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Bronchoscopic Measurement of Collateral Ventilation: State of the Art

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Chartis assessment · Endobronchial valve treatment · Lung volume reduction · Collateral ventilation · Fissure integrity

Abstract
Endoscopic lung volume reduction procedure with valves is a well-studied treatment option for advanced lung emphysema to target lung hyperinflation in carefully selected patients with COPD. Before valve implantation, collateral ventilation (CV) of the target lobe needs to be assessed to obtain an optimal treatment effect. The analysis of CV according to current standards occurs via an in vivo assessment with the Chartis® system (PulmonX Inc., Redwood City, CA, USA) and a computed tomography (CT) scan of the thorax with interlobar fissure analysis. The focus of this review is to provide detailed information about the Chartis® procedure and interpretation of Chartis® phenotypes. As a main tool in the assessment of CV and being a safe procedure, the Chartis® assessment should be performed by default to confirm interlobar fissure analysis in most emphysema patients. Based on the obtained results, lung volume reduction therapy options should be discussed in an interdisciplinary emphysema conference.

Introduction

A. Aim of the Review

- The aim of this review was to inform in detail about the assessment of collateral ventilation (CV) and the planning of endoscopic lung volume reduction (ELVR) with valves, with a special focus on the endoscopic Chartis® assessment system.

Today, ELVR procedures are an established procedure to treat hyperinflation in chronic obstructive pulmonary disease with emphysema. Several endoscopic methods have been developed in the last years to improve dyspnoea, exercise capacity, and life quality for patients with advanced emphysema. The goal of ELVR is to address hyperinflation and to improve breathing mechanics. The technique most frequently used is the implantation of endobronchial and intrabronchial one-way valves (EBV and IBV) [1–5]. Treatment with valves is the best studied and most effective ELVR procedure. The implantation of one-way valves in bronchial segments of a previously selected target lobe allows air to exit during expiration while also impeding air inflow during inspiration. This results in lung volume reduction as a complete or partial atelectasis. Studies have confirmed that an intact lobar fissure,

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meaning absent CV between two adjacent lobes, is the most important predictor for treatment response and for respective success. An in vivo assessment with the Chartis® system (PulmonX Inc., Redwood City, CA, USA) and a computed tomography (CT) scan of the thorax with interlobar fissure analysis are performed in order to assess CV according to current standards [6].

B. What Is Collateral Ventilation?

- CV is the main mechanism through which atelectasis is prevented following airway obstruction. There are three main pathways for CV: the interalveolar pores of Kohn, the bronchioalveolar channels of Lambert, and, most importantly, the interbronchiolar pathways of Martin.

CV is a long-known phenomenon occurring in human lungs to modulate imbalances of ventilation and was first described by Van Ellen et al. [7]. However, its clinical implications were small until the appearance of new ELVR. The first attestations of connections between two adjacent alveoli are attributed to the German physician Kohn in 1893, who discovered interalveolar communication in a patient with organizing pneumonia/acute fibrinous pneumonia [8]. In 1931, Van Ellen et al. [7] were the first to describe the mechanism of CV. Their research showed that passage of air, thin liquids, and fine particulate matter was possible between lobules belonging to the same lobe. They concluded that the occlusion of a lobular division would not result in atelectasis since air would enter and leave that part of the lung by CV and named this mechanism "collateral respiration" [7]. Electron microscopic images of the respective tissues led to the supposition that the very small (<5 μm), often fluid-filled pores of Kohn associated with type II pneumocytes could not solely explain the mechanism of CV [9]. In today's understanding, CV occurs mainly via the larger Lambert channels and via the interbronchiolar pathways of Martin. The Lambert channels are larger (30 μm in diameter), epithelium-lined, tubular alveolar ducts which connect distal bronchioles with the surrounding alveolar systems [10]. Additionally, the interbronchiolar pathways of Martin (80–150 μm) between terminal bronchioles from adjacent lung segments permit interlobar CV [11].

The exact role of CV has not yet been elucidated completely. Under normal respiratory conditions, airflow occurs through the pathway of least resistance and thus through the bronchial tree instead of through the intraparenchymal bridges that lead to CV and which usually remain inactive in healthy individuals [12, 13]. Hence, CV prevents atelectasis in cases of tumour obstruction, mucus impaction, or foreign body aspiration. Another interesting insight about CV is that fissure integrity appears to be genetically impacted. Genome-wide association analyses in non-Hispanic White subjects and African-American subjects derived from the COPDGene study showed a higher fissure integrity for African-American subjects than for non-Hispanic and for White subjects. No association with other clinical or environmental factors, such as sex, smoking, COPD, or emphysema, was identified [14].

C. How Can Collateral Ventilation Be Excluded?

- CV can be assessed by CT analysis or/and via Chartis® evaluation.

The cornerstones to assess CV in the lung are quantitative CT-based fissure analysis, together with the direct in vivo measurement with the Chartis® assessment system. The Chartis® assessment system enables airflow and resistance measurement in an occluded pulmonary lobe and visual categorization according to Chartis® phenotypes. The exact technique and the procedure are described below.

Quantitative assessment of fissure integrity using CT scans can be performed visually by experienced thoracic radiologists and pulmonologists or automated by computer software. Studies have shown only a fair to moderate interrater reliability among expert CT assessors and accuracy for visual CT-based interpretation of fissures was 77% [15, 16] Hence, software-based analysis was developed to improve diagnostic sensitivity, and various software products are now commercially available for calculating the fissure completeness score (FCS) [17]. The most commonly used software tools are StratX® (Pulmonx Inc., Redwood City, CA, USA), Apollo (VIDA Diagnostics, Coralville, IA, USA), and LungQ™ (Thirona, Nijmegen, The Netherlands), and their diagnostic accuracy to predict a target volume reduction of >350 mL was 78.8–96.4% depending on the cut-off values for the FCS [6, 18–20]. The main problem with the interpretation of these studies is that treatment failure due to valve dysfunction or errors in the assessment of CV cannot be distinguished from software-related problems of quantitative CT-based fissure analysis results. Discordant results in visual CT analysis versus Chartis® measurement regarding fissure completeness are seen in 31.9% of cases [19].

