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Magnetic resonance analysis of abnormal diaphragmatic motion in patients with emphysema

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Magnetic resonance analysis of abnormal diaphragmatic motion in patients with emphysema. T. Iwasawa, S. Kagei, T. Gotoh, Y. Yoshiike, K. Matsushita, H. Kurihara, K. Saito, S. Matsubara. ©ERS Journals Ltd 2002.

ABSTRACT: The purpose of this study was to quantitatively evaluate paradoxical diaphragmatic motion using magnetic resonance (MR) imaging.

A total of 27 subjects were examined, including 12 normal young adults, six control individuals, and nine patients with emphysema. With subjects in the supine position, 30 sequential sagittal MR images of the entire right lung were obtained during tidal and deep slow breathing.

Diaphragmatic movement between sequential images was estimated as the displacement area and the total diaphragmatic movement in a respiratory cycle was calculated. The paradoxical motion of the diaphragm, representing the inverted movement to increase or decrease lung area, since paradoxical movement ratio (M_{pr}=(total paradoxical diaphragmatic movement/total diaphragmatic movement)×100), was evaluated.

In patients with emphysema, paradoxical diaphragmatic motion was observed on MR images during deep breathing. The mean M_{pr} in emphysematous patients during deep breathing was 10±4%, which was significantly higher than 0.5±0.2% in young adults ($p<0.05$), and 1.2±0.6% in aged-matched controls ($p<0.05$).

The present results indicate that magnetic resonance images could be used to detect paradoxical diaphragmatic motion in patients with emphysema.
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Magnetic resonance imaging (MRI) has recently been used to assess chest wall motion, since the technique can noninvasively visualize the chest wall with high tissue contrast [1–4]. GIERADA *et al.* [1] described diaphragmatic motion in normal subjects using sequential magnetic resonance (MR) images taken during quiet breathing, and GAUTHIER *et al.* [2] evaluated the shape of the diaphragm at different lung volumes. CLUZEL *et al.* [3] obtained fast three-dimensional (3D) MRI during short periods of breath-holding, and the reconstructed images were used to measure the diaphragmatic area as well as changes in this area with respect to lung volume. SUGA *et al.* [4] reported asynchronous movement between the ribcage and diaphragmatic motion by measuring the anteroposterior distance at the upper and lower thorax on sequential MRI.

The authors have recently reported that subtraction images constructed from sequentially-obtained MR images could identify paradoxical motion of the diaphragm in patients with emphysema; the ventral and dorsal parts of the diaphragm moved paradoxically [5]. The method that used subtraction images, however, was not suitable for detailed analysis because of the low signal-to-noise ratio. In the present study, the paradoxical diaphragmatic motion was evaluated quantitatively by measuring the area through which the diaphragm moved between two sequential images. Paradoxical diaphragmatic motion and its correlation with pulmonary function tests was investigated.

Subjects and methods

Subjects

The subjects included 27 adults, with 12 young adults (six males and six females), six control males and nine male patients with emphysema. The characteristics of each subject, including pulmonary function tests, are summarized in table 1. The study

Table 1. – Characteristics of the subjects

Group	Young adults	Control subjects	Patients with emphysema
Subjects n	12	6	9
Sex M:F	6:6	6:0	9:0
Age yrs	22.7±1.05	68.2±3.12	71.1±1.05
Smoking pack-yrs	0	37.2±6.2	69.6±12.3
FEV_1 L	3.62±0.27	2.19±0.21	0.75±0.07
FEV_1 % pred	98.3±3.41	94.9±6.94	34.3±3.21
VC % pred	109.0±4.61	95.1±8.81	76.0±3.45

Data are presented as mean±SD unless otherwise stated. FEV_1: forced expiratory volume in one second; VC: vital capacity; % pred: percentage of predicted. All long volumes were measured seated.

protocol was approved by the institutional review board, and informed consent was obtained from each subject. The 12 young adults were recruited from the local community. They were healthy nonsmokers, and pulmonary function tests were normal. All control subjects were recruited from the local community, including three patients who were treated for abdominal aortic aneurysms (n=2), or arterial obliteration with sclerosis (n=1). The control subjects were selected based on the following criteria: 1) age was 60–80 yrs, 2) no chest disease or previous thoracic surgery, and 3) no obvious emphysematous changes on chest radiographs. There was no significant difference in the mean age between patients and control subjects.

