Special Article

Therapeutic application of collateral ventilation in diffuse pulmonary emphysema: study protocol presentation*

Aplicação terapêutica da ventilação colateral no enfisema pulmonar difuso: apresentação de um protocolo

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Abstract

We present a protocol to test a new surgical procedure for the treatment of patients with diffuse lung emphysema who, after having received the golden standard treatment (pulmonary rehabilitation), continue to present respiratory failure with disabling dyspnea. Ten patients with severe lung hyperinflation will be evaluated. The method proposed is designed to create alternative expiratory passages for air trapped in the emphysematous lung by draining the lung parenchyma, thereby establishing communication between the alveoli and the external environment. The ten patients selected will be required to meet the inclusion criteria and to give written informed consent. Those ten patients will be included in the study pending the approval of the Ethics in Research Committee of the São Paulo Santa Casa School of Medicine, São Paulo, Brazil. The protocol we will employ in order to evaluate the proposed procedure is feasible and will show whether debilitated patients suffering from diffuse pulmonary emphysema can benefit from this procedure, which could represent an alternative to lung transplant or lung volume reduction surgery, the only options currently available.

Keywords: Pulmonary Emphysema; Pulmonary Disease, Chronic Obstructive; Lung, Hyperlucent.

Resumo

Apresentação de um protocolo, para testar uma nova opção de tratamento operatório nos doentes portadores de enfisema pulmonar difuso, nos quais a terapêutica clínica máxima, incluindo a reabilitação pulmonar, foi realizada e ainda assim, existe falência respiratória com dispnéia incapacitante. Serão avaliados dez doentes portadores de hiperinsuflação pulmonar grave. O método propõe promover passagens expiratórias alternativas à via aérea principal para o ar aprisionado no pulmão enfisematoso, por meio de uma drenagem do parênquima pulmonar, comunicando os alvéolos ao meio exterior. Serão selecionados dez doentes, com os consentimentos informados assinados, e com a aprovação do Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da Santa Casa de São Paulo. Os doentes selecionados deverão obedecer os critérios de inclusão para participar deste estudo. O protocolo de avaliação do procedimento proposto é viável e ao final será capaz de mostrar, se de fato há ou não benefício para um doente debilitado e sofrido, quando hoje as únicas soluções são o transplante de pulmão ou a cirurgia redutora de volume pulmonar.

Descritores: Enfisema pulmonar; Doença pulmonar obstrutiva crônica; Pulmão hipertransparente.

The American Thoracic Society defines chronic obstructive pulmonary disease as chronic, progressive airway obstruction, accompanied by chronic bronchitis and emphysema.[1] Chronic bronchitis is defined as a clinical syndrome characterized by chronic cough with mucous or mucopurulent expectoration, for at least three months over a two-year period, when other causes of chronic cough have been ruled out. Pulmonary emphysema is an alteration characterized by an abnormal increase in the air spaces distal to the terminal bronchioles, accompanied by destruction of the alveolar walls.[1]

The treatment for pulmonary emphysema consists of counseling (regarding hygiene and diet), antibiotic therapy, bronchodilator use, oxygen therapy and corticosteroid therapy, as well as administration of mucolytics, immunization and respiratory rehabilitation programs. Despite treatment, the

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decreased functional capacity, in the severe stage, leads to incapacitating dyspnea and respiratory insufficiency.[2] Patients with pulmonary emphysema are unable to exhale appropriately, which leads to lung hyperinflation (air trapping). The debilitating effects of the hyperinflation are extreme respiratory effort and the inability to conduct gas exchanges in satisfactory proportions. For these patients, the only option is surgical treatment: lung volume reduction surgery, lung transplantation or both.[3]

It is important to emphasize that diffuse pulmonary emphysema can be classified as homogeneous, when all lobes are equally affected, and heterogeneous when the pulmonary alterations are unequally distributed. The most common scenario is that of less affected areas in the lower lobes and the most severely affected areas in the upper lobes. Lung volume reduction surgery is only indicated in patients with heterogeneous diffuse pulmonary emphysema, in whom the majority of the affected area of the lung is resected, allowing the remaining tissue to work more efficiently, as well as improving respiratory mechanics.

For patients with heterogeneous diffuse pulmonary emphysema, lung volume reduction surgery and lung transplantation, which are the only remaining treatment options, both result in high cost, high morbidity rates and high mortality rates.

In the present study, our objective was to propose an affordable treatment alternative that can relieve the debilitating effects of emphysema without incurring high rates of morbidity and mortality. To that end, we present a protocol designed to evaluate a new surgical technique based on the so-called collateral ventilation.

Study protocol

In this study, the efficacy of a surgical procedure used in combination with pulmonary drainage will be evaluated in ten patients with severe lung hyperinflation.

Selection of patients

Individuals will be provided with all standard and usual care for the primary diagnosis of emphysema with clinical symptoms of dyspnea prior to, during and after the procedure evaluated.

