



Incomplete pulmonary fissures evaluated by volumetric thin-section CT: Semi-quantitative evaluation for small fissure gaps identification, description of prevalence and severity of fissural defects

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ABSTRACT

Objective: To assess the interobserver agreement for a semi-quantitative evaluation of the interlobar fissures integrity in volumetric thin-section CT images, looking for more detailed information regarding fissural defects; and describe prevalence and severity of fissural defects between the different functional groups of subjects.

Materials and methods: Volumetric scans of 247 individuals exposed to tobacco with different functional status (normal to severe COPD), were retrospectively and independently evaluated by 2 chest radiologists, with a consensual reading additionally with a third reader in disagreement cases. Right oblique (RO), right horizontal (RH) and left oblique fissures (LO) integrity was estimated using a 5% scale. GOLD classification was available for all subjects.

Results: Interobserver agreement (weighted Kappa-index) for fissural categorization was 0.76, 0.70 and 0.75, for RO, RH and LO, respectively. Final evaluation found 81%, 89% and 50% of RO, RH and LO to be incomplete, with respective mean integrity of 80%, 58% and 80%. Small fissure gaps (<10%) were present in 30% of patients. Prevalence and severity of fissural defects were not different between the GOLD categories.

Conclusions: A substantial agreement between readers was found in the analysis of interlobar fissures integrity. The semi-quantitative method allowed a detailed description of the fissural defects, information that can be important, for example, in endoscopic lung volume reduction therapies for emphysema. Small fissure gaps, overlooked in previous studies, were found in almost a third of the patients. A higher than previously described prevalence of fissural defects was described, but without significant differences among the distinct functional groups.

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1. Introduction

Many studies using different techniques and methodologies have already demonstrated that the pulmonary fissures are highly variable among individuals, and that the interlobar fissures are frequently incomplete [1–8]. However, these studies differ greatly with regard to the severity (percentage) of fissural defects, prevalence of incomplete and accessory pulmonary fissures and their relation to pulmonary diseases. Severity of fissural defects has been showed to vary from short gaps of few centimeters to almost complete absence [9,10]. It has long been known that fissures anatomy may affect the distribution and spread of diseases, influence the allocation of pleural effusion and must be addressed in surgical approaches to the lungs and pleural space. The fissures status has recently gained renewed attention after description of its importance in novel endoscopic lung volume reduction (ELVR) therapies for severe emphysema. A recent multi-center study group (VENT) demonstrated that patients with severe emphysema and complete fissures depicted on CT images presented a better response to endobronchial valves (EBV) treatment [11]. The authors implied that incomplete or defective fissures probably represent collateral ventilation pathways between the pulmonary lobes (parenchymal bridges), and this hypothesis has been subsequently confirmed by other studies using bronchoscopy techniques [12,13]. Also, interlobar collateral ventilation, which is increased in emphysematous patients, has been correlated with emphysema distribution, occurring in greater extent in patients with radiological homogeneous disease [14].

The pulmonary fissures are mostly evaluated with thin-section high-resolution computed tomography (HRCT). Although computerized methods to automatically quantify the fissural integrity have been suggested [15,16], these techniques still need to be validated, especially in heterogeneously diseased lungs. Visual inspection of thin-section CT images is still the most used method for assessing the pulmonary fissures anatomy.

Previous CT studies focusing on pulmonary fissures evaluation were done in disease-free populations, some using thick slices, others using incremental acquisitions with gaps, and, if present, a quantitative assessment of fissural defects was done using large-scale categories like 25% intervals. Criteria for definition of a complete fissure also differed between studies, and some authors considered a fissure complete when being >90% present, therefore not taking into account smaller fissural defects [8–11]. In our group's experience, we commonly face exams where small fissure gaps of few centimeters are identified in COPD patients, probably representing a defect <10%, mainly in the medial mediastinal/hilar fissure attachment.