In addition to improving fissure integrity analysis, most software tools can perform lung density analysis and calculate volume and the emphysema score of each pulmonary lobe (based on voxel density > −910/−950 Houndsfield units). Pathologically hyperinflated lung ar-

Table 1. Cut-offs for fissure completeness score

Cut-offs for the right major fissure, %	Cut-offs for the left major fissure, %	Cut-offs for the right minor (or the right upper lobe) fissure, %	Recommendation
<80	<80	<80	CV positive, no further Chartis® needed
80–95	80–95	80–95	CV intermediate, Chartis® needed
>95	>95	>95	CV negative, valve treatment possible without further Chartis®

eas on the CT scan are summed up by measuring quantity of voxels with low density so as to obtain the emphysema score and thus to quantifying the degree of emphysematous destruction. The volume is expressed in millilitres and the emphysema score in percent, and both are important markers to select target lobes.

D. Development of Endobronchial in vivo Measurement of Collateral Ventilation (Chartis®)

- The Chartis® assessment is a new method for assessing collateral flow. It has been developed over several years and was initially presented in 2009. It has since found its place as a guide for ELVR therapy.

First attempts in lung volume reduction therapy relied on surgical resection of emphysematous lung segments. While improvements after lung volume reduction surgery were observed in lung function, as well as in exercise capacity and quality of life, this method was also associated with significant morbidity and mortality [21]. One of the main advantages of ELVR with valves over surgical emphysema treatment is its reversibility [22]. Consequently, attention shifted toward endoscopic procedures, aiming at inducing atelectasis of a target lobe. Initial treatment results showed only moderate success, given the lack of assessment of CV prior to implantation of occlusive devices. Based on the realization that prior careful selection of emphysema patients would improve treatment response, L. Freitag and N. Aljuri developed a CV assessment device able to provide a targeted measure of airflow and pressure changes in an occluded lobe in real time. Their method exhibited an improved treatment response after exclusion of CV, resulting in a higher rate of complete atelectasis [23]. Subsequent studies corroborated usefulness of the Chartis® assessment system in evaluating CV and as a valuable clinical tool in guiding treatment decisions in endobronchial valve therapy [24, 25]. A diagnostic accuracy of 74–83.3% for the Chartis® assessment is reported [6, 16, 19].

E. Fissure Integrity as Surrogate Parameter for Collateral Ventilation

- Exact fissure integrity cut-off values are still disputed but are an important tool to assess CV. Therefore, confirmatory Chartis® assessment is advised.

The human lung's left upper lobe and left lower lobe are separated by the left major fissure, while the right lower lobe (RLL) and the right middle lobe (RML) are separated by the right major fissure (Fig. 1). The right upper lobe fissure consists mainly of the minor fissure and a part of the major fissure. Considerable variation in the prevalence of incomplete fissures has been reported based on autopsies, cadaver studies, and radiologic evaluation. The prevalence ranges from 17–85% for the right major fissure, 19–74% for the left major fissure, and 20–90% for the right minor fissure. The minor fissure is most frequently incomplete, and the defects are often near the hilus [26]. African-American subjects show higher FCSs than non-Hispanic white subjects which suggests a genetic determination. Other clinical factors like COPD severity have no influence on fissure completeness [14]. The precise cut-off values for the FCS remain subject to scientific discussion, as different study protocols used divergent cut-offs [27, 28]. Usually the fissure integrity is categorized as "open/incomplete" (FCS <80%), "intermediate" (FCS between 80%–95%), and "complete" (>95%) (Table 1) [6, 16, 19, 29–33]. A different approach was chosen in research recently performed, focussing on anatomical differences in the fissure formation for the right and left lung. The suggested cut-offs are summarized in Table 2 [34]. The Chartis® assessment is recommended for confirming CV status in the event that all results for FCS are intermediate and if the right upper lobe is the target lobe for EBV treatment. It should be kept in mind that the quality of the QCT employed determines reliability of fissure quantification and thus the indication for Chartis® utilization, meaning that completely reliable cut-offs are almost impossible to define.

