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Can we use the end systolic volume index to monitor intrinsic right ventricular function after repair of tetralogy of Fallot?☆

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ABSTRACT

Background: After tetralogy of Fallot (ToF) repair the right ventricle (RV) is commonly exposed to abnormal volume load resulting from pulmonary regurgitation (PR) leading to progressive RV dilatation. The objective of this study was to assess the relationship between RV volumes, especially the end systolic volume index (ESVi), and RV contractility in patients after ToF repair and significant PR and to determine whether RV dilatation reflects intrinsic RV dysfunction in these patients.
Methods: Twenty-nine ToF patients were studied 11.6 (range: 1.9–30.1) years after repair with the pressure–volume conductance system. The patient cohort was divided into two groups according to the median ESVi (*group 1*: ESVi<34.7 ml/m$^{2\times1.18}$, $n=14$; *group 2*: ESVi≥34.7 ml/m$^{2\times1.18}$, $n=15$).
Results: The slope of the end systolic pressure–volume relationship (end systolic elastance, E*es*) was higher in *group 1* compared to *group 2* both at baseline and during dobutamine infusion (0.87 ± 0.36 vs. 0.46 ± 0.28 mm Hg/ml and 1.50 ± 0.77 vs. 0.92 ± 0.37 mm Hg/ml; $P<0.005$ and $P=0.02$, respectively).
Overall, E*es* at baseline correlated significantly with ESVi and also with the end diastolic volume index ($r=-0.64$, and $P<0.001$ for both). Receiver operating characteristic curve analysis revealed that ESVi was superior to RV ejection fraction (EF) in predicting an E*es* in the lowest quartile of the study group (area under curve ESVi vs. EF: 0.84 (0.64–0.95) vs. 0.68 (0.47–0.85); $P=0.015$).
Conclusion: ESVi is a valid estimate of intrinsic RV function in repaired ToF patients with residual PR and in this respect seems superior to EF. These data underscore the importance of serial ventricular volume assessment in the follow-up of these patients.

1. Introduction

The major cause of late morbidity in repaired tetralogy of Fallot (ToF) patients is pulmonary regurgitation (PR) which results in progressive right ventricular (RV) dilatation and is associated with RV dysfunction, exercise intolerance, sustained ventricular arrhythmia and sudden cardiac death [1–4].

With pulmonary valve replacement, PR is targeted and RV volume may decrease or even normalise after surgery [5,6]. Although controversy remains regarding the optimal timing of pulmonary valve replacement, there is consensus that the indication for this intervention should not only be based on clinical symptoms and grade of PR but, particularly, RV volume and function should be considered [7,8].

However, an association between the volume of the RV and its intrinsic function has not been proven in repaired Fallot patients. It hence remains unclear whether progressive RV dilatation always reflects a decrease in RV myocardial contractility and, vice versa, whether a normalisation in contractility can be assumed in patients where complete reverse RV remodelling is observed after pulmonary valve replacement.

In the present study, therefore, we measured RV volume and also assessed load-independent indices of RV myocardial function (i.e. contractility) using the pressure–volume conductance system in patients with repaired ToF and significant PR to investigate the relationship between intrinsic RV function and volume. We paid particular attention to the end systolic volume index as measures of end systolic chamber size are established as the most important determinants of survival and postoperative left ventricular function in patients undergoing aortic valve replacement for chronic aortic regurgitation [9].

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2. Materials and methods

2.1. Patients

A total of thirty-two repaired ToF patients were recruited to be studied with the conductance system between April 2004 and January 2007 at the time of routine diagnostic cardiac catheterisation. The patients were prospectively selected for the study when significant PR was evident on clinical and echocardiographic assessments. To estimate the degree of PR using Doppler echocardiographic techniques the width of the regurgitant jet the Doppler profile across the regurgitant valve, distal flow reversal and the size of the volume loaded right ventricle were taken into consideration [10]. Patients with pulmonary atresia, absent pulmonary valve, and double outlet right ventricle were excluded. All patients or their parents gave informed consent to a study protocol approved by the institutions human research ethics committee.

2.2. Clinical data

Data on patient characteristics were collected and included age, history and technique of previous surgery, number of previous operations, and New York Heart Association (NYHA) functional class. Standard 12-lead electrocardiograms were acquired for all patients at the day of admission at a paper speed of 50 mm/s and QRS duration was measured manually.

2.3. Cardiac catheterisation

Routine diagnostic cardiac catheterisation was performed under general anaesthesia including full haemodynamic assessment and biplane (posterior–anterior and lateral) RV angiocardiography. Angiocardiograms were recorded and digitally stored on a UNIX workstation for offline analysis. RV volumes were calculated at end diastole (EDV) and end systole (ESV) using custom made software that allows optimal image pairing and semiautomatic contour detection. The technique has previously been validated and described by our group [11,12]. EDV and ESV were corrected with factors appropriate for projection and cardiac phase [13]. PR was quantified using X-ray densitometry [12,14].

The diameter of the RV pulmonary trunk junction at the level of the pulmonary annulus was measured from the lateral angiocardiogram. In this study the term 'pulmonary annulus' was used even though postoperative angiograms were analysed. The pulmonary annulus area was calculated and normalised for body surface area to obtain a pulmonary annulus index [12].

