Non-pharmacological Treatment of Emphysema

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Outline

- Long Term Oxygen Therapy
- Pulmonary Rehabilitation
- Surgical Treatment for Emphysema
- Endobronchial Lung Volume Reduction

Long Term Oxygen Therapy (LTOT)

Thomas L Petty, MD, Master FCCP

University of Colorado
Father of Pulmonary Rehabilitation
Chaired the Nocturnal Oxygen Therapy Trial (NOTT), co-chaired all six Long Term Oxygen Consensus Conferences.

Nocturnal Oxygen Therapy Trial

- At six centers, 203 patients with hypoxemic COPD
- Randomly allocated to either continuous oxygen (O2) therapy or 12-hour nocturnal O2 therapy and followed for at least 12 months (mean, 19.3 months)
- Overall mortality in the nocturnal O2 therapy group 1.94 times that in continuous O2 therapy group ($P = 0.01$)

Ann Intern Med. 1980 Sep;93(3):391-8

NOTT

- More striking in patients with CO_2 retention and also present in patients with relatively poor lung function, more severe brain dysfunction, and prominent mood disturbances
- Continuous O2 therapy also appeared to benefit patients with low mean pulmonary artery pressure and pulmonary vascular resistance and those with relatively well-preserved exercise capacity

Ann Intern Med. 1980 Sep;93(3):391-8

Report of the Medical Research Council Working Party

- Three centres in the U.K.
- 87 patients all under 70 years of age with chronic bronchitis or emphysema with irreversible airways obstruction, severe arterial hypoxaemia, CO_2 retention, and a history of CHF
- Randomised to oxygen therapy (treated) or no oxygen (controls)
- Well matched, both clinically and in terms of lung function and other laboratory findings
- Oxygen (nasal prongs) > 15 h daily, usually at 2 1/min

Lancet. 1981 Mar 28;1(8222):681-6

MRC Trial

- 19 of the 42 oxygen treated patients died in the 5 years of follow-up compared with 30 out of 45 controls
- 500 days for survival advantage of oxygen to emerge in males
- No slowing of progression of respiratory failure in those who died early
- In longer term survivors on oxygen, arterial oxygenation stopped deterioration

Lancet. 1981 Mar 28;1(8222):681-6

Other Benefits

- Reduction in hematocrit
- Modest neuropsychological improvement
- Improvement in pulmonary hemodynamics
- Improvement in dyspnea and the work of breathing
- Dramatic reduction in the prevalence of cor pulmonale

Reduces Pulmonary HTN

- 16 patients with severe COPD (Baseline: mean FEV1, 891 ml; PaO_2, 50.2 mmHg; $PaCO_2$, 51.0 mmHg)
- 3 consecutive right heart catheterizations
- Timing
  - T0: 47 $\pm$ 28 months before the onset of LTOT
  - T1: Just before the onset of LTOT
  - T2: After 31 $\pm$ 19 months of LTOT

Weitzenblum E. Am Rev Respir Dis. 1985 Apr;131(4):493-8

Reduces PHTN….

- From T0 to T1, mean PaO2 decreased from 59.3 to 50.2 mmHg, and mean Ppa worsened from 23.3 to 28.0 mmHg ($p < 0.005$)
- From T1 to T2, PaO2 was stable, whereas Ppa decreased from 28.0 to 23.9mmHg ($p < 0.05$)
- Pulmonary hypertension improved in 12 of the 16 patients

Weitzenblum E. Am Rev Respir Dis. 1985 Apr;131(4):493-8

Would Oxygen Cause CO_2 retention?

- Effect of supplemental nocturnal oxygen on blood gases in 15 patients with severe but stable COPD
- Sleep variables and measures of gas exchange determined on two consecutive nights
  - N1: supplemental oxygen
  - N2: room air
- Supplemental O_2 sufficient to keep O_2 sats $\geq$ 90%

Goldstein RS et al. N Engl J Med. 1984 Feb 16;310(7):425-9

.....Fear of CO_2 Retention

- Less than 6 mm Hg increase in PCO_2 throughout sleep, as compared with values while subjects were breathing room air
- Increase in PCO_2 occurred early in the night and was not progressive

Goldstein RS et al. N Engl J Med. 1984 Feb 16;310(7):425-9

What about O_2 toxicity?

