LUNG VOLUME REDUCTION SURGERY : The Groote Schuur Experience

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ABBREVIATIONS:

COPD	:	Chronic obstructive pulmonary disease
LVRS	:	Lung volume reduction surgery
FEV_1	:	Forced expiratory volume in one second
FVC	:	Forced vital capacity
TLC	:	Total lung capacity
RV	:	Residual volume
TLCO	:	Carbon monoxide diffusion capacity
Nd:YAG	:	Neodymium:yttrium-aluminium garnet
GRF-glue	:	Gelatin-resorcinol-formaldehyde glue
HIV	:	Human immuno-deficiency virus
pO_2	:	Partial pressure for oxygen
pCO_2	:	Partial pressure for carbon dioxide
H_2O	:	Water
SF-36	:	Short Form 36 Questionnaire
PHS	:	Physical Health Score
MHS	:	Mental Health Score
GSH	:	Groote Schuur Hospital

CONTENT:

1. INTRODUCTION:

1.1. Importance of Chronic Obstructive Pulmonary Disease (COPD)

From recent statistics (79,59) it has been concluded that COPD is the most common lung disease in the United States affecting almost 16 million people. The mortality is rising, COPD is the fourth most common cause of death in USA after myocardial infarctions, cancer and stroke (91).

COPD is clearly under diagnosed in the early stages (101). Early smoking cessation would have an enormous impact on the progression of the disease (7,24,25,58,106).
This was independently proven by the National Health and Nutrition Examination Survey III 1988-1994, which included 16 084 patients undergoing a questionnaire and full lung function studies, and a huge European Study (27,79,116). Europe and America see COPD as a major health problem. COPD is the only disease among the top leading ones, which is rising in prevalence and mortality (117). It is already among the twelve leading causes of disability worldwide. Estimations state that by the year 2020 COPD will be fifth among the conditions, that will be the most burden to society considering HIV- and other infectious disease epidemiology (92).

In developing countries, like South Africa, we see a similar trend. Hard data is difficult to get, but several observations in the past and the recent survey by Ehrlich, White et al. (40) demonstrate the importance that COPD will have in future affecting the health of millions of South African.

The most important risk factor for COPD in developed countries is tobacco smoking, although genetic predisposition, early childhood respiratory infection, passive smoking, occupational exposures and outdoor air pollution play a role (12,25,123).
In developing countries, like South Africa, COPD is also on the rise mainly due to the same risk factors as increasing tobacco consumption and people getting older (risk of COPD increases with age).
The smoking rate in 1998 was 42% for men and 11% for women, which translates as more than 7 million South Africans 15 years or older smoke regularly. Higher smoking rates have been observed in urban areas, more educated groups smoke less than their less educated counterparts. Tobacco consumption is higher among coloured men and women and the lowest among non-urban Africans (118).
In their recent survey Ehrlich, White et al. (40) and Bumgarner (26) identified additional risk factors, which play a role in SA, those being:
Indoor pollution, chronic infections such as TB and the combination of sub optimal nutrition and respiratory tract infections early in life as well as occupational air pollution (i.e. dust, mining).

There is little data regarding accurate morbidity and mortality for emphysema in SA, mainly due to limited access of the population to health care, lack of early diagnosis and unavailability of spirometry for most of the population. The reporting and certification system lacks completeness.
The figures available indicate, that during the 1980's total mortality from chronic lung disease rose, whereas that for acute respiratory infection fell, in 1990 they both were lying around 4 percent of all deaths. Death rates were much higher among the white and coloured population group than the African race (40).
Morbidity data is gained from cross-sectional surveys of selected population.Wicht et al. (133) demonstrated a high prevalence of COPD of a white population sample in Cape Town. The data from Ehrlich and White indicate a prevalence of 2-3 % in men aged less than 44 years. In women of this age group it was slightly higher, but a sharp increase to 6.5-8.5 % was noted in men over 44 years. These figures are comparable to a self-reported diagnosis for chronic bronchitis and/or emphysema in America of 6.2 % (124).

Urban rates of reported emphysema/bronchitis were higher than non-urban rates.
The association with education is complex. Among men the rates for people with the least and most education were somewhat higher than those with intermediate education. Among women, the trend was for those with highest education to report the highest prevalence of emphysema/bronchitis (10.6 %). The highest rates were among the white race.

Exact prevalence figures are not possible to obtain, because lung function testing is essential for exact evaluation of emphysema. The recent survey (40) however showed a few interesting observations:

1. Confirmation of the high impact of smoking
2. A specific group of fast decliners
3. A significant risk factor is exposure to indoor pollution from cooking fuels
4. Occupational air pollution including mining, construction, manufacturing and agriculture play a significant role in the development of COPD
5. A strong impact on COPD due to previous TB

1.2. Pathology, Pathophysiology and Physiological Impairment of COPD and Emphysema

COPD is a disorder characterized by reduced maximum expiratory flow and slow forced emptying of the lungs, which does not change markedly over several months and has to be distinguished from asthma where air flow limitation is usually variable and reversible over short periods of time.

The British Thoracic Society (23) defines COPD as follows:

"COPD is a slowly progressive disorder characterized by airflow obstruction (reduced FEV_1 and FEV_1/FVC ratio) that does not vary markedly over several months of observation. Most

of the lung function impairment is fixed, although some reversibility can be produced by bronchodilator (or other) therapy."

There is general agreement that airflow limitation in COPD is the result of increased peripheral airway resistance, secondary to a mixture of small airways disease and emphysema (30).

Three conditions contribute to the picture of COPD:

1. Chronic bronchitis:

Chronic bronchitis is an inflammatory condition, clinically apparent as chronic cough and recurrent increase in bronchial secretions (mucus hypersecretions) (61). It becomes more clear in recent years, that mucus hypersecretion and sputum volume are associated with a decline in FEV_1, increased hospital admissions and increased mortality (103,126). Mucus does have a detrimental effect on the stability of small airways in COPD.

2. Chronic bronchiolitis:

Chronic bronchiolitis (small or peripheral airway disease) is an inflammatory condition of small bronchi and bronchioles, in which there are predominantly CD8+ and pigmented macrophages involved.

3. Emphysema:

Emphysema is an inflammatory condition of the alveoli in which T-lymphocytes, neutrophils and pigmented alveolar macrophages are involved associated with the release of excessive amounts of elastase. Emphysema is a result of an imbalance between proteolytic enzymes and protease inhibitors in the lung. Lung tissue, primarily elastin, undergoes repeated destruction, synthesis and degradation (68). In addition an excessive oxidant burden degrades the normal protease inhibitor screen.

Anatomically emphysema is defined as permanent destructive enlargement of airspaces distal to the terminal bronchiole without fibrosis.

There are two basic types corresponding to a persistent enlargement of the bronchiolar and alveolar portions of the respiratory acinus.
The bronchiolar (=centrilobular) and the alveolar emphysema. The panacinar emphysema involves the entire acinus (Figure 1d). It is often difficult to distinguish between confluent centrilobular and panacinar emphysema.

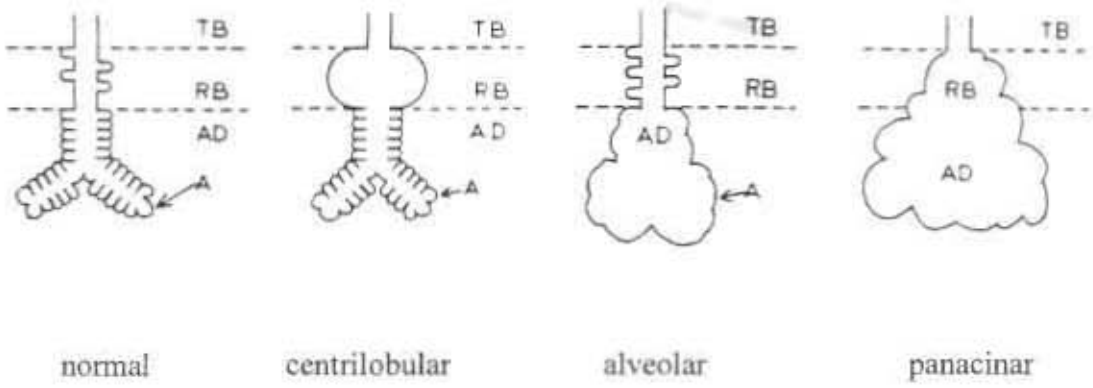


Figure1: a, Diagram of a respiratory acinus. TB=terminal bronchioles, RB=respiratory bronchioles, AD=alveolar ducts, A=alveoli.There are respiratory and alveolar parts of a respiratory acinus and different forms of emphysema are caused by permanent dilatation of either part. The terminal bronchiole divides into three to four generations of respiratory bronchioles, but this is not shown in the diagram. b, centrilobular emphysema with permanent dilatation distal to the terminal bronchiole involving first the respiratory bronchiole. c, alveolar duct emphysema with permanent dilatation distal to the terminal bronchiole involving first the alveolar ducts and alveoli. d, panacinar emphysema with permanent dilatation involving both the alveolar ducts and respiratory bronchioles (52).

Figure 2: Centrilobular emphysema. The specimen is part of a slice of lung, which had been fixed in inflation by the formalin steam method of Weibel and Vidone. The dilated respiratory bronchioles produce localized areas of emphysema associated with carbon pigment and seperated by normal tissue, x2 (52).

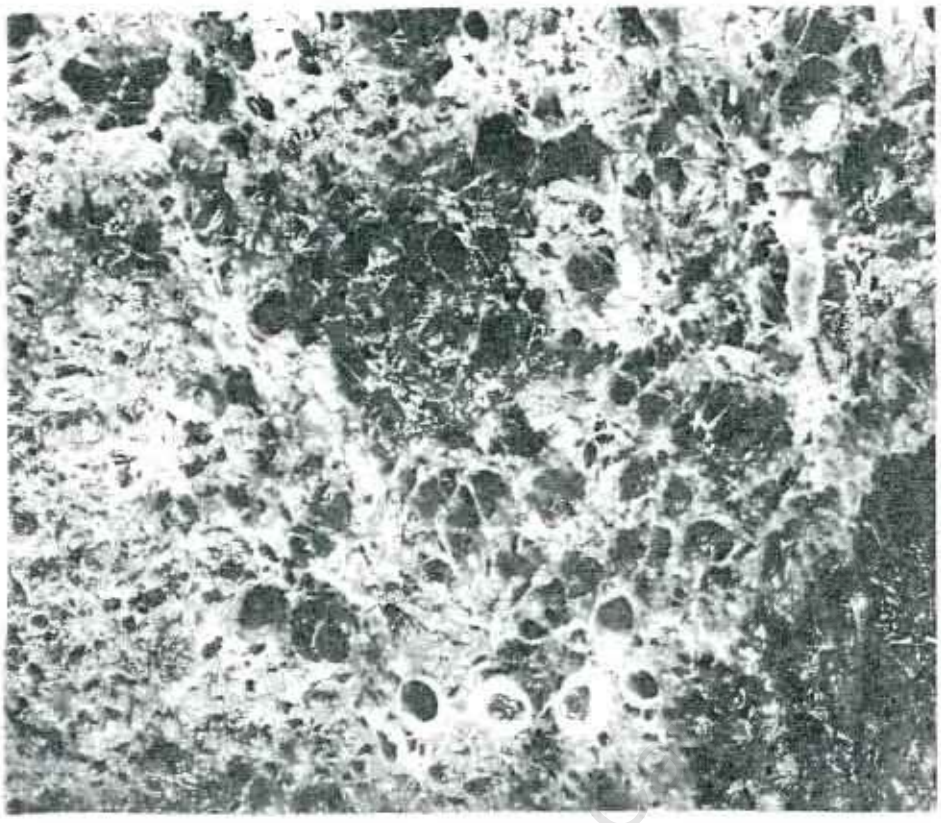


Figure 3. Panacinar emphysema. The specimen is part of a slice of lung, which had been fixed in inflation by the formalin steam method of Weibel and Vidone. There are confluent areas of lung destruction, so that the appearances contrast sharply with those of centrilobular emphysema shown in Figure2. x2 (52).

The lung internal surface for a 6000 ml lung is approximately 70 m^2, in alveolar emphysema the mean value is decreased to approximately 46 m^2, whereas in bronchiolar emphysema it is less reduced (approx. 61 m^2), which equals 87% of the figure in a normal lung.
The same applies to the number of alveolar spaces, which is markedly reduced in alveolar emphysema, less pronounced in bronchiolar emphysema. It seems to be, that the bronchiolar (=centrilobular) emphysema is more likely to give rise to serious pulmonary hypertension.
Development of pulmonary hypertension in emphysema is mainly due to the development of muscularized pulmonary arterioles and therefore increased pulmonary vascular resistance (Figure 4) and not so much due to loss of the pulmonary bed or fibrosis. It seems to be more periodic in nature, unlike the severe pulmonary hypertension in acquired and congenital heart disease, occurring during attacks of respiratory infection or fluid retention.
It is believed, that this muscularization of the terminal portions of the pulmonary artery tree is due to hypoxia and it is not only found in centrilobular and panacinar emphysema, but also in other chronic hypoxic conditions like Monge's disease or severe kyphoskoliosis (52, 53).
Hypoxic hypertensive pulmonary vascular disease seems to be partially or fully reversible.

Emphysema is characterised by decreased expiratory flow rates, increased pulmonary resistance and overinflation of the lungs (11).

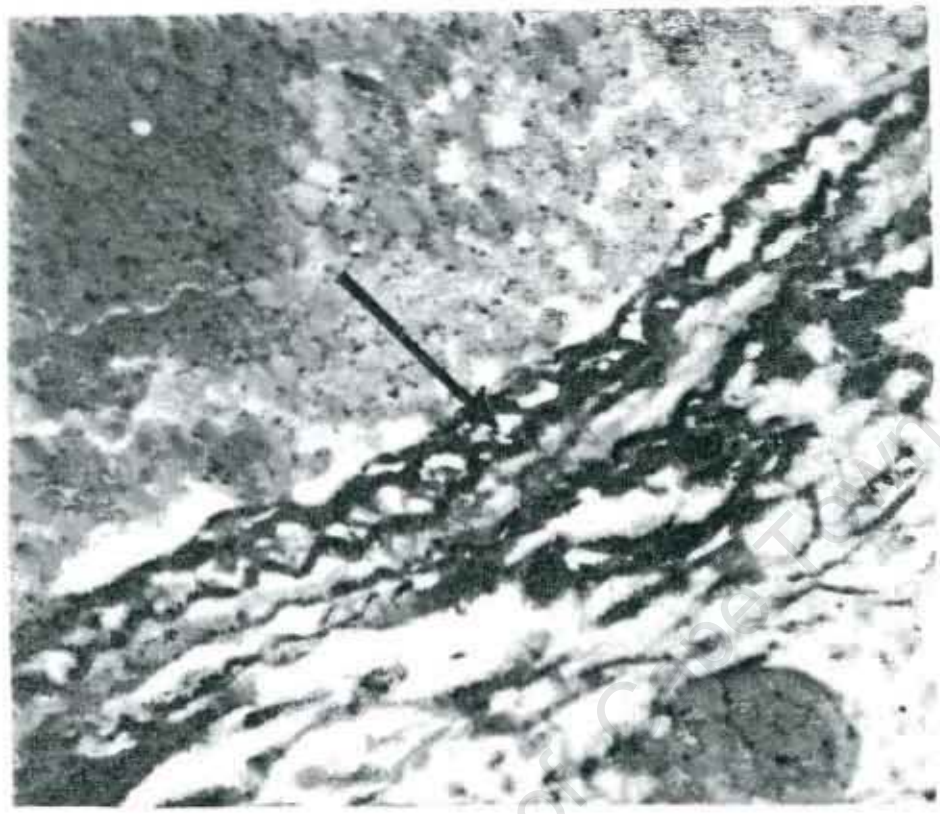


Figure 4: Transverse section of part of a muscular pulmonary artery from a case of centrilobular emphysema. The media of the artery is thin walled and is bounded by internal and external elastic laminae. Fasciculi of longitudinal muscle (arrow) are seen internal to the inner elastic lamina (52).

Airway resistance in emphysema:

It has been demonstrated by Hogg et al., that in both centrilobular and panacinar emphysema there is an increased resistance to airflow in airways less than 2 mm (57).
In centrilobular emphysema it is mainly due to inflammation and narrowing of the bronchioles, whereas in panacinar emphysema the bronchioles are rarely affected. Evidence of chronic inflammation in main, lobar and segmental bronchi was present in all cases of emphysema.
Catheter studies showed, that there were two mechanisms of airway resistance. One was situated in the smaller airway and was relatively fixed. The other one was situated in the larger airways and became greatly increased during expiration.
It was shown, that in a normal lung the smaller airways only contribute approx. 25% to total airway resistance, whereas in patients with emphysema there is an increase in total airway resistance, the smaller airways now contributing as much as 90 % (52).

Such observations suggest that, as far as an increased airway resistance is concerned, it is the abnormality of the small bronchi and bronchioles which is primary, the expiratory collapse of larger airways being secondary.
The flow related collapse of the smaller airways occurs more easily in emphysema, a phenomenon also called air trapping:
It is mainly due to the destruction of parenchyma and results in loss of elastic recoil, which usually keeps the smaller airway open. **The concept of the equal pressure point** applies as follows:
The cartilaginous airways have a considerable structural resistance to collapse, airways beyond generation 11 have no structural rigidity and are fully dependant on traction on their walls from elastic recoil of the lung tissue they are embedded (97). They collapse when the transmural pressure reverses (Figure 5):

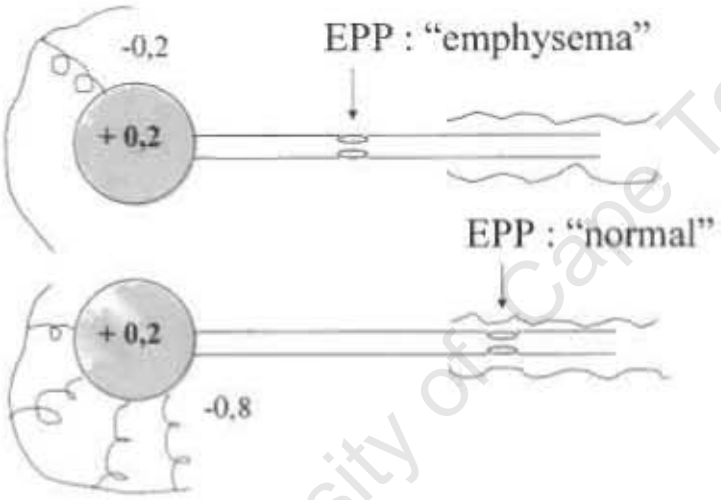


Figure 5: Simplification of the concept of shifting the equal pressure point (EPP) into unsupported airways with loss of elastic recoil

In summary of the previously outlined mechanism these functional abnormalities result from inflammation of small conducting airways causing them to be narrowed and close prematurely (14,35,57,100). There is destruction of lung tissue distal to the terminal bronchioles, which interferes with the supportive function of the peripheral airways (28,109) and shifts the equal pressure point, and decreases the elastic recoil force responsible for driving air out of the lung (84). In these circumstances the lungs hyperinflate. This overinflation grossly impairs the ability of the respiratory muscles to generate required force. The diaphragm becomes lower and flatter and the apposition of the diaphragm to the lower rib cage diminishes. Inspiration then leads to an inward pull on the lower rib cage. This diminishes the force generating ability of the inspiratory muscles and increases dyspnea through an awareness of increased neural stimulation to ventilate and eventual fatigue of the respiratory muscles (18,74). The hyperinflated lungs act mechanically on both the atria and ventricles to limit their respective diastole filling especially during exercise (29). In addition, in patients with marked overinflation, inspiration results in a decrease in venous return to the

heart rather than the normal increase (94). The net result is a marked reduction in mixed venous oxygen tension and cardiac output leading to increased dyspnea (89).

1.3. Medical management of Emphysema:

From the pathophysiologic descriptions it is clear, that medical treatment has a limited role in the management of emphysema, there is no medical cure. The medical treatment of emphysema consists of a combination therapy with bronchodilators, corticosteroids and treatment of acute exacerbations of infections. It has been summarized in a recent consensus report from the American Thoracic Society and the Canadian Thoracic Society (5,31,62). Medication and smoking cessation do have a supportive affect on the symptoms, but cannot reverse the amount of destruction. Exacerbations and infections can be successfully treated with antibiotics and/or steroids. Influenza vaccination is advisable. Nutrition and protein replacement in patients with alpha 1 anti-trypsin deficiency may be helpful. Cardiopulmonary rehabilitation can improve exercise capacity and dyspnea, the values of spirometry or gas exchange are not altered. Long-term home oxygen is often the only therapy, which improves quality of life and survival in these patients, but is a major expense.

The goals of medical therapy include diagnosis, assessment of severity and evaluation of comorbid disease as well as dealing with complications. Patients should undergo regular surveillance to prevent further decline, to optimise pulmonary function and reduce disability. Despite all these efforts of aggressive and appropriate medical treatment the patient's symptoms, effort tolerance and therefore quality of life decline within years, resulting in the endpoint of therapy being often only lung transplantation.

1.4. Rehabilitation program:

Pulmonary rehabilitation grew out of an attempt by physicians to use breathing control and exercise to help chronic lung disease patients cope with dyspnea. The consensus definition from 1993 established at a workshop of the National Institutes of Health (NIH USA) states: "Pulmonary rehabilitation is a multidimensional continuum of services directed to persons with pulmonary disease and their families, usually by an interdisciplinary team of specialists, with the goal of achieving and maintaining the individual's maximum level of independence and functioning in the community." (43)

It is agreed upon by all participants that pulmonary rehabilitation is an essential part before LVRS and should be completed by all patients prior to surgery. It not only aims to improve the symptom of dyspnea, but also addresses psychosocial problems and motivation. In selected cases it should be offered to patients with COPD, who are not candidates for LVRS. Several randomised trials have proven that dyspnea is reduced and exercise tolerance improves as well as quality of life (2,67).

Pulmonary rehabilitation is organized in three phases. The first phase is the inpatient program, which consists of education, psychosocial support and light activity. Phase two is an outpatient program, which consists of a more extensive educational component, an exercise training program and continued psychosocial support. The third phase or maintenance is a continuum of phase two, but patient take responsibility for their own exercise program and use skills learned in phase two regarding self-management of their disease. Education, exercise and psychosocial support are integral components of all three phases, but each is adjusted to the individual patient and situation (102).

In our study all patients underwent such a rehabilitation program prior to surgery.

1.5. Surgical management:

Lung volume reduction surgery (LVRS) has been advocated for patients with severe emphysema and marked lung hyperinflation. It is not a new technique, but experiences its revival recently.

1.5.1. History:

There is little doubt traditionally about the value of bullectomy for bullous emphysema to relief normal compressed lung and consequently improve lung function. Many good reviews proof that point and these patients in general have a favourable outcome (4,13,33,32,46,56, 90,110).
Diffuse generalized emphysema represents a different entity, often accompanied by poor quality of life, limited survival and poor response to medical treatment.
At the beginning of the 20th century a few different surgical strategies have been followed with varying success. One concept was based on elevating the flattened diaphragm either by the application of an abdominal compression device (i.e. belts) or creating a pneumoperitoneum, none of which could improve dyspnea or quality of life (3,105). Another ill-defined concept was to diminish the space of the thoracic cage and therefore counteract the hyperinflation of the lung and extension of the rib cage by thoracoplasty or phrenic nerve ablation, which most of the time led to worsening of the symptoms (95,128).
Slightly better results in some patients could be achieved by allowing the hyperinflated lung to fill more space. Costochondrectomies were performed (45), but the outcome proved to be fairly unpredictable. Pleurectomies were performed in the hope to enhance blood flow from collaterals; this could never proof measurable advantages.
Operations aiming at the nervous system, like glomectomies to reduce bronchoconstriction lacking the physiological reasoning and therefore could never demonstrate any improvements for the patients with diffuse emphysema (1,93,36).
These early attempts for a surgical solution all together failed and it needed new concepts to come one step closer to the problem.

Brantigan was the pioneer of the idea to perform multiple wedge resections to reduce lung volume and improve mechanics. His theory was that in a normal patient the bronchi are relatively pliable and held open by a circumferential elastic pull of the expanded lung. In emphysema patients this elasticity is lost, resulting in collapse of bronchi. By reducing the

volume of the lung this radial traction on the bronchi would be restored, expiratory airflow obstruction and dyspnea would be reduced (19-21).
Brantigan presented his series in 1959, Kennedy (64) in 1960, for a variety of reasons including the 16-22% operative mortality and lack of spirometric documentation this procedure did not gain support. Brantigan received a lot of criticism from his colleagues, who found it hard to believe, that one can improve lung function with taking away lung tissue in a diffuse process, which is characterized by a loss of parenchyma (65).
Delarue in 1977 reported a series of surgical interventions for patients with emphysema and dyspnea, he also had a 20 % mortality (38) and the enthusiasm for surgery remained low.

In the late 1980's surgery for emphysema resurfaced using laser or argon beam coagulators (71,130).
It took as long as 1995, when Cooper et al revived Brantigan's concept, especially after some observations in his lung transplant patients. Firstly he saw chest wall configurations of emphysema patient returning to almost normal after having received a smaller lung.
Secondly he found adequate gas exchange with single lung ventilation while these patients underwent single lung transplants and therefore was encouraged to operate on these severely compromised patients.
In his initial series twenty patients underwent LVRS bilateral via a mediansternotomy and his early results were encouraging (33).

1.5.2. Different techniques used internationally :

Laser ablation:

Various lasers have been used (Table 1), marked variation in technique is noted (CO_2 versus Nd:YAG, free beam versus contact). Widespread use by Wakabayashi and his colleagues did not convince the thoracic fraternity. Two prospective randomised studies by Hazelrigg (54) and Little (73) showed only small improvements in lung functions with the laser technique, not being anywhere near to the early results of Cooper et al.
Problems with prolonged air leaks occurred in over 50% of cases, and moderate to severe subcutaneous emphysema developed in 45% of cases (73).
Mc Kenna showed in a prospective randomised study a clear advantage of the stapler versus the laser treatment (83). Therefore most groups have abandoned laser ablation.