2.4. Conductance study

Once the routine part of the catheterisation procedure was completed a 4F or 7F combined pressure–conductance catheter with 12 electrodes (CD Leycom, Zoetermeer, The Netherlands) was placed in the RV via the inferior caval vein in order to acquire RV pressure–volume loops. Pressure–volume signals were displayed online and digitized at a sample rate of 250 Hz (CFL 512, CD Leycom, Zoetermeer, The Netherlands) using a value of blood resistivity determined before data acquisition. The pressure signal was calibrated with a standard calibration pulse from the amplifier (Sentron, Roden, The Netherlands). Conductance derived RV volume was calibrated for parallel conductance and gain factor α using the EDV and ESV obtained from biplane angiocardiography. A standard 7F thermodilution catheter (Baxter Healthcare, Boston, Massachusetts) was placed in the pulmonary artery and connected to a dedicated cardiac output processing computer (Com2, Baxter, Edwards). Finally, a 25-mm Latex balloon catheter (Numed, Hopkinton, NY) was placed at the junction of the inferior vena cava and the right atrium and prepared to modify preload.

Pressure–volume data were recorded for 10–15 s with the respirator temporarily interrupted at end expiration. Pressure and volume signals were collected along with the ECG during steady state conditions and progressive vena caval occlusion to generate pressure–volume loops over a wide range of filling pressures. Measurements were repeated at the end of a 10 min infusion of 10 $\mu g\ kg^{-1}\ min^{-1}$ of dobutamine (Fig. 1). All data acquisition runs were repeated in triplicate and all runs containing premature ventricular contractions were excluded from analysis.

2.5. Data analysis

Analysis of pressure–volume loops was performed with custom made software (Circlab 2008). Steady state haemodynamic data were calculated from pressure–volume loop recordings at baseline and after dobutamine infusion as means of all beats during a 10-second period.

Heart rate, cardiac index, stroke volume, EDV and ESV, RV ejection fraction (EF), end systolic and end diastolic pressure (ESP and EDP), maximal and minimal rate of RV pressure change (dP/dt_{max}, dP/dt_{min}) were analysed. The RV volumes were normalised for body surface area with an exponent appropriate for end diastole and end systole since RV volumes increase in an over proportional manner with respect to body surface area (EDVi, ESVi) [15]. The time constant of relaxation (τ), reflecting the early active relaxation process, was calculated as the time constant of monoexponential pressure decay during isovolumic relaxation. The isovolumic period was defined as the period between the time point of dP/dt_{min} and the time point at which dP/dt reached 10% of the dP/dt_{min} value. Stroke work (SW) was calculated as the area enclosed by the pressure–volume loop.

Indices of systolic and diastolic function were derived from pressure–volume loops recorded during the preload reduction manoeuvre. For systolic function, we determined end systolic elastance (E*es*) as the slope of the end systolic pressure–volume relationship (ESPVR: ESP vs. ESV). Diastolic stiffness (E*ed*) was determined as the slope of the end diastolic pressure–volume relationship (EDPVR: EDP vs. EDV). These slopes are regarded as the optimal load-independent indices of intrinsic systolic (E*es*) and diastolic (E*ed*) ventricular function, reflecting contractility and lusitropy, respectively [16,17].

All functional data were evaluated by a single investigator (AU) blinded to the clinical and normalised volumetric data.

2.6. Statistical analysis

Data were expressed as mean ± SD. Comparisons between groups were made with Student *t*-test after testing for normality with the Kolmogorov–Smirnov method and χ^2 test for categorical data. Comparisons within one group between baseline and dobutamine data were made with Student *t*-test for paired samples. We used a linear mixed-effects model to account for repeated measurements on each patient. In this model, patients were included as random effects and group (*group 1*, *group 2*)

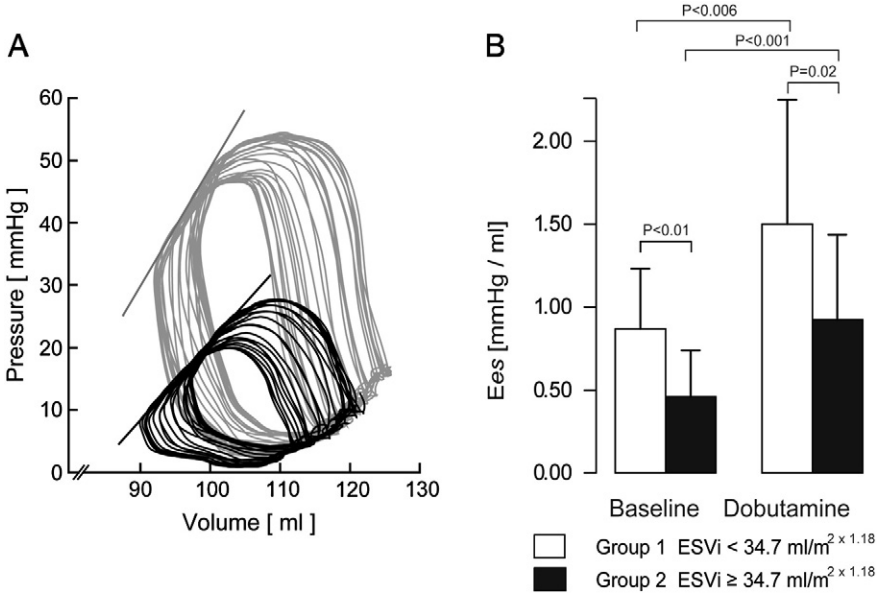

Fig. 1. Panel A: Pressure–volume loops recorded at baseline (black) and after 10 min of dobutamine infusion (grey) of a patient after repair of tetralogy of Fallot. Panel B: End systolic elastance (E*es*) at baseline and during dobutamine infusion in the two different groups of patients with repaired tetralogy of Fallot. ESVi, end systolic volume index.