Bronchoscopic Lung volume reduction using valves
Key studies

- EMPROVE
  - This is the largest randomized multicenter trial demonstrating efficacy of the Spiration valve system in COPD. This study was powered for a primary outcome of 15% improvement in FEV1, and it builds on smaller previous studies. Prior studies had shorter term follow up and/or did require an intact lobar fissure. 174 Subjects were enrolled across 41 sites and were randomized in a 2:1 fashion.
  - PICO
    - Population (n=174) –
      - Age > 40, FEV1 < 45%, TLC > 100%, RV > 150%, 6MWD > 140 meters, PCO2 < 50 mmHg, PO2 > 45 mmHg, BMI > 15
      - Target lobe Emphysema score > 40% (-920 Hounsfield Units)
      - Emphysema heterogeneity (delta of > 10% between the target and ipsilateral lobes)
    - Intervention (n=113)–
      - Endobronchial valve placement
    - Comparison (n=59) –
      - Standard of care
    - Outcome –
      - Statistically and clinically significant improvement of FEV1 over 1 year
      - Statistically and clinically significant improvement of SGRQ
      - No significant improvement of 6MWD
      - ~45% of enrolled patients were prescribed Oxygen at enrollment
      - 12.4% (intervention) vs. 0% rate of pneumothorax over one year
      - 1% (intervention) vs 0% rate of death
      - 30% (intervention) vs 19% COPD exacerbation rate
  - Take home message
    - In the correct patient population, Spiration valves can be beneficial; however, there is a non-insignificant risk morbidity including pneumothoraces. There is not a significant improvement in 6MWD,
- LIBERATE
  - This is the largest randomized multicenter trial demonstrating efficacy of the Zephyr valve system in COPD with the use of the Chartis system to help measure collateral ventilation. This study was powered for a primary outcome of 15% improvement in FEV1 over 1 year. 190 subjects were randomized in a 2:1 fashion, across 24 sites
  - PICO
    - Population (n=190)–
      - Age 40-75, 15% < FEV1 < 45%, TLC > 100%, RV > 175%, DLCO > 20%, 100m < 6MWD < 450m, BMI < 35, PaCO2 < 50 (Denver < 55), PaO2 > 45 (Denver > 30)
      - Target lobe Emphysema score > 50% (-910 Hounsfield Units)
      - Heterogeneous emphysema (delta of > 15% between the target and ipsilateral lobes)
      - Emphysema score < 75% in all ipsilateral lobes
    - Intervention (n=128)–

        - Endobronchial valve placement
    - Comparison (n=62)–
        - Standard of care
    - Outcome –
        - Statistical and clinically significant improvement of FEV1, 6MWD, and SGRQ
        - Initial improvements noted after the procedure persisted over the course of the 1 year subjects were followed
        - 33% (intervention) vs. 0% rate of pneumothorax over one year
        - 4% (intervention) vs 1.6% rate of death
        - 30% (intervention) vs 35% COPD exacerbation rate
- Take home message
    - In the correct patient population, Zephyr valves can be beneficial; however, there is a non-insignificant risk morbidity and mortality.

- IMPACT
    - This was the first study to evaluate the use of endobronchial valves only in homogeneous emphysema. 93 patients were enrolled with 43 in the experimental arm and 50 in the control arm in this randomized trial. This was 3-month evaluation with the primary endpoint being improvement in FEV1
    - PICO
        - Population (n=93)–
            - Age > 40, 15% ≤ FEV1 ≤ 45%, TLC > 100%, RV ≥ 200%, 6MWD ≥ 150 meters
            - < 20% perfusion difference between the left and right hemithorax
            - Homogeneous emphysema, <15% difference in emphysema scores between the target and ipsilateral lobes
            - No collateral ventilation by the Chartis system
        - Intervention (n=43)–
            - Endobronchial valve placement
        - Comparison (n=50)–
            - Standard of care
        - Outcome –
            - Clinically and statistically significant improvement of FEV1 and 6MWD
            - Average heterogeneity index (targe lobe emphysema score minus ipsilateral lobe emphysema score)
                - Intervention group, 6.88
                - Control group, 4.56
            - 0 deaths in the experimental arm and 1 death in the control arm
            - In the experimental arm, Increased risk of COPD exacerbation (16% vs 12%) and pneumothorax (26% vs 0%)
    - Take home message
        - Homogeneous emphysema can be successfully treated with endobronchial valves. This along with the STELVIO study demonstrate a patient population that can be treated outside of the surgical lung volume reduction cohort of only heterogeneous apical predominant emphysema from NETT.

<u>The Bottom Line</u>

Bronchoscopic lung volume reduction with valves has been well studied over more than 10 years and has demonstrated significant symptom improvement. BLVR allows for expanding the patient

population with advanced emphysema that can be treated without the morbidity/mortality associated with surgical lung volume reduction. The greatest advantage of BLVR is the minimally invasive nature and reversibility should complications arise. Ultimately, the most important aspect of a BLVR program is the selection/screening process and the close follow up to monitor for adverse effects such as COPD exacerbation, pneumothorax, or incomplete lobar collapse requiring valve revision. Patients and other Pulmonologists often will require education regarding the extensive screening and follow up process. The procedure itself is the most straight forward part of the entire process, and the interventional pulmonologist must be intimately familiar with the subtleties of the limitations of the clinical trials, the pathophysiology of COPD, and specifics of pulmonary function testing.

References:

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