Comparison of 1-, 3-, and 6-Minute Walk Tests in the Post-lung Transplant Period

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INTRODUCTION

After exhausting all treatment modalities, the definitive treatment of many end-stage lung diseases has been lung transplantation in recent years. The 6-minute walk test (6MWT) was used to evaluate the functional status, response to treatment, and prognosis of end-stage lung diseases. The 6MWT is a simple, inexpensive, reproducible, and easy-to-administer test for patients. Additionally, it has been shown that the patients reflect their ability for daily living activities better in this test than in other walk tests. The 6MWT fully evaluates the responses of all systems involved in completing the exercise, including the pulmonary and cardiovascular systems, as well as the muscle metabolism.^[1-6] The use of the 6MWT after lung transplantation on outcomes has not been sufficiently studied.^[7] By previous studies, the 6MWT is associated with posttransplant survival and also as a predictor for pretransplantation waiting mortality in lung transplant patients.^[8] Since a lower 6-minute walk distance (6MWD) is associated with a worse prognosis in end-stage lung diseases, the 6MWT

ABSTRACT

Objective: The 6-minute walk test (6MWT) values have an important role in pretransplant patient management, as they are an indicator of increased mortality in end-stage lung patients awaiting lung transplantation. However, there are not enough studies on the follow-up role of the 6MWT after lung transplantation. Although the 6MWT is widely used, it may not be an effective measure of functional endurance in some conditions and disease groups. Therefore, we investigated the relationship between the classical distance covered in 6 min and the distance walked in the first I or 3 min.

Methods: The study was compared with the preoperative 6MWT results and posttransplant results of patients who underwent lung transplantation between 2016 and 2021. The correlations of distances traveled during posttransplantation at 1, 3, and 6 min were analyzed. The subjects who completed the 6MWT during the follow-up were included in the study.

Results: There was a significant difference found between the pretransplantation 6-minute walk distance (6MWD) and posttransplantation 6MWD in the sixth month. A strong correlation between the distances of the I-minute walk test (IMWT) and the 6MWT was found in the first month of posttransplantation. IMWT and 3-minute walk test (3MWT) distances were significantly correlated with 6MWD in the sixth month posttransplantation.

Conclusion: In the early posttransplantation period, IMWT and 3MWT can be an alternative to the 6MWT to evaluate the functional status in this patient group.

has become one of the parameters used in the scoring calculation developed to evaluate this patient group for lung transplantation.^[9,10]

6MWD has no widely accepted threshold for prognosis after lung transplantation. Furthermore, its usefulness as a predictor of outcomes following a lung transplant is also insufficient. In a study comparing the 3-minute walk test (3MWT) and 6MWT in individuals with systemic hypertension, the correlation between walking distances was demonstrated.^[11] However, there were no studies comparing walking in less than 6 min in the posttransplant period and the classical 6MWT.^[7]

The distance traveled during the 6MWT is used as a measure of cardiopulmonary and musculoskeletal adaptation to pulmonary impairment. In a study on walk tests for different durations, which can be an alternative to 6MWT, the distance covered in the 2-minute walk test (2MWT), 6MWT, and 12-minute walk test (12MWT) in stroke patients was compared. In another study, they mentioned that they could use the 3MWT as an alternative to the standard 6MWT in patients with hypertension.^[11,12] Studies on the IMWT were conducted in the pediatric age group. According to studies in children with cerebral palsy, the IMWT is a valid and simple assessment to monitor changes in walking capacity in children with chronic conditions. In addition, it has been suggested that it may be an alternative test that is easy for the user to cooperate with and has less risk of falling due to the need for rest or loss of balance.^[13] The relationship between IMWT and 6MWT was investigated in the patient group with idiopathic pulmonary fibrosis (IPF).^[14] To the best of our knowledge, there were no studies of walk tests performed with different durations than the standard 6-min duration to assess functional capacity in the posttransplant period.

