Supplementary material

Bronchoscopic procedure.

Interlobar collateral ventilation (CV) was evaluated in all subjects using Chartis® (Pulmonx Corporation, Redwood City, CA) pulmonary assessment system under general anesthesia and endotracheal intubation using a tube with an internal diameter of 9 mm. The primary ventilator settings were positive pressure ventilation with low ventilation frequency and long expiratory settings (12). All Chartis® measurements were performed by one interventional pulmonologist. Chartis® measurement in the target lobe for EBV treatment was terminated when either absence of CV was confirmed by an airway flow gradually to zero in combination with immediate return of airway flow upon release of the balloon catheter, or when the presence of CV was confirmed by the observation of a continuous and persisting expiratory airway flow during at least 5 minutes or a total volume of air recorded of at least 1 Liter (12). Subjects with a CV positive read-out were allocated to the no-ELVR (control) group in whom a physical activity coaching intervention (by use of a step counter and smartphone application) provided between 3 to 6 months of follow-up. These control subjects (no-ELVR) were potentially eligible for LVRS after 6 months of follow-up (6m FU) and repeat MEET discussion. Subjects with a CV negative read-out underwent placement of EBVs (Zephyr®, Pulmonx Corporation, Redwood City, CA) with the intention of complete lobar occlusion. No prophylactic antibiotic therapy was given. These ELVR subjects were hospitalized for 4 nights regardless of their clinical status with bed rest and cough suppression during the first 48 hours after EBVs insertion (13). ELVR subjects were evaluated during clinical site visits at 30 days, 3 and 6 months after the procedure. At 30 days, a low dose CT scan (DLP 30 mGycm) was performed to check for lobar occlusion. In the absence of lobar occlusion, a follow-up bronchoscopy was

considered to check for valve position, valve function and when indicated valve replacement. A physical activity coaching intervention was provided between 3 to 6 months post intervention. After the 6-month evaluation, a definite non-response was considered if a patient didn't respond on measured minimal important differences. The valves were electively removed and these non-responding ELVR subjects were given the option to undergo LVRS when eligible based on MEET discussion.

Surgical procedure.

All LVRS procedures were performed by anterior 2 or 3-ports video-assisted thoracic surgery. All subjects received epidural analgesia and were installed at the operation table on their back on a vacuum mattress. Cefazolin was given at induction as prophylactic antibiotic therapy, in case of penicillin allergy clindamycin was administered. Targeted lung tissue was chosen based on MEET decision after careful evaluation of heterogeneous zones on CT scan and perfusion scintigraphy imaging, and intraoperative findings of parenchyma with trapped air upon deflation of the lung. These areas were resected with standard stapling technology without routine buttressing. The upper lobe was shaved in all patients. Seven patients had additional target zones removed in the lower lobe. One or two chest tubes were placed on water seal at the end of the operation. The subject remained intubated breathing spontaneously and was transferred to the intensive care unit. LVRS subjects were evaluated during clinical site visits at 42 days, 3 and 6 months after the procedure. All subjects received a physical activity coaching intervention between 3 to 6 months post LVRS.

Table S1: Changes (mean ± SEM) from primary and secondary outcome measures in ELVR group and no-ELVR group measured at baseline, 3 months and 6 months.

Table S2: Changes (mean ± SEM) from primary and secondary outcome measures in ELVR group and LVRS group measured at baseline, 3 months (3M) and 6 months (6M).

Table S3: Baseline characteristics ELVR versus LVRS.

Table S4: Percentage of MCID responders for key outcome measures for unilateral ELVR and bilateral LVRS group at 3 and 6 months follow-up.

Figure S1: Changes from baseline in key outcome measures at 3 and 6 months post allocation for ELVR group (full black line), no-ELVR group (dotted grey line) and LVRS group (dotted black line). Data are presented as mean ± SEM for FEV_1 (panel A), RV (panel B), FRC (panel C), TLC (panel D), six-minute walk distance (panel E) and BODE index (panel F).

Figure S2: Changes from baseline in key outcome measures at 3 and 6 months post allocation for ELVR group (full black line), no-ELVR group (dotted grey line) and LVRS group (dotted black line). Data are presented as mean ± SEM for Saint-George Questionnaire total score (panel A) and subdomains (panel B-D).

Table S1: Changes (mean ± SEM) from primary and secondary outcome measures in ELVR group and no-ELVR group measured at baseline, 3 months and 6 months.

