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Improvement of right ventricular dysfunction after pulmonary endarterectomy in patients with chronic thromboembolic pulmonary hypertension: Utility of echocardiography to demonstrate restoration of the right ventricle during 2-year follow-up

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ABSTRACT

Background: Pulmonary endarterectomy (PEA) is an effective treatment for chronic thromboembolic pulmonary hypertension (CTEPH) by dissecting the residual thrombus from the native vessel wall. The goal of PEA is to improve pulmonary hemodynamics and right ventricular dysfunction, and thus increase exercise capacity, alleviate symptoms and decrease mortality. The aim of this study, accordingly, was to assess the ability of echocardiography to provide a mechanism to monitor the time course of RV functional improvement after PEA.
Methods: Twenty-six consecutive adult patients who underwent PEA for CTEPH were included in the study. All the patients underwent transthoracic echocardiography and right heart catheterization before surgery. Follow-up echocardiography was performed within 3, 12, and 24 months of surgery. The parameters of right ventricle were compared with baseline data.
Results: In all cases, the RV was enlarged and systolic function was impaired before surgery. RV systolic pressure fell from 92 ± 16 mm Hg before surgery to 41 ± 9 mm Hg by the 3 month post-PEA follow-up ($P<0.001$). RV end-diastolic area and end-systolic area likewise decreased from 35.8 ± 4.4 cm^2 to 26.6 ± 4.8 cm^2 ($P<0.001$) and from 27.1 ± 3.8 cm^2 to 17.9 ± 3.8 cm^2 ($P<0.001$), respectively. The RV myocardial performance index also decreased from a ratio of 0.8 ± 0.1 to 0.5 ± 0.1 ($P<0.001$). The tricuspid annular plane systolic excursion increased from 8.8 ± 0.6 mm to 10.1 ± 0.9 mm ($P<0.001$). Tricuspid regurgitation (TR) improved from a mean grade of 3.1 ± 0.5 to 2.2 ± 0.7 ($P<0.001$). At the 12 and 24 month follow-up examinations, RV systolic pressure and function remained improved, respectively. The RV systolic pressure remained above 50 mmHg in only two cases.
Conclusion: In patients with CTEPH who undergo PEA, echocardiography is a useful tool for the evaluation of RV function. Echocardiographic measurements of RV size, systolic pressure, systolic function, and TR show significant improvement, and this effect is sustained for up to 24 months after surgery.

Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is a life-threatening complication of acute pulmonary embolism that results from intraluminal thrombus organization and fibrous stenosis or complete obliteration of pulmonary arteries. CTEPH is characterized by intravascular organization of emboli and occurs in 0.1–8.8% of all cases after acute pulmonary embolism(PE) [1,2]. Some patients with CTEPH

Abbreviations: ACT, acceleration time; CI, confidence interval; CO, cardiac output; CTEPH, chronic thromboembolic pulmonary hypertension; CVP, central venous pressure; IVC, inferior vena cava; LV, left ventricular; LVEDd, LV end-diastolic diameter; LV-EF, LV ejection fraction; NYHA, New York Heart Association; PAP, pulmonary artery pressure; PEA, Pulmonary endarterectomy; PFO, patent foramen ovale; PVR, pulmonary vascular resistance; RA, right atrial; RAP, RA pressure; RV, right ventricle; RV-EDA, RV end-diastolic area; RV-ESA, RV end-systolic area; RV-FAC, RV fractional area change; RV-MPI, RV myocardial performance index; RVSP, RV systolic pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

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have impaired fibrinolysis, likely due to structural abnormalities of fibrin or the fibrin clot. Pulmonary vascular resistance (PVR) is increased due to the obstruction of pulmonary artery branches following episodes of pulmonary embolism with incomplete thrombus resolution, formation of fibrosis and remodelling of pulmonary blood vessels. The proximal vascular occlusion in CTEPH, may result in a disconnection between ventilator inefficiency and hemodynamics and thus prognosis in CTEPH. A significant change of PVR will lead to pulmonary hypertension and progressive right heart failure [3].

Pulmonary endarterectomy (PEA) is the therapy of choice for patients with surgically accessible CTEPH. PEA is an effective treatment for CTEPH, which involves dissecting the residual thrombus from the native vessel wall. PEA improves pulmonary hemodynamic and right ventricular dysfunction, and thus increases exercise capacity, alleviates symptoms, and decreases mortality [4,5].

Most patients with CTEPH will show a significant RV dysfunction and pulmonary hypertension. Although CTEPH should be confirmed by direct measurement of pulmonary artery pressures via right heart catheterization, echocardiography is a useful tool for the follow-up evaluation after surgery. The aim of this study, accordingly, was to assess the ability of echocardiography to provide a mechanism to monitor the time course of RV functional changes after PEA, without the need of invasive catheterization.

