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Predictors of Response to Endobronchial Coil Therapy in Patients With Advanced Emphysema

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BACKGROUND: The Lung Volume Reduction Coil Treatment in Patients With Emphysema (RENEW) trial reported improvements in quality of life, pulmonary function, and exercise performance following endobronchial coil treatment.

OBJECTIVES: The purpose of this post hoc analysis was to identify baseline predictors, including quantitative CT measures, that identify patients most likely to significantly benefit from endobronchial coil therapy.

METHODS: Quantitative CT analysis by an independent radiology laboratory and a qualitative evaluation by five blinded experts of the baseline thoracic CT imaging were performed. Univariate and multivariate logistic regression analyses were performed to elucidate characteristics associated with clinical response.

RESULTS: In total, 125 patients underwent coil treatment and had evaluable 12-month follow-up results. Of these, 78 patients received treatment of lobes with the highest emphysematous destruction determined by quantitative CT analysis (quantitative visual match [QVM]+), and 47 received treatment in at least one lobe that was not the most destroyed (QVM–). From the 78 patients with QVM+ treatment, a subgroup of 50 patients (64%) was identified with baseline residual volume > 200% predicted, emphysema score > 20% low attenuation area, and absence of airway disease. In this subgroup, greater lobar residual volume reduction in the treated lobes was achieved, which was associated with significant mean ± SE improvement in FEV_1 (15.2 ± 3.1%), St. George's Respiratory Questionnaire (–12 ± 2 points), and residual volume (–0.57 ± 0.13 L).

DISCUSSION: This post hoc analysis found that both significant hyperinflation (residual volume ≥ 200% predicted) and CT analysis are critical for patient selection and treatment planning for endobronchial coil therapy. Quantitative CT analysis is important to identify optimal lobar treatment and to exclude patients with insufficient emphysema (< 20% low attenuation area), whereas visual assessment identifies patients with signs of airway disease associated with worse outcomes.

TRIAL REGISTRY: ClinicalTrials.gov; No.: NCT01608490; URL: www.clinicaltrials.gov.

CHEST 2019; 155(5):928-937

KEY WORDS: bronchoscopy; COPD; emphysema; endobronchial coils; HRCT; lung volume reduction

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Patients with COPD with advanced emphysema and severe lung hyperinflation have limited effective treatment options. Generally, lung volume reduction surgery or lung transplantation can be offered to those who meet strict criteria. However, these procedures are infrequently performed due to significant morbidity and mortality.[1] Alternatively, use of endobronchial valves is limited to individuals with intact lobar fissures. Bronchoscopic lung volume reduction using shape-memory nitinol endobronchial coils is a minimally invasive treatment option.[2,3] The safety and effectiveness of endobronchial coils have been evaluated in several studies, showing significant benefit of coil treatment on pulmonary function outcomes, exercise performance, and quality of life.[4-11]

Lung Volume Reduction Coil Treatment in Patients With Emphysema (RENEW),[12] an international, multicenter, randomized controlled trial, assessed endobronchial coil treatment in patients with severe lung hyperinflation and homogeneous or heterogeneous emphysema.[4] The primary outcome measure showed a small but statistically significant improvement in the 6-min walk distance (6MWD). Larger and statistically significant improvements were observed in outcome measures of residual volume, FEV_1, and St. George's Respiratory Questionnaire (SGRQ) scores vs control group patients (regular care) at 12 months. The RENEW primary analysis described prespecified subgroups with superior outcomes, namely patients with more hyperinflation (residual volume $\geq$ 225% predicted) and patients with heterogeneous emphysema distribution, but a statistical analysis for predictors of response was not performed. Of note, quantitative measures of the inspiratory and expiratory CT scans were not assessed in the primary analysis.

In this post hoc analysis of the RENEW trial, we performed lobar-based quantitative CT (QCT) measurements and a qualitative expert image review. The purpose of this analysis was to identify baseline predictors, including QCT measures, that identify patients most likely to significantly benefit from endobronchial coil therapy.

Methods

Patient Population

The patients' characteristics and primary results of the RENEW trial have previously been reported.[4] Of 158 patients randomized to the RENEW treatment group, 125 completed bilateral treatment and the 12-month follow-up and had evaluable inspiratory and expiratory CT scans at baseline and 12-month follow-up; these 125 patients are included in the post hoc analysis (Fig 1). Baseline characteristics are shown in Table 1. The RENEW trial was approved by all the 31 trial site medical ethical review committees, and all patients provided written informed consent.