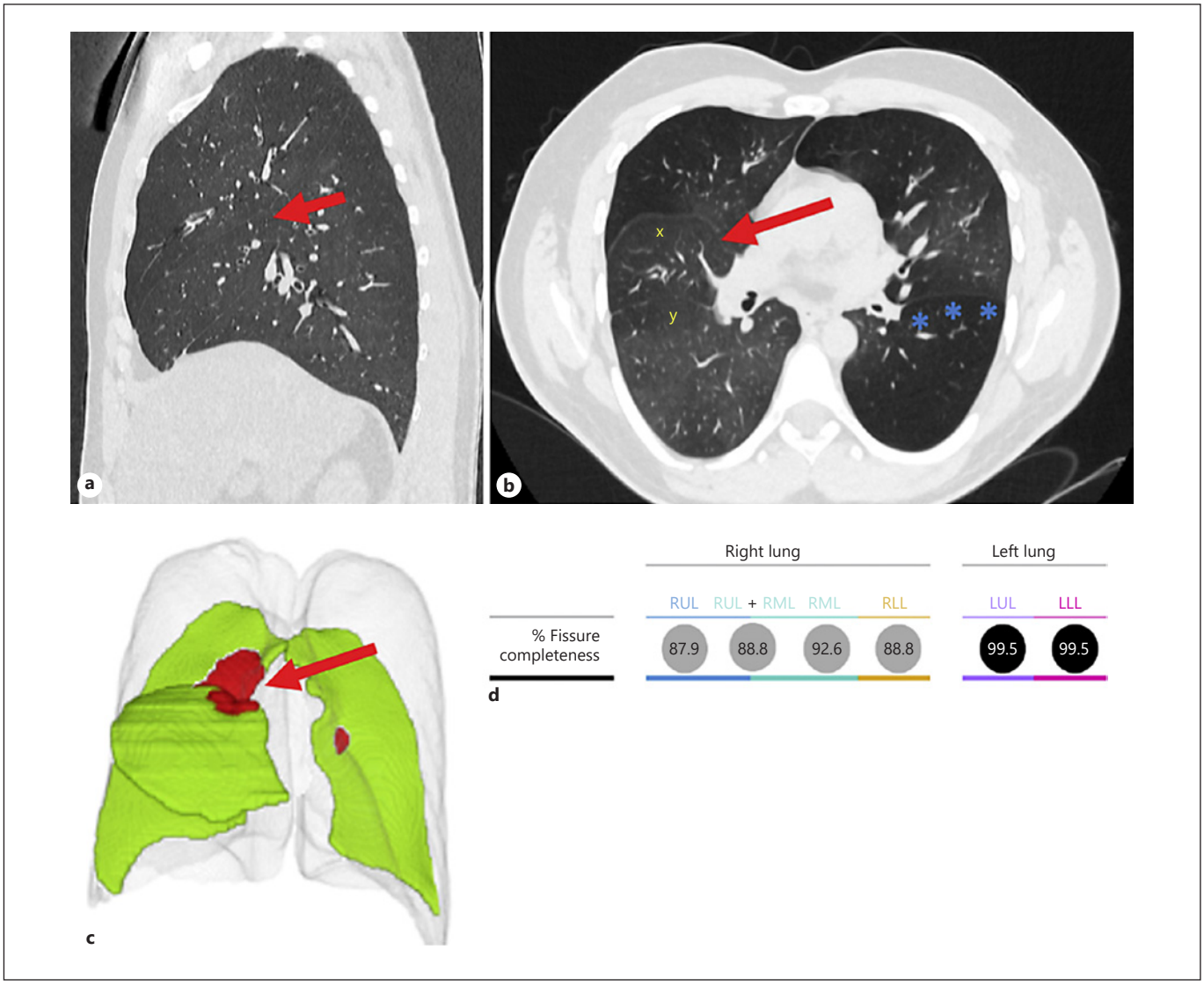

Fig. 1. Patient example. Computed tomography (CT) of the thorax in sagittal (**a**) and transversal (**b**) reconstruction. **a** CT thorax. Sagittal reconstruction. The red arrow shows a small fissure defect. **b** CT thorax. Transverse reconstruction. "x" marks the right upper lobe fissure. "y" shows the right major fissure. The red arrow shows a small fissure defect. * indicates the (intact) left major fissure. **c** Software reconstruction of the lung fissures. The fissure defect is represented in red (red arrow). **d** Software-calculated fissure completeness score (FCS) for the right and left lung. The FCS of the right lung was intermediary between 80% and 95%. The FCS of the left lung was >95% representing a complete left major fissure.

Table 2. Newer approach for fissure completeness score cut-offs

Cut-offs for the right major fissure, %	Cut-offs for the left major fissure	Cut-offs for the right minor (or the right upper lobe) fissure, %	Recommendation
<80	<80	<75	CV positive, no further Chartis® needed
90–100	80–95	75–100	CV intermediate, Chartis® needed
	>95		CV negative, valve treatment possible without further Chartis®