In this study, it has been investigated whether we can use a walk test, which takes less than 6 min after transplantation, as an alternative in the frail patient group that has undergone lung transplantation. The study sought an answer to the hypothesis question. The primary aim of the study was to evaluate whether the IMWT or 3MWT could replace the classical 6MWT after transplantation and to evaluate the walk test results in the first- and sixth-month periods after the transplantation. The secondary aim was to determine the change of the 6MWT in patients undergoing lung transplantation in their 6-month follow-up compared with their pretransplantation results.

MATERIALS AND METHODS

This retrospective single-center cohort study was conducted in the Department of Lung Transplantation of a tertiary hospital. The study was approved by the local ethics committee. The ethical approval was obtained in accordance with the Declaration of Helsinki. The data were collected from the patients' files in the hospital database. Due to the retrospective nature of the study, informed consent was not required from the patients for the use of medical data for publication purposes with the approval of the local scientific ethics committee. All patients' identifying information was kept confidential.

Study population

Of the 71 patients who underwent lung transplantation, 12 patients died in the first year of follow-up and were excluded from the study. We evaluated 59 patients who underwent transplantation in our clinic with end-stage lung disease between December 2016 and May 2021.

The consensus report on patient selection criteria was first published by the International Heart and Lung Transplantation Society (ISHLT) in 1998, and it is periodically updated with the increase in experience in transplantation over the years. In these guidelines, lung transplantation indications and contraindications, the stage at which patients should be referred to transplantation centers, and the criteria for being placed on transplantation waiting lists are detailed according to the underlying disease groups. In the selection of patients, not only the criteria specified in these international guidelines but also their country and center conditions should be taken into consideration. Our patients who apply to the lung transplantation clinic are first evaluated by the chest diseases and thoracic surgery specialist team with their disease history and current preliminary examinations. If there is no obstacle in terms of general indications and contraindications, further examinations are continued. Candidates go through a detailed examination process such as evaluation of the primary disease, general functional evaluation, determination of comorbidities and regulation of their optimal treatment, screening for chronic infections and malignancy, investigation of substance use, and examination of psychosocial status. Those placed on the transplant waiting list as lung transplant candidates are referred to diet and pulmonary rehabilitation.

Donors had PaO_2/FiO_2 (ratio of arterial oxygen partial pressure to fractional inspired oxygen) ratios above 300 mmHg [positive end-expiratory pressure (PEEP): 5 cmH_2O] and normal or near-normal chest radiographs. Bronchoscopy examinations performed before lung harvesting were performed for the evaluation of airway secretions. All the donors were younger than 55 years old, and the number of years of smoking was less than 20 years. It was made sure that all donors included in the study were in compliance with rules and protocols. The donor did not have any signs of chest trauma or previous heart-lung surgery. Furthermore, it was also checked that there were not any past signs of aspiration/sepsis.^[15]

Patients were also categorized according to the presence of underlying diseases such as obstructive lung disease (OLD), interstitial lung disease (ILD), enfective lung disease (ELD), and idiopathic pulmonary arterial hypertension (IPAH).

Our posttransplant follow-up protocol includes pulmonary function tests, laboratory parameters, 6MWT, imaging results, and controls with transbronchial biopsy of patients evaluated in the first, third, sixth, ninth (if a transbronchial biopsy is indicated, it is done in this month), and 12th months. The 6MWT was performed by a physiotherapist specialized in lung transplantation. Distances at the first and third minutes were recorded during the 6-min standard treatment. Patients who were able to perform the walk test and maintained their controls for I year were included in the study. Patients who could not perform the 6MWT for any reason were excluded from the study.

Data collection

The data were collected from the hospital database and patients' files. The data on patients' demographics and characteristics, including age, gender, and body mass index (BMI, kg/m²), were obtained. The results of laboratory examinations recorded at the time of diagnosis included complete forced expiratory volume in 1 s (%), forced vital capacity (%), and distance (m). During the 6MWT, distance, test start saturation of oxygen (SpO₂, %), test start heart rate (HR, beats per minute), end of test SpO₂, and HR values were recorded. Distances at the first and third minutes were recorded during the 6MWT.

