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Computer-aided recognition of emphysema on digital chest radiography

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ABSTRACT

Background: Computed tomography (CT) is the benchmark for diagnosis emphysema, but is costly and imparts a substantial radiation burden to the patient.
Objective: To develop a computer-aided procedure that allows recognition of emphysema on digital chest radiography by using simple descriptors of the lung shape. The procedure was tested against CT.
Methods: Patients ($N = 225$), who had undergone postero-anterior and lateral digital chest radiographs and CT for diagnostic purposes, were studied and divided in a derivation ($N = 118$) and in a validation sample ($N = 107$).
CT images were scored for emphysema using the picture-grading method. Simple descriptors that measure the bending characteristics of the lung profile on chest radiography were automatically extracted from the derivation sample, and applied to train a neural network to assign a probability of emphysema between 0 and 1. The diagnostic performance of the procedure was described by the area under the receiver operating characteristic curve (AUC).
Results: AUC was 0.985 (95% confidence interval, 0.965–0.998) in the derivation sample, and 0.975 (95% confidence interval, 0.936–0.998) in the validation sample. At a probability cutpoint of 0.55, the procedure yielded 92% sensitivity and 96% specificity in the derivation sample; 90% sensitivity and 97% specificity in the validation sample. False negatives on chest radiography had trace or mild emphysema on CT.
Conclusions: The computer-aided procedure is simple and inexpensive, and permits quick recognition of emphysema on digital chest radiographs.

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1. Introduction

Emphysema is defined as an abnormal, permanent enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls and without obvious fibrosis [1]. Since emphysema is a structural abnormality of the lung, its recognition requires tests that reflect lung structure rather than function.

Computed tomography (CT) of the thorax is regarded as the benchmark for diagnosing emphysema *in vivo* [2]. However, it is costly and imparts a substantial radiation burden to the patient [3].

Chest radiography has long been used in clinical practice for the evaluation of emphysema [4]. Even though it is less sensitive than CT in detecting emphysema, is far less expensive and entails a much lower radiation exposure, particularly when digital acquisition is used [3].

Recently, the diagnostic performance of chest radiography was reappraised using high resolution CT as the reference standard [5]. The diagnosis of emphysema on postero-anterior and lateral chest radiographs was based on the identification of at least two of four explicit criteria that had been originally validated against lung pathology [6]. Chest films were examined independently by five raters with varying degree of experience. The weighted sensitivity was 90%, and the weighted specificity 98% [5].

In the present study, we introduce a computer-aided procedure that allows the recognition of emphysema on digital chest radiographs by using simple descriptors of the lung shape. This method can be used by any physician, medical student or technologist with little or no experience in chest film interpretation. The procedure is aimed solely at evaluating structural emphysema; it cannot be relied upon to identify airflow obstruction.

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2. Methods

2.1. Sample

The study sample comprised 225 consecutive patients who were evaluated at the Institute of Clinical Physiology, Pisa (Italy) between June 1, 2007 and July 31, 2008. In these patients, CT of the thorax and postero-anterior and lateral digital chest radiographs were obtained for diagnostic purposes within a week of each other.

Most of the patients (85%) underwent CT for the presence of a solitary pulmonary nodule on chest radiography. The other patients had CT as part of their investigation for suspected pulmonary arterial hypertension.

For the sake of the present study, the patients were divided in two groups: (a) derivation sample ($N = 118$), whose chest radiographs were used to develop the computer-aided procedure for emphysema recognition, and (b) validation sample ($N = 107$), whose chest radiographs were used to test the diagnostic accuracy of the procedure.

The patients in the derivation sample had a median age of 65 years (interquartile range [IQR], 56–70 years); 96 (81%) of them were males. In the validation sample, the patients' median age was 66 years (IQR, 57–73 years), and the proportion of males 56%.

Chronic obstructive pulmonary disease (COPD) was rated present on spirometry if the post-bronchodilator ratio of forced expiratory volume in 1 s (FEV_1) over forced vital capacity (FVC) was less than 0.70. The severity of COPD was staged according to the GOLD guidelines as mild, moderate, severe, or very severe if FEV_1 was >80%, 50–80%, 30–49%, or <30% of the predicted value, respectively [7].