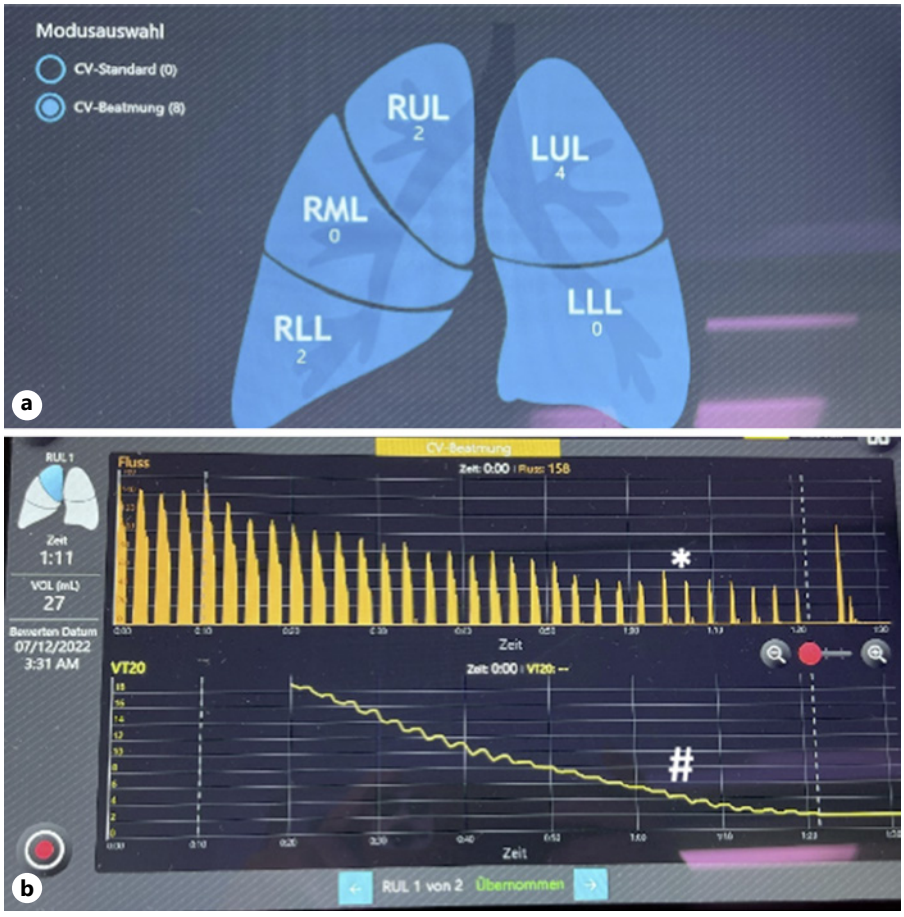

Fig. 2. Chartis console from Pulmonx®. **a** Start menu for selecting the lobe before starting the measurement. **b** Screen during the Chartis® assessment. This example shows a decrease in the expiratory flow (orange spikes*) during the measurement indicating an exclusion of collateral ventilation (CV negative). In line, the volume trends over the past 20 s were below 6 mL (#).

Additionally, all the cut-off values mentioned here rely on retrospective data analysis. A prospective randomized controlled trial would help to confirm the respective values.

F. Why Measuring Collateral Ventilation Is Important

- Measuring CV is indispensable for identifying suitable patients for ELVR with valves in cases when incomplete fissures are suspected, as well as to guide treatment decisions for different ELVR procedures.

Endobronchial valve treatment has become an established treatment option to manage hyperinflation in emphysematous lungs. Treatment success is highly dependent on careful prior assessment of CV in the target lobe. If CV is present between adjacent lung lobes, air can enter in the valve-occluded lobe, thereby preventing the development of atelectasis. The results of the first randomized controlled study for endobronchial valve treatment were modest, but a subgroup analysis showed significant response in patients with intact fissures on lung CT scans [33].

The Chartis® system was thus developed in order to improve treatment response. Subsequent research on its application verified it to be a safe and effective procedure to evaluate CV [25]. Since then, the Chartis® assessment and FCS have become principal diagnostic tools in planning treatment options for patients with advanced emphysema. This is particularly so, because combining both the Chartis® and the FCS results has led to increased diagnostic accuracy and to considerably improved treatment responses [6]. The exact diagnostic algorithm still remains to be elucidated, especially since randomized controlled studies used different study protocols, including different software tools and cut-offs for the FCS [27–31, 33, 35, 36].

In order to choose the optimal lung volume reduction treatment technique and target lobe for each patient for optimal treatment success, results from complete patient assessments are discussed in the interdisciplinary emphysema board, which consists of interventional pulmonologists, thoracic surgeons, and radiologists.

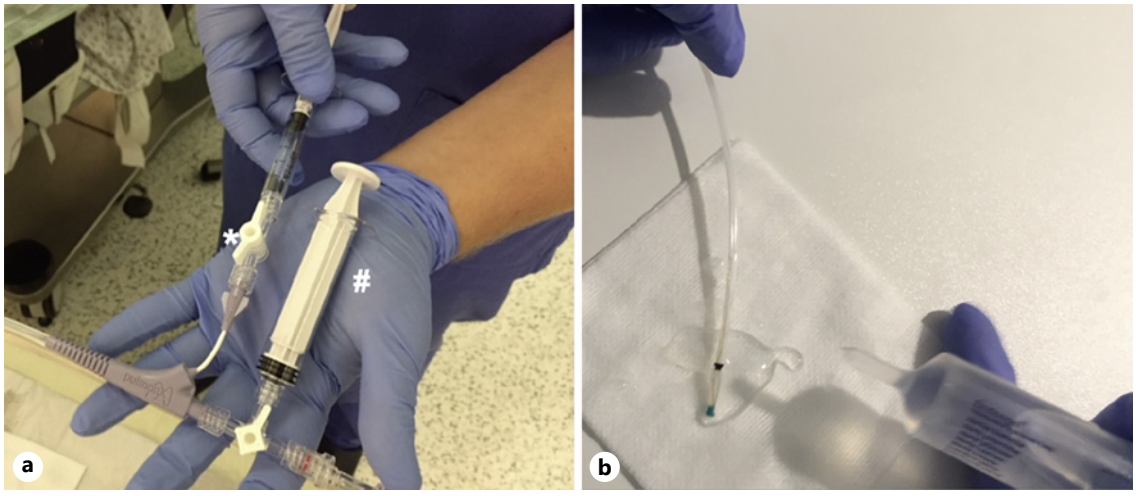

Fig. 3. Preparation of the Chartis® catheter. **a** Proximal end of the catheter with connections for two syringes. * Small syringe with one-way stopcock for in- or deflating the Chartis® balloon. # Big syringe with two-way stopcock for flushing the catheter. **b** Catheter tip with deflated balloon. Lubrication of the tip helps to push the Chartis® catheter through the bronchoscope's working channel.

Bronchoscopy and the Chartis® Procedure

A. Indication

- Chartis® measurement is advised when CT-guided fissure analysis indicates an intermediate fissure integrity score.

Either an experienced physician or a quantitative fissure integrity analysis usually gives an estimate of fissure status. With respect to which cut-off levels are best employed for defining fissure integrity, we recommend using Chartis® whenever there is doubt about fissure integrity. If more than one lobe is severely affected by emphysematous changes, we recommend including FCS to select the target lobe and treat the lobe with the most intact fissures [26, 37].

