HIGHLIGHTED TOPIC | The Respiratory Muscles in Chronic Obstructive Pulmonary Disease

Effect of lung transplant and volume reduction surgery on respiratory muscle function

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Estenne M. Effect of lung transplant and volume reduction surgery on respiratory muscle function. J Appl Physiol 107: 977–986, 2009; doi:10.1152/japplphysiol.91620.2008.—Lung transplantation and lung volume reduction surgery have opened a new therapeutic era for patients with advanced emphysema. In addition to providing impressive clinical benefits, they have helped us better understand how the chest wall and respiratory muscles adapt to chronic hyperinflation. This article reviews the effects of these procedures on respiratory muscle and chest wall function. Inspiratory (including diaphragm) and expiratory muscle strength are often close to normal after unilateral and bilateral transplantation, although some patients have marked weakness. After bilateral transplantation for emphysema, graft volume is normal at full inflation but remains greater than normal at end expiration, which results from structural changes in the chest wall. In contrast, patients with unilateral transplantation have a reduction in graft volume at full inflation. The mediastinum is displaced toward the graft at end expiration, which reduces the surface area of the diaphragm on the transplanted side, and it moves toward the native lung during tidal and full inspiration and toward the graft during tidal and forced expiration. Lung volume reduction produces an increase in contractility, length and surface area of the diaphragm, and increases its contribution to tidal volume; at the same time, neural drive to the muscle and respiratory load are reduced, such that diaphragm neuromechanical coupling is improved. Diaphragm configuration and rib cage dimensions are only minimally affected by the procedure. Single-lung transplantation and lung volume reduction favorably impact on the disadvantageous size interaction by which the lungs are functionally restricted by the chest wall in emphysema.

airflow obstruction; chest wall; transplantation; volume reduction; hyperinflation; diaphragm

OVER THE LAST 15 YEARS, two surgical treatments, lung transplantation and lung volume reduction surgery (LVRS), have opened a new therapeutic era for patients with advanced emphysema; for many of these, they have dramatically improved both quality of life and survival prospects. Furthermore, they have given a fantastic impetus to research programs aimed at understanding how the chest wall and respiratory muscles adapt to chronic hyperinflation. In this article, I will review the impact of lung transplantation and LVRS on chest wall mechanics and respiratory muscle function, with particular emphasis on single lung transplantation (SLT), which results in a marked imbalance between the volume and mechanical properties of the native lung and the graft and, as such, leads to a unique physiological situation.

This review focuses on transplant studies done in patients with well-functioning grafts and does not address alterations in chest wall physiology associated with specific complications.

With regard to LVRS, only studies of patients who have undergone surgical volume reduction of both lungs will be reviewed; unilateral surgical procedures and bronchoscopic lung volume reduction result in smaller and less durable physiological changes, and the impact of these approaches on chest wall mechanics has not been studied.

The studies discussed here require careful interpretation because most of them involved a small number of patients who were studied after, but not before, surgery; in addition, many studies were performed on a single occasion after the surgical procedure and did not provide longitudinal data.

LUNG TRANSPLANTATION

Respiratory Muscle Function

Muscle strength and endurance. Maximum inspiratory pressures and endurance time. A number of studies have assessed inspiratory muscle strength after lung transplantation. Their results are somewhat inconsistent, which may be explained by...
differences in the methods used to assess muscle strength and in the patients' characteristics (type of transplant, time elapsed after surgery, underlying disease, graft function at the time of study...); in addition, interpretation of many studies is limited by the small number of patients (<10–15) and the lack of appropriate control group.

Early studies in patients with heart-lung transplantation (HLT) reported markedly decreased maximal static inspiratory mouth pressure (MIP; Refs. 51, 52), but many later studies in recipients of HLT (1, 9, 16, 23, 34, 40) or bilateral lung transplantation (BLT; Refs. 9, 34, 40, 50, 61) found MIP values that were within normal limits, or only slightly reduced. Five of the six studies that assessed MIP in recipients of single grafts found normal values (10, 34, 40, 45, 61), but one reported a 40% reduction (49). This alteration, however, was only present in patients transplanted for emphysema, which contrasts with several other studies showing no reduction in MIP after SLT, BLT, or HLT for this indication (10, 45, 61).

