# Role of Echocardiography in the Diagnosis and Follow-up of Patients with Pulmonary Arterial and Chronic Thromboembolic Pulmonary Hypertension

Alexandros Stefanidis, George Koutroulis, George Kollias, J Simon R Gibbs, Petros Nihoyannopoulos

*Department of Cardiology, Hammersmith Hospital, Imperial College School of Medicine, National Heart & Lung Institute, London, United Kingdom*

Key words:
**Echocardiography, pulmonary hypertension.**

*Manuscript received:*
June 26, 2003;
*Accepted:*
July 11, 2003.

*Corresponding Author:*
Alexandros Stefanidis

*Echocardiography Laboratory, Hammersmith Hospital, Du Cane Road, W12 0HS, London, United Kingdom*
*e-mail:*
*plato203@yahoo.com*

Pulmonary Arterial and Chronic Thromboembolic Pulmonary Hypertension (PAH, CTPH) are two closely related conditions, characterised by high morbidity and mortality. Historical databases of the US National Institute of Health Registry have shown that, untreated PAH has a poor prognosis with survival rates at 1, 3 and 5 years of 68%, 48% and 34%, respectively[1].

The remarkable progress in the treatment of these patients that has occurred with either the use of novel drugs (e.g. prostacyclin and its analogues, sildenafil, endothelin receptor antagonists) or with technical advances in pulmonary thromboendarterectomy (PTE), has reduced mortality but led to an increased morbidity which requires serial assessment of the applied therapy with the use of clinical and imaging techniques.

Clinical examination is crucial for the initial evaluation of these patients. However, echocardiography appears to be the ideal test for unravelling the diagnostic 'algorithm', first, by excluding cardiomyopathies, valvulopathies, congenital heart diseases and other causes, followed by the evaluation of the severity and finally, the follow-up of these patients.

Although several echocardiographic parameters have been utilised for the evaluation of the severity of these diseases, none is sufficiently robust on its own, capable of-accurately assessing the progress of the disease in a simple, quick and reproducible way.

## Echocardiography and pulmonary hypertension

Primary target of each laboratory examination for the diagnosis and follow-up of PAH and CTPH, is the anatomical and haemodynamic evaluation of the pulmonary circulation, as well as risk stratification of the individual patient, when possible. Selection criteria of the best available method should take into consideration its diagnostic accuracy, patient risk, reproducibility, cost and availability of local expertise.

Right heart catheterisation and pulmonary angiography is characterized by a significant risk for adverse events and hence, except from baseline measurements, it is not an ideal test for follow-up. Spiral computed tomography (CT) is required as an adjunctive imaging technique to pulmonary angiography for the differential diagnosis and localization of chronic thromboembolic disease (Figure 1). Magnetic resonance imaging (cardiac MRI), is a method that provides useful information for the complex right ventricular (RV) architecture, volume, mass

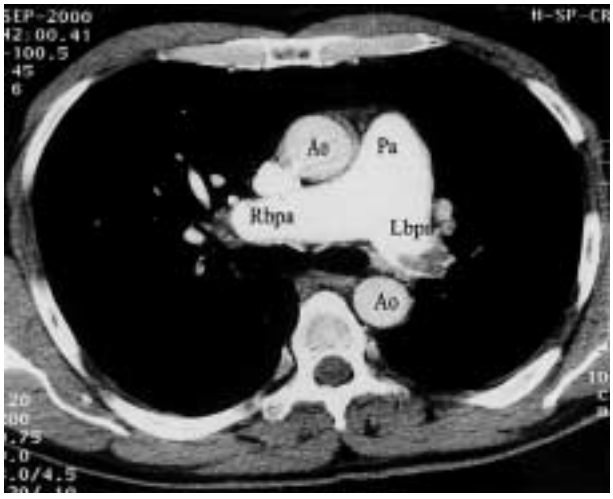


**Figure 1.** Spiral CT image confirming enlarged pulmonary artery and branches with thromboembolic material. Ao = Aorta, Pa = Pulmonary Artery, Rbpa = Right branch of pulmonary artery, Lbpa = Left branch of pulmonary artery.

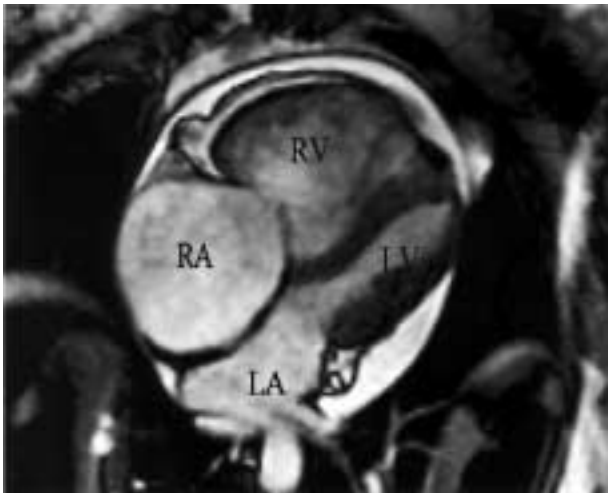


**Figure 2.** Cardiac MRI image revealing grossly dilated right heart chambers in a patient with primary pulmonary hypertension. LV = Left ventricle, LA = Left atrium, RV = Right Ventricle, RA = Right atrium.

and function. However, it is time consuming, expensive, not available in the clinical ward, while data are also still lacking on its prognostic value and use for serial assessment of RV function[2] (Figure 2).