QCT Analysis

After the RENEW 12-month primary end point follow-up visit and study unblinding, high-resolution CT (HRCT) scans for the coil-treated group were analyzed quantitatively (QCT) (Thirona). The QCT analysis included volumetric and densitometry assessments at a lung and lobar basis. Percent emphysema was calculated as percentage of low attenuation areas below –950 Hounsfield units on inspiratory scans (%LAA950). Percent air trapping was calculated as %LAA below –856 Hounsfield units on expiratory scans. Percent heterogeneity (difference in %LAA950 between ipsilateral lobes) and percent fissure integrity (for major fissures on inspiratory scans) were also measured. A "heterogeneous" patient was defined as having $\geq$ 15% ipsilateral difference in %LAA950 in both lungs, and a "homogeneous" patient was defined as having < 15% ipsilateral difference in %LAA950 in both lungs. A "mixed" patient had one heterogeneous lung and one homogeneous lung.

Lobar volume change was calculated as the total change in lobar volume of both treated lobes comparing baseline vs 12 months' post-coil treatment, assessed both with expiratory scans (lobar residual volume change) and inspiratory scans (lobar total lung capacity change).

Agreement Between Quantitative and Visual Analyses of the HRCT

The most damaged lobe of each lung determined according to QCT analysis was compared vs the lobe target determined by the RENEW

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*Collaborators from the RENEW Study Group are listed in the Acknowledgments.

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┌─────────────────────────────────────────────────────────────────┐
│ 125 RENEW Patients received bilateral coil treatment with        │
│ completed 12-mo follow-up visit[a] and analyzable CT scans        │
│ ("RENEW QCT Cohort")                                              │
└─────────────────────────────────────────────────────────────────┘
                              │
                              │──────────▶ 47 Patients that were not treated in the lobes
                              │            determine by QCT [QVM–]
                              ▼
┌─────────────────────────────────────────────────────────────────┐
│ 78 Patients treated in the lobes determined by QCT [QVM+]         │
│ ("Responder Analysis Cohort")                                     │
└─────────────────────────────────────────────────────────────────┘
                              │
                              │──────────▶ 28 Patients with low hyperinflation (baseline residual
                              │            volume < 200% predicted), or low emphysema (lobar
                              │            percent emphysema < 20% in either of the treated lobes),
                              │            or visual presence of airway disease
                              ▼
┌─────────────────────────────────────────────────────────────────┐
│ 50 Patients treated in the lobes determined by QCT and meeting    │
│ baseline criteria for volume reduction ("Volume Reduction         │
│ Criteria")                                                        │
└─────────────────────────────────────────────────────────────────┘
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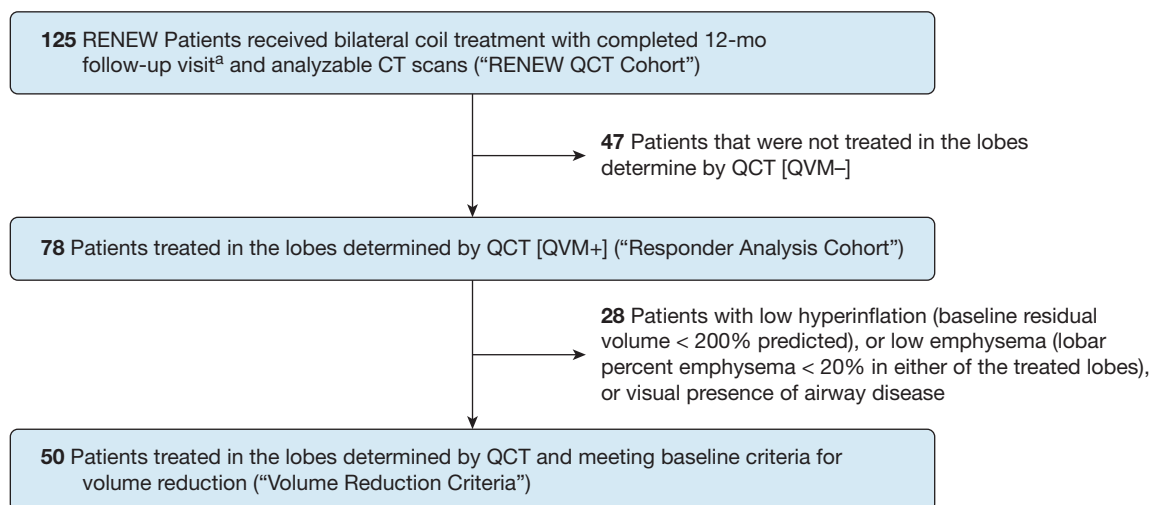
Figure 1 – Flow diagram of subjects included in this analysis. [a]Any one of the pulmonary function tests was measured at 12 months. QCT = quantitative CT; QVM– = quantitative-visual match-negative; QVM+ = quantitative-visual match-positive; RENEW = Lung Volume Reduction Coil Treatment in Patients With Emphysema trial.

