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Abnormal right atrial and right ventricular diastolic function relate to impaired clinical condition in patients operated for tetralogy of Fallot☆

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ABSTRACT

Background: Atrial enlargement may reflect ventricular diastolic dysfunction. Although patients with tetralogy of Fallot (TOF) have been studied extensively, little is known about atrial size and function. We assessed bi-atrial size and function in patients after TOF repair, and related them to biventricular systolic and diastolic function, and clinical parameters.

Methods: 51 Patients (21 ± 8 years) and 30 healthy controls (31 ± 7 years) were included and underwent magnetic resonance imaging to assess bi-atrial and biventricular size, systolic and diastolic function. Patients also underwent exercise testing, and N-terminal prohormone brain natriuretic peptide (NT-proBNP) assessment.

Results: In patients, right atrial (RA) minimal volume (34 ± 8 ml/m^2 vs. 28 ± 8 ml/m^2, $p = 0.001$) and late emptying fraction were increased; RA early emptying fraction was decreased. Patients had longer right ventricular (RV) deceleration time (0.24 ± 0.10 vs. 0.13 ± 0.04, $p < 0.001$), reflecting impaired RV relaxation, and larger RV volumes. Patients with end-diastolic forward flow (EDFF) had larger RA and RV size, abnormal RA emptying, higher NT-proBNP levels, higher VE/VCO_2 slope (ventilatory response to carbon dioxide production), and the most abnormal LV diastolic function (impaired compliance). Patients with abnormal RA emptying (reservoir function <30% and pump function >24%) had higher NT-proBNP levels and worse exercise capacity. RA minimal volume was associated with RV end-diastolic volume ($r = 0.35$, $p = 0.013$).

Conclusions: In TOF patients with moderate RV dilatation, abnormal bi-atrial function and biventricular diastolic dysfunction are common. Abnormal RA emptying was associated with signs of impaired clinical condition, as was the presence of EDFF. These parameters, together with RA enlargement, could serve as useful markers for clinically relevant RV diastolic dysfunction.

1. Introduction

Chronic pulmonary regurgitation (PR) with subsequent right ventricular (RV) dilatation is an important cause of late morbidity and mortality in patients long after surgical repair of tetralogy of Fallot (TOF) [1–4]. Up to now, it remains difficult to predict the course of RV dilatation and deterioration in TOF patients, and the precise indications and optimal timing to perform a pulmonary valve replacement (PVR) have therefore not been fully clarified.

Biventricular size and systolic functional parameters have been studied extensively in TOF patients, but little information is available on atrial size and function. The atria play a crucial role in the filling of the ventricle during ventricular diastole. It has been reported that left atrial (LA) enlargement reflects the burden of left ventricular (LV) diastolic dysfunction and that LA volumes increase with the severity of diastolic dysfunction [5]. This emphasizes the need for measurement of atrial size and function if diastolic function is assessed.

Diastolic dysfunction may be important as a marker preceding systolic dysfunction [6,7], but isolated diastolic dysfunction with preserved ejection fraction (EF) may also be an independent parameter influencing patient outcome [8]. The relationship between RV

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diastolic function and clinical parameters has been debated in TOF patients [9–13], but relatively little is known on the effects of right sided abnormalities on LV diastolic function.

Magnetic resonance imaging (MRI) is the gold standard technique for the assessment of biventricular size and function [14], and it has also been demonstrated to be an accurate tool for the analysis of atrial size and function [15].

The aim of our study was to assess bi-atrial size and function in patients after repair of tetralogy of Fallot and to evaluate the clinical value of these parameters by relating them to biventricular systolic and diastolic function, exercise capacity, electrocardiographic (ECG) parameters, and N-terminal prohormone brain natriuretic peptide (NT-proBNP) levels.

2. Methods

2.1. Patients

This study is part of a larger, prospective serial follow-up study, for which the inclusion criteria were: 1) surgical repair of tetralogy of Fallot without associated cardiac lesions, 2) the availability of an MRI study at least 3 years before the current study. Patients with more than mild tricuspid regurgitation or evidence of a residual ventricular septal defect were excluded.

Fifty-four patients were included in the current cross-sectional study between September 2007 and February 2010. Patients underwent an MRI study with imaging of the atria, 12-lead ECG, 24-hour Holter monitoring, NT-proBNP assessment, and exercise testing, all on the same day.

Results of MRI parameters were compared to a group of 30 healthy controls (15 male, 31 ± 7 years), within our center. Healthy controls were volunteers without cardiac symptoms.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Our study protocol was approved by the local Ethical Committee; all participants, and if required parents, gave written informed consent.

2.2. Magnetic resonance imaging

Cardiac MRI was performed at a Signa 1.5 Tesla system (General Electric, Milwaukee, WI, USA) and an 8-channel phased-array cardiac surface coil. All patients were monitored by vector cardiogram gating and respiratory monitoring. All images were obtained during breath-hold in end-expiration. A multi-slice, multi-phase data set was acquired using steady-state free precession cine imaging in a short axis direction, covering the whole heart, including the atria. Typical imaging parameters were: repetition time 3.4 ms, echo time 1.4 ms, flip angle 45°, slice thickness 8–10 mm, inter-slice gap 1 mm, field of view 380×380 mm, and matrix 160×128 mm. Flow measurements of the pulmonary valve were performed perpendicular to flow, using a velocity-encoded MRI sequence. Typical imaging parameters were: repetition time 4.5 ms, echo time 2.4 ms, flip angle 18°, slice thickness 7 mm, field of view 290×220 mm, and matrix 256×128 mm. Velocity encoding was set at 150 cm/s and was increased whenever phase aliasing occurred.