All nine patients had smoking-related emphysema and had been treated in the authors′ centre. The criteria used to select the patients were as follows: 1) moderate-to-severe airflow obstruction as evidenced by pulmonary function tests and forced expiratory volume in one second (FEV_1 % predicted) <50%; 2) emphysema was confirmed by computed tomography (CT) imaging; and 3) age was 60–80 yrs. Hyperinflation was present in all patients, with a mean±SD (TLC % pred) of 138±7.0%, and air trapping (mean residual volume (RV % pred) of 188±13%). TLC and RV were measured by using body plethysmography. Five patients required continuous oxygen supplementation while one patient required oxygen during exercise.

Magnetic resonance imaging

MRI was performed with subjects lying supine inside a 1.5 tesla (T) magnet (Horizon, GE Medical System, Milwaukee, WI, USA) with a body coil. Thirty sequential images of the right lung, from the lung apex to the base, during tidal and deep slow breathing were obtained. The sequence was a single-shot fast-spin echo with a half-Fourier transformation (echo time (TE): 41.5 ms, field of view (FOV): 40× 23–28 cm, matrices: 256×128, slice thickness=10 mm). The acquisition time was 0.53–0.73 s·image^{-1} for young subjects and 0.73 s for controls and patients. Respiration was monitored using a pressure belt during the examination. During tidal breathing, the mean respiratory frequency was 13.6±1.5 breaths·min^{-1} in young adults, 11.5±0.9 breaths·min^{-1} in controls and 11.2±0.9 breaths·min^{-1} in patients with emphysema. There was no difference in the respiratory frequency among the three groups. For deep slow breathing, subjects were instructed to attempt maximum breathing. Thus, at least 10 images were obtained during one deep slow breath.

The original images were examined in the cine mode with commercially-available software (Advantage Windows 2.0, GE Medical Systems, Milwaukee, WI, USA). Two parameters that related to diaphragm movement during deep slow breathing were measured manually: diaphragmatic excursion and diaphragmatic length displacement (see fig. 1 for details). Firstly, two images were selected, in which the lung area increased to a maximum and decreased to the minimum, respectively. Diaphragmatic excursion represented the vertical distance between the highest points of the diaphragm on the two images. The length displacement of the diaphragm was calculated by subtraction of the vertical height of the lung, from the lung apex to the base, measured on the two images. Diaphragmatic excursion was not equivalent to displacement (fig. 1).

Quantitative analysis

Quantitative analysis of the images was performed on a remote workstation using software originally developed by two of the present authors (S. Kagei and T. Gotoh). The lung field was extracted from a threshold value, which was digitally selected using the mode method [6]. Three anatomical landmarks, the lung apex and the ventral and dorsal costophrenic angles, were identified on each image using a pointing device (fig. 2a). A lung field with a lower signal intensity than the threshold was then extracted and its contour traced after smoothing (fig. 2b). A histogram (fig. 2c) shows measurements of the intensity of the image in the rectangular area surrounding the three points (see fig. 2a). The intensity level of the threshold value represented the minimum frequency between two peaks; the large peak of the lung field area and the small peak of the chest wall.

The lung area in each constructed image represented the region contained by three boundaries: the hemidiaphragm, and the ventral and dorsal ribcage lines. With this definition, the lung area comprised all lung compartments, including large pulmonary vessels and lobar and/or segmental bronchi. Changes in the lung area represented the difference in the areas between two subsequent images. The movement of the diaphragm was estimated as the area swept by the diaphragmatic line in subsequent images. The increase and decrease in lung areas was measured separately. The lung area and diaphragmatic movement were measured in pixel numbers, and then converted to cm^2.