Standard procedures

The 6MWT was performed indoors, along a flat and straight 50-m corridor supervised by a physiotherapist, according to the ATS guidelines. Pulse oximetry was used for continuous recording of the oxygen saturation (SpO_2) level in 6MWT. Dyspnea was assessed using the Borg scale for each minute during the 6MWT, and the maximum dyspnea level was recorded. Patients were encouraged every minute to use the standardized recommended sentences: "you are doing well" or "keep up the good work." Patients were allowed to stop during the test, but instructed to resume walking as soon as they felt they were able to walk. All the pulmonary function data were obtained as absolute values and expressed as percent predicted reference values.^[16] All transplant patients followed by our center were included in the rehabilitation program by the pulmonary rehabilitation department during the pre- and posttransplant periods.

Statistical analyses

The data obtained in this study were analyzed statistically using IBM SPSS Statistics 23.0 software. Descriptive statistics were used to illustrate the demographic and clinical characteristics of the patients. Medians and interquartile ranges were provided for nonparametric variables, while values of mean±standard deviation were used for parametric variables. The 6MWD before transplantation and the 6MWD at the sixth month after transplantation were compared using the Wilcoxon signed-rank test. The correlation between the distance covered by the classical 6-min walk and the distance walked for the 3-min period was determined using Spearman's correlation coefficient (r). In addition, Spearman's correlation coefficient (r) was used to determine the relationship between the percentage change in the 6MWD and the 1MWD and 3MWD in the first month and sixth month after the transplantation.

RESULTS

Overall, 59 patients were included in the study. Of these, 14 were females and 45 were males (23.7% and 76.3%, respectively) with a median age of 48 (28–56) years. The most common underlying diseases of these lung transplant candidates were OLD, ILD, ELD, and IPAH (n=11, 18.6%; n=26, 44.1%; n=21, 35.6%; and n=1, 1.7%, respectively). The median value of SpO_2 at the beginning of 6MWT was 92 (89–95)%, SpO_2 at the end of 6MWT was 83 (76–89)%, the heart rate at the beginning of 6MWT was 98 (84–110), the heart rate at the end of 6MWT was 121 (106–134), and 6MWD in the pretransplantation period was 250 (161–335) m. The demographic characteristics and clinical data of the participants are presented in Table 1.

The median distance of the IMWD was 80 (69–94.25) m, 3MWD was 212.50 (201–275) m, and 6MWD was 353.50 (298.5–400) m at first month after transplantation. The median value of IMWD was 80 (69–94.25) m, 3MWD was 184 (150.25–208.50) m, 6MWD was 475 (398.75– 512.50) m at 6 months after transplantation (Table 2). There was a significant difference between the pretransplantation 6MWD and posttransplantation 6-min distance in the sixth month (p<0.001) (Table 3). The relationship between the pretransplant and posttransplant 6MWD is shown in Figure 1, and the comparison of 6MWD in

Table I. Demographic characteristics period	n the pretransplant		
Age, median (IQR)	48 (28–56)		
BMI, median (IQR)	24 (19.7–26.8)		
Gender, male, n (%)	45 (76.3)		
FEV ₁ (%), median (IQR)	28 (20–45)		
FVC (%), median (IQR)	33 (26–43)		
FEV ₁ /FVC (%), median (IQR)	97 (65–115)		
PAP by catheterization	27 (21–34)		
Underlying diseases group (n=59), n (%)			
OLD	(8.6)		
ILD	26 (44.1)		
ELD	21 (35.6)		
IPAH	l (l.7)		
Pretransplantation 6MWT			
6MWD	250 (161–335)		
BT SpO ₂ , median (IQR)	92 (89–95)		
ET SpO ₂ , median (IQR)	83 (76–89)		
BT HR, median (IQR)	98 (84–110)		
ET HR, median (IQR)	121 (106–134)		