Maximum inspiratory pressures thus seem close to normal in most transplant recipients.

In seven patients with BLT for cystic fibrosis or bronchiectasis, Reynaud-Gaubert et al. (50) reported substantial improvements in endurance time to sustained inspiratory efforts performed after, compared with before, surgery; they also noted that endurance time continued to increase throughout the first postoperative year. In another study, Brath et al. (5) found no difference in endurance time between transplanted (SLT and BLT) and non-transplanted emphysema patients. Interpretation of these two studies, however, is limited by the absence of comparison with a group of healthy controls.

DIAPHRAGM FUNCTION. Pinet et al. (47) measured bilateral twitch transdiaphragmatic pressure (Pdi\textsubscript{tw}) in a group of patients with HLT or BLT for cystic fibrosis and found values that were similar to those of matched controls. Three studies have specifically assessed diaphragm function in patients transplanted for emphysema. Wanke et al. (60) measured bilateral Pdi\textsubscript{tw} in eight patients with BLT and six patients with SLT (using percutaneous electrical stimulation in the neck), Brath et al. (5) measured sniff Pdi (Pdi\textsubscript{sniff}) in six patients with BLT and six patients with SLT, and Martinez et al. (40) measured maximal Pdi (Pdi\textsubscript{max}) and Pdi\textsubscript{sniff} in 12 patients with BLT and eight patients with SLT. Overall, Pdi values in the patients were close to those reported in previous studies of healthy subjects and did not differ significantly in recipients of single vs. bilateral grafts (5, 40, 60). Interpretation of these results, however, requires caution because no contemporary control group was studied. Additional studies are thus needed to establish the time course of changes in diaphragm strength after transplantation and determine if it eventually fully recovers.

MAXIMUM EXPIRATORY Pressures. Three studies of expiratory muscle strength after lung transplantation showed a reduction in maximal expiratory mouth pressure (MEP; Refs. 45, 49, 52), but four reported near-normal or normal values (1, 9, 10, 34). More recently, a study in patients who had undergone HLT or BLT for cystic fibrosis demonstrated normal values of abdominal muscle strength assessed using a nonvolitional technique (magnetic stimulation of the lower thoracic nerve roots) (47). This suggests that the low MEP values previously reported may relate, in part, to the patients' inability to perform the required tasks.

MECHANISMS OF MUSCLE WEAKNESS. Collectively, these studies indicate that respiratory muscle contractility is relatively well preserved in recipients of bilateral and single grafts, whatever the indication for transplantation. Yet a striking feature is the marked between-patient variability in muscle strength, with some patients having evidence of pronounced weakness. Several factors may contribute to this alteration. First, phrenic nerve injury producing partial or complete paralysis of one or both hemidiaphragms can occur during the transplant procedure. The incidence varies widely from 3 to 43%, which is explained by differences in the techniques used to diagnose diaphragm paralysis and in the type of surgical procedure—the complication occurs more frequently after HLT than after BLT or SLT (20). Second, chest wall mechanics may be altered by complications like sternal wound malunion with rib cage instability or significant pleural thickening (21, 23), both of which may reduce maximal inspiratory pressures. Finally, there is ample evidence of decrements in limb muscle strength (due to wasting) and endurance (due to impaired oxidative metabolism and Ca\textsuperscript{2+}/K\textsuperscript{+} regulation) after lung transplantation (18). These alterations may be a reflection of risk factors already present in the pretransplant condition (e.g., altered nutritional status, immobilization, muscle deconditioning), but they may also develop, or be amplified, after surgery due to the use of immune suppressive agents, in particular cyclosporine A and corticosteroids. It is possible that some of these factors affect respiratory muscle function, but this deserves further investigation.

