

## Therapeutic application of collateral ventilation with pulmonary drainage in the treatment of diffuse emphysema: report of the first three cases\*

Aplicação terapêutica da ventilação colateral com drenagem pulmonar no tratamento do enfisema pulmonar difuso: relato dos três primeiros casos

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### Abstract

**Objective:** To report the results obtained in three patients with diffuse pulmonary emphysema during the pre- and post-operative periods following a new surgical technique: collateral ventilation with lung parenchyma drainage. **Methods:** Patients suffering from pulmonary failure and disabling dyspnea, despite having received the gold standard treatment, including pulmonary rehabilitation, were selected for the evaluation of pulmonary drainage. During the pre- and post-operative periods, patients were submitted to plethysmography and six-minute walk tests, as well as completing the following quality of life questionnaires: Medical Outcomes Study 36-item Short-Form Health Survey, Saint George's Respiratory Questionnaire, Eastern Cooperative Oncology Group Performance Status and Medical Research Council Scale. In all three cases, the post-operative follow-up period was at least 300 days. The tests were performed at the following time points: during the pre-operative period; between post-operative days 30 and 40; and on post-operative day 300. Data were analyzed using profile plots of the means. **Results:** When the results obtained in the pre-operative period were compared to those obtained at the two post-operative time points evaluated, improvements were observed in all parameters studied. **Conclusions:** The results suggest that the surgical technique proposed for the treatment of patients suffering from severe diffuse emphysema successfully reduces the debilitating symptoms of these patients, improving their quality of life considerably.

**Keywords:** Pulmonary emphysema; Lung diseases, obstructive; Lung, hyperlucent.

### Resumo

**Objetivo:** Relatar os resultados obtidos no pré- e pós-operatório de três pacientes portadores de enfisema pulmonar difuso grave, empregando uma nova técnica: ventilação colateral com drenagem do parênquima pulmonar. **Métodos:** Para a avaliação da drenagem pulmonar, foram selecionados pacientes que já haviam sido submetidos à terapêutica clínica máxima, incluindo a reabilitação pulmonar, e que ainda assim sofriam de falência respiratória com dispnéia incapacitante. Os pacientes foram submetidos, no pré- e no pós-operatório, à pletismografia e ao teste da caminhada de seis minutos, assim como responderam aos seguintes questionários de qualidade de vida: *Medical Outcomes Study 36-item Short-Form Health Survey*, *Saint George's Respiratory Questionnaire*, *Eastern Cooperative Oncology Group Performance Status* e *Medical Research Council Scale*. Todos os pacientes tiveram seguimento de no mínimo 300 dias de pós-operatório. Os testes foram realizados no pré-operatório, entre 30 e 40 dias de pós-operatório e após 300 dias de pós-operatório. Os dados foram analisados pelo método de gráficos de perfis de médias. **Resultados:** Quando comparados os resultados do pré-operatório com os do pós-operatório nos dois momentos, verificou-se que houve melhora em todos os parâmetros estudados. **Conclusões:** Os resultados sugerem que a técnica operatória proposta para o tratamento de doentes portadores de enfisema pulmonar difuso grave foi capaz de diminuir os sintomas debilitantes destes pacientes, tornando sua qualidade de vida muito melhor.

**Descritores:** Enfisema pulmonar; Pneumopatias obstrutivas; Pulmão hipertransparente.

### Introduction

In a previous study, we proposed a protocol to test a new surgical treatment for patients with diffuse pulmonary emphysema, based on the concept of collateral ventilation (in press). The concept of collateral ventilation is not new, having been described in 1930.<sup>(1)</sup> In normal venti-

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lation, the inhaled and exhaled air flows through the respiratory airways, since there is no obstruction to this flow. However, in the patient with emphysema, the airways are obstructed, impeding expiratory flow. Consequently, there is an increase in the intra-alveolar pressure, forcing the air flow to the neighboring alveoli through passages or channels (Khon, Lambert and Martin pores) which divert it from the natural airway.<sup>(2,3)</sup> The air circulating among the alveolar air sacs causes pulmonary hyperinflation and remains trapped in the parenchyma, the consequences of which are all well known. In 1978, a proposal, based on this concept, was made.<sup>(4)</sup> The proposal, which had potential clinical applications, involved the creation of artificial airways (spiracles) from the lung to the exterior, that is, outside the chest wall, which would allow the liberation of (an alternative exit for) the trapped air, decreasing hyperinflation and improving the respiratory mechanics.

The term airway bypass was proposed for the first time in 2003.<sup>(5)</sup> The term was applied to procedures which allowed communication between this trapped air (collateral ventilation) and the main respiratory airway in an extra-anatomical manner, allowing the trapped air to escape from the lung, thus decreasing the hyperinflation.

