

# Survival following lung volume reduction procedures: results from the UK Lung Volume Reduction (UKLVR) registry

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## ABSTRACT

**Introduction** Lung volume reduction surgery (LVRS) and endobronchial valve (EBV) placement can produce substantial benefits in appropriately selected people with emphysema. The UK Lung Volume Reduction (UKLVR) registry is a national multicentre observational study set up to support quality standards and assess outcomes from LVR procedures at specialist centres across the UK.

**Methods** Data were analysed for all patients undergoing an LVR procedure (LVRS/EBV) who were recruited into the study at participating centres between January 2017 and June 2022, including; disease severity and risk assessment, compliance with guidelines for selection, procedural complications and survival to February 2023.

**Results** Data on 541 patients from 14 participating centres were analysed. Baseline disease severity was similar in patients who had surgery n=244 (44.9%), or EBV placement n=219 (40.9%), for example, forced expiratory volume in 1 s (FEV<sub>1</sub>, 32.1 (12.1)% vs 31.2 (11.6)%. 89% of cases had discussion at a multidisciplinary meeting recorded. Median (IQR) length of stay postprocedure for LVRS and EBVs was 12 (13) vs 4 (4) days (p=0.01). Increasing age, male gender and lower FEV<sub>1</sub>% predicted were associated with mortality risk, but survival did not differ between the two procedures, with 50 (10.8%) deaths during follow-up in the LVRS group vs 45 (9.7%) following EBVs (adjusted HR 1.10 (95% CI 0.72 to 1.67) p=0.661)

**Conclusion** Based on data entered in the UKLVR registry, LVRS and EBV procedures for emphysema are being performed in people with similar disease severity and long-term survival is similar in both groups.

## INTRODUCTION

Lung volume reduction therapies can have significant benefits for people with chronic obstructive pulmonary disease (COPD) who, despite optimal medical care, remain burdened by breathlessness.<sup>1</sup> In recent years, interest in these interventions has grown as research has shown improvements in lung

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Lung volume reduction (LVR) procedures have been shown to produce significant benefits for carefully selected people with severe chronic obstructive pulmonary disease who, despite optimal management, remain limited by breathlessness.

## WHAT THIS STUDY ADDS

⇒ There are limited data about the delivery of these treatments in clinical practice. The UK Lung Volume Reduction registry was established to support quality standards and assess outcomes for people undergoing LVR procedures in the UK.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Findings suggest that LVR procedures are being carried out in appropriately selected patients with emphysema and few high-risk procedures are performed. Survival is similar in patients undergoing LVR either surgically or by endobronchial valve placement, but long waits for intervention indicate that future work should focus on streamlining the pathway to allow timely access to LVR interventions.

function, exercise capacity, quality of life and survival.<sup>1-6</sup> As a result, these specialist interventions have been adopted by an increasing number of centres in the UK. Lung volume reduction surgery (LVRS) and endobronchial valve (EBV) placement are included in UK National Institute for Health and Care Excellence (NICE) recommendations for the management of COPD,<sup>7</sup> have grade A evidence globally<sup>8</sup> and have been adopted for specialist commissioning by National Health Service (NHS) England.<sup>9</sup>

Identification of individuals with COPD who can benefit from LVR procedures requires careful selection based on their



lung function, pattern of emphysema and overall health status including exercise capacity, multimorbidity and frailty.<sup>10–12</sup> LVR procedures should only be conducted in centres with an experienced multidisciplinary team (MDT) and outcomes should be audited.<sup>11</sup> The UK Lung Volume Reduction (UKLVR) register was set up to support and guide LVR MDTs in collecting the appropriate data needed for decision making, to understand what the characteristics of people undergoing LVR procedures in the UK are, and to collect treatment outcomes. This resource is intended to be useful for clinical audit, the development of treatment pathways and to address clinical research questions.

We present a description of the UKLVR registry and analysis of data that have been entered, comparing the characteristics of people undergoing LVRS and EBV placement, reviewing the completeness of the data entry and considering the extent to which assessment matches NICE recommendations. The key outcome of interest was a comparison of survival between those undergoing LVRS and Bronchoscopic lung volume reduction (BLVR) as well as identifying important characteristics that may increase mortality risk.

## METHODS

The UKLVR registry was set up with support from Asthma+Lung UK. A web-based platform was developed by the investigators and hosted by Westcliffe Solutions in accordance with information governance requirements and GDPR. Where data entry was retrospective the requirement for individual patient consent was waived by the ethics committee to avoid bias, but for prospective data entry participants were asked to provide written, informed consent at the time of their procedure.

The registry allows sites to enter data about baseline assessments prior to LVR, the LVR procedure itself and then outcomes at 3 and 12 months postprocedure. Baseline measures include demographic data, confirmation that the case had been discussed in an MDT, symptoms, lung function, imaging and exercise capacity, and further collected data were complications, length of hospital stay and survival. Only LVRS and EBV procedures were included in statistical analysis due to their robust evidence base, adoption in clinical guidelines and being clinically commissioned procedures.

Participant characteristics were assessed in terms of a number of established risk criteria. The BODE/i-BODE index is a composite measure of health status that has been used in previous LVR trials due to its association with prognosis and healthcare utilisation.<sup>13 14</sup> A score between 0 and 10 is calculated based on four commonly used COPD outcome measures, 0 representing the best health and 10 the worst. The Glenfield BFG score categorises people as low, medium or high risk following LVRS based on their B= body mass index (BMI), F=forced expiratory volume in 1s (FEV<sub>1</sub>%) predicted, and G= gas transfer (carbon monoxide transfer factor (TLco)).<sup>12</sup> The

proportion of patients undergoing a procedure with both an FEV<sub>1</sub>% and TLco<20% was also determined as a measure of risk based on results from the National Emphysema Treatment Trial (NETT).<sup>15</sup>

Any centre carrying out LVR procedures was eligible to be involved in the study and could register their interest by contacting the trial coordinator directly. Training was provided to sites to aid with data collection, registry use and the consent process for the trial.

Adult patients with COPD, undergoing an LVR procedure (either surgical or bronchoscopic), were eligible for the present analysis if their procedure had been carried out between January 2017 and June 2022. Survival data were collected from the NHS Spine up until February 2023. The present analysis includes data from 14 UK centres that are currently inputting data into the registry. A list of sites entering data into the UKLVR registry can be accessed in online supplemental appendix 1.