Echocardiography is ideally suited to assess individual patients of known or suspected pulmonary hypertension (PHT). It reveals the primary and secondary anatomical and haemodynamical changes, that occur during the adaptation of the heart to the slow and chronic haemodynamic overload due to the increased pulmonary arterial resistance caused both by PAH and CTPH.

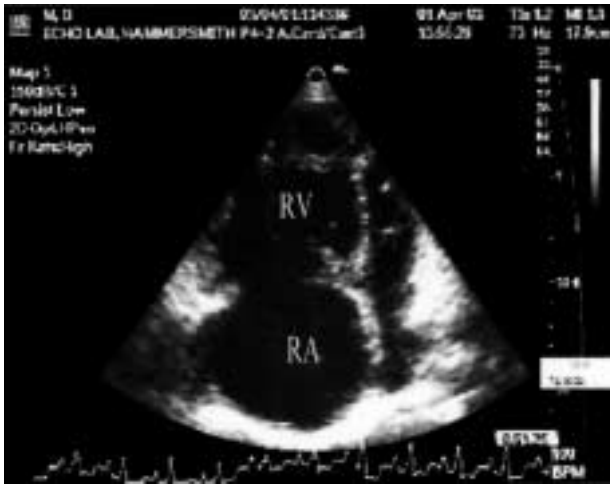


**Figure 3.** RA = Right atrium, RV = Right ventricle.

In brief, these changes are: 1) elevated pulmonary artery pressures, 2) RV hypertrophy and dilatation (Figure 3) (due to adaptation of the RV to chronic pressure overload); progressive volume overload due to further RV dilatation and functional tricuspid valve incompetence, 3) flattening and paradoxical movement of the interventricular septum, 4) RV systolic dysfunction (first sign of the failing RV is hypokinesia of the free wall), and 5) diastolic dysfunction of the left ventricle (LV) due to the marked impairment of the geometry, its interdependence with the RV and the large decrease of its preload, while the severity of LV diastolic dysfunction is closely related to the severity of PHT[3].

## Two-dimensional echocardiography. From the tradition towards the new techniques

Two–dimensional assessment of the RV should take various factors into account (Table 1). Difficulty of imaging is not an issue for PAH and CTPH (as it is for patients with chronic obstructive pulmonary disease), where the increased size of the RV allows very clear images. Nevertheless, for the evaluation of the RV, accuracy and reproducibility are factors that should be taken into consideration. Earlier studies in patients with pulmonary disease, showed a great variation regarding the reliability of measurements, basically due to lack of standardization[4]. Once those right heart measurements have been established[5,6]

**Table 1.** Two dimensional echocardiographic assessments.

| |
|---|
| LV & RV dimensions - wall thickness |
| Eccentricity index |
| LV & RV outflow tract diameter |
| Aortic root & main pulmonary artery diameter |
| Left & right atrial dimensions |
| End-diastolic and end-systolic RV cavity areas |
| Assessment of pericardial effusion |
| Inferior vena cava dimensions |

good reproducibility has been achieved and used in different clinical settings[7].

Two-dimensional imaging evaluates the dimensions, shape and thickness of the RV using several tomographic planes. A useful parameter for the assessment of the degree of RV dilatation is the measurement of the end-diastolic diameter of the RV from the specific parasternal right ventricular inflow tract or the apical four-chamber projection (Figure 4)[6].

The RV end-diastolic (RV-EDA) and end-systolic cavity areas (RV-ESA) are conventionally determined by tracing the endocardial borders in the apical 4-chamber view. Both are useful parameters, integrated in several area-length mathematical formulas for RV volume calculations. Although these formulas have been used some times with great enthusiasm, their geometric model-based approach is generally accepted with scepticism[8].

Automatic endocardial border detection correlates well with the angiographic evaluation of the RV[9]. However, the reliability of this method for volume evaluation is also questioned, due to the limited application of geometric assumptions in RV already mentioned[10]. The use of contrast agents improves accuracy[11].

