Isovolumic contraction acceleration before and after percutaneous closure of atrial septal defects

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A b s t r a c t

Aim: To compare systemic right ventricular function by isovolumic myocardial acceleration before and 6 months after the percutaneous closure of atrial septal defects (ASD).

Material and methods: Patients admitted to our tertiary center for the percutaneous closure of atrial septal defects between January 2010 and August 2012 constituted the study group. Right ventricular function of patients was assessed by tissue Doppler echocardiography before and after surgery. Echocardiographic data in patients were compared to age-matched controls without any cardiac pathology and studied in identical fashion mentioned below.

Results: A total of 44 patients (24 males, 20 females) and 44 age-matched controls (25 males, 19 females) met the eligibility criteria for the study. Right ventricular end-diastolic and end-systolic volume, right ventricular end-diastolic diameter measurements on echocardiogram, and pulmonary artery pressures in both pre- and post-ASD groups were significantly higher than in controls. Tricuspid annular plane systolic excursion and isovolumic myocardial acceleration measurements significantly increased after the percutaneous closure of the defect; however, post-ASD measurements were still significantly lower than the controls.

Conclusions: Atrial septal defect device closure resulted in a significant increase of isovolumic myocardial acceleration measurements. Tissue Doppler analysis of regional myocardial function offers new insight into myocardial compensatory mechanisms for acute and chronic volume overload of both ventricles.

Key words: atrial septal defect, isovolumic myocardial acceleration.

Introduction

Atrial septal defect (ASD) is a common congenital defect (1 in 1000 live births) and accounts for up to 40% of clinically relevant acyanotic shunts in adults [1]. While large ASDs may present in childhood with signs of heart failure, a significant proportion of patients present in the 3rd–4th decade of life [2]. Surgical closure is the most common therapy for these defects; however, a surgical procedure requires cardiopulmonary bypass, a significant postoperative recovery, and a sternotomy scar that may be undesirable to young patients. Catheter-based techniques for the treatment of ASD were pioneered by King and Mills in 1974 [3]. Percutaneous therapy is now the preferred strategy for closure of secundum ASD, by patients and physicians alike, in the absence of complicated anatomy or another indication for traditional cardiac surgery, because it is technically simple and associated with negligible morbidity and mortality [4].

Tissue Doppler echocardiography (TDE) has emerged as a useful tool to quantify regional ventricular function [5]. A TDE-based index of right ventricular (RV) contractile function, isovolumic myocardial acceleration (IVA), has been shown experimentally to measure contractile function accurately [6]. Isovolumic myocardial acceleration is an easily obtained, noninvasive index of ventricular contractile state that is unaffected by physiological changes in preload and afterload [5–7]. The ability to detect changes with the force-frequency relationship and during pharmacological manipulation makes this a potentially attractive method for clinical and experimental evaluation of systolic cardiac function *in vivo*.

Aim

The aim of this clinical study was to compare systemic RV function before and 6 months after the percutaneous closure of secundum ASDs by means of a relatively new

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load-insensitive marker, IVA, which is derived from myocardial velocity traces.

Material and methods

Study design

This study was approved by the local Institutional Review Board (No: 180913-3). Written informed consent was obtained from patients. Patients admitted to the Department of Cardiology of our tertiary center for the percutaneous closure of secundum ASDs between January 2010 and August 2012 constituted the study group.

Right ventricular function of patients was assessed by TDE before (pre-ASD group) and 6 months after (post-ASD group) the percutaneous closure of the defect. The TDE data in patients were compared to age-matched controls without any cardiac pathology (control group) and studied in identical fashion mentioned below. Patients with known mitral valve pathology and those with right ventricular hypertrophy due to cor pulmonale were excluded from the study.

Outcome parameters

Transthoracic imaging of the heart was performed using a 2.5 MHz phased-array transducer and a transthoracic echocardiographic recorder system (Philips Medical Systems, Andover, MA, USA). The RV and left ventricular (LV) free wall was separately imaged from an apical position, and color-coded myocardial velocities were recorded at the base immediately below the insertion of the atrioventricular valve leaflets. Recordings were made during apnea in the catheter laboratory; and, during held expiration in the ambulatory patients, tissue Doppler data were acquired with a simultaneous electrocardiogram. The peak myocardial velocities during isovolumic contraction, systole (S wave), early diastole (E wave), late diastole (A wave), tricuspid annular plane systolic excursion (TAPSE), and IVA were measured. The IVA was calculated as the peak isovolumic myocardial velocity divided by time to peak velocity were obtained from an apical four-chamber view using a sampling gate of 2 mm to 4 mm and swep of 100 to 150 mm/sn. Doppler tissue imaging was performed at the tricuspid lateral annulus. Isovolumic relaxation time was measured from the onset of the second heart sound to the beginning of the myocardial E wave. Measurements of myocardial acceleration and velocities were performed on three consecutive heartbeats, and the average of the three measurements was calculated. Regional RV and LV function were also assessed by TDE.

