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Morphologic grading of emphysema is useful in the selection of candidates for unilateral or bilateral reduction pneumoplasty☆

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Abstract

Objective: Radiologic morphology of emphysema proves useful in the selection of candidates for bilateral reduction pneumoplasty. We developed a simple morphologic grading system capable of identifying subsets of patients who had maximal functional improvement after unilateral or bilateral operation. **Methods**: Fifty-two patients who underwent unilateral ($n = 34$) or bilateral ($n = 18$) reduction pneumoplasty were evaluated. Emphysema morphology was visually scored by digital roentgenograms and high-resolution computed tomography. In each lung, severity of emphysema (ES), heterogeneity (DHT) and hyperinflation (DHF) degrees, were assessed. Asymmetric ratio of emphysema (ARE) between the lungs was expressed as: higher ES/lower ES scores. Morphometric data were correlated with absolute preoperative–postoperative FEV_1 change (ΔFEV_1). **Results**: No difference was found between the unilateral and the bilateral group for ES and DHT. DHF was greater in the bilateral group (3.1 vs. 2.7, $P = 0.02$) whereas ARE was greater in the unilateral group (1.29 vs. 1.05, $P = 0.0001$). Stepwise logistic regression extracted as best predictors of maximal ΔFEV_1, ARE (odds ratio = 238, Wald test $P = 0.04$) in the unilateral group, and DHT (odds ratio = 24, $P = 0.03$) in the bilateral group. Unilateral group ΔFEV_1 was greater in patients with ARE $\geq$ 1.3 (0.44 vs. 0.24 l, $P = 0.02$). Bilateral group ΔFEV_1 was greater in patients with DHT $>$ 1 (0.50 vs. 0.31 l, $P = 0.03$). No difference was found when comparing ΔFEV_1 resulting from unilateral RP and ARE $\geq$ 1.3, and bilateral RP (0.44 vs. 0.41 l, not significant). **Conclusions**: This morphologic grading system identified subsets of patients who had maximal functional benefit from unilateral or bilateral reduction pneumoplasty and might be useful in the preoperative screening of candidates for either approach. © 2000 Published by Elsevier Science B.V.

Keywords: Emphysema; Reduction pneumoplasty; Lung volume reduction surgery; Grading system

1. Introduction

Reduction pneumoplasty is an effective palliative surgical treatment for selected patients with severe emphysema. On the basis of early work by Brantingan et al. [1] and the recent refinements by Cooper et al. [2], the procedure involves non-anatomical resection of the most severely destroyed tissue to reduce lung volume by 20–30%. The rationale is that removal of nonfunctioning, hyperinflated lung tissue may improve respiratory mechanics, lung recoil pressure, and ventilation–perfusion matching.

Many groups intentionally perform bilateral reduction pneumoplasty since it usually produces greater functional improvement than the unilateral operation [3–5]. However, we have found that in patients with an asymmetric distribution of emphysema in the lungs, unilateral reduction pneumoplasty may produce functional improvement in the range of that achieved with bilateral operation [6]. Moreover, it has been recently reported that bilateral reduction pneumoplasty may be followed by a more rapid functional deterioration than unilateral operation [7]. These observations suggest that both approaches may have a role in the surgical management of emphysema. Appropriate patient selection based on physiologic parameters and radiologic morphology has been stressed as an important prerequisite for predicting maximal functional improvement after reduction pneumoplasty [2]. Morphologic grading systems have been developed to quantify parameters such as type, severity, and distribution of emphysema to help identify candidates for bilateral operation [5,8,9]. However, no precise and repro-

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ducible morphologic criteria have been yet provided to aid the selection of candidates for unilateral reduction pneumoplasty.

The purpose of our study was twofold: (i) to develop a simple and reproducible morphologic grading system that might be applied in the selection process for unilateral or bilateral reduction pneumoplasty; and (ii) to evaluate whether this system identifies morphologic patterns predicting maximal functional benefit after either approach.