- Home oxygen therapy does not result in pulmonary oxygen toxicity

Petty TL. Ann Intern Med. 1971 Sep;75(3):361-7

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- Stage IV COPD with
  - Waking PaO2 < 55mmHg or SaO2 < 88%, with or without hypercapnia (Evidence B)
  - PaO2 between 55 and 60mmHg or SaO2 of 88% with evidence of pulmonary HTN or peripheral edema suggesting CCF or polycythemia (Hct > 55%) (Evidence D)

Important Points

- Criteria met after optimal treatment regimen for at least 30 days in stable ambulatory patients
- Patients recovering from acute respiratory failure may be given ambulatory oxygen treatment
- Revaluated after 1 month to ascertain that they meet the necessary criteria for long-term oxygen

*Rx Always Mentions…

- Source of oxygen
- Method of delivery
- Duration of use
- Flow rate at rest, during exercise and during sleep

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Also….

- At least 15 hours and preferably longer*
- Maintain the PO_2 above 60 mm Hg and the SaO_2 above 90%
- ABG 30 minutes after initiating oxygen therapy, both to ensure adequate oxygenation and to assess for CO_2 retention
- *A supply that allows patient to leave house for some time and exercise without SaO_2 falling below 90%

*GOLD 2009

Oxygen during Exercise

- Patients with an arterial PO2 of 60 mm Hg or higher while breathing room air may develop worsening hypoxemia with exercise
- Oxygen therapy improves exercise endurance
- Benefit from supplemental oxygen, even in the absence of hypoxemia[1]

[1]Emtner M et al. *Am J Respir Crit Care Med* 2003; 168:1034-1042

Oxygen during Sleep

- Nocturnal drop in oxygen saturation in 50% of patients with daytime resting SaO2 less than 95%[1]
- Alveolar hypoventilation during REM sleep
- Occurs in the absence of frank sleep apnea[2]

[1]Lewis CA et al. *Thorax* 2008; 5:878-883

[2]Weitzenblum E et al. *Sleep Med Rev* 2004; 8:281-294

- Common practice to increase the resting oxygen flow rate by 1 L/min during sleep and exercise to prevent falls in arterial PO2 during these periods
- Need more studies

Modes of Administration

Modes of Administration

- Nasal cannula
- Facemask
- Transtracheal catheter

Source of Oxygen

- Oxygen cylinder
- Oxygen concentrator
- Ambulatory systems
  - Electrically driven concentrators with a 50-ft length of tubing
  - Small tanks of compressed O_2 for portable use
  - Portable concentrators powered by self-contained batteries

Conserving Devices

- Improve the efficiency of oxygen delivery by collecting oxygen flowing during expiration or by providing oxygen flow only during inspiration
- Result in oxygen savings of 50% or more

Transtracheal Catheters

- Inserted permanently into the trachea
- Respiratory dead space filled with undiluted high-concentration O_2 early in inspiration
- Invasive
- Complications including occasional life-threatening tracheal obstruction by mucous balls
- Pts refractory to high flow O_2 by nasal cannula
- Concealed → increased compliance

Commercial Air Travel

- Cabins of commercial airliners pressurized to an altitude between 5000 and 10,000 ft
- Reduced inspired oxygen partial pressure
- In flight desaturation can be measured by a hypoxic challenge, which correlates well within flight saturation[1]

[1]Kelly PT et al. *Chest* 2008; 133:920-926

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- Increase flow rate by 1-2 L/min during flight
- Maintain PaO2 of at least 50mmHg
- 3L/min by cannulae or 31% by Venti
- Those with sea level PaO2 > 70mmHg likely safe, but can desaturate

Beware….

- Major bullous disease -- warn patient about life-threatening pneumothorax
- Probably not fly

Pulmonary Rehabilitation (PR)

Definition by ATS/ERS

"An evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities. Integrated into the individualized treatment of the patient, pulmonary rehabilitation is designed to reduce symptoms, optimize functional status, increase participation, and reduce health care costs through stabilizing or reversing systemic manifestations of the disease."

Am J Respir Crit Care Med 2006; 173:1390-1413

How does Pulmonary Rehabilitation work?