Data analysis

All diaphragmatic movements between the sequential images, in terms of the maximum numbers of respiratory cycles in a MRI series, were summed

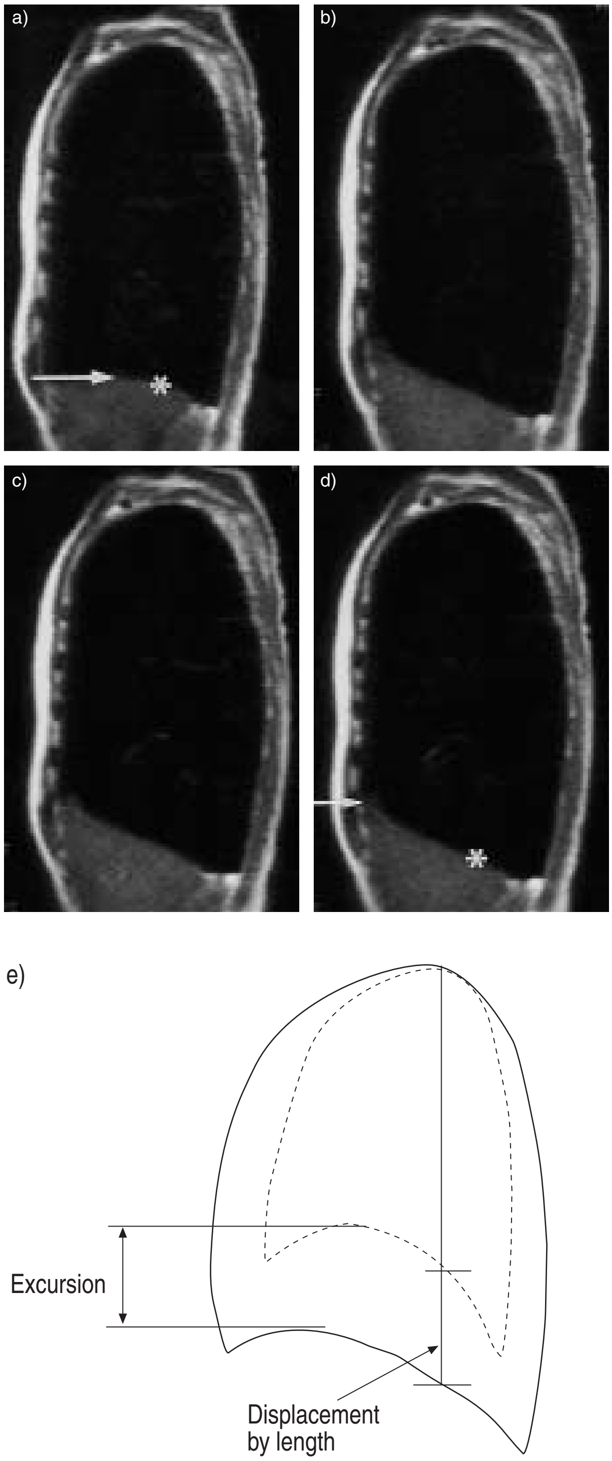

Fig. 1. – Sequential images of the right lung in a 71-yr-old male patient with emphysema obtained during deep, slow inspiration (a–d). e) Measurement of diaphragmatic excursion. The highest line of the diaphragm was selected on each image in the deep expiratory (a) and deep inspiratory phases (d) (arrow) and the vertical distance between them was measured. The vertical distance between the lung apex and hemidiaphragm on each image was measured at deep expiration (a) and inspiration (d) (asterisk), and the two dimensions were subtracted to obtain the diaphragmatic displacement by length (d). The sequential images show that the ventral part of the diaphragm moved upward during inspiration. In this case, excursion was -3.6 cm and displacement was 2.6 cm. The paradoxical movement ratio (M_{pr}) during deep breathing was 42.3%.