Considering the recent demonstration of the importance of incomplete fissures in new less invasive therapies for emphysema [11], its probable role as a marker for interlobar collateral ventilation and the crescent use of thin-section multidetectors CT (MDCT) images in COPD evaluation, we aimed in this study to characterize the incomplete pulmonary fissures in a population of individuals exposed to tobacco, ranging from normal lung function and parenchyma to severe COPD and emphysema, studied by thin-section MDCT. First, we assessed the interobserver agreement for a semi-quantitative evaluation method of the severity of fissural defects, looking for more detailed information regarding fissures integrity. Then, based on this method, we described the prevalence and severity of incomplete fissures between the different functional groups of patients. We also reported the prevalence of accessory fissures.

2. Materials and methods

2.1. Patients

This evaluation was approved by our institutional review board and informed consent for scientific evaluation of data was available from all individuals enrolled in the study, prior to scanning. In this retrospective study, the dataset analyzed included volumetric MDCT scans of a total of 247 individuals (168 men; 79 women; mean age 60 years; age ranging from 43 to 79 years). All patients were active or former smokers (average 47.5 pack-years; smoking history ranging from 5 to 141 pack-years). Clinical indications for a chest CT scan varied from asymptomatic volunteers participating in a lung cancer screening program [17], symptomatic patients in evaluation for suspected emphysema, as well as patients with known COPD and emphysema in investigation for suspected alterations. This way, the studied population was comprised of patients with normal to severe compromised function and CT exams ranging from normal lung parenchyma to severe emphysematous destruction. GOLD (Global Initiative for Chronic Obstructive Lung Disease) classification was available for all patients, based on spirometric examinations performed within the same week of the CT scans. Subjects with normal function were designated as GOLD category 0.

2.2. MDCT scans

All volumetric data was obtained using either a 4-detector (Somatom Volume Zoom, Siemens Medical Solutions, Erlangen, Germany) or a 16-detector (Aquilion 16, Toshiba, Japan) CT system. Scans were obtained at end-inspiration breath-hold, without intravenous administration of iodinated contrast media. CT parameters were: 120-kV tube voltage, 210 mAs (range 110–270 mAs) tube current and 1.0 or 1.25 mm slice thickness (16- and 4-detector scanners, respectively). Image data was reconstructed using standard (B40f) and high-resolution algorithm (B70f), 1.0 mm reconstruction interval, field of view of 350–400 mm and a 512×512 matrix. All datasets were transferred to a PACS system (Synapse, Fuji Medical System) at calibrated workstations. In our institution, all patients with suspected airway disease undergo quantitative CT emphysema analysis, which was also available for all subjects enrolled in this study. Quantification was performed with a fully automated in-house software (YACTA) [18] in the same exams where the fissures analyses were performed on.

2.3. Image evaluation

Two chest radiologists (MKS, 5 years of experience; WDP, 8 years of experience) retrospectively reviewed all MDCT images separately, blinded to any clinical information, using the dedicated PACS workstations. The readers had previous experience with fissures evaluation and also used the interactive multiplanar reformation tools to help categorizing each fissure, which enhances the analysis accuracy [19]. The pulmonary fissures were analyzed using the standard lung window settings (level: –600 HU, width: 1600 HU). The axial images were used for the purpose of the semi-quantitative analysis, and fissure integrity was estimated in a 5% scale, therefore ranging from 0% (absent) to 100% (fully complete). The right oblique (RO) fissure was examined taking into account its superior and inferior halves, with the right horizontal (RH) fissure as the landmark for this division; the left oblique (LO) was examined in its apical, middle and basal thirds. Location of the fissure defect may have clinical implication, especially for the right upper lobe, which is delimited by the RH and the superior half of the RO. In case this lobe is selected as target for EBV therapy, these are the fissure components most important to be addressed. In this study