Muscle length and configuration. A remarkable feature in recipients of SLT for emphysema is the displacement of the mediastinum toward the graft, which always appears radiographically "smaller" than the hyperinflated native lung (Fig. 1). One study in these patients assessed diaphragm dimensions and curvature during voluntary relaxation in supine posture using computerized tomography (7). It showed that the shift of the mediastinum reduced the surface area of the dome of the hemidiaphragm on the transplanted side. So, the surface area of...
the dome was smaller on this side than on the side the native emphysematous lung (Fig. 2); the surface area of the dome on the transplanted side was also smaller than the surface area of the dome of the ipsilateral hemidiaphragm in normal controls. These data thus suggest that, despite the marked reduction in the volume of the hemithorax on the transplanted side, diaphragm length may not come back to normal after transplantation. This might explain why Wanke et al. (60) failed to find a significant difference in unilateral Pdiw between the transplanted and the native side in six recipients of SLT for emphysema; it is unknown, however, if changes in esophageal pressure in response to unilateral phrenic stimulation can accurately reflect the strength of one hemidiaphragm. In contrast to the surface area of the dome, its curvature on the side of the graft was similar to that of healthy controls (7).

Additional studies are required to further explore how the asymmetry between the volume and the mechanical properties of the native lung and the graft after SLT for emphysema (or fibrosis) impacts on 1) the length and pressure-generating ability of the two hemidiaphragms and their mechanical coupling; 2) the process of muscle remodeling that may develop in response to changes in length and load [e.g., sarcomere adaptation (56), shift in muscle fiber type. . .]; and 3) the length and pressure-generating ability of rib cage muscles on each side of the chest.

Muscle activation and neural drive. Brath et al. (5) recorded surface electromyograms of the right and left hemidiaphragms during inspiratory threshold loading in patients with SLT for emphysema and computed changes in root mean square voltage to estimate neural drive. They found no difference in neural drive to the muscle on the transplanted vs. the native side. Similarly, Ratnovsky et al. (49) reported similar levels of activation during vital capacity maneuvers in the external intercostals, rectus abdominis, and external oblique muscles on
the native and transplanted sides in recipients of SLT for emphysema or fibrosis. Several important methodological flaws, however, limit interpretation of these data; for example, none of these studies used quantification of single motor unit firing rate (24) to compare neural drive to respiratory muscles on the native vs. the transplanted side, and on each side vs. in normal controls. In an experimental study, De Troyer and Leduc (15) assessed the response of the parasternal intercostals to acute single-lung inflation; they observed that the electromyographic activity of these muscles during occluded breaths was unaffected by lung inflation and remained similar on both sides of the chest.

Chest Wall Mechanics

Bilateral lung transplantation. After bilateral grafting, total lung capacity (TLC) is unaffected by the disease of the recipient and by the size of the donor lung. By 6 mo after surgery, patients have TLC values that are within the range predicted for the recipient, even when there are large disparities between the donor’s predicted TLC and the recipient’s preoperative, or predicted, TLC (9, 25, 46, 57). In contrast, the preoperative disease may influence values of functional residual capacity (FRC) and residual volume (RV) achieved after BLT or HLT. Whereas patients transplanted for pulmonary hypertension (who have nearly normal lung volumes before surgery) have normal or near normal values of FRC and RV after HLT (25, 57), patients transplanted for diseases that produce chronic hyperinflation (e.g., cystic fibrosis, emphysema) show a persistent increase in FRC (range 130–141% of predicted) and RV (range 151–164% of predicted) (9, 25, 46, 57; Fig. 3). These alterations are not seen in all patients, but when present, do not seem to improve with time (9, 23, 46). The increase in FRC is not related to a decrease in lung elastic recoil or to airflow obstruction (25), but appears to relate to persistent hyperinflation of the chest wall (i.e., corresponding to a displacement of the chest wall pressure-volume curve to higher volumes with consequent resetting of the balance between the now normal inward recoil of the lungs and the persisting increased outward recoil of the chest wall). Measurements of the anteroposterior diameter of the rib cage at FRC using computerized tomography showed increased values in patients transplanted for cystic fibrosis compared with patients transplanted for pulmonary hypertension and normal controls (25). Thus patients with emphysema and cystic fibrosis may have preoperative struc-