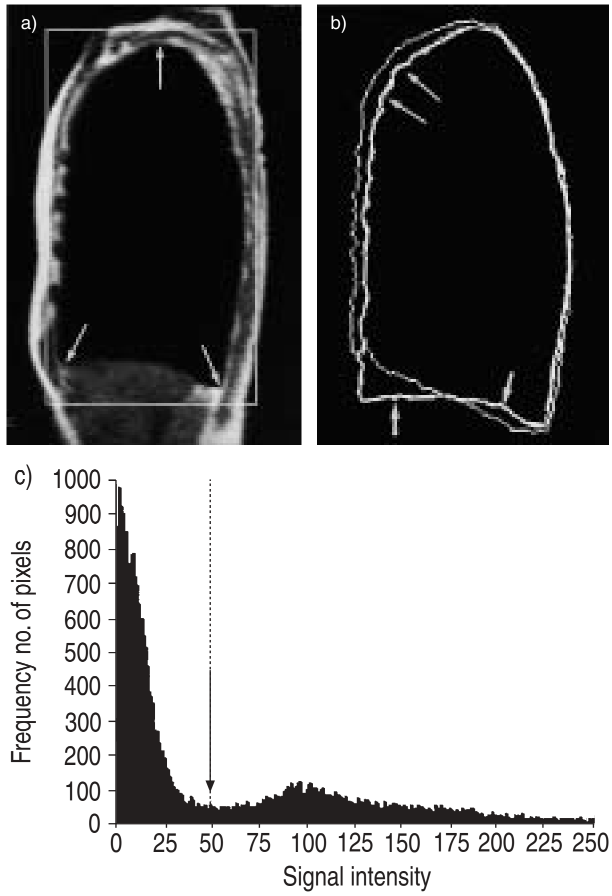

Fig. 2. – Process of image segmentation. a) The same image as figure 1b. Firstly, three landmarks, including the lung apex, ventral and dorsal costophrenic angles (arrows), were fixed on each image. A rectangular area surrounding the three points was drawn automatically (white box), and a histogram of the area was obtained. b) Segmented image constructed from figure 1b (thick line) and figure 1c (thin line). These lung area contours were traced using the image segmentation method described previously. The ventral side is on the left of the image. The image shows that the ventral ribcage moves anteriorly (small arrows) when the ventral part of the diaphragm moves upwards (arrow). At the same time, the dorsal portion of the diaphragm moves downward likes a see-saw (arrow). c) A histogram of the rectangular area shown in a). Although the absolute values of the signal intensity varied among magnetic resonance images, a histogram pattern consisting of two peaks, with a large peak of the lung area and a small peak of the chest wall, was recognized on all images. The value of the signal intensity at the minimum frequency between the two peaks was selected as the threshold value in each image, and the lung area with low signal intensity was computed. Threshold value in b) is indicated by a dotted line and an arrow.

and divided by the number of respiratory cycles in order to calculate the average movement in one respiratory cycle. The initial or the last data in a series, which did not complete one respiratory cycle, were excluded from analysis. Spirometry was not used during MR examinations, and pressure-belt data could not be recorded in the system (respiratory frequency was recorded separately by an operator). The respiratory cycle was defined based on changes in the lung area. It was found that the diaphragm did not always move synchronously with the change in the lung area, *i.e.* paradoxical movement.

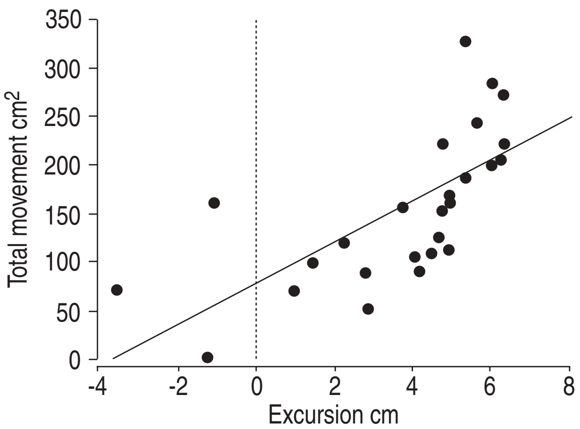

Fig. 3. – Correlation between diaphragmatic excursion and diaphragmatic movement by area. Note the strong relationship between these parameters ($p<0.001$, $r=0.91$). Diaphragmatic movement was different in three patients with negative excursion.

