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POSTERS
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YOUNG INVESTIGATOR AWARDS

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序

心房颤动一直是心律失常研究中最薄弱的环节，其机制和治疗学的演变一直存在着困惑和挑战。然而，我们欣喜地看到，近十年来随着对房颤认识的逐步深入及消融、外科等治疗技术的不断成熟，极大推动了房颤的临床研究和学术进展。房颤已成为当今心电生理学领域中的“HOT SPOT” 目前我国已建立起数个房颤研究和治疗中心，心房颤动国际论坛的成长亲历了我国房颤研究、治疗的不断进步和发展，成绩令人鼓舞，正逐渐步入国际先进水平。

本届论坛汇集了国内一年来房颤研究治疗中心和相关学科的最新研究进展，论文数量和质量创历届论坛之最，充分展示了我国房颤研究蓬勃发展和勃勃生机。本届论坛特节选60余篇优秀论文展示，并现场评选“优秀青年论文”，以表彰我国房颤研究工作者的突出贡献。

心房颤动国际论坛的成长倾注了国内外同道的共同心血，我们完全有理由，经过各位同仁的不断努力和辛勤耕耘，房颤——这片心脏电生理最活跃的沃土，必将结出更加诱人的胜利果实！

2006年7月9日

Young Investigator Awards

Chair Poster

POSTER (session 1)

Poster (Session 2)

Young Investigator Awards

Strain Rate Imaging for Noninvasive Functional Quantification of the Left Atrium in Hypertensive Patients with Paroxysmal Atrial Fibrillation

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Abstract: Strain rate (SR) imaging has been applied to the detection of regional left ventricular dysfunction but not as much to the assessment of left atrial function. We aimed to assess atrial myocardial properties during atrial fibrillation (AF) by myocardial velocity, SR, and strain, focusing on the effects of hypertension and atrial arrhythmias, especially paroxysmal AF.

Methods: We compared 3 groups of a total of 110 consecutive patients with hypertension presenting to our institution: 20 with brief atrial tachycardia, 20 with paroxysmal AF, and 70 with hypertension alone. These patients and 32 controls underwent transthoracic echocardiography, tissue velocity imaging (TVI), strain examination and SR imaging. Atrial tissue velocity, strain, and SR values of hypertensive patients were compared with those of age-matched controls.

Results: Compared with controls, hypertensive patients with paroxysmal AF showed significantly increased atrial myocardial features as assessed by TVI ($P<0.05$-0.001). Time to peak late diastolic SR corrected for heart rate (TASRc) and early diastolic SR (Δ ESR) were significantly increased ($P<0.05$ for both) and late diastolic SR (Δ ASR) ($P<0.05$) and Δ TASRc ($P<0.001$) significantly decreased; moreover, systolic SR (SSR), Δ ASR , and Δ TASRc were significantly decreased ($P<0.05$, $P<0.01$, and $P<0.001$, respectively), with Δ ESR significantly increased ($P<0.01$) as compared with hypertensive patients without arrhythmia. AV, strain, Δ S, TS, Δ TS, Δ SSR, ASR, TASR, and Δ TASR did not differ among the 4 groups.

Conclusions: Noninvasive quantification of LA function by SR imaging combined with TVI enables evaluation of LA dysfunction due to hypertension and paroxysmal AF. With paroxysmal AF in hypertensive patients, the efficiency of left atrial myocardia to reserve potential energy decreases but not the ability, which suggests that left atrial myocardial reservoir function decreases. The conductivity of the left atrium is impaired by paroxysmal AF, which leads to decreased total active atrial contraction and prolonged inter-atrial conduction. Thus, the temporal asynchrony of the atria is enhanced, but atrial systole tends to be synchronous.

Key words: atrial fibrillation; strain rate; hypertension;

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is a major risk factor for stroke and mortality[1]. In the past, AF was frequently a consequence of rheumatic heart disease[2]. Currently, hypertension is the most prevalent, independent, and potentially modifiable risk for AF[3,4]. Hypertension is associated with left atrial enlargement, changes in left atrial mechanical function, altered left atrial electrophysiologic features, and increased atrial ectopic activity. These changes in cardiac structure and physiology favor the development of AF[5].

The left atrium (LA) modulates left ventricular filling and cardiovascular performance by serving as a reservoir during left ventricular systole, as a conduit during early left ventricular diastole, and as a booster pump during late diastole. The hemodynamic importance of the LA for cardiac performance has been studied by both invasive and noninvasive methods[6,7,8].

However, quantitative assessment of LA function with use of invasive methods has been clinically difficult, because it requires simultaneous measurements of LA volume and pressure. Although several noninvasive methods have been used to assess LA function, major limitations, including single-plane assessment, dependence on altered left ventricular hemodynamics, and image quality, have prevented clinical application. Furthermore, Doppler assessment of mitral flow has been used to evaluate left atrial and left ventricular function, but these are surrogate markers of LA function that represent only blood flow during the atrial contraction phase, not intrinsic changes of the LA wall.