COPD is not all about a low FEV_1

Factors causing health status limitation

- Reduced exercise capacity
- Nutritional depletion
- Deconditioning and debilitation due to
  - Poor pacing techniques,
  - Maladaptive coping skills, and
  - Fear of dyspnea-producing activities

Predictors of survival

- 6-minute walk distance (better than FEV_1)[1]
- Mid-thigh cross-sectional area[2]
- Mid-arm cross-sectional area
- BODE index (BMI, FEV1, 6-min walk distance and dyspnea score)

[1]Pinto-Plata VM. Eur Respir J. 2004 Jan;23(1):28-33
[2]Marquis K et al. Am J Respir Crit Care Med. 2002 Sep 15;166(6):809-13

Factors Contributing to Exercise Intolerance in Chronic Respiratory Disease

Factors…

- Increased ventilatory requirements
- Gas exchange limitation
- Cardiac dysfunction
- Skeletal muscle dysfunction
- Respiratory muscle dysfunction

Cardiac dysfunction

- Increase in right ventricular afterload due to
  - Elevated pulmonary vascular resistance from direct vascular injury
  - Hypoxic vasoconstriction
  - Increases in effective pulmonary vascular resistance due to erythrocytosis
- Right ventricular hypertrophy
- Right ventricular failure
- Compromised LV filling through septal shifts
- Tachyarrythmias

Skeletal muscle dysfunction

- Weight loss and consequent peripheral muscle wasting (30% of COPD pts)
- Peripheral muscle dysfunction due to
  - Inactivity- induced deconditioning
  - Systemic inflammation
  - Oxidative stress
  - Blood gas disturbances
  - Corticosteroid use
  - Reductions in muscle mass

- Leg fatigue also contributes to poor exercise tolerance in chronic respiratory disease, and in some patients is the main limiting symptom
- In patients who developed leg fatigue during exercise, ipratropium failed to increase endurance time despite an 11% improvement in FEV1[1]

[1]Saey D et al. *Am J Respir Crit Care Med* 2003;168:425–430.

Respiratory muscle dysfunction

- Adaptation of diaphragm to chronic overload with greater resistance to fatigue
- More inspiratory force generated at identical absolute lung volumes than that in healthy control subjects
- Mechanical disadvantage due to hyperinflation
- Functional inspiratory muscle strength reduced
- Inspiratory muscle endurance compromised
- Respiratory muscle weakness

Evidence favoring Exercise Training

Casaburi R et al (1991)

- 19 COPD patients (average FEV1 56%) in an inpatient rehabilitation program
- Randomized to 5/7 cycle ergometer training for 8 wk
  - 45 min/day at a high work rate (average, 71 W) or
  - at a low work rate (average, 30 W) for a proportionally longer time
- Testing- 2 cycle ergometer exercise tests at a low and a high work rate
- ABG and arterial lactate before and after the training

Casaburi R et al. Am Rev Respir Dis. 1991 Jan;143(1):9-18.

Casaburi R et al (1991)

- No change in average FEV1
- Less lactate (4.5 versus 7.2 mEq/L) and less VE (48 versus 55 L/min) after training
- Decrease in lactate and ventilation significantly less in low work rate training group ($p < 0.01$)
- Increase in endurance time 73% in high work rate training group, 9% in low work rate training group

Casaburi R et al. Am Rev Respir Dis. 1991 Jan;143(1):9-18.

Goldstein RS et al (1994)

- RCT of respiratory rehabilitation in 89 subjects with severe but stable COPD
- Rehabilitation or conventional community care
- Rehabilitation as inpatients for 8 weeks and supervised as outpatients for 16 weeks
- Primary outcome measures: exercise tolerance and quality of life

Goldstein RS et al. Lancet. 1994 Nov 19;344(8934):1394-7

Goldstein RS et al (1994)

- 6 min walk distance (37.9 m, p = 0.0067)
- Submaximal cycle time (4.7 min)
- Significant improvement in dyspnoea (p = 0.0061), emotional function (p = 0.0150) by questionnaire assessment
- Improvements sustained for the 6 month study period

Goldstein RS et al. Lancet. 1994 Nov 19;344(8934):1394-7.

Ries et al

- Comprehensive outpatient pulmonary rehabilitation with exercise training better than education alone
- Positive results declined over time, approaching those of the control group by 18 to 24 months

Ries et al . *Ann Intern Med* 1995; 122:823-832.