TABLE 1] Baseline Characteristics of All RENEW Coil-treated Patients and Patients Stratified According to QCT Subgroup

Characteristic	RENEW (N = 125)[a]	QVM+ (n = 78)	QVM– (n = 47)	P Value[b]
Age, y	63.2 ± 8.1	62.9 ± 8.1	63.7 ± 8.3	.6102
Male	46.4 (58)	47.4 (37)	44.7 (21)	.8536
BMI, kg/m^2	24.9 ± 4.6	24.9 ± 4.6	24.9 ± 4.6	.9649
BODE	6.0 ± 1.3	6.1 ± 1.3	5.8 ± 1.2	.3184
Mean comorbidities	2.6 ± 2.1	2.7 ± 2.1	2.3 ± 1.9	.2910
≥4 Comorbidities	29.6 (37)	32.1 (25)	25.5 (12)	.5449
Cardiac comorbidities	24.8 (31)	30.8 (24)	14.9 (7)	.0555
6MWD, m	314.1 ± 79.9	313.8 ± 76.9	314.6 ± 85.6	.9582
Residual volume % predicted	244.9 ± 38.5	246.8 ± 40.6	241.8 ± 34.8	.4883
Residual volume ≥ 225%	71.2 (89)	74.4 (58)	66.0 (31)	.4149
Residual volume/TLC	66.8 ± 6.7	67.1 ± 7.3	66.4 ± 5.7	.5851
FEV$_1$ % predicted, PB	25.6 ± 6.1	25.8 ± 6.4	25.5 ± 5.8	.7813
SGRQ total score	60.0 ± 12.7	60.2 ± 13.6	59.7 ± 11.1	.8344
% Heterogeneous[c]	19.2 (24)	28.2 (22)	4.3 (2)	.0001
% Homogeneous	56.8 (71)	43.6 (34)	78.7 (37)	
% Mixed	24.0 (30)	28.2 (22)	17.0 (8)	
% Emphysema (–950 HU)[d]	44.0 ± 13.2	46.9 ± 12.9	39.2 ± 12.2	.0012
% Air trapping (–856 HU)[d]	75.2 ± 11.6	77.7 ± 10.4	71.1 ± 12.4	.0017

Continuous variables are presented as mean ± SD; categorical variables as percent (number) of patients. 6MWD = 6-min walk distance; BODE = BMI, airflow obstruction, dyspnea, and exercise capacity; HU = Hounsfield unit; PB = postbronchodilator; QVM– = quantitative-visual match-negative; QVM+ = quantitative-visual match-positive; RENEW = Lung Volume Reduction Coil Treatment in Patients With Emphysema; SGRQ = St. George's Respiratory Questionnaire; TLC = total lung capacity.
[a]All RENEW patients bilaterally treated with coils and with evaluable inspiratory and expiratory scans at baseline and 12 months.
[b]P values comparing densitometry-targeted and non-densitometry-targeted groups are based on the two-sided Student t test for continuous variables and the Fisher exact test for categorical variables.
[c]Requires ≥ 15% difference in percent emphysema between upper and lower lobes –950 HU, in both lungs.
[d]Average value for two QCT-targeted lobes.

visual analysis. The RENEW trial used a visual CT analysis to select the most damaged lobes for coil treatment based on a 0 to 5 scoring system of lobar destruction (e-Appendix 1, e-Table 1). If the quantitative and visual analyses agreed on both treated lobes, the patient was determined to be "quantitative-visual match-positive," or QVM+. If disagreement was observed in one or both treated lobes, the patient was designated as "quantitative-visual match-negative," or QVM−.