The standard measurements of RV volumes and ejection fraction are difficult and sometimes impossible to perform, due to the complex geometry and the increased RV trabeculation. Although three-dimensional (3-D) echocardiography is capable of more accurate estimation of RV volumes, overriding the limitation of the geometric models, it can avoid neither the necessary planimetry of the endocardial borders nor the time consuming off-line analysis[12]. Nevertheless, in the era of new commercially available 3-D systems and workstations for later analysis, an accurate measurement of both RV size and function has now been achieved with acceptable reproducibility[13]. The advent of real time 3-D imaging, allows for a shorter examination time while promising to revolutionize cardiac imaging (Figure 5). A recent study with real time 3-D in an animal model, demonstrated that RV stroke volume could be measured sufficiently in chronic RV volume overload state[14].

Measurement of the inferior vena cava diameter and its variation during the respiratory cycle is important for the indirect evaluation of right atrial pressure and could be of value since central venous

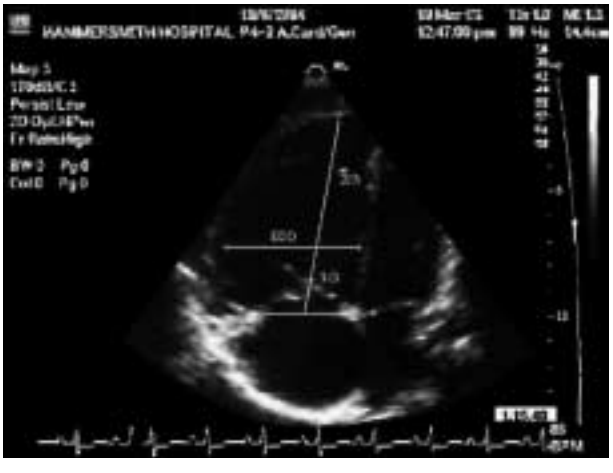

**Figure 4.** The minor axis of the right ventricular inflow tract (end-diastolic diameter) taken within one third of the distance below the tricuspid valve annulus towards the right ventricular apex. EDD = End-diastolic diameter.

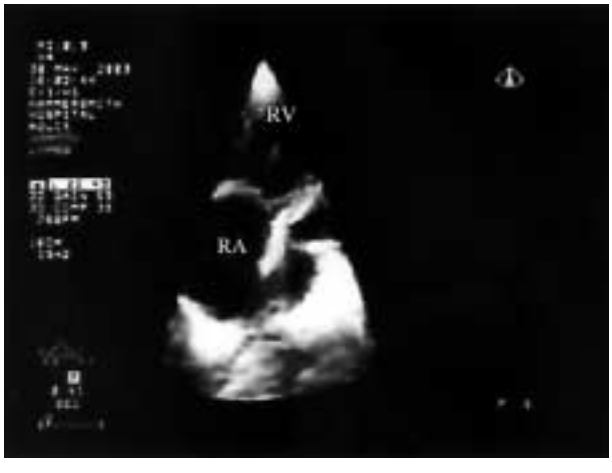


**Figure 5.** 3-D image from a patient with pulmonary arterial hypertension. RA = Right atrium, RV = Right ventricle.

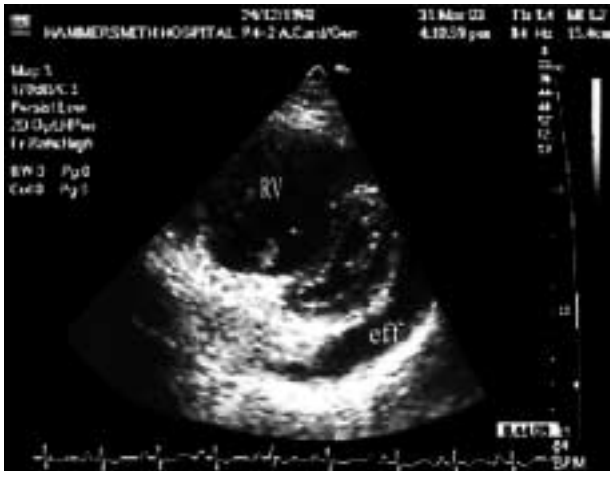


**Figure 6.** RV = Right ventricle, eff = pericardial effusion.

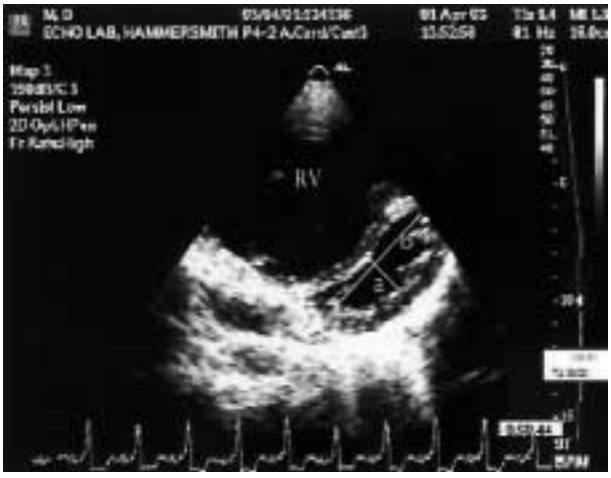


**Figure 7.** Eccentricity index. RV = Right ventricle.

pressure is itself an independent prognostic factor[15,16]. Reproducibility however is uncertain since the reference point for the measurement of the diameter and precise acoustic window, are ill-defined.