![Figure 3](http://jap.physiology.org/)

Fig. 3. Mean values (±SD) of TLC, FRC, residual volume (RV), and RV/TLC before (B) and at 6-mo intervals after heart-lung transplantation (HLT) or bilateral lung transplantation (BLT). Indications for transplantation included diseases associated with pulmonary hyperinflation: cystic fibrosis (n = 25), bronchiectasis (n = 3), emphysema (n = 3), and miscellaneous diagnoses (n = 2). Data are shown for 33 patients before transplantation, and for 33 patients at 6 and 12 mo, 21 patients at 18 and 24 mo, and 17 patients at 30 and 36 mo after the procedure. The horizontal dashed line represents 100% of the recipients’ predicted value. Note that FRC, RV, and RV/TLC remain greater than predicted after surgery (despite correction of the obstructive ventilatory defect). [Reprinted with permission (46). Copyright European Respiratory Society Journals Ltd.]
tural changes in rib cage shape that persist in part after transplantation and lead to persistent increases in FRC and RV. Additional studies are needed to determine the nature of these changes and understand why the increase in FRC and RV is seen in many, but not all, patients after HLT/BLT for emphysema and cystic fibrosis.

Single Lung Transplantation

Static lung volumes. As mentioned above, one major feature of SLT for emphysema is the displacement of the mediastinum toward the graft (Fig. 1). In two previous studies, the angle of mediastinal shift measured by computerized tomography in supine posture averaged 20–25° at FRC (14, 17). This displacement is likely due to the imbalance between the elastic recoil pressure of the graft and of the native lung, but the role of other factors like the size of the donor lung relative to that of the native lung is unknown.

Three studies have used standard chest radiographs (11) or computerized tomography scans (14, 17) to assess the volumes of the graft and the native lung at full inflation. On average, the graft and native lung had values corresponding to 33–39% and 55–75% of predicted TLC, respectively, with no obvious impact of differences in posture (upright for radiographs and supine for computerized tomography) and active vs. passive conditions. One study also showed that the volume of the graft at full inflation was decreased by ~20% compared with that of the same lung in normal controls (17; Fig. 4). This reduction may reflect functional restriction, as proposed by Hoppin (27), Fessler and Permutt (22), and Loring et al. (37). Functional restriction may be due to hyperinflation of the native lung overfilling the chest wall, to inspiratory muscle weakness causing inability to normally lower pleural pressure at full inspiration, or to a combination of both mechanisms. Inspiratory muscle weakness may be related to persistent hyperinflation of the chest and consequent shortening of the inspiratory muscles at shorter than optimal lengths.

In a recent study in 19 SLT recipients for emphysema, Loring et al. (38) suggested that inspiratory muscle weakness played a predominant role; in this study, however, patients had smaller than normal TLC values, which is very uncommon in this patient population, and much lower values of lung recoil pressure at full inflation (P_{Lmax}) than reported in earlier studies (10, 11). In addition, De Troyer and Leduc (15) showed in an animal model that acute single-lung inflation decreased the pressure-generating ability of inspiratory muscles, but that the ability of the diaphragm to lower pleural pressure was much better preserved on the side of the noninflated, than on the side of the inflated, lung. Although the precise mechanism(s) responsible for the reduced TLC of the graft remain to be clarified, the phenomenon of functional restriction likely accounts for the observation that patients with SLT for emphysema have smaller values of vital capacity (VC) and forced expiratory volume in 1 s (FEV$_1$) than patients operated for restrictive lung diseases (10, 37).