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences 19.0 for Windows (SPSS Inc., Chicago, IL). A normal distribution of the quantitative data was checked using Kolmogorov-Smirnov and Shapiro-Wilk tests. Parametric tests were applied to data of normal distribution and non-parametric tests were applied to data of questionably normal distribution. Independent-samples *t*-test was used to compare independent groups. Paired *t*-test was used to compare groups of independent continuous variables. The distribution of categorical variables in both groups was compared using Pearson χ^2 test. Data are expressed as mean ± SD or median (interquartile range), as appropriate. All differences associated with a chance probability of 0.05 or less were considered statistically significant.

Results

A total of 44 patients (24 males, 20 females) and 44 controls (25 males, 19 females) met the eligibility criteria for the study. The mean age of the patients was 31.64 ±15.85 (range: 9–63) years, while the mean age of the control group was 31.36 ±15.68 (range: 9–66) years. The groups did not differ from each other in terms of gender or age ($p = 0.830$, and $p = 0.936$, respectively).

Every patient in this series had normal right atrial and ventricular pressures confirmed by invasive measurements before the percutaneous closure of the defect. Right ventricular end-diastolic volume, right ventricular end-systolic volume, and right ventricular end-diastolic diameter measurements on echocardiogram, and systolic pulmonary artery pressures in both pre- and post-ASD groups were significantly higher than in controls (Table I).

The TAPSE measurements significantly increased after the percutaneous closure of the defect ($p < 0.001$); however, post-ASD measurements were still significantly lower than the controls ($p < 0.001$). Similarly, IVA measurements significantly increased after the closure of the defect ($p < 0.001$); however, post-ASD measurements were again significantly lower than the controls (Table I).

All percutaneous closures of atrial septal defects were performed successfully. There were no repeated interventions in either group. Complications such as cardiac perforations, device malposition or embolization, vascular trauma, residual shunts, thrombus formation, atrial arrhythmias, atrioventricular valve regurgitation, infectious endocarditis and sudden death were not observed. No wound infection was observed for any patient.

Discussion

In this study, we attempted to compare systemic RV function by IVA before and 6 months after the percutaneous closure of ASD. Our study showed that IVA can be used, in a way similar to invasive measurements of load-independent indexes, to describe the response of RV contractility to ASD repair in patients with a systemic RV.

The ASD represent a clinical model for chronic right ventricular volume overload. Closure of the defect results

Table I. Tissue Doppler echocardiographic parameters in pre- and post-ASD groups and controls

Parameter	Pre-ASD Closure	Post-ASD Closure	Controls	Value of *p*
RVEDV [ml]	60.39 ±5.23	51.11 ±5.09	45.76 ±3.41	(pre vs. post) < 0.001 (pre vs. control) < 0.001 (post vs. control) < 0.001
RVESV [ml]	24.39 ±4.22	19.27 ±3.07	15.93 ±2.38	(pre vs. post) < 0.001 (pre vs. control) < 0.001 (post vs. control) < 0.001
RVEDD [mm]	42.59 ±1.60	35.64 ±1.77	33.93 ±1.09	(pre vs. post) < 0.001 (pre vs. control) < 0.001 (post vs. control) < 0.001
PAP [mm Hg]	27.45 ±3.62	22.16 ±3.31	17.70 ±2.50	(pre vs. post) < 0.001 (pre vs. control) < 0.001 (post vs. control) < 0.001
TAPSE [cm]	21.48 ±1.81	24.22 ±2.28	26.71 ±1.47	*p* (pre vs. post) < 0.001 *p* (pre vs. control) < 0.001 *p* (post vs. control) < 0.001
IVA [m/s^2]	1.97 ±0.09	2.43 ±0.22	2.78 ±0.14	*p* (pre vs. post) < 0.001 *p* (pre vs. control) < 0.001 *p* (post vs. control) < 0.001

RVEDV – right ventricular end-diastolic volume, RVESV – right ventricular end-systolic volume, RVEDD – right ventricular end-diastolic diameter, TAPSE – tricuspid annular plane systolic excursion, PAP – systolic pulmonary artery pressure, IVA – isovolumic myocardial acceleration. Values are given as mean ± SD

in acute volume unloading of the right side of the heart and redirection of the pulmonary venous return toward the LV. The consequences for the regional wall motion in the ventricles are currently not completely understood [7]. In recent years there has been increased interest in the assessment of RV function in both acquired and congenital heart disease [8–10]. Because of its complex geometric shape and other spatial considerations, it has been notoriously difficult to noninvasively assess RV function [11]. Although RV ejection fraction can now be derived from volumetric data obtained by MRI or 3-dimensional echocardiography, the load dependency of ejection fraction limits its utility [11, 12]. Indeed, the validity of any single beat-derived ejection phase index of RV contractile function is questionable because changes in loading conditions, especially afterload, markedly influence such measurements. Furthermore, the RV in congenital heart disease is frequently characterized by pressure or volume overload, obviating useful comparison of these ejection phase indexes with data derived in the normal RV [8].