VARIABLE	ELVR GROUP			NO-ELVR GROUP			Absolute change at 3M FU	P-value	Absolute change at 6M FU	P-value
	Baseline	3M	6M	Baseline	3M	6M				
FEV_1 (L)	0.79 ± 0.06	1.00 ± 0.06	0.96 ± 0.06	0.83 ± 0.07	0.81 ± 0.07	0.78 ± 0.07	0.22 ± 0.05	<0.0001	0.21 ± 0.05	<0.0001
RV (L)	4.88 ± 0.21	4.16 ± 0.21	4.13 ± 0.21	4.86 ± 0.22	4.95 ± 0.23	5.06 ± 0.22	-0.81 ± 0.22	0.0004	-0.95 ± 0.21	<0.001
FRC (L)	5.94 ± 0.25	5.44 ± 0.25	5.42 ± 0.25	6.22 ± 0.26	6.28 ± 0.27	6.29 ± 0.26	-0.55 ± 0.17	0.0018	-0.59 ± 0.17	0.0009
TLC (L)	7.26 ± 0.30	6.85 ± 0.30	6.89 ± 0.30	7.63 ± 0.31	7.63 ± 0.31	7.64 ± 0.31	-0.40 ± 0.14	0.0053	-0.39 ± 0.14	0.007
6MWD (m)	356 ± 17	385 ± 17	394 ± 17	380 ± 17	359 ± 18	360 ± 17	51 ± 18	0.0052	58 ± 17	0.0013
SGRQ Total score, points	61 ± 3	41 ± 4	41 ± 3	63 ± 4	64 ± 4	60 ± 4	-21 ± 5	0.0002	-18 ± 5	0.0012
SGRQ Symptoms, points	64 ± 5	42 ± 5	48 ± 5	60 ± 5	60 ± 5	53 ± 5	-21 ± 7	0.007	-9 ± 7	0.25
SGRQ Activities, points	85 ± 3	62 ± 4	59 ± 3	82 ± 4	83 ± 4	84 ± 4	-24 ± 6	0.0001	-28 ± 6	<0.0001
SGRQ Impact, points	47 ± 4	28 ± 4	28 ± 4	52 ± 4	54 ± 4	50 ± 4	-20 ± 6	0.0018	-16 ± 6	0.008
BODE index score	5.4 ± 0.3	3.5 ± 0.3	4 ± 0.3	4.9 ± 0.4	5.8 ± 0.4	5.1 ± 0.4	-2.7 ± 0.4	<0.0001	-1.6 ± 0.4	<0.0001

Definition of abbreviations: ELVR = endoscopic lung volume reduction by Zephyr endobronchial valve; FEV_1 = forced expiratory volume in one second; FRC = functional residual capacity; RV = residual volume; TLC = total lung capacity; 6MWD = six-minute walking distance; SGRQ = Saint George's Respiratory Questionnaire (total and sub scores ranges from 0 to 100, with lower score indicating better quality of life); BODE index = Body mass index, airflow obstruction, dyspnea and exercise capacity (score ranges from 0 to 10 with higher scores indicating larger mortality risk).

Table S2: Changes (mean ± SEM) from primary and secondary outcome measures in ELVR group and LVRS group measured at baseline, 3 months (3M) and 6 months (6M).

