Turkish Journal of Thoracic and Cardiovascular Surgery 2022;30(4):584-592
http://dx.doi.org/doi: 10.5606/tgkdc.dergisi.2022.21855

Original Article / Özgün Makale

Effectiveness of echocardiographic evaluation of lung transplant candidates: Could it be an alternative to right heart catheterization?

Akciğer nakli adaylarının ekokardiyografik değerlendirmesinin etkinliği: Sağ kalp kateterizasyonuna alternatif olabilir mi?

Pınar Atagün Güney, Murat Ersin Çardak

Lung Transplantation, Kartal Koşuyolu High Speciality Educational and Research Hospital, Istanbul, Türkiye

ABSTRACT

Background: In this study, we aimed to evaluate the value of transthoracic echocardiography in the estimation of pulmonary artery pressure and to identify the presence of pulmonary hypertension in lung transplant candidates with end-stage lung disease.

Methods: Between January 2012 and September 2020, a total of 244 patients (166 males, 78 females; mean age: 48.6±13.8 years; range, 18 to 77 years) who were diagnosed with end-stage lung disease due to various underlying conditions and underwent right heart catheterization and transthoracic echocardiography within 72 h were retrospectively analyzed. Hemodynamic parameters of the patients were compared. Correlation analysis was performed among the values estimated by transthoracic echocardiography and measured by right heart catheterization for pulmonary artery pressure measurements.

Results: The median pulmonary artery systolic pressure with right heart catheterization was 43 mmHg and 40 mmHg using transthoracic echocardiography. A positive correlation was seen between the pulmonary artery systolic pressure estimated by transthoracic echocardiography and right heart catheterization (r=0.718; p<0.001). The sensitivity, specificity, and positive and negative predictive values of pulmonary artery systolic pressure measurement were 76.30%, 64.22%, 72.54%, and 68.63%, respectively.

Conclusion: This study revealed a strong positive correlation between the pulmonary artery systolic pressure evaluated with transthoracic echocardiography and measured with right heart catheterization. Pulmonary hypertension detection by these two methods showed acceptable sensitivity and specificity. Transthoracic echocardiography may be a useful and practical method to monitor pulmonary artery pressure trends both initially and in the subsequent follow-up of cardiac hemodynamics in lung transplant candidates.

Keywords: Lung transplantation, right heart catheterization, transthoracic echocardiography.

ÖZ

Amaç: Bu çalışmada son dönem akciğer hastalığı olan akciğer nakli adaylarında pulmoner arter basıncının tahmininde transtorasik ekokardiyografinin rolü değerlendirildi ve pulmoner hipertansiyon varlığı belirlendi.

Çalışma planı: Ocak 2012 - Eylül 2020 tarihleri arasında altta yatan çeşitli nedenlere bağlı son dönem akciğer hastalığı tanısı konan ve 72 saat içinde sağ kalp kateterizasyonu ve transtorasik ekokardiyografi yapılan toplam 244 hasta (166 erkek, 78 kadın; ort. yaş: 48.6±13.8 yıl; dağılım, 18-77 yıl) retrospektif olarak incelendi. Hastaların hemodinamik özellikleri karşılaştırıldı. Pulmoner arter basınç ölçümleri için transtorasik ekokardiyografi ile tahmin edilen ve sağ kalp kateterizasyonu ile ölçülen değerler arasında korelasyon analizi yapıldı.

Bulgular: Sağ kalp kateterizasyonu ile medyan pulmoner arter sistolik basıncı 43 mmHg iken, transtorasik ekokardiyografi kullanılarak 40 mmHg idi. Sağ kalp kateterizasyonu ve transtorasik ekokardiyografi ile hesaplanan pulmoner arter sistolik basıncı arasında pozitif bir ilişki görüldü (r=0.718; p<0.001). Pulmoner arter sistolik basıncı ölçümünün duyarlılık, özgüllük ve pozitif ve negatif prediktif değerleri sırasıyla %76.30, %64.22, %72.54 ve %68.63 idi.

Sonuç: Bu çalışma, transtorasik ekokardiyografi ile değerlendirilen pulmoner arter sistolik basıncı ve sağ kalp kateterizasyonu ile ölçülen arasında güçlü bir pozitif ilişki olduğunu ortaya koydu. Bu iki yöntemle pulmoner hipertansiyon tespiti, kabul edilebilir duyarlılık ve özgüllük gösterdi. Transtorasik ekokardiyografi, akciğer nakli adaylarında hem başlangıçta hem de sonraki kardiyak hemodinamiğin takibinde pulmoner arter basınç eğilimlerini izlemek için yararlı ve pratik bir yöntem olabilir.

Anahtar sözcükler: Akciğer nakli, sağ kalp kateterizasyonu, transtorasik ekokardiyografi.