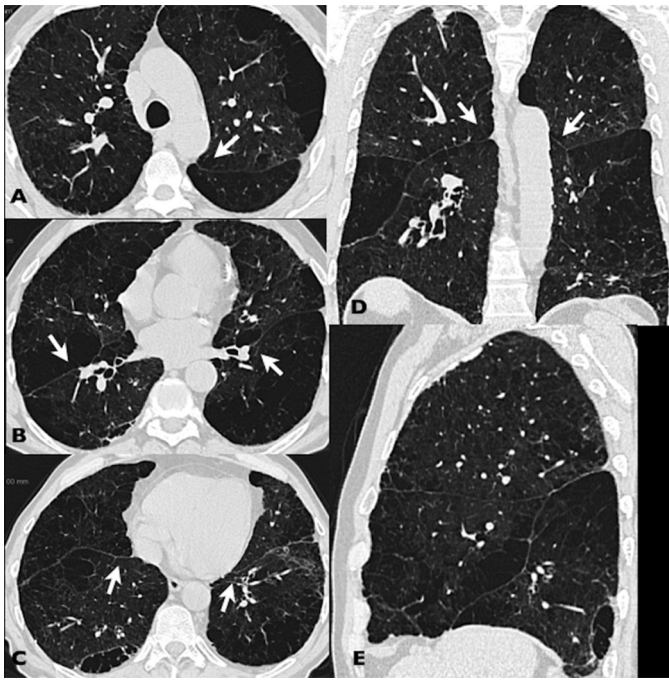


Fig. 1. Example of thin-section CT images (lung window) of a subject with COPD GOLD category 3, emphysema and complete fissures. Even in the presence of prominent emphysema and anatomy distortion, the normal fissure medial attachments to the mediastinum and hilum can be well depicted (arrows) in the axial (A–C) and reformatted images (coronal in D, right sagittal in E). Fissure integrity was estimated in a 5% scale, ranging from 0% (absent) to 100% (fully complete), and assigned considering the whole fissure extent. A fissure was considered fully complete only if it could be identified in all its extension in all examined segments, i.e., superior and inferior halves of the right oblique, and apical, middle and basal thirds of the left oblique fissure. Both readers assigned this patient as having the oblique fissures fully complete.

we used such subdivisions to identify if the readers were describing the same fissural defects, especially when considering small defects. Even though, the severity (percentage) of fissural defect was always assigned considering the whole fissure. A fissure was considered fully complete only if it could be identified in all its extension, with special attention to the medial attachment at the mediastinum and hilum. Afterwards, for the purpose of describing prevalence and severity of fissural defects in the studied population, average values were also calculated for all subjects, based on both readers evaluation. When the two readers disagreed in relation to the fissure status (complete vs. incomplete) or location (subdivision) of the fissural defect, a consensual reading with a third senior chest radiologist (MP, 12 years of experience) was obtained, and a final value for the fissure integrity was assigned. **Figs. 1 and 2** exemplify how the fissures evaluation was performed. Description of the accessory pulmonary fissures was also done in the consensual evaluation with the third reader when the two original readers did not describe them similarly, and nomenclature was used as previously described by Cronin et al. [9]. For the accessory fissures, only presence was reported.

2.4. Statistical analysis

Statistics was performed with Prism 6 software (Graphpad Software Inc, USA). Agreement between the two original readers was described taking into account the same rating, but also rating differences between the readers. The weighted Kappa index (wKI) was obtained, and for its calculation the integrity of each fissure as evaluated by each reader was divided in a restricted number of categories. Based on previous studies and clinical relevance, we chose