"Paradoxical movement (Mp)" was used to measure these paradoxical motions of the diaphragm, where Mp (cm^2)=average of paradoxical movement of the diaphragm in one respiratory cycle, and Mp ratio (Mpr)=100×Mp/total movement of the diaphragm in one respiratory cycle. "Paradoxical movement" refers to the downward (or upward) movement of the diaphragm when the lung area decreases (or increases). Mp was measured in both directions: downward (Mp+ and Mpr+) and upward movement (Mp- and Mpr-) of the diaphragm.

The values of diaphragmatic excursion, displacement by length, total diaphragmatic movement based on changes in the area, Mp and Mpr were compared among the three groups. The authors compared the diaphragmatic excursion to total diaphragmatic movement by area. Repeated analysis of variance and Fisher's exact test were used for subgroup comparisons. A p-value of <0.05 was considered statistically significant. These values were compared with FEV_1 % pred, and TLC % pred (TLC was not measured in one young adult and four control subjects).

Results

The original images showed paradoxical movement of the diaphragm in seven patients during deep breathing. It consisted of upward movement of the ventral portion of the hemidiaphragm when the dorsal part moved downward during deep inspiration and *vice versa* during expiration. The Mp was especially marked in three patients (fig. 1). In these three patients, the value of the excursion was negative because the highest point of the diaphragm at full inspiration was at the anterior costophrenic angle, although the displacement by length was positive. Paradoxical diaphragmatic motion could not be detected in the control and young adults, nor in emphysematous patients during tidal breathing.

Analysis of data showed that diaphragmatic excursion correlated with total diaphragmatic movement by area during deep, slow breathing ($p<0.001$, $r=0.91$, fig. 3). However, the diaphragmatic movement by area varied in the three patients who showed negative diaphragmatic excursion. The excursion correlated positively with FEV_1 % pred ($p<0.001$, $r=0.87$) and negatively with TLC % pred ($p<0.01$, $r=0.57$). The mean excursion in emphysematous patients was significantly smaller than in control subjects (table 2).

Figure 4 shows the correlation between total movement of the diaphragm during deep breathing and TLC. The total movement of the diaphragm significantly decreased with increases in TLC % pred ($p<0.01$). Furthermore, the total movement of the diaphragm tended to decrease with decreasing FEV_1 % pred (data not shown).

Figure 5 shows changes in Mp and Mpr during tidal and deep, slow breathing in the three groups of subjects. During tidal breathing, the mean values of Mp and Mpr in the total downward and upward movements of the diaphragm were not significantly different among the three groups. During deep, slow breathing, Mp increased in all subjects. However, the

Table 2. – Average values of diaphragmatic movement during deep, slow breathing

Group	Young adults	Control subjects	Patients with emphysema	p-value	p-value between controls and patients
Excursion cm	5.53±0.17	4.38±0.17	1.20±0.97	<0.0001	0.002
Displacement length cm	8.63±0.43	5.28±0.53	4.27±0.73	<0.0001	NS
Total diaphragmatic movement cm^2	227.6±18.9	121.9±11.0	99.5±21.2	<0.0001	NS
Paradoxical movement					
Total Mp cm^2	1.2±0.5	1.6±0.9	6.9±3.5	NS	NS
Mp %	0.46±0.18	1.20±0.60	10.79±4.89	0.0267	0.0429
Mp+ cm^2	0.59±0.2	0.86±0.5	3.13±1.8	NS	NS
Mpr+ %	0.25±0.10	0.66±0.37	4.85±2.42	NS	NS
Mp- cm^2	0.57±0.3	0.73±0.5	3.78±1.7	NS	NS
Mpr- %	0.21±0.09	0.54±0.32	5.93±2.50	0.0151	0.0027

Data are presented as mean±SD. Mp: paradoxical movement; Mp+: downward Mp during a decrease lung area; Mp-: upward Mp during an increase in lung area; Mpr: paradoxical movement ratio; Mpr+: ratio of downward Mp during an decrease in lung area; Mpr-: ratio of upward Mp during an increase in lung area; NS: nonsignificant.