Of the 225 patients reported on here, 141 (63%) had COPD (77 in the derivation, and 64 in the validation sample). The relative proportions of mild, moderate, severe, and very severe COPD were 9%, 37%, 41%, and 13%, respectively.

The protocol was approved by the Institutional Review Board. A written permission was obtained from all the patients to use their radiologic imaging data anonymously for the present study. This incorporated the consent to take part in the study.

2.2. Computed tomography

Volumetric CT was performed on a Toshiba Aquilion 64 detector row scanner (Toshiba, Japan) with the patient breath-holding at full inspiration for 10 s. Acquisition setting was 120 kVp with mAs modulated according to the patient's attenuation as assessed before scan acquisition (range, 60–250 mAs). Slice thickness was set at 0.65 mm. No contrast medium was infused.

Scans were reconstructed in the axial, sagittal and coronal planes. Images were viewed using a window level of −600 Hounsfield Units (HU) and a width of 1500 HU, and were examined independently by a chest radiologist and a chest physician for the presence of areas of low attenuation and vascular disruption. The two raters were blinded to clinical and chest radiography data.

Maximum intensity projection technique was used to evaluate vascular disruption, and minimum intensity projection to highlight focal areas of low attenuation in the lung parenchyma [8].

The severity of emphysema was scored on a nonparametric scale from 0 (no emphysema) to 100 using the panel grading (PG) method of Thurlbeck et al. [9].

This consists of 16 inflation-fixed, paper-mounted, midsagittal whole lung sections that are arranged at intervals of 5 between 0 and 50, and at intervals of 10 between 60 and 100. A score of 5 or less is consistent with trace emphysema, a score of 10–30 indicates mild emphysema, a score >30–50 moderate emphysema, and a score >50–100 severe emphysema.

In scoring emphysema on CT, the two raters examined sagittal lung sections, and gave them the score of the standard most closely similar, or a score between two standards. The PG scores by the two independent raters were averaged.

2.3. Chest radiography

Postero-anterior and lateral digital chest radiographs (Thorax 2000, IMIX, Finland) were obtained at a standard 2-m focus to detector distance with the patients upright holding their breath at full inspiration. Each radiographic image was 2000 × 2000 pixels (198 μm per pixel) in size with a dynamic range of 12 bits. Images were obtained by the acquisition equipment in standard operational conditions, and no further post-processing was applied. Chest radiographs had the identification data removed, and were stored in DICOM format for further analysis as described below.

2.4. Descriptors of the lung shape

The procedure begins with the extraction of the lung contours in the postero-anterior and lateral chest radiographs. This is the only interactive part of the procedure that is accomplished by locating a number of knot points along the boundaries of the lungs in each radiograph. In the present study, this step was carried out by a chest physician who was blinded to clinical and CT data. The lung contours are automatically drawn by means of cubic splines (Fig. 1).

The program then identifies 4 points in the postero-anterior view corresponding to the apex and the costophrenic angle of the right and left lung, respectively (Fig. 2a). In the lateral view, the 4 points are the costophrenic angle posteriorly, the cardiophrenic angle anteriorly, the lung apex, and the maximum vertical distance of the perpendicular drawn from the line joining the costophrenic to the cardiophrenic angle (Fig. 2b). The 4 points identified on each radiograph are the corners of a polygon, the area of which is measured.

Next, on each radiograph, the program identifies 3 triangles with their base on 3 sides of the polygon and their height equal to the maximum vertical distance from the triangle base to the superjacent lung segment (Fig. 2). Each triangle is described by 3 numerical features: (i) normalized area, or the ratio of the triangle area to the total area including the polygon and triangles; (ii) height ratio, or the ratio of the triangle height to the triangle base; (iii) base ratio, or the projection of the triangle minor side on the triangle base divided by the base length.

In emphysematous lungs, the normalized area of the triangle below the diaphragms is expected to decrease due to the depression and flattening of the diaphragmatic contours associated with chronic hyperinflation. Conversely, the normalized area of the triangles under the costal and retrosternal aspects of the lungs is expected to increase.