Table1: Reported experience with laser reduction surgery (54)

Reference Nr.	Patients	Laser	Follow up	FEV_1 improvement	ET improvement	Operative mortality
130	22	CO_2	1-3 m	x 0.74 -1.06	5.4 - 8 min	9.1%
131	443	ND:Yag	12-39 m	23-31% pred	87%	4.8%
55	141	ND:Yag	3 m	x 0.80± 0.30	846ft in 6min	5.7%
83	33	ND:Yag	6 m	6 ±3%	-	0.0%
63	10	ND:Yag	-	-	-	20%
22A	16	CO_2	1-3 m	0.2± 0.2	-	21%

Combined technique:

Eugene et al (41) and Wakabayashi (130) combined Nd-YAG laser ablation with stapled resections and came up with slightly better results concerning lung functions and relief from dyspnea compared to only laser ablation. Both reports do not provide details regarding the extent of either resection or laser ablation and therefore reproducibility and fair judgement of this technique is impossible.
Mortality was acceptable (~6%), increase in FEV_1 was around 30% and the patients noted subjective improvements.
Prolonged air leaks occurred in almost 50% of patients, reflecting the same problem mentioned above with the laser ablation.

Unilateral versus bilateral approach:

Most groups found a bigger improvement in patients undergone bilateral procedures (54,82,83,114).
Mc Kenna in his study found an even higher mortality in the unilateral group, which is supporting arguments pro the bilateral approach (83). The complication rate was similar in both groups.
In patients with only unilateral target zones or contraindications (previous thoracotomy, TB, pleurodesis etc.) a unilateral approach is indicated.

Thoracoscopic LVRS versus mediansternotomy:

Some investigators thought that the minimal invasive approach would be of benefit to these fragile patients.
Early reports from Keenan (63), Mc Kenna and Naunheim showed that thoracoscopy is a feasible option with mortality rates between 2.5-5,3 %, significant improvements in FEV_1 (27-35%) and marked decrease in the use of oxygen (82,95,96).
As mentioned before the bilateral approach seems to be superior (82,83). Other authors report similar success (48,16,22).
Other experienced centres report similar results with LVRS performed via a median-sternotomy (8,33,37,87,88).

Arguments for bilateral VATS are:
- all areas of the lung can be accessed
- less pain
- shorter hospital stay

Arguments for mediansternotomy:

- less airleaks and better control over bleeding and leaks
- remodelling of the remaining lung more physiologic
- target areas are better to identify
- less costs

Reports indicate equal short-term outcome. A slightly better long-term outcome in the mediansternotomy group is noted, but that can be due to the fact, that the teams, who now have a 5-6 y follow up, started doing LVRS via mediansternotomies.

Acceptable results have been demonstrated with both techniques (10,33,63,83,87,88). Wisser et al demonstrated equal results with both techniques in terms of functional improvements and complication rates (135).

Lung transplantation:

Lung transplantation, single or double, provides excellent palliation for selected patients with advanced emphysema.
Emphysema is in fact the most common indication for lung transplantation (51).
Nevertheless several problems arise from this approach. First there is at least a 1-2 year waiting period for an organ, the annual mortality for patients on the waiting list is 10%. Second, the requirement of immunosuppressive medication does have negative effects like hypertension, diabetes, infections and an increased risk of haematologic malignancies. Nearly everybody will suffer from significant infectious complications in their lifetime. Third, transplantation, the medication and follow up are extremely expensive. Fourth, although short-term survival following lung transplantation is in the range of 90% in big centres, 4-year survival is only 30-40% (51,99), largely as a result of obliterative bronchiolitis.

Methods used in GSH:

As a conclusion of the literature review we decided on the following approach:
All our patients were operated in a standard fashion via a mediansternotomy, bilateral wedge resections aimed to reduced the lung volume by approximately 30%. No pericardial buttressing was used, but GRF glue was applicated to prevent air leaks.
The team consisting of the pulmonologists, surgeons, anaethetists and experienced nursing staff ensured correct indications, technique, pain relief and best postoperative care in ICU. A thoracic epidural catheter was inserted in all patients preoperatively, enabling us to extubate all but one patient in theatre postop and to transfer them to the ICU spontaneously breathing on a 40% oxygen mask. The surgical technique is described in detail in the following chapter.

1.5.3. Current status of LVRS:

Recent enthusiasm for the procedure has resulted in a large number of case reports claiming dramatic results. Meanwhile there are several trials published, which confirm Cooper's findings from 1995 (33,34,39,47,81,85,107,108,112,113,119), most of them showing a benefit for patients with severe emphysema regarding lung functions and quality of life.

Nevertheless LVRS is high risk and expensive. It has yet to be evaluated in a prospective randomised trial enrolling a large number of patients. This is under way as a combined effort of several universities in Canada and England at the moment. The University of Cape Town, respectively the Department of Cardio-Thoracic Surgery and the Respiratory Clinic will participate in the study. Results are expected in a few years, patients recruitment is behind schedule. Until these studies are published one has to rely on data provided by small series.

Until now a few questions about the best approach, technique and patients selection seem to be solved. As described in the previous chapter the bilateral approach is superior (39,85, 114), the laser technique is abandoned and there is equal distribution in the surgical fraternity favouring mediansternotomy or thoracoscopic methods.
Two groups used a plication- or loop techniques instead of stapling the lung (72,121) via the thoracoscopic approach resulting in multiple small wedge resections. Sabanathan emphasizes that the lung resection (> 30%) and not the operative approach is critical to the success of the operation (108). Very little discussion about the patient selection in the recent literature indicates, that most inclusion and exclusion criteria are agreed upon.

LVRS as an alternative or bridge to transplantation is regarded as a viable option by many authors (51,95,125,136), even as a salvage operation in chronic allograft rejection (111) or LVRS in the native lung post single lung transplantation (6).

Nevertheless the topic is still controversial until big prospective randomised trials with a reasonable follow-up period are published. Many questions remain and are subject of several multicenter trials (87,88,125), which will not produce any results before the next 2-4 years. We therefore still rely on results from small series. They seem to show following trends in short- and median follow-ups after LVRS (34,39,47,81,85,95,96,107,112,113,119):

- relief of breathlessness (dyspnea)
- improvement in FEV_1, FVC and RV
- improvement in quality of life
- decrease in oxygen dependancy
- slow decline of lung function after one year parallel to the natural history
- clinical and physiological improvements after > 3 years (48)
- LVRS is palliative in nature

2. GROOTE SCHUUR EXPERIENCE: MATERIAL AND METHODS:

2.1. Study Design:

We performed LVRS on ten patients so far, starting in 1995. The relatively small number is consequence of careful patient selection and financial constraints.
We retrospectively analysed our data to determine the impact of LVRS on airflow limitation, symptoms of breathlessness, quality of life and costs in patients with severe emphysema. Therefore the purpose of this study was the following:

- Assessment of pulmonary physiology, exercise tolerance, morbidity and mortality of LVRS as practiced in Groote Schuur Hospital (optimal medical management including respiratory rehabilitation followed by surgery) in a retrospective study.

  Inclusion and exclusion criteria, modified techniques and postoperative Management, short- and long-term results over a period of 5 years are reported

- Evaluation of the

  a: Cost effectiveness of LVRS in a state hospital and its impact upon

  b: Assessment of Quality of Life

to investigate, whether LVRS is an acceptable form of treatment for severe emphysema in countries like South Africa.

Limitations of this study are the relatively small number of patients, but all were selected according to our strict inclusion- and exclusion criteria, and therefore it is a relative homogenous group. No change in surgical technique or selection took place over these 5 years. The second problem is, that the follow up data show significant gaps, which are mainly due to long distance travelling necessary for 5 patients and cost constraints in the SA health system. Especially the plethysmography values could not be obtained on a regular basis, making these results worthless for statistical analysis.
Despite the fact, that the quality of life scores were evaluated retrospectively and patients tend to forget the downsides and hard times in life easier than the successes, the reliability and accuracy of these questionnaires was confirmed when compared with the physician's notes in the folders. The almost uniform results for the six patients evaluated reflect the general outcome in terms of quality of life.

Participants:

Four males and six females, the age ranging between 44-59 years with disabling dyspnea due to severe emphysema.

2.2. Inclusion- and exclusion criteria:

Inclusion Criteria:

Radiographic evidence of emphysema,
Disabling dyspnea
Air flow limitation (FEV1 less 35% predicted),
Gas trapping (TLC > 120%, RV/TLC >60%),
Hyperinflation RV > 200% predicted
Ability to complete preoperative rehabilitation program
Cessation of smoking

Exclusion Criteria:

Absolute:

Age >75 y,
Severe obesity,
Hypercapnia (pCO_2 >55 mmHg),
Isolated bulla > 20% of hemithorax,
Malignancies and significant medical illnesses

Relative:

Ventilated patients,
Chest wall deformities,
Previous thoracotomy or pleural disease (including previous PTB),
Bronchiectasis
Asthma

2.3. Methods used in Groote Schuur Hospital:

10 patients were suitable for LVRS according to the above-mentioned inclusion and exclusion criteria, the patients' data to be demonstrated in Table 4 (see page 27):
Factors assessed were pre- and postoperative forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), total lung capacity (TLC), residual volume (RV), pO_2, pCO_2, carbon monoxide diffusing capacity with a single breath method (TLCO) and the 6 min walk test.

A thoracic epidural catheter was placed and a T1-T8 block was established on the awake patient.
All LVRS was performed under general anaesthesia using a double lumen tube (Figure 6), peak inspiratory pressure was limited to < 20 cm H_2O, I:E = 1:4.

Figure 6: Double lumen tube

All patients were operated via a median sternotomy in supine position, the patients were ventilated with 100% O_2 for 20 min to preoxygenate and to demonstrate areas of high ventilation/perfusion mismatch, because these areas will deflate slower after the lung is vented and allowed to collapse. The non collapsed areas were primarily selected as target areas for resection and grasped with clamps (Figure 7 and Figure 8).

After precoating a 90 mm stapler device (TA 90, Ethicon, Johnson&Johnson) with GRF glue (= Gelatine-resorcinol-formaldehyde) these areas were resected paying attention to regain a shape of the remaining lung, which can fill the chest cavity appropriately.
The stapled lung was removed and the stapled edge sealed with GRF glue (Figure 9 + 10), avoiding contact of the formalin to other parts of the lung except the stapler line. After 10 min the glue had set and the lung was carefully reexpanded and checked for leaks (Figure 11).
This procedure was repeated on the other side. We aimed for resected area of ~ 30% of the lung (Figure 12). We left four 28 Ch drains in situ (2 on each side) and closed the chest

rewiring the sternum. Local anaesthesia was given to the drain sites and the manubrium sterni, the thoracic epidural was maintained with 0.25 % bupivacaine.
The patients were extubated in theatre after reversal of the anaesthetics, usually changing to a single lumen tube allowing the pCO_2 to come down and transfer the patient awake to the ICU. Postoperative monitoring and treatment included 3 hourly blood gases, O2 saturation monitoring, urinary catheter and thoracic epidural for adequate analgesia and oxygen mask, humidification, nebulization and experienced physiotherapy for sufficient oxygenation of the spontaneously breathing patient (Figure 14).

LVRS was performed as described in the previous chapter by two surgeons, the technique was not altered or changed for the ten cases.

Figure 7: Areas of gas trapping

Figure 8: Target areas selected

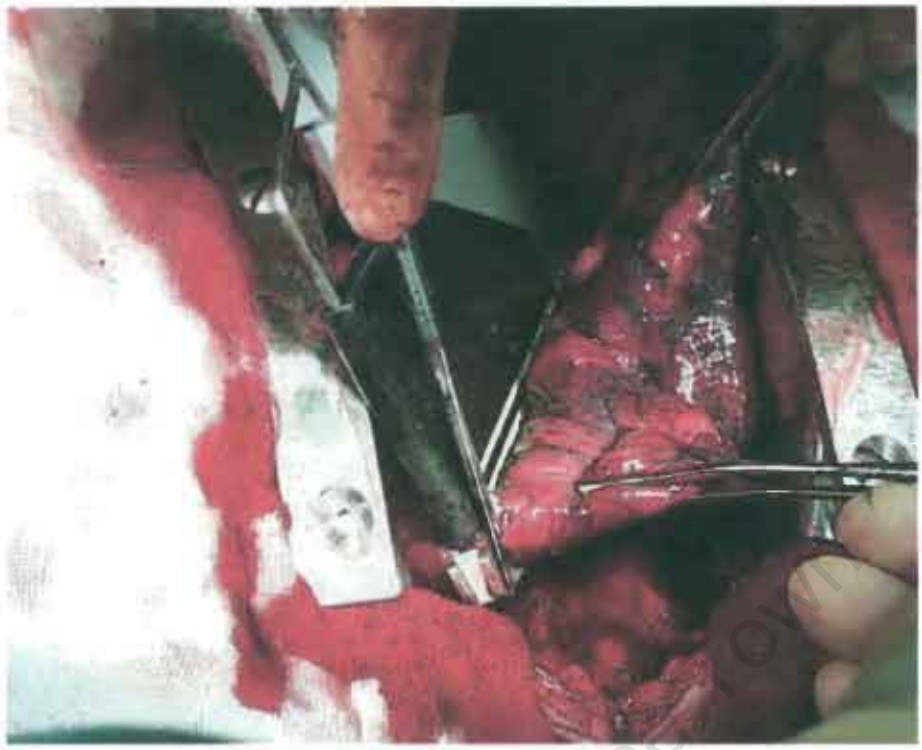


Figure 9: Lung stapled and removed

Figure10: Application of GRF – glue at the stapler line

Figure 11: Careful expansion of the lung after the glue has dried

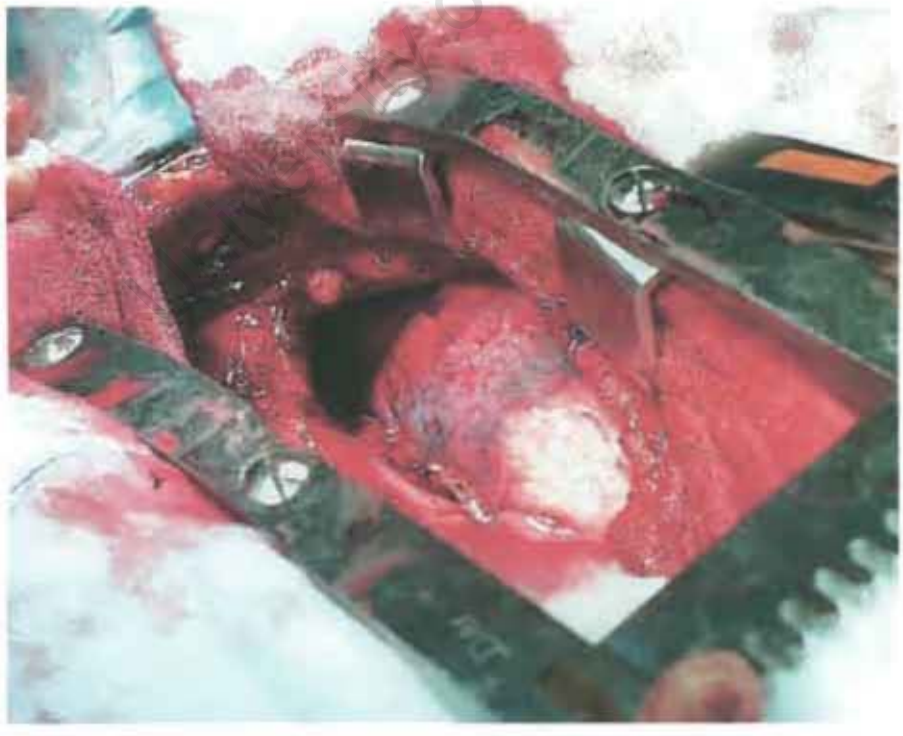


Figure 12: Final result

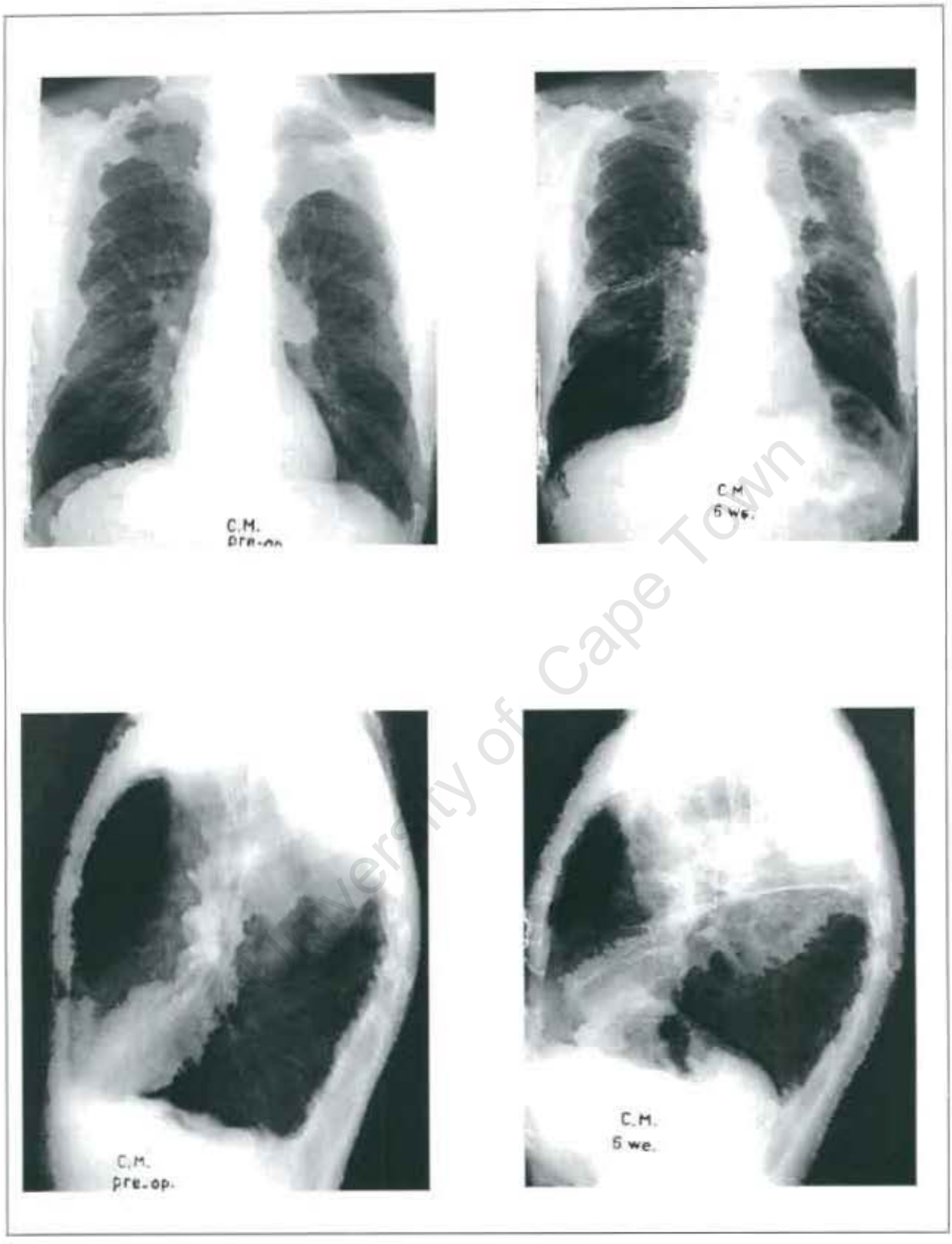


Figure 13: preoperative CXR a.p and lateral (left) and 6 weeks postoperative (right). A marked difference is noted in shape of the diaphragm, lung volumes and the retrosternal space

Figure 14: Patient in the ICU postoperatively

2.4. Cost analysis:

For the cost analysis recent pricing with the best values available to a state hospital (year 2000) and /or fees according to the MASA guidelines were used. The scale of benefit values were applied for all procedures and diagnostic tests, as well as for most of the consultation fees. Only where the price available to GSH was lower than the scale of benefit fees we used the lower price (i.e. for medication and some laboratory items). The costs for each patient (Table 9) were retrieved from the folders and microfilms and individually calculated. No estimations were applied.
The one patient, who died on day 1 postoperative, was excluded from the average calculation.

To compare the costs for patients who received LVRS with the costs of patients with medical treatment alone we have chosen a period of 5 years, because the natural history of the disease in end stage emphysema would make a longer period unrealistic and would bias the results in favour of a better cost effectiveness of the surgical group.
Three different scenarios were calculated, based on information retrieved from the patient's folders and personal experience of the attending pulmonologists:

1. An average year of a patient with severe emphysema on medical treatment
2. An average year of a patient, who has done well after LVRS
3. An average year of a patient with end stage COPD (bedridden, oxygen dependant)

For comparison purposes the costs of the medication are listed with state tender prizes and wholesale prices, which are more realistic and reflect, what a chronic COPD patient costs over the 5-year period.

Statistics:

For the statistical analyses the SPPS Base 7.5 for Windows 1997 software was applied. Both descriptive statistics ($\pm$ 2SD) and the paired t-test were used for the physiological parameters.

2.5. Quality of life:

To assess quality of life two intruments were used.

- The Medical Outcome Study Short Form 36 (MOS SF 36)

The MOS SF 36 is a generic health- related quality of life measure. The instrument is used widely to evaluate health-related quality of life. It can be self or interviewer administered. It tests 8 domains: physical functioning; role limitations due to physical health problems; bodily pain; social functioning; general mental health; role limitations due to emotional problems; vitality, energy or fatigue and general health perceptions.
In the MOS SF 36 zero is the worst and 100 is the best score, clinical significant difference is reached with a change in score of more than 20 .

- Chronic Respiratory Disease Questionnaire (CRQ)

The CRQ is an interviewer-administered questionnaire measuring both physical and emotional aspects of chronic respiratory disease. It tests four categories: dyspnea, fatigue, emotional function and mastery on a numerical 7 point modified Likert Scale.
Minimal important difference is reflected by a change in score of 0.5 on a seven-point scale, a change of more than 1 represents a clinically significant difference.

Both instruments were administered by the same interviewer preoperative and 6 months postoperative retrospectively.

In addition the use of home oxygen and the degree of activities are reported at different time intervals postoperative (Table 10).

3. RESULTS:

3.1.Overview:

Table 4 gives an overview of the ten patients who underwent LVRS after careful selection according to above mentioned inclusion and exclusion criteria.
Six female and four male patients with a median age of 50.8 years (range from 41–59) were operated on bilaterally via a mediansternotomy. In two patients an alpha 1 anti-trypsin deficiency was known, the others were tested normal.
Seven have been smokers with a median pack year history of 37 pack years (range 15-100), all of them stopped smoking before the rehabilitation program started. Three patients were non-smokers.

Seven patients had grade IV dyspnea, according to the Dyspnea score in Table 2, three had grade III dyspnea. Of the ones severely short of breath at rest five used home oxygen more than 8 h, three of them were absolutely bed bound.

Table 2: Modified Medical Research Council Dyspnea Scale (60)

Grade	Symptoms
0	Not troubled with breathlessness except with strenuous exercise
I	Troubled by shortness of breath when hurrying on the level or walking up a slight hill
II	Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level
III	Stops for breath after walking about 100 yards or after a few minutes on the level
IV	Too breathless to leave the house or breathless when dressing or undressing

The CT- and Perfusion scan results revealed a homogenous pattern in four cases and a inhomogeneous pattern in six patients, describing a centrilobular appearance in five, a pan-acinar in one and a mixed type in four patients.

3.2. Mortality and morbidity:

The 30 day mortality was 10%. This patient was the only one, who could not be extubated directly postoperatively. He died the first postoperative night due to respiratory failure. This was the only major complication, and lead to the death of this patient.

Of the remaining nine patients minor complications occurred in six, mainly prolonged air leaks or residual pneumothoraces (Table 3).

Table 3: Morbidity of LVRS in GSH (1995-1999)

Morbidity*	
Prolonged air leak > 5 days	6
Small apical pneumothorax	3
Rethoracotomy (air leak)	1
Respiratory tract infection	1
Superficial wound infection	1
Sternal wound pain	2

* In 6 out of 9 patients, 3 patients had no complication

The actuarial survival is depicted in Figure 15.
One patient died a few hours after surgery. In the 5 year follow up period another two patients died after 3 years and 4 years post LVRS, both in respiratory failure due to endstage emphysema.