Visual CT Assessment

Five experts (one radiologist and four pulmonologists) conducted a post hoc blinded visual assessment of all baseline inspiratory CT scans. Experts noted visual findings, including bronchial wall thickening, bronchiectasis, fibrosis/scarring, and suspected pulmonary hypertension. Methods are described in e-Appendix 1.

Statistical Analysis

Univariate analysis and Pearson correlation coefficients were used to investigate associations between QCT-measured outcomes, potential baseline predictors, and clinical response outcomes. A multivariate logistic regression model was used to identify the association between baseline measures, including QCT and lobar volume reduction at 12 months. Multivariate logistic regressions were performed with stepwise control using the minimum Akaike Information Criterion stopping rule in the forward direction. Clinical response was measured by using the original RENEW study end points at 12 months (6MWD, FEV$_1$, residual volume, SGRQ, and the minimum clinically important difference [MCID] for these end points (MCID: 6MWD of 25 m,[13] FEV$_1$ of 10%,[14] residual volume of −0.35 L,[15] and SGRQ total score of −4 points[16]).

The QCT measures used in this analysis were percent emphysema, percent air trapping, percent heterogeneity, QVM+, and percent fissure integrity. Patient baseline characteristics included demographic characteristics (age and BMI), pulmonary function tests (plethysmographic lung volumes and forced spirometry), visual CT findings, and treatment factors (total number of coils per lobe volume and percent proportion of each coil size).

Differences in baseline characteristics between QVM+ and QVM− patients were evaluated by using the two-sample Student t test or Fisher exact test. All statistical analyses were performed by using SAS version 9.4 (SAS Institute, Inc.). P values < .05 were considered statistically significant.

Results

Association Between Change in QCT Measures and Clinical Response Measures

We examined the association between change in QCT measures and clinical response MCIDs from baseline to 12 months' follow up (e-Table 2). Change in lobar residual volume in the treated lobes was the only QCT measure that was significantly associated ($P < .05$) with all four clinical outcomes. This finding establishes reduction in expiratory lobar residual volume as a mechanistically plausible primary effect of the coils that can be analyzed in establishing baseline predictors of response.

Impact of Matching QCT and Visual CT Targeting of Lobe With Greatest Emphysema (QVM)

Using targeting based on the visual scoring algorithm, 38% of patients (47 of 125) received one or both treatments in the ipsilateral lobe of lesser QCT emphysematous destruction and were designated QVM−. The majority of the QVM− treatments occurred in lungs defined as homogeneous according to QCT (Fig 2). The QVM+ subgroup, in which the visual algorithm matched the QCT lobe of greatest destruction, had greater heterogeneity at baseline ($P < .0005$), greater percent emphysema ($P < .005$), and more air trapping ($P < .005$) compared with the QVM− group (Table 1).
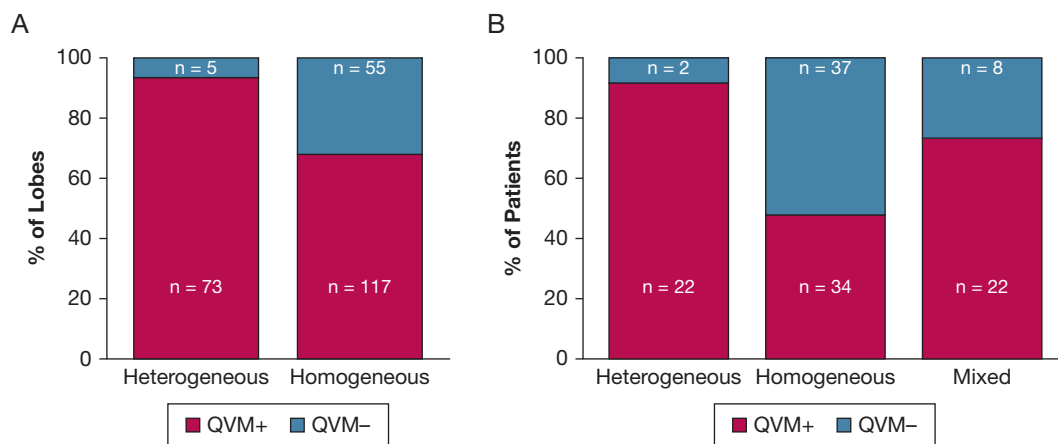

Figure 2 – Baseline QCT characteristics stratified according to QCT subgroup. A, Proportion of treated heterogeneous lobes (≥ 15% ipsilateral difference in percent low attenuation area −950 Hounsfield units) and homogeneous lobes (< 15% ipsilateral difference), stratified according to whether the treated lobes were QVM+ or QVM−. B, Proportion of treated patients with heterogeneous (both lungs), homogeneous (both lungs), or mixed (one heterogeneous lung and one homogeneous lung) disease, stratified according to whether both lobes were QVM+ or whether one or both lobes were QVM+. See Figure 1 legend for expansion of abbreviations.