2. Material and methods

2.1. Study design

The first 52 consecutive patients who underwent unilateral ($n = 34$) or bilateral ($n = 18$) reduction pneumoplasty at our institution between October 1995 and March 1998 were retrospectively evaluated. There were 50 men and two women with a mean age of 61 ± 8.1 years (range 44–75 years). All patients had emphysema radiologically graded as severe as well as significant functional disability. Exclusion criteria included patients with prevailing intrinsic disease of the airway as indicated by excessive sputum production, asthma or clinically significant bronchiectasis, metastatic cancer, and cigarette smoking within the previous 4 months. Patients with giant bullae occupying at least one third of the hemithorax and surrounded by relatively normal lung were not included in this study.

Preoperatively, patients were enrolled in a comprehensive respiratory rehabilitation program that was continued postoperatively for up to 10 weeks.

In typical cases reduction pneumoplasty regarded nonanatomical staple resection of maximally destroyed and nonperfused lung tissue (target areas) carried out by means of video-assisted thoracoscopic surgery, as previously described [6]. A tailored approach entailing both unilateral and bilateral operations was applied on the basis of emphysema morphology. As a rule, unilateral operation was intentionally carried out in patients with an asymmetric distribution of emphysema between the lungs, and the worst lung was operated on. A bilateral treatment was preferred in patients with symmetrically distributed emphysema and bilateral operation was performed either as a simultaneous procedure or as a staged procedure, usually with a 1-month interval. Two patients with an obliterated pleural space not amenable of a thoracoscopic approach were operated on via muscle-sparing lateral thoracotomy.

2.2. Morphologic assessment

Radiologic assessment included digital inspiratory and expiratory chest radiographs in posteroanterior and lateral views, and high-resolution computed tomography (CT) of the chest: thickness 1 mm, index 10 mm (Tomoscan SR 7000, Philips, Eindhoven, The Netherlands). The scans were taken at a window width (1500 HU) and level (−600 H) appropriate for lung detail. Six standard lung scans obtained from lung apex to base at end-inspiration, which were exactly defined by anatomic structures (brachiocephalic trunk, aortic arch, main pulmonary artery, middle lobe bronchus, ventricular chambers, and 1 cm above the diaphragm), were chosen as reference levels in each patient. Emphysema was visually identified by areas of decreased density with loss of vascular lung structures. Morphologic parameters were independently assessed by three blinded readers (two radiologists and one surgeon) unaware of the patient's preoperative clinical test results and outcome. In each lung the degree of hyperinflation as well as the severity and degree of heterogeneity of emphysema were assessed (Table 1). The degree of hyperinflation was expressed by the degree of impairment of diaphragmatic excursion. Excursion was estimated in centimeters by superimposing the inspiratory and expiratory posteroanterior chest radiographs using the spine for registration. As a result a four-grade scale was created in a way that the less the diaphragmatic excursion, the higher the degree of hyperinflation: grade 1, >5 cm; grade 2, 4–5 cm; grade 3, 2–3 cm; grade 4, 0–1 cm.

In each CT layer, the severity of emphysema (ES) was graded by estimating the percentage of destroyed lung tissue according to the criteria outlined by Hunsaker et al. [10]: grade 1, 0–25%; grade 2, 25–50%; grade 3, 50–75%; grade 4, $> 75\%$. In each lung all six level scores were summed up to give the single lung score (ES_{sl}) whereas the sum of both lungs score has given the global score (ES_{gl}). As a result, by this method scores from 12 to 48 were possible.

In each lung, the difference between the median ES score in the three worst sections and the three best sections was calculated to express the degree of heterogeneity according to the criteria outlined by Wisser et al. [5]. In bilaterally operated patients the overall degree of heterogeneity was expressed by the mean of the lungs scores (Fig. 1).

Finally, the asymmetric ratio of emphysema between the lungs was expressed by the ratio: higher ES_{sl}/lower ES_{sl} scores.