## Statistical analysis

Data were analysed by using IBM Statistical Package for Social Sciences (SPSS) V.28 and Stata V.17.0 (StataCorp). A descriptive analysis is provided for all outcomes. Quantitative variables are presented as mean (SD) or median (IQR) where data were not normally distributed. Categorical variables are reported as number and percentage (%). Between-treatment comparisons were carried out using t-test or Mann-Whitney U test as appropriate and  $\chi^2$  or Fisher's exact test for categorical data. A Kaplan-Meier survival analysis was conducted to estimate overall comparative survival using a log-rank tests, and Cox proportional hazard modelling was used to estimate HRs. Patients were considered to be at risk from time of procedure until either date of death or end of follow-up period (73 months/6 years). Death was defined as all-cause mortality during the follow-up period. Univariable cox regression analysis was carried out investigating the relationship between treatment (LVRS/EBVs) and important covariates: FEV<sub>1</sub>%predicted, residual volume (RV%) predicted, CAT score and exercise capacity (distance walked on either 6 min walk test (6MWT) of incremental shuttle walk test (ISWT)) and survival. In addition, we report a multivariable analysis including all confounders. The proportional hazards assumption was applied based on Schoenfeld residuals method with no significant violations found (p=0.205). Significance was set at p<0.05 for all statistical analyses.

## Patient and public involvement

Discussion with Asthma+Lung UK Breathe Easy groups was highly supportive during the early design phase of the registry. Patients and the public were not involved in the conduct, reporting or dissemination of this research.

**Table 1** Baseline characteristics of patients in the UKLVR registry

	All LVR patients n=541	LVRs n=244	EBVs n=219	Missing data
Gender n (%Female)	222 (41.8)	94 (38.5)	91 (41.6)	3 (0.6%)
Age (years)	64.8 (8.54)	63.4 (8.58)	65.9 (8.31)	18 (3.9%)
BMI kgm <sup>-2</sup>	24.2 (4.4)	24.6 (4.6)	24.2 (4.3)	126 (23.3%)
FEV <sub>1</sub> %predicted	31.8 (12.1)	32.1 (12.1)	31.2 (11.6)	61 (11.3%)
RV% predicted	224.2 (51.3)	220.2 (51.5)	225.4 (52.4)	84 (15.5%)
TLco% predicted	36.1 (18.0)	37.0 (16.2)	35.9 (18.8)	83 (15.3%)
MRC dyspnoea score	4.0 (0.89)	3.7 (0.85)	3.8 (0.87)	147 (27.2%)
Pattern of emphysema				
Heterogeneous	386 (71.0)	190 (77.9)	159 (72.6)	0 (0.0%)
Homogeneous	155 (28.5)	54 (22.1)	60 (27.4)	
Alpha1-antitrypsin deficiency Yes	69 (13.0)	26 (10.7)	35 (16.0)	252 (49.9%)

Data are presented as n (%) and mean (SD). Where numbers do not add up to 100% these missing data represent 'other LVR procedures' carried out but due to small numbers and to ensure these individuals remain non-identifiable, have not been presented in this table. BMI, body mass index; EBCs, endobronchial coils; EBVs, endobronchial valves; FEV<sub>1</sub>, forced expiratory volume in 1s; LVRs, lung volume reduction surgery; MRC, Medical Research Council; RV, residual volume; TLco, carbon monoxide transfer factor.

## RESULTS

### Baseline characteristics of people undergoing LVR

Data on 541 patients undergoing LVR were available (online supplemental table S1); 42% female, mean (SD) age 64.8 (8.54), FEV<sub>1</sub> 31.8 (12.1) %predicted, BMI 24.2 (4.4) kg/m<sup>2</sup> (table 1). The majority had undergone either LVRs 244 (44.9%) or EBV placement 219 (40.9%). In addition, 65 (12%) endobronchial coil treatments (EBC), 9 (1.8%) bullectomies and 4 (0.7%) bronchosopic thermal vapour ablation (BTVA) treatments were recorded but are not included in this analysis. 386 (71.0%) were described as having a heterogeneous pattern of emphysema on their CT thorax and 155 (28.5%) had a homogeneous pattern. 60 (38.7%) of the patients described as having homogeneous emphysema were treated with EBVs and 55 (35.5%) underwent LVRs. 69 (13.0%) of patients in the registry were recorded as having alpha-1 antitrypsin deficiency, and of these 35 (50.7%) had EBVs, 26 (37.7%) LVRs, 7 (10.1%) EBCs and 1 (1.4%) had BTVA.

People undergoing BTVA and bullectomy were excluded from further analysis in this paper due to the very low numbers in these groups and endobronchial coils are excluded as this treatment is no longer available in the UK outside of clinical trials. However, further details on EBC procedures are presented for interest in online supplemental appendix 2.

Baseline lung function parameters in the LVRs and EBV groups were similar (online supplemental table S2); FEV<sub>1</sub>%predicted: 32.2 (11.9) % vs 31.4 (11.3)% (p=0.46); RV/TLC 64.6 (22.1)% vs 68.9 (37.8)% (p=0.19). In those undergoing LVRs 88.5% had lung function tests recorded, compared with 89.5% in the BLVR group.