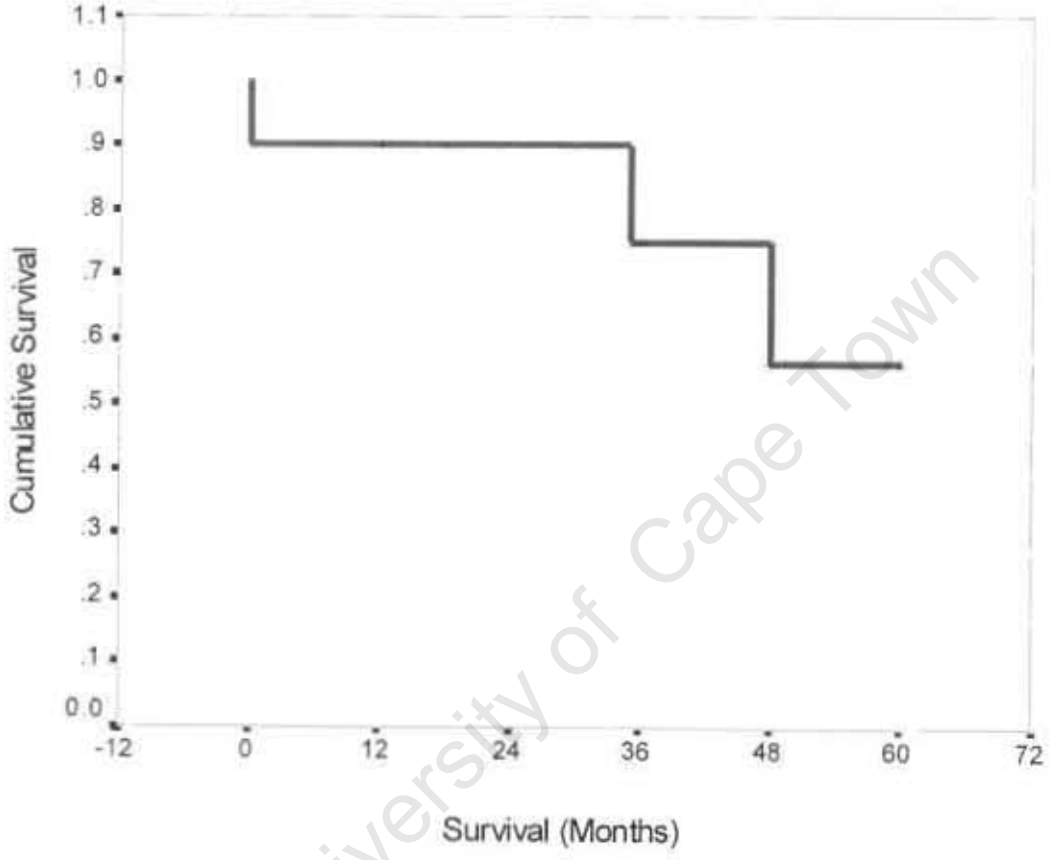


Figure 15: Actuarial survival for our ten patients after LVRS

3.3 Lung function tests:

Preoperative values:

Table 4 summarises FEV_1, FVC, RV, TLC, diffusion capacity (=TLCO) , 6 min walk test and blood gas analysis in all ten patients preoperatively:

Table 4: Overview of preoperative data:

Patient	FEV_1 (ml) %FEV_1	FVC (ml) %FVC	Ratio	TLC (ml) %TLC	RV (ml) %RV	TLCO %TLCO	6Min (metres)
1(KA)	400 **12.6**	1420 **36.9**	28	7620 **126**	5520 **280**	11.70 **43.2**	358
2(VN)	620 **21.0**	2170 **62.9**	28	8970 **160**	5780 **301**	9.69 **35.6**	360
3(MI)	440 **15.7**	1320 **40.4**	33	*	*	*	70
4(MY)	880 **29.0**	2180 **58.1**	40	8730 **143**	6080 **286**	7.24 **27.9**	246
5(VDB)	520 **20.6**	2490 **84.7**	21	7300 **158**	4790 **309**	11.68 **50.3**	385
6(SCH)	520 **18.1**	2190 **61.0**	24	6680 **111**	4580 **209**	6.80 **27.2**	277
7(NE)	500 **17.4**	1380 **41.4**	36	6890 **151**	5340 **356**	8.30 **31.8**	75
8(TR)	720 **27.0**	2900 **92.7**	25	7490 **143**	4550 **243**	12.60 **50.6**	325
9(SM)	440 **19.1**	2310 **84.6**	28	7280 **150**	5450 **296**	5.66 **24.9**	350
10(SN)	520 **16.4**	2960 **83.4**	18	7320 **121**	4650 **236**	6.20 **22.9**	245
Average in % predicted	**19.7**	**64.6**	**28**	**140**	**279**	**34.9**	**269**

+ post bronchodilator response > 10%
* stops necessary

Only in one patient no values for residual volume (RV), total lung capacity (TLC) and diffusion capacity (TLCO) could be established preoperative, because the patient was unable to tolerate the body box test.
We have taken the best values after bronchodilators, the " + " is indicating, if the dilator response was more than 10%.

In average the FEV_1 was 19.7 % of predicted (12.6% – 29.0%), the FVC 64.6 % of predicted (36.9% - 92.7%), with a ratio of 28.

The RV was on average 279% higher than predicted values (209% – 356 %), the TLC 140% of predicted (111% - 160%).

The TLCO single breath was 34.9 % of predicted (22.9% - 50.6%), established by the carbon monoxide diffusion method.

The results of the 6 min walk test preoperative differed from 70 – 385 m and are compared later with the postoperative values.

Blood gas analysis revealed an average pCO_2 of 4.38 mmHg (3.76 – 6.1), and a pO_2 of 9.47 mmHg (8.6 – 12.26).

Table 5: Blood gas analysis for 9 patients preoperative:

Patient	pH	pCO_2	pO_2
1			
2	7.38	5.20	12.17
3	7.40	5.30	11.10
4	7.40	6.10	8.70
5	7.40	3.80	11.80
6	7.41	3.76	12.26
7	7.47	4.60	8.60
8	7.40	4.70	11.43
9	7.38	5.70	8.65
10	7.49	4.65	10.00
Average		**4.38**	**9.47**

Postoperative values:

For the statistical analysis the % predicted values were rounded up or down.
Figure 16 - 21 summarize the trend including all available data of the nine patients over a five year follow up period. The mean values are demonstrated as a square $\pm$ 2SD. If there were less than 3 patients no mean is shown any more.
All physiological parameters are measured as the % predicted values instead of absolute figures, which represents the adjustments to age, sex and height.
We did a paired sample analysis on all measurements, only the statistically significant results are illustrated (FEV_1, residual volume and 6 min walk test).
All individual results and curves of each patient are shown in Annexure A, as well as the detailed statistics for the paired t-test.

Forced expiratory volume in 1 second (FEV_1) in % predicted

There is a significant improvement in FEV_1 3months, 6 months and 12 months after LVRS compared to the preoperative values ($p < 0.05$). After 4 years the mean value is still above baseline and in the two patients with the longest follow up there are still measured higher values of FEV_1 than preoperatively. Table 6 and Figure 16 are demonstrating these results:

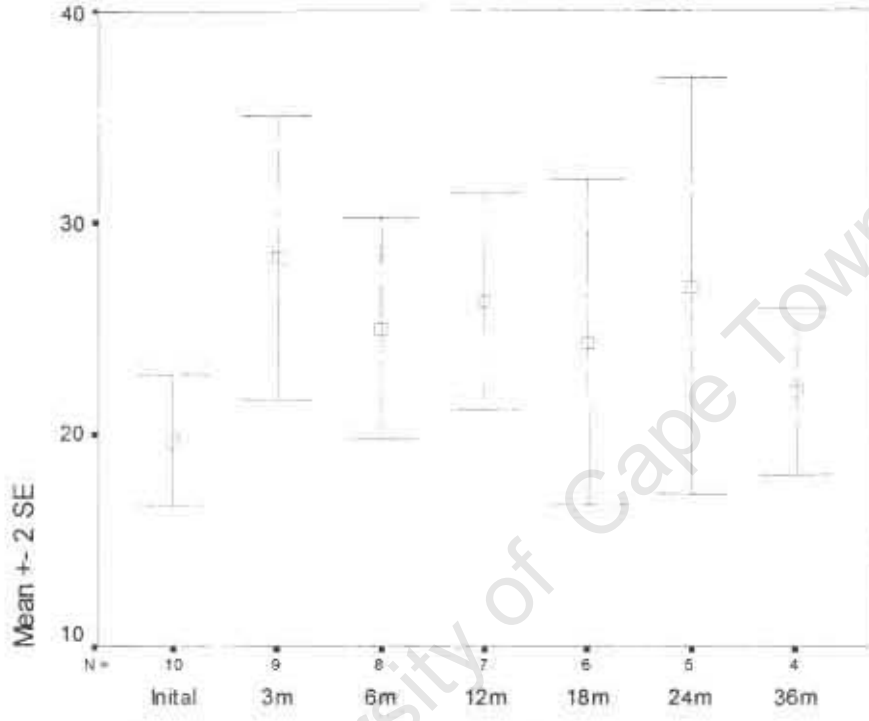


Figure 16: Mean values of forced expiratory volume in 1 second (FEV_1)

Paired Samples Test

		Paired Differences					t	df	Sig (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Inital - 3m	-8.22	8.20	2.73	-14.52	-1.92	-3.009	8	.017
Pair 2	Inital - 6m	-5.75	7.07	2.50	-11.66	16	-2.302	7	.055
Pair 3	Inital - 12m	-5.43	3.41	1.29	-8.58	-2.28	-4.214	6	.006
Pair 4	Inital - 18m	-2.67	7.45	3.04	-10.48	5.15	-.877	5	.421
Pair 5	Inital - 24m	-2.50	7.06	2.88	-9.91	4.91	-.867	5	.426
Pair 6	Inital - 36m	-1.00	2.94	1.47	-5.68	3.68	-.679	3	.546
Pair 7	Inital - 48m	-7.50	4.95	3.50	-51.97	36.97	-2.143	1	.278

Table 6: Paired t-test FEV_1 (preop to follow up at 3m, 6m, 12m, 18m, 24m, 36m, 48m), significance is shown in the far right column

Forced vital capacity (FVC) in % predicted

A similar trend is seen measuring the forced vital capacity, although it did not reach stastistical significance. The squares in Figure 17 represent the mean values of FVC in % predicted. Starting preoperatively at 65% predicted a steady improvement is noted until the second year, where it reaches 81% of predicted.

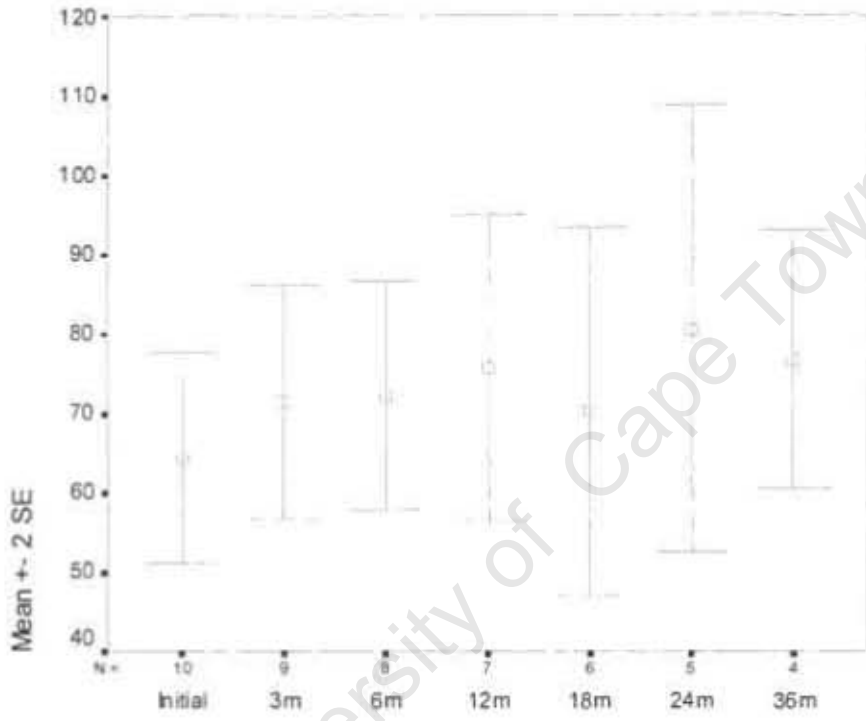


Figure 17: Mean values for forced vital capacity (FVC)

Total lung capacity (TLC) and residual volume (RV) in % predicted

Unfortunately the follow up for TLC and RV was not complete due to inaccessability of body plethysmography. Six months after LVRS the values for only two patients could be determined and therefore Figure 18 and 19 only show the means preoperative, 3 months, 12 months and 18 months after LVRS. The trend is visible , both TLC and RV are diminished after LVRS, which could be expected according to the literature, and are increasing at 18 months again.

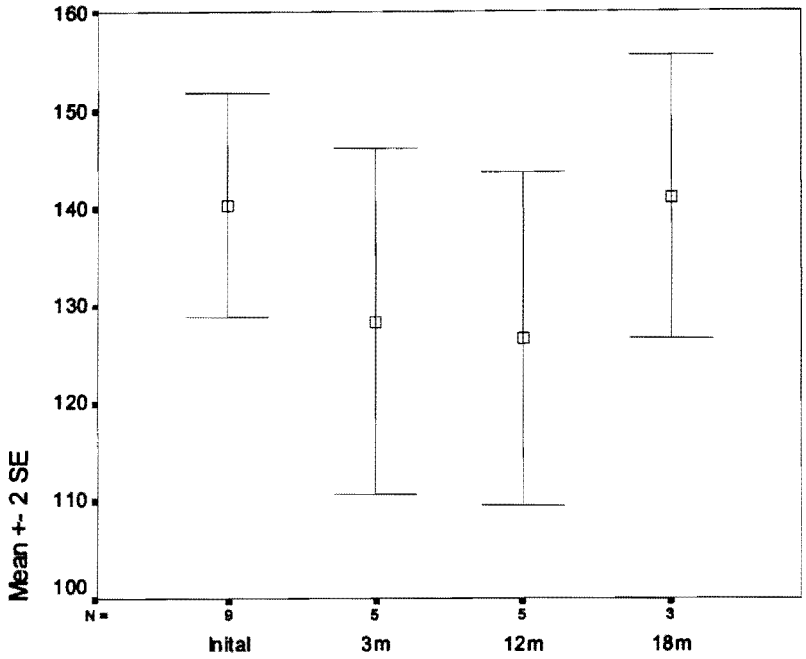


Figure 18: Mean values for total lung capacity (TLC)

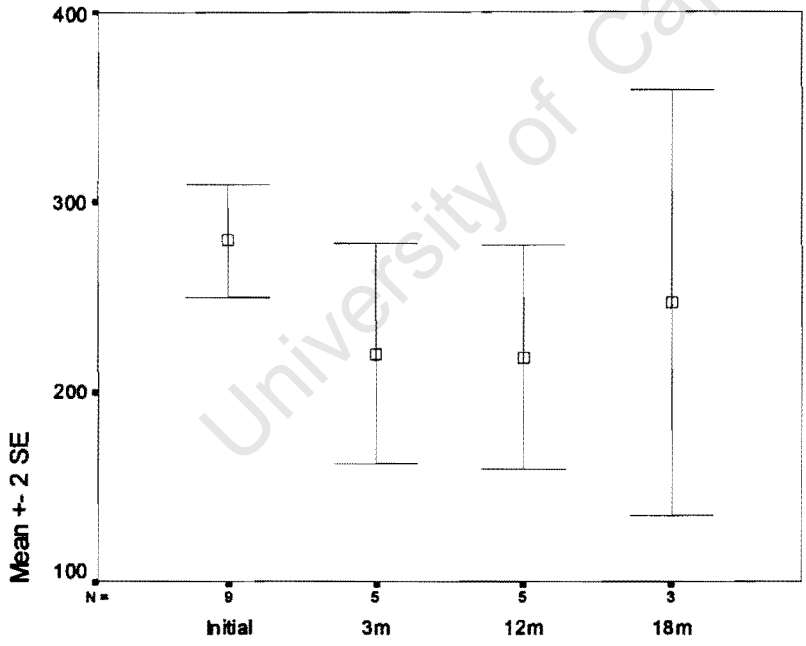


Figure19: Mean values for residual volume (RV)

Nevertheless there is a significant decrease in residual volume (RV) 3 months , 12 months and 18 months postoperatively compared to the baseline values preoperatively ($p< 0.05$), as shown in Table 7:

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Initial - 3m	79.00	38.45	19.23	17.81	140.19	4.109	3	.026
Pair 2	Initial - 6m	49.50	33.23	23.50	-249.10	348.10	2.106	1	.282
Pair 3	Initial - 12m	67.60	52.75	23.59	2.11	133.09	2.866	4	.046
Pair 4	Initial - 18m	82.50	6.36	4.50	25.32	139.68	18.333	1	.035
Pair 5	Initial - 24m	44.00	14.14	10.00	-83.06	171.06	4.400	1	.142

Table 7: Paired t-test (preop to follow up at 3m, 6m, 12m, 24m), significance is shown in the far right column

Carbon monoxide diffusion capacity (TLCO) in % predicted

The single breath method determining the carbon monoxide diffusion capacity was applied in nine patients preoperatively. The patient with the lowest value (22.88% of predicted) died a few hours after surgery in respiratory failure.
We did not exclude patients with TLCO lower than 30% of predicted.
The trend towards improvement of the diffusion capacity after LVRS is demonstrated in Figure 20:

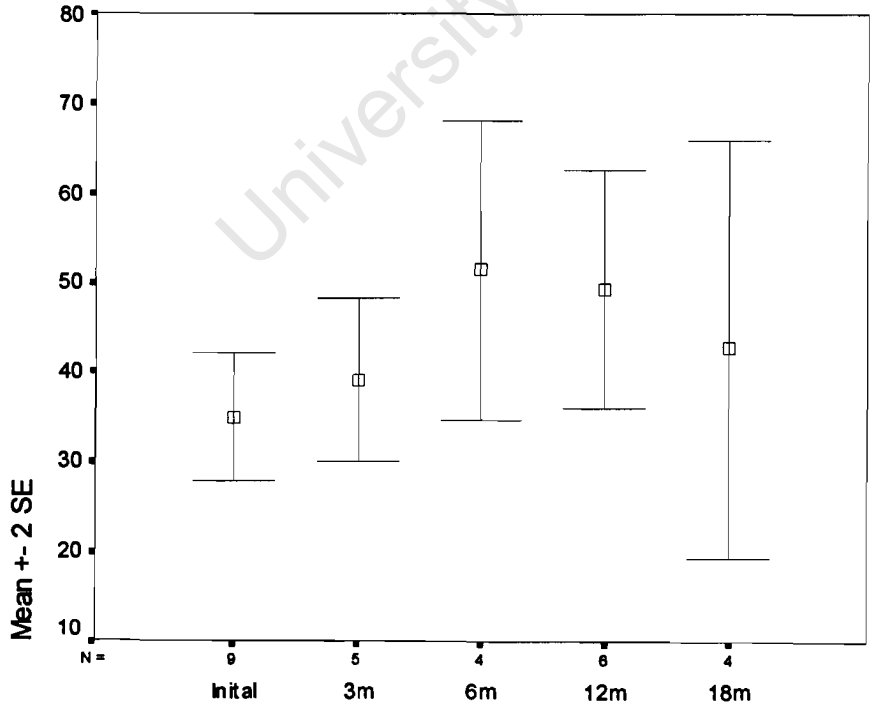


Figure 20: Mean values carbon monoxide diffusion capacity (TLCO single breath method)

6 min walk test

The 6 min walk test could be performed on all ten patients preoperatively and is an easy test to determine effort tolerance. Figure 21 and Table 8 demonstrate the significant changes in the six minute walk test after LVRS and the lasting effect of LVRS concerning walking distance and indirectly dyspnea.

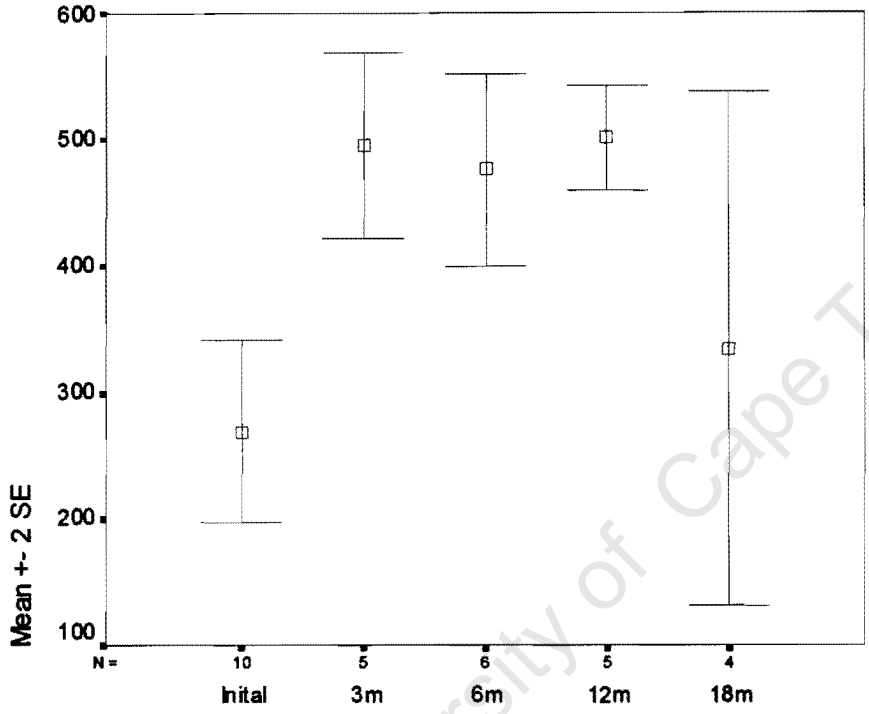


Figure 21: Mean values for the six minute walk test

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Inital - 3m	-217.60	130.16	58.21	-379.21	-55.99	-3.738	4	.020
Pair 2	Inital - 6m	-232.67	137.61	56.18	-377.08	-88.25	-4.141	5	.009
Pair 3	Inital - 12m	-145.60	54.30	24.28	-213.02	-78.18	-5.996	4	.004
Pair 4	Inital - 18m	-52.50	75.44	37.72	-172.55	67.55	-1.392	3	.258
Pair 5	Inital - 24m	-25.00	28.28	20.00	-279.12	229.12	-1.250	1	.430

Table 8: Paired t-test 6 min walk (preop to follow up at 3m, 6m, 12m, 18m, 24m), sigificance is shown in the far right column

3.4. Costanalysis:

A detailed list of all items is enclosed in Annexure B. The basis of this cost analysis are prices of the year 2000 in a state hospital reflecting the hospital stay of the patients undergoing LVRS with all costs covered (Table 9).
The average amount spent for LVRS is approximately 30.000 Rand.

Table 9: Costs for LVRS

Patient	1	2	3	4	5	6	7	8	9	10	Average
	KA	VN	MI	MY	VDB	SCH	NE	TR	SM	SN	
ICU costs	8292.00	8292.00	12438.00	16584.00	16584.00	4146.00	4146.00	4146.00	4146.00	2073.00*	
days	4	4	6	8	8	2	2	2	2	1	
Ward costs	5628.00	1876.00	9849.00	3752.00	938.00	4690.00	4690.00	8911.00	3283.00		
days	12	4	21	8	2	7	10	19	7		
Subtotal	**13920.00**	**10168.00**	**22287.00**	**20336.00**	**17522.00**	**7429.00**	**8836.00**	**13057.00**	**7429.00**		
Costs for:											
preop consultation	149.00	149.00	149.00	149.00	149.00	149.00	149.00	149.00	149.00	149.00*	
Diagnostic tests	1952.80	2033.00	1563.70	2033.00	2033.00	2033.00	2046.20	2033.00	2033.00	2033.00*	
Procedures	3322.20	3322.20	5259.28	3322.20	3322.20	3322.20	3322.20	3322.20	3322.20	3487.48*	
ICU registrar	566.40	566.40	849.60	1132.80	1132.80	283.20	283.20	283.20	283.20	141.60*	
Thoracic surgeon	298.00	298.00	298.00	298.00	149.00	298.00	298.00	298.00	298.00	298.00*	
Pulmonologist	298.00	298.00	298.00	298.00	149.00	149.00	298.00	298.00	298.00	298.00*	
Physio	964.00	394.40	942.00	854.60	602.50	361.50	591.60	602.50	832.40	0.00	
Medication	474.60	566.75	798.76	343.75	289.02	179.93	145.76	228.25	160.53	53.78*	
Nutrition	131.34	92.84	265.75	375.79	77.84	55.58	264.40	128.20	74.69	425.38*	
Oxygen/Gas	465.74	461.52	297.20	164.16	385.04	334.80	323.46	416.16	261.88	330.58*	
Ventilation	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	354.00*	
Laboratory	916.22	904.25	1716.73	1955.61	1216.03	945.89	1007.88	1012.87	640.31	565.58*	
Bloodbank	99.00	99.00	99.00	99.00	99.00	99.00	99.00	99.00	99.00	770.00*	
Consumables	6961.47	6961.47	7679.44	7685.41	6888.64	6961.47	8888.99	5966.11	7653.81	6649.28*	
X-rays	584.90	537.00	898.60	941.10	845.30	675.30	494.50	669.90	223.30	90.40*	
Subtotal	**17183.67**	**16683.83**	**21115.06**	**19652.42**	**17338.37**	**15847.87**	**18212.19**	**15507.10**	**16329.32**		
Total cost/pat.	**31103.67**	**26851.83**	**43402.06**	**39988.42**	**34860.37**	**23276.87**	**27048.19**	**28564.10**	**23758.32**		**30983.76**

* excluded from average

These prices include the preoperative diagnostic tests routinely performed before LVRS, the hospital stay, the medication, the laboratory costs, the consumables and the doctors fees according to the scale of benefit values in the MASA guidelines. Costs are calculated accurately from the patients folders and range from 23276.87 - 43402.06 Rand. The highest costs (patient 3) were due to the need for a reoperation for a prolonged air leak. This caused higher costs for the procedures, the consumables and the hospital stay. The patient, who died, was excluded from the calculations. Table 9 shows the details.

1. Medical treatment scenario 1:

Patient with severe emphysema on optimal medical treatment:
Evaluation is based on the information in the folders of our 10 patients preoperative and information of experienced pulmonologists, who treat many of these emphysema patients. These patients are still working or doing their household, no hospital stays are required and they are managing with intermittent home oxygen. The costs are estimated for one year.

Medication:		state tender	wholesale
Ventolin refill	x 12:	95.52	260.76
Atrovent refill	x 24:	435.12	1498.80
Euphyllin ret tbl. bd	700:	79.31	964.48
Prednisone 10mg daily	1000:	60.50	124.67
Nebulizer solution twice daily 1ml f.e. Berotec 20 ml	x 36.5:	320.47	1326.05
Saline bags 200ml	x 15:	135.90	193.50
Beconase 50 ml aerosol	x 2:	20.04	249.92
(or Inflamide + Spacer		not available	261.00)
Amoxil/Augmentin tds (5days)	x 4:	150.00	404.64
Mistabron		not available	60.19
Influenza vaccination		13.16	31.64
Subtotal:		**1310.02**	**5114.65**

Home oxygen:

LTDOT for 12-16h per day 7320.00 (State pat.)