2.3. Functional assessment

All patients underwent pulmonary function tests, arterial blood gas analysis, 6-min walking test, and modified Medical Research Council dyspnea scores preoperatively, and 3, 6, and 12 months postoperatively. Morphometric data were correlated with clinical outcome measured by means of

Table 1
Evaluated morphologic parameters

	Abbreviation	Type of measurement
Degree of hyperinflation	DHF	Calculated
Severity of emphysema	ES	Estimated
Degree of heterogeneity	DHT	Calculated from ES
Asymmetric ratio of emphysema	ARE	Calculated from ES

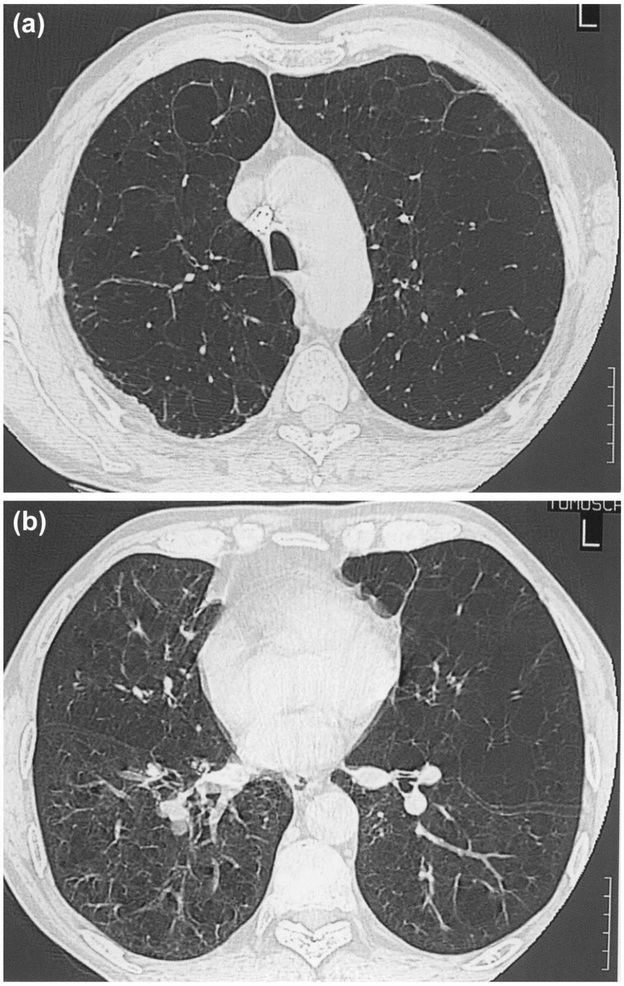

Fig. 1. High resolution CT scans showing heterogeneous emphysema. (a) ES: left = 4; right = 4. ES: (b) left = 3; right = 2. DHT = 1.5, ARE = 1.1. Bilateral RP, $\Delta FEV_1 = 0.52$ l.

improvement in pulmonary function test results. The forced expiratory volume in 1 s (FEV_1) was selected as the most important measurement of outcome because it is one of the most reliable, best understood, and widely accepted clinical measurements of emphysema [11]. The postoperative measurements obtained between 3 and 6 months after surgery were taken into account to calculate the absolute improvement (ΔFEV_1). The FEV_1 values were always expressed as the best of three postbronchodilator measures. Absolute improvement was preferred to the percentage of improvement to avoid that minimal changes in patients with severe functional impairment could appear exaggerated.

In evaluating ΔFEV_1 a cutoff of 0.25 l was chosen on the basis of the finding that in a worst-scenario case FEV_1 deterioration as high as 255 ml per year has been reported [7]. Thus we assumed that acceptable postoperative FEV_1 improvement should last at least 1 year.

2.4. Statistical analysis

Group descriptive statistics are presented as mean ± SD. The degree of agreement among the readers was calculated using intraclass correlation or weighted κ [12] coefficients, as appropriate. The Wilcoxon signed rank sum test or the Mann–Whitney nonparametric test were respectively used to compare paired or unpaired data not normally distributed. The Fisher exact test was used to compare categoric variables. The predictive values, sensibility and specificity of the various predictive features studied were determined. Binomial receiver operating characteristic (ROC) curves based on maximum likelihood estimation were constructed, using cumulative frequency distribution of true positive fraction (SE) or false positive fraction (1 − SP) at different cutoff values for the morphologic variables. Finally, a stepwise logistic regression analysis was performed to identify the best predictors of maximal ΔFEV_1 after unilateral or bilateral treatment. The importance of each variable was assessed by the value of Wald statistic (coefficient/standard error). In this model satisfactory ΔFEV_1 was considered as a dependent variable (outcome). A *P*-value of less than 0.05 was considered significant. BMDP statistical software version 7 [13] was used for the analysis.