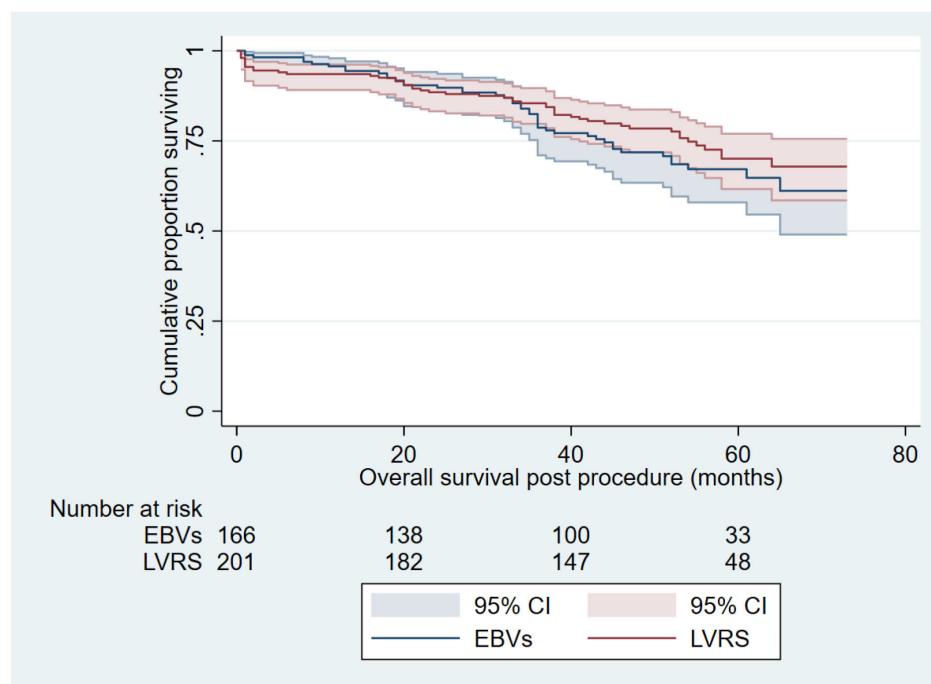
### LVR assessment pathways

A majority, 414 (89.4%) of people undergoing LVRs or EBV, were reported to have been discussed at a specialist MDT meeting prior to a decision being made on their suitability for treatment. The median (IQR) time between being discussed at an MDT meeting and receiving treatment was 175 (195) days. Only 126 (24.3%) of patients were documented as having pulmonary function test (PFT) investigations within the 3 months prior to receiving their treatment with 195 (233) days being the median (IQR) length of time between having PFT and receiving treatment. 428 (92.4%) had a CT scan date recorded prior to treatment with a median of 219 (259) days between having the scan and receiving intervention. 339 (73.2%) had undergone a nuclear medicine ventilation-perfusion isotope (VQ) scan and the median length of time between investigation and treatment was 248 (231) days. Although those receiving LVRs waited longer between receiving treatment and all steps of the pathway than those undergoing a bronchoscopic treatment, there was only a significant between-group difference in CT scan and PFT wait times (CT scan: LVRs: 242(270)/BLVR:199(258) (p=0.038) (PFTs; LVRs: 221(245)/BLVR :153(212) (p<0.001). Although statistically significant, this time difference is unlikely to have made an important difference to outcomes (online supplemental table S3).

### LVR procedures

The median (IQR) length of stay postprocedure for LVRs and EBVs was 12 (13) and 4 (4) days, respectively (p=0.01). 209 (87.1%) LVRs treatments were done via a video-assisted thoracoscopic approach; 71 (29.6%) had





**Figure 1** Kaplan-Meier survival analysis showing absolute survival between patients undergoing either LVRS or BLVR. The blue (LVRS) line shows significantly more perioperative deaths (0–90 days) compared the red (BLVR) line. At around 20 months, the two lines meet and then from around 20 months LVRS has a non-significant survival advantage. BLVR, bronchoscopic lung volume reduction; EBV, endobronchial valve; LVRS, lung volume reduction surgery.

a lobectomy. 18 (7.5%) LVRS patients were admitted to the intensive care unit post-treatment and 15 (6.3%) required ventilatory support. The median length of time postsurgery with an intercostal drain was 11 days.

Prior to EBV treatments, 143 (66.5%) were reported to have had a Chartis (PulmonX, Redwood City, California, USA) procedure to confirm whether collateral ventilation (CV) was present. Of these 14 (9.9%) had an indeterminate result compared with 122 (85.3%) with a negative result. 7 (4.8%) were treated with EBV despite having been recorded as CV positive.

On average, patients received four valves (range 1–7). 153 (69.9%) were carried out under general anaesthetic and 55 (25.1%) under sedation. Only two patients did not have a CXR postintervention recorded (0.9%). 27 (12.3%) patients were reported to have a postprocedure pneumothorax, 7 (3.2%) having one after hospital discharge.

### Outcomes postprocedure

There were 95 deaths during the follow-up period to February 2023; 50 (10.8%) in the LVRS group and 45 (9.7%) following EBVs. Kaplan-Meier survival curves did not differ between the two groups (figure 1) (log rank=1.028,  $p=0.298$ ) and unadjusted Cox regression analysis showed no significant difference between the groups (HR 1.24 (95% CI 0.83 to 1.85,  $p=0.301$ ). It was not possible to report median survival time because the mortality rate did not reach 50% but 5-year survival was 75% following LVRS and 73% following EBVs. Early

postprocedural deaths (0–90 days) were proportionally higher in the LVRS group (5.5% vs 1.8%), although this difference was not statistically significant ( $p=0.068$ ). There were 4 (1.6%) deaths during the perioperative (30 days) period following LVRS and 7 (2.9%) in the 31–90 days postprocedure. There were no perioperative deaths in the EBV group but 3 (1.4%) 30–90 days postprocedure. The adjusted HR 1.30, 95% CI 0.86 to 1.98,  $p=0.216$  showed no evidence that time modifies the treatment effect (table 2).

Covariates associated with an increased risk for mortality in univariable analyses were age, being male or having a lower FEV<sub>1</sub>%predicted (age 1.06 95% CI 1.03 to 1.09,  $p\leq 0.001$ , gender: HR 0.62, 95% CI 0.40 to 0.96  $p=0.032$ , FEV<sub>1</sub>%: HR 0.98, 95% CI 0.96 to 0.99,  $p=0.003$ ) but only age and FEV<sub>1</sub>%predicted remained significant in a multivariable model (age 1.07, 95% CI 1.04 to 1.11,  $p\leq 0.001$ , FEV<sub>1</sub>%HR 0.97, 95% CI 0.96 to 0.99,  $p=0.002$ ) (table 2). Due to high percentage of missing data, Medical Research Council (MRC) dyspnoea score and exercise capacity were not included as covariates in the regression model. However, a sensitivity analysis was carried out including both in the univariate analysis, which indicated that breathlessness had a significant association with survival (online supplemental table S4).