Received: March 27, 2021 *Accepted*: August 17, 2021 *Published online*: October 31, 2022

Correspondence: Pınar Atagün Güney, MD. Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Akciğer Nakli Bölümü, 34865 Kartal, İstanbul, Türkiye.
Tel: +90 535 - 967 44 90 e-mail: atagunpnar@yahoo.com

Cite this article as:
Atagün Güney P, Çardak ME. Effectiveness of echocardiographic evaluation of lung transplant candidates: Could it be an alternative to right heart catheterization?. Turk Gogus Kalp Dama 2022;30(4):584-592

Pulmonary hypertension (PHT) refers to high blood pressure in the lungs, and five groups of PHT have been identified based on different etiologies. Pulmonary hypertension impairs health-related quality of life (QoL), often signals advanced pulmonary disease, and can result in early mortality if left untreated during the course of pulmonary vascular disease, lung parenchyma, or airway disease.[1] Detection of PHT is typically an indicator of a poor prognosis. Since a variety of etiologies can lead to the development of PHT, classifying patients and assessing the clinical outcomes is complex. The prognosis is associated with the underlying disease, with the worst prognosis seen in cases of PHT due to lung diseases, such as chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis (IPF).[2]

Some medical treatment is available for PHT; however, surgery is often necessary. The severity of PHT affects decisions regarding surgical options to treat end-stage lung disease. The presence of significant PHT often requires evaluation of suitability for lung transplantation (LTx).[2] The most appropriate time for LTx is determined based on the PHT diagnosis and an increasing trend in pulmonary artery pressure (PAP) values.[3]

Right heart catheterization (RHC) and transthoracic echocardiography (TTE) are routine tests performed in patients undergoing transplant assessment at LTx centers. Although RHC is the gold-standard method to measure pulmonary pressure, it is invasive, expensive, and requires an experienced team and equipment. It also has significant risks, including morbidity (1.1%) and mortality (0.055%).[4] Transthoracic echocardiography is an inexpensive, non-invasive, and practical method to estimate PAP and monitor cardiac functions. It has become a popular means of non-invasive pulmonary artery systolic pressure (PASP) evaluation in the last two decades and provides useful information about right ventricular structure and function.[5] Additionally, a study by Buyukbayrak et al.[6] showed that the TTE played a critical role in the assessment of postoperative hemodynamic impairment in open-heart surgical patients. Another important aspect of TTE is that it can facilitate prediction of hemodynamic changes that may occur following transplantation and is helpful in the postoperative patient management.[7-10] Current guidelines recommend TTE for the evaluation of LTx candidates.[11]

Lung transplantation has evolved into a life-saving treatment option that can increase survival and QoL in selected patients with end-stage lung disease.[10] An accurate PASP estimation using TTE without the need for an invasive procedure such as RHC would be of great benefit. In the present study, we aimed to analyze the correlation between PAP estimated by TTE and RHC to evaluate the performance of TTE in the estimation of PAP and to identify the presence of PHT in LTx candidates with end-stage lung disease.

PATIENTS AND METHODS

This single-center, retrospective cohort study was conducted at the Department of Lung Transplantation of Kartal Koşuyolu High Speciality Educational and Research Hospital between January 2012 and September 2020. The study included a total of 244 consecutive patients (166 males, 78 females; mean age: 48.6±13.8 years; range, 18 to 77 years) who were diagnosed with end-stage lung disease due to various underlying conditions such as obstructive lung disease (OLD), interstitial lung disease (ILD), end-stage infectious lung disease, or pulmonary vascular disease (PVD), who were referred for LTx. Of the initial 317 patients selected for the study, 11 were excluded, as TTE and RHC were not both performed within 72 h. Another 38 patients were eliminated, as PASP could not be estimated using TTE, and 24 patients were found not to have sufficiently appreciable tricuspid regurgitation. Finally, 73 patients were excluded due to insufficient data for this study. The study flow chart is shown in Figure 1.

Data collection

The data used were extracted from patient files and the hospital database. Patient demographic details, smoking history, body mass index (BMI), arterial blood gas values, results of respiratory function test and a 6-min walk test (6MWT), long-term oxygen therapy use, need for non-invasive mechanical ventilation, PASP estimated by TTE, PASP measured by catheter, PAPmean, cardiac output (CO) results, and cardiac index (CI) assessments were recorded.

Standard procedures

The 6MWT was performed without any oxygen assistance according to the American Thoracic Society (ATS) guideline by an experienced physiotherapist.[12]

The RHC was regulated with a balloon-tipped and flow-directed pulmonary artery catheter. The catheter was placed through the right femoral vein or the right internal jugular vein utilizing local anesthesia and the Seldinger technique. Pulmonary artery occlusion pressure, right atrial pressure, pulmonary artery systolic and diastolic pressure, and CO were each measured