3. Results

All patients were highly symptomatic and the disease had a major impact on their quality of life despite maximal bronchodilator therapy. Indications for unilateral operation were: asymmetric emphysema ($n = 20$), major air leak at the completion of the first reduction during planned bilateral procedure ($n = 6$), patient deemed high-risk for one-stage bilateral procedure ($n = 5$), and previous pleurodesis ($n = 2$) or thoracotomy ($n = 1$). For the group as a whole, preoperative FEV_1 was 0.88 ± 0.3 l (29.4 ± 9.7%), modified MRC dyspnea index 3.3 ± 0.6, and the 6-min walking test 394 ± 48 m. A significant difference was found in the FEV_1 between the unilateral and the bilateral group (0.96 ± 3.1 vs. 0.7 ± 0.1 l, $P = 0.03$).

Morphologic data regarding the evaluated factors are summarized in Table 2. Interobserver agreement for each evaluated parameter was satisfactory as illustrated in Table 3. When comparing morphologic data in patients undergoing unilateral or bilateral reduction pneumoplasty, no difference was found in DHT and ES (*P* not significant). Conversely, the DHF was higher in the bilateral group ($P = 0.02$) whereas ARE was higher in the unilateral group ($P = 0.0001$) (Table 2).

The perioperative mortality rate was 1.9% (one out of 52 patients). No patient was lost to follow-up.

For the group as a whole, ΔFEV_1 was 0.38 ± 0.23 l (43.2 ± 26.1%). No difference was found between the unilateral and the bilateral group regarding the number of patients that achieved a satisfactory ΔFEV_1 (25/34 patients (73.5%) vs. 13/18 patients (72.2%), *P* not significant).

Table 2
Morphologic data according to treatment

	DHF	ES_{gl}	ES_{sl}	DHT	ARE
Unilateral RP					
Mean	2.7 ± 0.5	28.6 ± 7.5	15.9 ± 4.0	1.26 ± 0.8	1.29 ± 0.2
Range	1–4	14–46	8–23	0–2	1–1.63
Bilateral RP					
Mean	3.1 ± 0.5	30.3 ± 7.2	–	1.17 ± 0.7	1.05 ± 0.06
Range	2–4	20–45	–	0–2	1–1.26

3.1. Correlation of morphologic parameters with functional improvement

Grouping the patients undergoing unilateral reduction according to ARE and taking as cutoff the value of 1.3 (Fig. 2a), ΔFEV_1 was greater in patients with ARE $\geq$ 1.3 (0.44 vs. 0.24 l, $P = 0.02$). In the same manner, grouping the bilaterally treated patients according to DHT and taking as cutoff the value of 1.0 (Fig. 2b), ΔFEV_1 was greater in patients with DHT > 1 (0.50 vs. 0.31 l, $P = 0.03$). Table 4 indicates sensibility, specificity and predictive values of the cutoff chosen for ARE and DHT. Both the cutoffs had an 88% positive predictive value that corresponds to a high probability of identifying patients who may have a satisfactory functional outcome after either unilateral or bilateral reduction pneumoplasty. No difference was found when comparing ΔFEV_1 resulting from unilateral reduction and ARE $\geq$ 1.3, and bilateral reduction (0.44 vs. 0.41 l, P not significant) (Fig. 3). Stepwise logistic regression analysis confirmed as best predictors of maximal ΔFEV_1, ARE in the unilateral group (odds ratio = 238, Wald test $P = 0.04$), and DHT in the bilateral group (odds ratio = 24, Wald test $P = 0.03$).