Among the 115 patients with homogeneous emphysema, there were 27 (23.5%) deaths in the follow-up period; 12 (20%) in the LVRS group and 15 (27.3%) in the BLVR group (figure 2) ( $p=0.194$ ). There was one perioperative death in the LVRS group and one in the

**Table 2** Univariate and multivariable Cox regression analysis investigating predictors of survival following LVR

	Patients (n=367)	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Gender (male as reference)	349	0.62 (0.40 to 0.96)	0.032	0.81 (0.50 to 1.31)	0.393
Age	355	1.06 (1.03 to 1.09)	<0.001	1.07 (1.04 to 1.11)	≤0.001
Pattern of emphysema (homogeneous)	349	1.02 (0.65 to 1.60)	0.935	0.93 (0.59 to 1.49)	0.775
Fev <sub>1</sub> % predicted	347	0.98 (0.96 to 0.99)	0.003	0.97 (0.95 to 0.99)	0.003
RV% predicted	347	1.00 (1.00 to 1.00)	0.122	1.00 (1.00 to 1.01)	0.006
CAT score	348	1.00 (0.99 to 1.02)	0.738	1.01 (0.99 to 1.02)	0.620
BMI	347	0.99 (0.97 to 1.01)	0.157	0.98 (0.96 to 1.00)	0.092
Treatment arm (LVRS/BLVR)	367	1.24 (0.83 to 1.85)	0.216	1.10 (0.72 to 1.67)	0.661

HRs, 95% CIs and p values estimated from univariable and multivariable Cox models.

BLVR, bronchoscopic lung volume reduction; BMI, body mass index; CAT, COPD assessment test; EBVs, endobronchial valves; FEV<sub>1</sub>, forced expiratory volume in 1 s; LVR, lung volume reduction; LVRS, Lung volume reduction surgery; RV, residual volume.

90-day postintervention period in the BLVR arm. Cox regression analysis showed no statistically significant difference between survival in the LVRS and EBV arms (HR 1.65, 95% CI 0.77 to 3.54, p=0.200).

In 61 patients with alpha-1 antitrypsin deficiency, there were 12 (17.4%) deaths in the follow-up period; 8 (30.8%) in the LVRS group and 4 (11.4%) in BLVR (figure 2) (p=0.119). One death following LVRS was in the 90-day postoperative period. Again, there was no difference in mortality rate between the those receiving LVRS or EBVs (HR 0.40, 95% CI 0.12 to 1.32, p=0.132).

Follow-up data were entered into the register for 221/541 (40.9%) participants. There were 136 follow ups entered between 0 and 3 months postprocedure, 134 between 3 and 12 months, 40 between 12 and 24 months and 12 up to 36 months. Table 3 describes the complications recorded for each LVR treatment. Of note, exacerbations and hospitalisations were higher in those who underwent EBV treatment but not by a statistically significant amount. Complications including pneumothorax and haemoptysis were more frequent in the EBV group and postoperative pain in the LVRS group (table 3).

### Completeness of selection criteria

The basic recommendations for selecting patients who may be eligible for LVR include being a non-smoker, FEV<sub>1</sub><50%, CT evidence of hyperinflation and a sufficient exercise capacity for the procedure to be undertaken safely (6MWD>140 m or ISWT>80 m). The proportions of missing data for the four criteria were as follows: FEV<sub>1</sub>% predicted: 55 (11.9%), smoking status: 89 (19.2%), MRC dyspnoea score: 137 (29.6%), ISWT or 6MWT: 257 (55.5%). The mean of each of the four individual outcomes fits within the criteria thresholds that are recommended by NICE.<sup>11</sup> However, 48 (10.1%) of patients did not meet one of more of the NICE criteria (online supplemental table S5). 252 (54.4%) of patients had an exercise capacity test recorded as part of their LVR assessment: 179 (86.9%) 6MWT and 76 (36.9%) ISWT,

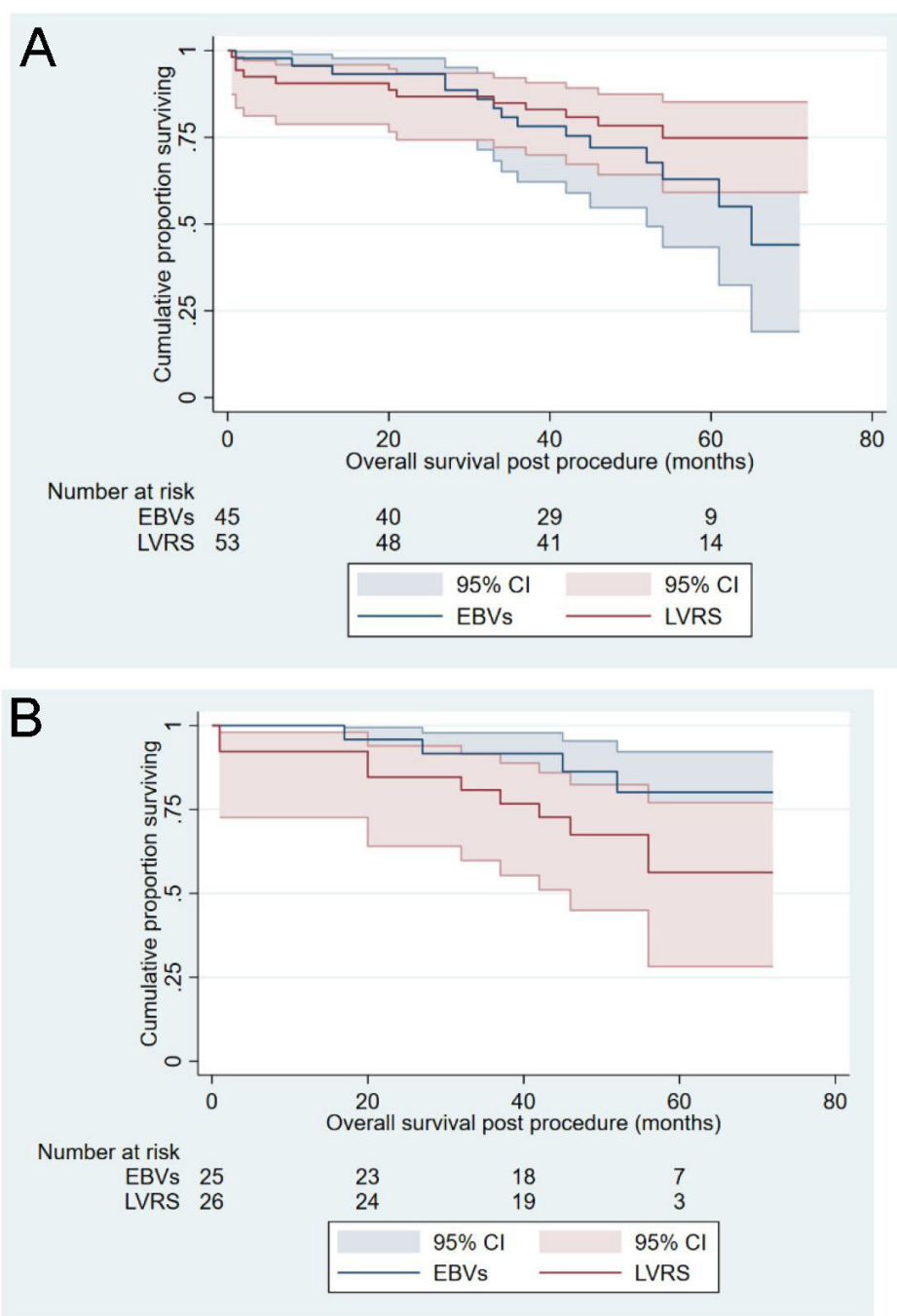
3 (0.6%) patients had both. The mean (SD) distance achieved on these tests was 280 (102.6) m for the 6MWT and 244 (117.8) m for the ISWT. Of those patients with a walking test recorded 40 (19.3%) were able to walk a distance that would put them at the lowest threshold on the BODE/iBODE index; 5 (7.1%) walking>350 m on the 6MWT and 35 (25.5%) walking>250 m on the ISWT.