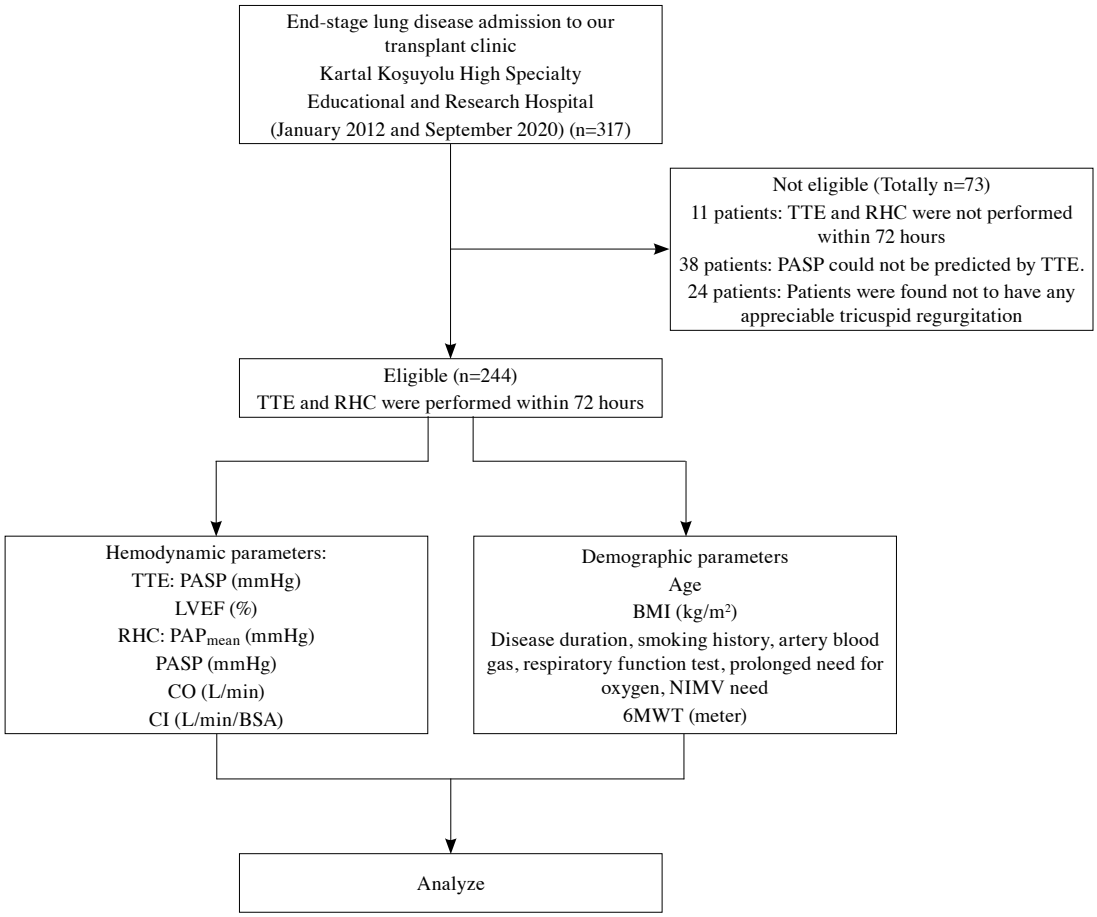

Figure 1. Study flow chart.

TTE: Transthoracic echocardiography; RHC: Right heart catheterization; PASP: Pulmonary artery systolic pressure; LVEF: Left ventricular ejection fraction; PAP: Pulmonary artery pressure; CO: Cardiac output; CI: Cardiac index; NIMV: Non-invasive mechanical ventilation; 6MWD: 6-min walking distance; BSA: Body surface area.

twice. The TTE was performed using conventional clinical echocardiographic equipment (il53 xMATRIX ultrasound system; Philips Healthcare, Inc., Andover, MA, USA). Transthoracic Doppler and two-dimensional images were retrieved from parasternal long and short-axis, apical four-chamber, and subcostal four-chamber views. Right ventricular size and function were assessed. The color flow Doppler technique was used to discern tricuspid regurgitate flow, and maximum jet velocity was calculated with continuous-wave Doppler without intravenous contrast. The right ventricular systolic pressure was approximated according to the modified Bernoulli equation and was considered equal to PASP without right ventricular outflow obstruction: PASP (mmHg) = right ventricular systolic pressure = trans tricuspid gradient + right atrial pressure, where tricuspid gradient 4×v2 (v= peak speed of tricuspid regurgitation m/second).[4,13,14]

The 2015 European Society of Cardiology (ESC)/ European Respiratory Society (ERS) Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension definition of PHT of a PAPmean at rest of ≥25 mm Hg was used.[15]

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were presented in mean ± standard deviation (SD), median and interquartile range (IQR) or number and frequency, where applicable. The relationship between RHC and hemodynamic changes detected with the TTE was evaluated according to the Pearson correlation analysis. The Bland-Altman analysis was used to determine the clinical compatibility of the TTE estimates of PASP/PAPmean with the values determined by RHC, and TTE estimates of PASP/PAPmean were considered accurate at 95%