4. Discussion

Several reports have demonstrated the beneficial effects of reduction pneumoplasty on subjective dyspnea, lung function and quality of life. However, the reported range of functional improvement, expressed in term of ΔFEV_1 vary widely. The variability in response to surgery may relate to several factors including the type of approach that is employed. As a matter of fact, ΔFEV_1 ranged from 250 to 500 ml after bilateral operation and from 151 to 270 ml after unilateral operation, in recent reports [2,14–17], suggesting that the bilateral treatment is more effective in improving lung function.

Hence, is there any role for unilateral reduction pneumoplasty? To answer this question McKenna et al. [3] compared the results achieved by unilateral and bilateral operation in a large series of patients. They concluded that

Table 3
Interobserver agreement for the evaluated parameters[a]

	DHT	P-value	DHF	P-value
Reader 1–2	$\kappa = 0.918$	0.0001	$\kappa = 0.686$	0.0001
Reader 1–3	$\kappa = 0.671$	0.0001	$\kappa = 0.681$	0.0001
Reader 2–3	$\kappa = 0.695$	0.0001	$\kappa = 0.681$	0.0001
	ES		ARE	
All readers	$r_I = 0.947$	0.007	$r_I = 0.879$	0.009

[a] κ, weighted κ coefficient; r_I, intraclass correlation.

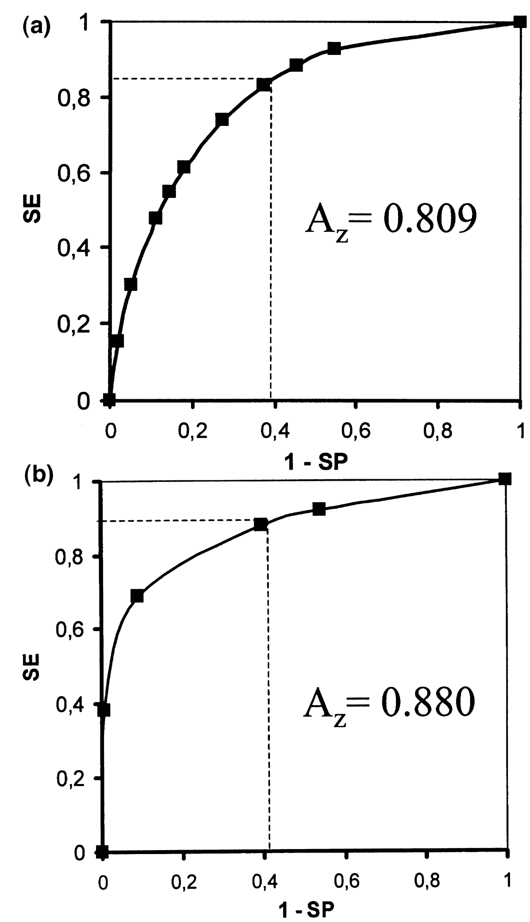

Fig. 2. Receiver operating characteristic analysis of asymmetric ratio of emphysema scores for the unilateral group (a) and of the degree of heterogeneity for the bilateral group (b). Dotted lines refer to the cutoff chosen for each variable. The A_z values (areas under the receiving operating characteristic curves) obtained are also shown.

Table 4
Predictive values for satisfactory improvement of the cutoffs chosen[a]

	Unilateral operation (ARE cutoff = 1.3)	Bilateral operation (DHT cutoff = 1.0)
SE	0.74	0.88
CI 95% SE	0.35–0.93	0.31–0.95
SP	0.73	0.60
CI 95% SP	0.42–0.95	0.28–0.95
PPV	0.88	0.88
NPV	0.51	0.60

[a] SE, sensibility; CI, confidence interval; SP, specificity; PPV, positive predictive value; NPV, negative predictive value.

bilateral reduction pneumoplasty produces a greater overall improvement in FEV_1, oxygen independence, and dyspnea index and should thus be the standard operation. Also, they stated that unilateral operation should be limited to patients with unilateral heterogeneous emphysema or patients with contraindications for a bilateral treatment. More recently, however, the same authors [7] have reported that FEV_1 deterioration after bilateral treatment averaged 255 ml/year whereas it averaged 107 ml/year after unilateral operation. These results suggest that simultaneous bilateral reduction pneumoplasty, though more effective, may increase the mechanical stress in the lung parenchyma that has been hypothesized by West [18] as one of the leading causes of progression of lung destruction in emphysema. Furthermore, no comparative data are yet available as regards the duration of functional improvement following simultaneous bilateral operations, or unilateral operation followed by contralateral treatment at the reappearance of symptoms.