BMI: Body mass index; PAP: Pulmonary artery pressure; FEV1: Forced expiratory volume in 1 s; FVC: Forced vital capacity; OLD: Obstructive lung disease; ILD: Interstitial lung disease; ELD: Enfective lung disease; IPAH: Idiopathic pulmonary arterial hypertension; BT: Beginning of test; ET: End of test; 6MWT: 6-Minute walk test; 6MWD: 6-Minute walk distance; HR: Heart rate; IQR: Interquartile range; SpO,: Arterial oxygen saturation.

First month		
6MWD, median (IQR)	353.50 (298.5–400)	
IMWD, median (IQR)	80 (69–94.25)	
3MWD, median (IQR)	D, median (IQR) 212.50 (201–275)	
BT SpO ₂ , median (IQR)	96 (96–98)	
ET SpO ₂ , median (IQR)	95 (92.25–96.75)	
BT HR, median (IQR)	97.50 (89.25–107.75)	
ET HR, median (IQR)	121 (109.75–139)	
Sixth month		
6MWD, median (IQR)	475 (398.75–512.50)	
IMWD, median (IQR)	80 (69–94.25)	
3MWD, median (IQR)	184 (150.25–208.50)	
BT SpO ₂ , median (IQR)	92 (89–95)	
ET SpO ₂ , median (IQR)	83 (76–89)	
BT HR, median (IQR)	98 (84–110)	
ET HR, median (IQR)	121 (106–134)	

6MWD: 6-Minute walk distance; IMWD: I-Minute walk distance; 3MWD: 3-Minute walk distance; BT: Beginning of test; ET: End of test; HR: Heart rate; IQR: Interquartile range; SpO₂: Arterial oxygen saturation.



Figure 1. Variation of six-minute walking distances before and after transplantation.

the first and sixth months after transplantation is shown in Figure 2. The correlation analysis of walk distances at first-, third-, and sixth-minute posttransplantation is listed in Table 4. A strong correlation between 6MWD and IMWD was found in the first month at posttransplantation (r=0.796, p<0.001, CI (95%)=0.060-0.91). At the sixth month after transplantation, it was observed that 3MWD highly correlated with 6MWD (r=0.36, p<0.001, CI (95%)=0.48-0.84). Furthermore, there was a moderate correlation between the percentage change of 3MWD and 6MWD at the first and sixth months

Table 3. Comparison of pre-LTX 6MWD and post-LTX 6MWD at the sixth month					t-LTX
	n	Median ranks	Sum of ranks	Z	р
Negative ranks	l a	10.00	10.00	-5.228 ⁵	<0.001
Positive ranks	37⁵	19.76	731.00		
Ties	0 ^c				
Total	38				

Wilcoxon signed-rank test. 6MWD: 6-Minute walk distance; LTX: Lung transplantation. ^aSixth month 6MWD < pre-TX 6MWD. ^bSixth month 6MWD > pre-TX 6MWD. ^cSixth month 6MWD = pre-TX 6MWD.



Figure 2. Follow-up of six-minute walking distances in the first and sixth months after transplantation.

(r=0.699, p<0.001, CI (95%)=0.45–0.85). There was a significant correlation between the percentage change of IMWD and 6MWD at the first and sixth months (r=0.750, p<0.001, CI (95%)=0.53–0.89) (Table 5).

DISCUSSION

The primary findings of this study showed that walk distance at 3 min correlated with the distance walked in 6 min in the first month and the sixth month at posttransplant period. Another finding of the study was that there was a correlation between the percentage change of 3MWD and 6MWD in the first and sixth months. Posttransplant 6MWD values were found to be significantly higher than pretransplant values.

The study by Seoane et al.^[7] showed that the distance walked for 6 min in lung transplant patients continued to improve during the first year. Similarly, in our study, we found that the walk distance of the patients increased in the 6-month follow-up compared with the pretransplantation period.