### High-risk patients

None of the patients in the registry that received treatment would be considered ‘high risk’ when assessed against the Glenfield BFG score criteria. 39 (12.5%) would be considered medium-risk and 273 (87.5%) low-risk patients (online supplemental table S6). Broken down per individual criteria that make up the high-risk score, 151 (48.4%) patients had an FEV<sub>1</sub><0.71 L, 22 (7.1%) a BMI<18.5 kg/m<sup>2</sup> and 26 (8.3%) a TLco<20%. 4 (1.1%), 1 LVRS and 3 EBV (p=0.54), had both FEV<sub>1</sub> and TLco below 20% predicted (online supplemental table S6).

### DISCUSSION

This first report from the UKLVR registry provides evidence about the practice of lung volume reduction in the UK. Key findings are that those undergoing LVRS and EBV have similar characteristics at baseline, and that long-term survival does not differ between the two procedures. Compliance with NICE and NHS Clinical Commissioning recommendations for LVR patients to have been discussed in an MDT was high. Only a small proportion of those undergoing procedures met criteria to be deemed high risk. There were some gaps in data collection, in particular objective assessment of exercise capacity. Finally, the pathway to LVR procedures was characterised by substantial delays and lack of timely reassessment of lung function and imaging prior to procedure. The findings presented must be interpreted within the



**Figure 2** Kaplan-Meier survival analysis showing absolute survival between patients with (A) homogeneous pattern of emphysema and (B) alpha-1 antitrypsin deficiency, undergoing either LVRS or BLVR. BLVR, bronchoscopic lung volume reduction; EBV, endobronchial valve; LVRS, lung volume reduction surgery.

context of varying clinical practices between the centres that contributed to the registry.

### Significance of findings

Patients selected for LVRS or EBV did not differ in terms of disease severity, suggesting that decisions between procedures are being based appropriately on the pattern of emphysema and the completeness of interlobar fissures. An absence of CV is necessary for benefit post-EBV placement. The results do support the perception that LVRS

carries a greater short-term risk. The 90-day mortality rate for LVRS (6%) is comparable to that reported in previous studies<sup>16–18</sup> as is the 2% seen with EBVs.<sup>19</sup> However, it is important to stress that survival longer term did not differ statistically, suggesting that once the immediate perioperative period has been exceeded, higher risks do not extend into the medium to long term. The 5-year survival postprocedure for people entered into UKLVR was 75% following LVRS and 71% following EBVs. This is within the 63%–78% range previously reported for

**Table 3** Complications per treatment

Complication	Whole cohort (n=289)	LVRS (n=118)	EBVs (n=171)	P value
Haemoptysis	12 (2.6)	0 (0)	12 (5.5)	0.002
Pneumonia	33 (7.1)	12 (4.9)	21 (9.6)	0.568
Pneumothorax	31 (6.7)	11 (4.5)	20 (9.1)	0.518
Pneumothorax occurring after hospital discharge	9 (1.9)	3 (0.8)	8 (3.2)	0.534
Valve expiration, aspiration or migration	10 (2.2)	n/a	10 (4.6)	n/a
Bronchospasm	1 (0.2)	0 (0)	1 (0.5)	1.000
Exacerbation of COPD	75 (16.2)	26 (10.7)	49 (22.4)	0.198
Post-operative pain	13 (2.8)	11 (4.5)	2 (0.9)	<0.001
Hospitalisations (up to 12 months postprocedure)	42 people (12.5)/52 admissions	13 people (14.3)/17 admissions	29 people (22.3)/35 admissions	0.120
Hospitalisations requiring NIV (up to 12 months postprocedure)	5 people (1.1) 7 NIV admissions	0 (0)	5 people (2.3)/7 admissions	0.059
Hospitalisations requiring intubation (up to 12 months postprocedure)	6 (1.3)	1 (0.4)	5 (2.3)	0.215
Survival analysis	Whole cohort (n=367)	LVRS (n=201)	EBVs (n=166)	
Death	95 (25.9)	50 (24.9)	45 (27.1)	0.298*
Death within 0–90 days of procedure	14 (3.8)	11 (5.5)	3 (1.8)	0.068

Data are presented as n (%) p values represent  $\chi^2$  or Fisher's exact test.

\*Log rank test.

COPD, chronic obstructive pulmonary disease; EBVs, endobronchial valves; LVRS, lung volume reduction surgery; NIV, non-invasive ventilation.

LVRS<sup>20–22</sup> and 75% for EBVs<sup>3 23</sup> in previous cohorts and significantly higher than reported in other severe COPD cohorts that had not undergone an LVR intervention (around 33%).<sup>24 25</sup> The mean (SD) BODE/i-BODE score in this cohort at baseline for those receiving LVRS and EBVs was 4.8 (1.8) and 5.0 (1.8), respectively, a severity score associated with around 57% survival over 4 years (52 months).<sup>14</sup> Although those undergoing LVR procedures are subject to various forms of selection, these registry data are certainly consistent with the evidence base indicating that undergoing an LVR procedure can substantially increase life expectancy.<sup>1–4</sup> Regression analysis indicated that only gender, age and FEV1% predicted were significantly associated with mortality risk but it should be noted that 6MWT and ISWT records were combined as one 'exercise capacity variable' for the purpose of inclusion in the regression analysis, despite these being different tests. Therefore, the influence of baseline exercise capacity on survival should be investigated further.