The multivariate analysis with adjustment for the identified baseline imbalances between the two subgroups showed that QVM+ patients achieved significantly more expiratory lobar volume reduction at 12 months compared with QVM– patients (mean of –0.37 ± 0.05 L vs –0.13 ± 0.08 L; $P = .0064$), even after accounting for baseline differences in percent heterogeneity, percent air trapping, and percent emphysema (e-Table 3). In addition, between-group differences in change in 6MWD (15.4 m; 95% CI, –12.1 to 42.9), FEV$_1$ (6.7%; 95% CI, –0.8 to 14.2), residual volume (–0.12 L; 95% CI, –0.41 to 0.17), and SGRQ (–0.6 point in total score; 95% CI, –5.5 to 4.3) all favored QVM+ patients. Furthermore, QVM+ emerged as the only significant QCT-based predictor of lobar residual volume change ($P = .02$) (e-Table 4).

Thus, lobar selection with QCT emerged in this analysis as a previously unknown covariate in RENEW that may have obscured the response profile of endobronchial coil therapy in this trial. To account for this finding, we excluded QVM– patients from the subsequent analyses in which baseline predictors of response were examined.

Baseline Predictors of Superior Response to Coil Treatment in QVM+ Population

Higher baseline percent emphysema score and absence of airway disease on visual CT review were associated ($P < .05$) with lobar residual volume reduction at 12 months (Figs 3A, 3B, Table 2). Higher baseline residual volume percent predicted approached significance ($P = .071$) in the multivariate stepwise model.

We next applied a lobar residual volume change threshold of –320 mL to determine the lowest baseline value for residual volume percent predicted and percent emphysema score that resulted in a lobar residual volume response at 12 months. The threshold of –320 mL for lobar residual volume change was determined by using an MCID analysis anchored to residual volume change measured via body plethysmography (e-Tables 5, 6). Patients with baseline residual volume < 200% predicted or with percent emphysema score < 20% in either targeted lobe did not achieve clinically meaningful lobar residual volume reduction (e-Fig 2).

Sixty-four percent of patients in the QVM+ subgroup (50 of 78) met all three identified volume reduction criteria: residual volume ≥ 200% predicted, % LAA ≥ 20%, and no visually determined presence of
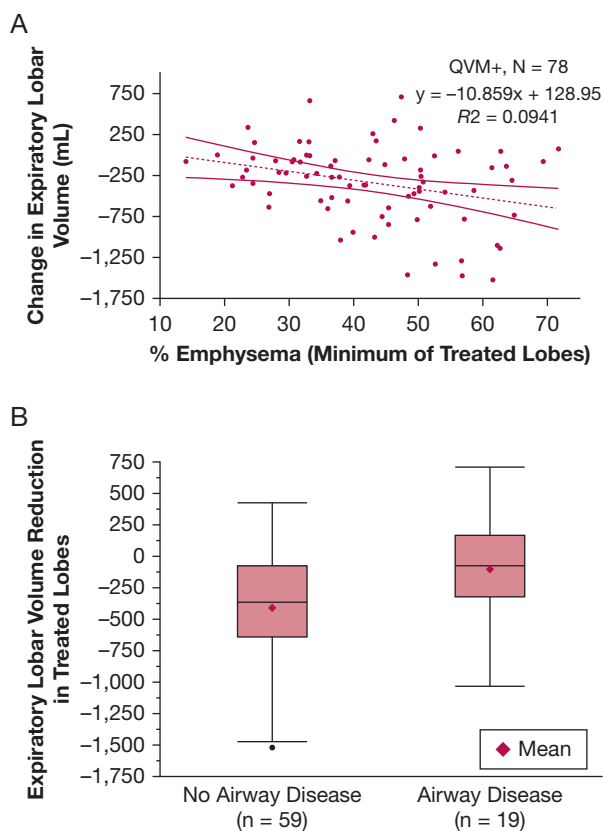
Figure 3 – A, Scatterplot of emphysema score vs lobar residual volume reduction in responder analysis cohort (N = 78). The relationship between lobar residual volume change and baseline percent emphysema score in treated patients. In this figure, percent emphysema is represented as the smaller lobar percent low attenuation area –950 Hounsfield units score of the two treated lobes. B, Expiratory lobar volume reduction in treated lobes by visual presence of airway disease in responder analysis cohort (N = 78). Subjects receiving a score of "2" or "3" (n = 19) for presence of airway disease (Airway Disease) on visual CT scan achieved significantly (P = .0117) less expiratory lobar volume at 12 months' post-coil treatment than patients with scores of "0" or "1" (N = 59) (No Airway Disease).