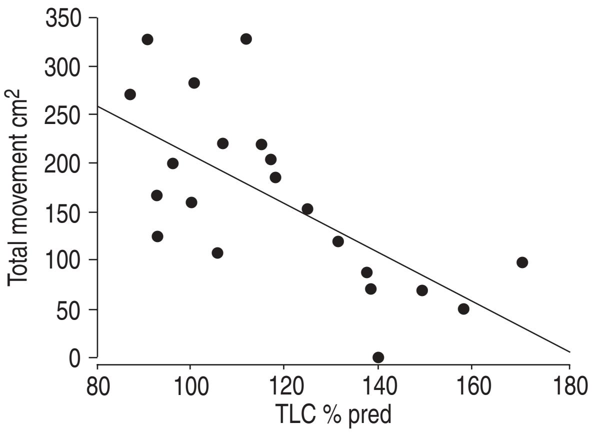

Fig. 4. – Correlation between total movement of the diaphragm during deep breathing and total lung capacity (TLC) % predicted. The total movement of the diaphragm decreased significantly with increases m TLC % pred, and the correlation was significant $p<0.01$ and $r=0.68$.

largest increase in Mp was noted in emphysematous patients. There was no significant difference in the mean Mp during deep breathing, although, the mean Mpr in patients with emphysema was significantly greater than in the controls ($p<0.05$) and young adults ($p<0.05$). As for the direction of diaphragmatic movement, the difference in Mpr+ was not significant although the difference in Mpr- was significant between the two groups ($p<0.05$). The mean Mpr- in patients with emphysema was significantly greater than that in controls ($p<0.05$) and young adults ($p<0.01$).

The correlation between Mpr- during deep, slow breathing and FEV_1 % pred (fig. 6a) and TLC % pred (fig. 6b) was also examined. Patients with low FEV_1 % pred showed large Mpr- during deep, slow breathing. On the other hand, during deep, slow breathing, Mpr- was large in patients with mildly high TLC % pred, but it was low in those patients with very large TLC % pred.

