Impact of a Rescue Program on the Operability of Patients With Bronchogenic Carcinoma and Chronic Obstructive Pulmonary Disease

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OBJECTIVE: Bronchogenic carcinoma and chronic obstructive pulmonary disease (COPD) are strongly associated in our setting, occurring together in around 70% of cases. Approximately 60% of COPD patients who require resection for bronchogenic carcinoma are considered unfit for surgery because of seriously impaired lung function. The purpose of this study was to evaluate the extent to which a rescue program could improve lung function in COPD patients who had previously been considered unfit for surgery because of poor lung function.

PATIENTS AND METHODS: The study enrolled COPD patients who had not been considered for surgical resection because they had a predicted postoperative forced expiratory volume in 1 second (FEV_1) of less than 1 L. All of the patients participated in a 2-week rescue program that involved optimization of drug treatment (inhaled bronchodilators and/or corticosteroids) and intensive respiratory physiotherapy. Lung function was analyzed before and after the program.

RESULTS: We evaluated 30 patients (26 men and 4 women) with a mean (SD) age of 66.7 (8.15) years and an initial FEV_1 of 1.497 (0.27) mL (FEV_1% of 55.7% [20.14%]). None of the patients had respiratory failure (PaO_2 of 77.0 [9.4] mm Hg and $PaCO_2$ of 41.6 [2.4] mm Hg). Twenty-four patients (80%) showed significant improvement in lung function (P<.001) after the program and were admitted for resection.

Two wedge resections, 18 lobectomies, 2 pneumonectomies, and 2 exploratory thoracotomies were performed (based on oncologic indications). Nineteen of the 24 patients who underwent surgery had no complications. Two patients had prolonged air leaks, 1 empyema, and 1 hemothorax. One patient died from sepsis.

CONCLUSIONS: A large number (80%) of COPD patients previously considered unfit for surgical resection because of seriously impaired lung function can be admitted for surgery following an intensive drug and respiratory physiotherapy rescue program.

Key words: *Bronchogenic carcinoma. COPD. Surgical resection. Respiratory physiotherapy.*

Influencia de un programa de rescate en la decisión quirúrgica en pacientes con carcinoma broncogénico y EPOC

OBJETIVO: La asociación entre carcinoma broncogénico y enfermedad pulmonar obstructiva crónica (EPOC) se sitúa en torno al 70% en nuestro medio. Aproximadamente un 60% de los pacientes con dichos diagnósticos son rechazados para cirugía de resección del carcinoma broncogénico debido a la intensa alteración de su función pulmonar. El objetivo del presente trabajo es evaluar el efecto de un programa de rescate en la mejoría de la función pulmonar de pacientes con EPOC y previamente descartados para cirugía por la alteración de su función pulmonar.

PACIENTES Y MÉTODOS: Se incluyó en el estudio a pacientes con EPOC descartados inicialmente porque se había calculado que su volumen espiratorio forzado en el primer segundo (FEV_1) tras la intervención quirúrgica sería menor de 1 l. Todos ellos participaron en un programa de rescate de 2 semanas de duración que incluía: optimización del tratamiento farmacológico (broncodilatadores inhalados y/o corticoides) y fisioterapia respiratoria intensiva. Se analizó la función pulmonar antes y después del programa.

RESULTADOS: Se evaluó a 30 pacientes (26 varones y 4 mujeres) con una edad media ± desviación estándar de 66,7 ± 8,15 años y FEV_1 inicial de 1,497 ± 0,27 ml (FEV_1%: 55,7 ± 20,14 l), que no presentaban insuficiencia respiratoria (presión arterial de oxígeno: 77,0 ± 9,4 mmHg; presión arterial de anhídrido carbónico: 41,6 ± 2,4 mmHg). Tras el programa 24 pacientes (80%) pudieron ser aceptados para la resección propuesta al objetivarse una mejoría significativa en la función pulmonar (p < 0,001).

Se realizaron 2 resecciones en cuña, 18 lobectomías, 2 neumonectomías y 2 toracotomías exploradoras (por criterios oncológicos). De los 24 pacientes a los que se intervino, en 19 no hubo complicaciones, 2 presentaron fugas aéreas mantenidas, hubo un caso de empiema pleural y otro de hemotórax. Un paciente falleció por sepsis.