Physiotherapy:

Percussion and breathing exercise x 20: 872.00

Special motivation:

i.e. Nebulizer or home oxygen 56.10

Visits/Consultations:

Physician	x 4:	299.90
Pulmonologist	x 2:	290.30

Diagnostic tests:

Chest radiograph	x 3:	271.20
Lungfunction test (limited)	x 2:	377.60
Bloodgas	x 2:	89.20

Total:		**10886.32**	**14690.95**

Medical treatment scenario 2:

Patient with endstage emphysema:
These patients are bedridden, fully oxygen dependant and cannot care for their own needs, nursing is required. Three of our patients were preoperatively in such a bad state, one patient post LVRS, who is still alive 4 years postop, also falls in this category.

Medication:		state tender	wholesale
Ventolin refill	x 12:	95.52	260.76
Berotec refill	x 12:	134.76	630.30
Euphyllin ret tbl. bd	700:	79.31	964.48
Prednisone 10mg daily	1000:	60.50	124.67
Nebulizer solution twice daily 1ml			
i.e. Atrovent 20 ml	x 36.5:	1291.61	1991.80
Ventolin 20 ml	x 36.5:	229.95	637.66
Saline bags 200ml	x 30:	271.80	387.00
Beconase 50 ml aerosol	x 10:	100.20	1249.60
(or Inflamide + Spacer	x 5:	not available	1305.00)
Cefuroxime 750 mg 8 hourly	x 4:	581.40	2529.60
Amoxil/Augmentin tds (5days)	x 2:	75.00	202.32

Moduretic 25 mg daily	x 365:	33.54	164.01
Mistabron		not available	60.19
Influenza vaccination		13.16	31.64
Vitamins tbl. daily	x 365:	not available	23.64
Subtotal:		**2966.75**	**9197.49**

Home oxygen:

LTDOT for 12-16h per day	7320.00 (State pat.)

Hospital stay:

20 ward days/year	9380.00
4 ICU days/year	8292.00

Physiotherapy:

Percussion and breathing exercise	x 30:	1308.00

Visits/Consultations:

Physician	x 4:	299.90
Pulmonologist	x 2:	290.30
in hospital	x 12:	747.60
ICU registrar	x 4:	566.40

Diagnostic tests:

Chest radiograph	x 6:	542.40
Lungfunction test (limited)	x 4:	755.20
Bloodgas	x 8:	356.80
ECG	x 4:	127.50
Laboratory		~ 1000.00

Homeopathy/Psychiatrist:	~ 400.00	
Nursing:		
Excluding meals on wheels 5 days homevisit (morning, lunch, evening) * not cost effective 4 hours daily (7.00 – 13.00h)	23504.00	(67860.00*)
Total:	**57856.85**	**64087.59**

Medical treatment scenario 3:

Patient with good result after LVRS (f.e. second year):
The patient is fully independent, is exercising, does not need home oxygen, Dyspnea score II (Table 2) and is looked after by his general practitioner.

Medication:		state tender	whole sale
Ventolin refill	x 12:	95.52	260.76
Atrovent refill	x 24:	435.12	1498.80
Euphyllin ret tbl. bd	700:	79.31	964.48
Prednisone 5mg daily	500:	30.25	62.34
Amoxil/Augmentin (5 days)	x 1:	37.50	101.16
Visits/Consultations:			
Physician	x 4:	299.90	
Diagnostic tests:			
Chest radiograph	x 2:	180.80	
Lungfunction test (limited)	x 2:	377.60	
Total:		**1536.00**	**3745.84**

These three scenarios represent the cornerstones of the following estimations:
The worst case scenario is reached in the endstage of the disease without or with LVRS. Our experience and others (47,65,86), as well as taking into account the natural history of severe emphysema (41) one can assume, that LVRS is shifting the time until this endstage is reached by 3-4 years, for some of the patients even longer.

With medical therapy alone the estimated costs will develop as follows:

First year	second year	third year	fourth year	fifth year	Subtotal
10886.32	22628.95	34371.58	46114.21	57856.85	**171 857.91**
14690.95*	27040.11*	39389.27*	51738.43*	64087.59*	196 946.35*

Once in this 5 year period the special investigations (f.e. CT scan, alpha 1 anti-trypsin test, skin prick test, full lung functions etc.) have to be added, which brings us to an estimated cost over a five year period of:

Total: 173 226.81 (198 315.25 *)

* calculation with whole sale prices for the outpatient medication

A realistic outcome after LVRS is the following estimation, based on the mean costs of LVRS in our ten patients plus the yearly costs in the five year follow up period in a patient, who responded well to the operation, but follows the natural history parallel to the medical treatment alone, assuming that he is back to baseline after 3 years:

First year	second year	third year	fourth year	fifth year
30983.76 + 1408.00 (11 m at home)	1536.00	6211.16	10886.32	22628.95
30983.76 + 3433.69* (11m at home)	3745.84*	9218.40*	14690.95*	27040.11*

Total: 73654.19 (89112.75*)

With LVRS and reasonable response to the operation an estimated 100 000.- Rand are saved in a 5 year period. In the following years the gap will decrease again due to the natural history of the disease. The most costsaving factor is the independency gained (Table 10) and the improved effort tolerance, nicely demonstrated in the 6 min walk test (Figure 21).

3.5. Quality of life:

An overview of the well being of our nine patients is shown in Table 10.
This information was gained from the folders and notes at the follow up visits at GSH and from the pulmonologists or general practitioners involved in the follow up and from the patients themselves.

Table 10: Summary of daily activities until the last follow up:

Patient	Follow up	Well being	O2 use	Steroids
KA	12 m	Feels fine, is looking for a new job, Fully independent	N	N
VN	12m	Markedly increased ET, walks on the beach as long as she wants, moved from Pretoria to Durban, own shopping, fully independent	N	N
MI	12 m	Back at work fulltime, walks her dogs every day, full independence	PRN	Y
	18m	Still working, but decreased ET (50m), decline noted, multiple hospital stays, almost back to baseline		
SCH	12m	Full independence, own shopping, ET well above baseline	N	Y
	24m	Decline noted, depressed, on home oxygen	Y	Y
		Died 3 years post LVRS		
VDB	12m	Full independence, 15 min cycling/day	N	N
	24m	Doing well, still exercising	N	N
	36m	Slow decline	N	N
	48m	No change, still fully independent well above baseline	N	N
MY	12m	Full independence, walking on his own pace	N	Y
	24m	Back to baseline	Y	Y
	4 y	Bedridden, nursing required 12 h, O2 continously	refuses	Y
NE	12m	Full independence, doing her household	N	Y
	24m	Slow decline, ET decreasing, but well above baseline	Y	Y
	36m	Wheelchair, physio 2x/week	Y	Y
		Died 4 y post LVRS		
SM	12m	Full independence, own shopping, exercising 30min/day	N	N
	24m	Still good ET, doing her household	N	Y
	36m	Functions above baseline,but moved to JHB and feels a decline in high altitude environment	PRN	Y
TR	12m	Full independence, regular exercise (gym)	N	Y
	24m	Slow decline, still exercising, goes shopping, does her household	N	Y
	36m	Gained weight!!, ET decreased, still doing her household	PRN	Y
	48m	Stopped going to the gym	PRN	Y
	60m	Walking on her own pace, still independent	PRN	Y

Two different questionnaires could be completed by 6 patients. They were administered by one interviewer in July 2000, retrospective for the time before LVRS and 1 year after LVRS.

The Medical Outcome Study Short Form 36 (MOS SF 36):

This instrument measures general health-related quality of life and is divided in 8 domaines:

1. PH = physical function
2. RP = role limitation due to physical health
3. BP = bodily pain
4. GH = general health
5. VT = vitality
6. SF = social function
7. RE = role limitation due to emotional problems
8. MH = mental health

The best score is 100 and the worst score is 0. A change of 20 points is regarded as significant.

The mean overall score in our 6 patients improved from 28.3 preoperative to 70.95 one year postoperative, this and all individual domains except bodily pain showed a significant difference in the quality of life score pre- and postoperatively, as shown in Figure 22:

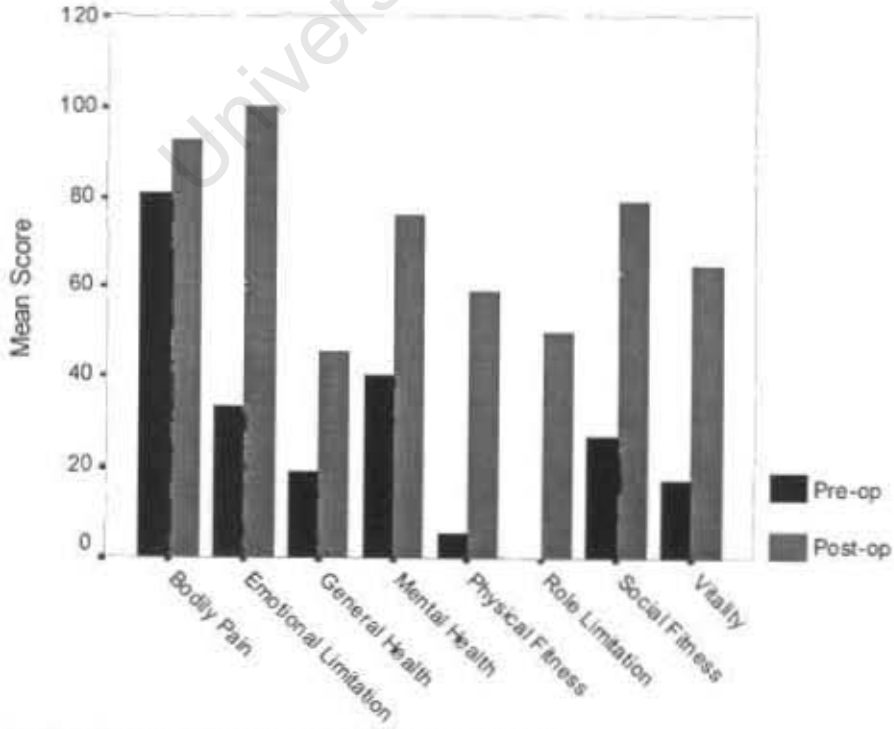
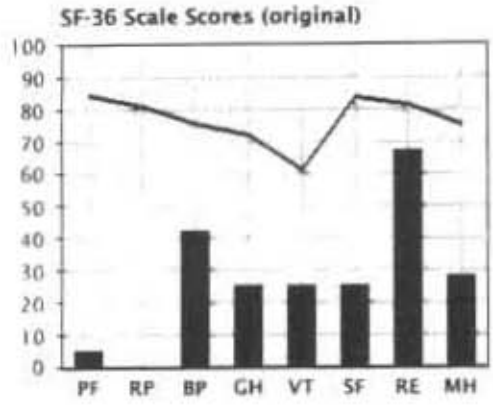
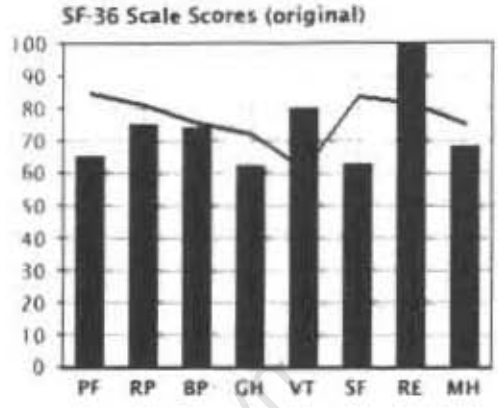


Figure 22: Mean scores of the 36-Item Short-Form Questionaire (SF-36)

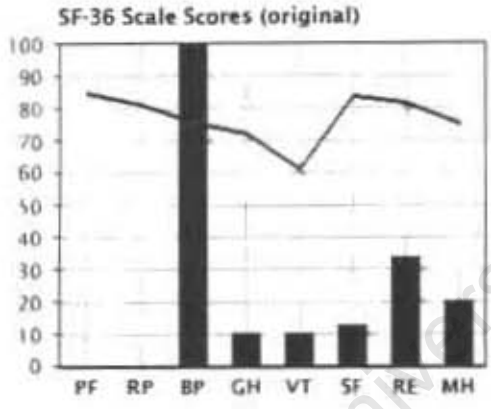
Based on the general U.S. population mean score (black line) in each category the individual outcomes preoperatively (left) and 1 year after LVRS (right) are depicted in Figure 23:

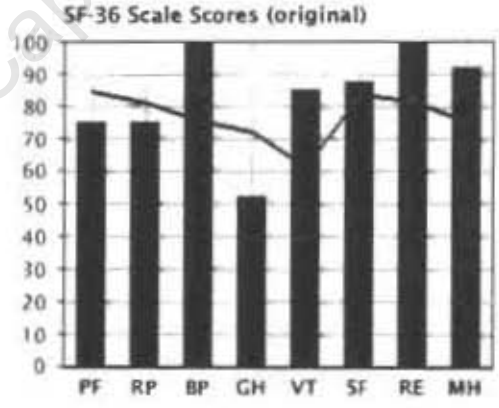
Patient 1



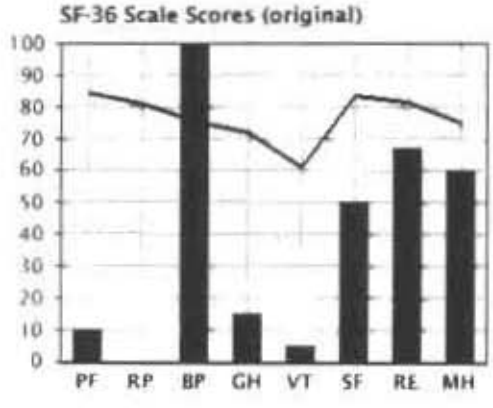


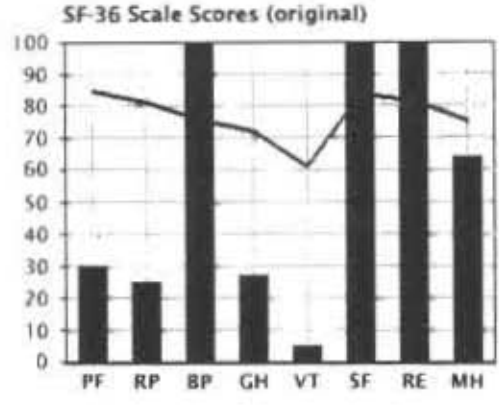
Patient 2



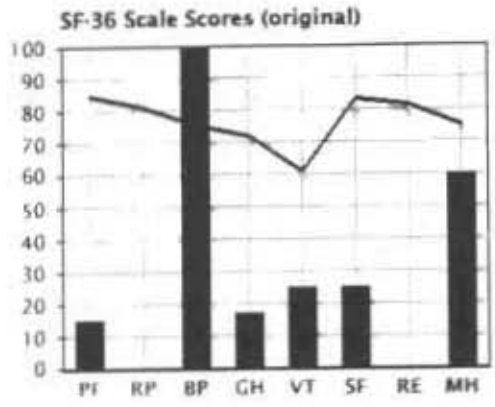


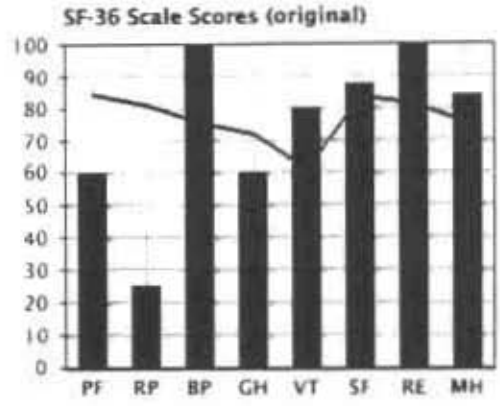
Patient 3



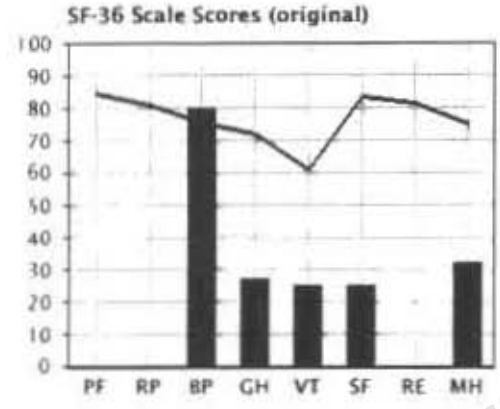


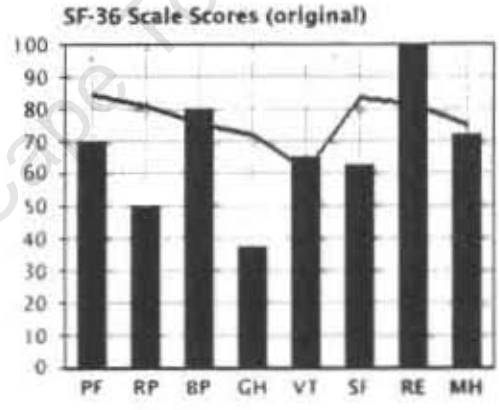
Patient 4



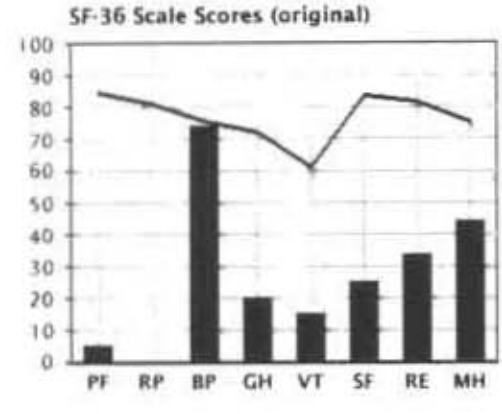


Patient 5





Patient 6



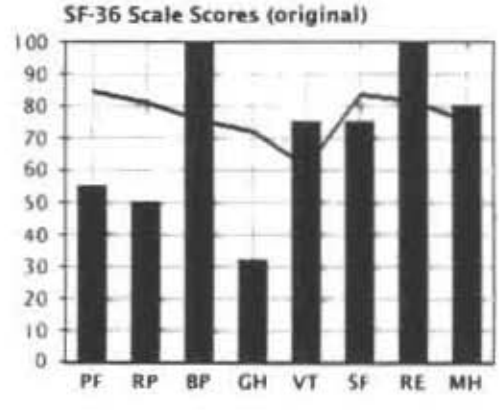
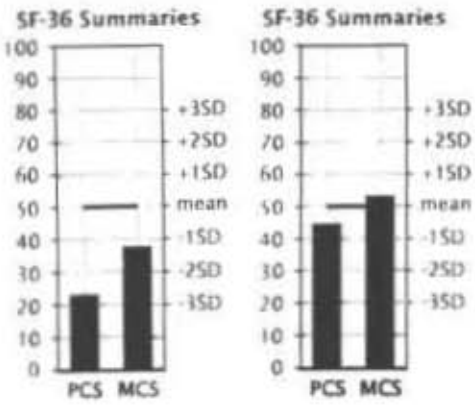
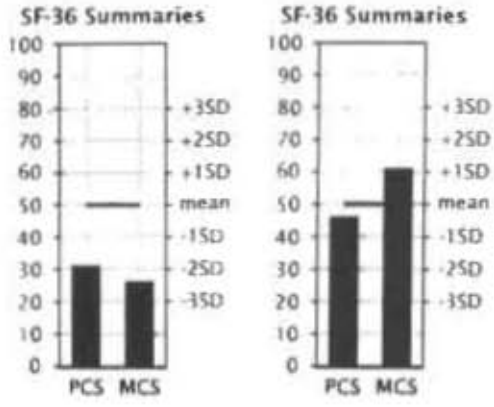


Figure 23: Preoperative (left) and 1 year after LVRS (right) SF-36 scores for each individual patient. The black line demonstrates the average scores for the general US population

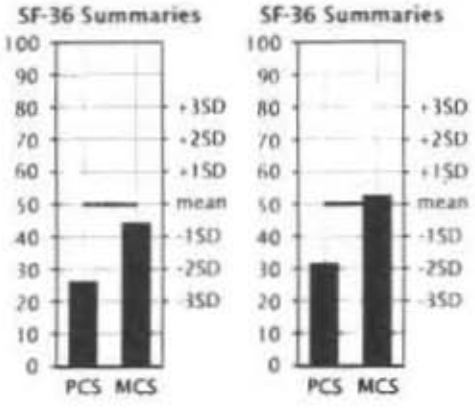
Patient 1



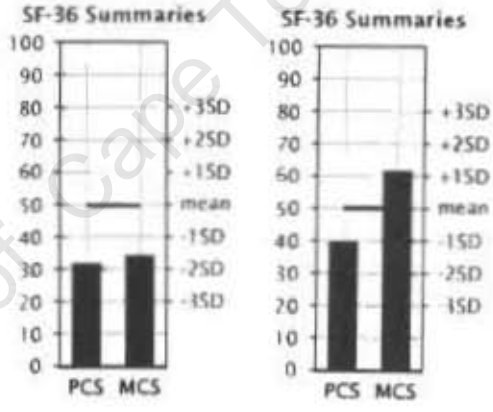
Patient 2



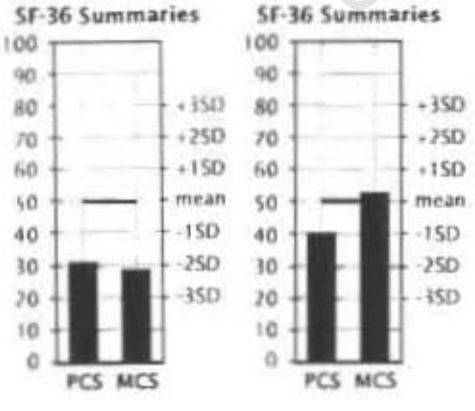
Patient 3



Patient 4



Patient 5



Patient 6

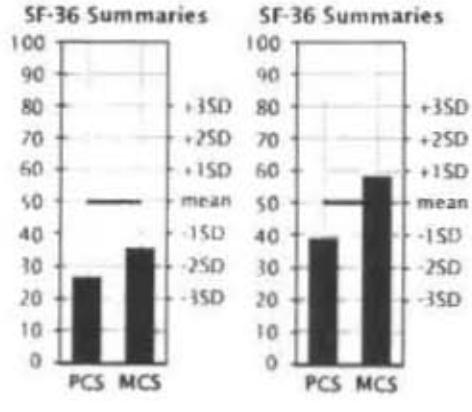


Figure 24: The Physical Component Score (PCS) and Mental Component Score (MCS) preoperatively (left) and 1 year after LVRS (right) for each individual patient. The "50" line represents the mean score for the general U.S. population

The Physical Component Score (PCS) and Mental Component Score (MCS) depicted above are the physical and mental summaries for the SF-36, and are displayed on what's called a standardized "50-10" scale.
The mean score for the general U.S. population for PCS and MCS is 50, and the standard deviation of those scores is 10. Both scores are directly comparable, and the extent of the variation of each score from the mean is standardized in equivalent standard deviation units. Each 10 point difference is equal to one standard deviation. This makes the interpretation of the results easier. Preoperative values are put next to the results 1 year after LVRS for each patient (Figure 24).
In all patients the PCS (mean 28) was preoperative 2 or more standard deviations below the general U.S. Population and improved 1 year after LVRS in average 12 points, still ranging below mean values.
The Mental Component Score started in average 16 points below mean, but was in all patients above the mean of the general U.S. population 1 year after LVRS. It increased in average 23 points (> 2 SD), which demonstrates the mental strength and confidence these patients gained.
Figure 25 shows the 8 different domaines preoperatively (right) and 1 year after LVRS (left), only bodily pain did not change significantly, mainly because the patients did not have a lot of pain preoperatively, all other qualities changed dramatically and reached significance (change > 20 points).

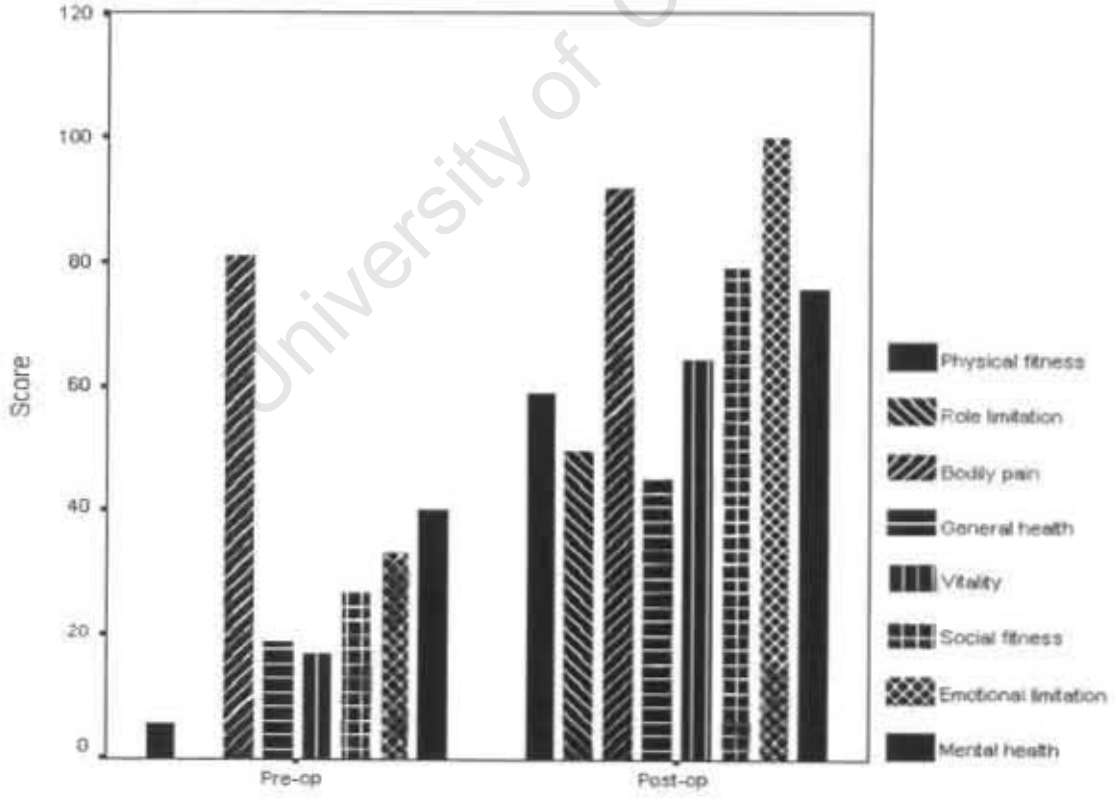


Figure 25: Preoperative values and 1 year after LVRS for the 8 different domaines

The Chronic Respiratory Disease Questionnaire (CRQ):

This instrument is a disease specific 20 item-questionnaire. It measures symptoms in the area of :

1. Dyspnea (5 questions)
2. Fatigue (4)
3. Emotional function (7)
4. Mastery (4)

During self-selected day-to-day activities. Each domain is scored on a scale of 1-7. A change in score of 0.5 per item has been associated with a minimally important difference in health-related quality of life, a change of 1 is moderate and a change of more than 1 is a large = significant difference (60). It takes 20 min to administer.

