Invasive techniques in the management of severe Pulmonary Emphysema. Which and when?

The role of Imaging with CT

Collateral Ventilation

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Radiologists
The pattern of emphysema observed on the CT scan
- centrilobular emphysema
- panlobular emphysema
- paraseptal emphysema
Pulmonary emphysema
Centrilobular emphysema

- Centrilobular is by far the most common type.
- Common finding in asymptomatic elderly patients.
- The centrilobular pattern affects the proximal respiratory bronchioles which are seen as focal lucencies measuring from hardly visible defects up to 10-20 mm in diameter
- Located centrally within the secondary pulmonary lobule.
- Upper lobes or the apical segments of the lower lobes
Severe centrilobular emphysema CT

It appears as focal lucencies (emphysematous spaces) which measure up to 1-2 cm in diameter, located centrally within the secondary pulmonary lobule, often with a central or peripheral dot representing the central bronchovascular bundle.
Pulmonary emphysema
Panlobular emphysema

- **Panlobular emphysema** affects the entire secondary pulmonary lobule
- More pronounced in the lower zones or even bigger defects, matching areas of maximal blood flow lobes
- Tends to lead to more homogeneous involvement.
Panlobular emphysema
Radiological Assessment
CT
Pulmonary emphysema

Paraseptal emphysema

• Located adjacent to the pleura and septal lines with a peripheral distribution within the secondary pulmonary lobule.
• The affected lobules are almost always subpleural. Demonstrate small focal lucencies up to 10 mm in size.
• Well preserved more central lung tissue.
Paraseptal emphysema
Radiological Assessment
Endobronchial Valves

- Valve treatment is targeted to the most emphysematous destroyed lung lobe, which will need to be completely occluded by the valves.
- EBVs are placed bronchoscopically to occlude the emphysematous lobe.
- The goal is to create an atelectasis of the region of the lung
- The valves allow the air to be expelled during expiration but not to enter the lobe during inspiration, thus facilitating the creation of a full lobar atelectasis.
Radiological Assessment prior to the procedure

Standardized CT scans are required to
- Characterize the emphysema.
- Evaluate the distribution of the emphysema destruction.
- Measure for emphysema heterogeneity.
- Evaluate the interlobar collateral flow. Determine the integrity of the lobar fissures.
Multidetector CT

CT protocol

CT protocol should be a standardized non-contrast volume acquisition on a multidetector scanner platform with thin (0.6-1.25 mm) series with some overlap.
The primary assessment should also ensure the absence of significant comorbidity or abnormalities that require further assessment.

If there are unexpected findings like bronchiectasis, pulmonary nodules, suspected lung cancer and interstitial fibrosis then the patients should be evaluated and treated based on the underlying disease.

It would be inappropriate to consider them for endoscopic lung volume reduction.
Radiological Assessment
Emphysema quantification

- Emphysema quantification on CT is usually expressed as the proportion of pixels of $<-910$ or -950 Hounsfield units (HU).
- The -910 HU density threshold is commonly used for thick-slice (>3 mm) CT scans.
- This threshold yielded the best correlation between emphysema, as determined from resected lung tissue and 10-mm-thick slice CT measurements.

For thin-slice volumetric chest CT scans, -950 HU is nowadays the most commonly used threshold. The strongest correlation between the pathology of macroscopic and microscopic emphysema and CT measurements has been reported at a threshold of -950 HU in 1-mm non-contrast chest CT scans.

Radiological Assessment
Measurement of emphysema heterogeneity

• Using emphysema quantification scores, a relative lobar difference of this measure is regarded as heterogeneity.
• This can be done by simple visual analysis, but more accurate results are produced using software systems.
• Heterogeneity is the relative or percentage difference in the emphysema scores between ipsilateral lobes.
• To date, no clear definition exists for heterogeneity.
• In most trials reported, a >25% difference in the proportion of pixels of <-910 HU or a >15% difference in the proportion of pixels of <-950 HU has been used.

Herth FJ, Slebos DJ, Rabe KF, Shah PL. 
Respiration. 2016;91(3):241-50
Heterogeneous pulmonary emphysema

Heterogeneous pulmonary emphysema
The phenomenon of collateral ventilation in the human lung is defined as “the ventilation of alveolar structures through passages or channels that bypass the normal airways”.

- This phenomenon seems to be prominent in emphysema and is emerging as a key issue for those working in the new and exciting field of bronchoscopic techniques for treating emphysema.
Collateral ventilation

Too small to appear visible on CT, their existence being confirmed through electron microscopy.

Intra- and interlobar collateral ventilation

The fissure: interlobar collateral ventilation and implications for endoscopic therapy in emphysema.
Koster TD, Slebos DJ.
Int J Chron Obstruct Pulmon Dis. 2016 Apr 13;11:765-7
What’s the significance of CV?

The resistance to collateral flow in human lungs has been measured and found to be 50 times greater than the resistance to flow through the normal airways. It therefore seems that collateral ventilation has NO SIGNIFICANCE in subjects with NORMAL AIRWAYS.