airway disease at baseline. This volume reduction criteria subgroup (n = 50) exhibited significant clinical improvement at 1-year posttreatment (mean) for residual volume (–570 mL), FEV$_1$ (97 mL), FEV$_1$ % predicted (15.2%), and SGRQ (–12 points) ($P < .01$) but not for 6-min walk test (0.1935) (Table 3) compared with patients who did not meet these criteria. Importantly, this scenario resulted in significant improvements in clinical responder rates when the volume reduction criteria subgroup was compared with those who did not meet these criteria (Fig 4).

Safety in Improved Patient Selection Group

We examined the 1-year safety profile in all RENEW treatment patients who completed the 12-month follow-up visit (n = 125) to assess the safety impact of

TABLE 2] Baseline Characteristics Associated With Lobar Residual Volume Change at 12 Months in Responder Analysis Cohort (N = 78)

Parameter	Correlation	P Value	Correlation Coefficient, r
Bivariate			
% Emphysema, minimum of both treated lobes	−	.0063	−0.3067
Visual CT presence of airways disease	+	.0117	0.2841
% Heterogeneity between ipsilateral lobes	−	.0118	−0.2837
BMI	+	.0464	0.2262
Multivariate (stepwise) R^2 = 0.1773, P = .0023			
% Emphysema, minimum of both treated lobes	−	.0244	
Visual CT image presence of airways disease	+	.0313	
Residual volume % predicted	−	.0710	

Only statistically significant predictors are shown for univariate analysis ($P < .05$). Multivariate regression model with stepwise control using minimum Akaike Information Criterion stopping rule in forward direction.

improved patient selection. No differences approached significance between the volume reduction criteria subgroup and the subgroup without all volume reduction criteria (Table 4).

Discussion

Following early lung volume reduction trials, post hoc subgroup analysis proposed responder profiles that still define the current use of both surgical therapies and valve therapies.[17,18] The responder subgroup identified in the randomized controlled Endobronchial Valve for Emphysema Palliation Trial (VENT) trial has been confirmed prospectively, providing necessary selection criteria for real-world therapeutic adoption of endobronchial valves.[19-23] Similarly, this RENEW post hoc analysis offers rational predictors of response to

coil therapy that can now be prospectively confirmed as well.

Endobronchial coils have shown effectiveness in both heterogeneous and homogeneous disease; however, no clear single mechanism of action has been defined. Although valves and other therapies based on atelectasis or injury-response fibrosis benefit from the rich evidence base of response mechanisms in lung volume surgery, the mechanisms driving the effects of coil treatment have yet to be defined.[24,25] Despite its early stage, there is accumulating evidence supporting multiple mechanistic effects on the lung induced by coil placement such as reducing static hyperinflation, improving airway resistance, promoting the airway tethering effect, and reducing dynamic hyperinflation.[10,26-28] RENEW has provided substantial

TABLE 3] Clinical Outcomes According to Volume Reduction Criteria in Responder Analysis Cohort (N = 78)