In a study conducted in 2007,<sup>(6)</sup> patients with severe emphysema were submitted to airway bypass through the endoscopic application of paclitaxel-eluting stents. The patients were submitted to general anesthesia. Subsequently, with the aid of fiberoptic bronchoscopy and Doppler ultrasound, a site in a segmental bronchus, free of blood vessels, was elected. Subsequently, an opening was made in the bronchial wall and the stent was put into place, creating a new passage between the respiratory tree and the adjacent pulmonary tissue. It was concluded that this procedure reduces hyperinflation, improving pulmonary function and reducing dyspnea in selected patients with severe pulmonary emphysema.

Based on these concepts,<sup>(7)</sup> the Santa Casa in São Paulo Group proposed an alternative procedure for the treatment of patients with severe pulmonary emphysema: drainage of the lung parenchyma, creating communication between the lung and the environment (spiracle). We initiated this pilot study 15 months ago.

The clinical and biochemical evolution of three patients submitted to this procedure is described with the objective of showing the results obtained in this period.

## Methods

Patients were included in or excluded from the study based on the criteria detailed below. The inclusion criteria were as follows: having been diagnosed with emphysema, with chest X-ray (inhalation and exhalation) and HRCT evidence of homogeneous or heterogeneous diffuse emphysema showing pulmonary hyperinflation (Figure 1); being less than 75 years of age; being incapacitated despite having received the gold standard treatment (pulmonary rehabilitation) for at least 6 months; postbronchodilator FEV<sub>1</sub> < 30% of predicted; residual volume ≥ 150% of predicted; total lung capacity > 100% of predicted; smoking cessation at least 6 months prior to the procedure; and being considered a candidate for lung transplantation or lung volume reduction surgery.

We elected the following exclusion criteria: having had a myocardial infarction in the preceding six months; presenting a ventricular ejection fraction < 45%; interstitial or pleural disease which could impede the procedure; clinically significant bronchiectasis; pulmonary nodule; giant lung bullae (>1/3 of the lung volume); pulmonary hypertension (= 35 mmHg); comorbidities presenting five-year mortality rates > 50%; abnormal weight loss (< 70% or > 130% of ideal body weight); and evidence of systemic disease/neoplasia expected to impair survival.

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

Prior to, during and after the procedure investigated, enrolled individuals were provided with full care in relation to the clinical evalua-



**Figure 1** - Tomographic view (patient 2) showing lung hyperinflation and severe diffuse emphysema.

tion and diagnosis of the disease (emphysema with clinical symptoms of dyspnea). Individuals were fully informed regarding the procedure and the purpose of the study. All participating patients gave written informed consent. The following data were obtained from all of the participants using forms for subsequent analysis: written informed consent; identification; age; date; documentation showing that the individual met all of the inclusion criteria; anamnesis; significant physical examination findings; and pre-operative evaluation data. The selected patients were submitted to plethysmography and six-minute walk tests, in addition to completing quality of life questionnaires (Medical Outcomes Study 36-item Short-Form Health Survey; Saint George's Respiratory Questionnaire; Eastern Cooperative Oncology Group Performance Status; and Medical Research Council Scale). For all of the patients, the post-operative follow-up period was at least 300 days. The tests were performed at the following time points: during the pre-operative period (T0), between post-operative days 30 and 40 (T1) and on post-operative day 300 (T2).

### ***Surgical technique***

Patients were 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, with the objective of performing conventional chest tube drainage in the hemithorax chosen for the performance of the pulmonary drainage. The choice of the side of the surgery was based on chest X-rays and on HRCT scans of the chest. Subsequently, a 4-cm incision was made in the selected hemithorax, under local anesthesia, in the third intercostal space, in the midclavicular line. Careful layer-by-layer dissection was performed until the pleural cavity was reached. Once the pleural cavity had been accessed, the lung parenchyma was secured with forceps in order to be opened safely. Four cardinal sutures were made in order to attach the lung to the parietal pleura. A 2- to 3-cm opening in the lung was sufficient. Through this opening, a chest tube was introduced (5 to 7 cm into the lung parenchyma) and affixed to the lung. A fenestrated 30 F silicone chest tube was used. The use of water-seal drainage was not required, since a patient can lead a normal life with the tube exposed to the environment (Figure 2). The chest tube is designed to be left in place for the lifetime of the patient. After the surgery, the

patient, awake, was maintained in the postanesthesia care unit for at least 1 h and subsequently taken to the room.

The results for the three first patients submitted to this procedure are described below.

The statistical analysis of the data was performed using profile plots of the means.<sup>(8,9)</sup>

### **Results**

All patients were hospitalized for 3 days. Chest tubes were removed after 24 h.