B. Technical Aspects

- The Chartis® system consists of a catheter with an inflatable balloon inserted via the bronchoscope's working channel. The system also includes a console with flow and pressure sensors.

The Chartis® system consists of a balloon catheter and a console (Fig. 2, 3). The Chartis® catheter length is 72 cm. A balloon is located at the end of the catheter and can be inflated with air to a diameter of 5–12 mm, with a maximal volume of 3 mL (Fig. 3). The working channel needs to have a diameter of at least 2.8 mm as to enable insertion of the catheter into the bronchoscope. The catheter consists of a central lumen initially containing an internally-located stylet. The stylet has to be removed to enable the initiation of airflow measurements through its central lumen. The Chartis® console has flow and pressure sensors. Only expiratory flow is registered through a valve mechanism in the console. The expired airflow volume, pressure, and resistance are measured and visualized on the monitor. Newer Chartis® consoles also show a VT20 trend (flow trend of the last 20 s). Recent studies suggest that if the VT20 reaches 6 mL, CV is not present and the Chartis® assessment can be stopped, thereby reducing the measurement time by 60 s [38].

C. Sedation versus General Anaesthesia, Ventilation Mode

- Chartis® measurement can be performed under all types of sedation modes. General anaesthesia ensures an easier and faster procedure.

Chartis® measurement can be performed under conscious sedation with spontaneous breathing, as well as under general anaesthesia with pressure-controlled ventilation, or under high-frequency jet ventilation. Some difficulties might be faced under conscious sedation, including longer procedure time due to repeated measurements by increased coughing, secretions, bronchoconstriction, and swelling of the mucosa. Furthermore, an optimal level of sedation is necessary during spontaneous breathing to maintain adequate measurement conditions. For this reason, Chartis® measurement is frequently performed under general anaesthesia. Different Char-

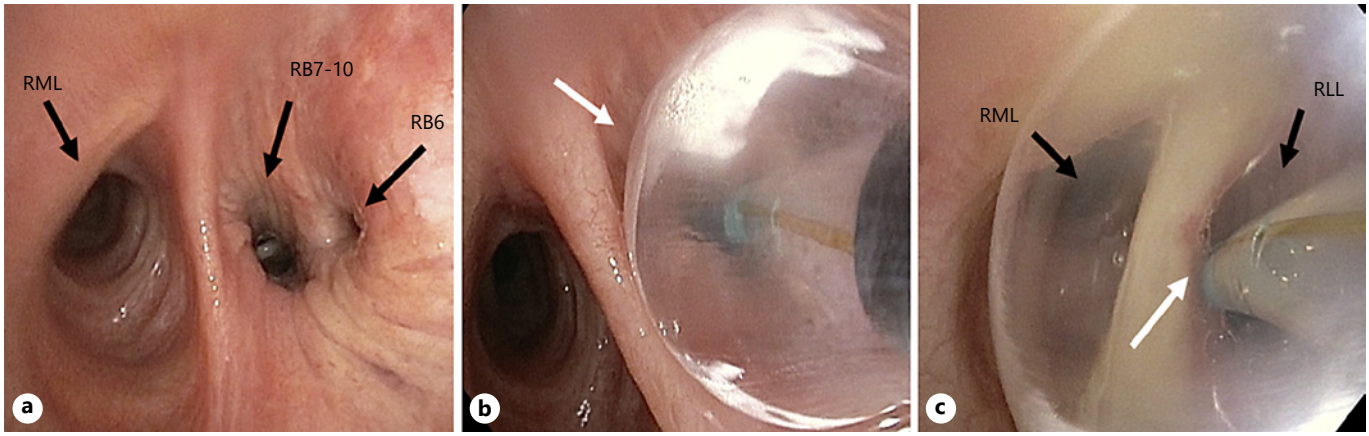

Fig. 4. Difficult positioning of the Chartis® balloon in the right lung. **a** Anatomical configuration of the right lower lobe (RLL) bronchus prevents the proper positioning of the balloon. **b** Insufficient occlusion of the bronchus with the balloon (white arrow) will lead to false CV-positive Chartis® results. **c** Overinflation of the Chartis® balloon presses the catheter tip against the mucosa (white arrow) which inhibits airflow through the catheter leading to false CV-negative Chartis® results. CV positive, detection of collateral ventilation; CV negative, exclusion of collateral ventilation; RML, right middle lobe.

tis® measurement phenotypes are observed with all types of sedation, and ventilation modes with no significant differences in the quality of measurement or in treatment outcome. The bronchoscopist should choose the preferred ventilation mode at the beginning of the Chartis® measurement. Depending on the type of ventilation mode selected, the observed flow curves might differ [39–41].

For conscious sedation, a combination of midazolam and propofol is frequently used after the instillation of topical lidocaine 1% in the trachea-bronchial tree for local anaesthesia. Furthermore, pethidine and atropine can be used to reduce intraprocedural coughing and endobronchial secretion. Atropine should be avoided if pulse rate is above 100 beats/minute. Tracheobronchial secretions can be obtained for microbiological analysis before starting the procedure.

D. The Chartis® Procedure: Balloon Placement

- The Chartis® assessment should be performed in the target lobe for valve implantation if feasible. If not, indirect measurement of the neighbouring lobe is also possible. A carefully guided insertion and placement of the catheter is recommended.