Presence of pericardial effusion and the size of the right atrium are also two prognostic factors in patients with PAH[17]. Nevertheless, pericardial effusion is rather uncommon and can only be assessed semiquantitatively (Figure 6). In contrast, right atrial size measurement is more accurate and reproducible. Right atrial enlargement is a manifestation of high right atrial pressure and may be viewed as an indicator of right ventricular decompensation[17].

Finally, measurement of LV dimensions as a prognostic or follow-up factor may also be important. Right-sided volume or pressure overload can alter LV systolic and diastolic function and may have unpredictable clinical consequences between individuals even with the same degree of severity of RV disease[18,19]. Although LV is displaced due to the clockwise rotation of the heart, measurement of the end-diastolic diameter is accurate and reproducible as well. Eccentricity index appears a reproducible measurement with an established clinical value for the evaluation of the severity of the pressure overload of the RV, due to the displacement of the interventricular septum[20]. It is calculated from the parasternal short axis projections as the ratio of the minor axis of the LV parallel to the septum at the level of the chordae (b), divided to minor-axis perpendicular to and bisecting the septum at the same section (a) (Figure 7). Intravenous prostacyclin infusion of 12 weeks duration, was able to improve significantly this index' values[21].

## Doppler echocardiography and doppler-index of myocardial performance of the right ventricle. Back to the future...

From Doppler parameters (Table 2), peak tricuspid regurgitation velocity is probably the most robust measurement for screening suspected pulmonary hypertension patients. When present, it can be easily measured with high reproducibility in nearly all cases. It is clinically important for the estimation of the pulmonary artery systolic pressure using the modified Bernoulli equation[22] and the staging of the severity of pulmonary hypertension.

In one study, Hinderliter et al[21] noted that peak tricuspid regurgitation velocity was reduced in patients who received prostacyclin intravenously when compared to the control group. However, these differences before and after treatment seemed to be particularly small and certainly within the limits of the repeated measurements error, although the authors did not discuss this. In a similar study in a small group of patients who received prostacyclin

**Table 2.** Doppler echocardiographic assessments.

| |
|---|
| E & A waves of trans-mitral & trans-tricuspid velocities |
| Assessment of tricuspid regurgitation severity |
| Peak tricuspid regurgitant velocity |
| Pulmonary artery flow acceleration time |
| Early and end-regurgitant flow velocity across the pulmonary valve |
| Pulsed tissue-Doppler of tricuspid and mitral annulus |
| RV myocardial performance index |
| Assessment for patent foramen ovale |
| Velocity-time integral of right and left ventricular outflow tract |
| Positive dP/dt |

intravenously, the authors also noticed a small decrease (15%) of pulmonary artery systolic pressure[23].

Small differences of the peak tricuspid regurgitation velocity may occur due to the fall of the RV systolic pressure. However, when pressure reduction occurs in parallel to a drop of right atrial pressure, this fall may lead to an unchanged pressure gradient overall between the two chambers, despite the presence of an obvious improvement of the symptoms and the functional stage of the patients. Therefore, lack of max TR velocity changes should be evaluated with caution when evaluating the progress of such patients[24].

Tricuspid regurgitation severity is an independent prognostic factor in patients with primary pulmonary hypertension[25]. However, due the substantial error of repeated measurements it cannot be considered a robust parameter. Tricuspid regurgitation may be under or overestimated due to the variable colour-Doppler gain adjustments or the variable size and compliance of the right atrium. The tricuspid regurgitation area over 30 $cm^2$ as well as the ratio of the regurgitation area to the area of the right atrium >34%, had sensitivity for the detection of severe tricuspid regurgitation of 66% and 76% respectively[26].

Pulmonary artery flow acceleration time (AT) is another hemodynamic parameter, which has been related to the mean pressure of the pulmonary artery[27]. However, the short duration of AT and its potential variation with a relatively small movement of the cursor during the measurement result to poor reproducibility.

Measurement of the regurgitant flow across the pulmonary valve is useful for the evaluation of the pulmonary artery diastolic pressure[28]. Along with tricuspid regurgitation, it is a useful parameter for estimation of the pulse pressure of the pulmonary artery. The difference of the pulmonary artery pulse pressure has been proposed as a method of differential diagnosis between PAH and CTPH[28].