CONCLUSIONES: El diseño de un programa intensivo farmacológico y de fisioterapia respiratoria permite rescatar para cirugía a un número alto (80%) de los pacientes con EPOC a los que inicialmente se descarta por una alteración importante de la función pulmonar.

Palabras clave: *Carcinoma broncogénico. EPOC. Cirugía de resección. Fisioterapia respiratoria.*

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Introduction

According to the EUROPREVAL study, the current prevalence of bronchogenic carcinoma in Spain is 1863 cases per 100 000 population and a firm diagnosis is made in approximately 10 500 of these individuals every year.[1] Between 1978 and 1992, 150 000 males and 19 000 females died of lung cancer and only 14% to 17% of those diagnosed were able to receive surgical treatment.

Surgical resection is the treatment of choice for early stages of bronchogenic carcinoma. It is, however, first necessary to assess surgical risk and weigh the risks and benefits of the procedure for each candidate.[2-4] Assessment criteria include a range of clinical, tumor, and lung function parameters. Lung function evaluation is essential, not only for calculating perioperative risk but also for predicting respiratory failure. Surgical resection is generally ruled out if the patient is expected to have a forced expiratory volume in 1 second (FEV_1) of less than 800 mL after the operation, although the cutoff point varies from group to group.[5,6]

Chronic obstructive pulmonary disease (COPD) and lung cancer are strongly associated in Spain, occurring together in 73.8% of cases. COPD is the most common concomitant disease in lung cancer patients[5] and it presents serious problems when it comes to establishing an operability/inoperability threshold. A survey conducted by the Lung Cancer Working Group attached to the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR)[7] found 19 different sets of guidelines (17 for clinical use and 2 for research) containing recommendations on how to establish the best possible cutoff values for resectability without incurring further risk.[8-10]

Our hypothesis was that by participating in an intensive, short-term preoperative "rescue" program that involved cessation of smoking, optimization of drug treatment, and various pulmonary rehabilitation exercises, certain lung cancer patients who had previously been considered unfit for surgery due to impaired lung function could be admitted for surgical resection.

Patients and Methods

We conducted a prospective study of lung cancer patients considered unfit for surgical resection following an initial lung function test. The patients were enrolled consecutively at our center between January 2000 and December 2003. All had impaired lung function and a predicted postoperative FEV_1 of less than 1 L, calculated according to the recommendations of Olsen et al[11] and Boysen et al[12] and the treatment protocol for bronchogenic carcinoma at our center.

One surgeon from our team performed a clinical, radiological, and functional assessment of all the patients. The lung function test, conducted at the time of diagnosis and on completion of the rescue program, revealed significant differences between pretreatment and posttreatment values for all the parameters analyzed: forced vital capacity (FVC), FVC%, FEV_1, and FEV_1% (Datospir-91; Sibelmed, Barcelona, Spain). The bronchodilator test was performed with salbutamol and readings were taken after 15 minutes. Response was considered positive when FEV_1 increased by 15% or 200 mL. Arterial blood gas analysis was also performed. All the patients underwent perfusion scintigraphy with technetium Tc 99m to assess the contribution of each lung to overall lung function. The reasons for the program were explained before testing and consent was obtained from all the patients.

The rescue program was undertaken by a medical team and included rehabilitation exercises administered by the team's physiotherapist. It lasted 2 weeks and involved a 1-hour session 2 days a week. Patients were instructed to continue their exercises at home on the other days. Four patients with comprehension difficulties underwent intensive treatment on an inpatient basis for 3 days. Drug treatment included long-acting bronchodilators combined with anticholinergic agents (salmeterol and ipratropium bromide) at standard doses, and inhaled corticosteroids (budesonide) in the case of patients with a positive bronchodilator test response. Pulmonary rehabilitation exercises were designed specifically to improve diaphragmatic breathing, thoracic expansion, and drainage of secretions where necessary.[13]

Statistical Analysis

The Student *t* test for repeated measures was used to compare pretreatment and posttreatment values. Data were analyzed using the Statistical Package for Social Sciences software package, version 14.0.

Results

The study enrolled 30 patients (26 males and 4 females) with a mean (SD) age of 67 (8.15) years and a moderate to severe airflow limitation. A positive response was observed in 53.3% of the patients and there were no cases of respiratory failure. Arterial blood gas analysis revealed a PaO_2 of 77 (9.4) mm Hg, a $PaCO_2$ of 41 (2.5) mm Hg, and an arterial oxygen saturation of 94.7% (2%). Twenty-six of the 30 patients underwent the program on a fully outpatient basis and 4 were admitted to the hospital for a 3-day intensive treatment program.