The longer length of stay following surgery (LVRS 12 days vs EBV 4 days  $p=0.01$ ) and the greater number of hospitalisations post-EBV, although not statistically significant (LVRS  $n=22$  vs EBV  $n=54$   $p=0.06$ ) both have health economic implications and should be explored further.

The need for specialist MDTs and careful patient selection to ensure the best results from LVR procedures is widely acknowledged<sup>9 26–29</sup> and similar multi-centre open label registries have been set up in Germany (Lung Emphysema -Registry)<sup>30</sup> and the Netherlands

(Bronchoscopic Emphysema Treatment in THE Netherlands (ClinicalTrials.gov Identifier: NCT02815683)) collecting data on patients undergoing LVR procedures. Our registry data demonstrate that the majority of LVR cases were being considered by a specialist MDT and that patients receiving LVR treatments in the UK generally meet the NICE recommendations set out for selection<sup>11</sup> with only small amounts of missing data for these criteria with the exception of an objective test of exercise capacity.

There were long delays between assessment, MDT discussion and procedures. One approach to this is consolidating the role of PR services in the LVR pathway.<sup>10</sup> People meeting the basic eligibility criteria for LVR who still experience limiting breathlessness at the end of PR should be assessed systematically for suitability (presence of hyperinflation, emphysema on CT thorax and absence of exclusion criteria such as pulmonary fibrosis).<sup>7 10</sup> Specialist LVR services should also have capacity to perform all necessary investigations, to ensure that procedures are performed in a timely way. Of note, the period covered in the registry includes that of the COVID-19 pandemic and the inevitable disruption to clinical practice caused by this. It is well recognised that the pandemic has in some circumstances had a profound effect on surgical waiting lists, particularly for benign disease. This is a real cause for concern, especially when dealing with a cohort of patients where there is a limited therapeutic window for intervention before the





risks associated with declining physiological status make these interventions impossible. This period would have undoubtedly influenced the pathway delays, but other factors should be considered such as seasonal variation in the performance of procedures at some centres.<sup>31</sup>

The patients in this registry had significant airflow obstruction and hyperinflation comparable to those seen in trial cohorts.<sup>2 19 32</sup> These levels are substantially worse than those at which guidelines suggest LVR ought first to be considered. The recent development of a decision-making tool<sup>33</sup> embedded into PR programmes that may be used to ensure the systematic consideration and onward referral of potentially eligible patients using broad eligibility criteria suggested by NICE should help to deliver this. Very few cases were carried out in patients considered to be at high risk according to a range of criteria, but severity measures such as FEV1 were at the more severe end of the window of suitability. This may be due to delays in a referral being made and previous research illustrates that individuals have had to ‘fight to get a referral’.<sup>34</sup> In addition, patients being discussed in a specialist MDT may require further workup for a procedure to address multimorbidity before finally determining their eligibility. Identifying and treating multimorbidity is the fifth of the Five Fundamentals of COPD Care set out by NICE guidance for COPD, but a significant proportion of patients with COPD do not receive adequate attention to this.<sup>7 35</sup>

### Methodological issues

We do not have data from centres that have not taken part in the UKLVR study or what percentage of procedures carried out have been entered into the registry, which may introduce bias. However, the data presented here come from a network of specialist centres across the UK carrying out LVR procedures, and therefore, the results can be generalised in a broad population and a variety of settings. Observing a large number of LVR procedures within clinical practice confirms that patient selection criteria and outcomes postintervention are comparable to those seen in research trials. Furthermore, the results of this data analysis report on procedures that were carried out in all severity levels, rather than excluding higher-risk patients as is often the case in clinical trials.

We do acknowledge a number of limitations. First, it is possible that some errors exist in data entry. For example, some patients receiving treatments may not have been entered in the registry and therefore our results may not reflect the entire population of people receiving these treatments, which may be a source of bias if this was not random. Additionally, the database did not dictate that all data must be completed, therefore, there was a large proportion of data entry that was incomplete which may bias our results. For example, when considering the proportion of patients that had been recorded as ‘not discussed at an MDT meeting’ it was evident that they were from centres that had discussed other patients

at an established MDT, raising the possibility of a data entry error. Participation in the registry and data entry are currently voluntary, and this means the absence of clinical data points does not necessarily mean the appropriate investigations were not conducted. 14 centres in the UK contributed data to the registry, so the findings are necessarily limited to these. This emphasises the import of providing both the time and personnel to maintain registry information.

Second, although survival data were complete, limited amounts of follow-up data were entered, which may have led to an underestimate of adverse events post-LVR. A more streamlined dataset, collecting only the most fundamental information to guide good practice, should be considered going forward. Third, the UKLVR data only include those proceeding to an intervention and therefore will not capture the full range of patients being discussed at MDT—an MDT-based audit registry rather than the current procedure-based approach would broaden understanding in this area and may be more convenient for clinicians. Finally, other criteria may make a patient more suited to LVRS than EBVs, or vice-versa, including individual preference. This information was not collected in the registry and these decisions are complex and made by a specialist MDT, highlighting the importance of shared decision-making. Although broadly similar, caution is, therefore, needed about ‘matching’ the LVRS and EBV population.

### Conclusion

The UKLVR registry provides a database for recording all LVR procedures carried out across the UK. The results from this analysis confirm that in the centres entering data into the registry, procedures are being carried out are generally being conducted in line with quality standards set out by NICE, and only a small number of high-risk cases being performed.

Future research should focus on streamlining and standardising the LVR pathway, in particular the interface with pulmonary rehabilitation,<sup>10 33 34</sup> MDT process and data collection, establishing how risk should be categorised in EBV therapy, and ensuring we are effectively identifying and treating those who will benefit the most from LVR therapies. Delays in the pathway, further exacerbated by the COVID-19 pandemic, indicate the need to ensure equity of access to a proven intervention.