In contrast to TLC, the FRC of the graft measured using computerized tomography was similar to that of the same lung in normal controls (17). This observation is best explained by overexpansion of the rib cage at end expiration on the transplanted side, resulting from the interdependence between the two sides of the cage. This overexpansion may in part offset the restrictive effect that the mediastinal displacement has on the volume of the graft (17). Consistent with this observation, De Groote et al. (14) showed using optoelectronic plethysmography in recipients of SLT for emphysema that the two sides of the thoracic cage have similar volumes at end expiration.

Chest wall dynamics. De Groote et al. (14) also showed that the two sides of the cage undergo similar volume changes during FVC maneuvers and CO$_2$-stimulated breaths in seated posture, i.e., there is no volume distortion between the native and transplanted sides of the chest wall. Further studies using computed tomography indicated that the larger expiratory volume and shorter expiratory time constant of the graft (37) were accommodated for, at least in part, by displacement of the mediastinum toward the graft (Fig. 5). So, the mediastinum was displaced toward the graft during tidal and forced expiration and moved back toward the native lung during inspiration. This observation is consistent with the results of Lin et al. (36) who studied the mechanical effects of asymmetrical lung inflation in patients undergoing thoracic surgery and suggested that the external boundaries of the chest wall have a much greater resistance than the mediastinum to displacement and/or deformation. Displacement of the mediastinum toward the native lung during inspiration may be caused by a greater fall in pleural pressure on this side, by stretching produced by descent of the diaphragm dome and ventral motion of the sternum, or by a combination of the two mechanisms.

Dynamic lung volumes. Two studies have shown that most patients with SLT for emphysema develop expiratory flow limitation and dynamic hyperinflation at peak exercise (40, 42); this phenomenon likely originates in the native lung, as predicted by the model analysis of Loring et al. (37). Analysis of tidal flow volume loops demonstrated encroachment on the maximal expiratory limb during exercise, and patients who did exhibit flow limitation had greatest dyspnea scores.

Fig. 4. Average (±SE) values for the volumes of the native lung and of the graft (Tx) at full inflation (TLC) and at end-expiration (FRC) in 10 patients with SLT for emphysema (open bars). These values are compared with those obtained in 10 matched normal control subjects (hatched bars). Note that the volume of the graft is similar to that of controls at end expiration, but smaller than that of controls at full inflation. Statistical differences are shown only for adjacent bars: **P < 0.005; ***P < 0.0005. [Reprinted with permission (17). Official journal of the American Thoracic Society].
Several studies have assessed the effects of LVRS on diaphragm strength by measuring Pd\textsubscript{disniff}, Pd\textsubscript{max}, or Pd\textsubscript{itw} before, and 1 to 24 mo after the procedure (2, 12, 26, 29–32, 41, 53, 58). These studies are qualitatively consistent, all showing an increase in the pressure-generating capacity of the muscle after surgery; four studies also showed increases in MIP (12, 41, 53, 58). The increase in MIP and Pd\textsubscript{disniff} was already present at 1 mo after LVRS in one study (58), and in the study by Bellemare et al. (2), Pd\textsubscript{max} (but not Pd\textsubscript{itw}) continued to increase throughout the first postoperative year. Laghi et al. (30) reported that values of Pd\textsubscript{itw} at 2 yr after surgery had decreased to values intermediate between those recorded before, and those recorded at 3 mo after the procedure; values of FRC showed a similar trend. The magnitude of changes in indexes of diaphragm strength was variable among patients and among studies; so, increases in Pd\textsubscript{disniff}, Pd\textsubscript{max}, and Pd\textsubscript{itw} ranged between 23 and 51%, 37 and 43%, and 50 and 100% of the preoperative value, respectively.

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LUNG VOLUME REDUCTION SURGERY

Diaphragm Strength

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lung volume, but Laghi et al. (29) found an improvement in diaphragm strength that was out of proportion with the reduction in lung volume. The validity of such comparisons, however, is questionable because they imply several postulates that have not been proven to be true.