Maltais et al

- Exercise training led to increased levels of oxidative enzymes in muscle biopsy specimens
- Correlated with reduced lactic acid production during exercise

Maltais et al. *Am J Respir Crit Care Med* 1996; 154:442-447

Griffiths et al

- Compared 6 weeks of multidisciplinary pulmonary rehabilitation and standard medical management
- Reduced health care utilization following pulmonary rehabilitation

Griffiths et al. *Lancet* 2000; 355:362-368

Walker et al

- Directly measured activity (from activity monitors) increased following 8 weeks of pulmonary rehabilitation
- Effectiveness in promoting increased activity in the home and community setting

Walker et al. *Thorax* 2008; 63:68

Statements and Guidelines

Statements and Guidelines

- 1997: European Respiratory Society
- 1999: American Thoracic Society
- 2006: American Thoracic Society/European Respiratory Society Statement on Pulmonary Rehabilitation[1]
- 2007: Pulmonary rehabilitation: Joint ACCP/AACVPR evidence-based clinical practice guidelines[2]

[1]Am J Respir Crit Care Med 2006; 173:1390–1413

[2]Chest 2007; 131:4-42

Indications

- Severe dyspnea and/or fatigue
- Decreased exercise ability
- Interference with performing activities of daily living
- Impaired health status
- Decreased occupational performance
- Nutritional depletion
- Increased medical resource utilization

Exclusion Criteria

- An associated condition that might interfere with the rehabilitative process, eg. disabling arthritis and severe neurologic, cognitive, or psychiatric disease
- A comorbid condition that might place the patient at undue risk during exercise training, eg. severe pulmonary hypertension or unstable cardiovascular disease

Components of a Comprehensive Pulmonary Rehabilitation Program (CPRP)

CPRP Components

- Exercise Training
- Education
- Psychosocial training and support
- Respiratory muscle training and chest physical therapy
- Nutritional support
- Oxygen assessment and therapy
- Vaccination

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Exercise Training

- Cornerstone of pulmonary rehabilitation
- Best available means of improving muscle function in COPD[1]
- Reduce mood disturbance[2]
- Decrease symptoms
- Improve cardiovascular function

[1]Sala E et al. *Am J Respir Crit Care Med* 1999;159: 1726–1734

[2]Emery CF et al. *Chest* 1991;100:613–617.

Before exercise training....

- Optimise medical treatment, including bronchodilator therapy
- Long-term oxygen therapy
- Treatment of comorbidities
- A maximal cardiopulmonary exercise test to assess
  - The safety of exercise
  - Factors contributing to exercise limitation, and
  - Exercise prescription

Exercise programs in COPD

Program duration and frequency

- Minimum duration of exercise training not known
- Outpatient exercise training with twice to thrice weekly sessions for 4 weeks less benefit than similar training for 7 weeks[1]
- 20 sessions considerably more improvement in multiple outcomes than 10 sessions[2]
- Short-term, intensive programs (20 sessions condensed in 3–4 weeks) also effective
- Larger, more endurable training effects with longer programs

[1]Green RH et al. *Thorax* 2001;56:143–145.
[2]Rossi G et al. *Chest* 2005;127:105–109.

ATS/ERS 2006 guidelines[1]

- Exercise at least 3/7 under regular supervision
- 2/7 supervised exercise training and and one or more unsupervised session at home an acceptable alternative
- Once-weekly supervised sessions insufficient

[1]Am J Respir Crit Care Med 2006; 173:1390–1413

Intensity of exercise

- Attempt to achieve maximal physiologic training effects
- Modified according to
  - Disease severity
  - Symptom limitation
  - Comorbidities
  - Level of motivation
- Low-intensity targets may be more important for long-term adherence

Specificity of exercise training

- Upper limb exercises should also be incorporated into the training program
- Arm cycle ergometer, free weights, and elastic bands

Endurance Training

- Most commonly applied exercise training modality
- In the form of cycling or walking exercises
- Optimal: Long exercise sessions time > 30 minutes at high intensity (60% max work rate)
- Alternative: Interval training (several smaller sessions separated by periods of rest or lower intensity exercise)

Strength Training

- Greater potential to improve muscle mass and strength than endurance training[1]
- Two to four sets of 6 to 12 repetitions at appropriate intensities
- Advantage: Less dyspnea during the exercise period, easier to tolerate than aerobic training

[1]Simpson K et al. *Thorax* 1992;47:70–77

ATS/ERS Guidelines 2006[1]