In our series, by tailoring both approaches on the basis of individual emphysema morphology, a ΔFEV_1 of more than 0.25 l was achieved in more than 73% of the patients. This feature confirms our preliminary finding [6] that in patients with an asymmetric distribution of emphysema, unilateral reduction pneumoplasty may produce a degree of functional improvement that compares to that of the bilateral treatment. Several definitions have been empirically used to qualify candidates for unilateral treatment, including heterogeneous unilateral disease [3], asymmetric distribution of perfusion or parenchymal disease [16], and marked difference in distribution and/or severity of emphysema within the lungs in at least two CT layers [6]. Although suggestive, these definitions are vague and do not allow to apply practical and reproducible criteria.

Computed tomography-based visual scoring systems for quantifying emphysema have been shown to correlate well with pathologic grade of disease assessed at autopsy and with densitometry measurements of parenchymal destruction [19]. Moreover, CT has been shown to be a more sensitive predictor of emphysema than simple spirometry because physiologic changes similar to those of emphysema can occur in small airways disease even in absence of centrilobular emphysema [20]. In this light, Slone and Gierada [8] developed an excellent grading system that visually scores severity and heterogeneity of emphysema as well as the degree of hyperinflation in order to help identify surgical candidates. Subsequently, Weder et al. [9]. proposed a simpler classification that identifies three different patterns of heterogeneity and correlated these patterns with functional outcome. More recently, Wisser et al. [5] developed a further system modifying in part the criteria of Slone and Gierada in order to facilitate a mathematical quantification of heterogeneity and severity of the disease. All these systems identified specific patterns of emphysema predicting a favorable outcome after bilateral reduction pneumoplasty. However, unfortunately none has provided specific criteria capable of identifying candidates for unilateral operation.