Whether diaphragm strength fully recovers after LVRS is uncertain because only one of the studies quoted above included a control group; in this study, values of Pdimax and Pditw measured at 6 mo after surgery were similar to those of controls. This observation, however, needs to be confirmed by larger studies because it was obtained in only six patients. In addition, several factors that may impair diaphragm contractility before LVRS may not fully recover after surgery, e.g., muscle shortening (see below), reduced force generation at single-fiber level (44), right ventricular dysfunction, altered nutritional status, electrolyte abnormalities and CO₂ retention, corticosteroid use. . . . These factors, as well as differences in patients’ characteristics and time elapsed between surgery and study, may explain why LVRS produces variable improvements in diaphragm strength. The impact of this variability on the gains in lung function and quality of life remains to be established (see FUNCTIONAL RESTRICTION).

Diaphragm Length and Configuration

Human studies. A number of studies have assessed the impact of LVRS on diaphragm length or surface area and configuration, three using plain chest radiographs (2, 13, 32), one using ultrasound and magnetometers (24), and one using computerized tomography (8). Lando et al. (32) made measurements at active TLC in upright posture and demonstrated an increase in diaphragm length in the coronal but not in the sagittal plane, and a cranial motion of the dome after vs. before surgery. Bellemare et al. (2) and Gorman et al. (24) showed no significant effect of LVRS on diaphragm length at active TLC in upright posture. In contrast, total muscle length and the length of the zone of apposition increased at FRC in three studies (2, 13, 24) by 5–40% and 30–95%, respectively. In the study by Cassart et al. (8), the surface area of the whole muscle and of the zone of apposition increased at supine FRC by 17 and 43%, respectively. Relationships between diaphragm surface area and lung volume before and after surgery fitted almost a single line, i.e., at a given absolute lung volume, the surface area was identical [or very similar (24)] before and after the procedure (Fig. 6). Despite these improvements, diaphragm length and surface area after LVRS remained smaller than those of healthy individuals (2, 8); for example, in the study by Cassart et al. (8), the surface areas of the whole muscle and of the zone of apposition at FRC averaged ~1,000 and ~500 cm² after LVRS compared with ~1,200 and ~700 cm² in normal controls (6).

The curvature of the dome changed little with surgery. The dome shape factor did not increase in either the coronal, or the sagittal plane after LVRS in the study by Bellemare et al. (2), and the increase in the curvature reported by Cassart et al. (8) was only observed at TLC in the sagittal plane.

The response of skeletal muscles to sustained changes in length is a process that develops over time. Animal studies have shown that skeletal muscles adapt to chronic changes in length by deleting (in case of shortening) or adding (in case of lengthening) sarcomeres in series within muscle fibers; this leads to a shift of the length-tension curve that brings optimal length closer to precontraction length and restores the muscle pressure-generating ability. This response has been demonstrated in the diaphragm of emphysematous hamsters (19). It also probably develops in patients with emphysema and explains that Pditw at FRC is higher in these patients than the value obtained at a similar lung volume in normal individuals (2, 56); sarcomere deletion, however, seems unable to fully compensate for muscle shortening (43) since Pditw remains below normal in emphysema patients (2, 56, 48).

If optimal length were actually achieved close to the spontaneous end-expiratory level in emphysema patients, an acute decrease in volume (as occurs with LVRS) would be expected to stretch the muscle beyond optimal length and produce a short-term decrease in force generation, followed by a progressive increase over time as length adaptation (addition of sarcomeres) develops. Studies by Loring et al. (38) and Ingenito et al. (28) showed that in many patients studied 4–6 mo after LVRS, the relationship of maximal inspiratory esophageal pressure and lung volume was shifted toward lower volumes after compared with before surgery, i.e., there was a loss of force-generating ability at isovolume. In addition, three studies demonstrated that Pdimax, Pdisniff, or sniff nasal inspiratory pressure continued to improve throughout the first postoperative year (2, 13, 31). These observations, however, cannot be interpreted as providing convincing evidence that LVRS is followed by an initial loss of diaphragm contractility; there is no study comparing pre- and early postoperative data, and interpretation of the results is made difficult by many confounding factors.