The height ratio is a numerical index of the maximum bending of a given anatomic segment of the lung, and the base ratio indicates the position, along the triangle base, where the maximum bending occurs.

The procedure ends by creating one vector from each radiograph that includes 9 numerical features as descriptors of the lung shape. The two vectors are then fed to a neural network that operates as follows.

2.5. Neural network training and testing

A feed-forward multi-layer neural network was employed to recognize emphysema from the descriptors of lung shape on chest radiography. Based on a preliminary study with different net-

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work architectures [10], we chose a neural network featuring 18 input units, two hidden layers with 10 and 4 units respectively, and a single output unit whose activation yields the probability that the input pattern belongs to the “emphysema” category.

The network was trained using the standard error back-propagation algorithm with adaptive learning rate [11]. The chest radiographs from the derivation sample were used for the training process, adopting the “leave-one-out” approach [11]. For each case, the descriptors of the lung shape are the training pattern, and the corresponding target value is 0 for “no emphysema”, and 1 for “emphysema”.

After training, the performance of the neural network was tested in both the derivation and the validation samples using CT as the reference diagnostic standard. The descriptors of lung shape were fed to the network inputs, and the output unit returned the probability of emphysema between 0 and 1.

2.6. Statistical analysis

The scatter plot of the PG of emphysema by the two independent raters was tested for departure from perfect agreement by fitting a simple linear regression model and verifying the null hypothesis that the intercept is equal to zero and the slope is equal to one, jointly.

The prevalence of emphysema in the derivation and in the validation samples was compared by Fisher exact test. Differences in the severity of emphysema across the two samples were assessed by Mann–Whitney nonparametric test. The relation between the severity of COPD and the severity of emphysema on CT, or the probability of emphysema on chest radiography, was tested for by Kruskal–Wallis nonparametric test.

The diagnostic performance of the computer-aided procedure in the derivation and validation samples was described by receiver operating characteristic (ROC) curves, using the area under the