Figure 26 shows the mean scores in each domaine preoperatively and 1 year after LVRS and the overall score. The overall score changed from 2.3 preop to 5.6 one year after surgery, which is highly significant, as were the changes in the domaines.

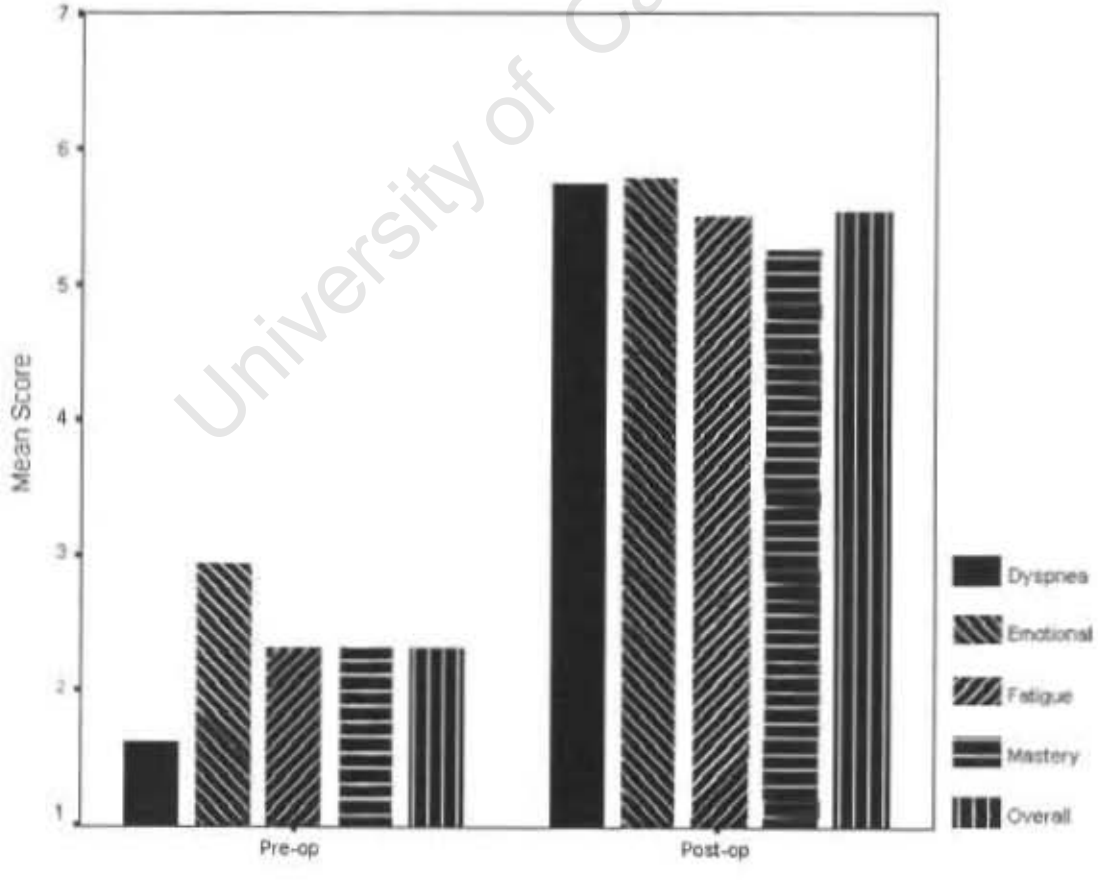


Figure 26: Scores of the 4 domaines and the overall score preoperatively and 1 year after LVRS

The individual scores in each domaine and the overall score for each patient are showing Figure 27:

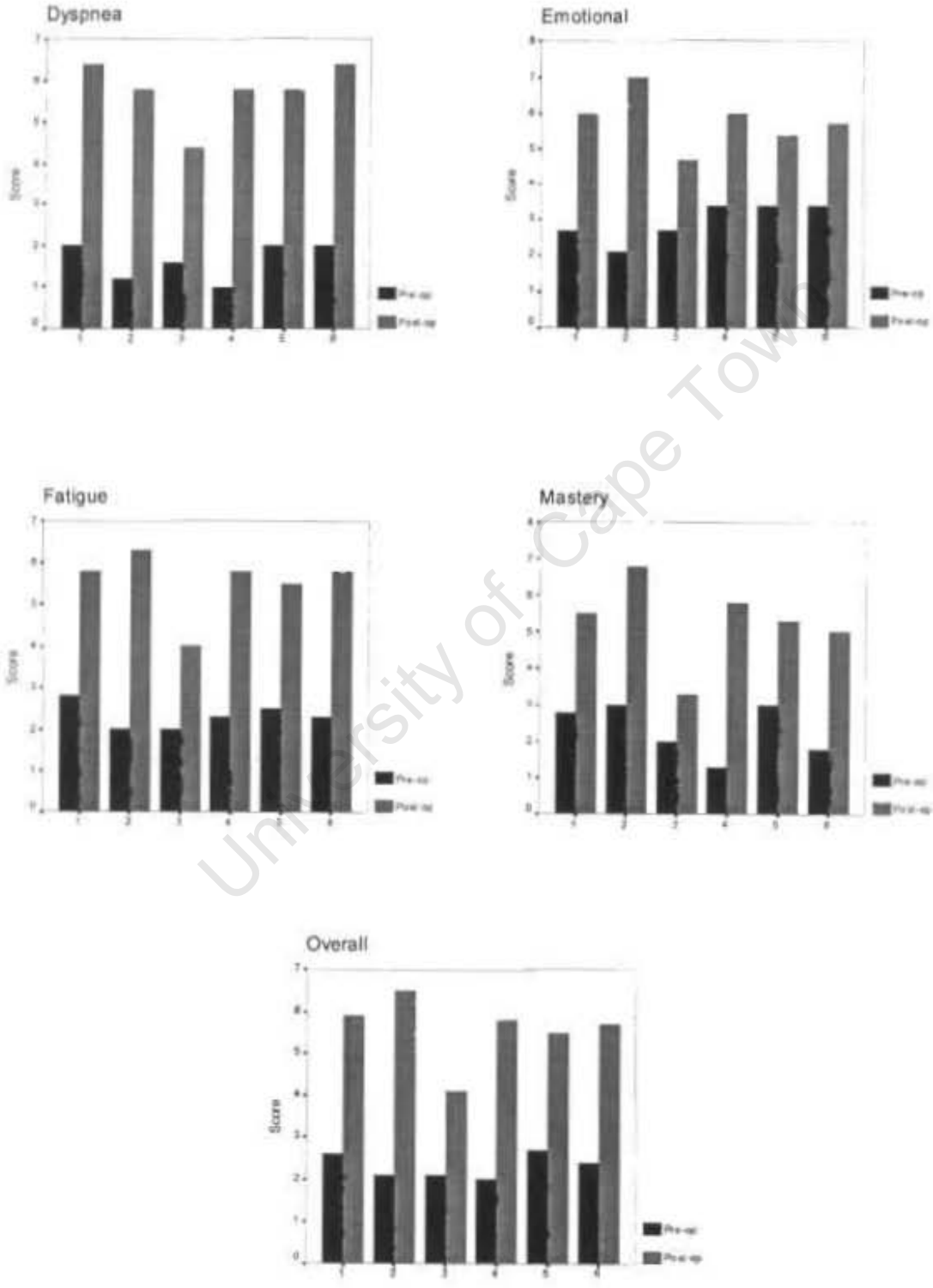


Figure 27: Scores of the 4 domaines and the overall score for each patient

4. DISCUSSION:

With the revival of Brantigan's idea of multiple wedge resections for severe emphysema by Cooper et al in 1995 a large number of small series, trials and publications have flooded the medical literature. As with every "new" technique it took a few years until the cornerstones of the method had been established. Most of the selection criteria and surgical techniques are now standardized within certain limits. The main short come is that no big prospective, rando-mised study has been completed. Two major studies are underway but still in their enrolment phase, one is the NETT=National Emphysema Treatment Trial (125) and the second is the CLVR-Study = Canadian Lung Volume Reduction Study (87,88). One has to rely on small studies with short- and median follow-ups (33,34,39,47,81,85,107,108,112,113,119).

Due to restricted manpower and budget constraints at the moment in South Africa we can only analyse our data retrospectively and investigate, whether we can keep up with international standards. Especially for South Africa it is of utmost importance to investigate not only the technical feasibility and physiological outcome after LVRS, but also evaluate the costs and the benefits for the patients in terms of quality of life.
The presented data can be looked at from different angles. We are aware, that it is a small series with gaps in the follow up and it is a retrospective analysis. Nevertheless a few interesting points need to be emphasized:

- The choice of operating via a mediansternotomy on both lungs and the use of GRF (gelatin-resorcinol-formaldehyde/glutaraldehyde) glue to prevent major air leaks seem to have resulted in a fairly low and acceptable morbidity (Table 3). Only one patient went back to theatre because of a prolonged air leak, all other patients "stopped bubbling" in less than 14 days and could leave hospital without a bottle or a Heimlich valve.
  Postoperative pain and therefore respiratory function are not as significantly impaired as with a thoracotomy and the target areas bilaterally can be easily reached.
  We can staple the lung in such a way, that it will fit well into the thoracic cage and we try not to staple away triangles or amputate the apex.
  It has to be emphasized, that the utmost care is necessary to use the GRF glue only on the stapling device and the stapled edge, avoiding contact with lung tissue or other structures. The toxic component formaline could otherwise cause necrosis (9,129).
  Personal communication with some overseas thoracic surgeons draw the attention to the fact, that prolonged air leaks are a major problem, not only with the laser technique (73) but also with stapling these emphysematous lungs. The Brompton group therefore does not hesitate to send their patients home with a Heimlich valve, accepting a comorbidity in these patients. The use of GRF glue in our experience worked well, it is cheaper than bovine pericardium or PTFE felts and easy applicable.
  A previous review (88) reported morbidity and complications after LVRS as high as the following figures: prolonged air leaks (40-55%), tracheobronchitis (46%), postoperative pneumonia (17-22%), prolonged postoperative mechanical ventilation (13-17%), arrhythmia (21%), reoperation for air leaks (10%), reoperaton for bleeding (5%), pneumothoraces (50%) and postoperative myocardial infarction (0.9%).

- Strict adherence to the inclusion and exclusion criteria resulted in a limited number of patients offered LVRS. Especially in South Africa with financial limitations and ongoing

budget cuts this operation is offered only to a small group of patients, who are already imposing major costs on the community. This selection process will prohibit inflational use of this technique and, as pointed out in later sections, it is cost effective at least over the next five years and provides impressive and valuable improvements quality of life.

A 30 day mortality of 10 % , in our study one patient, is compatible with international standards, 0-20% reported in various series (8,33,47,82,119). One interesting observation from the recent prospective randomised study from Brompton (47) is that they changed their exclusion criteria regarding the carbon monoxide diffusion capacity and excluded patients with values lower than 30 % predicted. The reason was that they had 5 deaths out of the first 15 patients, all of them with values lower than 30 % of predicted. The patient, who died in our group, had the lowest TLCO value of all with 22.88% of predicted.

This leads to the question: **Who benefits the most?**
Inhomogeneous distribution of emphysema and clear target areas makes it easier for the surgeon to resect most affected areas. Demarcation is facilitated by preoxygenation with 100 % oxygen and consequently collapsing the lung. Areas with severe gas trapping stay pink longer and can be identified as target areas.
Four of our patients had a homogenous pattern, confirmed by both high resolution CT-scan and a perfusion scan, but two of them are doing exceptionally well, one died 4 years post LVRS and one is back to baseline after 18 months.
As demonstrated by Gelb et al (48) it seems, that in each study there are some patients, who do not show the expected benefit from LVRS, he calls them "short term-responders", others would say "non-responders". In our study there is at least one patient, who has returned to her preoperative status 18 months postoperatively, probably due to a combination of low preoperative lung function and a homogenous pattern of emphysema. She was the only patient, who was unable to perform a bodyplethysmography preoperative, so we have no values for residual volumes or diffusion capacity before LVRS.
Alpha 1 anti-trypsin deficiency is not regarded as a contraindication per se, one patient is now bedridden 5 years after LVRS, the other one is doing very well 4 years after LVRS.
The question, why some people have an impressive and long-lasting benefit as opposed to others, who are deteriorating soon after LVRS, remains unanswered.

- One central issue in the assessment of any procedure designed to improve function in patients with COPD is **the dyspnea.** Dyspnea is a subjective sensation and the severity may or may not correlate with physiological measurements (78).

Five parameters reflect the degree of dyspnea:

- the dyspnea score
- the quality of life assessment CRQ and PH in the SF-36
- performance was evaluated by the 6 min walk test
- the use of home oxygen as an indirect reflection on dyspnea (Table 10)
- physiological evaluation by spirometry and plethysmography

Our data clearly showed an improvement of all these parameters for the first 12 months, most patients had a measurable benefit for more than 2 years.

The 6 minute walk test is a very reliable indicator of effort tolerance. It was significantly improved up to 24 months postoperative. This reflects the findings of Geddes et al (47) in their prospective randomised study.
It was shown impressively, that the medical arm continues to follow the expected deterioration according to the natural history of severe emphysema (Figure 28). The surgical arm follows parallel on an improved level, hitting the baseline (=preoperative values) after approximately 2 years and keeps on deteriorating in the next few years parallel to the medical arm.

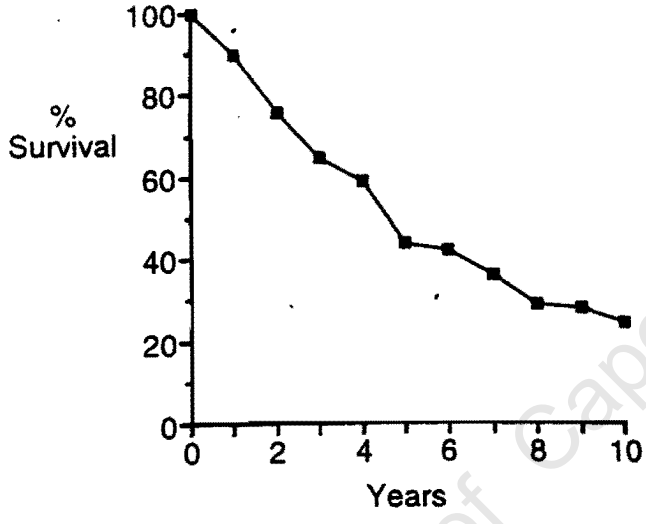


Figure 28: Survival in patients diagnosed with chronic obstructive pulmonary disease who have a forced expiratory volume in 1 second less than 30% of predicted (95)

Probably the best reflection of the natural history of patients with severe emphysema is gained from a report from Meyers et al.(86). He followed up 22 patients, who were selected for LVRS, but were denied the operation by Medicare. He compared these patients with the ones, who underwent LVRS. He showed an actuarial survival after 36 months of 64% in the patients denied the operation and a 83% survival for patients undergone LVRS. He also showed a significant improvement in FEV_1 after 12 and 24 months, as well as sustained improvements in the frequency of oxygen use at rest and at exercise, relief of dyspnea and a decrease in steroid requirements.

Considering all above mentioned points, our spirometry values showed the least reliable correlation between subjective relief from dyspnea and measurable improvements of lung functions. This was noted by other authors before (13,33,48).

- A second central issue is the question : **How cost effective is this treatment ?**
The techniques of economic evaluation offer a systematic framework for identifying, measuring and valuing the resource input (costs) to a health care program (i.e. a new drug or surgical procedure) and the health benefits associated with the intervention. Especially in view of the situation in America and the precedence, that Medicare does not pay for LVRS

until beneficial effects are proven (54), one should look at the costs, these patients accumulate over the years with their severe disability.
Figure 28 demonstrates the natural history of severe COPD. According to our findings and that of many other small series (47,48,113), five years would be a realistic time interval to look at. The costs of medical treatment alone and costs of LVRS plus medical treatment required for the following 5 years are calculated at the endpoints of year 1 and year 5 and extrapolated in between. Knowing the natural history (44) and the requirements with progression of the disease (hospital stays, medication, loss of independence etc.) this is a fair assumption.
A longer period is unrealistic, because many patients would drop out because of death. According to Bergner 70-80% of these patients will be dead within 5 years (15).

An economic evaluation does look not only at the costs, but also analyses the effects and benefits gained by a treatment or procedure. A simplification of this is shown in Table 11:

Table 11: Dominance and trade offs in economic evaluation (98)

	More effective	**Less effective**
More costly	Trade off	Dominance to reject
Less costly	Dominance to accept	Trade off

If a new intervention is demonstrated to be both less costly and more (or equally) effective, then there would be a dominance (= "win-win" situation) to adopt the new therapy, which is the case in our study for LVRS. It clearly demonstrated, that over a five year period a substantial amount in the region of 100 000 – 110 000 Rand can be saved, if patients undergo LVRS.
All economic evaluations distinguish between direct cost and indirect costs. Direct costs are the value of resources consumed in delivering care (i.e. medication, hospital costs etc.). Indirect costs are the value of lost or gained production due to the patient's inability or ability to work as a consequence of the disease or treatment.
In our study we neglected these indirect costs from the societal viewpoint, because our patients were either pensioners, did not work before or after LVRS or did work before and after LVRS. So there was no change in indirect costs.

If there is evidence, that health outcome from a new therapy is equivalent or better than the comparison therapy, then it is legitimate to consider costs only (98). Cost analysis is not only including the costs of the procedure (Table 9), but also costs over the following years as outpatients and if necessary inpatients.

A cost utility study looks at costs plus quality of life gained. The cost utility could not be assessed accurately, because the quality of life score, which allows to measure quality

adjusted life years (= QALY's) was not made available to us. But this leads to the third central issue:

- The question to answer is: **Do patients undergone LVRS gain quality of life and if yes, for how long?**

In bigger, randomised studies usually one general health index (i.e. SF-36, Nottingham Health Profile) and one or two disease specific instruments are used to assess quality of life. Both tests used in our study are proven to test quality of life and are sensitive and specific to changes in the respiratory status. They have been used for COPD and LVRS in previous studies. They are easily administered, reliable and reproducible (49,50,69,76,77,80,104, 120,122,127,132,134).
Unfortunately the third test, the Health Utility Index 2/3, a 40 item questionnaire was assessed, but the algorithm and therefore the evaluation of outcomes is not freely available and subject to royalties in the United States and Canada.
HUI 2/3 would have been the only test, which allows the assessment of deaths during the follow up period, integrates the quality of life and survival in a single outcome (Quality of life years=QALY's) and could be used in the economic evaluation for cost utility and cost effectiveness (42).

A significant difference was shown between quality of life preoperative and 1 year postoperative, the patients were mobile on basic medication, off home oxygen and gained an enormous amount of independency. Both the physical scores and the mental scores improved significant. The mental health score in the SF-36 (MHS) was lying over that of the general U.S.population.
Unfortunately four patients either died before the evaluation or were not willing to complete the questionnaire, but from the existing notes by the Respiratory Clinic their outcome after one year would not have been different concerning quality of life (Table 10).
In 4 out of 9 patients a steady decline was noted after 2 years, following the natural history of COPD, all nine patient's records confirm a marked improvement of quality of life one year post surgery.
Even taken into consideration that the questionnaires were applied retrospectively, the consistency of the results and the clear differences shown in all scores (Figures 22-27) emphasize, that this part of the study shows a clear advantage for LVRS.
The patients could remember clearly and described in detail, what their condition was preoperatively and one year post LVRS, which is reflected in the two quality of life scores.

CONCLUSIONS:

- We have proven, that LVRS is a safe and cost effective procedure for carefully selected patients with severe emphysema. These patients gained physical and mental strength, evaluated in two quality of life scores.

- Our results are in line with international standards, and our hypothesis is proven to be valid.

- We will be able to participate in the prospective randomised multicenter study from Canada, which will further decrease the impact on our own health budget.
  Only a big study like this can give conclusive proof and answers to unresolved questions around LVRS.

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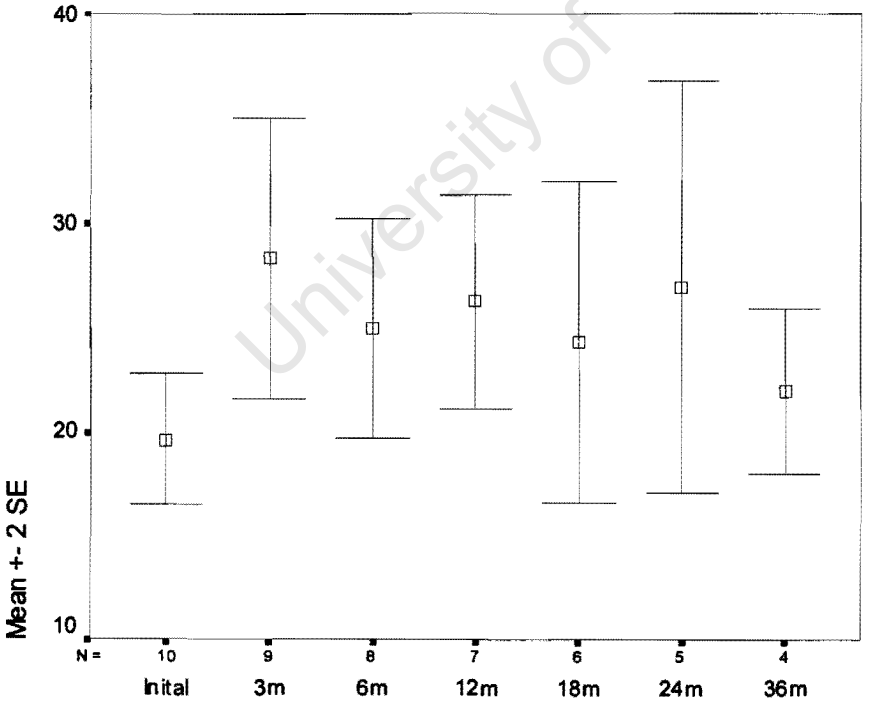
Annexure A:

FEV_1 in % predicted

Pt. Nr.	preop	3m	6m	12m	18m	24m	36m	48m	60m
1	13	17	17	20					
2	21	28	26	23					
3	16	39	37	22	23				
4	29	32	32	32	24	38			
5	21	25	28	24	26	27	24	25	
6	18	17	15		13	15			
7	17	24	25				21		
8	27	48		39	41	38	26	38	34
9	19	25	20	24	19	17	17		
10	16								
Mean	**20**	**28**	**25**	**26**	**24**	**24**	**22**		
Number	10	9	8	7	6	6	4		



Mean values for forced expiratory volume in 1 second (FEV_1)

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Inital	20.11	9	5.13	1.71
	3m	28.33	9	10.07	3.36
Pair 2	Inital	19.25	8	4.74	1.68
	6m	25.00	8	7.48	2.65
Pair 3	Inital	20.86	7	5.67	2.14
	12m	26.29	7	6.75	2.55
Pair 4	Inital	21.67	6	5.20	2.12
	18m	24.33	6	9.37	3.83
Pair 5	Inital	21.83	6	5.00	2.04
	24m	24.33	6	11.83	4.83
Pair 6	Inital	21.00	4	4.32	2.16
	36m	22.00	4	3.92	1.96
Pair 7	Inital	24.00	2	4.24	3.00
	48m	31.50	2	9.19	6.50

Paired Samples Correlations

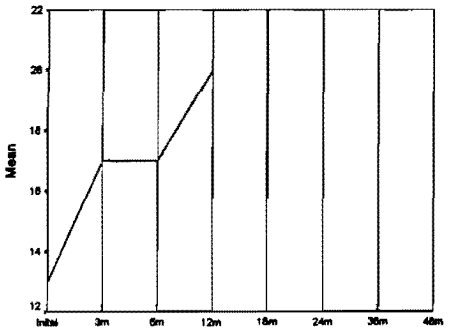
		N	Correlation	Sig.
Pair 1	Inital & 3m	9	.586	.097
Pair 2	Inital & 6m	8	.402	.323
Pair 3	Inital & 12m	7	.863	.012
Pair 4	Inital & 18m	6	.610	.199
Pair 5	Inital & 24m	6	.972	.001
Pair 6	Inital & 36m	4	.749	.251
Pair 7	Inital & 48m	2	1.000	.000