For the left lung, the left upper lobe or, alternatively, the left lower lobe can be measured in order to determine possible CV, as there is only one fissure present on the left side. If the target lobe for valve implantation is the right upper lobe, the right upper lobe needs to be evaluated. If this is not possible because of inconclusive results or challenging anatomy, the Chartis® balloon catheter can be placed in the bronchus intermedius to occlude and to measure the RML and the RLL together. In case that the right lower lobe is the target lobe, Chartis® measurement is particularly challenging because it is difficult to occlude RLL due to the higher location of the right segment 6 (Fig. 4). Another possibility of assessing the right major fissure is to occlude the RML with a regular balloon or Watanabe spigot and to measure the right upper lobe. If, in rare cases, the middle lobe or a single segment is the target for valve implantation, the RML or a single segment can be assessed as well [42].

Initially, the lobe must be selected in the menu of the Chartis® console, and the ventilation mode has to be chosen according to the patient's cardio-respiratory requirements. The catheter is then connected to the console, and the Chartis® balloon catheter is introduced into the bronchoscope. A lubricating gel can be applied at the tip of the catheter in order to facilitate sliding of the catheter in the working channel (Fig. 3). Next, the Chartis® balloon catheter is inserted into the bronchoscope and held within the working channel at the onset to prevent kinking and blocking the catheter with secretion. The bronchoscope is then positioned in front of the target ostium, and the Chartis® balloon catheter is subsequently pushed out until the black marker on the catheter is visible (Fig. 5a). Only then should the stylet be removed. Ensuing, measurement can be initiated as to document correct catheter position and measurement functions via adequate flow

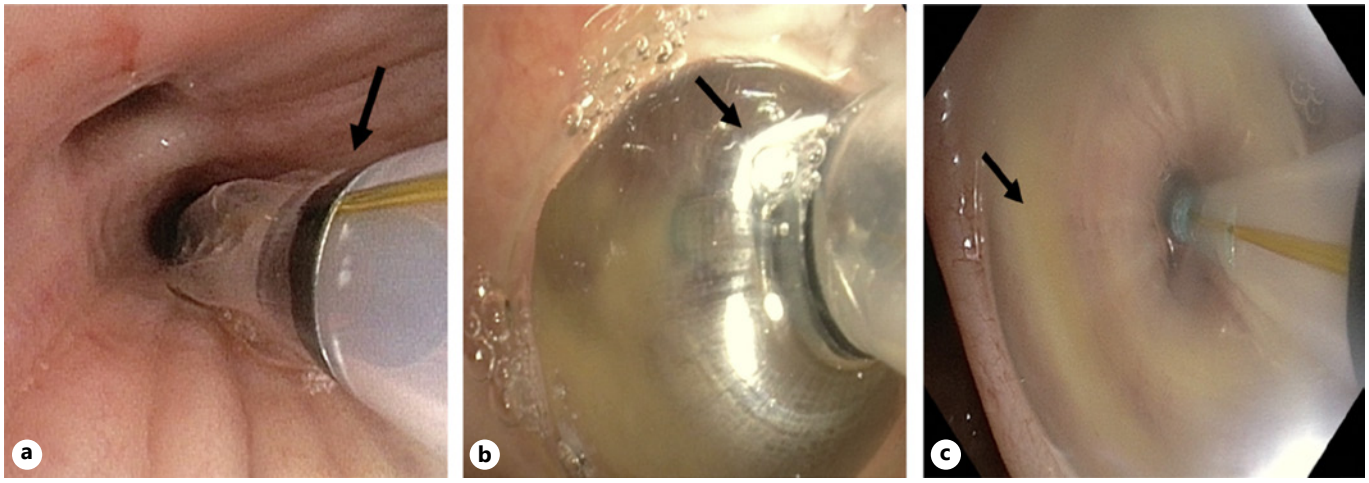

Fig. 5. Catheter and balloon placement in the right lung. **a** The catheter has to be pushed out until the black marker becomes visible. **b** The balloon is sufficiently inflated when a reflection sign appears on the surface. **c** Proper sealing of the lobar bronchus can be confirmed visually through the blanching of the mucosa.

curves. The balloon is inflated by the assistant while the bronchoscopist places the balloon in the target ostium. It is very important to carefully position the balloon centrally in the bronchus in order to ensure perfect contact of the balloon with the airway wall (Fig. 5b) and to avoid contact of the catheter tip with either the carina or the bronchial wall (Fig. 3c). Once adequate contact is confirmed by circumferential blanching of the mucosa (Fig. 5c), the bronchoscope is advanced over the Chartis® catheter, and gentle pressure is applied on the balloon with the bronchoscope. The bronchoscopist can confirm visually through the balloon that the end of the catheter is free in the lumen and not blocked by the airway wall or by secretions. The balloon should occlude all segments of the target lobe. Complete sealing of the lobar bronchus during the assessment should be confirmed visually and aided by a characteristic flow curve on the Chartis® console. Confirmation of the unobstructedness of the catheter is very important or else a sudden drop in the flow curve will be observed. If CV is negative, a decreasing flow is expected after 1–2 min. A positive CV can be concluded if the airflow measured exceeds 500–750 mL or if there is no significant decrease in airflow after 5 min. After a CV-negative result is obtained, the Chartis® balloon should be deflated which should in turn lead to an immediate increase in flow. If the flow curve does not increase after deflating, blocking of the catheter by endobronchial secretion during the procedure can be assumed, and the measurement should be repeated. ("negative probe"). In cases of very low flow rates, the amount of time for the flow to cede completely can be significant, typically made apparent by a decrease in the flow curve. The latest version of Chartis® console additionally displays the volume trend for the previous 20 s as "VT20". When this value reaches an expiratory volume ≤6 mL, the lobe can be assumed to be CV negative. By proceeding this way, the length of the entire procedure can be reduced by approximately 60 s on average. Importantly, this feature can only be used when a persistent and continuous decreasing flow with a total volume of exhaled air >50 mL is observed, and it has only been validated for procedures performed under general anaesthesia [37].