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**ONLINE SUPPLEMENT: Survival following Lung Volume Reduction procedures- results from  
the UK Lung Volume Reduction (UKLVR) Registry**

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Table S1; Procedures carried out per site

Patient data collected	All n= 541	LVRS n=244 (44.9%)	EBV's n=219 (40.9%)	EBC's n=65 (12%)	Bullectomy n=9 (1.8%)	BTVA n=4 (0.7%)
<b>Centre:</b>						
Addenbrookes	27 (5.0)	19 (7.8)	8 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
Birmingham	55 (10.2)	18 (7.4)	27 (12.3)	10 (15.4)	0 (0.0)	0 (0.0)
Bristol (BRI)	20 (3.7)	1 (0.4)	11 (5.0)	8 (12.3)	0 (0.0)	0 (0.0)
Glenfield	79 (14.6)	49 (20.1)	21 (9.6)	7 (10.8)	2 (22.2)	0 (0.0)
Golden Jubilee	10 (1.8)	4 (1.6)	3 (1.4)	2 (3.1)	1 (11.1)	0 (0.0)
Liverpool	23 (4.3)	15 (6.1)	8 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
New Cross	15 (2.8)	7 (2.9)	8 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
Northern General	17 (3.1)	8 (3.3)	9 (4.1)	0 (0.0)	0 (0.0)	0 (0.0)
RBHT	244 (45.1)	118 (48.4)	94 (42.9)	25 (38.5)	6 (66.7)	1 (25.0)
Preston	6 (1.1)	0 (0.0)	0 (0.0)	3 (4.6)	0 (0.0)	3 (75.0)
Southampton	36 (6.7)	4 (1.6)	22 (10.0)	10 (15.4)	0 (0.0)	0 (0.0)
Southmead	6 (1.1)	1 (0.4)	5 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)
Nottingham	3 (0.6)	0 (0.0)	3 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)

Data presented as n(%).

LVRS: Lung volume reduction surgery; EBVs: Endobronchial valves; EBCs: Endobronchial coils; BTVA: bronchosopic thermal vapour ablation



Table S2; Lung function data whole cohort and per treatment

	Whole cohort	LVRs	EBVs	P value
<b>FEV1 (L)</b>	0.87 (0.42)	0.90 (0.44)	0.85 (0.39)	0.23
<b>FEV1%</b>	32.3 (11.7)	32.2 (11.9)	31.4 (11.3)	0.46
<b>FVC (l)</b>	2.91 (1.52)	3.10 (2.02)	2.79 (0.89)	0.04
<b>FVC% predicted</b>	101.7 (375.0)	123.5 (558.7)	83.4 (23.9)	0.31
<b>TLco% predicted</b>	36.1 (18.0)	37.0 (16.2)	35.9 (18.8)	0.56
<b>Kco% predicted</b>	46.5 (17.1)	48.2 (16.3)	46.5 (15.4)	0.31
<b>TLC (litres)</b>	8.9 (10.6)	8.24 (4.28)	10.0 (15.7)	0.57
<b>TLC% predicted</b>	134.2 (20.7)	133.7 (21.1)	133.9 (21.5)	0.93
<b>RV (litres)</b>	5.43 (9.61)	4.94 (1.37)	6.10 (14.7)	0.31
<b>RV% predicted</b>	223.8 (51.1)	220.4 (51.4)	225.4 (52.4)	0.34
<b>RV/TLC</b>	67.1 (30.3)	64.6 (22.1)	68.9 (37.8)	0.19
<b>FRC% predicted</b>	188.6 (38.4)	186.8 (42.9)	191.0 (34.7)	0.36
<b>FRC (litres)</b>	8.50 (20.4)	9.25 (24.2)	8.04 (18.1)	0.63
<b>PaO2</b>	10.0 (1.84)	10.0 (1.81)	10.1 (1.76)	0.76
<b>PaCO2</b>	5.27 (0.93)	5.22 (0.99)	5.26 (0.90)	0.77

Data are presented as mean(SD).

FEV<sub>1</sub>: forced expiratory volume in 1 sec; FVC: forced vital capacity; TLco: carbon monoxide transfer factor; Kco: carbon monoxide transfer coefficient; TLC: total lung capacity; RV: residual volume; FRC: functional residual capacity; PaO<sub>2</sub>: partial pressure of oxygen; PaCO<sub>2</sub>: partial pressure of carbon dioxide

Table S3; treatment related data for whole UKLVR cohort and per treatment (LVRS/EBVs)

	All n=463	LVRS n=244	EBVs n=219	p-value
<b>Discussed at MDT meeting:</b>				
Missing data	18 (3.9)	11 (4.5)	7 (3.2)	
Yes	414 (89.4)	221 (90.6)	193(88.1)	
No	31 (6.7)	12 (4.9)	19 (8.7)	
Time between MDT and treatment (days)	175 (195)	198(198)	150(161)	<0.001
<b>CT scan</b>				
Missing data	35 (7.6)	20 (8.2)	15 (6.8)	
Yes	428 (92.4)	224 (91.8)	204 (93.2)	
Time between CT scan and treatment (days)	219(259)	242(270)	199(318)	0.220
<b>VQ scan</b>				
Missing data	46 (9.9)	16 (6.6)	30 (13.7)	
Yes	339 (73.2)	188 (77.0)	151 (68.9)	
Time between VQ scan and treatment (days)	248(231)	259(241)	231(217)	0.105
<b>PFTs</b>				
Missing data	51 (11.0)	28 (11.5)	23(10.5)	
Yes	412 (89.0)	216 (88.5)	196 (89.5)	
Time between PFTs and treatment (days)	195(233)	221(247)	153(212)	<0.001

Data are presented as n (%) or median (IQR). P values correspond to the comparative number of days between investigation and treatment.

LVRS: Lung volume reduction surgery; EBVs: Endobronchial valves; MDT: Multidisciplinary team; CT scan: computer tomography scan; VQ scan: Ventilation perfusion scan; PFTs: Pulmonary function tests.

Table S4; Sensitivity analysis- Univariate and multivariable Cox- regression analysis investigating predictors of survival following LVR with MRC dyspnoea and exercise capacity in models

	Patients (n=367)	Unadjusted HR (95%CI)	p value
MRC dyspnoea score	263	1.52(1.10-2.08)	0.010
Exercise capacity (6MWT/ISWT)	164	1.00 (1.00-1.00)	0.077

Hazard ratios, 95% confidence intervals and p values estimated from univariable and multivariable cox models.

LVRs: Lung volume reduction surgery; EBVs: Endobronchial valves; BMI: body mass index; FEV<sub>1</sub>: forced expiratory volume in 1 sec; RV: residual volume; 6MWT: 6-minute walk test; ISWT: incremental shuttle walk test.