Bohannon et al.,^[17] in their study comparing the 2MWT and 6MWT in healthy individuals, showed that the distances covered in both walking times were highly cor-

	First month 6MWD	First month IMWD	First month 3MWD	Sixth month 6MWD	Sixth month IMWD	Sixth month 3MWD
First month 6MWD		r=0.796	r=0.065	r=0.123		
		p<0.001	р=0.697	p=0.462		
		CI (95%):	CI (95%):	CI (95%):		
		0.60-0.91	0.27-0.36	0.25-0.43		
Sixth month 6MWD					r=0.322	r=0.719
					p=0.049	p<0.001
					CI (95%):	CI (95%):
					0.00-0.15	0.48-0.84

Table 4. Correlation of walk distances at first-, third-, and sixth-minute post-LTX

Spearman's correlation test. 6MWD: 6-Minute walk distance; 3MWD: 3-Minute walk distance; IMWD: I-Minute walk distance; LTX: Lung transplantation; CI: Confidence interval.

	Percentage change of 6MWD
Percentage change of distance 3MWT between the first and sixth month in post-LTX	r=0.699
	p<0.001
	CI (95%): 0.45–0.85)
Percentage change of distance IMWT between the first and sixth month in post-LTX	r=0.750
	p<0.001
	CI (95%): 0.53–0.89

related. Similarly, in our study, we found a high positive correlation between 3MWD and 6MWD at the postoperative sixth month. We also found a high positive correlation between walk distances of I and 6 min in the shorter postoperative period (first month). In the early posttransplantation period, while the patient is still in the adaptation period, walking for less than 6 min may also be more comfortable and beneficial in the progression follow-up. In another study that investigated the comparison of the 2MWT, 6MWT, and 12MWT, the 2MWT was found to be the most efficient of the three test times and correlated well. In this study, the 2-min assessment with less fatigue inhibition can be considered a valid measure of self-selected walking speed. The 6MWT and 12MWT, which can cause significant fatigue and the need to rest, can be considered measures of endurance rather than speed.^[12] 3MWT and 6MWT were compared in a study conducted by Ibikunle et al.[11] According to this study, the 3MWT stood out as the submaximal walk test that could reach the maximum exercise capacity. On the other hand, it is not known whether it can initiate adequate changes in the cardiovascular system in the same way as the 6MWT in functional capacity assessment. On the other hand, in the study of Goel et al.,[18] which investigated the 3MWT and 6MWT in the assessment of the progression of COVID-19 patients, there was no significant correlation found between walking for 3 min and walking for 6 min. In the light of this evidence, we believe that the duration of walking the distance as long as the patient can do effectively can provide as efficient results as the classical 6MWT.

Studies on IMWT have generally been conducted in childhood. In a study, a case was excluded due to orthopedic limitations. This was shown as an indicator of the functional adequacy of the selected period. It was emphasized that the long-term tests performed on children with more serious disabilities would face the problem of not completing the test.^[19] In another study conducted by Kerr et al.^[20] in the pediatric age group, it was revealed that it could provide useful information about both the effective completion of walking and the functional ability of the subjects. Thus, it was emphasized that IMWT could be an alternative test showing functional endurance. In a study by Nunes et al.,^[14] IMWT showed a strong correlation with

6MWT in the group of adults with IPF, and they concluded that it could predict transplant-free survival. Since shorter walking times are logistically advantageous and provide similar prognostic information, the IMWT has been emphasized as a more practical test than the 6MWT. Similarly, in our study, a significant relationship was found between IMWD and 6MWD data. Considering the variable conditions, the severity of the pretransplant diseases of our patients, the different waiting times on the transplant waiting list, the follow-up of some patients in intensive care units due to the need for advanced life support systems such as a bridge to ECMO, every patient has not the same functional status during the chance of transplantation. As it is a heterogeneous patient population, IMWT can be shown as an alternative test to 6MWT in terms of completion and sustainability of the test in 1 min instead of the most commonly used 6 min to evaluate the functional adequacy of patients.