- High-intensity exercise encouraged; however, low-intensity training also effective
- Interval training in more symptomatic patients
- Both upper and lower extremity training
- Combination of endurance and strength training esp for those with significant muscle atrophy

[1]Am J Respir Crit Care Med 2006; 173:1390–1413

Severe Pulm HTN

- Not a contraindication
- High-intensity exercise and weight lifting avoided
- Low intensity aerobic exercise, pacing, and energy conservation techniques recommended
- Telemetric monitoring of arrhythmias
- Stop if chest pain, light-headedness or palpitations
- Blood pressure and pulse monitored closely during exercise

Additional Strategies to Improve Exercise Performance

Bronchodilation

- Reduces dyspnea and improve exercise tolerance by
  - reducing airway resistance
  - reduction of resting and dynamic hyperinflation
- Effectiveness judged not only by improvement in FEV1, but improvements in markers of hyperinflation, such as inspiratory capacity
- Primary cause of exercise limitation changes from dyspnea to leg fatigue– better peripheral muscle training

Oxygen

- Three distinct populations
  - Already on LTOT (continue O_2 at higher rate)
  - Those with exercise-induced hypoxemia
  - Those without exercise-induced hypoxemia

- Supplemental oxygen therapy during exercise allows for higher intensity training in hypoxemic and even in nonhypoxemic patients with COPD[1]
- Several mechanisms:
  - dose-dependent lowering of respiratory rate → decrease in dynamic hyperinflation
  - decrease in pulmonary artery pressures
  - decrease in lactic acid production

[1]Emtner M et al. *Am J Respir Crit Care Med* 2003;168:1034–1042.

ATS/ERS Guidelines 2006[1]

- Oxygen supplementation during pulmonary rehabilitation, regardless of whether or not oxygen desaturation during exercise occurs, often allows for higher training intensity and/or reduced symptoms in the research setting. However, at the present time, it is still unclear whether this translates into improved clinical outcomes.

[1]Am J Respir Crit Care Med 2006; 173:1390–1413

CPRP Components

- Exercise Training
- Education
- Psychosocial training and support
- Respiratory muscle training and chest physical therapy
- Nutritional support
- Oxygen assessment and therapy
- Vaccination

Respiratory Muscle Training

- Improvement in exercise capacity with IMT in patients with poor initial inspiratory muscle strength more than exercise training alone[1]
- Adjunctive therapy primarily in patients with suspected or proven respiratory muscle weakness (ATS 2006)

[1] Wanke T et al. *Eur Respir J* 1994;7:2205–2211.

Neuromuscular electrical stimulation

- Involves passive stimulation of contraction of the peripheral muscles to elicit beneficial training effects in patients with severe peripheral muscle weakness
- Can be applied in the home setting
- Larger studies needed
- Adjunctive therapy for patients with severe chronic respiratory disease who are bedbound or suffering from extreme skeletal muscle weakness (ATS 2006)

Physical Therapy

- Postural drainage in patients who are major sputum producers (>30 mL/day) and who have difficulty coughing up their secretions
- Safe in COPD patients
- Routine use of postural drainage and chest percussion and vibration in COPD patients not indicated especially for patients who produce only small quantities of sputum

Physical Therapy

- Inhaled bronchodilator 20 to 30 minutes before postural drainage
- Cupped-hand chest wall percussion or use of an electromechanical percussor

CPRP Components

- Exercise Training
- Education
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Nutritional supplementation

- Caloric support is indicated
  - to match elevated energy requirements during pulmonary rehabilitation
  - to maintain or restore body weight and fat mass
- Adequate protein intake to maintain or restore lean body weight not only in underweight but also in normal-weight patients

ATS 2006

- Caloric supplementation intervention should be considered for the following conditions:
  - a BMI less than 21 kg/m2
  - involuntary weight loss of more than 10% during the last 6 months or more than 5% in the past month, or
  - depletion in lean body mass
- Consists of adaptation in the patient's dietary habits and the administration of energy-dense supplements

Exercise and Body Composition

- Strength training may selectively increase FFM by stimulation of protein synthesis via insulin like growth factor 1 (IGF-1, whereas body fat tended to decrease[1]
- Enhanced bilateral mid-thigh muscle cross-sectional area, assessed by computed tomography, was seen after 12 weeks of aerobic training combined with strength training in normal-weight patients with COPD

Franssen et al. *Chest* 2004; 125:2021–2028.

