Radiologic and Functional Analysis of Compensatory Lung Growth After Living-Donor Lobectomy

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Background. **Whether compensatory lung growth occurs in adult humans is controversial. The aim of this study was to confirm compensatory lung growth by analyzing ipsilateral residual lung after lower lobectomy in living lung transplant donors with quantitative and qualitative computed tomography assessments.**

Methods. **Chest computed tomography and pulmonary function tests were performed in 31 eligible donors before and 1 year after donor lobectomy. Ipsilateral residual lung volume was measured with three-dimensional computed tomography volumetry. The computed tomography-estimated volumes of low, middle, and high attenuations in the lung were calculated. Assessment of the D value, a coefficient of the cumulative size distribution of low-density area clusters, was performed to evaluate the structural quality of the residual lung.**

Results. **Postoperative pulmonary function test values were significantly larger than preoperative estimated values. Although postoperative total volume, low attenuation volume, middle attenuation volume, and high attenuation volume of the ipsilateral residual lung were significantly larger than the preoperative volumes, with 50.2%, 50.0%, 41.5%, and 43.1% increase in the median values, respectively (all $p < 0.0001$), the differences in D values before and after donor lobectomy were not significant ($p = 0.848$). The total volume of ipsilateral residual lung was increased by more than 600 mL (50%).**

Conclusions. **The volume of ipsilateral residual lung increased, but its structural quality did not change before and after donor lobectomy. The existence of compensatory lung growth in adult humans was suggested by quantitative and qualitative computed tomography assessments.**

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Compensatory lung growth (CLG) is defined by an absolute increase in the quantity of functioning lung tissue in response to injury or disease, or both [1]. Whether CLG occurs in adult humans and large mammals is still controversial. In particular, an experimental pneumonectomy model has been studied as a useful model of CLG because of advantages related to ease of defining loss of functional lung tissue and of evaluating the compensatory responses in the residual lung [2–4]. Increases in lung volume after lung resection in adult humans have been widely considered to be alveolar dilatation, not CLG [2]. However, Butler and colleagues [5] reported a case of lung regeneration in the contralateral residual lung after pneumonectomy in an adult patient.

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Various studies have reported radiologic increases in the volume of the residual lung and postoperative pulmonary functional restoration in lung cancer patients with heterogeneous backgrounds [6, 7]. In contrast to such studies, we previously reported functional restoration after lower lobe resection of living lung transplantation (LLT) donors who were considered homogeneous, healthy subjects by pulmonary function test (PFT) results, quantitative three-dimensional (3D) computed tomography (CT), and radiologic Hounsfield unit (HU) evaluations [8, 9]. In the present study, other CT imaging parameters, the percentile of low attenuation volume (%LAV) within the lung, and D-value assessments were used to evaluate the structural quality of the residual lung after lower lobectomy. Several reports noted that increased %LAV reflects the loss of lung tissue associated with emphysematous change [10, 11]. The cumulative size distribution of low attenuation area clusters follows a power law characterized by the exponent D [12]. The D-value measurement reflects the fractal dimension of terminal air space geometry and has also been widely

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Abbreviations and Acronyms

- CLG = compensatory lung growth
- CT = computed tomography
- DLCO = diffusing capacity of the lung for carbon monoxide
- FEV_1 = forced expiratory volume in 1 second
- HAV = high attenuation volume
- HU = Hounsfield units
- L = lower lobe
- LAV = low attenuation volume
- LLT = living lung transplantation
- M = middle lobe
- MAV = middle attenuation volume
- PFT = pulmonary function test
- U = upper lobe
- VA = alveolar ventilation
- VC = vital capacity
- %HAV = percentile of high attenuation volume within the lung
- %LAV = percentile of low attenuation volume within the lung
- %MAV = percentile of middle attenuation volume within the lung
- 3D = three-dimensional

used for early emphysema detection [10–13] because the D value can sensitively detect alveolar tissue destruction and provide additional information about the morphologic features of emphysema [11–13].