Doppler estimation of the trans-tricuspid diastolic velocity is based on the same pathophysiologic principles as the trans-mitral velocity. However, it requires an average number of at least 5 consecutive cardiac cycles due to the influence of respiration on pressure gradient through the tricuspid valve. Essential measurements are the peak velocity of E and A waves and the deceleration time of the E wave. In most cases, the E/A ratio is < 1 due to the increased RV hypertrophy and reduced compliance. In an advanced stage with ensuing systolic RV failure or with severe tricuspid regurgitation, diastolic dysfunction becomes progressively pseudonormalized, with a reversed E/A ratio (>1). It has to be emphasized that tricuspid flow pattern is strongly influenced by loading conditions of the RV. Different patterns may be seen hours to days apart in the same patient, depending on the RV preload or afterload[29]. In addition, a quantitative relationship between the degree of PHT and LV diastolic filling has been established. Especially in patients with CTPH, the E/A ratio varies inversely with mean pulmonary artery pressure, directly with cardiac output, while increases post-PTE[30].

The use of pulsed Tissue Doppler echocardiography is a recent modality to evaluate RV function[31]. Assessment of tricuspid annular excursion is a simple and quick method with good reproducibility. Systolic velocity < 11.5 cm/sec can identify the presence of RV dysfunction with a sensitivity and specificity of 90% and 85% respectively[31].

The Doppler-index of myocardial performance (Tei-index or myocardial performance index-MPI) is a parameter, which, although it was initially used for the evaluation of the overall LV performance[32], was also used for the evaluation of the RV function[32]. It is expressed by the formula [(Isovolumic contraction time + isovolumic relaxation time) / RV ejection time] (Figure 8). It is relatively unaffected by heart rate, loading conditions or the presence and the severity of tricuspid regurgitation[34]. In patients with primary pulmonary hypertension, the index had a good correlation with symptoms, while also proved

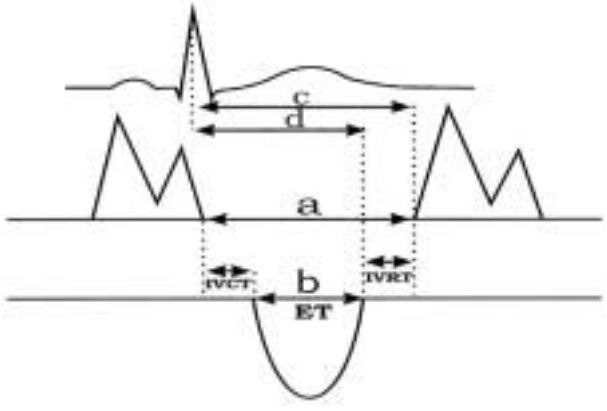


**Figure 8.** Myocardial performance index. IVCT = isovolumetric contraction time, IVRT = isovolumetric relaxation time, ET = ejection time.

to be a good prognostic factor[34]. The advantages of its use are good reproducibility, quick calculation, no need for use of geometric models and appliance even in the presence of a difficult acoustic window. The disadvantages are the lack of familiarity among physicians when compared to other more traditional indices (e.g. ejection fraction) and the overlapping which often occurs between the end of tricuspid regurgitation signal and the pulsed signal of the early diastolic filling (E) of the trans-tricuspid flow that challenges the accurate estimation of the isovolumic relaxation time. Nevertheless, MPI has become a robust prognostic factor with good reproducibility and makes it a useful measurement for patients' follow-up.

Finally, a recent report showed that the ratio of peak tricuspid regurgitant velocity to the right ventricular outflow tract velocity-time integral ($TRV/VTI_{RVOT}$) provides a clinically reliable non-invasive assessment of pulmonary vascular resistance[35].

## Need for national referral centres

Patients with PHT require life-long monitoring in a specialist institution with the initiation of proper therapies related to the progression of the disease. Referral of these patients should not be delayed and usually is made after the basic diagnostic tests (electrocardiogram, chest radiography, simple spirometry and echocardiography). In the referral centre, the diagnosis and aetiology should be confirmed with right heart catheterization and other diagnostic tests (spiral CT and cardiac MRI) in order to determine optimal treatment[36].