\*for exercise capacity either 6MWT or ISWT was used depending on which one had been recorded for an individual

Table S5; NICE recommendation criteria

	Whole cohort (n=463)			LVRs (n=244)			EBVs (n=219)		
	n (%) meeting NICE criteria	n (%) Not meeting NICE criteria	n (%) missing criteria	n (%) meeting NICE criteria	n (%) Not meeting NICE criteria	n (%) missing criteria	n (%) meeting NICE criteria	n (%) Not meeting NICE criteria	n (%) missing criteria
<b>Smoking status</b>	371 (80.1)	3 (0.6)	89 (19.2)	191 (78.3)	1 (0.4)	52 (21.3)	180 (82.2)	2 (0.9)	37 (16.9)
<b>FEV1</b>	432 (93.3)	26 (5.6)	55 (11.9)	227 (93.0)	14 (5.7)	27 (11.1)	205 (93.6)	12 (5.5)	28 (12.8)
<b>MRC</b>	303 (65.4)	23 (5.0)	137 (29.6)	161 (66.0)	14 (5.7)	69 (28.3)	142 (64.8)	9 (4.1)	68 (31.1)
<b>Walking test</b>	187 (40.4)	19 (4.1)	257 (55.5)	81 (33.2)	10 (4.1)	153 (62.7)	106 (48.4)	9 (4.1)	104 (47.5)
<b>6MWT</b>	56 (12.1)	14 (3.0)	393 (84.9)	33 (13.5)	9 (3.7)	202 (82.8)	23 (10.5)	5 (2.3)	191 (87.2)
<b>ISWT</b>	131 (28.3)	6 (1.3)	326 (70.4)	48 (19.7)	1 (0.4)	195 (79.9)	83 (37.9)	5 (2.3)	131 (59.8)

Data are presented as n (%)

LVRs: Lung volume reduction surgery; EBVs: Endobronchial valves; NICE: National Institute of Clinical Excellence; FEV1: forced expiratory volume in 1 sec;

MRC: medical research council; 6MWT: 6 minute walk test; ISWT: Incremental Shuttle Walk Test.



Table S6; Risks associated to procedures carried out; 4-year survival rates based on BODE/i-BODE score, Glenfield BFG score, other important risk predictors

Risk criteria	Number (%) all procedures (n=463)	Number (%) LVRS (n=244)	Number (%) EBV's (n=219)	P value
<b>BODE/i-BODE index (n=177 whole cohort)</b>		(n=80)	(n=99)	
0-2 points (80% survival)	18 (10.12)	8 (10.0)	10 (10.1)	0.95
3-4 points (67% survival)	59 (33.3)	27(33.8)	32 (32.3)	0.65
5-6 points (57% survival)	67 (37.9)	30 (37.5)	37 (37.4)	0.69
7-10 points (18% survival)	33 (18.6)	15 (18.8)	18 (18.2)	0.97
<b>BFG score components (n=312)</b>		(n=163)	(n=149)	
FEV1 < 0.72	151 (48.4)	73 (44.8)	78 (52.3)	0.26
BMI <18.5	22 (7.1)	13 (8.0)	9 (6.0)	0.56
TLco <20%	26 (8.3)	11 (6.7)	15 (10.1)	0.40
<b>BFG score (n=312)</b>		(n=163)	(n=149)	
High risk (4-5)	0 (0.0)	0 (0.0)	0 (0.0)	0
Medium risk (2-3)	39 (12.5)	20 (12.3)	19 (12.8)	0.95
Low risk (0-1)	273 (87.5)	143 (87.7)	130 (87.2)	0.95
<b>FEV<sub>1</sub>/TLCO (n=359)</b>		(n=190)	(n=169)	
FEV <sub>1</sub> and TLco <20% predicted	4 (1.1)	1 (0.5)	3 (1.8)	0.54

Data are presented as n (%). LVRS: Lung volume reduction surgery; EBVs: Endobronchial valves; EBCs: Endobronchial coils; BMI: body mass index; FEV: forced expiratory volume in 1 sec; TLco: Transfer capacity of the lung.

**Appendix 1; List of specialist UK sites inputting data into UKLVR registry**

Specialist LVR centre collecting and inputting data into UKLVR registry	Lead clinicians
<b>Royal Brompton and Harefield Hospitals (London, UK)</b>	Professor Nicholas Hopkinson (Study CI) Professor Pallav Shah/Mr Simon Jordan
<b>Addenbrookes Hospital, Cambridge, UK</b>	Dr Ravi Mahedeva
<b>Birmingham Heartlands Hospital, Birmingham, UK</b>	Mr Babu Naidu
<b>Bristol Royal Infirmary, Bristol, UK</b>	Dr Katrina Curtis
<b>Glenfield Hospital, Leicester, UK</b>	Mr Sridhar Ratinham
<b>Golden Jubilee Hospital, Glasgow, UK</b>	Mr Alan Kirk
<b>Liverpool Heart and Chest Hospital, Liverpool, UK</b>	Mr Michael Shackcloth
<b>New Cross Hospital, Wolverhampton, UK</b>	Dr Ahmed Habib
<b>Northern General Hospital, Sheffield, UK</b>	Miss Sara Tenconi/ Dr Rod Lawson
<b>Nottingham University Hospitals Trust.</b>	Professor Charlotte Bolton/ Dr Amy Binnion
<b>Royal Preston Hospital, Lancashire, UK</b>	Mr Mohammad Munavvar
<b>Southampton Hospital, Southampton, UK</b>	Dr Tom Havelock
<b>Southmead Hospital, Bristol, UK</b>	Dr James Dodd
<b>Wythenshawe Hospital, Manchester, UK</b>	Dr Richard Barraclough

**Appendix 2: Endobronchial coil (EBCs) data**

There were 112 EBC procedures in 65 cases. Median (IQR) LOS post EBCs was 2 (2) days for the first treatment and 2(1) for the second treatment, giving a combined number of hospital days post procedure of 4 (2.3). An average of 10 (range 4-18) coils were placed in the first treatment received in the EBCs group and 8 (range 4-18) in the second. The decision to not proceed to the second treatment was made in 18 (28.6%) patients and the mean number of days between first and second treatment was 77 (122). There were 25 deaths reported in participants receiving EBC's none of which were within the perioperative period, but one occurred at 47 days post procedure. 2 patients experienced haemoptysis, 3 pneumonias, 4 bronchospasms and there were 19 COPD exacerbations in 10 people. There were 14 hospitalisations, and 1 further hospitalisation requiring intubation.