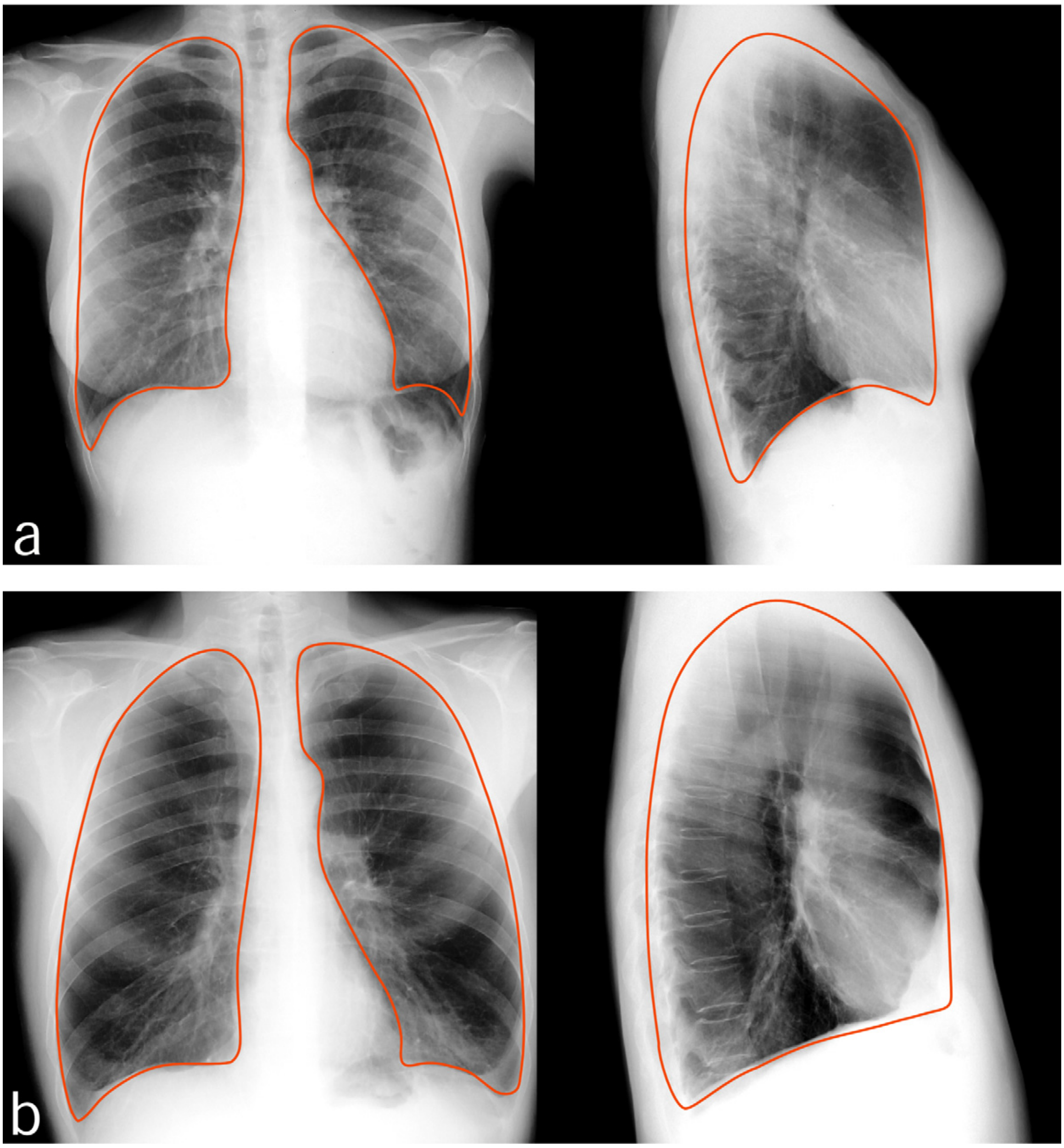

Fig. 1. Identification of lung contours in postero-anterior and lateral chest radiographs from two patients: (a) no emphysema on CT; (b) emphysema on CT. Note the different shape of the lungs in (a) with respect to (b).

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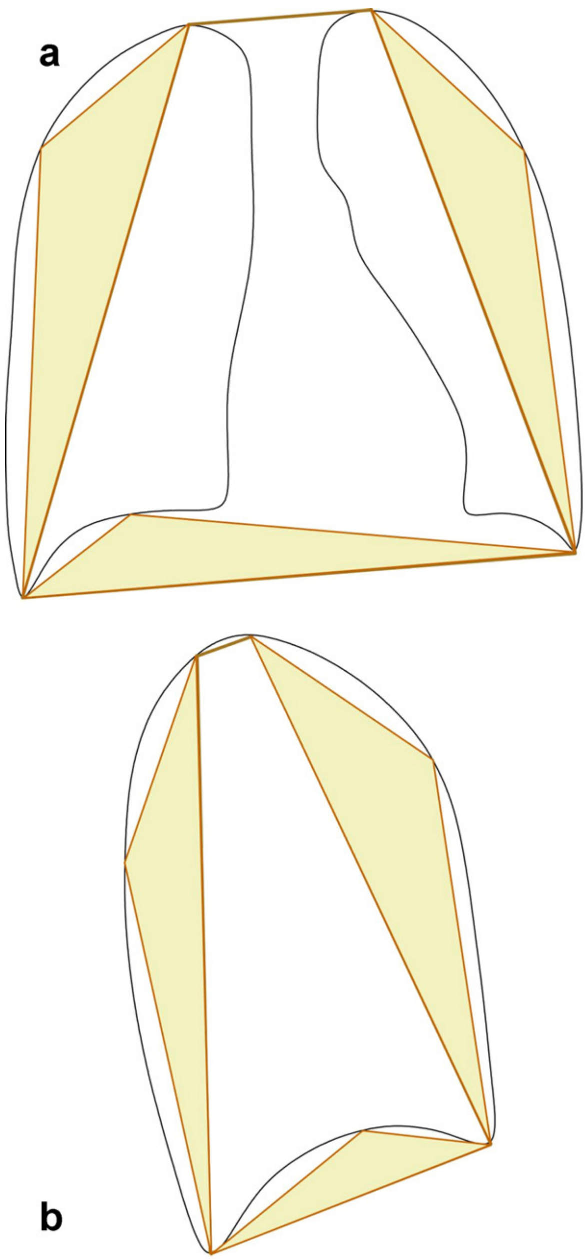

