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The Role of Transthoracic Echocardiography in Predicting Mortality in Patients with Chronic Thromboembolic Pulmonary Hypertension

Jola Klosi[1], Aneida Hodo Vevecka[2], Prof. Elizana Petrela[1] , Prof. Mihal Tase[1]

[1]Corresponding Author: **JolaKlosi**
University Hospital "Mother Theresa", Tirana, Albania
Jklosi[at]yahoo.com

[1]Elizana Petrela, e-mail: elapetrela[at]yahoo.com

[1]Mihal Tase, e-mail: mihaltase[at]hotmail.com

[2]Aneida Hodo Vevecka: Regiomedkliniken - Cardiology clinic, Coburg, Germany
e-mail: aneidahodo[at]yahoo.com

Abstract: ***Aim: To identify echocardiographic parameters who predict mortality of patients with chronic thromboembolic pulmonary hypertension (CTEPH) who did not performed surgical treatment or specific pulmonary vasodilator therapy. Methods: Prospective study, conducted at Department of Internal Medicine, University Hospital Center "Mother Theresa" in Tirana, Albania. During 2012 – 2015, 43 patients, survivors of an acute pulmonary embolism (PE) were included in the study and were followed periodically, after 3, 9, 15 and 24 months. Mean age of patients was 64.23±10.70 years old (31 females). Diagnosis of PE has been determined through pulmonary computer tomography andscintigraphy. CTEPH was diagnosed in 12 (28%) of 43 patients (pulmonary artery systolic pressure (PAsP)>45 mmHg, at least 3 months after PE und effective anticoagulation) among which 5 patients (41%) died during follow up period. We have determined through a detailed statistical analysis the echocardiographic parameters predictors of mortality in this study. Results: It was seen a strong statistical correlation between mortality and TAPSE (13.34±1.42; p=0.008). Moreover there is a relation between mortality and right ventricle ejection fraction (RVEF) (36.74±1.43; p=0.01) also between mortality and pulmonary velocity acceleration time (PVAT)(74.3±11.45; p=0.001).There is no correlation between mortality and PAsP(p=0.14); Conclusion: The most important echocardiographic parameters which are found statistically significant as predictive factors of mortality, in our group of patients, reflect mainly the systolic function of the right ventricle (RVEF, TAPSE and TAP). In the present study, PAsP was not a predictive factor of mortality.***

Keywords: CTEPH, mortality, predictive factors, echocardiography

1. Introduction

Chronic thromboembolic pulmonary hypertensionis primarily a complication of acute Pulmonary Embolism (PE). The incidence of it is still not very well defined ranging between 0.1 – 9.1% in survivors of an acute PE [1].CTEPH is caused by non complete resolution of thrombotic material in main or lobar pulmonary arteries which organizes causing a remodeling process of pulmonary arteries and progressive increase of pulmonary vascular resistance, pulmonary hypertension and death due to right heart failure [2]. The diagnosis is made by right heart catheterization and pulmonary angiography at least after 3 months of successful anticoagulation, but these 2 invasive and expensive examinations are not always available, especially in developing countries. The treatment of this condition is pulmonary endarterectomy performed by a very specialized team of surgeons, pulmonologists, cardiologists and radiologists. Unfortunately this treatment cannot be applied to all patients diagnosed with CTEPH, because of the late diagnosis or due to the inability of the medical system of different countries to apply this service (lack of technical and professional resources), especially in third world countries.

In this study we attempted to evaluate the role of transthoracic echocardiography in predicting mortality in patients with CTEPH, since this examination is non-invasive and broad available. Our main goal is to describe the profile of patients with high risk of mortality that must receive optimal surgical treatment immediately.

2. Methods

This is a prospective study, conducted at University Hospital Center "Mother Theresa", Tirana, Albania. During 2012 – 2015 were examined 43 patients who had survived an acute PE. Mean age in this patient group was 64.23±10.70 years old (31 females). We have excluded patients with pulmonary hypertension due to left heart diseases and other terminal severe diseases which affect directly the mortality. Diagnosis of acute PE has been determined through pulmonary computer tomography and scintigraphy. All patients are checked up on regular basis every 3, 9, 15 and 24 months. We have collected from this group of patients the anthropological and anamnestic data. ECG, chest X-Ray, computerized tomography, lung V/Q scan, transthoracic echocardiography (performed by an accredited cardiologist), 6mWD, and biochemical data were registered.

CTEPH was diagnosed in 12 (28%) of 43 patients (pulmonary artery systolic pressure (PAsP) >45 mmHg, at least 3 months after acute PE and effective anticoagulant treatment), among which 5 patients (41%) died during follow up period **[3]**.Among various data collected for our group of patient, we analyzed the echocardiographic parameters which could therefore serve as predictors of mortality in patients

with CTEPH. Right heart catheterization and pulmonary endarterectomy were not performed. Our Patients did not receive any pulmonary vasodilator therapy. Each patient included in this study agreed with the examinations and the follow-up plan.

