination, with an AUC of approximately 0.95, which is significantly better than that of our physicians in pneumothorax detection. Importantly, using lead I alone can provide

similar performance compared with 12-lead ECG. Patient characteristics enhanced the performance of our DLM, providing an AUC of 0.994. Increasing evidence supports conservative management for atraumatic pneumothorax [26]. Our DLM system might not guide the treatment for pneumothorax, but this study definitively provides a promising diagnostic supportive system for detecting spontaneous pneumothorax.

Our AI-ECG has extraordinary performance in detecting pneumothorax and side discrimination, even with a single lead, lead I, which can be applied to wearable devices to monitor high-risk patients in prehospital care and ED, and used in continuous ECG monitoring. Compared with chest plain film and computed tomography, ECG machines are widely available and cheaper devices. Although ultrasonography exhibits feasibility, high sensitivity and specificity for pneumothorax diagnosis, electrocardiography is a widespread and convenient examination even in rural areas or clinics. In ED, ECG is the first exam used for chest pain,





across a series of conditions. The diagnostic OR, which is the ratio of the positive likelihood ratio (sensitivity/(1 – specificity)) to the negative likelihood ratio [(1 – sensitivity)/specificity], as well as the associated 95% CI, is shown for each situation. All analyses were checked for problematic zero counts, and a fixed value of 0.5 was added to all cells of tables where the problems Fig. 5 Subgroup analysis and matched analysis for pneumothorax diagnosis by the AI system in the validation cohort. The sensitivity and specificity in detecting pneumothorax is tabulated occurred



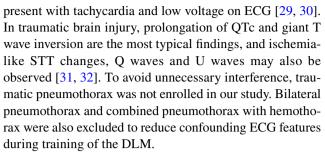
which is the most common symptom of spontaneous pneumothorax. Applying the AI-ECG system for pneumothorax detection may shorten the diagnostic process and avoid unnecessary examinations. Furthermore, taller individuals, smokers and patients with secondary pneumothorax have a high risk of recurrent pneumothorax [27, 28]. In such patients, we can use a wearable device with a lead I ECG monitor that will sound an alarm when it reoccurs, which is not easily performed by an imaging diagnostic method. Collectively, although the overall incidence of pneumothorax is low, our system can be applied in the field of wearable devices to monitor high-risk patients in prehospital care and ED and thus serve as a diagnostic supportive system to detect spontaneous pneumothorax.

We found that some left-side-pneumothorax ECGs present with low voltage and poor R wave progression in the lateral precordial lead, which might be due to the accumulation of air in the left pleural space. In right-side pneumothorax, some ECGs present with a rightward shift of QRS in the precordial lead and a negative QRS wave with low voltage in the lead aVL. Among right-side-pneumothorax ECGs enrolled in our study, the proportions of counterclockwise rotation, clockwise rotation and no rotation were 28%, 20% and 52%, respectively. According to the findings, the rotation of pneumothorax ECG was not a specific feature to discriminate the lesion side. The detailed mechanisms for distinguishing pneumothorax by ECG remain unclear. By using a large, annotated dataset, our AI-ECG both identified pneumothorax and conducted side discrimination from ECGs.

In the subgroup analysis in Fig. 5, we found that there was no obvious difference in the diagnostic OR between the age < 40 group and the age > 40 group. We knew that the incidence of pneumothorax shows a bimodal age distribution, with a peak in individuals aged approximately 15–34 years relating to primary spontaneous pneumothorax and another peak in elderly individuals relating to secondary spontaneous pneumothorax [3–5]. Accordingly, we suggest that our AI-ECG could perform equally well in primary and secondary pneumothorax detection and location discrimination. Interestingly, our results indicated that the diagnostic OR in the female subgroup was lower than that in the male subgroup, and the lowest diagnostic OR existed in the male, young (age < 40), and lean (BMI < 20) subgroups. These results suggest that our AI-ECG took age, BMI, and sex into consideration when identifying pneumothorax, which warrants further investigation

. [21].

Traumatic pneumothorax was excluded from our study due to variant changes in heart rate, rhythm or ECG caused by trauma. For instance, cardiac or vascular injury can induce arrhythmia, left ventricular injury can cause STT changes or T wave inversion, and cardiac tamponade can



There are certain limitations in our study. First, there may be some concern about the number of pneumothorax cases in our model. Although the AI-ECG has shown good performance in pneumothorax detection, there is still room to improve it with a large dataset. Second, we do not categorize primary, secondary or tension pneumothorax in our model. Among 108 pneumothorax ECGs enrolled in the study, only 7 ECGs were obtained from patients who underwent needle compression due to suspicion of tension pneumothorax. Third, the small sample size of tension pneumothorax is a limitation of our study. Further investigation is needed to determine whether the current AI-ECG can be applied to detect ventilated patients, bilateral pneumothorax and traumatic pneumothorax. Finally, the mechanism by which ECG distinguishes pneumothorax remains unclear. Prospective studies and prognostic changes after applying the AI-ECG in clinical practice were not performed in the current study and warrant further evaluation in future studies.

Conclusion

We developed a DLM that can both detect pneumothorax with an AUC of 0.9469 and a sensitivity and specificity of 94.7% and 88.1%, respectively, and perfectly discriminate the location of pneumothorax. Using +*ead I alone provides similar performance to a 12-lead ECG (sensitivity: 94.7%, specificity: 86.0%, AUC: 0.930), which could be applied to early recognition of pneumothorax, especially in prehospital settings, ED and continuous monitoring, although further prospective and large studies are needed to confirm the performance of our AI-ECG.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00068-022-01904-3.

Author contributions C-CL, CL and CSL are the guarantors of the content of the manuscript. C-CL, CL and CSL contributed to the conception of the work, had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. C-CL, CL, CSL, CST, TPT, CCC, JTL, WSL, CCL, and JTC contributed substantially to the study design, data acquisition, analysis and interpretation. All authors contributed substantially to the writing of the manuscript, have read and approved the manuscript and agree to be 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.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request. Some data may not be made available because of privacy or ethical restrictions.

Code availability The codes presented in this study are available on request from the corresponding author.

Declarations

Role of the sponsors The sponsors had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

Conflict of interest The author(s) declare no competing interests.

Ethics approval The study was ethically approved by the institutional review board (IRB NO. C202005055).

Consent for participation Not required.

Consent for publication Not required.

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