Patient selection before endobronchial valve treatment

To the Editor:

We read with great interest the study by HERTH *et al.* [1]. They investigated the ability of the bronchoscopic Chartis Pulmonary Assessment System to predict the response to unidirectional endobronchial valve (EBV) treatment by determining the presence of collateral ventilation (CV) and the Chartis system showed an accuracy level of 75% in predicting whether or not the target lobe volume reduction (TLVR) cut-off ($\geqslant$350 mL) would be reached.

As previously reported [2], EBV treatment brought emphysema patients significant but modest improvement of forced expiratory volume in 1 s (FEV_1), exercise capacity and quality of life compared with controls, while another type of unidirectional valve, intrabronchial valve treatment, did not [3]. However, only a subgroup of patients could benefit more from EBV treatment. Therefore, defining and selecting this subgroup of patients is of great help to improve the clinically significant benefit of EBV treatment. To date, three methods can be used before EBV placement to predict therapeutic effect, which are CV detected by Chartis [1], and heterogeneity and fissure completeness assessed by high-resolution computed tomography (HRCT) [2, 4, 5]. This raises two questions.

First, which of these three methods has the highest capability to predict response to EBV treatment? Regrettably, HERTH *et al.* [1] did not provide information about heterogeneity and fissure completeness. GOMPELMANN *et al.* [6] studied whether the accuracy of CV assessment was comparable to fissure analysis from HRCT in predicting clinically significant lung volume reduction following EBV treatment. Preliminary results of this study showed that Chartis and HRCT matched 24 (77.4%) times in 31 patients, and did not match seven (22.6%) times. Complete results of this study were not available when we were reviewing the literature, so we could not know the difference in the accuracy of predicting response to EBV treatment between these two methods. Therefore, we tried to extract comparable data from other studies. HERTH *et al.* [1] reported that CV-negative patients had a median TLVR of 752.7 mL compared to 98.6 mL in CV-positive patients; 43% of CV-negative patients showed change in (Δ)FEV_1 $\geqslant$15% at 1 month from baseline after EBV treatment. SCIURBA *et al.* [2] reported patients with complete fissure had a median TLVR of 713 mL compared to 196 mL in patients with incomplete fissure; 42.6% of patients with complete fissure showed ΔFEV_1 $\geqslant$15% at 6 months from baseline after EBV treatment. HERTH *et al.* [4] reported that 35.2% of patients with more heterogeneous emphysema showed ΔFEV_1 $\geqslant$15% at 6 months from baseline after EBV treatment. So, it seems that CV detected by Chartis and fissure completeness assessed by HRCT are comparable in predicting response to EBV treatment.

Second, does combining those two or three methods have a higher capability to predict response to EBV treatment than a single one? Data from HERTH *et al.* [1] showed that the false-positive value and the false negative value for Chartis system were 38% and 12%, respectively. LINDQUIST *et al.* [7] reported that nine out of 49 patients screened with HRCT had intact fissures and went onto Chartis assessment and EBV placement, seven of whom were CV-negative and two were CV-positive on Chartis. The CV-negative group showed clinically significant improvement of lung function and St George's Respiratory Questionnaire, while the CV-positive group did not. Thus, combining these methods may further improve the predictive value.

As discussed here, further studies are warranted to investigate these two questions, which may help build an effective workflow for patients selection before EBV treatment.

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Combining Chartis and HRCT may help build an effective workflow for patients selection for endobronchial valve treatment http://ow.ly/qn0sn

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Infant lung function and wheeze in later childhood in the Southampton Women's Survey

To the Editor:

We were interested to read the study by VAN DER GUGTEN *et al.* [1] reporting associations between increased neonatal respiratory resistance and wheezing illnesses during infancy, and between reduced neonatal respiratory compliance and wheezing illnesses during the first 5 years of life and late-onset and persistent wheeze phenotypes. Reduced respiratory compliance was also associated with asthma, defined both according to primary care consultations and prescriptions or referral for wheezing illnesses, and according to patient-reported symptoms and lung function at the age of 5 years. The authors proposed that compliance and resistance might reflect different lung characteristics that are associated with symptoms in different age periods. Our data from normal-term infants in the Southampton Women's Survey birth cohort provide further evidence that impaired physiological measurements soon after birth are associated with specific wheeze phenotypes. We previously reported an association between lower maximal flow at functional residual capacity ($V'max_{FRC}$) in early infancy and later transient wheeze [2]. The paper by VAN DER GUGTEN *et al.* [1] has led us to analyse our data further with regards to compliance of the respiratory system (C_{rs}) and we have found that lower C_{rs} is associated with asthma in our cohort too. Using the raised volume thoracoabdominal compression technique, we also measured forced expiratory volume in 0.4 s ($FEV_{0.4}$); lower $FEV_{0.4}$ measurements were associated with increased childhood asthma risk.

We have previously described our methods [3]. In brief, lung function was measured between 5 and 14 weeks of age in 147 term infants. Infants were tested lying supine in quiet sleep, augmented by oral chloral hydrate (75–100 $mg \cdot kg^{-1}$). $V'max_{FRC}$ and $FEV_{0.4}$ were calculated from partial and raised volume expiratory flow–volume curves, respectively. C_{rs} was calculated from passive flow–volume curves following single occlusions. Wheeze data were collected at 6, 12, 24 and 36 months and 6 years using questions from the ISAAC (International Study of Asthma and Allergies in Childhood) core questionnaire wheezing module. 95 children provided questionnaire data and spirometry at age 6 years. Associations between infant lung function measurements and wheeze phenotype were assessed using regression; significant confounders were included in multivariable models (as described in [2]). Table 1 shows an association between lower early infancy C_{rs} and childhood asthma together with an association between lower $V'max_{FRC}$ and transient wheeze. The former confirms the finding of VAN DER GUGTEN *et al.* [1] of reduced early-life C_{rs} in children later diagnosed with asthma and the latter; although not identical to the findings of VAN DER GUGTEN *et al.* [1], it is, however, consistent with their proposal that low airway calibre is a likely contributor to wheeze