Enrolled individuals will be informed regarding the procedure, its purpose in the treatment and the objective of the study, after which they will be invited to participate in the study. All participating patients will be required to give written informed consent.

For all participants, the following data will be collected using a form designed to allow subsequent analysis:

1) written informed consent
2) identification and age of the individual; current date
3) documentation showing that the individual meets all of the eligibility criteria
4) anamnesis and results of a complete physical examination
5) Information regarding the routine pre-operative evaluation and the placement of the catheter

Study design

As can observed in Chart 1, the individuals selected will have to undergo the following examinations in the pre-operative period and in the fourth post-operative week:

1) pulmonary function tests - plethysmography:
   - forced vital capacity
   - forced expiratory volume in one second
   - forced expiratory flow between 25 and 75% of forced vital capacity
   - peak expiratory flow
   - forced inspiratory flow at 50% of the inspiratory loop of the flow-volume curve
   - total lung capacity
   - vital capacity
   - functional residual capacity
   - expiratory reserve volume
   - residual volume
   - diffusing capacity of the lung for carbon monoxide (DLCO)
   - DLCO adjusted for the hemoglobin concentration
   - alveolar volume
   - airway resistance
   - airway conductance
   - elasticity
   - inspiratory pressure
   - expiratory pressure
2) six-minute walk test
3) quality of life questionnaires: the Medical Outcomes Study 36-item Short-Form

Chart 1 - Study design.

T0	Diagnosis of pulmonary hyperinflation.
T1	Clinical treatment and pulmonary rehabilitation. Counseling by a pulmonologist. Treatment duration: minimum of 6 months.
T2	Pulmonologist diagnosis of clinical treatment failure. Surgical treatment indicated: lung transplantation, lung volume reduction surgery or both.
T3	Interview with the thoracic surgeon, in which the inclusion criteria in the proposed study will be discussed based on laboratory test results and imaging. In this phase, quality of life questionnaires will be applied.
T4	Patients selected to be included in this study will be informed with the details of the procedures, will give written informed consent and will voluntarily be submitted (or not) to the proposed treatment.
T5	Proposed operation.
T6	Repeat all examinations performed in the pre-operative period, including the quality of life questionnaires, within at least 30 days.

T: time.

Health Survey, the St. George's Respiratory Questionnaire, the Performance Status scale of the Eastern Cooperative Oncology Group and the Medical Research Council Scale

4) chest X-rays during inspiration and expiration
5) high-resolution computed tomography scans of the chest during inspiration and expiration

The cases included in this study should be in accordance with the inclusion and exclusion criteria.

Inclusion criteria

The inclusion criteria were as follows: having been diagnosed with emphysema; not being older than 75 years of age; being incapacitated despite having received the full clinical treatment (pulmonary rehabilitation); presenting evidence of homogeneous or heterogeneous diffuse emphysema on high-resolution tomography scans of the chest; and presenting lung hyperinflation on chest X-rays taken during inspiration and expiration.

Pulmonary function test criteria:

a) post-bronchodilator forced expiratory volume in one second <35-40% of predicted
b) total lung capacity >250% of predicted
c) DLCO <50% of predicted

Additional criteria:

a) cardiac evaluation
b) evaluation of the pre-operative clinical status
c) smoking cessation for 3 to 6 months prior to the procedure
d) being considered a candidate for lung transplantation or lung volume reduction surgery

Exclusion criteria

The following exclusion criteria were applied: presenting bradycardia (heart rate, 50 bpm) at rest; having complex ventricular arrhythmia; presenting sustained ST-segment elevation; having been diagnosed with heart disease (infarction in the previous six months); and presenting a ventricular ejection fraction <45%. In addition, patients presenting interstitial lung disease or pleural disease that might preclude the operation were excluded, as were those with clinically significant bronchiectasis, pulmonary nodules requiring surgery, giant lung bullae (larger than 1/3 of the lung volume), pulmonary arterial hypertension (≥35 mmHg), comorbidities presenting five-year mortality rates >5%, abnormal weight loss (<70 or >130% of ideal body weight), or evidence of systemic disease/neoplasia expected to impair survival.

Surgical technique

1) Patient is taken to the operating room, maintained in the supine position and submitted to local anesthesia, in the sixth intercostal space and extending for 2 cm in each direction, with the objective of performing conventional chest tube drainage in the hemithorax chosen for the performance of the pulmonary drainage. This procedure prevents the occurrence of pneumothorax.

2) Subsequently, a 4- or 5-cm incision is made in the selected hemithorax, under local anesthesia and in the third intercostal space.
3) Careful layer-by-layer dissection is performed until the pleural cavity is reached.
4) Once the pleural cavity has been accessed, the lung parenchyma is secured with forceps in order to be opened safely.
5) Four cardinal sutures are made in order to attach the lung to the parietal pleura.
6) A 2- to 3-cm opening in the lung is sufficient.
7) Through this opening, a tube is affixed to the lung.
8) A fenestrated silicone tube (28-32 F) is introduced 5 cm into the lung.
9) The use of a water seal is not required.