Variable	Patients With Volume Reduction Criteria (n = 50)				Patients Without Volume Reduction Criteria (n = 28)				P Value[a]
	Mean	SE	Median	IQR	Mean	SE	Median	IQR	
Residual volume, L	−0.57	0.13	−0.44	−1.19 to −0.10	−0.20	0.16	−0.02	−0.67 to 0.38	.0793
VC, L	0.31	0.06	0.27	0.09 to 0.55	0.11	0.08	0.09	−0.25 to 0.32	.0470
FEV$_1$, %	15.2	3.1	13.6	1.4 to 21.9	0.6	3.5	−0.9	−13.3 to 10.1	.0038
FEV$_1$, L	0.097	0.022	0.075	0.010 to 0.145	−0.005	0.024	−0.005	−0.103 to 0.067	.0040
Lobar volume, mL	−467	64	−402	−670 to −128	−103	78	−68	−264 to 145	.0007
6MWD, m	16	11	24	−2 to 63	−7	12	−13	−46 to 41	.1935
SGRQ, points	−12	2	−13	−19 to −3	−4	3	−2	−9 to 6	.0100
mMRC, points	−0.8	0.2	−1.0	−2.0 to 0.0	−0.8	0.2	−1.0	−1.8 to 0.0	.9040

Volume reduction criteria are as follows: QVM+, percent emphysema ≥ 20% and residual volume ≥ 200% predicted, and no visual CT presence of airway disease. IQR = interquartile range; mMRC = modified Medical Research Council dyspnea score; VC = vital capacity. See Table 1 legend for expansion of other abbreviations.
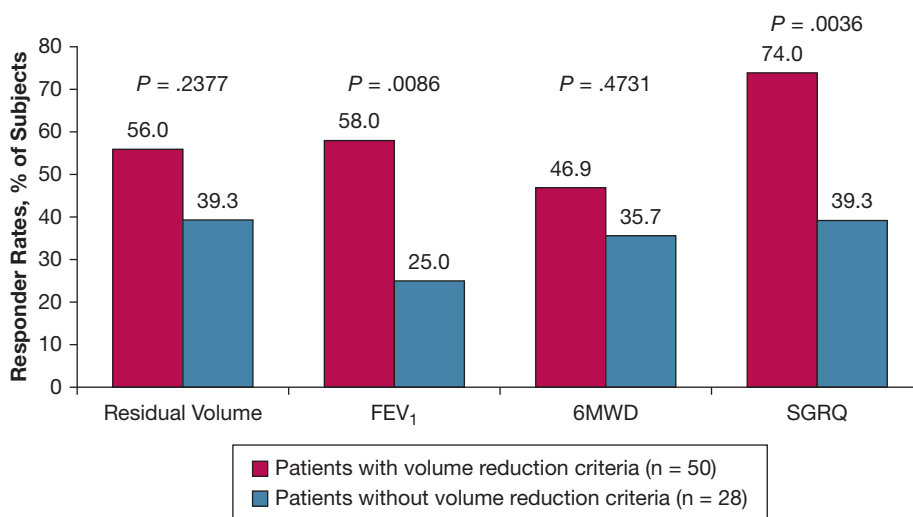[a]Analysis of variance for continuous outcomes, two-tailed Fisher exact test for categorical outcomes.

Figure 4 – *Responder rates in patients with and without identified predictive criteria for response. Volume reduction criteria were no airway disease, low attenuation area ≥ 20%, and residual volume residual volume ≥ 200% predicted. Patients who met those criteria had significantly higher response rates in clinical end points, using standard minimum clinically important difference levels: residual volume, –350 mL; FEV₁, 10%; 6MWD, 25 m; and SGRQ, –4 points. 6MWD = 6-min walk distance; SGRQ = St. George's Respiratory Questionnaire.*

opportunity for post hoc analysis and improved understanding of coil mechanisms and predictors of response.[4] Although the design of coils as local, nonblocking devices creates the potential for multiple mechanisms of action, we propose volume reduction as the primary objective of coil therapy and have confirmed the association of lobar residual volume reduction with clinical responsiveness at 1-year posttreatment. We also identified three baseline criteria with proposed inclusion thresholds (residual volume ≥ 200% predicted, emphysema score %LAA ≥ 20, and no presence of airway disease on visual CT scanning) that defined a patient subgroup achieving clinically significant pulmonary function and volume reduction outcomes at 12-months' post-coil treatment.