Table 1. Demographic and clinical data of patients

	All patients (n=244)	OLD (n=64)	ILD (n=111)	End-stage infectious lung disease (n=55)	PVD (n=14)	*p*
Age (mean±SD)	48.6±13.8	55.1±10.0	51.5±13.1	38.7±12.3	34.4±10.0	<0.001
Sex						<0.001
Female, n (%)	78 (32%)	11 (14.1%)	35 (44.9%)	24 (30.8%)	8 (10.3%)	
Smoking, n (%)	119 (48.8%)	59 (49.6%)	48 (40.3%)	7 (5.9%)	5 (4.2%)	<0.001
Time since disease's diagnosis (mean±SD)	7.61±6.93	7.35±6.3	5.06±3.8	13.6±8.9	5.3±5.7	<0.001
BMI (mean±SD)	23.3±4.3	23.2±3.4	23.9±4.5	22.2±4.8	22.3±3.1	0.110
$PaCO_2$ (mean±SD)	45.1±13.6	50.4±11.7	45.8±13.1	51.1±15.7	36.8±6.7	<0.001
PaO_2/FiO_2, median (25-75%)	250 (250-307)	257 (233-280)	255 (236-273)	286 (254-317)	289 (223-355)	0.210
6MWD, meters, median (25-75%)	210 (210-312)	226 (196-255)	219 (197-241)	211 (176-247)	180 (104-257)	0.635
FEV1, % (mean±SD)	34.7±18.0	27.5±14.9	41.1±17.4	27.5±12.1	45.7±28.6	<0.001
NIMV, n (%)	66 (27%)	40 (22.5%)	97 (54.5%)	29 (16.3%)	12 (6.7%)	<0.001
LTOT, n (%) (>12 h)	184 (75.4%)	52 (28.3%)	79 (53.3%)	43 (23.4%)	4 (5.4%)	0.462
RHC PAP_{mean}, median (25-75%)	43 (33-56%)	26.8 (23.6-30.0)	26.8 (24.3-29.4)	29.6 (26.4-32.9)	60.9 (51.6-70.2)	<0.001

Data are given in mean±standard deviation (SD), median and interquartile rate (IQR), or n (number) and (%); OLD: Obstructive pulmonary disease; ILD: Interstitial lung disease; PVD: Pulmonary vascular disease; SD: Standard deviation; BMI: Body mass index; $PaCO_2$: Partial arterial pressure of carbon dioxide; PaO_2: Partial arterial pressure of oxygen; FiO_2: Fraction of inspired oxygen; 6MWD: 6-min walking distance; FEV1: Forced expiratory volume in 1 sec; NIMV: Non-invasive mechanical ventilation; LTOT: Long-term oxygen treatment; RHC PAP: Right heart catheterization Pulmonary artery pressure;

limits of agreement within 10 mmHg. A *p* value of <0.05 was considered statistically significant.

RESULTS

The patients were divided into subgroups according to underlying lung disease: OLD (n=64, 26.2%), ILD (n=111, 45.5%), end-stage infectious lung disease (n=55, 22.5%), and PVD (n=14, 5.7%). The mean time from diagnosis to the evaluation of the patient for a LTx candidate in the inpatient setting was 7.61±6.93 years. The mean BMI was 23.3±4.3 kg/m^2 and the mean forced expiratory volume in 1 sec (FEV1) was 34.75±18%. Demographic data, pulmonary function test results, and hemodynamic characteristics of the participants are presented in Table 1 according to the underlying lung disease group. The mean age was higher in ILD and OLD subgroups than end-stage infectious lung disease and PVD groups (p<0.001). When the ILD and OLD groups (p=0.17) and end-stage infectious lung disease and PVD groups (p=0.52) were evaluated among themselves, there was no statistically significant difference. However, smoking was significantly higher in the ILD group than in the OLD, end-stage infectious lung disease, and PVD groups (p<0.001). End-stage infectious lung disease according to the time elapsed after diagnosis; ILD was short compared to OLD and PVD (p<0.001). The mean FEV1 in ILD group was higher than that of the OLD and end-stage infectious lung disease subgroups (p<0.001), but no significant difference was found compared to the PVD subgroup (p=1.00). The mean FEV1 value was similar in the OLD and end-stage infectious lung disease (p=1.00) groups and in the PVD and other disease groups (p=0.93). There was no statistically significant difference among the subgroups in terms of the mean BMI and 6MWT values (p=1.00 and p=1.00, respectively). The mean TTE PASP value was higher in the PVD group than that of the ILD, OLD, and end-stage infectious lung disease groups (p<0.001). The mean PASP value measured with the RHC was higher in the PVD group than that of the ILD, OLD, and end-stage infectious lung disease groups (p<0.001). The mean CO and CI values were similar among the subgroups (p=1.00 and p=1.00, respectively).

The median RHC PASP value was 43 (IQR: 33 to 56.75) mmHg, while it was 40 mmHg (IQR: 30 to 60) mmHg when TTE was used. The TTE results indicated a median left ventricular ejection fraction of 63.56% (IQR: 63.09 to 64.03%), a median CO of 4.5 L/min (IQR: 4.3 to 4.6 L/min), and a median CI of 2.5 L/min/body surface area (BSA) (IQR: 2.5-2.6 L/min/BSA). The RHC and TTE hemodynamic measurements are presented in Table 2.