Limitations

First, the sample size may be limited. Due to the nature of the retrospective study, the Borg Dyspnea Scale during the 6MWT, SpO_2 , and HR changes during the 1MWT and 3MWT were not included in the study to avoid lack of data. Our study has several limitations.

CONCLUSION

The walk distance at 3 min correlated with the 6-min result in the first month and the sixth month at the posttransplant period. Also, the percentage change of the 3MWD and 6MWD correlated between the first- and sixth-month periods. Posttransplant 6MWD were found to be significantly higher than pretransplant values. We thought the IMWT and 3MWT have great potential in predicting the functional status of transplant patients. As far as we know, the present study is the first study to investigate the posttransplant follow-up of patients with IMWT and 3MWT in the lung transplant population. Based on the distances walked, and particularly the significant correlation between 3MWD and 6MWD, the 3MWD can be considered an alternative to the 6MWD to demonstrate the relative functional endurance.

Ethics Committee Approval

This study approved by the Kartal Koşuyolu Higher Specialized Training and Research Hospital Non-Interventional Clinical Research Ethics Committee (Date: 08.05.2020, Decision No: 2020.4/35-340).

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: P.A.G., M.E.Ç.; Design: P.A.G.; Supervision: S.Ç.; Fundings: E.T.; Data: A.N.H., E.S.; Analysis: P.A.G.; Literature search: M.V.; Writing: P.A.G., M.E.Ç.; Critical revision: E.T., P.A.G.

Conflict of Interest

None declared.

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Akciğer Nakli Sonrası Dönemde 1-, 3- ve 6- Dakikalık Yürüme Testlerinin Karşılaştırılması

Amaç: Altı dakika yürüme testi değerleri, akciğer transplantasyonu bekleyen son dönem akciğer hastalarında mortalite artışının bir göstergesi olması nedeniyle transplantasyon öncesi hasta yönetiminde önemli bir yere sahiptir. Ancak, akciğer transplantasyonundan sonra altı dakika yürüme testinin takipteki rolü konusunda yeterli çalışma bulunmamaktadır. Altı dakika yürüme testi yaygın olarak kullanılmasına rağmen bazı durumlarda ve hastalık gruplarında fonksiyonel dayanıklılığın etkili bir ölçüsü olarak uygulanamayabilir. Bu nedenle, altı dakikada kat edilen klasik mesafe ile ilk bir veya üç dakikada yürünen mesafe arasındaki ilişkiyi araştırdık.

Gereç ve Yöntem: Çalışma, 2016–2021 yılları arasında akciğer nakli yapılan hastaların ameliyat öncesi altı dakika yürüme testi sonuçları ve nakil sonrası sonuçları ile karşılaştırıldı. Nakil sonrası bir, üç ve altı dakikada kat edilen mesafelerin korelasyonları analiz edildi. İzlemde altı dakika yürüme testini tamamlayan olgular çalışmaya dahil edildi.

Bulgular: Altıncı ayda nakil öncesi altı dakika yürüme mesafesi ile nakil sonrası altı dakika yürüme mesafesi arasında anlamlı fark bulundu. Transplantasyondan sonraki birinci ayda bir dakika yürüme testi ile altı dakika yürüme testi mesafeleri arasında güçlü bir ilişki bulundu. Bir ve üç dakikalık yürüme testi mesafeleri, transplantasyon sonrası altıncı aylık dönemde altı dakikalık yürüme mesafeleri ile korelasyonu anlamlı idi.

Sonuç: Özellikle transplantasyon sonrası erken dönemde bu hasta grubunda fonksiyonel durumu değerlendirmek için bir veya üç dakika yürüme testi altı dakika yürüme testine alternatif olabilir.

Anahtar Sözcükler: I-Dakika Yürüme Testi; 3-Dakika Yürüme Testi; 6-Dakika Yürüme Testi; akciğer nakli.