Treating the most damaged lobe was shown to be most strongly associated with lobar volume reduction, and we discovered that more than one-third of patients treated in RENEW did not receive bilateral treatment in the most destroyed lobes according to QCT. When the most damaged lobes were treated (QVM+ subgroup), substantial improvements in physiological and clinical outcomes were shown compared with the QVM– subgroup. This finding suggests that using QCT, rather than visual analysis, to target the most damaged lobes for treatment may be associated with improved outcomes in coil-treated patients. QCT-visual mismatching was much more common in homogeneous patients compared with heterogeneous patients. This finding has important

TABLE 4] Summary of Major Complications Through 12 Months (N = 125)

Major Complication Event	Patients With Volume Reduction Criteria (n = 50)		Group Without All Volume Reduction Criteria (n = 75)		P Value[a]
	Subject Counts	Event Counts	Subject Counts	Event Counts	
Total major complication events	14 (28.0%)	17	19 (25.3%)	31	.8365
Death	0	0	0	0	NA
Pneumothorax	1 (2.0%)	1	0	0	.4000
Hemoptysis	0	0	1 (1.3%)	1	> .9999
COPD exacerbation	5 (10.0%)	5	8 (10.7%)	11	> .9999
Lower respiratory infection	8 (16.0%)	10	12 (16.0%)	16	> .9999
Respiratory failure	1 (2.0%)	1	3 (4.0%)	3	.6492
Unanticipated bronchoscopy	0	0	0	0	NA

[a]By Fisher exact test. Subjects are counted at most once for each major complication event. NA = not applicable.

implications given that most volume reduction studies focus almost exclusively on heterogeneous patients in whom the difference between QCT and visual lobar targeting is small and/or negligible. This analysis suggests important limitations of visual lobe targeting for complex and novel interventional therapies, especially in the context of homogeneous patients.

There are limitations to this post hoc analysis, mainly the small number of patients because of the exclusion of QVM– treated patients. This study was a retrospective subgroup analysis with potential "n" effects. However, the National Emphysema Treatment Trial post hoc responder subgroup represented 11% of the total study population (139 of 1,218 patients with upper lobe predominant, heterogeneous emphysema, and low baseline exercise tolerance), and the VENT post hoc responder subgroup represented approximately 20% of the study population (68 of 321 patients with intact fissures and heterogeneous emphysema). These post hoc analyses from 2003[18] and 2010[17] have effectively established appropriate patient selection criteria for these therapies still in use today. We also acknowledge the potential of confounding influences among the factors that emerged as significant in the present analysis, particularly for the findings of airway wall thickening, which was not under protocol for this analysis.

The present analysis was based on a quantitatively measured end point (CT expiratory lobar volume) that is somewhat independent of patient effort, although the expiratory scans were not gated using spirometry (e-Appendix 1). Many of the predictors found in this analysis reached statistical and clinical significance despite small subgroups. Our findings are clinically rational and consistent with published literature from earlier emphysema trials.[11,17-19] Our results are promising given that nearly one-half (44%) of the volume reduction criteria subgroup is composed of patients with bilateral homogeneity of disease (< 15% ipsilateral

difference at –950 Hounsfield units), a group of patients not generally considered for lung volume reduction surgery.[1] The Identifying Responders and Exploring Mechanisms of Action of the Endobronchial Coil Treatment for Emphysema (REACTION) trial exploring physical activity change and physiologic response patterns in coil-treated patients is ongoing and may shed light on this intriguing hypothesis.[29]

Although quantitative assessment of the HRCT is much more reliable in precise emphysema scoring and fissure completeness,[30,31] subtle airway wall changes, magnitude of bronchial wall thickening and mild bronchiectasis, and postinfectious consolidations are much more difficult to quantify. Although expert CT readers do not have a solid consensus,[32] it is possible to make a judgment with clinical implications.[30,33] A thorough qualitative inspection with clinical interpretation regarding the findings of these features, in addition to routine QCT, is key in excluding patients with relevant airway disease, who are less likely to benefit from coil treatment.

Conclusions

We identified three baseline criteria with proposed inclusion thresholds (residual volume ≥ 200% predicted, emphysema score %LAA ≥ 20, and absence of airway disease on visual CT imaging) that defined a patient subgroup achieving clinically significant pulmonary function and volume reduction outcomes at 12 months' post-coil treatment. Patients selected for lobar volume reduction with endobronchial coil treatment should meet all these criteria, and lobe targets should be confirmed with densitometry analysis to ensure treatment in the lobes of greater destruction. This post hoc analysis of RENEW data proposes patient selection criteria that improve response to endobronchial coils. These findings warrant prospective confirmation to establish the profile of patients with severe emphysema who should be offered this treatment.

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