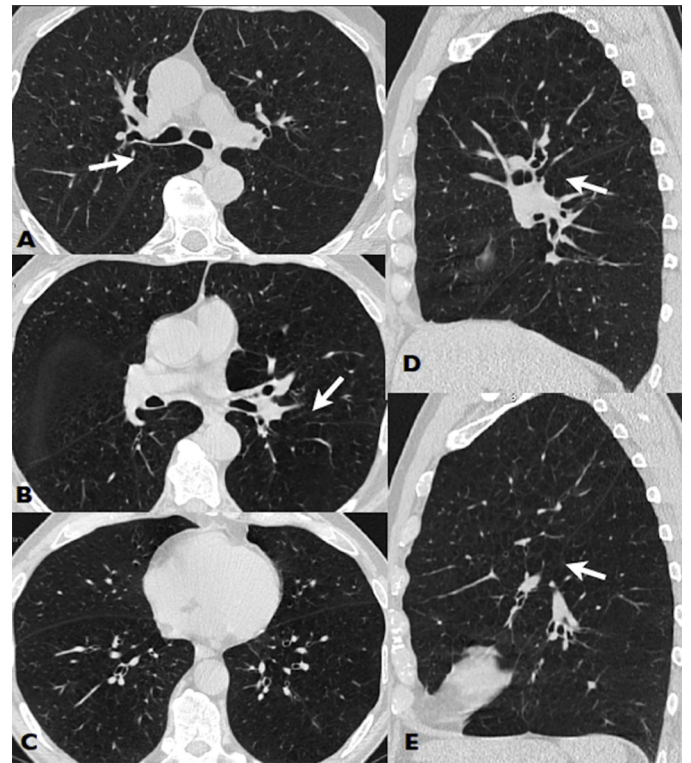


Fig. 2. Example of thin-section CT images (lung window) of a subject with COPD GOLD category 2, emphysema and incomplete oblique fissures, with small fissure gaps. Small medial fissural defects of approximately 2–3 cm were identified by both readers in the upper half of the right oblique (RO) fissure (arrow in A) and in the middle third of the left oblique (LO) fissure (arrow in B). Sagittal reformatted images (right side in D and left side in E) help to assure the presence of fissural defects (arrows). In this case, one reader assigned the subject as having both oblique fissures 90% complete (10% fissural defect), while the second reader assigned an integrity of 90%/95% for the RO/LO fissure. As they agreed regarding the fissures status (complete vs. incomplete) and defects location, no consensual reading with a third reader was necessary. Finally, to include in the population description of prevalence and severity of incomplete fissures, integrity for this subject was assigned as 90%/93% (average between both readers) for the RO/LO, respectively.

to divide it in seven categories: absent, 1–20%, 21–40%, 41–60%, 61–80%, 81–99%, and fully complete. Interpretation of the wKI for agreement was: 0 = absent; 0.01–0.2 = slight; 0.21–0.40 = fair; 0.41–0.60 = moderate; 0.61–0.8 = substantial; 0.81–0.99 = almost perfect; 1 = perfect agreement [20]. Continuous quantitative data, e.g. patients' age and emphysema index, was compared using two-tailed *T*-tests. Prevalence of incomplete fissures between the different GOLD categories of COPD was compared using the Chi-square test, while comparison of fissural defects severity was done with the Mann–Whitney test. *P* values of <0.05 were considered statically significant for all comparisons.

3. Results

Table 1 shows the clinical data summary for all patients in relation to the GOLD categories. No significant differences were observed between the COPD categories for patients' gender prevalence, age and smoking history. Quantitative CT analysis showed a higher emphysema index in GOLD 3 and 4 patients ($P < 0.01$) when compared to categories 0, 1 and 2, therefore confirming that patients with worse obstructive disease also had a more severe degree of emphysema.

The readers described exactly the same severity of fissural defects (in the 5% scale categorization) in 88 (36%), 60 (24%) and 125 (51%) cases, for the RO, RH and LO fissures respectively (**Table 2**). When considering a rating difference maximum of 10%, they agreed

Table 1

Resume of the clinical data for the studied population of 247 subjects in relation to the GOLD categories of COPD. Subjects with normal functional parameters were designated as GOLD category 0.

GOLD category	Patients (N)	Gender		Age (years)		FEV1%		FEV/FVC		Smoking history (py)	Emphysema index
		Male	Female	Mean	SD	Mean	SD	Mean	SD		
0	61	42	19	59	5	97.1%	14.0%	77.4%	5.8%	47	6.9
1	34	23	11	60	7	91.0%	11.0%	64.1%	5.1%	45	12.0
2	48	37	11	61	6	69.3%	23.7%	57.8%	8.5%	49	18.8
3	52	30	22	60	19	41.1%	11.6%	42.7%	6.3%	46	35.7
4	52	36	16	59	7	28.7%	15.0%	33.6%	5.6%	50	41.2
All	247	168	79	60	10	64.7%	31.6%	55.2%	17.5%	48	23.2

FEV1%: forced expiratory volume in first second; FEV/FVC: Tiffeneau index; py: pack-years; emphysema index as evaluated by quantitative CT analysis (Yacta software); SD: standard deviation.