Additional studies are thus needed to establish the time course of changes in diaphragm strength after LVRS, and to

![Fig. 6. Measurements of diaphragm surface area obtained in supine posture using computerized tomography in 11 patients with emphysema before and after LVRS. Average values (±SE) for the total surface area of the diaphragm (Adi), the surface area of the dome (Ado), and the surface area of the zone of apposition (Aap) were measured at FRC, mid-inspiratory capacity, and TLC and are plotted as a function of supine lung volume. Note that LVRS produced a reduction in Adi and Aap but not in Ado; however, at a given absolute volume, Adi and Aap were similar before vs. after the procedure. [Reprinted with permission (8). Official journal of the American Thoracic Society].](http://jap.physiology.org/Downloadedfrom http://jap.physiology.org/ by 10.220.32.247 on April 1, 2017)
determine the characteristics of the muscle remodeling that may develop in response to changes in length and load [e.g., sarcomere adaptation (56) and shift in muscle fiber type...].

Animal studies. Lewis et al. (35) showed in an emphysema hamster model that the acute fiber stretch produced by LVRS resulted in muscle injury characterized by sarcolemmal rupture and myofibrillar disruption of type I and IIA fibers and profound force deficit in vitro. This deficit, which may be amplified in vivo by muscle stretching (see above), may explain why the ventilatory pump of LVRS patients is so vulnerable in the early postoperative period.

Experimental studies in rats have shown that at 5 mo after LVRS, sarcomeres are added in series with a resultant increase in diaphragm optimal length (54, 55). The chemical signaling involved in this response may include diaphragm insulin-like growth factor-I (IGF-I), which is upregulated on day 1 after surgery (35). In the hamster model used by Marchand et al. (39), the increase in optimal length in LVRS animals was less marked and the difference with the sham-sternotomy group only reached significance after a single outlier in this group was removed from the analysis; in this study, however, animals were studied only 8 wk after LVRS, which may be too short for full-length adaptation to occur. Notably, Marchand et al. (39) reported a significant decrease in diaphragm mass and twitch tension, but an increased resistance to fatigue due to a shift from type IIX/b to type IIA fibers in the LVRS animals compared with emphysema controls.

Respiratory Muscle Recruitment and Neural Drive

LVRS is accompanied by a decrease in the $\Delta P_{ga}/\Delta P_{es}$ ratio during tidal breathing, a greater contribution of the abdomen to tidal volume, and a better synchronization of rib cage-abdominal motion with less frequent abdominal paradoxical motion during inspiration (3, 4, 29, 41). These changes likely reflect both an increased contribution of the diaphragm to tidal breathing (59) and a decreased recruitment of the abdominal and intercostal-accessory muscles. The latter factor did not play an important role at rest (3, 29, 41), but was obvious when the pattern of tidal pressure generation at equivalent workloads during exercise was compared after vs. before LVRS (3, 41). The increased contribution of the diaphragm to ventilation after surgery was accompanied by a reduction in neural drive, as evidenced by a 16% decrease in median motor unit firing frequency during tidal breathing (24) and a 35% reduction in esophageal EMG activity during inspiratory threshold loading (31). These observations are consistent with the decreased load placed on the respiratory muscle pump and the increase in diaphragm strength, resulting in an enhanced diaphragm neuromechanical coupling at rest and during exercise (29, 30).

Rib Cage Dimensions

Two studies using plain chest radiographs failed to show significant changes in rib cage dimensions after compared with before LVRS (2, 24). In contrast, one study performed at active TLC reported decreases in both rib cage anteroposterior and transverse diameters measured in upright posture using chest radiographs and in anteroposterior diameters measured supine using computerized tomography (33); these decreases, however, were small in magnitude (<5%). Because the diaphragm moved cranially after LVRS while rib cage dimensions were (nearly) unaffected, the height of the dome was smaller for any given rib cage surface area after compared with before surgery. Bellemare et al. (2) suggested that this might reflect an alteration in the distribution of pleural surface pressure with a preferential increase in axial stress caused by ressection of the apical parts of the lung. Additional studies are needed to assess how LVRS may impact on the length and geometry of rib cage inspiratory muscles.