Paired Samples Test

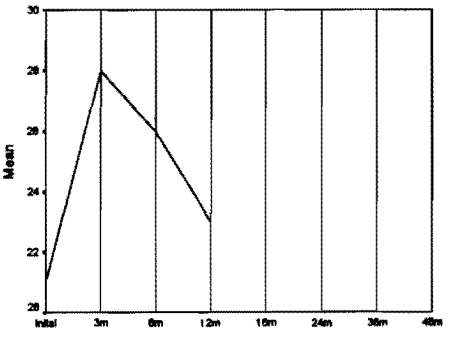
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Inital - 3m	-8.22	8.20	2.73	-14.52	-1.92	-3.009	8	.017
Pair 2	Inital - 6m	-5.75	7.07	2.50	-11.66	.16	-2.302	7	.055
Pair 3	Inital - 12m	-5.43	3.41	1.29	-8.58	-2.28	-4.214	6	.006
Pair 4	Inital - 18m	-2.67	7.45	3.04	-10.48	5.15	-.877	5	.421
Pair 5	Inital - 24m	-2.50	7.06	2.88	-9.91	4.91	-.867	5	.426
Pair 6	Inital - 36m	-1.00	2.94	1.47	-5.68	3.68	-.679	3	.546
Pair 7	Inital - 48m	-7.50	4.95	3.50	-51.97	36.97	-2.143	1	.278

Paired t-test FEV1 (preop to follow up at 3m,6m,12m,18m,24m,36,48m)

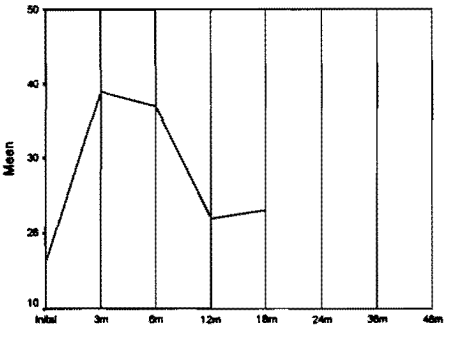
Patient 1



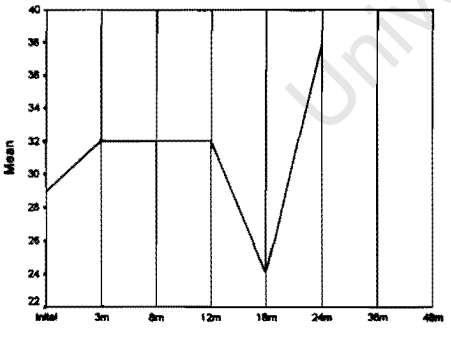
Patient 2



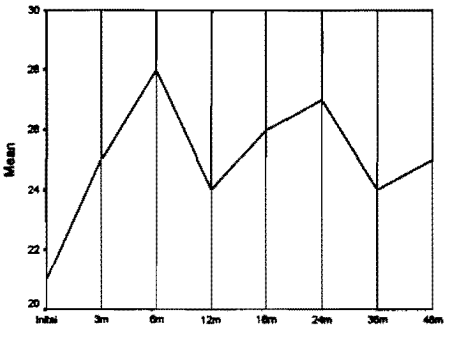
Patient 3



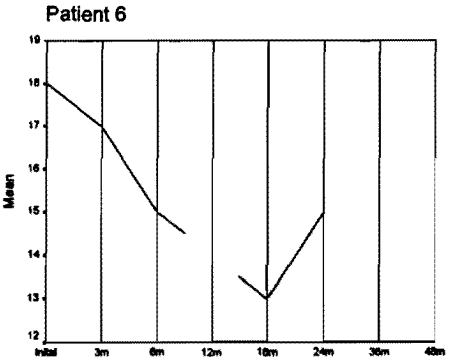
Patient 4



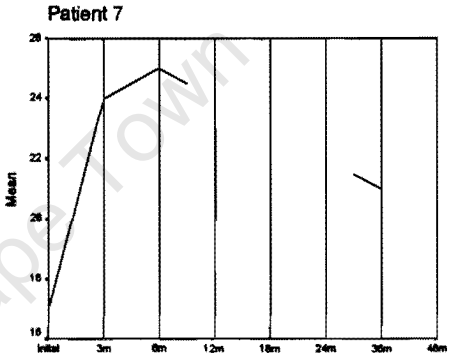
Patient 5



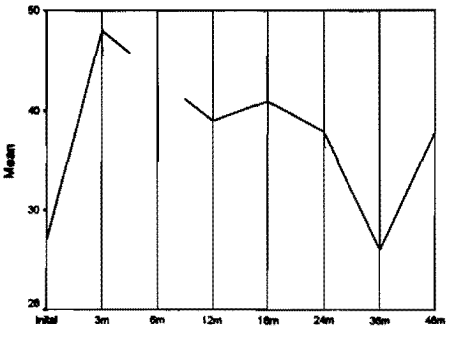
Patient 6



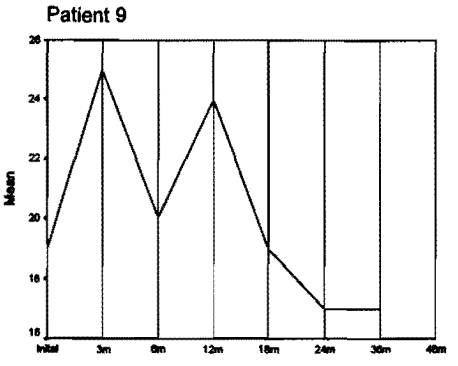
Patient 7



Patient 8

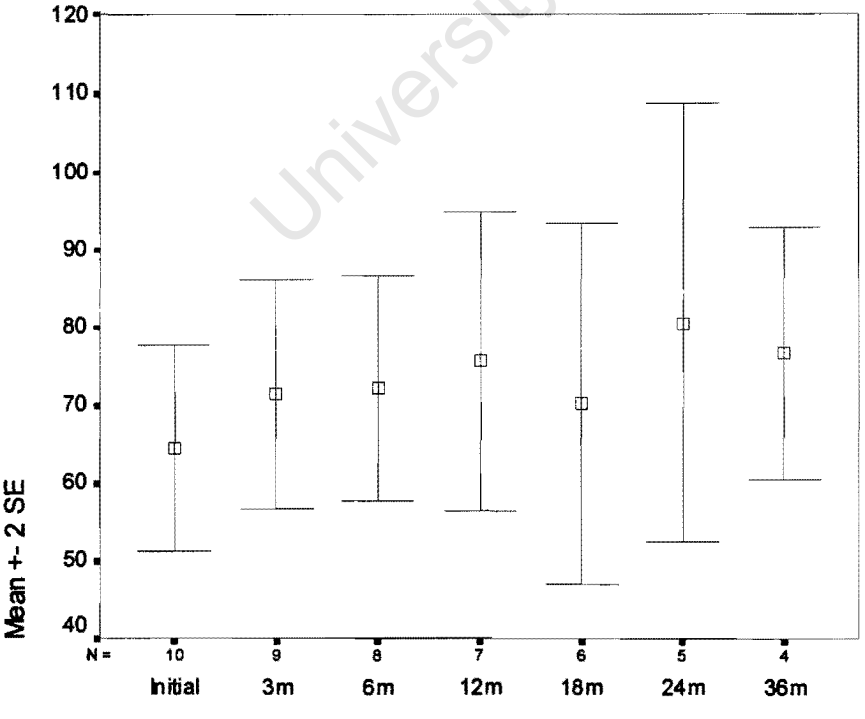


Patient 9



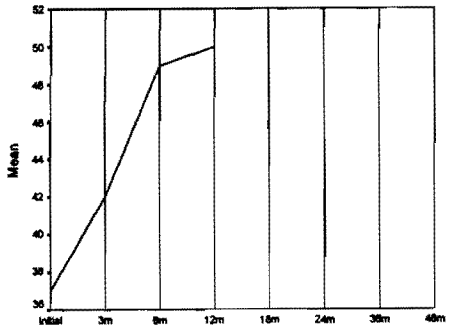
FVC in % predicted

Pt.Nr.	preop	3m	6m	12m	18m	24m	36m	48m	60m
1	37	42	50	50					
2	63	57	63	65					
3	40	85	84	48	62				
4	58	75	89	89	70	97			
5	85	94	110	98	104	105	94	118	
6	61	58	57		29	36			
7	41	56	67				60		
8	93	112		115	101	106	87	114	91
9	85	64	59	65	56	59	65		
10	83								
Mean	**65**	**71**	**72**	**76**	**70**	**81**	**77**		
Number	10	9	8	7	6	5	4		

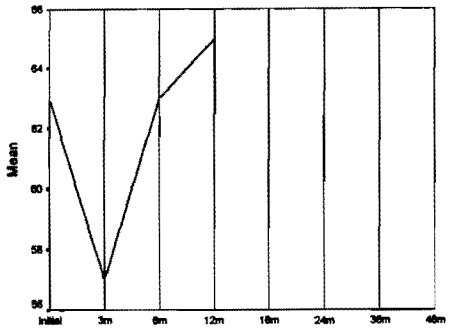


Mean values for forced vital capacity (FVC)

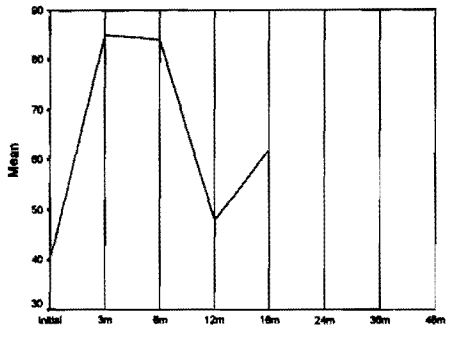
Patient 1



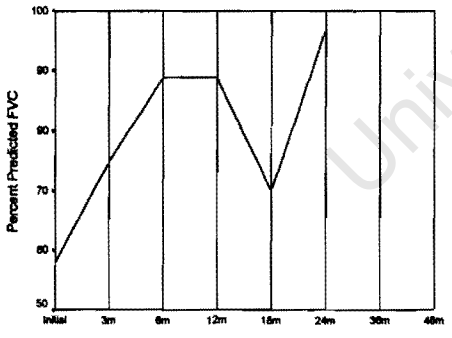
Patient 2



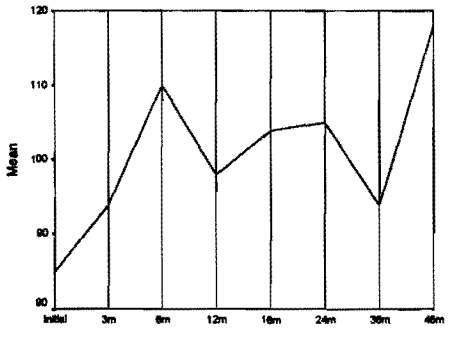
Patient 3



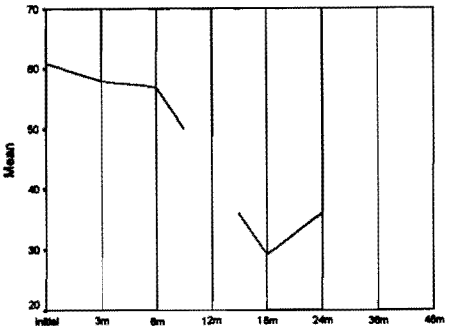
Patient 4



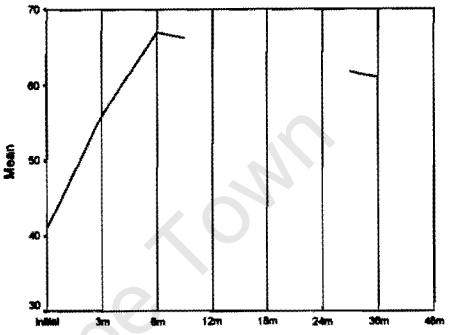
Patient 5



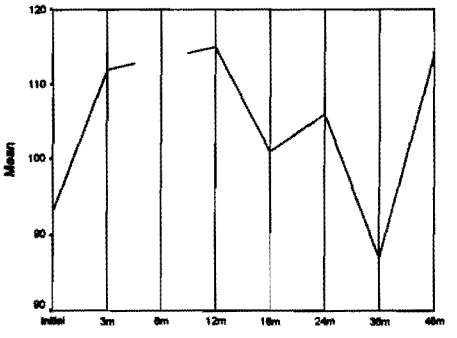
Patient 6



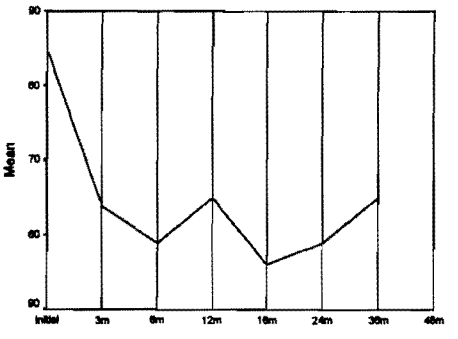
Patient 7



Patient 8

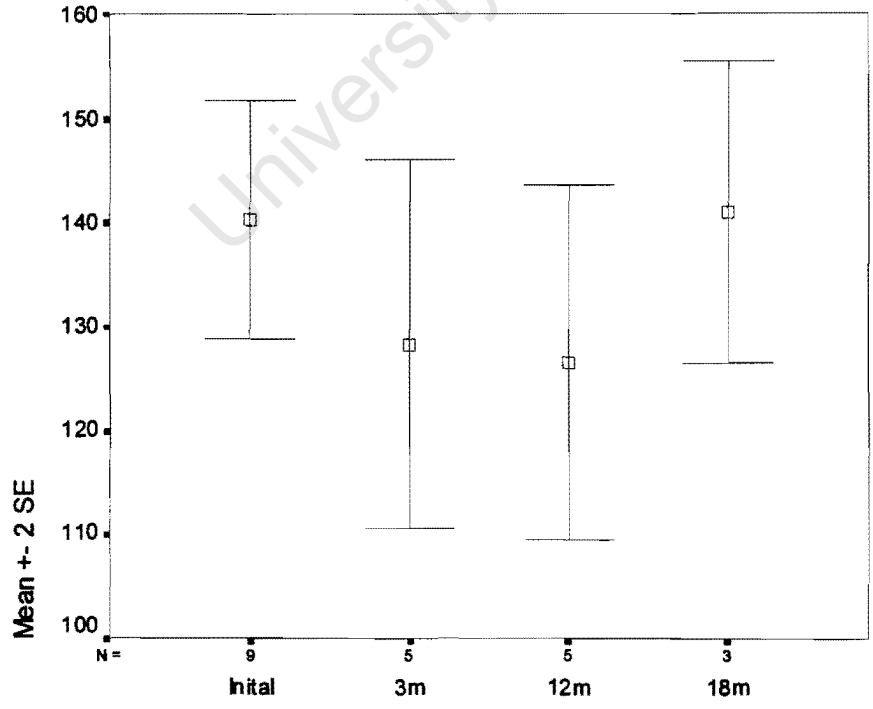


Patient 9

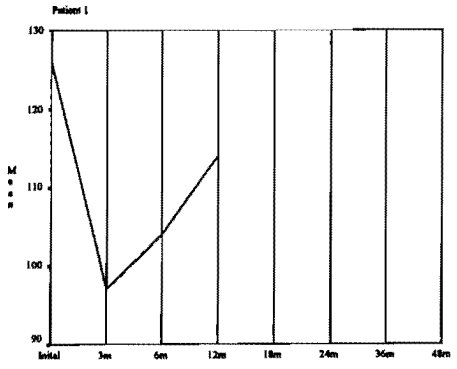


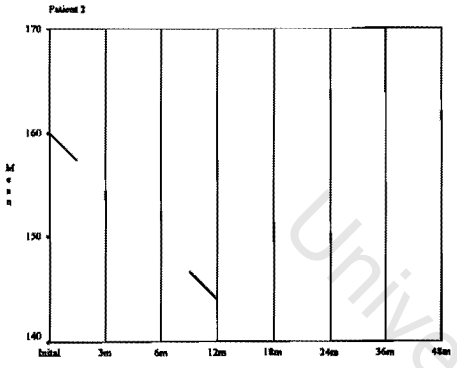
TLC in % predicted

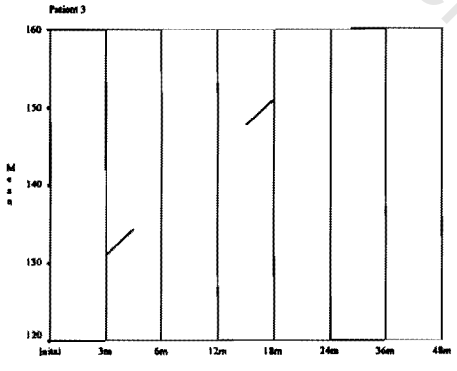
Pt.Nr.	preop	3m	6m	12m	18m	24m	36m	48m	60m
1	126	97	104	114					
2	160			144					
3		131			151				
4	143	134							
5	158	128		150	145		142		
6	111								
7	151	153	139						
8	143			119	127	128		144	129
9	150			107		133			
10	121								
Mean	**140**	**129**	**121**	**127**	**141**				
Number	9	5	2	5	3				

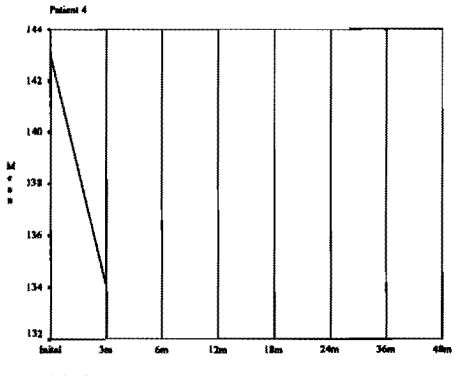


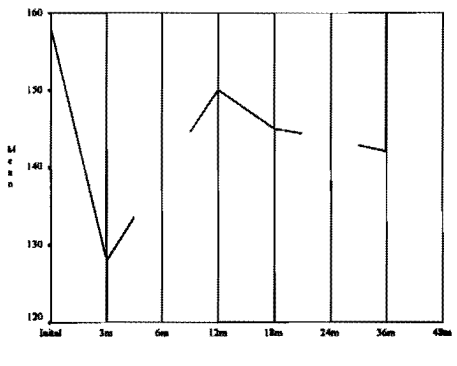
Mean values for total lung capacity (TLC)

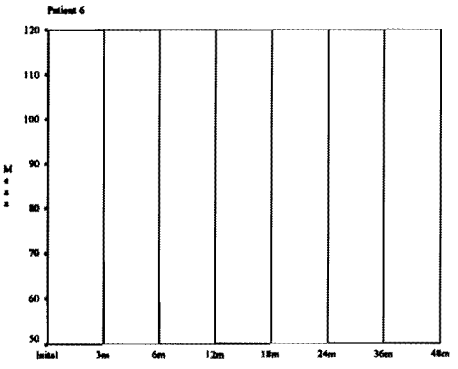


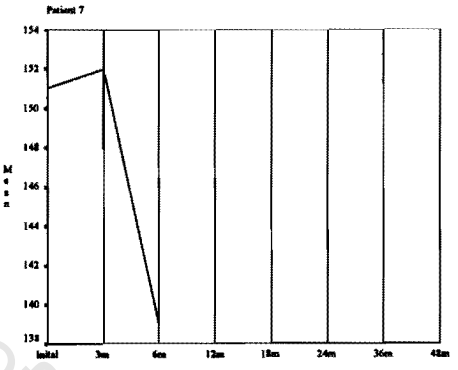


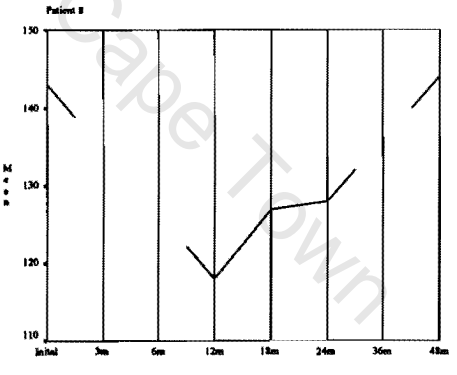


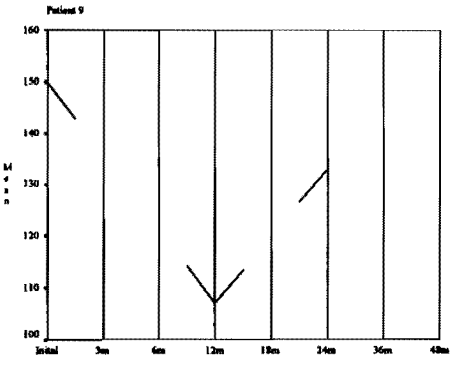






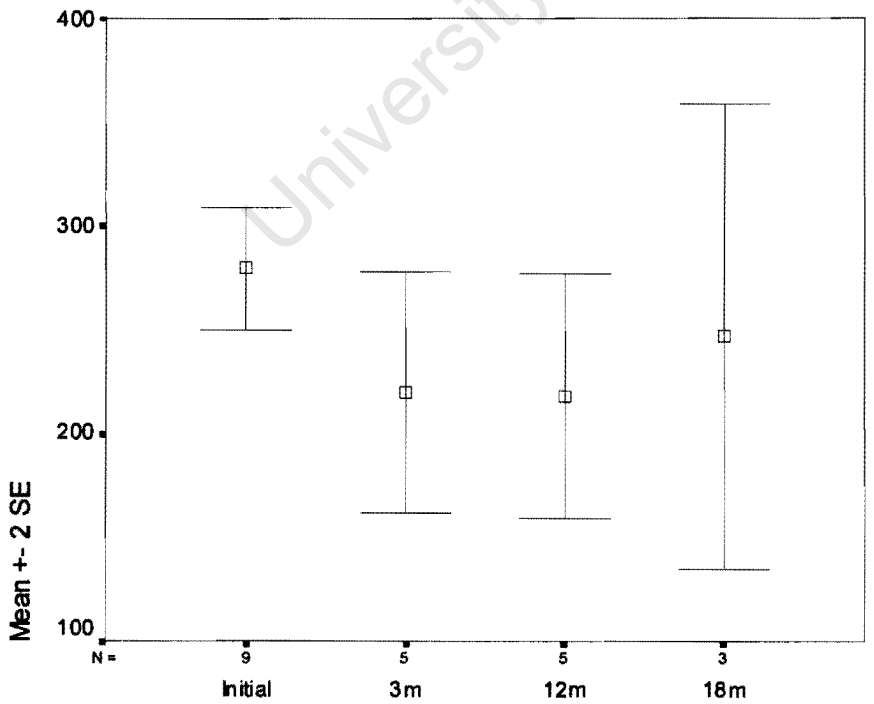






RV in % predicted

Pt.Nr.	preop	3m	6m	12m	18m	24m	36m	48m	60m
1	280	188	206	245					
2	301			310					
3		185			354				
4	286	181							
5	309	213		217	222		237		
6	209								
7	356	334	330						
8	243			135	165	189		231	199
9	296			184		263			
10	236								
Mean	**280**	**220**		**162**	**247**				
Number	9	5		5	3				



Mean values for residual volume (RV)

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Initial	308.00	4	34.30	17.15
	3m	229.00	4	71.33	35.67
Pair 2	Initial	318.00	2	53.74	38.00
	6m	268.50	2	86.97	61.50
Pair 3	Initial	285.80	5	26.17	11.70
	12m	218.20	5	65.65	29.36
Pair 4	Initial	276.00	2	46.67	33.00
	18m	193.50	2	40.31	28.50
Pair 5	Initial	269.50	2	37.48	26.50
	24m	225.50	2	51.62	36.50
Pair 6	Initial	309.00	1[a]	.	.
	36m	237.00	1[a]	.	.
Pair 7	Initial	243.00	1[a]	.	.
	48m	231.00	1[a]	.	.

a. The correlation and t cannot be computed because the sum of caseweights is less than or equal to 1.