Patient 1: male, 47 years old, diagnosed with COPD, lung transplantation was indicated.

This patient engaged in no social activities. He had stopped working, and was unable to ascend gentle slopes. He presented various attacks of dyspnea, which required treatment in the emergency room. He was enrolled in a pulmonary rehabilitation program and was monitored by a pulmonologist, receiving gold standard treatment.

He underwent surgery on 21 December 2006. At this writing, he had been in post-operative follow-up for 363 days. No serious complications were reported. He reported resuming work (pushing an ice-cream cart). As a minor complication, he reported pain at the drainage site for a period of 3 months.

Patient 2: male, 62 years old, diagnosed with severe COPD, lung transplantation was indicated.

He reported having had dyspnea for 7 years, with worsening of the symptoms for 3 years. He displayed respiratory arrest 2 years before, having



**Figure 2** - Chest tube put into place at the end of the procedure.

**Table 1** – Results of the plethysmography, six-minute walk tests, and quality of life questionnaires, during the preoperative and post-operative periods.

Variable	Patient 1			Patient 2			Patient 3		
	T0	T1	T2	T0	T1	T2	T0	T1	T2
FEV <sub>1</sub> (% of predicted)	32	34	45	27	41	38	24	28	34
RV (% of predicted)	149	-	117	231	-	118	257	-	204
TLC (% of predicted)	114	-	108	142	-	121	143	-	136
6MWD (m)	320	-	570	170	-	225	150	-	435
MRC (score)	4	0	1	4	1	0	4	0	1
SGRQ (score)	61	21	37	80	17	15	70	23	33
SF-36 (scores)									
Functional Capacity	15	70	55	15	75	45	15	75	85
Physical Limitation	0	100	100	0	100	25	0	100	100
Pain	31	62	87.5	41	90	100	31	100	100
General Health Status	30	82	72	35	82	42	30	57	82
Vitality	35	75	60	80	95	90	35	75	60
Social Aspects	37.5	62.5	62.5	37.5	100	100	37.5	65	65
Emotional Aspects	100	100	100	100	100	100	0	100	100
Mental Health	76	92	92	76	100	90	56	100	92

T0: pre-operative period; T1: between post-operative days 30 and 40; T2: post-operative day 300; RV: residual volume; TLC: total lung capacity; 6MWD: six-minute walk distance; MRC: Medical Research Council score; SGRQ: Saint George's Respiratory Questionnaire; and SF-36: Medical Outcomes Study 36-item Short-Form Health Survey.

been admitted to the intensive care unit and submitted to mechanical ventilation. He reported having been hospitalized, due to frequent infections, at least once a month. He was unable to live alone, since he could not perform even the simplest of tasks, such as showering and eating. Therefore, he lived with his daughter. He was receiving oxygen therapy 18 h per day. He was unable to sleep at night without oxygen therapy. He was enrolled in a pulmonary rehabilitation program and was monitored by a pulmonologist, receiving gold standard treatment.

He underwent surgery on 19 January 2007. At this writing, he had been in post-operative follow-up for 310 days. No serious complications were reported. He was again able to live alone, since he was now able to perform all tasks with rarely any symptoms.

As a minor complication, a hematoma developed in the chest wall.

Patient 3: female, 53 years old, diagnosed with severe COPD, lung transplantation was indicated.

She reported having dyspnea since 2003 (for 4 years). She used oxygen therapy 15 h per day, with a flow of 3 L/min, with the following schedule: 3 h in the morning, 3 h in the afternoon and 9 h at night. She reported experiencing extreme shortness of breath when bathing or ascending a flight of stairs. She had to stop working and was unable to walk. She suffered from constant panic attacks.

She was enrolled in a pulmonary rehabilitation program and was monitored by a pulmonologist, receiving gold standard treatment.

She underwent surgery on 20 January 2007. At this writing, she had been in post-operative follow-up for 310 days. No serious complications were reported. She reported improvement in her disposition, and she was sleeping all night without the use of oxygen therapy. There was no longer any need for emergency room visits due to attacks of dyspnea, and she became more socially active. As a minor complication, she presented cervical emphysema, which regressed a week after surgery.

For all three patients, the results obtained in the examinations carried out at the various time points are listed in Table 1.

In relation to the profile plots of the means of the analyzed variables, the differences between T0 and the other two time points were, in general, greater than those observed between T1 and T2.

The statistical analysis of the results involved only the three patients described. Due to the small sample size, the conclusions have a merely indicative (descriptive) character.