This study used IVA, which has been proposed as a tissue Doppler index of myocardial contractility [12, 13]. The IVA is sensitive to contractile change and relatively independent of changes in loading conditions over a physiologic range that might be expected postoperatively. It can also describe the myocardial force-frequency relationship and therefore is potentially ideal for describing postoperative changes [13]. In clinical practice, it has been far more difficult to quantify contractility than the other two independent determinants of preload and afterload. The reference standard of contractility requires simultaneous recordings of ventricular pressure and volume under different loading conditions, making it difficult to use clinically [14]. An alternative method to determine contractility is to measure peak endocardial acceleration with a microaccelerometer implanted in the RV on the tip of a pacemaker lead [15]. The highest values for endocardial acceleration have been registered during the isovolumic contraction phase of the cardiac cycle. Based on this principle, Vogel *et al.* measured IVA noninvasively [6]. The technique relies on measurements of the slope of the upstroke of the distinct pre-ejection wave seen during the isovolumic contraction phase of the cardiac cycle on myocardial velocity tracings. In the present study, we demonstrated a close correlation between IVA from tissue Doppler measurements and reference standard measurements of contractility.

In the present report, we have presented volume-dependent and tissue-dependent indices together. Both have strengths and weaknesses. It was shown that tissue velocities vary with age and heart rate. Eidem *et al.* showed that pulsed-wave tissue Doppler velocities correlate with cardiac growth variables, i.e., especially LV end-diastolic diameter and LV mass, indicating that tissue velocities are not independent of geometry [16]. Apart from the influence of geometry, changes in loading conditions also affect Doppler velocity measurements [17]. The IVA seems to be more valuable in the assessment of RV function in the ASD setting. The IVA resembles myocardial motion during the isovolumetric contraction period. During this time period there is myocardial motion, related to the shape change from a more spherical ventricle to an ellipsoid. The rate of myocardial acceleration during the isovolumic period has been described

to correlate with intrinsic myocardial contractility and is thought to be relatively independent of loading conditions [18]. The IVA has also been validated as a sensitive non-invasive index of LV and RV contractility [13]. In the present study, IVA measurements significantly increased after the closure of the defect; however, post-ASD measurements were significantly lower than the controls.

A high frame rate is critical to correctly analyze the fast events occurring throughout the cardiac cycle. Frame rates of at least 140 fps are required to adequately analyze myocardial events during each cardiac cycle in adults. Since the heart rate is higher in fetuses than in adults (110–180 beats/min), the temporal resolution permitted by the frame rate may limit this offline analysis. Any heart cycle subphases, especially such short ones as IVA, must be analyzed with a high number of frames, otherwise the reliability of analysis is jeopardized.

It has been shown that TAPSE is a reproducible index of RV systolic function and abnormal TAPSE (below 1.8 cm) had a high specificity for abnormal RV function in adults [19]. Adult studies describe the usefulness of TAPSE to diagnose RV systolic dysfunction; it has been shown that a TAPSE < 2 cm indicates an RV ejection fraction of < 40% [20–22]. Recently it has been reported that TAPSE measurement is a more reproducible indicator of RV function when compared to other echocardiographic variables such as the RV fractional area change [19]. In the present study, TAPSE measurements significantly increased after the percutaneous closure of the defect; however, post-ASD measurements were still significantly lower than the controls.

Limitations of our study are the relatively small size of our series and lack of definite criteria for selection of patients. In addition, some details of history and factors that may influence the outcome may not be completely documented. The IVA is relatively independent of changes in loading conditions within a physiologic range. Nonetheless, the responses of contractile indices, including IVA, are difficult to validate in human subjects, in which a complex interplay of changes in loading conditions and myocardial contractility are often interrelated. Due to these restrictions, associations should be interpreted with caution. Further randomized, prospective, controlled trials on larger series are necessary for making more precise interpretations.

Conclusions

The IVA is a noninvasive measurement of RV contractile function that is unaffected by RV loading conditions over a wide range, making it eminently suitable for assessment of patients. The ASD defect closure resulted in a significant increase of IVA measurements. The TDE analysis of regional myocardial function offers new insight into myocardial compensatory mechanisms for acute and chronic volume overload of both ventricles.

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