The follow-up of these patients includes: clinical examination, electrocardiogram, echocardiography, chest radiography, arterial blood gases, quality of life tests and lastly, exercise tolerance test which is a useful objective assessment of patients functional state since the severity of pulmonary hypertension and the exercise capacity are well correlated. The recommendation of any other follow-up investigations

**Table 3.** Echocardiographic pulmonary hypertension protocol.

| Projection | Measurement |
|---|---|
| Parasternal long axis | Interventricular septum and LV posterior wall dimension |
| | End-diastolic, end-systolic LV dimension |
| | Left ventricular outflow tract diameter |
| Parasternal short-axis (base) | Aortic root diameter |
| | Left atrial diameter |
| | RV outflow tract diameter |
| | Main pulmonary artery diameter |
| | RV isovolumetric contraction and ejection time* |
| | Peak velocity and velocity-time integral of pulmonary artery ejection flow |
| | Pulmonary artery ejection flow acceleration time |
| | Assessment of pulmonary regurgitation |
| Parasternal short-axis (chordae-tendinae level) | Eccentricity index |
| | End-diastolic, end-systolic RV dimension |
| Apical four-chamber | Peak mitral E and A wave velocity |
| | Deceleration time of mitral E wave |
| | Pulmonary vein velocities |
| | Peak velocity and velocity-time integral of Left ventricular outflow tract and Aortic flow |
| | Tricuspid regurgitation peak velocity |
| | RV positive dP/dt, |
| | Peak tricuspid E and A wave velocity |
| | Time duration from QRS complex to opening of tricuspid valve (start of E wave)* |
| | Pulse tissue Doppler of mitral and tricuspid annulus Severity of tricuspid regurgitation |
| Subcostal long-axis | Inferior vena cava dimensions (inspiration-expiration) |

* Measurements necessary for myocardial performance index calculation.

**Table 4** Demographic, clinical and echocardiographic variables*.

| | Pulmonary arterial hypertension | Chronic thromboembolic pulmonary hypertension |
|---|---|---|
| Age (years) | 46 (14) | 47 (13) |
| Women | 59 (81%) | 5 (63%) |
| Arterial systolic pressure (mmHg) | 106 (15) | 111 (17) |
| Central venous pressure (mmHg) | 13 (3) | 13 (4) |
| LV end-diastolic diameter (mm) | 38 (5) | 40 (6) |
| RV end-diastolic diameter (mm) | 44 (9) | 43 (11) |
| Left atrium (mm) | 35 (7) | 35 (6) |
| Right atrium (mm) | 57 (11) | 56 (11) |
| LV outflow tract (mm) | 19 (2) | 19 (2) |
| RV outflow tract (mm) | 27 (4) | 27 (3) |
| Peak velocity of tricuspid regurgitation (m/sec) | 4.3 (0.6) | 3.9 (0.6) |
| RV isovolumic contraction time interval (msec) | 72 (16) | 73 (15) |
| RV ejection time interval (msec) | 278 (37) | 285 (42) |
| RV isovolumic relaxation time interval (msec) | 105 (43) | 83 (30) |
| RV Doppler-index | 0.65 (0.22) | 0.56 (0.19) |
| Pulmonary artery flow acceleration time (msec) | 61 (20) | 58 (25) |
| End-diastolic velocity of pulmonic valve regurgitation (m/sec) | 2 (0.6) | 2 (0.2) |
| Inferior vena cava (expiration) (mm) | 22 (5) | 21(7) |
| Inferior vena cava (inspiration)(mm) | 18 (6) | 18 (8) |
| Pericardial effusion | Mild: 1 (12.5%) | Mild: 14 (18%), Moderate:1 (1.3%) |

All quantitative variables are expressed as mean value (standard deviation).
* For the comparison of all qualitative and quantitative variables p = non-significant.

needed is being made on an individual basis according to the diagnostic and treatment plan.

The orientation of the Echocardiography laboratory in patients of known or suspected PHT has two main directions. First, the diagnosis, classification and staging of types of PHT and second, detection of prognostic indicators. In our institution, one of the national referral centres, patients who are admitted or come through the Pulmonary Hypertension Clinic, undergo serial, thorough 2-D, pulse-wave, continuous-wave, colour flow and pulse tissue Doppler imaging echocardiographic examination in addition to the other diagnostic tests (CT, MRI) (Table 3).

Since January 2002, there have been 81 consecutive patients (64 women) with PAH or CTPH (8 with CTPH). Of them, 67 have Primary Pulmonary Hypertension, 3 Systemic Lupus Erythematosus, 1 Rheumatoid Arthritis, 1 Adamantiades-Behcét disease and 1 HIV infection.

Table 4 shows the basic demographic, clinical and echocardiographic characteristics of these patients.

It is evident that no echocardiographic parameter could separate PAH from CTPH. Therefore differential diagnosis is essentially based on the ventilation-perfusion scan of the lungs, spiral CT, cardiac MRI and angiographic appearance. Ventilation-perfusion scan is crucial to rule out thromboembolic disease. In PAH patients, the ventilation-perfusion scan may be normal or reveal non-segmental perfusion defects. On the contrary, in thromboembolic disease, there are larger segmental perfusion defects. If the perfusion scan or spiral CT is not diagnostic, selective pulmonary arteriography should be performed.

For follow-up of PHT patients MPI was found to be an essential echocardiographic parameter, since the differentiation of its values among consecutive studies was found to correlate well with the increase or decrease of patients' exercise capacity[37].