Statistical analysis

1) Explanatory variables
   - Time points: pre-operative period and post-operative day 30
2) Response variables
   - spirometric parameters
   - six-minute walk test
   - quality of life questionnaires
   - radiological evaluation

In the descriptive and inferred analysis, the generalized estimation equations model[4] will be used for the evaluation of qualitative variables, and the paired t-test (parametric) or the nonparametric Wilcoxon test will be used for the evaluation of continuous variables.[5] The level of statistical significance adopted will be 0.05.

This study protocol was submitted to and approved by the Ethics in Human Research Committee of the Santa Casa School of Medical Sciences in São Paulo.

Final comments

The concept of collateral ventilation is not new: it refers to the ventilation of the alveolar structures through passages or canals (Khon, Lambert and Martin pores) which deviate the air from the normal airway.

One aspect of an emphysematous lung is that the flow of communicating air between neighboring air sacs (collateral ventilation) is much more prevalent than it is in a normal lung. This phenomenon was demonstrated using lungs removed during autopsy[6] and later confirmed in a clinical context.[7]

The air circulating between the alveolar air sacs causes lung hyperinflation and is trapped in the parenchyma, since it encounters difficulty in reaching the exterior via the normal airways, which are obstructed.

If the phenomenon of the collateral ventilation could be used to expel the trapped air from the emphysematous lung, potential benefits would include increased expiratory airflow, decreased expiratory work, increased gas exchange, decreased residual volume, decreased dyspnea and increased ventilation/perfusion.

The concept of promoting alternative expiratory passages for the air trapped in the emphysematous lung was suggested by Macklen in 1978.[8]

Although these concepts have been discussed since 1978, there is as yet no accepted procedure or method to effectively remove the air trapped in the emphysematous patient without invasive resection of the pulmonary tissue.

Since 1994, the Surgeons Group at the Santa Casa School of Medical Sciences in São Paulo has been developing surgical procedures, culminating in a viable and quite safe alternative for the removal of this trapped air, thereby testing the concepts here stated.

In 1994, we analyzed the viability of the performance and maintenance of bronchotomy through an experimental study in dogs. In that study, we proved that, after lobectomy, suturing the corresponding proximal bronchial stump to the thoracic wall (bronchotomy) did not affect the life of the animal. The procedure was easily performed and maintained. We concluded that a bronchus of large diameter (lobar) can be exteriorized without harm to the animal.[9]

One option to treat large lung bullae is the technique proposed by Monaldi and modified by Head et al.: drainage and aspiration of the bulla.[10] In 1988, Venn et al. published their experience using the Brompton technique. Under general anesthesia, a 10-cm thoracotomy was performed, including resection of a segment of the costal arch and opening of the bulla (in order to section septa in its interior). Talcum powder was sprayed into the bulla. The authors reported good results, with symptom improvement in 16 of the 17 patients.[11]

The Surgeons Group at the Santa Casa School of Medical Sciences in São Paulo has, since 1997,

used bulla drainage to treat patients with large lung bullae. However, they have made a major modification in the original technique: local, rather than general, anesthesia is used. Therefore, 27 patients were submitted to 31 bulla drainage using thoracotomy under local anesthesia. We concluded that this surgical procedure is minimally invasive, reduces the duration of hospital stays, presents a lower incidence of complications than does conventional treatment (thoracotomy or video-assisted surgery) and carries no mortality risk.[11,12]

With the knowledge acquired (that the bronchus can be sutured to the thoracic wall, without causing any harm, and that the drainage of a large lung bulla can be performed under local anesthesia with good results), we decided to propose and test, in this new study, lung parenchyma drainage using local anesthesia, with the objective of providing an alternative route for the outflow of trapped air in patients whose lungs present diffuse emphysema.

The performance of this procedure is theoretically justified.

1) Individuals submitted to this procedure are severe patients, in whom the clinical treatment, including pulmonary rehabilitation, was performed and yet there is respiratory insufficiency and incapacitating dyspnea.
2) Lung volume reduction surgery or lung transplantation is indicated in these patients.
3) The option of operative treatment that we propose, drainage of the lung parenchyma, is a viable option, since it will allow the emptying of the air trapped in the lung, thus improving respiratory mechanics.
4) Pulmonary parenchyma drainage is a quite safe procedure.
5) Previous experiences with the performance of bronchotomy and bulla drainage allowed this conclusion.
6) It is a simple procedure, and, more importantly, it is performed under local anesthesia, the dangers of general anesthesia therefore being avoided.

The protocol designed to evaluate the proposed procedure is viable. At the study endpoint, the results of the evaluation will show whether or not the procedure can benefit debilitated patients suffering from diffuse pulmonary emphysema, for whom the only solutions currently available are lung transplantation and lung volume reduction surgery.

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