Paired Samples Correlations

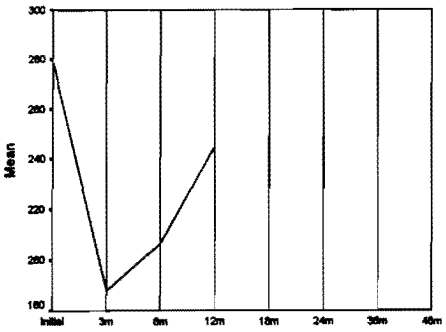
		N	Correlation	Sig.
Pair 1	Initial & 3m	4	.978	.022
Pair 2	Initial & 6m	2	1.000	.000
Pair 3	Initial & 12m	5	.644	.241
Pair 4	Initial & 18m	2	1.000	.000
Pair 5	Initial & 24m	2	1.000	.000

Paired Samples Test

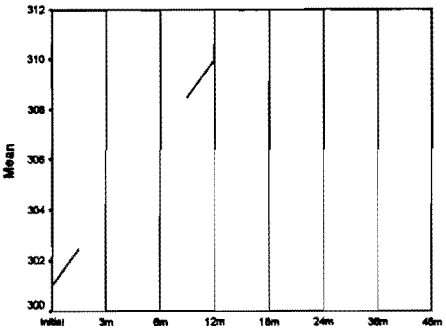
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Initial - 3m	79.00	38.45	19.23	17.81	140.19	4.109	3	.026
Pair 2	Initial - 6m	49.50	33.23	23.50	-249.10	348.10	2.106	1	.282
Pair 3	Initial - 12m	67.60	52.75	23.59	2.11	133.09	2.866	4	.046
Pair 4	Initial - 18m	82.50	6.36	4.50	25.32	139.68	18.333	1	.035
Pair 5	Initial - 24m	44.00	14.14	10.00	-83.06	171.06	4.400	1	.142

Paired t-test (preop to follow up at 3m,6m,12m,24m)

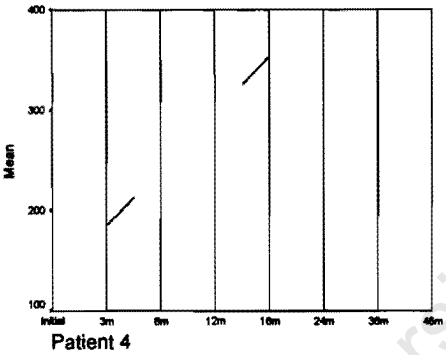
Patient 1



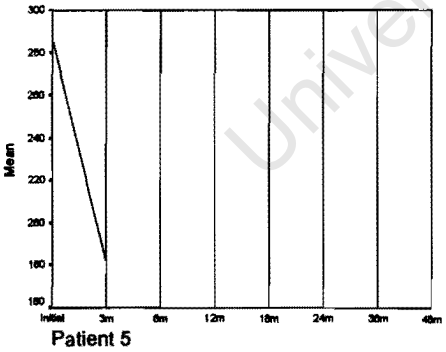
Patient 2



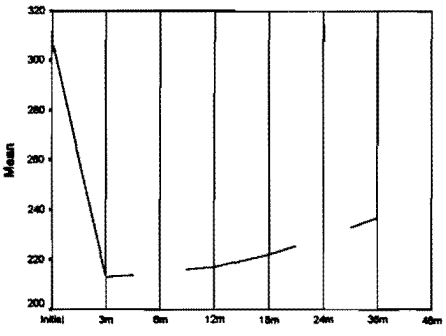
Patient 3



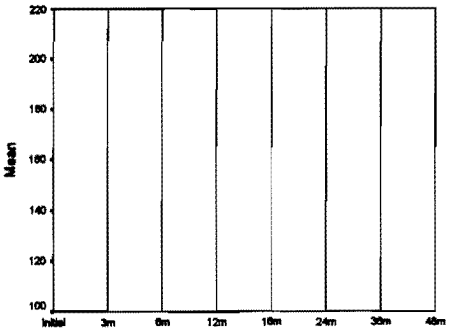
Patient 4



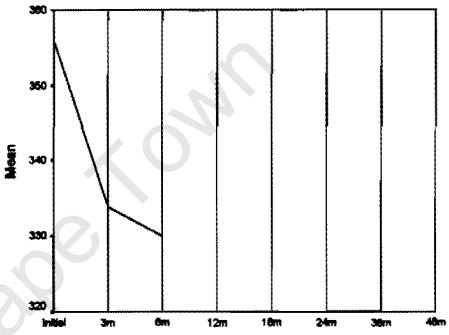
Patient 5



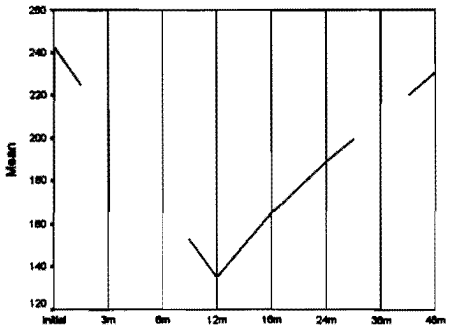
Patient 6



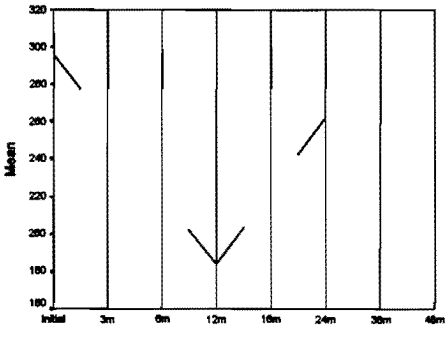
Patient 7



Patient 8

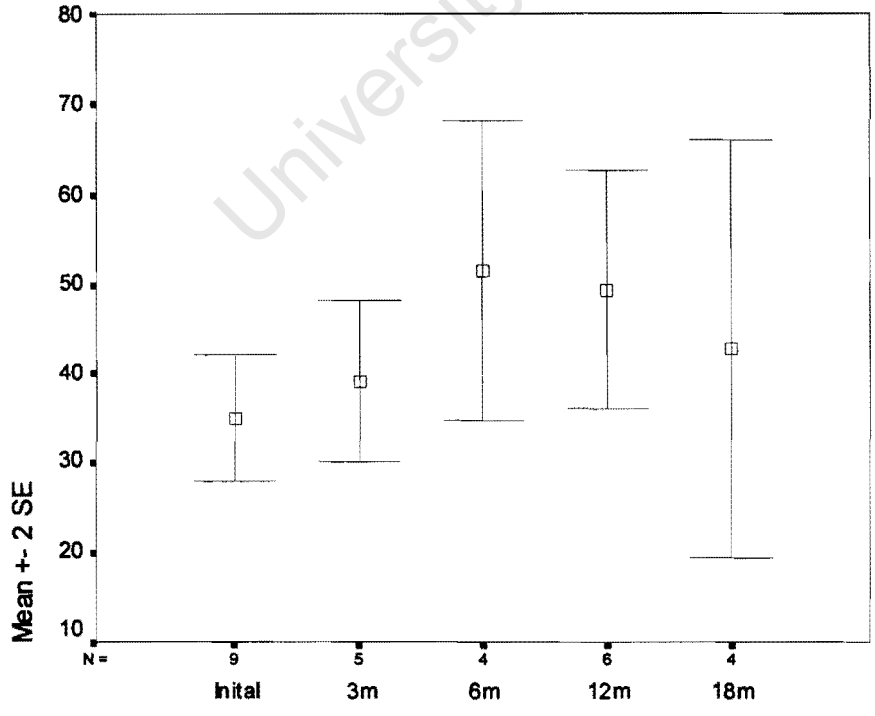


Patient 9



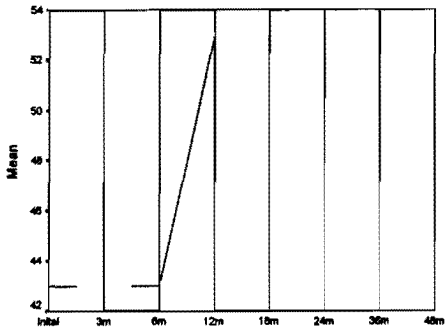
TLCO in % predicted

Pt.Nr.	preop	3m	6m	12m	18m	24m	36m	48m	60m
1	43		43	53					
2	36	43		31					
3			51		19				
4	28	53	75	58					
5	50	41		57	52		54		
6	27	26							
7	32	33	37						
8	51			69	71	68			51
9	25			28	29	26	36		
10	23								
Mean	**35**	**32**	**52**	**49**	**43**				
Number	9	5	4	6	4				

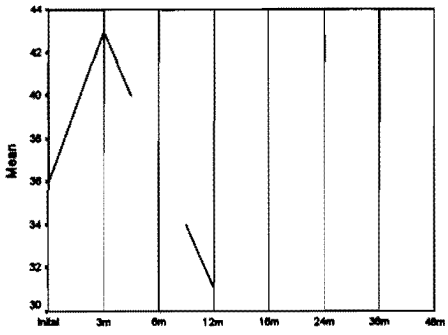


Mean values for diffusion capacity (TLCO single breath method)

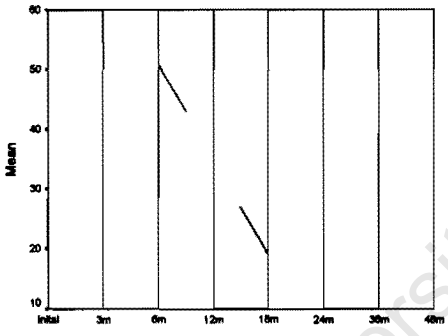
Patient 1



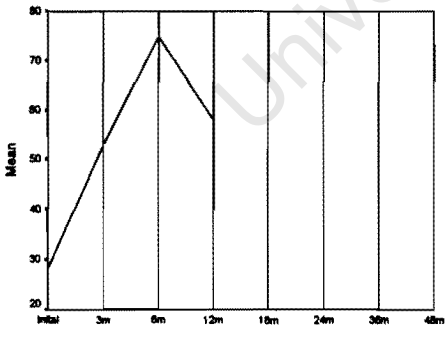
Patient 2



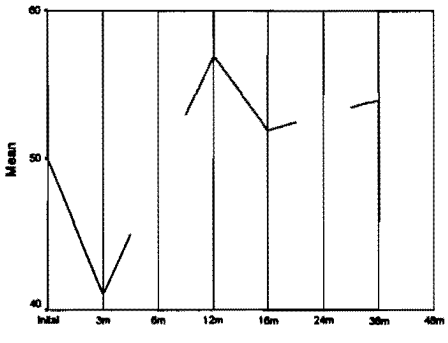
Patient 3



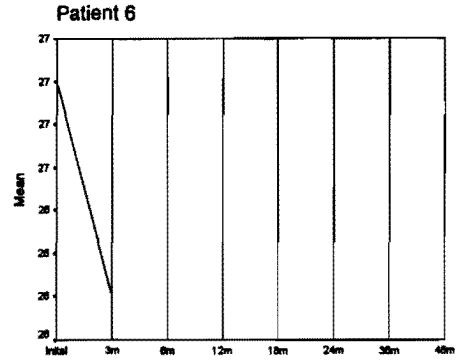
Patient 4



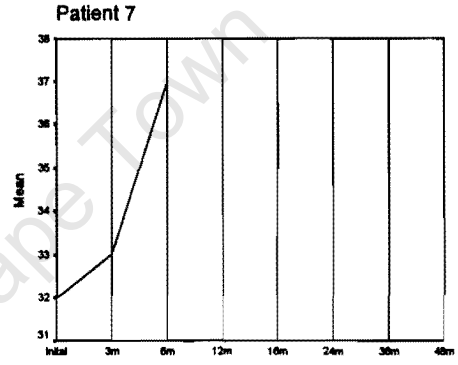
Patient 5



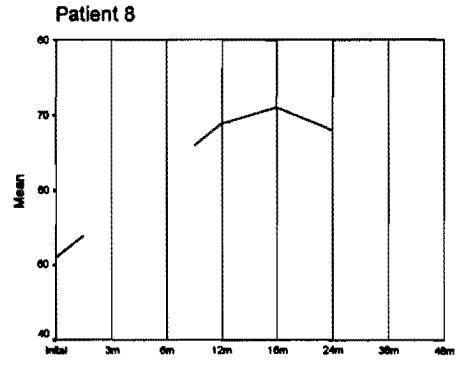
Patient 6



Patient 7



Patient 8



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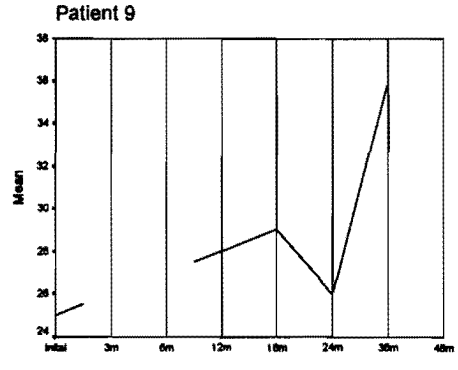
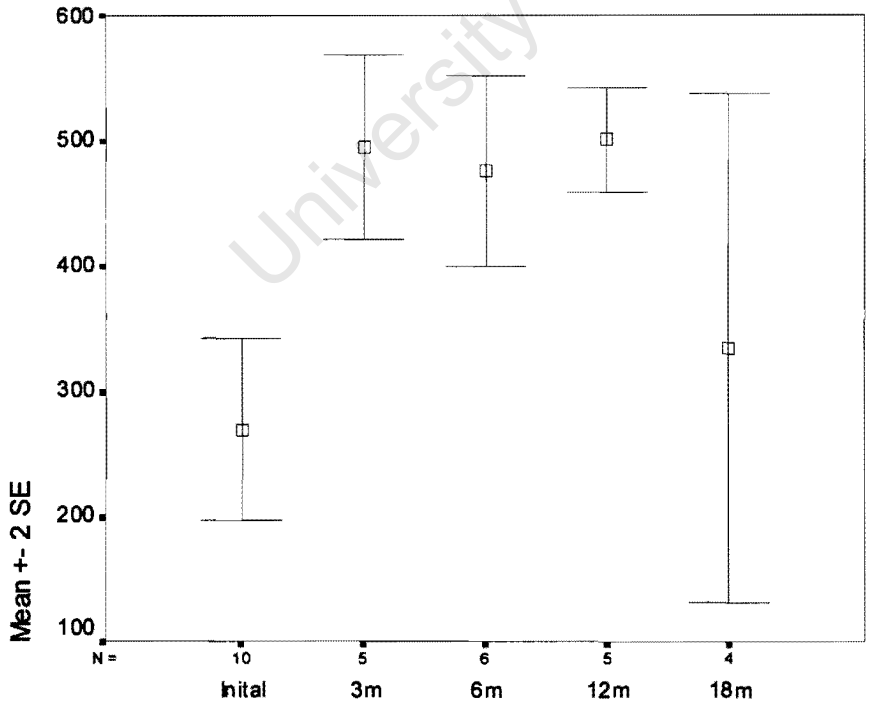


6 min walk test

Pt.Nr.	preop	3m	6m	12m	18m	24m	36m	48m	60m
1	358	447	440	420					
2	360		480	520					
3	70		415		50				
4	246	625	650						
5	385	520		520	525		525		
6	277								
7	75	410	390						
8	325	475		536	415	370		360	
9	350		480	510	350	355			
10	245								
Mean	**269**	**495**	**476**	**501**	**335**				
Number	10	5	6	5	4				



Mean values for the six minute walk test

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Inital	277.80	5	124.79	55.81
	3m	495.40	5	82.85	37.05
Pair 2	Inital	243.17	6	138.94	56.72
	6m	475.83	6	92.43	37.74
Pair 3	Inital	355.60	5	21.55	9.64
	12m	501.20	5	46.34	20.72
Pair 4	Inital	282.50	4	143.79	71.89
	18m	335.00	4	203.27	101.63
Pair 5	Inital	337.50	2	17.68	12.50
	24m	362.50	2	10.61	7.50
Pair 6	Inital	385.00	1[a]	.	.
	36m	525.00	1[a]	.	.
Pair 7	Inital	325.00	1[a]	.	.
	48m	360.00	1[a]	.	.

a. The correlation and t cannot be computed because the sum of caseweights is less than or equal to 1.

Paired Samples Correlations

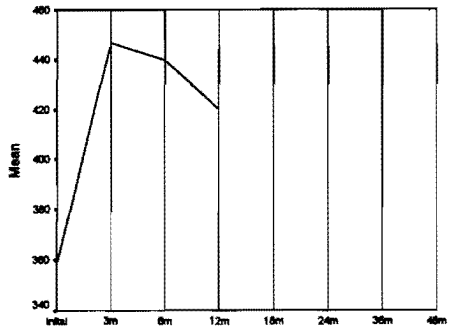
		N	Correlation	Sig.
Pair 1	Inital & 3m	5	.266	.666
Pair 2	Inital & 6m	6	.347	.500
Pair 3	Inital & 12m	5	-.169	.786
Pair 4	Inital & 18m	4	.963	.037
Pair 5	Inital & 24m	2	-1.000	.000

Paired Samples Test

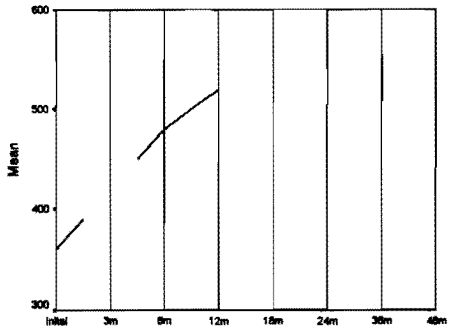
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Inital - 3m	-217.60	130.16	58.21	-379.21	-55.99	-3.738	4	.020
Pair 2	Inital - 6m	-232.67	137.61	56.18	-377.08	-88.25	-4.141	5	.009
Pair 3	Inital - 12m	-145.60	54.30	24.28	-213.02	-78.18	-5.996	4	.004
Pair 4	Inital - 18m	-52.50	75.44	37.72	-172.55	67.55	-1.392	3	.258
Pair 5	Inital - 24m	-25.00	28.28	20.00	-279.12	229.12	-1.250	1	.430

Paired t-test 6 min walk (preop to follow up at 3m,6m,12m,18m,24m)

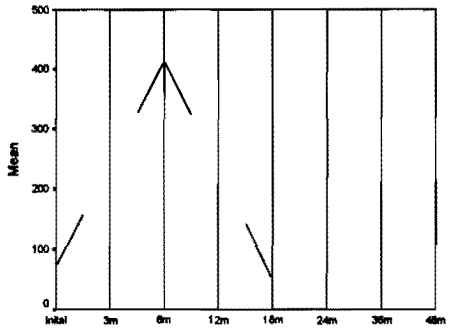
Patient 1



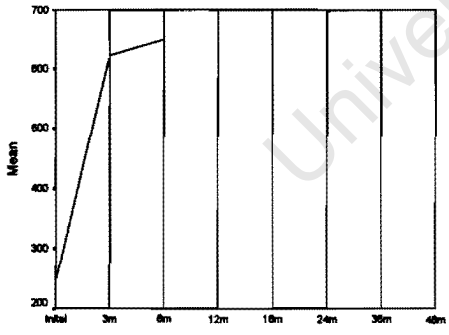
Patient 2



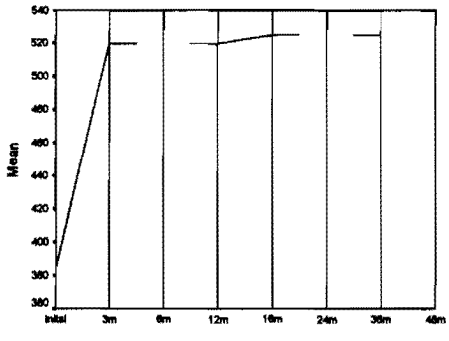
Patient 3



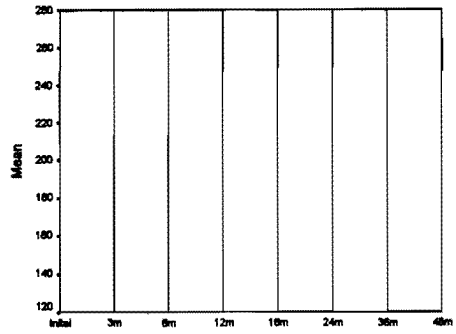
Patient 4



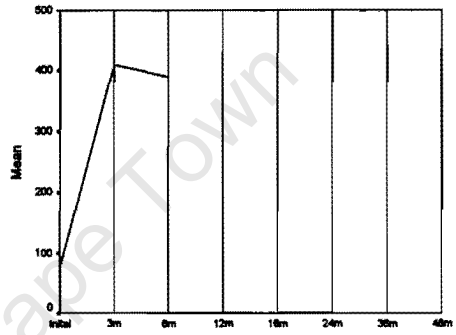
Patient 5



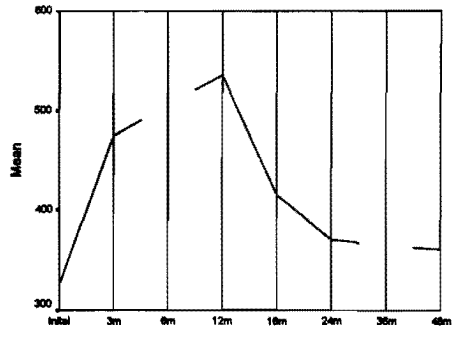
Patient 6



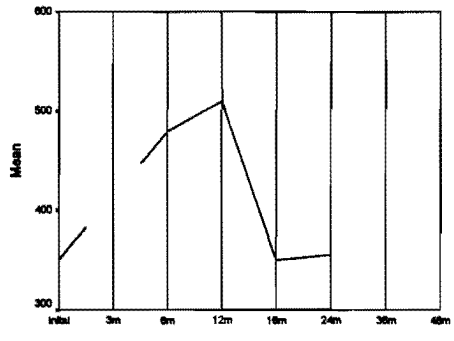
Patient 7



Patient 8



Patient 9



Annexure B

Detailed Listing of all costs

ITEM	2000 COST PER UNIT
Laboratory	
Microbiology: Urine or sputum microscopy	24.30
culture	31.20
Bloodculture	68.80
HIV - Elisa	65.80
Haematology: FBC + Diff	63.10
FBC	52.00
INR	29.70
ptt	29.00
bloodgas	44.60
Chemistry : CEUG	17.92
AST	26.73
ALT	26.73
Albumin	15.39
Total protein	15.39
Bilirubin	23.61
AP	25.64
alpha 1 anti-trypsin	35.60
emergency chemistry and haematology: after hours	50% more after hours
Transfusion: group and screen	99.00
crossmatch	170.00
Red pack cells	300.00
Whole blood	339.00
FFP	277.00
Diagnostic Tests:	
Limited PFT (FEV1/FVC) first visit	236.00
consequent visit	141.60
Full PFT (FEV1/FVC + Body box)	188.80
Transfer factor	113.30
6 min walk test	76.30
VQ scan	499.80
HRCT scan	941.70

CXR 1 view	
2 views	90.40
ECG	42.50
Cardiac echo + colour doppler	217.50
Skin prick test	13.20

Medication:

Antibiotics: Kefzol 1 g iv	5.73
Clindamycin 600 mg iv	21.50
Cefuroxime 750 mg iv	9.69
Gentamycin 240 mg iv	6.72
Penicillin 5 mill iv	4.07
Flagyl 500mg iv	5.52
Flagyl 400mg po tds	0.18
Erythromycin 250 mg po tds	1.16
Bactrim 2 tbl bd	0.25
Amoxycillin 250 mg po tds	0.34
Augmentin 375mg po tds	7.16
Flucloxacillin 500 mg qd	3.37
Analgesia: Morphin 20 mg po (500 ml)	20.00
Morphin 10 mg iv amp	0.83
Morphin 15 mg iv amp	0.86
Voltaren 25 mg po (20 tbl.)	0.84
Voltaren 75 mg im	0.60
Doxyphene po (100 capsules)	32.05
Fentanyl 2ml	4.62
Ketarolac 10mg iv amp	8.50
Brufen 400mg (100 tbl.)	9.05
Valoron 50 mg (20 caps)	28.50
Panadeine (20 tbl.)	2.30
Epidural: Bupivacain 0.5% 10 ml amp	7.58
Bupivacain 0.5% 5 ml amp	3.37
Lignocaine 2% 5ml iv	0.95
Pancuronium 2 ml	5.67
Suxamethonium 2 ml	0.98
Vecuronium 4 mg (1amp)	14.99
Neostigmin	0.92
Etomidate 10 ml	23.03
Propofol 20 ml	51.84
Thiopentone 0.5 g	7.01
Adrenalin iv 1mg/ml	1.14
Atropin iv 0.5mg	0.59
Glycopyrrolate 2ml	1.55

Naloxon iv amp	4.24
Calciumgluconate iv amp	2.03
KCl iv amp	0.83
Ephedrine 50mg/ml	7.80
Solumedrol 500mg	44.90
Hydrocortison 100 mg iv amp	4.02
Prednisone 5mg po (100 tbl.)	6.05
Maxalon iv amp	1.03
Maxalon po (500tbl.)	11.80
Aterax 25mg po (100 tbl.)	60.57
Serepax 10 mg po (250 tbl.)	8.37
Calciparin 5000 I.U. sc	5.82
Heparin 5000IU/ml vial	5.09
Aminophyllin iv amp	0.73
Euphyllin ret po 250 mg (100 tbl.)	11.33
Atrovent aerosol	18.13
nebulizer (x 60)	106.16
Berotec aerosol	11.23
nebulizer (x 60)	26.34
Ventolin aerosol	7.96
nebulizer (x 60)	18.90
po 2 mg (40 caps.)	20.90
po 4+A291 mg (60 caps.)	27.94
Beconase 50 mg aerosol	10.02
Metamucil 250g	21.30

Consumables for the operation:

TA 90 stapler	963.30
GRF Glue	1019.70
Steridrape	34.97
Gloves	14.46
Gown	34.63
Diathermy plate	7.19
Sutures 1 Nylon	4.49
1 PDS	25.30
2-0 Vicryl	6.54
3-0 Vicryl	5.42
Sternal wires	119.69
bulb syringe	15.16
Blades	0.53
Swabs: Abdominal swabs	20.03
Ratex	2.25
Blue cleaning swabs	2.18
Suction tubing	11.43
Urine catheter (silastic)	9.63

Urine meter bag	58.96
Chest drain	15.80
Tubing	6.99
Dressing big	3.21
Dressing small	1.97
Saline por bottle	8.34
Anaesthetics:	
Mask +Filter	28.90
Double lumen tube (Bronchocath) left	317.07
Double lumen tube (Bronchocath) right	1041.01
CVP double lumen	226.95
Percutanous CVP+sheat	154.12
Swan-Ganz cath.	724.40
Epidural minipack	70.06
guidewire 25 cm	41.37
Cannula	2.89
Syringe 2ml	0.39
Syringe 5ml	0.56
Syringe 10ml	0.72
Syringe 20ml	1.12
Needles	0.21
3-way tap	2.69
Airway	1.27
Nasogastric tube + bag	10.41
ECG electrode	1.16
Tegaderm large	6.63
Yankauwer suction	6.92
iv administration set 15 dropper	3.17
Transducer kit	296.82
extension line	5.36
Volatile gases:	
Halothane per minute	0.59
Forane	2.69
Oxygen	1.58
Consumables ICU/ward per day	10.00
Infusion: NACl 1l	10.77
NaCl 200 ml	9.06
NaCl 10 ml	0.83
HAES steril	61.56
Plasmalyte B 200ml	14.01
GMS 1l	9.47
Maintelyte 1l	11.84
Ringers Lactate 1l	10.67
Haemacel 500 ml	14.00
Dextrose 5% 1l	7.98
Dextrose/Saline 1l	11.52
Rehydration 1l	11.32
Water 10 ml	0.47

Water 20 ml	1.02
Infusion set: 15 dropper	3.17
bloodset	4.49
bloodset high capacity	7.70
Dressing Tegaderm large	6.63
Respiratory Therapy:	
Ventilation in ICU first day	354.00
subsequent day	236.00
O2 Therapy one day 5l / min	7.68
Nutrition/Hyperalimentation per day	70.80
Consultations:	
Thoracic Surgeon first visit	162.00
consequent	105.90
in hospital	62.30
Pulmonologist first visit	168.20
consequent	122.10
in hospital	62.30
Anesthesia pre op	99.70
ICU registrar per day	141.60
General practitioner first visit	75.50
consequent	74.80
home visit	113.20
home visit emergency	163.50
one off fee for consultations in hospital/day	149.00
Writing of special motivation (f.e. home oxygen)	56.10
Procedures:	
Bronchoscopy Surgeon/Physician	306.80
Anaethetist	142.50
Bullectomy bilateral via mediansternotomy (1184)	
Surgeon	2067.40
Assistant (20%)	413.40
Anaethetist	261.30
Anaethetist Assistant (66%)	174.20
Wedge resection Surgeon	1722.80
Assistant (20%)+A53	344.56
Anaethetist	261.30
Anaethetist Assistant (66%)	174.20