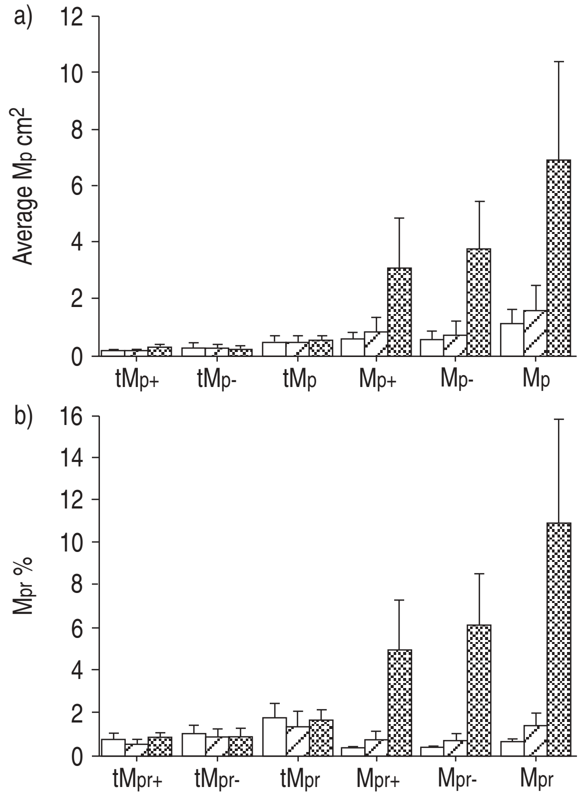

Fig. 5. – a) Paradoxical movement (Mp) during tidal and deep slow breathing. tMp: Mp in one tidal breath; tMp+: downward Mp in one tidal breath during a decrease in lunge area; tMp-: upward Mp in one tidal breath during an increase in lung area; Mp: Mp in one deep breath; Mp+: downward Mp during a decrease in lung area; Mp-: upward Mp during an increase in lung area. There was no significant difference among the three groups in mean tMp. b) Paradoxical movement ratio (Mpr) during tidal and deep, slow breathing. tMpr: the ratio of Mp in one tidal breath; tMpr+: ratio of downward Mp in one tidal breath during a decrease in lung area; tMpr-: ratio of upward Mp in one tidal breath during an increase in lung area; Mpr: ratio of Mp in one deep breath; Mpr+: ratio of downward Mp during a decrease in lung area; Mpr-: ratio of upward Mp during an increase in lung area. The mean Mpr- in emphysema patients (■) was significantly higher than that in young adults (□; $p<0.01$) and control subjects (▨; $p<0.05$).

Discussion

The main findings of the present study can be summarized as follows. 1) MR images showed that part of the diaphragm moved paradoxically, relative to the change in lung area. 2) Quantitative estimation of Mp and Mpr showed that Mpr was significantly highest in patients with emphysema. These results suggested that diaphragmatic movement does not contribute efficiently to the change in the lung area in emphysema, especially during the inspiratory phase.

The exact mechanism of the paradoxical motion of the diaphragm is not completely understood. However, it could be due to reduced efficiency of diaphragmatic contraction in emphysema. In fact, previous studies have shown that the apposition zone of the diaphragm is markedly reduced in patients with emphysema [7], and that contraction of the diaphragm reduces the proportion of the apposition zone area to the surface area of the diaphragm [8].

In the present study, Mpr was highly variable in patients with emphysema, ranging from 0–42.3%, although Mpr- tended to be large in patients with low FEV_1 % pred. However, the correlation between Mp and Mpr and pulmonary function tests could not be adequately examined due to the small number of patients. The present results showed that paradoxical diaphragmatic motion correlated with hyperinflation, although severe hyperinflation tended to restrict both normal and paradoxical diaphragmatic movements. Total diaphragmatic movement correlated negatively with TLC % pred, similar to previous findings reported by GEORGE and WEIL [9].

It should be stressed that the paradoxical movement of the diaphragm was "an appearance", not equal to voluntary diaphragmatic movement based on contraction. It included passive movement of the diaphragm due to muscle interaction, which is frequently altered in patients with emphysema [10]. In this study,