FUNCTIONAL RESTRICTION

Fessler and Permutt (22), Hoppin (27), and Loring et al. (37) proposed a theoretical analysis in which they describe the inescapable structural and functional linkage between volume-dependent expiratory lung function and volume-dependent inspiratory chest wall function and the way they are altered by emphysema, LVRS, and single-lung transplantation. In this landmark analysis, the authors proposed that emphysema causes dysfunctional interaction between the chest wall and the lungs. The hyperinflated lungs keep the chest wall greatly expanded, limiting the capacity of inspiratory muscles to generate adequate inspiratory pressures, flow rates, and tidal volumes. At the same time, the limited ability of the chest wall to expand keeps the emphysematous lungs from being inflated to the supernormal volumes at which greater recoil pressures and higher expiratory flow rates could be achieved. This mutually disadvantageous interaction between the lungs and chest wall can be seen as a problem of relative size, the lungs being too large for optimal function of the chest wall and the chest wall being too small for optimal function of the lungs. This disadvantageous interaction is altered by LVRS and transplantation.

Lung Volume Reduction Surgery

In the analysis proposed by Fessler and Permutt (22), Hoppin (27), and Loring et al. (37), improvements in lung function after LVRS are thus seen as being primarily due to a reduction of the mismatch between the size of the hyperinflated lungs and the size of the chest wall. So the increase in expiratory flows produced by LVRS would primarily be caused by an increase in lung recoil pressure at full inflation, rather than by an improvement in airway resistance or closure (i.e., LVRS does not work through improving tethering of the airways). As a result of the process of resizing the lung to the chest wall, RV would decrease to a greater extent than TLC, such that vital capacity (VC) and expiratory flows would increase. This analysis is supported by the observation that the preoperative ratio of RV to TLC (which reflects the degree of size mismatch) is the best predictor of the increase in VC after surgery, which largely accounts for the increase in FEV$_1$ (i.e., there is little improvement in FEV$_1$/FVC; Refs. 22, 28). In contrast, the model predicts a relatively small influence of lung recoil or heterogeneity of emphysema on outcome (22, 27).

For the process of resizing to result in a greater recoil pressure at full inflation, inspiratory muscle contractility should not be affected by LVRS. As noted above, however, Ingenito et al. (28) and Loring et al. (37, 38) reported a loss of force-generating ability of inspiratory muscles after surgery, which occurred in proportion to the magnitude of the reduction in volume subsequent to the procedure. It is critical to understand the mechanisms responsible for this alteration because by...
reducing TLC and the elastic recoil at this volume, it will inevitably minimize the functional benefits of the intervention (28).

**Single-Lung Transplantation**

After SLT for emphysema, functional restriction may occur when hyperinflation of the native lung overfills the chest wall, which is unable to lower pleural pressure sufficiently to expand the graft to its predicted maximal inspiratory volume (17). The model analysis of Loring et al. (37) simulates the changes in volumes and flow rates of the native lung and the graft during prolonged maximal inflation, forced expiration, and maximal voluntary ventilation (MVV) and predicts the effects of chest wall size and of the size of the graft on postoperative lung function. Consistent with the concept of functional restriction, increasing chest wall size increased VC and tidal volume during the MVV maneuver much more than increasing the size of the transplanted lung. Furthermore, lung volume reduction of the native lung after SLT increased markedly VC and expiratory flows.

**Conclusions**

This review provides an overview of the effects of LVRS and SLT for emphysema on chest wall and respiratory muscle function. Both procedures substantially improve diaphragm length and contractility and alter the neural drive and pattern of respiratory muscle activation. In addition, they produce remarkable alterations in the relationships between the sizes of the lungs and chest wall, which provide a unique opportunity to better understand the process of functional restriction.

**REFERENCES**