Table 2

Interobserver agreement (N cases and proportion) for the two independent readers according to the rating difference in the evaluation of integrity of the interlobar fissures.

Fissures	Rating difference between readers					
	0 (same rating)	0.1–5.0%	5.1–10.0%	10.1–15.0%	15.1–20.0%	>20.0%
Right oblique	88 (36%)	105 (43%)	33 (13%)	16 (6%)	3 (1%)	1 (<1%)
Right horizontal	60 (24%)	72 (29%)	57 (23%)	31 (13%)	14 (6%)	13 (5%)
Left oblique	125 (51%)	77 (31%)	28 (11%)	9 (4%)	5 (2%)	3 (1%)

Table 3

Prevalence (N subjects and proportion) of incomplete interlobar fissures in relation to the GOLD categories of COPD.

Gold category	Right oblique fissure	Right horizontal fissure	Left oblique fissure
0	52 (85%)	58 (95%)	30 (49%)
1	28 (82%)	28 (82%)	15 (44%)
2	39 (81%)	44 (92%)	28 (58%)
3	40 (77%)	43 (83%)	26 (50%)
4	40 (77%)	46 (86%)	25 (48%)
All	199 (81%)	219 (89%)	124 (50%)

in 226 (91%), 189 (77%) and 230 (93%) cases, respectively for the RO, RH and LO fissures. Overall interobserver agreement (wKI) between the two original readers was 0.76, 0.70 and 0.75, for the RO, RH and LO fissures, respectively.

Final evaluation found 199 (81%), 219 (89%) and 124/247 (50%) of RO, RH and LO to be incomplete (Table 3). Therefore, the RH was the most commonly incomplete fissure, while the LO presented the lowest proportion of fissural defects. Integrity of the incomplete fissures showed mean values of 80%, 58% and 80%, for the RO, RH and LO respectively (Table 4). This means that the incomplete oblique fissures presented similar severity of defects, while the incomplete RH fissures had larger defects.

Only 9 (4%) out of 247 subjects presented with all fissures being complete. Most of the incomplete fissures presented severity of defects between 10 and 50% (Table 5). A fissural defect <10% was present in 73 (30%) patients, mostly described as 2–3 cm medial fissural defects identified in few continuous slices, configuring small

Table 4

Average integrity (%) of the incomplete interlobar fissures in relation to the GOLD categories of COPD.

Gold category	Right oblique (%)		Right horizontal (%)		Left oblique (%)	
	Mean	SD	Mean	SD	Mean	SD
0	81	10	55	22	81	13
1	83	12	61	20	76	17
2	75	14	59	21	78	21
3	81	9	54	23	80	15
4	81	11	60	18	81	13
All	80	11	58	21	80	16

SD: standard deviation.

fissure gaps (Fig. 2). Between these cases with small fissure gaps, 29 were patients with severe COPD (GOLD 3/4), most of them also presenting higher emphysema index. Prevalence and severity of fissural defects were not statistically different between the GOLD functional categories of COPD (Tables 3–5).

Accessory fissures were found in 40 (16.2%) patients, with the left horizontal being the most common (18 patients). Other less frequent accessory fissures described were: the right inferior (17), right superior (6), azygos (3), lingula (1), left inferior (1), left superior (1) and middle lobe (1 patient).