## Conclusions

Assessing patients with PHT is demanding, particularly as they usually constitute a population of poor clinical state. Echocardiography is supportive of the clinical evaluation regarding the diagnosis, staging, prognosis and follow-up of these patients. However, for the differential diagnosis between

PAT and CTPH, other imaging modalities should be used.

Echocardiography has a clear advantage for the follow-up when compared to other laboratory examinations. The MPI appears to be a promising and robust method of assessment for prognosis and follow-up of this patient population. Anticipating the results of several multicenter trials related to diagnostic accuracy of all the available imaging techniques, spiral CT and MRI have an important complementary role for the diagnosis and treatment of those patients.

## References


1. McLaughlin V: Pulmonary arterial hypertension: current diagnosis and management. ACC Curr J Review 2002; 11: 17-21.
2. Helbing WA, Bosch HG, Maliepaard Ch, Rebergen SA, van der Geest RJ, Hansen B, et al: Comparison of echocardiographic methods with magnetic resonance imaging for assessment of right ventricular function in children. Am J Cardiol 1995; 76: 589-594.
3. Schena M, Clinic F, Errera D, Quadri A: Echo-Doppler evaluation of left ventricular impairment in chronic cor pulmonale. Chest 1996; 109: 1446-1451.
4. Kaul S, Tei Ch, Hopkins JM, Shah PM: Assessment of right ventricular function using two-dimensional echocardiography. Am Heart J 1984, 107: 526-531.
5. Nihoyannopoulos P, Dickele MC, Gauthier J, Mossard JM, Brechenmacher C, Voegtlin R: Diagnostic echocardiographique de l'hypertension arterielle pulmonaire. Arch Mal Coeur Vaiss 1982; 75: 169-176.
6. Foale RA, Nihoyannopoulos P, McKenna WJ, Kleinebenne A, Nadazdin A, Rowland E, et al: Echocardiographic measurement of the normal adult right ventricle. Br Heart J 1986, 56: 33-44.
7. Nihoyannopoulos P, McKenna WJ, Smith G, Foale RA: Echocardiographic assessment of the right ventricle in Ebstein's anomaly: relation to clinical outcome. J Am Coll Cardiol 1986; 8: 627-635.
8. Denslow S, Wiles H: Right ventricular volumes revisited: a simple model and simple formula for echocardiographic determination. J Am Soc Echocardiogr 1998; 11: 864-873.
9. Hausmann B, Muurling S, Simon R: Dynamic on-line quantification of biventricular function with acoustic quantification (AQ). Validation, reproducibility and normal values of a new echocardiographic approach. Int J Card Imaging 1997; 13: 463-474.
10. Oe M, Gorcsan J 3rd, Mandarino WA, Kawai A, Griffith BP, Kormos RL: Automated echocardiographic measures of right ventricular area as an index of volume and end-systolic pressure-area relations to assess right ventricular function. Circulation 1995; 92: 1026-1033.
11. Tokgözoglu SL, Caner B, Kabakci G, Kes S: Measurement of right ventricular ejection fraction by contrast echocardiography. Int J Cardiol 1997; 59: 71-74.
12. Munoz R, Marcus E, Palacio G, Gauvreau K, Wessel DL, Colan SD: Reconstruction of 3-dimensional right ventricular shape and volume from 3 orthogonal planes. J Am Soc Echocardiogr 2000; 13: 177-185.
13. Menzel T, Kramm T, Bruckner A, Mohr-Kahaly S, Mayer E, Meyer J: Quantitative assessment of right ventricular volumes in severe chronic thromboembolic pulmonary hypertension using transthoracic three-dimensional echocardiography: changes due to pulmonary thromboendarterectomy. Eur J Echocardiography 2002; 3: 67-72.
14. Shiota T, Jones M, Chicada M, Fleishman CE, Castellucci JB, Cotter B, et al: Real-time three-dimensional echocardiography for determining right ventricular stroke volume in an animal model of chronic right ventricular volume overload. Circulation 1998; 97: 1987-1900.
15. D'Alonzo GE, Barst RJ, Ayres SM, Bergofsky EH, Brundage BH, Detre KM, et al: Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. Ann Intern Med 1991; 115: 343-349.
16. McLaughlin VV, Shillington A, Rich S: Survival in primary pulmonary hypertension: the impact of epoprostenol therapy. Circulation 2002; 106: 1477-1482.
16. Raymond RJ, Hinderliter AL, Willis PW, Ralph D, Caldwell EJ, Williams W, et al: Echocardiographic predictors of adverse outcomes in primary pulmonary hypertension. J Am Coll Cardiol 2002; 39: 1214-1219.
18. Burgess MI, Bright-Thomas RJ, Ray SG: Echocardiographic evaluation of right ventricular function. Eur J Echocardiography 2002; 3: 252-262.
19. Louie EK, Lin SS, Reynertson SI, Brundage BH, Levitsky S, Rich S: Pressure and volume loading of the right ventricle have opposite effects on left ventricular ejection fraction. Circulation 1995; 92: 819-824.
20. Ryan T, Petrovic O, Dillon JC, Feigenbaum H, Conley MJ, Armstrong WF: An echocardiographic index for separation of right ventricular volume and pressure overload. J Am Coll Cardiol 1985; 5: 918-927.
21. Hinderliter AL, Willis PW, Barst RJ, Rich S, Rubin LJ, Badesch DB, et al: Effects of long-term infusion of prostacyclin (epoprostenol) on echocardiographic measures of right ventricular structure and function in primary pulmonary hypertension. Primary Pulmonary Hypertension Study Group. Circulation 1997; 95: 1479-1486.
22. Yock PG, Popp RL: Noninvasive estimation of right ventricular systolic pressure by Doppler ultrasound in patients with tricuspid regurgitation. Circulation 1984; 70: 657-662.
23. Sebbag I, Rudski L, Therrien J, Hirsch A, Langleben D: Effect of chronic infusion of epoprostenol on echocardiographic right ventricular myocardial performance index and its relation to clinical outcome in patients with primary pulmonary hypertension. Am J Cardiol 2001; 88: 1060-1063.
24. Higham MA, Dawson D, Joshi J, Nihoyannopoulos P, Morrell NW: Utility of echocardiography in assessment of pulmonary hypertension secondary to COPD. Eur Respir J 2001; 17: 350-355.
25. Bustamante-Labarta M, Perrone S, De la Fuente RL, Stutzbach P, De la Hoz RP, Torino A, et al: Right atrial size and tricuspid regurgitation severity predict mortality or transplantation in primary pulmonary hypertension. J Am Soc Echocardiogr 2002; 15: 1160-1164.
26. Shapira Y, Porter A, Wurzel M, Vaturi M, Sagie A: Evaluation of tricuspid regurgitation severity: Echocardiographic and clinical correlation. J Am Soc Echocardiogr 1998; 11: 652-659.