However, the resistance to collateral flow is markedly reduced in certain conditions including emphysema due to:

- Destruction of terminal bronchioles → opening of CV
Radiological Assessment
Assess interlobar collateral flow

• To assess interlobar collateral flow, dedicated endoscopic measurement of the collateral flow is possible with the Chartis Pulmonary Assessment system (Pulmonx). Whether a patient is a candidate can be decided using bronchoscopy.
• In a multicenter European study, it was shown that the fissure analysis and the endoscopic measurement have a high correlation.

Assessment of fissure integrity

- Patients with a complete interlobar fissure on the HRCT scan experienced the best outcome following EBV implantation.
- Unilateral lobar occlusion with EBV in patients with heterogeneous emphysema and intact interlobar fissures assessed on CT produces significant improvements in lung function as well as improvements in the quality of life.

The occurrence of incomplete fissures (IF) was first described in the 1940s.

Aziz et al. conducted a visual CT analysis of the completeness of fissures in 622 healthy patients, finding IF in 43% of left fissures, 48% of major right fissures and 63% of minor.

IF therefore is not the exception and cannot be regarded as pathological.

The frequency of IF in emphysema patients is approximately the same as that of the healthy population.

Assessment of fissure integrity in emphysema patients

- **Incomplete fissure** is present if CT shows $<90\%$ of the fissure to be traceably intact in a spatial plane.
- Frequently, CV is incorrectly used synonymously with IF.
- A complete fissure therefore appears to be a predictor of absent or only minor CV

Fissure analysis

- A pretreatment fissure analysis must be performed, and patients with an incomplete fissure should not be considered for treatment with valves.
- If the interlobar fissure between the treatment target lobe and adjacent lobe is less than 85% intact, proceeding to valve treatment is not useful because of the high likelihood of present collateral flow.
- If the fissure is between 95 and 100% complete on CT, there will be a very low occurrence of significant collateral flow.

Criteria for incomplete interlobar fissures

1) neither a clear avascular zone nor interlobar line is observed
2) vascular images in adjacent lobes cross over the interlobar region
3) pulmonary blood vessels, particularly the pulmonary vein penetrate the interlobar region
4) the pulmonary vein is observed in the interlobar region and is related to the vascular images in adjacent lobe

The fissure: interlobar collateral ventilation and implications for endoscopic therapy in emphysema.
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Automatic methods have been developed to quantify the completeness of the fissures
Automatic methods have been developed to quantify the completeness of the fissures.
Radiological Assessment

- Prior to the procedure itself, the preferred sites for stent placement were identified on the chest CT scans based on the areas of most emphysematous destruction within the lung parenchyma

<table>
<thead>
<tr>
<th></th>
<th>RIGHT LUNG</th>
<th>LEFT LUNG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RUL</td>
<td>RUL+RML</td>
</tr>
<tr>
<td>% Fissure Completeness</td>
<td>48.6</td>
<td>53.8</td>
</tr>
<tr>
<td>% Voxel Density Less Than -910 HU</td>
<td>63</td>
<td>68</td>
</tr>
<tr>
<td>% Voxel Density Less Than -950 HU</td>
<td>34</td>
<td>38</td>
</tr>
<tr>
<td>Inspiratory Volume (ml)</td>
<td>1256</td>
<td>2326</td>
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</tbody>
</table>
For visualization purposes, images are rendered for a voxel density less than -950 HU.
Post-treatment Radiological Assessment
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Lung Volume Reduction in Pulmonary Emphysema from the Radiologist's Perspective.
Doellinger F, Huebner RH, Kuhnigk JM, Poellinger A.
Post-treatment Radiological Assessment

- The problem limiting repeat CT scans for post-treatment assessment is the cumulative radiation dose.
- Standard-dose CT for follow-up of BLVR is limited by the risk of administration of a radiation dose of 8-12 mSv for each CT examination.
- Low-dose CT, in which the radiation dose is six to ten fold less than in conventional CT, has been used for the evaluation of emphysema patients
- This technique was recently used for the evaluation of the feasibility of thin-section low-dose CT in the radiologic monitoring of patients after placement of bronchial stents for airway bypass

Comparison of standard- and low-radiation-dose CT for quantification of emphysema.
Gierada DS, Pilgram TK, Whiting BR, Hong C, Bierhals AJ, Kim JH, Bae KT.

Low-dose MDCT for surveillance of patients with severe homogeneous emphysema after bronchoscopic airway bypass.
Grgic A, Wilkens H, Kubale R, Gröschel A, Buecker A, Sybrecht GW.
Conclusions

- EBV is a method in which the phenomenon of "collateral ventilation" (CV) is an issue, making patient selection especially important.
- Pre-interventional evaluation of this phenomenon through analysis of pulmonary fissures on the basis of CT scans
- An automated evaluation of the completeness of fissures, which would save both time and resources, would be desirable.
- Valve implantation should not be performed without the prior evaluations, as clinical success may otherwise be jeopardized.
- Quantitative computed tomography (qCT) is the method of choice for evaluating pulmonary emphysema lobe-by-lobe and recommending the optimal target lobes for ELVR the interventional pulmonologist.

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