Overall, 55.3% (n=135) of the study patients were diagnosed with PHT based on RHC measurements, while 58.2% (n=142) were diagnosed with TTE. Figure 2 shows the PASP values recorded by TTE

Table 2. Hemodynamic parameters determined by RHC and Doppler echocardiography

	Median	IQR
Transthoracic echocardiography		
PASP (mmHg)	40.0	30.0-60.0
LVEF (%)	63.56	63.0-64.0
Right heart catheterization		
PAP_{mean} (mmHg)	15.2	27.5-31.3
PASP (mmHg)	43.0	33.0-56.7
CO (L/min)	4.5	4.3-4.6
CI (L/min/BSA)	2.5	2.5-2.6

RHC: Right heart catheterization; IQR: Interquartile ratio; PASP: Pulmonary artery systolic pressure; LVEF: Left ventricular ejection fraction; CO: Cardiac output; CI: Cardiac index; BSA: Body surface area.

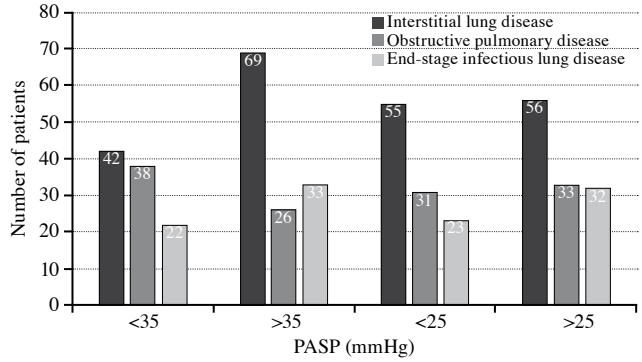

Figure 2. PASP in the sub-groups according to etiology of lung disease. First two groups estimated by TTE, last two groups measured by RHC.

PASP: Pulmonary artery systolic pressure; TTE: Transthoracic echocardiography; RHC: Right heart catheterization; PASP: Pulmonary artery systolic pressure.

and RHC for each of the subgroup. The overall median PASP was 40.0 (IQR: 45.57 to 52.33) mmHg as assessed by TTE and 43 (IQR: 33 to 56.75) mmHg as measured by RHC. The patients with ILD had a median PASP of 44 (IQR: 30 to 60) mmHg using TTE and the median RHC measurement was 43.0 (IQR: 31 to 53) mmHg. Patients with OLD had a median TTE PASP of 35 (IQR: 29 to 45) mmHg and the median RHC PASP was 38 (IQR: 33 to 51) mmHg. The end-stage infectious lung disease patients had a median PASP of 43 (IQR: 29 to 65) mmHg using TTE and a median of 46.0 (IQR: 35 to 58) mmHg using RHC. The PVD group had a median PASP by RHC of 93 (IQR: 76 to 138) mmHg.

Correlation analysis of TTE and RHC PASP measurements are shown in Table 3. A strong correlation between the two methods was seen in all of the study patients (r=0.718; p<0.001) (Figure 3). The Bland-Altman analysis results are illustrated in Figure 4. Analysis according to the underlying lung disease subgroups revealed a weak correlation in OLD patients (r=0.416; p=0.001) and a moderate correlation in the ILD (r=0.647; p<0.001) and end-stage infectious lung disease (r=0.590; p<0.001) groups. No significant correlation was observed in the PVD patients (r=0.428; p=0.127).

The sensitivity, specificity, and positive predictive and negative predictive values of TTE and RHC were analyzed based on the PHT criteria. The sensitivity, specificity, and positive and negative predictive values of PASP for a diagnosis of PHT using TTE was 76.30% (confidence interval [CI]: 68.22-83.19%), 64.22% (CI: 4.47-73.17%), 72.54% (CI: 66.88-77.55%), and 68.63% (CI: 61.05-75.33%), respectively (Table 4). Due to the small sample size, the PVD group was not included in the analysis.

DISCUSSION

The main finding of this study is that the results of TTE PASP assessment correlated with the RHC measurements with an acceptable sensitivity (76%) and specificity (64%) in transplantation candidates with end-stage lung diseases. Therefore, TTE can be used to non-invasively evaluate pulmonary hemodynamics.

Table 3. Correlation between RHC and TTE PAP values in subgroups*

	n	%	Correlation coefficient (r)	*p*
Obstructive lung disease	64	26.2	0.416	0.001
Interstitial lung disease	111	45.4	0.647	<0.001
End-stage infectious lung disease	55	22.5	0.590	<0.001
Pulmonary vascular disease	14	5.7	0.428	0.127
All patients	244	100	0.718	<0.001

RHC: Right heart catheterization; TTE: Transthoracic echocardiography; PAP: Pulmonary artery pressure; * Pearson correlation coefficient.