Fig. 2. Descriptors of lung shape in postero-anterior (a) and lateral (b) chest radiographs. In (a) the corners of the polygon are the apex and the costophrenic angle of each lung; in (b) the corners are the costophrenic angle posteriorly, the cardiophrenic angle anteriorly, the lung apex, and the maximum vertical distance from the line joining the costophrenic to the cardiophrenic angle. The triangles have their base on 3 sides of the polygon and their height equal to the maximum vertical distance from the triangle base to the superjacent lung segment.

curves as a numerical index. Ninety-five confidence intervals (95% CI) were estimated using the bias corrected accelerated bootstrap method.

3. Results

Inter-rater agreement in scoring emphysema on CT was excellent (Fig. 3).

Emphysema was diagnosed consistently by the two independent raters in 92 (41%) of the 225 patients. The prevalence of emphysema was slightly but not significantly higher in the derivation than in the validation sample (43% vs 38%, $p = 0.498$). Similarly, there was no significant difference between the two samples with regard to the severity of emphysematous lesions on CT; the median PG score was 50 (IQR, 35–68) in the derivation sample, and 50 (IQR, 30–75) in the validation sample ($p = 0.768$).

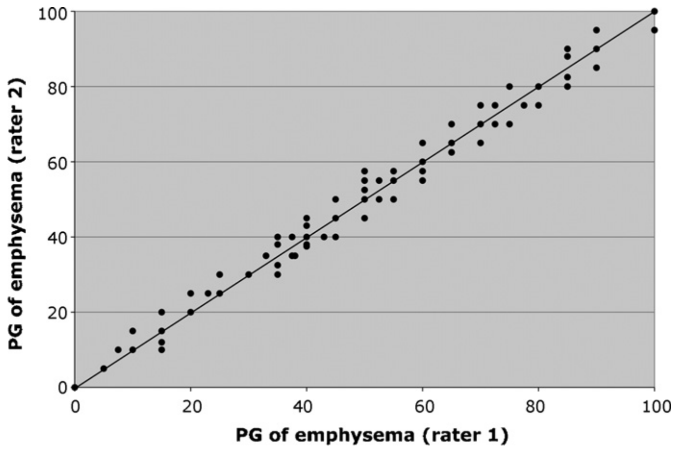

Fig. 3. Scatter plot of the panel grading (PG) of emphysema by two independent raters in 225 patients. The 45 degrees line represents perfect agreement. Departure from perfect agreement is tested for by fitting a simple linear regression model and verifying the null hypothesis that the intercept is equal to zero and the slope is equal to one, jointly. The resulting p-value is 0.7708, so indicating excellent inter-rater agreement. The two raters assigned the same PG in 167 cases of whom 133 were rated as not having emphysema (PG = 0).

ROC curves from the derivation and the validation samples are displayed in Fig. 4. Each curve is constructed using probability cut-points between 0 and 1 at steps of 0.05. The area under the ROC curve was 0.985 (95% CI, 0.965–0.998) in the derivation sample, and 0.975 (95% CI, 0.936–0.998) in the validation sample.

We chose a probability cutpoint of 0.55 to compute the sensitivity and specificity of the procedure in diagnosing or excluding emphysema on chest radiography (Table 1).

Overall, there were 8 false negative results, 4 in the derivation and 4 in the validation sample. Their characteristics are summarized in Table 2. In these patients, the PG score was consistent with mild or trace emphysema.

Five patients turned out to be false positive, of whom 3 in the derivation and 2 in the validation sample. Two of them had COPD on spirometry (FEV_1 46% and 69% predicted, respectively) but no emphysema on CT. The probability of emphysema in the 5 false positives was 0.56, 0.57, 0.57, 0.58, and 0.59.