On completion of the program, 24 patients (80%) showed a clinically and statistically significant improvement in all the lung function parameters analyzed ($P<.001$), with values above the cutoff points for resectability (Tables 1 and 2), and they were given the option of undergoing surgery. Table 3 shows the pretreatment and posttreatment values for the 30 patients, together with type of surgery, age, and outcome. The 6 patients (20%) who were conclusively ruled out for surgery were offered alternative therapy.

Two wedge resections, 18 lobectomies, and 2 pneumonectomies were performed. An exploratory thoracotomy was performed in the 2 remaining patients following the discovery of tumor spread to the pleura (M1).

TABLE 1
Pretreatment and Posttreatment Values for Patients Who Participated in the Rescue Program*

	Pretreatment	Posttreatment
FVC, L	2.72 (0.49)	3.04 (0.35)
FEV_1, L	1.49 (0.27)	1.69 (0.12)
PaO_2, mm Hg	77.0 (9.4)	81.4 (11.0)
$PaCO_2$, mm Hg	41.6 (2.5)	43.4 (3.4)
SaO_2, %	95 (1)	96 (1)

*Data are expressed as means (SD). FEV_1 indicates forced expiratory volume in 1 second; FVC, forced vital capacity; SaO_2, arterial oxygen saturation.

TABLE 2
Pretreatment and Posttreatment Percentages of Predicted Values for Patients Included in Program*

	Pretreatment	Posttreatment
FVC, % of predicted	72 (16)	76 (15)
FEV_1, % of predicted	55 (20)	60 (19)

*Data are expressed as means (SD) (P<.001). FEV_1 indicates forced expiratory volume in 1 second; FVC, forced vital capacity.

There were no postoperative complications in 19 (63%) of the patients. Four (13%) had complications, including 2 prolonged air leaks, 1 empyema, and 1 hemothorax. One patient (3%) died from sepsis.

Discussion

The present study shows that 80% of patients who had been declared unfit for surgery due to impaired lung function were admitted for surgical resection following a short-term intensive treatment optimization or so-called rescue program involving medical care, appropriate drug therapy, and pulmonary rehabilitation.

Several studies have demonstrated the efficacy of smoking cessation and the use of bronchodilators or respiratory physiotherapy in reducing postoperative complications.[14-16] To the best of our knowledge, however, this is the first time that such strategies have been combined in a single program to rescue patients considered unfit for surgery.

Smoking cessation has been shown to improve lung function and gas exchange almost immediately. It also reduces carboxyhemoglobin levels and, in turn, improves tissue oxygenation.[17] Furthermore, it has been widely demonstrated in the medical literature that the prolonged use of bronchodilators (β_2-adrenergic agonists and anticholinergic agents), whether in isolation or in association with inhaled corticosteroids, improves lung function.[18-22]

Respiratory physiotherapy adapted to the needs of each patient has also been shown to improve clinical and functional outcomes in COPD patients and patients with hypersecretion, particularly in lung volume reduction and transplant surgery.[23-25] In our review of the literature, we found that several authors had already discussed the benefits of using such strategies some years ago. In 1970, for example, Stein and Cassara[26] demonstrated the efficacy of respiratory physiotherapy in reducing postoperative respiratory complications in 48 randomly selected patients assigned to 2 groups. Parker[27] stated that preoperative preparation was of prime importance and that it was essential for the patient to quit smoking, and, if secretions

TABLE 3
Pretreatment and Posttreatment Values in Patients Who Participated in the Program, Type of Surgery Performed, Age, and Outcome*