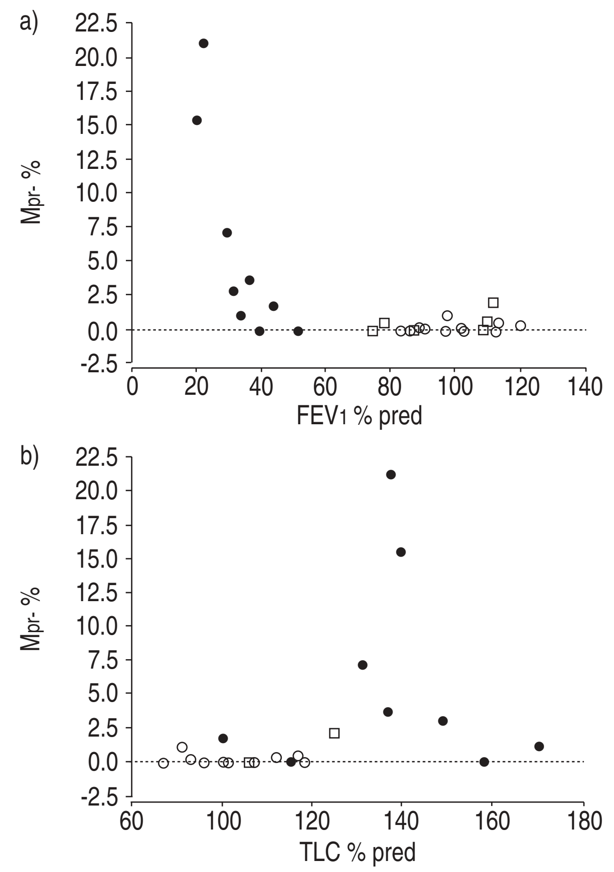

Fig. 6. – a) Correlation between forced expiratory volume in one second (FEV1) % predicted and the ratio of upward paradoxical movement (Mp) during an increase in lung area (Mpr-) during deep, slow breathing. b) Correlation between total lung capacity (TLC) % pred and Mpr- during deep, slow breathing. ○: young adults; □: controls; ●: patients with emphysema.

MR images demonstrated that the ventral portion of the diaphragm moved in paradox to the change in lung area; the ventral part of the diaphragm appeared to move upward with the outward movement of the ribcage. The parasternal inspiratory intercostal muscles and other accessory muscles such as the scalenes and sternocleidomastoid muscles that elevate the ribcage and prevent it from inward movement during diaphragmatic contraction, are less affected by hyperinflation because the muscle length change due to hyperinflation is smaller in these muscles [11, 12]. The action of the ribcage and cervical muscles would be related to the paradoxical diaphragmatic movement.

Abdominal muscle recruitment could also influence paradoxical diaphragmatic motion [13]. In the present study, *M*p in young subjects slightly increased during deep slow breathing. This finding was probably due to voluntary abdominal muscle recruitment [14]. Small *M*p, which was observed during tidal breathing in young adults and control individuals, would include measurement error since temporal resolution depends on the rate of image acquisition.

There are several limitations to this study. The method involved only a two-dimensional (2D) analysis, and is incomplete unless 3D views of the diaphragm and lungs are designed, due to the complex motion of the diaphragm, lungs and ribcage during breathing. Nevertheless, diaphragmatic paradoxical motion was observed in the authors′ patients, especially in the early or end inspiratory phase. Small paradoxical motion cannot be detected in images taken during breath-holding. Thus, at present obtaining 3D MR images requires breath-holding for a period of time, thus indicating that the 2D analysis using sequential images is appropriate.

In the present study, diaphragmatic movement was evaluated as the area of displacement. Previous studies evaluated diaphragmatic motion using various techniques and parameters such as diaphragmatic excursion on fluoroscopy [15], changes in abdominal and ribcage circumferences [16], changes in diaphragmatic length and area using 3D reconstruction of CT images [7] and thickness by using ultrasonography [17]. Diaphragmatic excursion measured in the present study was measured by subtraction of the highest points of the diaphragm during deep respiration, and thus corresponds to the anterior-posterior view of the diaphragm assessed by fluoroscopy [15]. The excursion data presented here are in reasonable agreement with those reported in other studies of normal subjects [15]. In the present study, diaphragmatic movement measured by area correlated significantly with diaphragmatic excursion. Thus, these data of diaphragmatic movement by area would be acceptable. It was impossible to compare the paradoxical movement of the diaphragm by area with similar data, because such analyses have not been reported previously. The increased Mpr- results observed during deep breathing are compatible with the data reported by GILMARTIN and GIBSON [18], in which paradoxical movement increased and mechanical efficiency decreased during diaphragmatic breathing in severe chronic obstructive pulmonary disease patients.

The results of the present study were derived from a small number of patients. Thus, comparative studies in a larger number of patients and age-matched controls are necessary. Three-dimensional images taken during breathing and volumetric analysis are ideal, although further methodological improvements are needed. The results, however, suggest a new application for magnetic resonance imaging and segmentation analysis, and indicate that magnetic resonance imaging and quantitative analysis of the images provides useful information regarding respiratory muscle motion.

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