Among the 141 patients who were diagnosed as having COPD, there was a highly significant relation ($p < 0.0001$) between the severity of airflow obstruction, as reflected by the GOLD stage, and the PG of emphysema on CT (Table 3). Similarly, there was a highly significant relationship ($p < 0.0001$) between the GOLD stage and the probability of emphysema on chest radiography (Table 3).

Table 1
Sensitivity and specificity of digital chest radiography against computed tomography in diagnosis or exclusion of emphysema*.

	Number	%	(95% CI)
Derivation sample			
Emphysema on CT	51/118	43	(34–53)
True positive on CXR	47/51	92	(80–97)
No emphysema on CT	67/118	57	(47–66)
True negative on CXR	64/67	96	(87–99)
Validation sample			
Emphysema on CT	41/107	38	(29–48)
True positive on CXR	37/41	90	(76–97)
No emphysema on CT	66/107	62	(52–71)
True negative on CXR	64/66	97	(89–99)

CI: confidence interval. CT: computed tomography. CXR: chest radiography.
* Based on neural network output (probability cutpoint 0.55).

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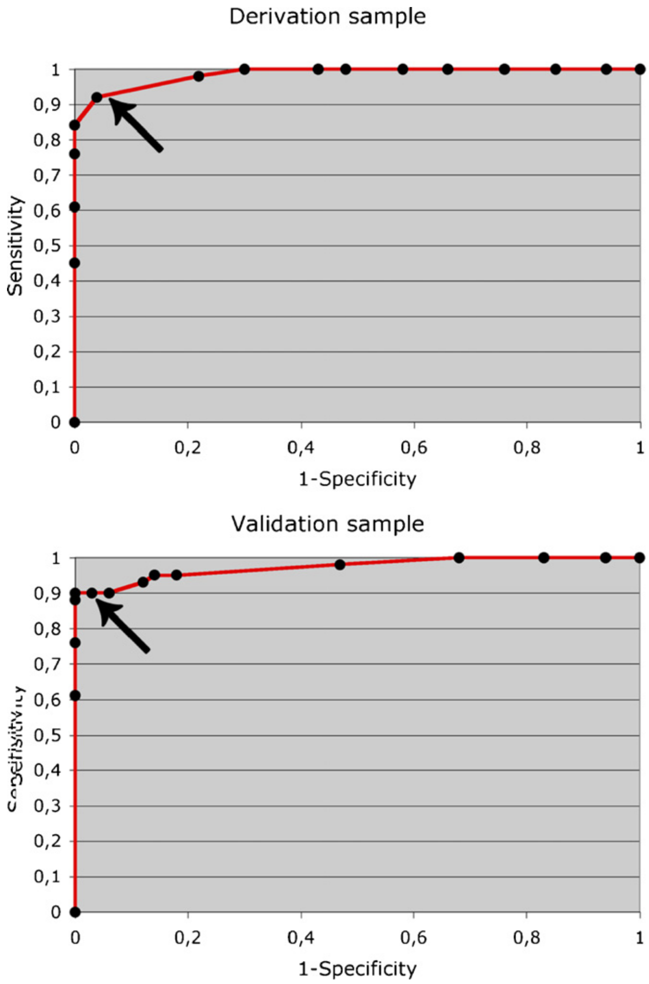

Fig. 4. Receiver operating characteristic curves from derivation and validation samples. Solid circles are probability cutpoints of emphysema from 0 (top right) to 1 (bottom left) as provided by neural network output. Arrows indicate the probability cutpoint (0.55) chosen to compute sensitivity and specificity of digital chest radiography.

Among the 225 patients included in the study, there was one patient only in whom emphysema and interstitial lung disease coexisted. This 68-year old male was GOLD stage 3 (FEV_1/FVC 43%, FEV_1 49% predicted), and had severe pulmonary arterial hypertension at right heart catheterization. The PG score of emphysema was 60, and the probability of emphysema on chest radiography 0.80. So, he was correctly classified as true positive for emphysema.

Fig. 5 shows the frequency distribution of the patients in the validation sample according to the estimated probability of emphysema on chest radiography. The computer-aided procedure provided a nearly complete discrimination between patients with and those without emphysema on CT.