Noninvasive mechanical ventilation

- Currently not recommended for routine use[1]
- Can be useful in a select subset of patients especially those with pronounced daytime hypercapnia

[1]GOLD 2009

Surgical Treatment for Emphysema

Lung Volume Reduction Surgery (LVRS)

- Dr. Otto Brantigan pioneered LVRS for diffuse emphysema in late 1950s
- Mortality rate of 16%
- "An operation directed at restoration of a physiologic principle. It is *not* concerned with the removal of pathologic tissue, because all of the lung is affected to one degree or another by the emphysematous process, and if you remove all of the the pathology you will not have anything left."

LVRS

- Advances in technology and in surgical technique resulting from experience with lung transplantation
- Led to a revival of surgical treatments of emphysema in 1990s.
- In 1995, Cooper and colleagues presented results of 20 patients who had undergone a resection of between 20% and 30% of each lung via median sternotomy

National Emphysema Treatment Trial

NETT Research Group. N Engl J Med 2003;348:2059-73

NETT

- Patients with severe emphysema (mean FEV_1 26%)
- Underwent 6-10 weeks of pulmonary rehabilitation
- Randomly assigned to
  - LVRS
  - Continued medical treatment
- Complete evaluations at baseline after PR and at 6 months, 12 months, and yearly thereafter

NETT Research Group. N Engl J Med 2003;348:2059-73.

Methods

- 17 clinics: 8– median sternotomy alone, 3 by VATS, 6 by either selected randomly
- Resection 20 to 35 percent of each lung, targeting the most diseased portions

Outcomes

- Primary
  - Overall mortality
  - Maximal exercise capacity
- Secondary
  - Pulmonary function
  - 6-min walk distance
  - HRQOL (SGRQ)
  - General quality of life (QOWS)
  - Dyspnea (UCSD-SOBQ)

Results

- 3777 patients evaluated, 1218 patients underwent randomization
- Mean duration of followup: 29.2 months
- 90-day mortality rate in surgery group was 7.9% (95% CI, 5.9 to 10.3), significantly higher than that in the medical-therapy group (1.3% [95% CI, 0.6 to 2.6], P<0.001)

Mortality

- The total mortality rate was 0.11 death per person-year in both groups (risk ratio for death in the surgery group, 1.01; P=0.90)
- No significant difference in overall mortality despite a higher early mortality rate in the surgery group

Exercise Capacity

- More than 10 W improvement in exercise capacity in 28%, 22%, and 15% of patients in the surgery group after 6, 12, and 24 months, as compared with 4%, 5%, and 3% of patients in the medical-therapy group ($P<0.001$ for the comparisons at all three time points)

Secondary Outcomes

- Improvements significantly more likely in patients in surgery group than patients in medical-therapy group in
  - 6 minute walk distance
  - Percentage of the predicted value for FEV_1
  - General and health-related quality of life
  - Degree of dyspnea

High-risk Patients

- Subgroup of 140 patients
  - Value for $FEV_1 \leq$ 20% predicted and
  - Either homogeneous emphysema or a DLCO $\leq$20% less of the predicted value
- 70 patients underwent LVRS and 70 patients treated medically
- 16 percent 30 day mortality and a 29 percent 90 day mortality in surgery arm as compared with no deaths in the medically managed group

High risk Group

- Patients who had LVRS and survived the early postoperative period had
  - modest increases in FEV1 and six-minute walk times
  - no difference in quality of life when compared to medically treated control patients.
- Excluded these high-risk patients from future enrollment

Non-High Risk Patients

- overall mortality in the surgery group was 0.09 death per person year, as compared with 0.10 death per person-year in the medical-therapy group (risk ratio, 0.89; $P=0.31$);
- exercise capacity after 24 months had improved by more than 10 W in 16 percent of patients in the surgery group, as compared with 3 percent of patients in the medical-therapy group ($P<0.001$).