VARIABLE	ELVR			LVRS			BETWEEN GROUP 3M	P-VALUE 3M	BETWEEN GROUP 6M	P-VALUE 6M
	Baseline	3M	6M	Baseline	3M	6M				
FEV1 (L)	0.79 ± 0.06	1.00 ± 0.06	0.96 ± 0.06	0.83 ± 0.06	1.16 ± 0.07	1.09 ± 0.07	0.12 ± 0.07	0.08	0.09 ± 0.07	0.15
RV (L)	4.88 ± 0.21	4.16 ± 0.21	4.13 ± 0.21	5.12 ± 0.22	3.65 ± 0.24	3.62 ± 0.24	-0.74 ± 0.27	0.009	-0.75 ± 0.27	0.008
FRC (L)	5.94 ± 0.25	5.44 ± 0.25	5.42 ± 0.25	6.34 ± 0.23	5.06 ± 0.24	5.09 ± 0.24	-0.79 ± 0.25	0.003	-0.75 ± 0.25	0.004
TLC (L)	7.26 ± 0.30	6.85 ± 0.30	6.89 ± 0.30	7.66 ± 0.26	6.60 ± 0.27	6.65 ± 0.27	-0.65 ± 0.24	0.008	-0.64 ± 0.24	0.01
6MWD (M)	356 ± 17	385 ± 17	394 ± 17	371 ± 17	424 ± 19	441 ± 19	23 ± 23	0.31	32 ± 22	0.15
SGRQ TOTAL SCORE	61 ± 3	41 ± 4	41 ± 3	54 ± 4	31 ± 4	37 ± 4	-4 ± 6	0.57	2 ± 6	0.68
SGRQ SYMPTOMS	64 ± 5	42 ± 5	48 ± 5	49 ± 5	29 ± 6	35 ± 6	1 ± 8	0.94	4 ± 8	0.64
SGRQ ACTIVITIES	85 ± 3	62 ± 4	59 ± 3	79 ± 4	50 ± 5	56 ± 5	-7 ± 7	0.37	0.3 ± 7	0.96
SGRQ IMPACT	47 ± 4	28 ± 4	28 ± 4	43 ± 4	19 ± 5	26 ± 4	-5 ± 7	0.48	2 ± 6	0.75
BODE	5.4 ± 0.3	3.5 ± 0.3	4 ± 0.3	4.5 ± 0.4	2.2 ± 0.4	2.4 ± 0.4	-0.4 ± 0.5	0.61	-0.6 ± 0.5	0.28

Definition of abbreviations: ELVR = endoscopic lung volume reduction by endobronchial valves; LVRS = lung volume reduction surgery; FEV1 = forced expiratory volume in one second; FRC = functional residual capacity; RV = residual volume; TLC = total lung capacity; 6MWD = six-minute walking distance; SGRQ = Saint George's Respiratory Questionnaire (total and sub scores ranges from 0 to 100, with lower score indicating better quality of life); BODE index = Body mass index, airflow obstruction, dyspnea and exercise capacity (score ranges from 0 to 10 with higher scores indicating larger mortality risk).

Table S3: Baseline characteristics ELVR versus LVRS.

Variable	ELVR group (n=20)	LVRS group (n=16)	*P* Value*
Age (years)	65 ± 6	62 ± 5	0.10
Gender (% female)	45%	56%	0.74 □
BMI (kg/m^2)	23 ± 3	23 ± 4	0.68
GOLD stage IV (%)	55%	63%	0.60 □
FEV_1, L	0.79 ± 0.22	0.78 ± 0.26	0.90
FEV_1 (% of predicted)	32 ± 8	30 ± 7	0.65
FRC (% of predicted)	192 ± 19	220 ± 33	0.003
TLC (% of predicted)	128 ± 12	144 ± 18	0.003
RV (% of predicted)	222 ± 31	256 ± 48	0.02
6MWD (meter)	356 ± 74	365 ± 56	0.70
SGRQ total score †	61 ± 12	56 ± 13	0.25
mMRC score ^	3 ± 0.6	3 ± 0.7	0.32 Δ
BODE index score ¶	5 ± 1	5 ± 1	0.35 Δ

* *P*-values obtained by unpaired t-test, Fisher's exact test□ and Wilcoxon rank sum testΔ

Table S4: Percentage of MCID Responders for key outcome measures for unilateral ELVR and bilateral LVRS group at 3 and 6 months follow-up. P values obtained by Fisher's exact test.

Variable (MCID)	ELVR 3M FU (%)	LVRS 3M FU (%)	*P* Value	ELVR 6M FU (%)	LVRS 6M FU (%)	*P* Value
FEV_1 (≥ +100 mL)	70	69	>0.99	45	63	0.34
RV (≤ -430 mL)	70	69	>0.99	70	69	>0.99
6MWD (≥ +30 m)	50	44	0.75	55	56	>0.99
SGRQ (≤ -4 points)	70	75	>0.99	85	63	0.15
SGRQ (≤ -7 points)	60	69	0.73	80	63	0.29

Definition of abbreviations: ELVR = endoscopic lung volume reduction; LVRS = lung volume reduction surgery; FU = follow-up; FEV_1 = forced expiratory volume in one second; RV = residual volume; 6MWD = six-minute walk distance; m = meter; SGRQ = Saint George's Respiratory Questionnaire.

Figure S1: Changes from baseline in key outcome measures at 3 and 6 months post allocation for ELVR group (full black line), no-ELVR group (dotted grey line) and LVRS group (dotted black line). Data are presented as mean ± SEM for FEV_1 (panel A), RV (panel B), FRC (panel C), TLC (panel D), six-minute walk distance (panel E) and BODE index (panel F).