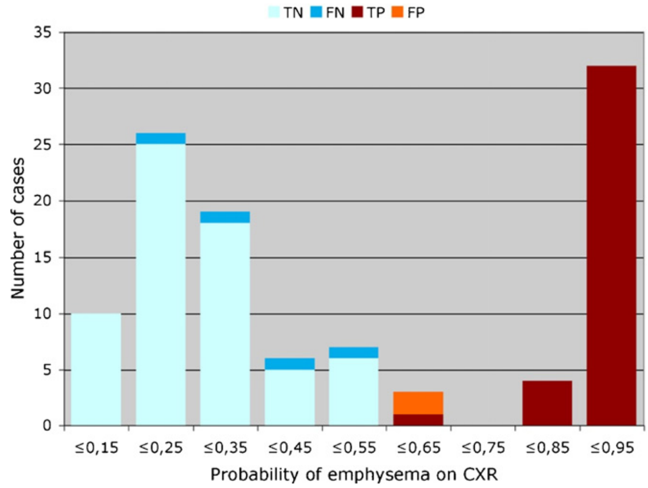

Fig. 5. Frequency distribution of patients in validation sample according to probability of emphysema. CXR: chest radiography. TN: true negative. FN: false negative. TP: true positive. FP: false positive.

4. Discussion

The recognition of emphysema on chest radiography is based on the identification of signs of hyperinflation and vascular disruption. Chronic hyperinflation is often manifested by depression and flattening of the diaphragmatic contours [6]. In the lateral chest radiograph, this determines a widening of the cardiophrenic junction such that the cardiophrenic angle is close to or greater than 90 degrees [6].

A widened restrosternal space is an additional sign of hyperinflation in the lateral view. It is defined as a space showing increased radiolucency and measuring 2.5 cm or more from the sternum to the most anterior margin of the ascending aorta [6].

In keeping with the pathology of emphysema, signs of vascular disruption or attenuation have also been described [6,12–14]. The identification of these vascular abnormalities, however, requires substantial medical expertise and is affected by the exposure of the chest radiograph. In fact, a grossly overexposed film makes the evaluation of vascular abnormalities nearly impossible.

Sometimes, it may be hard to establish whether a given diaphragmatic contour is flat. Similarly, it may be difficult to rate a retrosternal space "widened" in the presence of an unfolded ascending aorta, or "hyperlucent" if the anterior mediastinum is thickened by fibrotic tissue. We thought, therefore, to resort to a computer-aided recognition of emphysema.

Table 2
False negative results on digital chest radiography.

Patient	COPD	Probability of emphysema on CXR*	PG of emphysema	Type of emphysema	Distribution
1	Yes	0.54	15	Centrilobular	Upper lobe
2	No	0.23	15	Bullous	Upper lobe
3	No	0.36	10	Centrilobular	Upper lobe
4	Yes	0.49	7.5	Paraseptal	Upper lobe
5	No	0.48	5	Paraseptal	Upper lobe
6	No	0.23	5	Paraseptal	Upper lobe
7	No	0.32	5	Paraseptal	Upper lobe
8	No	0.41	5	Paraseptal	Upper lobe

COPD: chronic obstructive pulmonary disease; CXR: chest radiography. PG: picture grading. Patients 1–4 are from derivation sample. Patients 5–8 are from validation sample. Of the two COPD patients, one was GOLD stage 1 (FEV_1: 69% predicted), and the other GOLD stage 3 (FEV_1: 46% predicted).

* Based on neural network output.

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Table 3
Relationship between COPD, emphysema on computed tomography and probability of emphysema on digital chest radiography.