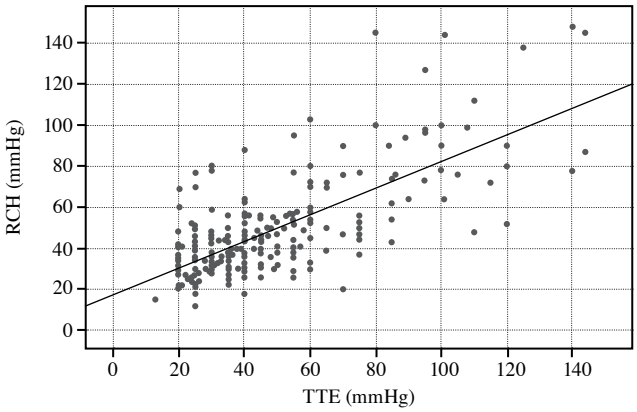

Figure 3. Correlation between pulmonary artery systolic pressure estimated by TTE and measured by RHC in lung transplantation candidates.

RHC: Right heart catheterization; TTE: Transthoracic echocardiography.

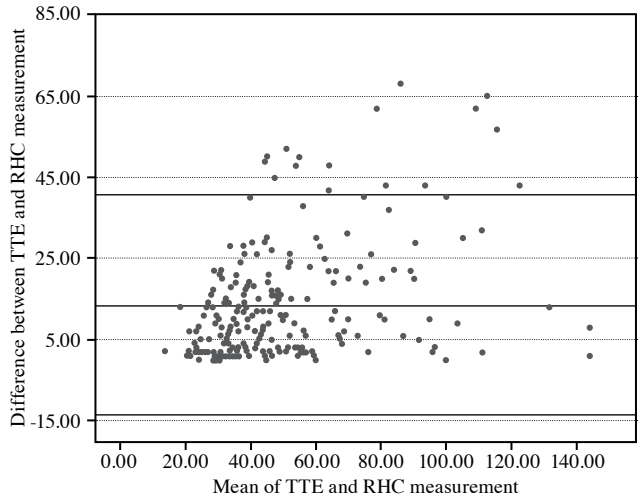

Figure 4. Bland-Altman plot of pulmonary artery pressure measurements by RHC and estimations by TTE.

RHC: Right heart catheterization; TTE: Transthoracic echocardiography.

However, the results also demonstrated that the correlation between TTE and RHC measurements of PAP differed in specificity and sensitivity according to the underlying lung disease. Although RHC is the gold standard for PHT, it is an invasive method that requires extensive equipment and limited application.[15] The TTE provides information about functional cardiac changes that may affect perioperative management in transplant candidates, as well as estimation of PAP. In addition, it can be used for PAP monitoring due to its reproducibility. The use of echocardiography in clinical practice may provide great value for transplant patients.

Previous studies have examined the correlation between TTE and RHC measurement of PASP in non-transplantation patients with various underlying diseases. Kim et al.[16] reported a strong correlation between PAP measured with TTE and RHC in patients with end-stage liver disease (r=0.718; p<0.001; sensitivity: 97%, specificity: 77%). In a recent study by Sohrabi et al.,[17] the PAP estimated by TTE correlated with RHC values in patients with rheumatic mitral valve stenosis (r=0.89; p<0.001; sensitivity: 92.8%, specificity: 86.6%).

The widespread application of LTx in many centers has led to greater use of TTE in clinical practice in the last decade. Recent studies have examined the correlation between TTE and RHC measurements of PAP in LTx candidates. Both Arcasoy et al.[2] and Ben-Dor et al.[18] reported a strong correlation (r=0.69; p=0.0001 and r=0.80; p<0.0001, respectively). Similarly, in our study, we found that the PAP values of both methods were strongly correlated in LTx candidates (r=0.71; p<0.001). Arcasoy et al.[2] reported a PHT prevalence of 25% using RHC and 44% using TTE, with a mean PASP of 49.08±24.13 mmHg using RHC and a mean of 48.95±26.78 mmHg using TTE. In contrast, we found that 93.9% of all patients were diagnosed with PHT with RHC and 58.2% with TTE. This difference can be explained by the fact that the PAP threshold value for the diagnosis of PHT, which is higher

Table 4. Sensitivity, specificity, and positive and negative predictive values of PAPs by Doppler echocardiography for diagnosis of pulmonary hypertension

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
All patients	76.3 (68.2-83.1)	64.2 (54.47-73.1)	72.5 (66.8-77.5)	68.6 (61.0-75.3)
Obstructive lung disease	41.6 (29.0-55.1)	75.0 (19.4-99.3)	96.1 (81.6-99.2)	7.89 (4.4-13.5)
Interstitial lung disease	66.9 (57.0-75.9)	100.0 (63.0-100.0)	100.00 (84.7-100)	19.05 (15.1-23.6)
End-stage infectious lung disease	61.54 (47.0-74.7)	66.67 (9.4-99.1)	96.9 (86.4-99.3)	9.09 (4.0-19.2)

PPV: Positive predictive value; NPV: Negative predictive value; PAP: Pulmonary artery pressure; CI: Confidence interval.

than that used in our study, is ≥45 mmHg. Similarly, the median PASP using TTE was 40.0 mmHg and 43 mmHg using RHC in our study. In the Arcasoy et al.'s[2] study, the estimation of PASP by TTE had an 85% sensitivity, 55% specificity, and 52% positive and 87% negative predictive values, which are similar to our rates (76.3%, 64.22%, 72.54%, and 68.63%, respectively).