E. Chartis® Phenotypes

- Phenotypes of Chartis® curves have specific characteristics and must be interpreted carefully. The results should correlate with the preprocedural fissure analysis.

Chartis® phenotypes are discriminated by changes in expiratory peak flow, changes in total exhaled volume after 1–5mins, and possible increases in resistance index. The expiratory flow curve is influenced by the ventilation mode and can be continuous in general anaesthesia and high frequency jet ventilation.

Flow curves of the different Chartis® phenotypes are depicted in Figure 6. The CV-negative phenotype is characterized by a steady decline of expiratory flow to at least 20% of baseline value, while no relevant changes in airflow are usually apparent for the CV-positive phenotype. Some console variants show a concomitant increase in

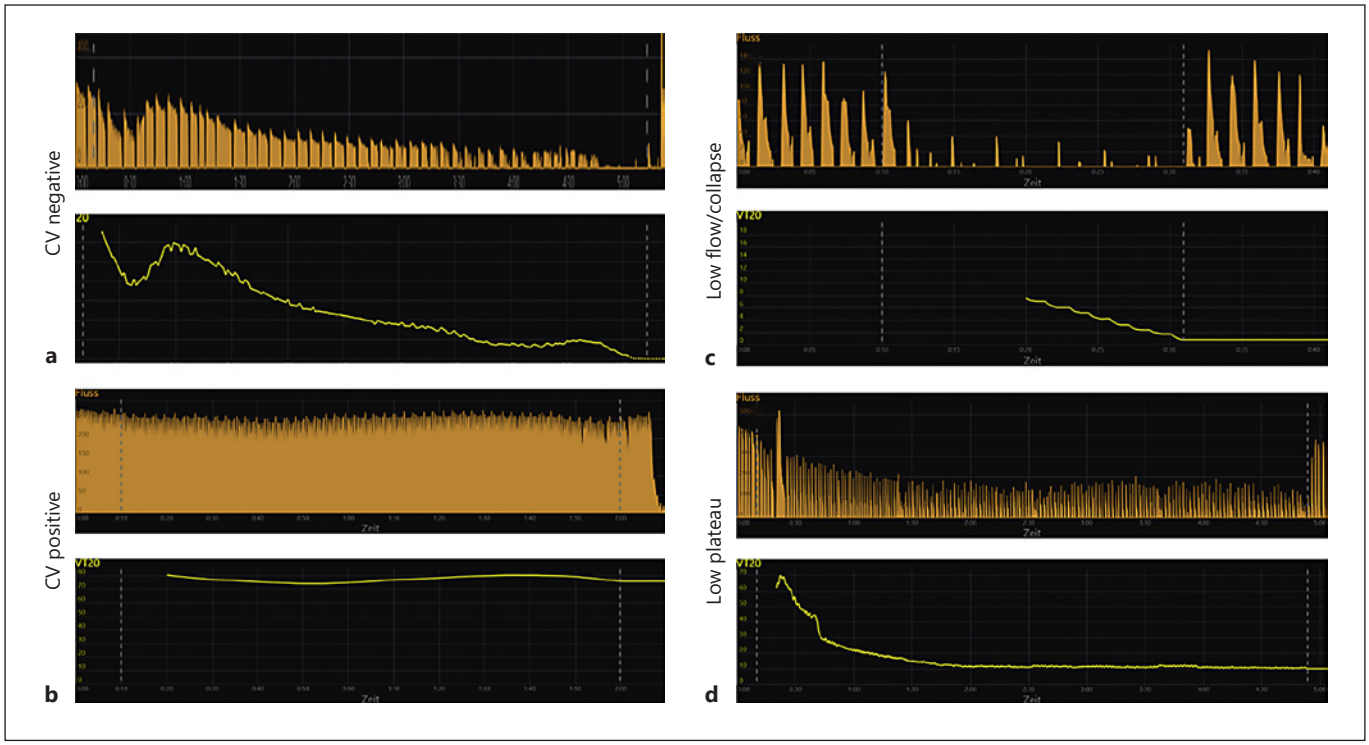

Fig. 6. Chartis phenotypes. **a** Collateral ventilation (CV) negative: gradual decrease in airflow until zero (orange curve). The yellow curve shows a gradual decrease in airflow of time (vt: volume trend over the past 20 s). **b** CV positive: continuous airflow and no decrease in volume trend. **c** Low flow (collapse): airflow stops abruptly and the occluded airway collapses. Simultaneous drop in volume trend. **d** Low plateau: gradual decrease in airflow until stabilizing at a plateau of 20–50% of baseline flow. The curve is mirrored by the volume trend.

resistance for CV-negative phenotypes and no change in case of CV-positive phenotypes.

The low flow or collapse phenotype is characterized by an airway collapse with little ventilated volume (<50 mL), a sudden drop in airflow, and an immediate increase in resistance readings. Collapse phenotype or low flow is observed in 31.5% of all patients and is more frequent in the lower lobes. 69.8% of all patients with collapse phenomena have complete fissures. Collapse phenomena in patients with emphysema and reduced elastic recoil are caused by dynamic expiratory airway collapse due to a sudden stop of airflow [43]. A rare Chartis® phenotype is the low plateau, characterized by a decrease in airflow between 20 and 50% from baseline and sometimes by an increase in resistance [24]. Visual interpretation of Chartis® phenotypes is intuitive, as confirmed by intraobserver and interobserver agreement [24].