GOLD stage[a]	No. of patients	PG of emphysema		Probability of emphysema on CXR[*]	
		Median	IQR	Median	IQR
1	13	0	0–0	0.37	0.33–0.49
2	52	0	0–37	0.52	0.32–0.86
3	58	45	10–60	0.89	0.56–0.92
4	18	78	70–90	0.93	0.91–0.94

PG: panel grading; CXR: chest radiography; IQR: interquartile range. GOLD stage vs PG of emphysema: $p < 0.0001$; GOLD stage vs probability of emphysema on CXR: $p < 0.0001$ (Kruskal–Wallis nonparametric test).
[*] Based on neural network output.
[a] GOLD stage is based on severity of airflow obstruction as reflected by FEV_1% predicted. Stage 1: $FEV_1 > 80\%$; stage 2: FEV_1 between 50 and 80%; stage 3: FEV_1 between 30 and 49%; stage 4: $FEV_1 < 30\%$.

The proposed method is entirely based on the identification of abnormalities in the lung shape that are brought about by chronic hyperinflation. It does not rely on linear measurements, such as lung height or width, that are related to body build and gender, and have limited value in either diagnosing or excluding emphysema on chest radiography [13].

Our method makes use of simple descriptors that measure the bending characteristics of the lung profile on the postero-anterior and lateral chest radiographs. Such descriptors are applied to train a neural network to assign the chest radiographs a probability of emphysema between 0 and 1.

A probability >0.55 makes a diagnosis of emphysema very likely, whereas a probability <0.55 makes the diagnosis very unlikely (Table 1 and Fig. 5). Below this cutpoint, mild emphysema may occasionally be found. The sensitivity and specificity attained with our method are in all similar to those reported by experienced physicians [5].

In the patients with established COPD, we found a significant relationship between the severity of airflow obstruction and the severity of emphysema on CT (Table 3). This is in keeping with the notion that severe emphysema is a major determinant of airflow limitation in COPD patients [5]. We also found that the probability of emphysema on chest radiography is strongly related to the GOLD stage (Table 3), the higher the probability of emphysema the greater the degree of airflow obstruction. It should be made clear, however, that the algorithm we propose cannot be used to predict COPD because airflow obstruction may occur in the absence of structural emphysema.

The procedure described requires a minimal interaction in extracting the lung contours from the postero-anterior and lateral chest radiographs. This step needs no particular expertise, and is carried out in less than 2 min. Then, the program returns at once the probability of emphysema.

Now that filmless technology is available in many hospitals worldwide, the computer-aided method can be used for the online evaluation of emphysema on digital chest radiographs. Our method can also be applied in epidemiological surveys to assess the prevalence of emphysema in samples of the general population, should digital chest radiography be incorporated in the diagnostic work-up.

The present study has some limitations. First, the method we developed requires that the lung boundaries be clearly discernible in both the postero-anterior and lateral chest radiographs. So, any disorder that obscure the lung profile, such as large pleural effusion or extensive lung consolidation, will hamper the radiologic recognition of emphysema.

Second, the procedure we propose is not expected to assess precisely the extent and regional distribution of emphysema, nor to identify the type of emphysematous lesions. Such features are better evaluated by CT.

Third, we used a semi-quantitative method to assess emphysema on volumetric CT. Such method was developed by the pathologists for the very purpose of establishing whether emphysema is absent, mild, moderate, or severe [9], and was utilized to assess emphysema on axial CT [5,15–17]. Since volumetric CT allows three-dimensional image reconstruction, it facilitates the application of the PG score that was originally described in lung specimens cut along the midsagittal plane [9].

Over recent years, quantitative assessment of emphysema on CT has been introduced, based on the measurement of the relative lung area (volume) with attenuation coefficients below a given threshold [3]. Such an approach is aimed at overcoming the inherent subjectivity of visual estimates of emphysema [3].

As of now, there is no consensus regarding the actual threshold to be used, nor it is clear what is the upper limit of the relative lung area (volume) below a given threshold which identifies the transition from a normal to an emphysematous lung. Therefore, we preferred to apply an old-fashioned but well-established approach.

5. Conclusions

In summary, we propose a computer-aided method that allows online recognition of emphysema on digital chest radiographs. This method could be advantageously used in clinical practice for it is simple and inexpensive, and requires no special expertise. Its application may cut down the costs of the diagnostic procedures for emphysema and minimize the radiation burden to the patient.

Conflict of interest

The authors have no financial, personal, or professional interest that may have influenced the study design, the analysis and interpretation of data, or the writing of the report.

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