## Discussion

In a recently published experimental study,<sup>(7)</sup> explanted lungs from lung transplant patients were evaluated. In the explanted native lung, a

small opening was made and a silicone tube was inserted in order to create a spiracle. Lungs were then ventilated through the bronchial tree or through transpleural communications. The flow-volume curve and the volume of air recovered from the lungs by the spiracles were determined. Magnetic resonance imaging was employed in order to study the spatial distribution of helium administered through the natural airway or through the spiracles. The authors concluded that, due to the presence of collateral ventilation in the lung with emphysema, the direct communication between the lung parenchyma and the environment improved the respiratory mechanics and, consequently, the ventilation. This study was the final result of many such studies conducted since 1930.<sup>(1)</sup> Therefore, 78 years after the study in which the concept was first defined, the existence of collateral ventilation in healthy lungs has been proven. In 1969, one group of authors measured the resistance of the interalveolar channels and demonstrated that, in the setting of hypertension (emphysema), collateral ventilation becomes fundamentally important for the redistribution of air in the parenchyma, resulting in the development of the pulmonary hyperinflation and all of its consequences.<sup>(2)</sup> In a study conducted in 1978, it was suggested that a new procedure, based on the concept of collateral ventilation, be used for the treatment of patients with emphysema.<sup>(4)</sup> The author of that study stated the following: "Although it seems ridiculous at first, the creation of spiracles, allowing direct air exchanges between the pulmonary parenchyma and the environment, bypassing the normal airways (which are diseased), can produce significant improvement in the ventilation and respiratory mechanics." In addition to these aspects, some authors defend the hypothesis that there are air passages among the pulmonary lobes, so that, when there is severe emphysema, the consequent collateral ventilation maintains direct communication among the alveoli of the pulmonary lobes.<sup>(3,4,10)</sup> Therefore, in theory, a procedure enabling the communication of the upper lobe, for instance, with the environment, would allow the drainage not only of this upper lobe but also of the lower lobe of the same side.

Since then, the procedure suggested in this context has been treatment with the aid of bronchoscopy, creating communication between the pulmonary parenchyma and the corresponding bronchus. In this procedure, the use of general anesthesia and of costly high technology is

necessary, translating to longer hospital stays and a risk of severe bleeding.<sup>(5,6,11,12)</sup>

Two other therapeutic methods currently used for the treatment of severe pulmonary emphysema are lung volume reduction surgery and lung transplantation.

In both methods, the use of general anesthesia, admission to the intensive care unit and long hospital stays are necessary. These methods present high morbidity and mortality, as well as high costs.

In the National Emphysema Treatment Trial,<sup>(13)</sup> mortality within 90 days after lung volume reduction surgery was found to be 7.9%. Lung volume reduction surgery is contraindicated for high-risk patients (those with an  $FEV_1 < 20\%$  of predicted). In selected patients submitted to this procedure, the following results were described<sup>(14)</sup>: post-operative clinical and functional improvement; a 30% decrease in residual volume; a 50% increase in  $FEV_1$ ; and the discontinuation of supplementary oxygen in 80% of the patients. However, 2 years after the intervention, all patients presented values equal to those observed in the pre-operative period.

It is known that the pre-operative mortality is 6.2% among lung transplant patients, whereas the survival rate after bilateral transplantation is 86.4% in 1 year and 66.7% in 5 years.<sup>(15,16)</sup> The complications most frequently observed in the first year after the procedure are as follows: infection, in 80% of the cases; pulmonary hypertension, in 51.1%; renal dysfunction, in 25.7%; diabetes, in 21.5%; dyslipidemia, in 17.7%; severe acute rejection, in 10.5%; primary graft failure, in 10.2%; bronchiolitis obliterans, in 8.8%; and malignant neoplasia, in 3.9%.

However, since 2000, the Thoracic Surgery Group of the Santa Casa School of Medical Sciences in São Paulo has been improving techniques for the treatment of giant lung bullae using local anesthesia and drainage.<sup>(17)</sup> Therefore, in the 7 years after that first publication, we have accumulated considerable experience and confidence in this technique,<sup>(18,19)</sup> and we can now propose this new type of procedure not only for patients with giant lung bullae but also for patients with diffuse lung emphysema, as proposed in 1978,<sup>(4)</sup> and as carried out in the explanted native lungs of patients submitted to lung transplantation.<sup>(7)</sup> Therefore, the results obtained in the post-operative period, using drainage of the lung parenchyma, in these three patients with severe diffuse pulmonary disease constitute the first



report of the therapeutic application of collateral ventilation in human beings.

Although the results obtained show that there was clinical improvement of the patients in the post-operative period, we cannot conclude that the surgical method proposed truly bring benefits. However, the findings of this pilot study convinced us to obtain further data from a larger sample of patients.

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