Editorial

Can pretransplant computed-tomographic assessment predict outcomes after lung transplantation?

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Survival after lung transplantation has improved over the last few decades (1). However, long-term survival after lung transplantation remains worse than that after other solid organ transplantations. To improve the outcomes after lung transplantation, patient selection is one of the important issues that needs to be reviewed. In fact, the International Society for Heart and Lung Transplantation (ISHLT) has continually upgraded the patient selection criteria for lung transplantation (2,3). Recently, pretransplant frailty (4) of lung transplant recipients was shown to be associated with decreased survival after lung transplantation. Frailty is a condition of increased vulnerability to adverse health outcomes, that represents the biologic rather than the chronologic age (4). Precise assessment of frailty is an important component for optimizing patient selection. The ISHLT consensus document included class I obesity [body mass index (BMI) 30.0–34.9 kg/m^2], progressive or severe malnutrition, and severe, symptomatic osteoporosis as relative contraindications (3); however, further standardization of the measurement techniques is required to assess the effect of frailty on the outcomes in lung transplantation.

In a recent study, Pienta *et al*. conducted a retrospective review of 200 patients who had undergone lung transplantation following morphomic analysis using computed-tomographic (CT) images obtained within a year prior to lung transplantation at their institution between 2003 and 2014 (5). The analytic morphomics conducted using pretransplant CT images covered the lungs, dorsal muscle groups, bones, subcutaneous and visceral fat areas, and bone density. They identified predictors of the body composition associated with the survival and other outcomes after lung transplantation on pretransplant CT images. They identified, by multivariate Cox regression analysis, subcutaneous fat area/total body area [hazard ratio (HR) 0.60, P=0.001], lung density 3 (–724 to –424 Hounsfield unit) volume (HR 0.67, P=0.013), serum creatinine (HR 4.37, P=0.010), and percentage predicted of the forced vital capacity (HR 0.98, P=0.021) as being independent predictors of the overall survival after lung transplantation. Moreover, multivariate logistic regression analysis also identified initial ventilatory support for more than 48 hours as being associated with a decrease of the distance from the vertebral body to the linea alba [odds ratio (OR) 0.49, P=0.002] and Zubrod score 4 (OR 14.0, P=0.0001). Visceral fat area (OR 0.17, P=0.023) was associated with prolonged air leak for more than 5 days. Increased bone mineral density (P<0.001) and increased cross-sectional body area (P<0.001) were associated with a decreased length of hospital stay, whereas supplemental oxygen (P<0.001), bilateral transplantation (P=0.002), cardiopulmonary bypass (P<0.001), and Zubrod score 3 (P<0.001) or 4 (P=0.040) were associated with an increased length of hospital stay. In summary, morphomic factors associated with lower metabolic reserve and frailty, including decreased subcutaneous fat, bone density, and body dimensions, were identified as independent predictors of survival, prolonged ventilation, and increased length of hospital stay. They concluded that analytic morphomics using pretransplant CT scans may improve patient selection and risk stratification for lung transplantation.

Basically, the physical characteristics of lung transplant recipients differ among countries and races. For example, in Japan, the BMI of lung transplant recipients tends to be very low, as the obesity rate in Japan is the lowest among the countries of the Organization for Economic Co-operation and Development (6). According to our recent report, the average BMI of the recipients who underwent living-donor lobar lung transplantation was 17.2±3.9 kg/m^2, which corresponds to the underweight category, and that of the recipients who underwent cadaveric lung transplantation was 19.3±4.5 kg/m^2 (7). Among these, the patients undergoing lung transplantation for pulmonary complications developing after hematopoietic stem cell transplantation, which is associated with a high risk of complications due to nutritional compromise and prolonged immunosuppressive therapy, had especially low BMI (8). Patients with BMI less than 18.5 kg/m^2 (underweight) have been reported to show increased morbidity and mortality rates after major lung resection (9) and increased mortality rates after lung transplantation (10). However, even though most of the recipients were underweight in our experience, both the recipients of living-donor lobar lung transplantation and those of cadaveric lung transplantation showed favorable and similar survival after lung transplantation (5-year survival rate, 80.6% *vs.* 69.8%; 10-year survival rate, 71.6% *vs.* 57.3%) (P=0.10). Although BMI is easily measurable and has been used in many researches, the reliability of BMI as an indicator of the body composition remains controversial (11). It has been suggested that the BMI does not adequately discriminate between muscle and fat and that it underestimates obesity prevalence (12). Furthermore, Pienta *et al.* identified differences between the subcutaneous fat area/total body cross-sectional area and BMI (5). In their study, in spite of having a normal BMI, many of the patients had a low subcutaneous fat area, and the authors could show no association between the BMI and survival after lung transplantation (5). As compared to BMI, analytic morphomics using pretransplant CT images is a more detailed and comprehensive approach to evaluate the body composition. Therefore, this technique might compensate for differences in the physical characteristics of the subjects of each country or race in the assessment of the body composition.

In regard to morphomic factors, psoas area has been shown to be associated with survival after lung transplantation (13), and the muscle volumes of the thigh muscles (14) and cross-sectional area of the quadriceps (15) have also been assessed in previous studies. Different from the analysis using these single morphomic muscle mass measurements, analytic morphomics using pretransplant CT images consists of multiple morphomic factors, including the lung density, dorsal muscle group area and density, subcutaneous and visceral fat area, bone density, and body dimensions such as the cross-sectional area (5). Interestingly, morphomic variables include not only muscle, fat and bone, which are generally assessed for the evaluation of frailty (4,16), but also the lung. In regard to the influence of variables of the lung, less severe lung disease was associated with improved survival as compared to more severe lung disease (5). Although these morphomic variables were acquired using automated algorithms in the dedicated application, analysis of multiple morphomic factors might provide more reliability and reproducibility to assess the frailty of the patients than analysis of a single factor.

Modalities for the measurement of muscle mass reported previously are bioelectrical impedance (17,18), CT (15,19) and magnetic resonance imaging (14). CT is inevitably performed to assess the general condition of the patients before listing them for lung transplantation. The use of standard CT would be practical and ideal to assess the frailty of the patients. In the study conducted by Pienta *et al.*, the preoperative CT obtained closest to the date of transplantation was analyzed, and the number of the patients who performed the CT immediately before the lung transplantation was veiled. They pointed out the unpredictable nature of transplantation and variability in waiting times, and implied the difficulty in standardizing the timing of CT. To reflect any changes occurring between the time of the CT and the transplantation, CT for analytic morphomics should be performed at the time of admission for lung transplantation. On the other hand, at our institution, CT is routinely performed to check the changes in the recipients at the time of admission for lung transplantation, because the national average waiting time for cadaveric lung transplantation is still very long, and more than two years in Japan. Except for the cost and effort, CT at the time of admission for lung transplantation would be ideal to assess the patient's condition, including for analytic morphomics.

In summary, analytic morphomics using pretransplant standard CT images is useful to assess the body composition related to metabolic reserve and frailty for lung transplantation. Although larger and prospective multicenter studies are required, as also mentioned by Pienta *et al.* in their report, analytic morphomics using pretransplant CT images may be one of the useful measurement techniques to optimize patient selection for lung transplantation and to improve the survival after lung transplantation.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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