4. Discussion

In this study, we performed a meticulous characterization of the incomplete pulmonary fissures as evaluated by thin-section MDCT images, in a population of tobacco-exposed individuals with different pulmonary functional categories. We found a substantial agreement between readers using a 5% scale semi-quantitative analysis of the interlobar fissures integrity. The readers frequently agreed even in the analysis of patients with heterogeneous disease and distorted anatomy by emphysema. Using this methodology,

Table 5

Distribution of incomplete interlobar fissures (N subjects) according to integrity intervals and in relation to the GOLD categories of COPD.

Fissures integrity	GOLD categories					
	0	1	2	3	4	Total
Right oblique						
<50%	0	0	3	0	1	4
51–75%	15	8	15	10	11	59
76–90%	30	11	15	24	21	101
91–99%	7	9	6	6	7	35
Total for fissure	52	28	39	40	40	199
Right horizontal						
<50%	23	8	12	14	15	72
51–75%	24	14	24	26	22	110
76–90%	10	5	6	2	7	30
91–99%	1	1	2	1	2	7
Total for fissure	58	28	44	43	46	219
Left oblique						
<50%	1	2	3	1	1	8
51–75%	8	4	5	4	6	27
76–90%	13	5	12	16	10	56
91–99%	8	4	8	5	8	33
Total for fissure	30	15	28	26	25	124

almost a third of the patients were identified with fissural defects <10% (small fissure gaps), and a high prevalence of incomplete fissures was described. No significant difference in prevalence or severity of fissural defects was found among the distinct functional groups.

Recently, several ELVR strategies have been developed for palliation in severe emphysematous patients, as alternative to surgery. These bronchoscopy-based techniques (valves, coils, glues and other agents) aim to obtain the collapse of the most diseased target lobe, and have been demonstrated to have lower treatment-associated morbidity and mortality when compared to surgery [21]. EBV are usually advantageous, since they are easy to employ and offer the possibility of temporal application. The VENT study showed that lobar volume reduction using EBV presented superior clinical results when there were CT findings suggestive of complete interlobar fissures [11]. A complete fissure was designated when more than 90% of the fissure length was present on at least one axis (axial, sagittal or coronal), as classified by a consensual reading at thin section CT images. Therefore, according to the authors' definition, small fissural defects <10% were not taken into account. Similar methodology and definition has also been used in subsequent studies evaluating ELVR therapies [22,23]. Air leak through collateral channels is the major concern following ELVR therapies, and knowledge of the precise incidence and extent of interlobar laterals is considered paramount [24]. After a meticulous evaluation of the fissures integrity, almost a third of the 247 patients evaluated in this study presented small fissure gaps (defects <10%). Even if the role of these small fissural defects as source of significant collateral ventilation has not been established, and its influence in pulmonary surgery and endoscopic procedures has to be determined, our results suggest that they may be more frequent than expected and therefore should be described. A semi-quantitative analysis can be used for this detailed description of the fissures integrity, while it showed clinical significant agreement between observers and it is simple enough to be applied in clinical routine.

A higher prevalence of incomplete fissures in patients with more severe COPD and emphysema was not described, and the defects were designated in similarly positions, related to the mediastinal or hilar insertion of the fissures, which did not match with areas of higher emphysema destruction or anatomy distortion. These findings also help to ensure that the small fissure gaps described in this study really represent partial absence of the fissures, and are not related to image artifacts or anatomy distortion by emphysema.

In the present study, a higher prevalence of fissural defects was found when compared to previous studies using thin-section CT images. The authors believe this is probably related to the applied methodology, with a more detailed evaluation of the fissures integrity, and use of different criteria for definition of complete fissure. In this population of 247 individuals with different degrees of lung disease, approximately 81%, 89% and 50% of the RO, RH and LO fissures were incomplete, respectively. Guelsuen et al. [8] evaluated HRCT scans of 144 patients with normal lung parenchyma and described 63% and 60% of the RO and LO to be respectively incomplete. Cronin et al. [9] retrospectively assessed MDCT exams of 150 patients without lung disease, and described 34%, 48%, and 25% of the RO, RH and LO fissures to be incomplete, respectively, and 40% of patients had an accessory fissure, most commonly the left horizontal. Ozmen et al. [10] studied 387 patients without significant thoracic changes scanned on a 64-row MDCT, fissures integrity was assessed in a 25% scale fashion, and the authors found 70%, 87% and 48% of the RO, RH and LO fissures to be incomplete, respectively. Accessory fissures were described in 42.4% of patients. van Rikxoort et al. [16] studied 96 subjects with homogeneous emphysema as depicted by MDCT, and used an automatic technique in comparison to a visual consensual reading of experienced radiologists. The authors classified the fissures as complete, partial or