27. Kitabake A, Inoue M, Asao M, Masuyama T, Tanouchi J, Morita T, et al: Noninvasive evaluation of pulmonary hypertension by pulsed Doppler technique. Circulation 1983; 68: 302-309.
28. Nakayama Y, Sugimachi M, Nakanishi N, Takaki H, Okano Y, Satoh T, et al: Noninvasive differential diagnosis between chronic pulmonary thromboembolism and primary pulmonary hypertension by means of Doppler ultrasound measurement. J Am Coll Cardiol 1998; 31: 1367-1371.
29. Nishimura R, Tajik J: Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta stone. J Am Coll Cardiol 1997; 30: 8-18.
30. Mahmud E, Raisinghani A, Hassankhani A, Sadeghi M, Strachan M, Auger W: Correlation of left ventricular diastolic filling characteristics with right ventricular overload and pulmonary artery pressure in chronic thromboembolic pulmonary hypertension. J Am Coll Cardiol 2002; 40: 318-324.
31. Meluzin J, Spinarova L, Bakala J, Toman J, Krejci J, Hude P, et al: Pulsed Doppler tissue imaging of the velocity of tricuspid annular systolic motion. Eur Heart J 2001; 22: 340-348.
32. Tei C, Ling LH, Hodge DO, Bailey KR, Oh JH, Rodeheffer RJ, et al: New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function-a study in normal and dilated cardiomyopathy. J Cardiol 1995; 26: 357-366.
33. Eidem BW, Tei C, O' Leary PW, Cetta F, Seward JB: Nongeometric quantitative assessment of right and left ventricular function: myocardial performance index in normal and patients with Ebstein anomaly. J Am Soc Echocardiogr 1998; 11: 849-856.
34. Tei C, Dujardin KS, Hodge DO, Bailey KR, McGoon MD, Tajik AJ, et al: Doppler echocardiographic index for assessment of global ventricular function. J Am Soc Echocardiogr 1996; 9: 838-847.
35. Abbas A, Fortuin D, Schiller N, Appleton C, Moreno C, Lester S: A simple method for noninvasive estimation of pulmonary vascular resistance. J Am Coll Cardiol 2003; 41: 1021-1027.
36. Gibbs JSR, Higenbottam TW: Recommendations on the management of pulmonary hypertension in clinical practice. Heart 2001; 86 (Suppl I): i1-i13.
37. Stefanidis A, Kollias G, Koutroulis G, Tunariu N, Gin-Sing W, Gibbs JSR, Nihoyannopoulos P: The role of echocardiography in follow-up of patients with pulmonary arterial hypertension. Time for reconsideration? Eur Heart J 2003; 24 (abstr suppl: No 3380).