In the present study, PAP values could not be obtained by TTE for 62 patients due to a poor tricuspid regurgitation signal or other technical inadequacies. The PAP estimation by TTE was possible in 76.9% of our patients. Ben-Dor et al.[18] reported TTE PASP evaluation of 74% in their study. Arcasoy et al.,[2] however, used TTE in only 44% patients, which we speculate that it may be a result of differing equipment quality and experience level in multiple specialists.

Difficulties associated with TTE assessment of pulmonary hemodynamics include obtaining insufficient echocardiographic images in a hyperinflated chest and potential rightward rotation of the heart, and difficult visualization of the tricuspid valve and vena cava in patients with obstructive lung disease due to the physiology of the disease. Fisher et al.[19] evaluated patients with severe emphysema and found that TTE and RHC PAP values were weakly correlated and the test characteristics (sensitivity, specificity, and predictive values) were poor for TTE diagnosis of PHT. They reported that the diagnosis of PHT was important in patients with emphysema and that TTE should be interpreted carefully and may need to be confirmed with RHC. The examination according to underlying disease in our transplant candidates revealed a noteworthy poor correlation between the two methods in OLD patients compared to the ILD and end-stage infectious lung disease groups ($r=0.416$ $p=0.001$; $r=0.647$, $p<0.001$; and $r=0.590$, $p<0.001$, respectively). The sensitivity and specificity of patients with OLD were also relatively low (41.67% and 75%, respectively). Our results are consistent with those of Arcasoy et al.,[2] despite the relatively low sensitivity and specificity rates due to poor image quality in the patient group with hyperinflation, and TTE may be preferable for LTx and perioperative management.

A long wait for listed LTx candidates contributes to annual mortality.[20] Pulmonary hypertension is a major risk factor for early and late mortality in LTx patients.[21] Mortality varies according to the underlying disease, and wait list mortality can be as much as 64%, particularly in cases of IPF. Nathan et al.[22] investigated transplant candidates with IPF and revealed that the incidence of PHT increased from 77 to 86% during the period between diagnosis and transplantation. Keir et al.[23] also estimated nearly 90% PHT in patients with non-transplant ILD using TTE. In our study, the correlation between TTE and RHC was higher in ILD patients compared to other underlying disease groups ($r=0.647$; $p<0.001$).

Right heart catheterization may be risky in detecting PHT in ILD patients due to the frequent accompanying cardiac hemodynamic disorders. Thus, TTE can be safely used as a non-invasive method for detecting PHT in these patients, as it enables the evaluation of cardiac parameters. According to our results, the TTE and RHC correlation of PASP measurement was higher in ILD patients compared to other underlying disease groups ($r=0.647$; $p<0.001$). Therefore, echocardiographic evaluation of cardiac hemodynamics in ILD patients who are candidates for transplant has a critical value.

To avoid the development of PHT, it is of utmost importance to refer this patient group for transplantation soon after diagnosis and to reduce the time on the waiting list as much as possible. In our study, the mean time after diagnosis in patients who are still waiting for LTx and who underwent LTx was 7.6±6.9 years. Among these, the patient groups with the shortest waiting time were PVD (3; 95% CI: 1-7) and IPF (5.1±3.8 months).

One of the main limitations to this study is that there is a 72-h time frame allowed for the use of the two methods. The PAP is a dynamic measurement and can vary up to 30% within 24 h as reported by Rich et al.[24] Another limitation is that, although we could not monitor and provide oxygen as needed during the RHC procedure, we were unable to monitor oxygen saturation or provide standardized oxygen during TTE. Hypoxemia that occurs during testing can cause pulmonary vasoconstriction.

In conclusion, our study results showed that pulmonary artery systolic pressure assessed using transthoracic echocardiography was strongly correlated with that measured using right heart catheterization in transplant candidates. These results suggest that transthoracic echocardiography may be a very useful, practical, non-invasive method of monitoring pulmonary artery systolic pressure changes, particularly in idiopathic lung disease patients, in the assessment of pulmonary hypertension and cardiac hemodynamics. In the obstructive lung disease group, due to transthoracic echocardiography imaging difficulties, evaluation of transthoracic echocardiography pulmonary artery

systolic pressure may need to be confirmed by right heart catheterization.