3. Statistical Analysis

All data collected in Microsoft Excel and then exported to SPSS (Statistical Package for Social Sciences) 20.0. Procedures and statistical techniques applied in the analysis of the data of this study are described in detail below: For all variables were calculated absolute numbers and corresponding percentages. For all numerical variables, when the data subject to normal distribution, arithmetic averages were calculated respective ± standard deviations. For non-parametric data (ordinal) correlation coefficients were calculated Kendal's tau. Differences between groups for discrete variables were performed by Chi-Square test. Differences between groups for quantitative variables were performed by the Student test and ANOVA analysis (when comparing the differences between more than two groups). Bonferroni procedures were applied to see which groups attributed the difference. To evaluate occasional relationships between dependent and independent variables was used the binary logistic regression analysis. For each of the variables was accounted the likelihood ratio (Odds) and 95% confidence interval. It was considered significant values of $p \leq 0.05$.

4. Results

Regarding the overall characteristics of the patient group, 12 patients (28%) from 43 patients included in our study developed CTEPH. Overall 2 year mortality in this category of patient's was41% (5patients/12 patients). We observed that themortalityin patients developing CTEPH was correlated to the right ventricular ejection fraction (RVEF) represented by a p value with high statistical significance (p= 0.01). Patients who died due to pulmonary hypertension had an average value of RVEF lower (36.74±1.43%) **(Table 1(a)**, **Figure 1)** than patients who developed CTEPH but survived after 2 years (46.74±7.2%), and much smaller than patients who did not developed pulmonary hypertension after acute pulmonary embolism (51.39±4.4%) **Table 1(b), Figure 2.** TAPSE, another parameter of the systolic function of the right ventricle parameter may serve as a predictor of mortality in patients with CTEPH (p=0.008). In our study we have noted that patients who died from CTEPH had a significant decrease of the TAPSE-value (13.34±1.42mm) compared with the patients with CTEPH who were still alive two years after diagnosis (18.16±3.03 mm)(**Table 1(a), Figure 2**). Patients who did not develop pulmonary hypertension after acute pulmonary embolism had primarily a normal TAPSE **Table 1(b), Figure 2.**

We also noticed that mortality was statistically correlated to pulmonary velocity acceleration time, which reflect the extent of the pulmonary vascular resistance (p=0.001). The average value of this parameter (PAVT) in patients who died due to pulmonary hypertension was74.3±11.45vs.109.54±15.06 of survived CTEPH patients **Table 1(a), Figure 3** and 115.09±14.15 of survived non CTEPH patients **Table 1(b), Figure 3**.

Very important is to note that in our study was not observed a significant statistical link between mortality and pulmonary artery systolic pressure (p=0.14) **Table 1 (a)**.

Table 1(a): Echocardiographic predictor parameters of mortality in group with CTEPH (compare of the two groups)

Variables	CTEPH		
	Death (nr-5)	Survival (nr=7)	P value
PAsP_mean	82.45±7.93	72.29±12.57	0.14
RVEF_mean	36.74±1.43	46.74±7.02	**0.01**
PVAT_mean	74.3±11.45	109.54±15.06	**0.001**
TAPSE_mean	13.34±1.42	18.16±3.03	**0.008**

Table 1(b): Echocardiographic predictor parameters of mortality in group Non CTEPH

Variables	non CTEPH		
	Death (nr=2)	Survival (nr=29)	P value
PAsP_mean	39±8.49	34.50±4.28	0.181
RVEF_mean	41.65±7.28	51.39±4.4	0.006
PVAT_mean	88.15±0.92	115.09±14.15	0.013
TAPSE_mean	15.45±4.17	19.91±2.43	0.022

Agenda: PVAT-pulmonary velocity acceleration time; TAPSE-tricuspid annular plane excursion; PAsP-pulmonary artery systolic pressure, RVEF-right ventricle ejection fraction

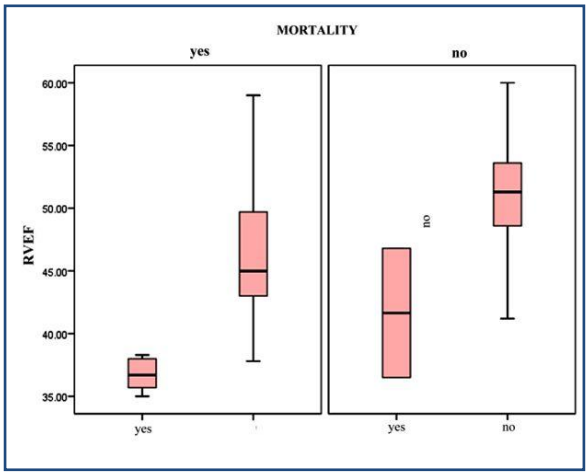

Figure 1: Statistical correlation between mortality and RVEF in Groups with CTEPH and non CTEPH (compare of the two groups)