Analysis was performed on a commercially available Advanced Windows workstation (General Electric Medical Systems), equipped with the software packages MASS and FLOW (Medis Medical Imaging Systems, Leiden, the Netherlands). Endocardial and epicardial borders of both ventricles were manually traced in end-systole and end-diastole. Endocardial borders of the right atrium (RA), LA, RV, and LV were subsequently defined in all phases and all slices of the short axis set using a previously described semi-automated full cardiac cycle contour detection method [16]. Contours were manually corrected if necessary. The atrial appendages were included in the atrial volumes. The superior and inferior caval veins, coronary sinus and pulmonary veins were excluded at their junction to the atrium. Papillary muscles and trabeculations were included in the ventricular cavity. The interventricular septum was included in the LV mass. When the pulmonary valve was visible in the basal slice, contours were drawn up to the junction with the pulmonary valve. All atrial data-sets were analyzed by 1 observer (RP) and supervised by another observer (SL), who also analyzed all ventricular data-sets and had 4 years of experience in cardiac contour tracing. Fig. 1 shows bi-atrial and biventricular endocardial contour tracing.

2.3. MRI parameters

Time volume curves for the RA, LA, RV, and LV were acquired by summation of the volumes of every slice of each phase. Additionally, time volume change curves were reconstructed (Fig. 2). The terms systole and diastole always refer to ventricular systole and ventricular diastole.

2.4. RA and LA function

The following parameters were assessed for RA and LA function (Fig. 2A, B), as described by Riesenkampff and colleagues [17]: 1) maximal volume (max.vol); 2) minimal volume (min.vol); 3) cyclic volume change, defined as the difference between maximal and minimal atrial volume; 4) cyclic volume change function, which is the cyclic volume change, expressed as percentage of maximal atrial volume; 5) reservoir function, calculated by subtracting the minimal atrial volume at middiastole from the maximal atrial volume, expressed as percentage of ventricular effective stroke volume (SV); 6) pump function, calculated by subtracting the minimal atrial volume from the maximal atrial volume at middiastole, expressed as percentage of ventricular effective SV; 7) conduit function, calculated by subtraction of the sum of reservoir and pump volume from the effective SV of the ventricle, expressed as percentage of ventricular effective SV; 8) early emptying fraction, defined as atrial volume decrease during the first 1/3 of ventricular diastole, expressed as percentage of the cyclic volume change; 9) early peak emptying rate (EPER), defined as the maximal atrial volume change in early ventricular diastole; 10) late emptying fraction, defined as the decrease in atrial volume after the onset of atrial contraction, expressed as percentage of the cyclic volume change; 11) late peak emptying rate (LPER), defined as the maximal atrial volume change in late ventricular diastole; and 12) E/A volume ratio, as the ratio of early emptying volume to late emptying volume. Volumetric parameters were indexed for body surface area (BSA); EPER and LPER were indexed for cyclic volume change.

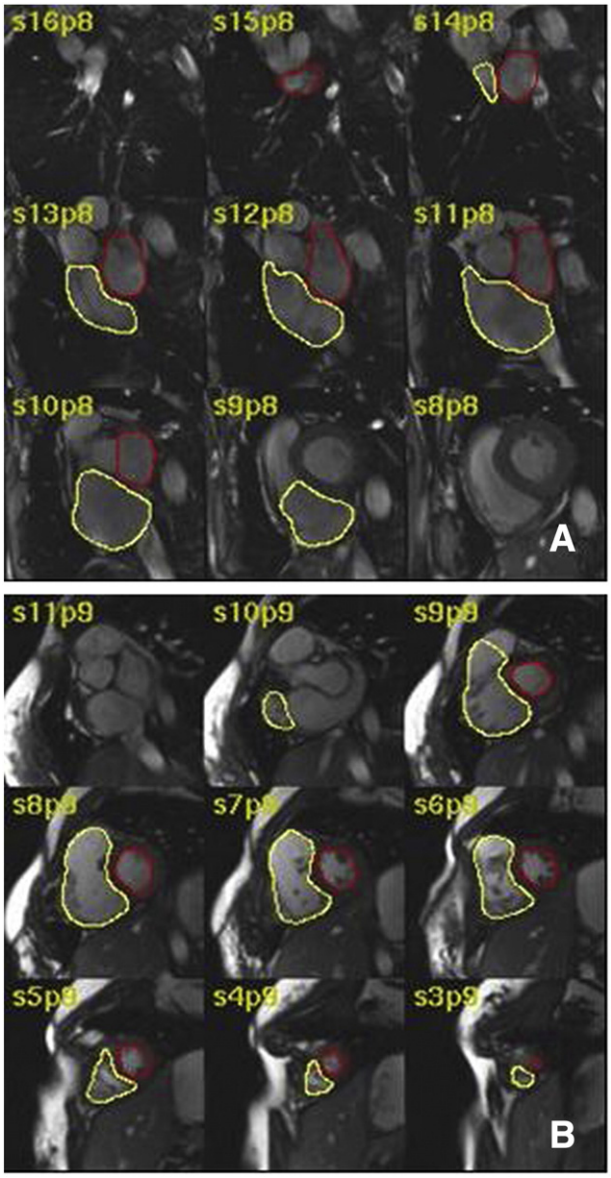

Fig. 1. Contour tracing of atrial and ventricular borders in short axis orientation. A) Right atrial and left atrial contours; B) right ventricular and left ventricular contours.

2.5. RV and LV function

The following parameters were assessed for RV and LV systolic and diastolic function (Fig. 2C, D): 1) biventricular end-diastolic volume (EDV); 2) end-systolic volume (ESV); 3) SV; 4) EF; 5) mass; 6) early filling fraction, defined as ventricular volume