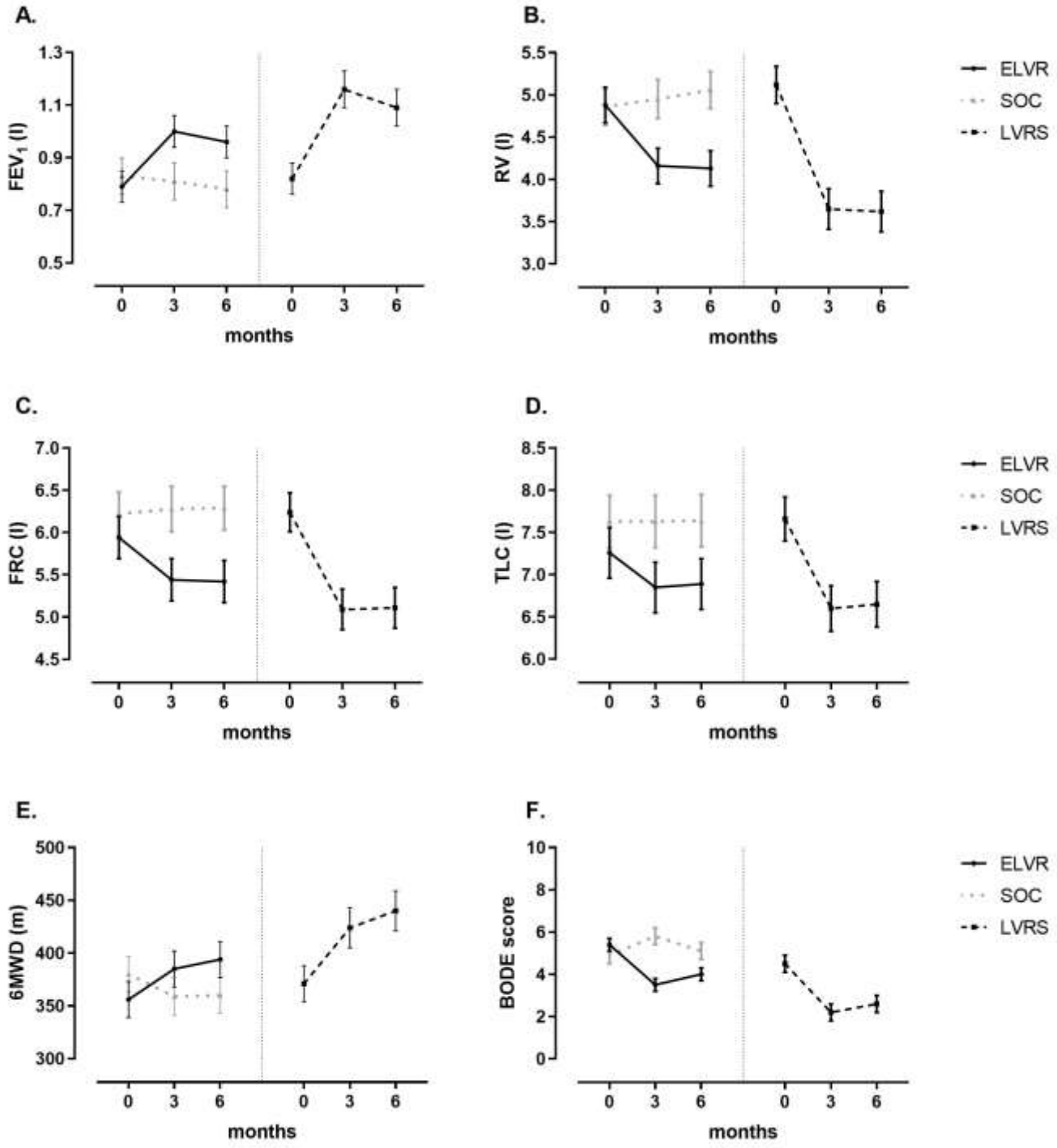

Figure S2: Changes from baseline in key outcome measures at 3 and 6 months post allocation for ELVR group (full black line), no-ELVR group (dotted grey line) and LVRS group (dotted black line). Data are presented as mean ± SEM for Saint-George Questionnaire total score (panel A) and subdomains (panel B-D).