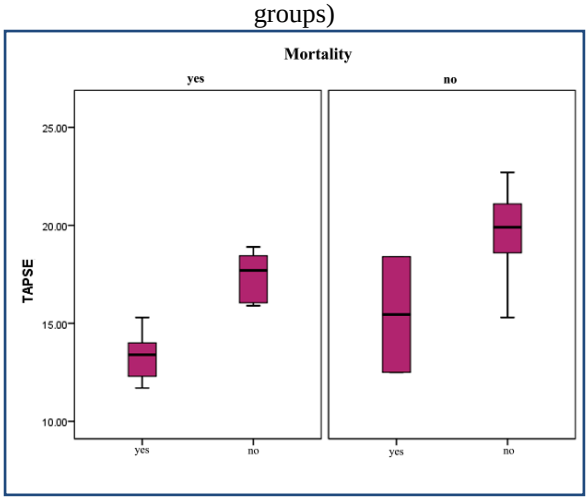

Figure 2: Statistical correlation between mortality and TAPSE in Groups with CTEPH and non CTEPH (compare of the two groups)

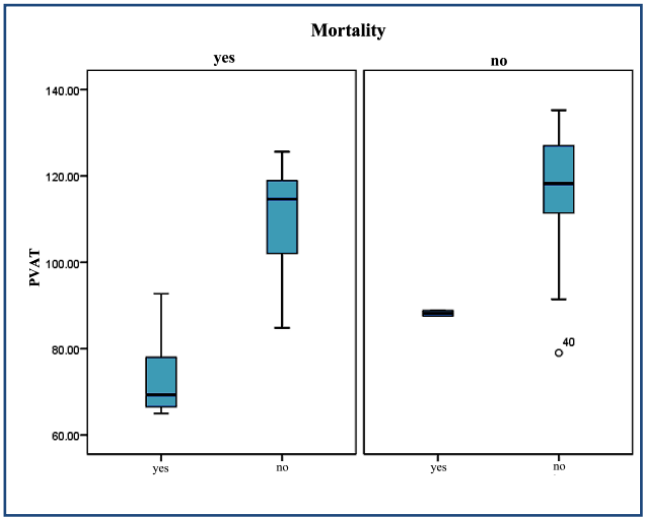

Figure 3: Statistical correlation between mortality and PAVT in Groups with CTEPH and non CTEPH (compare of the two groups)

5. Discussion

CTEPH is serious devastating disease with a very impaired survival because it proceeds to right heart failure and death, especially when left untreated [4]. However, unlike other forms of pulmonary hypertension, CTEPH can be totally cured through pulmonary endarterectomy, without needing a lung transplant. Patients are often diagnosed during the late stages of the disease when surgical treatment is no longer appropriate because of the associated high risk of mortality. In these conditions, an alternative treatment would be the use of specific pulmonary vasodilators that improve symptomatology but do not significantly increase life expectancy [5].Both modern methods of treatment are sometimes not available, especially in developing countries, due to high costs but also because of the lack of appropriate centers and specialists [6]. Identifying predictive factors of mortality and assessment of the clinical profile of patient with a high risk of mortality would help in the application of rapid optimal therapy, leading to reducing mortality in this category of patients. Therefore, assessment of right ventricular function and the impact of pulmonary hypertension on heart with transthoracic echocardiography are very important issues in evaluation of pulmonary hypertension and prediction of mortality in this group of patients.

We found that mortality in the group of our CTEPH patients was strongly correlated to right ventricle systolic function parameters. Like many other studies that have focused assessment of mortality in patients with CTEPH, the results of our study support once again the fact that the mortality rate of these patients is directly related to poor performance of the right ventricle due to high pulmonary resistance [7-9].Assessment of echocardiographic right ventricular function is easy, reliable, non-invasive and also available worldwide [10]. Presence of echocardiographic parameters that would indicate the right ventricular insufficiency should be an alarm system for the application of optimal therapy in specialized centers as soon as possible.

Evaluation of systolic pressure in the pulmonary artery through echocardiography do not correlated with mortality in our study. It is well known that one of the key parameters in the evaluation of this pressure is the systolic function of the right ventricle. In the context of a reduced systolic function of the right ventricle, the pressure recorded in pulmonary artery can be underestimated. For this reason we believe that pulmonary hypertension is not solitary leading to death in these patients, but rather is its impact on the right heart that makes their prognosis very unfavorable.

Despite the fact that this topic has been the main subject in many contemporary studies, new studies in this field are welcome considering the fact that CTEPH is becoming an important medical problem that despite the existence of good possibilities for medication, often remains undertreated.

6. Conclusions

Patient, who survived an acute pulmonary embolism, can develop chronic thromboembolic pulmonary hypertension. This disease has a poor prognosis because of the rapid progression towards the right ventricular failure, despite the fact that theoretically can be treated completely through pulmonary endarterectomy. In many cases, surgical treatment is not applicable for different reasons.

In this context we want once again to stress the importance of predictive factors of mortality in these patients, who can receive optimal treatment in useful time. We have found that the most important echocardiographic parameters which are statistically significant predictive factors of mortality, in our group of patients, reflect mainly the systolic function of the right ventricle. Pulmonary artery systolic pressure does not correlate with mortality in our group of patients.

Conflicts of Interest: none declared.

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