Theoretically, an ideal grading system should be precise,

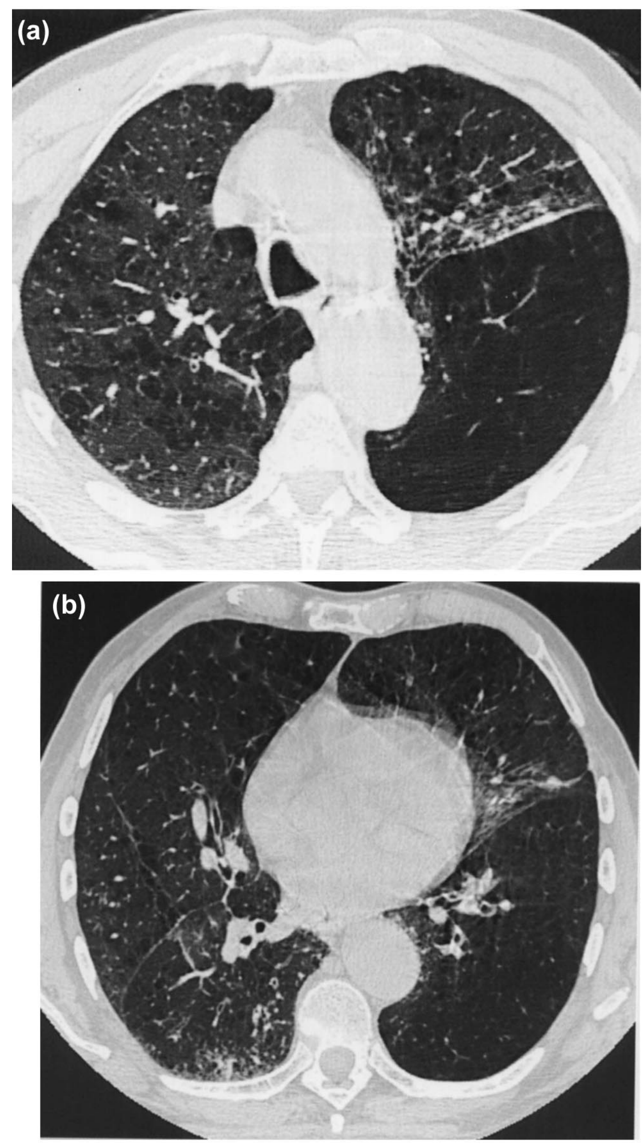

Fig. 3. HRCT scans showing asymmetric emphysema. (a) ES: left = 3; right = 1. (b) ES: left = 3; right = 1. ARE = 1.63. Unilateral RP, ΔFEV_1 = 0.43 l.

easy to apply, and reproducible. In our study we have taken from some of the proposed systems those criteria that we thought might fit better these principles. Also, we thought that reproducibility might be improved by limiting the number of ranks in each parameter in order to reduce inter-observer differences. Regarding the ES, we have preferred to apply criteria that include absence of emphysema and mild emphysema in the same rank (grade 1) since mild emphysema may be missed on CT scan, and the severity of emphysema, especially the panacinar type, may be under-estimated [20]. In this way a good interobserver agreement was achieved for assessment of the ES, ES-derived parameters DHT and ARE, and DHF.

The position and shape of the diaphragm has been shown to represent the best way of assessment of hyperinflation [8]. Accordingly, we have evaluated the DHF by measuring the diaphragmatic excursion on posteroanterior chest radiographs. In fact, although flattening of the diaphragm is shown to better advantage on the lateral examination, excursion of each hemidiaphragm can be better estimated on posteroanterior view. Moreover, Lando et al. [21] have recently shown no difference when measuring the height of the diaphragm before and after reduction pneumoplasty on either lateral or posteroanterior views.

In our series we have found no difference in ES and DHT when grouping the patients undergoing unilateral and bilateral operation. Conversely, either the mean preoperative FEV_1 and ARE were higher in the unilateral group. This difference is probably related to the presence of a greater proportion of functioning lung tissue in the nonoperated lung. Similarly Weder et al. [9], in an analysis conducted in patients undergoing bilateral reduction pneumoplasty, have found a higher baseline FEV_1 in the group with the highest degree of heterogeneity that also suggest the presence of a greater amount of preserved tissue in the lungs.

In our study, multivariate analysis identified the ARE and DHT as the best predictors of maximal functional improvement after unilateral and bilateral operation, respectively. Worth noting is that when grouping the unilaterally treated patients according to ARE, we found no difference in ΔFEV_1 between patients with ARE > 1.3 and bilaterally treated patients. This result is quite surprising and probably reflect some differences in the type of emphysema in the two groups. In fact, we have frequently found in patients with asymmetric emphysema the association of bullous and nonbullous disease that may explain at least in part the excellent outcome. Furthermore, we believe that unilateral reduction pneumoplasty might affect the function also in the nonoperated lung as a result of an interdependence between the hemithoraces. Accordingly, Becker et al. [22] have found that unilateral operation led to an increase in volume of the contralateral unoperated lung at total lung capacity. They also supposed that a degree of interdependence should exist, probably as a function of the compliance of the lung and the mediastinum.

The finding that a higher DHT correlated with better outcome after bilateral operation is in line with the results of previous reports [2,9] and confirms that the best outcome occurs in patients with greater degrees of heterogeneity, some compressed lung, and larger percentages of normally and mildly emphysematous lung.

Although the results presented here hold promise, they must be confirmed in a large cohort since cutoffs used in our analysis to determine predictors of maximal ΔFEV_1 may change when greater and more equal numbers in the subgroups are considered.

To conclude, this morphologic grading system allowed us to identify specific morphologic features that correlated with maximal functional improvement after unilateral or bilateral reduction pneumoplasty. Multivariate analysis extracted the ARE as the best predictor in the unilateral group and the DHT in the bilateral group, suggesting that a tailored approach based on the individual morphology of emphysema might be warranted. The good reproducibility achieved in applying this system suggest that it might be useful in the preoperative screening of candidates for reduction pneumoplasty.

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