The aim of this study was to evaluate the presence of CLG of the ipsilateral residual lung after lower lobectomy in LLT donors, which could be considered healthy and mature subjects, by PFTs and quantitative and qualitative CT assessments. In this study, PFTs and CT images were prospectively obtained at specified times, and CT images were analyzed retrospectively.

Material and Methods

The Kyoto University Graduate School and Faculty of Medicine Ethics Committee approved this study (approval No. E 2336).

Donors

From November 2010 to December 2012, 34 living donors (for 19 consecutive LLTs) were evaluated in our institute. The criteria for donor selection are reported elsewhere [9]. The living donors underwent chest CT before and 1 year after donor lobectomies. Included were 31 donors who underwent lower lobe resection and were monitored for 1 year; of these, 3 donors were excluded because thin-slice CT images were not available before or after donor lobectomies. PFTs, including vital capacity (VC), forced expiratory volume in 1 second (FEV_1), diffusing capacity of the lung for carbon monoxide (DLCO), and the ratio of DLCO to alveolar ventilation (DLCO/VA) were prospectively evaluated in enrolled donors before and after donor lobectomies. The estimated values for the PFTs (VC, FEV_1, and DLCO) after lung resection were calculated from preoperative values, as previously reported [14]. In detail, there were 19 segments in total in a donor's lungs, 5 segments in the right lower lobe, and 4 segments in the left lower lobe. Thus, to calculate the estimated postoperative PFT values, the preoperative PFT values for right-sided and left-sided lower lobectomy were multiplied by 14/19 and 15/19, respectively, taking into account the number of segments removed in a donor.

In the present study, chest CT and PFT assessments of 31 donors who underwent right or left lower lobectomy and were monitored for 1 year were retrospectively reviewed using several quantitative and qualitative assessments. The requirement for informed consent from each donor was waived for the retrospective part of the study design. Informed consent was obtained from each donor before the prospective part of the study.

CT Image Analysis

The CT images were analyzed retrospectively. Enrolled donors underwent noncontrast-enhanced chest CT (Aquilion 64; Toshiba Medical Systems, Tochigi, Japan). In addition to routine calibration using an air and water phantom, HU values of all images were corrected using tracheal air densities to eliminate the influence of X-ray tube aging, as previously reported [8, 11, 13]. The entire chest was scanned during one breath-hold with 0.5-mm collimation and a gantry rotation time of 500 ms, using automatic exposure control at 120 kVp. Thin-slice images ($\leq$1 mm) were reconstructed with a lung kernel. The processes were supervised by a board-certified diagnostic radiologist (T.K). The acquired CT data were then analyzed by AZE Virtual Place (AZE Ltd, Tokyo, Japan), and the volume of ipsilateral residual lung (right upper and middle lobes of right-sided donors, or left upper lobe of left-sided donors) evaluated before and 1 year after donor lobectomies was calculated semiautomatically (Fig 1). Thresholds of –950 and –700 HU were applied to the acquired lung CT data according to previous reports [15]. The volume between each HU threshold range was automatically calculated. The volume under –951 HU was defined and calculated as LAV, between –701 and –950 HU volume was defined and calculated as middle attenuation volume (MAV), and–700 HU and over was defined and calculated as high attenuation volume (HAV; Fig 2). The percentile of each volume of the lung was defined as %LAV, %MAV, and %HAV. The values of %LAV, % MAV, and %HAV were compared before and after donor lobectomy.

The D-value measurement is a power law analysis of a low attenuation area cluster [12, 16]. The size distribution of low attenuation area clusters follows a power law, and their analysis is useful for revealing the pattern of progression of emphysema [11–13]. The formula, $Y = K \times X^{-D}$, represents the concept of low attenuation area cluster analysis, with Y indicating the cumulative frequency distribution of low attenuation cluster size, K is the constant, and X is the low attenuation cluster size. Y can be described by a power law of X [12, 16]. The threshold of –960 HU was used to detect low attenuation clusters,