Repeat thoracotomy Surgeon	1652.00
Anaethetist	285.00
Open lung biopsy Surgeon	542.80
Anaethetist	261.30
Arterial line insertion	118.00
Epidural cath. Insertion	169.90
CVP line insertion via peripheral vein	47.20
CVP line insertion via central vein	118.00
Swan Ganz cath. Insertion	236.00
PCA pump supervision (once off charge)	141.60

Physiotherapy and Rehabilitation:

Rehabilitation program /day	48.20
Chest physio percussion	21.90
breathing exercise	21.90
nebulization	32.90

Hospital stay overheads

ward per day	469.00
ICU per day	2073.00

Outpatient treatment:	State tender/whole sale
Medication:	
Antibiotics:	
Amoxil/Augmentin (5 days course)	37.50 / 101.60
Cefuroxime (5 days course)	145.35 / 632.40
Erythromycin (5 days course)	5.81 / 26.48
Bactrim 2 tbl bd (5 days course)	1.25 / 10.04
Aerosols:	
Atrovent aerosol refill	18.13 / 62.45
nebulizer (20ml)	35.39 / 54.57
Beconase 50 mg aerosol	10.02 / 124.96
Berotec aerosol refill	11.23 / 52.55
nebulizer (20ml)	8.78 / 36.33
Ventolin aerosol refill	7.96 / 21.73
nebulizer (20ml)	6.30 / 17.47
Inflamide + Spacer	not available / 261.00
Others:	
Prednisone 5 mg (1000 tbl)	60.50 / 124.67
Euphyllin ret. tbl. (60)	6.80 / 82.67
Moduretic 25 mg (100 tbl)	9.19 / 44.93
Influenza vaccination	13.16 / 31.64
Multi vitamins (30 tbl)	not available / 1.97
Mistabron	not available / 60.19

Oxygen therapy:	
concentrator vital air medical aid pat./month	695.00
concentrator vital air state pat./month	610.00
Cylinder 2 kg lasts 4-6 h on 5l/min	107.13
Cylinder 4.9 kg lasts 12-15 h on 5l/min	169.00
Cylinder 9.7 kg lasts 24-30 h on 5ml/min	263.12
Rental equipment/month	105.00
General practitioner	75.50
General practitioner home visit	113.20
Psychologist	168.20
Physiotherapy	43.60
Occupational therapist visit at home	50.00
at the hospital incl. Transport/ session	41.00
Home care:	
Nurse full time 12 h shift	271.20
Sunday	406.80
part time/ per hour	22.60
Sunday	33.90
one home visit	87.00
Sunday	130.50

Annexure C:

THE MOS 36-ITEM SHORT-FORM HEALTH SURVEY (SF-36)

INSTRUCTIONS: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

(circle one)

Excellent 1

Very good 2

Good 3

Fair 4

Poor 5

2. Compared to one year ago, how would you rate your health in general now?

(circle one)

Much better now than one year ago 1

Somewnat better now than one year ago 2

About the same as one year ago 3

Somewhat worse now than one year ago 4

Much worse now than one year ago 5

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(circle one number on each line)

ACTIVITIES	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c. Lifting or carrying groceries	1	2	3
d. Climbing **several** flights of stairs	1	2	3
e. Climbing **one** flight of stairs	1	2	3
f. Bending, kneeling, or stooping	1	2	3
g. Walking **more than a mile**	1	2	3
h. Walking **several blocks**	1	2	3
i. Walking **one block**	1	2	3
j. Bathing or dressing yourself	1	2	3

4. During the ~~past~~ 4 weeks, have you had any of the following problems with your work or other regular daily activities *as a result of your physical health*?

(circle one number on each line)

	YES	NO
a. Cut down on the **amount of time** you spent on work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Were limited in the **kind** of work or other activities	1	2
d. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

5. During the past 2 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(circle one number on each line)

	YES	NO
a. Cut down the amount of time you spent on work or other activities	1	2
b. Accomplished less than you would like	1	2
c. Didn't do work or other activities as carefully as usual	1	2

6. During the past 2 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

(circle one)

Not at all 1

Slightly 2

Moderately 3

Quite a bit 4

Extremely 5

7. How much bodily pain have you had during the past 2 weeks?

(circle one)

None 1

Very mild 2

Mild 3

Moderate 4

Severe 5

Very severe 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one)

Not at all 1

A little bit 2

Moderately 3

Quite a bit 4

Extremely 5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks -

(circle one number on each line)

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
a. Did you feel full of pep?	1	2	3	4	5	6
b. Have you been a very nervous person?	1	2	3	4	5	6
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d. Have you felt calm and peaceful?	1	2	3	4	5	6
e. Did you have a lot of energy?	1	2	3	4	5	6
f. Have you felt downhearted and blue?	1	2	3	4	5	6
g. Did you feel worn out?	1	2	3	4	5	6
h. Have you been a happy person?	1	2	3	4	5	6
i. Did you feel tired?	1	2	3	4	5	6

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(circle one)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

None of the time 5

11. How TRUE or FALSE is each of the following statements for you?

(circle one number on each line)

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
a. I seem to get sick a little easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

CHRONIC RESPIRATORY INDEX QUESTIONNAIRE

First Administration, 7 Point Scale

INTERVIEWER FORM

This questionnaire is designed to find out how you have been feeling during the last 2 weeks. You will be asked about how short of breath you have been, how tired you have been feeling and how your mood has been.

1. I would like you to think of the activities that you have done during the last 2 weeks that have made you feel short of breath. These should be activities which you do frequently and which are important in your day-to-day life. Please list as many activities as you can that you have done during the last 2 weeks that have made you feel short of breath.

   [CIRCLE THE NUMBER ON THE ANSWER SHEET LIST ADJACENT TO EACH ACTIVITY MENTIONED. IF AN ACTIVITY MENTIONED IS NOT ON THE LIST, WRITE IT IN, IN THE RESPONDENT'S OWN WORDS, IN THE SPACE PROVIDED]

   Can you think of any other activities you have done during the last 2 weeks that have made you feel short of breath?

   [RECORD ADDITIONAL ITEMS]

2. I will now read a list of activities which make some people with lung problems feel short of breath. I will pause after each item long enough for you to tell me if you have felt short of breath doing that activity during the last 2 weeks. If you haven't done the activity during the last 2 weeks, just answer 'NO'. The activities are:

   [READ ITEMS, OMITTING THOSE WHICH RESPONDENT HAS VOLUNTEERED SPONTANEOUSLY. PAUSE AFTER EACH ITEM TO GIVE RESPONDENT A CHANCE TO INDICATE WHETHER HE/SHE HAS BEEN SHORT OF BREATH WHILE PERFORMING THAT ACTIVITY DURING THE LAST WEEK. CIRCLE THE NUMBER ADJACENT TO APPROPRIATE ITEMS ON ANSWER SHEET]

1. BEING ANGRY OR UPSET
2. HAVING A BATH OR SHOWER
3. BENDING
4. CARRYING, SUCH AS CARRYING GROCERIES
5. DRESSING
6. EATING
7. GOING FOR A WALK
8. DOING YOUR HOUSEWORK
9. HURRYING
10. MAKING A BED
11. MOPPING OR SCRUBBING THE FLOOR
12. MOVING FURNITURE
13. PLAYING WITH CHILDREN OR GRANDCHILDREN
14. PLAYING SPORTS
15. REACHING OVER YOUR HEAD
16. RUNNING, SUCH AS FOR A BUS
17. SHOPPING
18. WHILE TRYING TO SLEEP
19. TALKING
20. VACUUMING
21. WALKING AROUND YOUR OWN HOME
22. WALKING UPHILL
23. WALKING UPSTAIRS
24. WALKING WITH OTHERS ON LEVEL GROUND
25. PREPARING MEALS

3.a) Of the items which you have listed, which is the most important to you in your day-to-day life? I will read through the items, and when I am finished, I would like you to tell me which is the most important.

[READ THROUGH ALL ITEMS SPONTANEOUSLY VOLUNTEERED AND THOSE FROM THE LIST WHICH PATIENT MENTIONED]

Which of these items is most important to you in your day-to-day life?

[LIST ITEM ON RESPONSE SHEET]

b) Of the remaining items, which is the most important to you in your day-to-day life? I will read through the items, and when I am finished, I would like you to tell me which is the most important.

[READ THROUGH REMAINING ITEMS]

Which of these items is most important to you in your day-to-day life?

[LIST ITEM ON RESPONSE SHEET]

c) Of the remaining items, which is most important to you in your day-to-day life?

[LIST ITEM ON RESPONSE SHEET]

d) Of the remaining items, which is the most important to you in your day-to-day life?

[LIST ITEM ON RESPONSE SHEET]

e) Of the remaining items, which is the most important to you in your day-to-day life?

[LIST ITEM ON RESPONSE SHEET]

[FOR ALL SUBSEQUENT QUESTIONS, ENSURE RESPONDENT HAS APPROPRIATE RESPONSE CARD IN FRONT OF THEM BEFORE STARTING QUESTION]

4. I would now like you to describe how much shortness of breath you have experienced during the last 2 weeks while doing the five most important activities you have selected.

a) Please indicate how much shortness of breath you have had during the last 2 weeks while [INTERVIEWER: INSERT ACTIVITY LIST IN 3a] by choosing one of the following options from the card in front of you: [GREEN CARD]

1 EXTREMELY SHORT OF BREATH
2 VERY SHORT OF BREATH
3 QUITE A BIT SHORT OF BREATH
4 MODERATE SHORTNESS OF BREATH
5 SOME SHORTNESS OF BREATH
6 A LITTLE SHORTNESS OF BREATH
7 NOT AT ALL SHORT OF BREATH

b) Please indicate how much shortness of breath you have had during the last 2 weeks while [INTERVIEWER: INSERT ACTIVITY LISTED IN 3b] by choosing one of the following options from the card in front of you: [GREEN CARD]

1 EXTREMELY SHORT OF BREATH
2 VERY SHORT OF BREATH
3 QUITE A BIT SHORT OF BREATH
4 MODERATE SHORTNESS OF BREATH
5 SOME SHORTNESS OF BREATH
6 A LITTLE SHORTNESS OF BREATH
7 NOT AT ALL SHORT OF BREATH

c) Please indicate how much shortness of breath you have had during the last 2 weeks while [INTERVIEWER: INSERT ACTIVITY LIST IN 3c] by choosing one of the following options from the card in front of you: [GREEN CARD]

1 EXTREMELY SHORT OF BREATH
2 VERY SHORT OF BREATH
3 QUITE A BIT SHORT OF BREATH
4 MODERATE SHORTNESS OF BREATH
5 SOME SHORTNESS OF BREATH
6 A LITTLE SHORTNESS OF BREATH
7 NOT AT ALL SHORT OF BREATH

d) Please indicate how much shortness of breath you have had during the last 2 weeks while [INTERVIEWER: INSERT ACTIVITY LISTED IN 3d] by choosing one of the following options from the card in front of you: [GREEN CARD]

1 EXTREMELY SHORT OF BREATH
2 VERY SHORT OF BREATH
3 QUITE A BIT SHORT OF BREATH
4 MODERATE SHORTNESS OF BREATH
5 SOME SHORTNESS OF BREATH
6 A LITTLE SHORTNESS OF BREATH
7 NOT AT ALL SHORT OF BREATH

e) Please indicate how much shortness of breath you have had during the last 2 weeks while [INTERVIEWER: INSERT ACTIVITY LISTED IN 3e] by choosing one of the following options from the card in front of you: [GREEN CARD]

1 EXTREMELY SHORT OF BREATH
2 VERY SHORT OF BREATH
3 QUITE A BIT SHORT OF BREATH
4 MODERATE SHORTNESS OF BREATH
5 SOME SHORTNESS OF BREATH
6 A LITTLE SHORTNESS OF BREATH
7 NOT AT ALL SHORT OF BREATH

5. In general, how much of the time during the last 2 weeks have you felt frustrated or impatient? Please indicate how often during the last 2 weeks you have felt frustrated or impatient by choosing one of the following options from the card in front of you: [BLUE CARD]

1 ALL OF THE TIME
2 MOST OF THE TIME
3 A GOOD BIT OF THE TIME
4 SOME OF THE TIME
5 A LITTLE OF THE TIME
6 HARDLY ANY OF THE TIME
7 NONE OF THE TIME

6. How often during the past 2 weeks did you have a feeling of fear or panic when you had difficulty getting your breath? Please indicate how often you had a feeling of fear or panic when you had difficulty getting your breath by choosing one of the following options from the card in front of you: [BLUE CARD]

    1 ALL OF THE TIME
    2 MOST OF THE TIME
    3 A GOOD BIT OF THE TIME
    4 SOME OF THE TIME
    5 A LITTLE OF THE TIME
    6 HARDLY ANY OF THE TIME
    7 NONE OF THE TIME

7. What about fatigue? How tired have you felt over the last 2 weeks? Please indicate how tired you have felt over the last 2 weeks by choosing one of the following options from the card in front of you: [ORANGE CARD]

    1 EXTREMELY TIRED
    2 VERY TIRED
    3 QUITE A BIT OF TIREDNESS
    4 MODERATELY TIRED
    5 SOMEWHAT TIRED
    6 A LITTLE TIRED
    7 NOT AT ALL TIRED

8. How often during the last 2 weeks have you felt embarrassed by your coughing or heavy breathing? Please indicate how much of the time you felt embarrassed by your coughing or heavy breathing by choosing one of the following options from the card in front of you: [BLUE CARD]

    1 ALL OF THE TIME
    2 MOST OF THE TIME
    3 A GOOD BIT OF THE TIME
    4 SOME OF THE TIME
    5 A LITTLE OF THE TIME
    6 HARDLY ANY OF THE TIME
    7 NONE OF THE TIME

9. In the last 2 weeks, how much of the time did you feel very confident and sure that you could deal with your illness? Please indicate how much of the time you felt very confident and sure that you could deal with your illness by choosing one of the following options from the card in front of you: [YELLOW CARD]

    1 NONE OF THE TIME
    2 A LITTLE OF THE TIME
    3 SOME OF THE TIME
    4 A GOOD BIT OF THE TIME
    5 MOST OF THE TIME
    6 ALMOST ALL OF THE TIME
    7 ALL OF THE TIME

10. How much energy have you had in the last 2 weeks? Please indicate how much energy you have had by choosing one of the following options from the card in front of you: [PINK CARD]

    1 NO ENERGY AT ALL
    2 A LITTLE ENERGY
    3 SOME ENERGY
    4 MODERATELY ENERGETIC
    5 QUITE A BIT OF ENERGY
    6 VERY ENERGETIC
    7 FULL OF ENERGY

11. In general, how much of the time did you feel upset, worried, or depressed during the last 2 weeks? Please indicate how much of the time you felt upset, worried, or depressed during the past 2 weeks by choosing one of the following options from the card in front of you. [BLUE CARD]

    1 ALL OF THE TIME
    2 MOST OF THE TIME
    3 A GOOD BIT OF THE TIME
    4 SOME OF THE TIME
    5 A LITTLE OF THE TIME
    6 HARDLY ANY OF THE TIME
    7 NONE OF THE TIME

12. How often during the last 2 weeks did you feel you had complete control of your breathing problems? Please indicate how often you felt you had complete control of your breathing problems by choosing one of the following options from the card in front of you: [YELLOW CARD]

    1 NONE OF THE TIME
    2 A LITTLE OF THE TIME
    3 SOME OF THE TIME
    4 A GOOD BIT OF THE TIME
    5 MOST OF THE TIME
    6 ALMOST ALL OF THE TIME
    7 ALL OF THE TIME

13. How much of the time during the last 2 weeks did you feel relaxed and free of tension? Please indicate how much of the time you felt relaxed and free of tension by choosing one of the following options from the card in front of you: [YELLOW CARD]

    1 NONE OF THE TIME
    2 A LITTLE OF THE TIME
    3 SOME OF THE TIME
    4 A GOOD BIT OF THE TIME
    5 MOST OF THE TIME
    6 ALMOST ALL OF THE TIME
    7 ALL OF THE TIME

14. How often during the last 2 weeks have you felt low in energy? Please indicate how often during the last 2 weeks you have felt low in energy by choosing one of the following options from the card in front of you: [BLUE CARD]

    1 ALL OF THE TIME
    2 MOST OF THE TIME
    3 A GOOD BIT OF THE TIME
    4 SOME OF THE TIME
    5 A LITTLE OF THE TIME
    6 HARDLY ANY OF THE TIME
    7 NONE OF THE TIME

15. In general, how often during the last 2 weeks have you felt discouraged or down in the dumps? Please indicate how often during the last 2 weeks you felt discouraged or down in the dumps by choosing one of the following options from the card in front of you: [BLUE CARD]

1 ALL OF THE TIME
2 MOST OF THE TIME
3 A GOOD BIT OF THE TIME
4 SOME OF THE TIME
5 A LITTLE OF THE TIME
6 HARDLY ANY OF THE TIME
7 NONE OF THE TIME

16. How often during the last 2 weeks have you felt worn out or sluggish? Please indicate how much of the time you felt worn out or sluggish by choosing one of the following options from the card in front of you: [BLUE CARD]

1 ALL OF THE TIME
2 MOST OF THE TIME
3 A GOOD BIT OF THE TIME
4 SOME OF THE TIME
5 A LITTLE OF THE TIME
6 HARDLY ANY OF THE TIME
7 NONE OF THE TIME

17. How happy, satisfied, or pleased have you been with your personal life during the last 2 weeks? Please indicate how happy, satisfied or pleased you have been by choosing one of the following options from the card in front of you: [GRAY CARD]

1 VERY DISSATISFIED, UNHAPPY MOST OF THE TIME
2 GENERALLY DISSATISFIED, UNHAPPY
3 SOMEWHAT DISSATISFIED, UNHAPPY
4 GENERALLY SATISFIED, PLEASED
5 HAPPY MOST OF THE TIME
6 VERY HAPPY MOST OF THE TIME
7 EXTREMELY HAPPY, COULD NOT HAVE BEEN MORE SATISFIED OR PLEASED

18. How often during the last 2 weeks did you feel upset or scared when you had difficulty getting your breath? Please indicate how often during the past 2 weeks you felt upset or scared when you had difficulty getting your breath by choosing one of the following options from the card in front of you: [BLUE CARD]

1 ALL OF THE TIME
2 MOST OF THE TIME
3 A GOOD BIT OF THE TIME
4 SOME OF THE TIME
5 A LITTLE OF THE TIME
6 HARDLY ANY OF THE TIME
7 NONE OF THE TIME

19. In general, how often during the last 2 weeks have you felt, restless, tense, or uptight? Please indicate how often you have felt restless, tense, or uptight by choosing one of the following options from the card in front of you: [BLUE CARD]

1 ALL OF THE TIME
2 MOST OF THE TIME
3 A GOOD BIT OF THE TIME
4 SOME OF THE TIME
5 A LITTLE OF THE TIME
6 HARDLY ANY OF THE TIME
7 NONE OF THE TIME

CRQ RESPONSE SHEET

1. BEING ANGRY OR UPSET
2. HAVING A BATH OR SHOWER
3. BENDING
4. CARRYING, SUCH AS CARRYING GROCERIES
5. DRESSING
6. EATING
7. GOING FOR A WALK
8. DOING YOUR HOUSEWORK
9. HURRYING
10. MAKING A BED
11. MOPPING OR SCRUBBING THE FLOOR
12. MOVING FURNITURE
13. PLAYING WITH CHILDREN OR GRANDCHILDREN
14. PLAYING SPORTS
15. REACHING OVER YOUR HEAD
16. RUNNING, SUCH AS FOR A BUS
17. SHOPPING
18. WHILE TRYING TO SLEEP
19. TALKING
20. VACUUMING
21. WALKING AROUND YOUR OWN HOME
22. WALKING UPHILL
23. WALKING UPSTAIRS
24. WALKING WITH OTHERS ON LEVEL GROUND
25. PREPARING MEALS

OTHER ACTIVITIES

_____

_____

_____

_____

_____

Activity 3a) _____

Activity 3b) _____

Activity 3c) _____

Activity 3d) _____

Activity 3e) _____

'Y/11

CHRONIC RESPIRATORY DISEASE INDEX QUESTIONNAIRE

Follow-up, 7 Point Scale, Informed

You have previously completed a questionnaire(s) telling us about how you were feeling and how your lung disease was affecting your life. This is a follow-up questionnaire designed to find out how you have been getting along the last [insert length of time since last seen].

When you are answering the questions this time I will tell you the answer you gave us the last time. I would like you to give your answer today keeping in mind what you said the last time. For example, let's say that last time I asked you how short of breath you were while beating carpets [GIVE RESPONDENT GREEN CARD] and you said "4 Moderate shortness of breath". If you were exactly the same today, you would answer 4 once again. If you were more short of breath you would choose 1, 2, or 3 and if you were less short of breath you would choose 5, 6, or 7.

[FOR QUESTIONS 4a) to 4e) INSERT ACTIVITIES 3a) to 3e) FROM FIRST ADMINISTRATION ANSWER SHEET]

4. I would now like you to describe how much shortness of breath you have experienced during the last two weeks while doing each of the five most important activities you have selected.

   a) Please indicate how much shortness of breath you have had during the last two weeks while [INTERVIEWER: INSERT ACTIVITY LISTED IN 3a] by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [GREEN CARD]

   b) Please indicate how much shortness of breath you have had during the last two weeks while [INTERVIEWER: INSERT ACTIVITY LISTED IN 3b] by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [GREEN CARD]

c) Please indicate how much shortness of breath you have had during the last two weeks while [INTERVIEWER: INSERT ACTIVITY LISTED IN 3c] by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [GREEN CARD]

d) Please indicate how much shortness of breath you have had during the last two weeks while [INTERVIEWER: INSERT ACTIVITY LISTED IN 3d) by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [GREEN CARD]

e) Please indicate how much shortness of breath you had during the last two weeks while [INTERVIEWER: INSERT ACTIVITY LISTED IN 3e] by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [GREEN CARD]

5. In general, how much of the time during the last two weeks have you felt frustrated or impatient? Please indicate how often during the last two weeks you have felt frustrated or impatient by choosing one of the following from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMININSTRATION]. [BLUE CARD]

6. How often during the past two weeks did you have a feeling of fear or panic when you had difficulty getting your breath? Please indicate how often you had a feeling of fear or panic when you had difficulty getting your breath by choosing one of the following options from the card in front of you keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [BLUE CARD]

7. What about fatigue? How tired have you felt over the last two weeks? Please indicate how tired you have felt over the last two weeks by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [ORANGE CARD]

8. How often during the last two weeks have you felt embarrassed by your coughing or heavy breathing? Please indicate how much of the time you felt embarrassed by your coughing or heaving breathing by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [BLUE CARD]

9. In the last two weeks, how much of the time did you feel very confident and sure that you could deal with your illness? Please indicate how much of the time you felt very confident and sure that you could deal with your illness by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [YELLOW CARD]

10. How much energy have you had in the last two weeks? Please indicate how much by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [PINK CARD]

11. In general, how much of the time did you feel upset, worried or depressed during the last two weeks? Please indicate how much of the time you felt upset, worried, or depressed during the last two weeks by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [BLUE CARD]

12. How often during the last two weeks did you feel you had complete control of your breathing problems? Please indicate how often you felt you had complete control of your breathing problems by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [YELLOW CARD]

13. How much of the time during the past two weeks did you feel relaxed and free of tension? Please indicate how much of the time you felt relaxed and free of tension by choosing one of the following options from the card in front of you, keeping mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [YELLOW CARD]

14. How often during the last two weeks have you felt low in energy? Please indicate how often during the last two weeks you have felt low in energy by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTATION]. [BLUE CARD]

15. In general, how often during the last two weeks have you felt discouraged or down in the dumps? Please indicate how often during the last two weeks you have felt discouraged or down in the dumps by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [BLUE CARD]

16. How often during the last two weeks have you felt worn out or sluggish? Please indicate how much of the time you felt worn out or sluggish by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [BLUE CARD]

17. How happy, satisfied, or pleased have you been with your personal life during the last two weeks? Please indicate how happy, satisfied or pleased you have been by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [GRAY CARD]

18. How often during the last two weeks did you feel upset or scared when you had difficulty getting your breath? Please indicate how often during the last two weeks you felt upset or scared when you had difficulty getting your breath by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [BLUE CARD]

19. In general, how often during the last two weeks have you felt restless, tense, or uptight? Please indicate how often you have felt restless, tense, or uptight by choosing one of the following options from the card in front of you, keeping in mind that last time you answered the questionnaire you chose [INSERT PATIENT'S ANSWER FROM PREVIOUS ADMINISTRATION]. [BLUE CARD]

CRQ RESPONSE SHEET (cont'd)

Question_#	Date:_____	Date:_____	Date:_____	Date:_____
4a)	_____	_____	_____	_____
4b)	_____	_____	_____	_____
4c)	_____	_____	_____	_____
4d)	_____	_____	_____	_____
4e)	_____	_____	_____	_____
5.	_____	_____	_____	_____
6.	_____	_____	_____	_____
7.	_____	_____	_____	_____
8.	_____	_____	_____	_____
9.	_____	_____	_____	_____
10.	_____	_____	_____	_____
11.	_____	_____	_____	_____
12.	_____	_____	_____	_____
13.	_____	_____	_____	_____
14.	_____	_____	_____	_____
15.	_____	_____	_____	_____
16.	_____	_____	_____	_____
17.	_____	_____	_____	_____
18.	_____	_____	_____	_____
19.	_____	_____	_____	_____