Ethics Committee Approval: The study protocol was approved by the Kartal Koşuyolu High Speciality Educational and Research Hospital Ethics Committee (date: 06.10.2020, no: 2020/9/365). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, literature review: M.E.Ç.; Design, data collection and/or processing, analysis and/or interpretation, writing the article: P.A.G.; Control/supervision, critical review, references and fundings, materials: P.A.G., M.E.Ç.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J 2019;53:1801913.
2. Arcasoy SM, Christie JD, Ferrari VA, Sutton MS, Zisman DA, Blumenthal NP, et al. Echocardiographic assessment of pulmonary hypertension in patients with advanced lung disease. Am J Respir Crit Care Med 2003;167:735-40.
3. Hurdman J, Condliffe R, Elliot CA, Davies C, Hill C, Wild JM, et al. ASPIRE registry: Assessing the Spectrum of Pulmonary Hypertension identified at a REferral centre. Eur Respir J 2012;39:945-55.
4. Hoeper MM, Lee SH, Voswinckel R, Palazzini M, Jais X, Marinelli A, et al. Complications of right heart catheterization procedures in patients with pulmonary hypertension in experienced centers. J Am Coll Cardiol 2006;48:2546-52.
5. Currie PJ, Seward JB, Chan KL, Fyfe DA, Hagler DJ, Mair DD, et al. Continuous wave Doppler determination of right ventricular pressure: A simultaneous Doppler-catheterization study in 127 patients. J Am Coll Cardiol 1985;6:750-6.
6. Büyükbayrak F, Uyar İ, Aksoy E, Günay D, Selimoğlu Ö, Sarikaya S, et al. An evaluation of diagnostic sensitivity of transthoracic echocardiography in diagnosis of post-cardiac surgery tamponade. Turk Gogus Kalp Dama 2014;22:35-42.
7. Ritchie M, Waggoner AD, Dávila-Román VG, Barzilai B, Trulock EP, Eisenberg PR. Echocardiographic characterization of the improvement in right ventricular function in patients with severe pulmonary hypertension after single-lung transplantation. J Am Coll Cardiol 1993;22:1170-4.
8. Yeoh TK, Kramer MR, Marshall S, Theodore J, Gibbons R, Valantine HA, et al. Changes in cardiac morphology and function following single-lung transplantation. Transplant Proc 1991;23:1226-7.
9. Kramer MR, Valantine HA, Marshall SE, Starnes VA, Theodore J. Recovery of the right ventricle after single-lung transplantation in pulmonary hypertension. Am J Cardiol 1994;73:494-500.
10. Homma A, Anzueto A, Peters JI, Susanto I, Sako E, Zabalgoitia M, et al. Pulmonary artery systolic pressures estimated by echocardiogram vs cardiac catheterization in patients awaiting lung transplantation. J Heart Lung Transplant 2001;20:833-9.
11. Weill D, Benden C, Corris PA, Dark JH, Davis RD, Keshavjee S, et al. A consensus document for the selection of lung transplant candidates: 2014--an update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant 2015;34:1-15.
12. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111-7.
13. Yock PG, Popp RL. Noninvasive estimation of right ventricular systolic pressure by Doppler ultrasound in patients with tricuspid regurgitation. Circulation 1984;70:657-62.
14. Chan KL, Currie PJ, Seward JB, Hagler DJ, Mair DD, Tajik AJ. Comparison of three Doppler ultrasound methods in the prediction of pulmonary artery pressure. J Am Coll Cardiol 1987;9:549-54.
15. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Respir J 2015;46:903-75.
16. Kim WR, Krowka MJ, Plevak DJ, Lee J, Rettke SR, Frantz RP, et al. Accuracy of Doppler echocardiography in the assessment of pulmonary hypertension in liver transplant candidates. Liver Transpl 2000;6:453-8.
17. Sohrabi B, Kazemi B, Mehryar A, Teimouri-Dereshki A, Toufan M, Aslanabadi N. Correlation between pulmonary artery pressure measured by echocardiography and right heart catheterization in patients with rheumatic mitral valve stenosis (A Prospective Study). Echocardiography 2016;33:7-13.
18. Ben-Dor I, Kramer MR, Raccah A, Iakobishvilli Z, Shitrit D, Sahar G, et al. Echocardiography versus right-sided heart catheterization among lung transplantation candidates. Ann Thorac Surg 2006;81:1056-60.
19. Fisher MR, Criner GJ, Fishman AP, Hassoun PM, Minai OA, Scharf SM, et al. Estimating pulmonary artery pressures by echocardiography in patients with emphysema. Eur Respir J 2007;30:914-21.

20. Hayama M, Date H, Oto T, Aoe M, Andou A, Shimizu N. Improved lung function by means of retrograde flush in canine lung transplantation with non-heart-beating donors. J Thorac Cardiovasc Surg 2003;125:901-6.
21. Conte JV, Gaine SP, Orens JB, Harris T, Rubin LJ. The influence of continuous intravenous prostacyclin therapy for primary pulmonary hypertension on the timing and outcome of transplantation. J Heart Lung Transplant 1998;17:679-85.
22. Nathan SD, Shlobin OA, Ahmad S, Koch J, Barnett SD, Ad N, et al. Serial development of pulmonary hypertension in patients with idiopathic pulmonary fibrosis. Respiration 2008;76:288-94.
23. Keir GJ, Wort SJ, Kokosi M, George PM, Walsh SLF, Jacob J, et al. Pulmonary hypertension in interstitial lung disease: Limitations of echocardiography compared to cardiac catheterization. Respirology 2018;23:687-94.
24. Rich S, D'Alonzo GE, Dantzker DR, Levy PS. Magnitude and implications of spontaneous hemodynamic variability in primary pulmonary hypertension. Am J Cardiol 1985;55:159-63.