Case	Pretreatment					Posttreatment					Type of Surgery	Outcome	Age, y
	FVC, L	FVC, %	FEV_1 L	FEV_1, %	SaO_2	FVC, L	FVC, %	FEV_1, L	FEV_1, %	SaO_2			
1	3.01	89	1.87	84	95	3.05	89	2.03	88	96	Lobectomy	Good	53
2	2.72	122	1.91	122	98	2.54	114	2.01	128	96	ET	Good	72
3	2.57	55	1.29	39	94	2.79	61	1.52	48	97	Lobectomy	Good	76
4	3.14	72	1.60	50	97	3.24	73	1.82	55	97	Lobectomy	Complications	74
5	2.58	65	1.03	37	93	3.40	84	1.39	49	97	Lobectomy	Good	74
6	3.26	74	1.60	50	93	3.28	74	1.64	50	98	Lobectomy	Good	57
7	3.71	73	1.81	58	95	3.22	75	2.20	65	98	Lobectomy	Good	65
8	2.80	67	1.44	49	96	3.40	81	1.80	61	95	No surgery	–	73
9	2.52	80	1.55	72	94	2.41	76	1.72	69	96	Lobectomy	Good	75
10	2.24	48	0.99	30	93	2.55	54	1.44	43	95	Lobectomy	Good	71
11	3.21	72	1.44	45	93	3.61	81	1.72	54	94	Lobectomy	Good	65
12	2.78	62	1.44	43	95	3.58	57	1.90	57	95	Lobectomy	Good	54
13	1.51	74	0.92	66	94	1.75	86	.84	60	95	No surgery	–	75
14	2.65	69	1.85	49	95	4.05	77	2.00	53	94	Lobectomy	Death	68
15	3.14	82	1.37	49	95	3.22	84	1.76	63	98	No surgery	–	61
16	3.36	76	1.63	51	95	3.38	75	1.79	49	96	Lobectomy	Complications	65
17	2.24	54	1.28	43	93	3.45	78	1.76	59	96	Neumectomía	Good	67
18	2.84	62	1.85	55	92	3.19	70	2.15	64	94	Lobectomy	Complications	59
19	1.66	45	1.34	53	93	1.59	43	1.28	50	95	No surgery	–	77
20	2.52	113	1.82	116	92	2.72	122	1.91	122	98	ET	Good	72
21	2.50	74	1.17	48	94	2.17	64	1.08	44	94	No surgery	–	64
22	3.13	69	1.27	38	94	3.56	79	1.43	43	95	No surgery	–	61
23	3.35	67	1.86	49	95	3.54	71	2.02	53	96	Neumectomía	Good	48
24	2.90	77	1.38	53	95	3.18	83	1.67	55	95	No surgery	–	76
25	3.15	80	1.68	61	96	3.05	78	1.87	64	98	Lobectomy	Good	74
26	2.46	59	1.60	56	93	3.06	64	1.89	56	95	Lobectomy	Good	64
27	3.36	73	1.48	46	96	3.86	84	1.53	48	97	RC	Good	77
28	2.79	60	1.68	48	96	3.46	68	1.75	50	95	Lobectomy	Complications	53
29	1.96	69	1.15	56	94	2.50	88	1.31	64	95	Lobectomy	Good	65
30	2.18	55	1.57	55	96	2.47	65	1.45	53	97	Lobectomy	Good	67

*FEV_1 indicates forced expiratory volume in 1 second; FVC, forced vital capacity; SaO_2, arterial oxygen saturation; ET, exploratory thoracotomy.

existed, to have expert personnel administer aggressive pulmonary physiotherapy both before and after the operation to aid the patients. In another chapter in the same book, Auchincloss[28] wondered whether preoperative treatment of these patients would be best administered on an inpatient or outpatient basis. Lezius[29] commented that general and local treatment could keep bacterial infection under control in such a way that would make it unnecessary to operate on lungs containing large amounts of purulent expectoration. Epstein[3] analyzed response to preoperative treatment and indicated that optimized treatment reduced complications secondary to surgical resection. Other authors have demonstrated the efficacy of intensive diaphragmatic exercise in improving lung function following surgery in COPD patients.[30-32] Celli and colleagues[33] proposed using mechanical inspiratory incentives to increase thoracic expansion following general surgery, and Miller[34] demonstrated the efficacy of certain supervised respiratory exercises in improving the lung capacity of patients with chronic bronchopulmonary disorders.

When used in isolation, each of these strategies has proven to be capable of improving clinical and functional outcomes. Our aim was to combine them in a single program in order to optimize lung function and reverse the decision not to operate

The rate of surgical complications in the studied patients was relatively low (13%) and similar to that reported by other surgical teams faced with the complicated task of working with patients with considerably impaired lung function.[35] In the end, the prognosis of our patients was influenced more by the diagnosis of cancer than by their lung function.

In summary, our study shows that a large number of patients with bronchogenic carcinoma initially considered unfit for surgical treatment due to impaired lung function can be admitted for surgical resection following an intensive rescue program involving physician care, appropriate drug therapy, and respiratory rehabilitation.

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