Chartis® phenotypes can be conclusive or inconclusive with respect to the CV status. No definitive statement about the CV is possible if the collapse/low flow phenotype or low plateau are diagnosed based solely on the Chartis® assessment. The low flow phenotype seems to occur more often in patients with low or absent CV. If in doubt, valves can be positioned in the mentioned phenotypes "collapse, low flow, and low plateau." The neighbouring target lobe should be measured whenever possible to ensure good outcome. However, lobes with a low flow phenotype are less likely to respond to valve treatment than CV-negative phenotypes [37]. After a CV-negative Chartis® result, endobronchial valves can be implanted into the target lobe in the same bronchoscopy session.

F. Main Problems, Complications, and Safety Aspects

- The Chartis® procedure is a safe procedure. The catheter can cause minor damage to the airway mucosa. The main problems with this procedure are inconclusive or unattainable measurements because of hypersecretion or because of difficult anatomy. If this happens, assessment in correlation with fissure analysis of the CT scan will aid in treatment decision-making.

In patients with endobronchial hypersecretion, Chartis® measurement can be difficult because mucus blocks

the catheter. It is essential to clean the airway before commencing measurements and to flush the Chartis® catheter with air should secretion be suspected in the distal end. Another potential problem can be the difficulty to completely block the target lobe because of a challenging anatomy. It is difficult to occlude especially the RLL because the balloon often cannot be placed adequately to fully block segment 6. In this case, indirect measurement of the other lobes is possible and advised, as described above. Furthermore, segment 6 is often blocked but not included in the assessment of CV, also producing unreliable results. Complications regarding the Chartis® procedure are rare and only very few have been reported in literature or occurred in our personal experience so far. Only the Stelvio trial reported one pneumothorax after the Chartis® assessment [44]. And from the author's own experience, the surface of the airway walls can be damaged through manipulation with the catheter, which can lead to minor bleeding or mucosa scratching. This can be prevented by careful handling of the catheter. A notable decrease in oxygenation can possibly occur if a relevant part of the lung is obstructed; however, this can be managed by immediate deflation of the balloon.

The Chartis® assessment is a complex procedure, and its results should be evaluated in the context of patient history, readings of fissure measurements and the CT scan, and on the basis of the best medical judgement. Furthermore, treatment failure can also be a consequence of incorrect valve placement and not necessarily due to incorrect assessment of CV. In distinct cases, individual decisions and exceptions from the above-mentioned rules can be made after discussion of alternative approaches with members of the interdisciplinary emphysema board. We highly recommend the evaluation and treatment of patients in experienced centres as to improve respective quality because patient selection is a challenge and requires skills from experts from radiology, pneumology, and surgery [37]. Hence, a national non-profit multicenter prospective study was recently founded in Germany (Lungenemphysemregister e.V.), focussing on improving treatment quality by implementing procedural standards and on collecting real-world patient data independent of controlled study conditions [37].

Open Research Questions

The Chartis® assessment is a safe and frequently performed procedure to evaluate patients for ELVR therapy. Despite ongoing intense research for over almost two decades, several questions remain unresolved until today which can sometimes lead to difficulties in the treatment decision process. Especially, the low flow/collapse phenotype is a challenging result in the Chartis® assessment, as no definitive statement about the CV status is possible. Research has evidenced that this phenotype frequently appears in the lower lobes. Additionally, mismatching results can occur in clinical practice in up to 12.5% of cases if lobes are assessed twice during the Chartis® assessment. Furthermore, Chartis® can be technically very challenging. Yet another unresolved question is which cut-offs for FCS should be best applied.

All these yet-to-be resolved questions make treatment decisions more difficult. The authors therefore recommend a structured approach to the Chartis® assessment, including at least two measurements of a potential target lobe, especially if Chartis® result and fissure integrity analysis do not match. Additionally, the upper lobes should be assessed first if considered for EBV treatment, since low flow/collapse phenotypes occur more frequently in the lower lobes. If discordant Chartis® results appear in the target lobe, additional assessments and a correlation with the fissure integrity analysis are recommended. If different target lobes are assessed, the one with the most intact fissure integrity score should be chosen. Up until now, there are no recommendations regarding the approach after endobronchial valve treatment failure. The Chartis® assessment can be repeated if endobronchial valves are replaced due to insufficient treatment results. Naturally, this is only possible after removal of all valves, since the Chartis® assessment should not be performed with inserted valves.

Conclusion

Measuring CV via Chartis® has found its place in ELVR procedures ever since its initial application in patients in 2003. CV and presence of incomplete fissures have led to the development of different endoscopic lung volume reduction approaches. Fissure analysis of CT scans is essential in the evaluation of patients for endoscopic lung volume reduction. Analysis should preferably be performed by automated software or well-experienced physicians. Additional Chartis® assessment is often required when intermediate fissures are present. The measurement must be done carefully, and subsequent Chartis® phenotypes should be interpreted with caution. The main problems encountered during Chartis® assessment are inconclusive results or difficult measurements due to

secretions or complicated endobronchial anatomy. If performed well, Chartis® measurement guides the ELVR decision and thus guarantees better outcomes in ELVR.

The Chartis® assessment is one of the main tools in evaluating CV and in guiding ELVR treatment for incomplete fissures. Difficult anatomy and secretions sometimes impede adequate measurement, and preprocedural CT-guided fissure analysis as well as expectations for possible ELVR benefit should therefore always be kept in mind.

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Conflict of Interest Statement

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Author Contributions

Jacopo Saccomanno and Judith Brock: drafting the work, literature research, writing, interpretation, and critically revising the manuscript.

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Martin Witzenrath: drafting the work, interpretation, and critically revising the manuscript.

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