absent, and final consensual evaluation found 51%, 85% and 33% of the RO, RH and LO fissures to be incomplete, respectively. To our knowledge, the present study is the first to evaluate a semi-quantitative quantification of the integrity of interlobar fissures as assessed by thin-section MDCT images, addressing the presence of small fissural defects, and to analyze it in a population comprised of individuals with different degrees of pulmonary alterations, ranging from normal parenchyma to severe emphysema.

In the present study, no significant difference in prevalence or severity of fissural defects among the distinct pulmonary functional groups was described. The major interest in studying a heterogeneous population comprised of normal individuals and patients with severe emphysema was to verify if lung disease could influence fissures detectability, and the semi-quantitative method showed to be robust against distortion of the parenchymal anatomy related to emphysema. Even though, there was also interest in comparing the fissure status among the different COPD groups, especially because of the results described by Higuchi et al. [14], who showed that interlobar collateral ventilation occurred to a much greater extent in patients with radiologically homogeneous than in those with heterogeneous emphysema. The authors concluded that heterogeneity of emphysema may predict patients with a significant or reduced risk of interlobar collateral ventilation and this could influence in selection of patients to ELVR therapy. It is an interesting question whether the other-way relation can also be assumed, so that the presence of collateral ventilation pathways (already present in normal lungs and probably related to interlobar fissures integrity) as an individual characteristic could influence emphysema distribution and degree, and therefore be involved in the disease pathophysiology [25]. Besides the bronchoscopic studies demonstrating the presence of collateral ventilation between lobes [13], hyperpolarized gas magnetic resonance imaging (e.g. ^3He - or ^{129}Xe -MRI) as well as lung ventilation scintigraphy could also show that there is indeed airflow between the pulmonary lobes, and it is increased in COPD patients [26,27]. The lack of differences on the fissures status between the functional groups in this study could be explained by the absence of linear correlation between the degree of airflow limitation (spirometric test) and emphysema proportion [28]. Therefore, as a next step, we intend to determine a possible correlation between the fissures integrity, as a marker of collateral ventilation and assessed with this more detailing semi-quantitative method, and the emphysema degree and distribution assessed by quantitative CT in a lobar/lung-basis analysis.

This study has some limitations: we performed a semi-quantitative analysis, which is better than a simple qualitative classification of the fissures (complete versus incomplete), but does not give the same degree of confidence when compared, for example, with the measurements obtained by computerized tools; this study lacks a gold-standard anatomical evaluation for the fissures integrity to correlate with the CT description; and no other method was available to verify that there was significant collateral ventilation between lobes in cases of incomplete fissures, especially for the small fissure gaps, which could be clinically obtained, for example, with bronchoscopy [12].

5. Conclusions

In this study, the incomplete pulmonary fissures were characterized in a population of 247 individuals examined by thin-section MDCT images, including subjects with normal function/lung parenchyma and subjects with different degrees of COPD and emphysema. A substantial agreement between readers was described for a 5% scale semi-quantitative analysis of the interlobar fissures integrity. Using these detailed methodology, almost

a third of the studied patients presented small fissure gaps <10%, previously overlooked by other studies. Furthermore, a higher than previously described prevalence of incomplete fissures was found. Considering the crescent interest in pulmonary fissures anatomy, especially because of its proved importance for the new less invasive ELVR therapies for emphysema, the results in this study suggest that a semi-quantitative method could be used to evaluate the fissures anatomy with more details, inclusively in clinical routine.

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Conflicts of interest

All authors declare no conflicts of interest in this work.

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