Other subgroups

- Among patients with predominantly upper-lobe emphysema and low exercise capacity, mortality was lower in the surgery group than in the medical-therapy group (risk ratio for death, 0.47; P=0.005).
- Among patients with non–upper-lobe emphysema and high exercise capacity, mortality was higher in the surgery group than in the medical-therapy group (risk ratio, 2.06; P=0.02)

Subgroups

- Upper-lobe disease and high exercise capacity, mortality was similar, regardless of the treatment-group assignment (risk ratio for death in the surgery group, 0.98; P=0.70)
- However, patients in the surgery group more likely than those in the medical-therapy group to have improvement of more than 10 W in the maximal workload at 24 months (15% vs. 3%, P=0.001)

Subgroups

- Patients with non–upper-lobe disease and low exercise capacity had a similar risk of death, regardless of the treatment group (risk ratio for the surgery group, 0.81; $P=0.49$)
- Had similar chances of improvement of more than 10 W in the maximal workload at 24 months, regardless of the treatment group (12 percent vs. 7 percent, $P=0.50$)

Conclusions

- Overall, lung-volume–reduction surgery offered no survival benefit
- Survival benefit limited to patients with predominantly upper-lobe emphysema and a low base-line exercise capacity
- Functional benefits in patients with predominantly upper-lobe emphysema and a high base-line exercise capacity and in patients with non–upper-lobe emphysema and a low base-line exercise capacity

Lung Transplantation

- Initial report by Mal and colleagues
- Benefits
  - Improved function
  - Improved HRQOL
  - Survival benefit not clear
- COPD most common indication

- Single-lung transplant most common procedure of choice for emphysema
- Advantages
  - Easier
  - Cardiac bypass usually not necessary
  - 2 recipients may receive transplants
- Bilateral lung transplantation may provide better outcomes

Giant Bullae

- Mechanisms for impairment of lung function
  - Compression of nonbullous lung by a giant bulla whose internal pressure is high and whose volume does not change during respiration
  - Impairment of ventilation because of the large amount of space occupied in the thorax by the bulla, with resultant loss of linkage between the chest wall and the nonbullous lung tissue

Surgery for Bullous Lung Disease

- Considered in presence of large bullae
- Morbidity and mortality high if lung function not improved by the surgery
- CT at both full inspiration and full expiration
- Best outcomes
  - large bullae occupying at least 30% to 50% of the hemithorax and
  - FEV1 of about 50% predicted

- Determinants of poor outcome of surgery
  - Size of the bulla (less than one third)
  - Minimal impairment of function of the nonbullous lung tissue
  - Presence of generalized emphysema
  - Low FEV1
  - Hypercapnia
  - Cor pulmonale

Endobronchial Valves

Endobronchial Valve for Emphysema Palliation Trial (VENT)[1]

- Patients with heterogeneous emphysema (assessed on HRCT)
- Endobronchial-valve therapy versus standard medical care.
- Efficacy end points
  - Percent changes in the forced expiratory volume in 1 second (FEV1)
  - 6-minute walk test

[1]N Engl J Med 2010;363:1233-44

Results

- 321 patients
  - 220 endobronchial valves (EBV group) and
  - 101 standard medical care (control group)
- Flexible bronchoscopy used alone (in 98.6% patients) or in combination with rigid bronchoscopy
- Mean number of valves placed 3.8 per patient (range, 1 to 9)
- Mean (±SD) duration of the procedure was 33.8 ± 20.5 minutes

Results

- At 6 months, there was an increase of 4.3% in the FEV1 in the EBV group as compared with a decrease of 2.5% in the control group
- Mean between-group difference of 6.8% in the FEV1 ($P = 0.005$). Roughly similar between-group differences were observed for the 6-minute walk test

Results

- At 12 months, rate of the complications 10.3% in EBV group versus 4.6% in the control group (P = 0.17)
- At 90 days, in EBV group vs control group
  - Increased rates of exacerbation of COPD requiring hospitalization (7.9% vs. 1.1%, p = 0.03)
  - Hemoptysis (6.1% vs. 0%, p = 0.01)
- Pneumonia in target lobe in EBV group 4.2% at 12 months
- Greater radiographic evidence of emphysema heterogeneity associated with an enhanced response to treatment

Endobronchial Valves

More evidence needed

Summary

- Long term oxygen therapy is the standard of care in advanced COPD with proven benefits.
- Pulmonary rehabilitation forms an essential part of management of COPD patients.
- Lung Volume Reduction Surgery can be advised in highly selected patients with advanced disease.
- More evidence is needed on benefits and pitfalls of endoscopic lung volume reduction.