Materials and Methods

Study Patients

All the CTEPH patients referred to Beijing Chao-Yang Hospital and treated with PEA surgery were consecutively followed-up. The patients who had both baseline and 24 months follow-up echocardiograms were included in the analysis. An IVC filter was placed routinely several days in advance to the operation, PEA under general anesthesia and cardiopulmonary bypass was always performed through a median sternotomy on both main intrapericardial pulmonary arteries following the standardized technique which was described by the UCSD PEA group, which has been described in our previous study [4,5]. Two patients had coronary artery disease that underwent additional coronary bypass surgery and one had closure of the patent foramen ovale (PFO). All the patients were treated with standard anticoagulant therapy before and after surgery. The study was approved by the institutional review board at our hospital, and all the patients in the study gave informed written consent.

Transthoracic Echocardiography

Transthoracic echocardiography was performed using the Philips Sonos 5500 (S4 transducer, 2–4 MHz) or Philips iE33 (S3-1 transducer, 1–3 MHz). Images were obtained with patients lying in the left lateral position and monitored by surface ECG. The tricuspid annular plane systolic excursion (TAPSE) was acquired by placing an M-mode cursor through the tricuspid annulus to measure the amount of longitudinal motion of the annulus at peak systole. Right atrial pressure (RAP) was estimated by inferior vena cava (IVC) diameter and the presence of inspiratory collapse as seen in the subcostal view. An IVC diameter $\leq$21 mm that collapsed >50% with a sniff suggested normal RA pressure of 5 mm Hg, whereas an IVC diameter >21 mm that collapsed <50% with a sniff suggested high RA pressure of 15 mm Hg. The RAP was estimated to be approximately 10 mm Hg when the IVC diameter decreased by less than 50%. The RV end-diastolic area (RV-EDA) and RV end-systolic area (RV-ESA) were determined in the apical four-chamber view. The RV fractional area change (RV-FAC) was calculated as follows: RV-FAC = (RV-EDA − RV-ESA)/RV-EDA × 100. The RV myocardial performance index (RV-MPI) was measured by pulsed tissue Doppler (MPI = [TCO-ET]/ET). The tricuspid (valve) closure opening time (TCO) encompassed the isovolumic contraction time, ejection time (ET), and isovolumic relaxation time. The area of the tricuspid regurgitation (TR) was determined in the apical four-chamber view according to the following scoring system: 4 + TR, jet area >10 cm^2; 3 + TR, jet area >4 and $\leq$10 cm^2; 2 + TR, jet area >2 and $\leq$4 cm^2; and 1 + TR, jet area >0 and $\leq$2 cm^2 [4]. All above parameters were measured before and at 3, 12, and 24 months after surgery. All data were stored digitally for off-line post-processing and data analysis. The same echocardiographic protocol and the same measured variables were used during the study period.

Right Heart Catheterization

In all patient-cases included in this study, a hemodynamic examination was performed with a Swan-Ganz catheter to attain pre-operative and 3 months post-operative determinations of pulmonary vascular resistance.

Statistical Analyses

Continuous variables were expressed as mean ± standard deviation (SD). Baseline and postoperative continuous variables were compared using a two-tailed Wilcoxon signed rank test. A $P<0.05$ was considered significant. For statistical analysis and graphic representation, a statistical software package (SPSS, version 11.5 for Windows; SPSS; Chicago, USA) was used.

Results

Clinical Features

Between February 2002 and July 2010, 35 consecutive CTEPH patients (29 male, 6 female; age (43.5 ± 12.6) years, range 17–66 years at operation time) were referred to our hospital and treated with PEA surgery. Five (5/35) patients died of persistent pulmonary hypertension after PEA or serious bleeding complication in early stage. Four(4/35) patients could not come back to the hospital for the follow-up echocardiograms because of the distance issues. 26 patients (4 women and 22 men; average age, 44.5 ± 12.7 years; range, 17–64 years) who both survived PEA surgery were finally included in the study. The 26 study patients included 4 women and 22 men, and the mean age was 44.5 ± 12.7 years (range from 17–64 years). The mean duration of

Table 1
Baseline characteristic of patients with CTEPH (n = 26 patients).

	All patients (n = 26)
Age (years)	44.5 (17-64)
Gender (men/women)	22/4
Duration of symptomatic pulmonary hypertension (months)	34.1 (4-72)
Commodities	
Pre-existing coronary artery disease, n (%)	2 (7.7)
Deep venous thrombosis	21(81)
Antiphospholipd Syndrome	2 (7.7)
NYHA scale, n (IV/III/II)	
II	2
III	19
IV	5
mPAP (mmHg)	48 (33-84)
CO (L/min)	3.7 (2.5-5.0)
RVSP (mmHg)	92 (66-134)
PVR (dynes.s.cm^{-5})	944 (603-1324)
Echo Data	
RV-MPI	0.8 (0.6-1.1)
TR velocity (m/s)	4.8 (4.1-5.8)

NYHA = New York Heart Association; mPAP = mean pulmonary artery pressure; CO = cardiac output; RVSP = RV systolic pressure; PVR = pulmonary vascular resistance; RV-MPI = RV myocardial performance index; TR = tricuspid regurgitation.