The development of novel echocardiographic techniques, such as tissue Doppler imaging (TDI), has enhanced the ability to assess regional myocardial function noninvasively. Although this technique has been used for the assessment of both regional myocardial function [9,10], some problems to be overcome include overall heart motion, cardiac rotation, and the tethering effect. Recently, strain rate (SR) imaging has been introduced as an accurate technique for quantifying regional myocardial function, with high spatial and temporal resolution. The SR is the rate by which the deformation occurs. Thus, SR imaging enables quantitative measurement of regional function independent of cardiac rotational motion and the tethering effect[11,12]. SR imaging has been applied to the detection of regional left ventricular dysfunction but not as much to the assessment of LA function. We aimed to assess the feasibility of measuring regional longitudinal strain/SR profiles in the LA wall to quantify LA functions and to explore the changes in left atrial functions in hypertensive patients with atrial arrhythmias, especially paroxysmal AF.

Methods

The study cohort consisted of 142 subjects who were referred to our department between May 2005 and November 2005. Of these, 32 healthy subjects (16 males and 16 females, mean age 50 years [range 28 to 69 years]) without cardiovascular disease, hypertension, or diabetes mellitus were enrolled as controls. Every subject had no history of dysrhythmia and normal sinus rhythm on recent electrocardiography. No subjects showed abnormal findings on physical examination or conventional echocardiography, and none were receiving cardioactive therapy.

We also enrolled 3 groups of patients from a total of 110 patients (71 males and 39 females, mean age 52 years [range 24 to 77 years]) with hypertension (defined as having a blood pressure > 140/90 mmHg or taking antihypertensive medication) : 20 with brief atrial tachycardia, 20 with paroxysmal AF, and 70 with hypertension alone. Excluded were patients with secondary hypertension or underlying systemic disease such as diabetes mellitus shown on physical and laboratory examinations and those in whom significant abnormalities, such as valvular diseases, hypertrophic cardiomyopathy, left ventricular systolic dysfunction, or pericardial effusion, were found on echocardiography. Paroxysmal AF was diagnosed with both AF and sinus rhythm on electrocardiography. Brief atrial tachycardia was diagnosed with > 3 premature atrial contractions in a row on electrocardiography. All patients were in sinus rhythm at the time of the echocardiographic examination. Informed consent was obtained from all subjects. The study protocol was approved by the Committee on Clinical Investigation of Qilu Hospital of Shandong University.

Echocardiography

A commercially available ultrasound machine (Vivid 7 dimension; General Electric Medical Systems, Horten, Norway) equipped with a 2.5 MHz variable-frequency transducer was used for all echocardiography. Standard echocardiographic views, including parasternal long-axis and apical 4-, 3-, and 2-chamber views, were obtained in 2-D and color TDI modes with the subjects lying on the left side. The LV dimensions and ejection fraction (LVEF;%) were measured by 2-D guided M-mode in the parasternal long-axis view. LV end-diastolic and end-systolic diameters (LVd and LVs, mm) as well as septal and posterior end-diastolic wall thickness (IVSd and LVPWd, mm) were measured as recommended by the American Society of Echocardiography (ASE). LV mass was calculated by use of the formula proposed by Devereux et al.[13] and normalized for body surface area (LV mass index, g/m^2). LA dimension was defined as the largest distance between the posterior aortic and atrial walls in the parasternal long-axis view during systole. Final values were obtained from an average of 3 to 5 measurements.

Transmitral flow profile was assessed by 2-D guided pulsed wave Doppler from the apical 4-chamber view by positioning a 3-mm sized sample volume between the tips of the mitral leaflets in diastole and recording at a sweep velocity of 100 mm/s. Mitral flow parameters included peak velocities during early diastole (E) and late diastole (A), their ratio (E/A ratio), E wave deceleration time (EDT), and isovolumetric relaxation time (IVRT).

SR Imaging in the LA

After patients underwent echocardiography, tissue velocity imaging (TVI) was performed with 4-, 3-, and 2-chamber views in all subjects. Three to five cardiac cycles were recorded in each cine loop. Three cineloops recorded for each patient were saved digitally on a compact disk recordable (CD-R-700MB; IMATION, Japan) for later analysis.

Myocardial Doppler velocity profile signals were reconstructed off-line from the TVI color images. Curve analysis was performed on an average analysis of the 3 to 5 recorded cardiac beats. In apical 4-chamber view, the regional analysis consisted of placing the region of interest cursor at the level of the mitral and tricuspid annuli. In all subjects, curves of atrial strain and SR were assessed on the proximal part (about 1 cm away from the mitral valve annulus) of the corresponding walls of the LA. A region of interest with a sampling size of 1x1 mm was positioned on each wall of the LA in 4-, 3-, and 2-chamber views and manually tracked frame by frame to maintain its position within the LA wall. Thus, tissue velocity versus time curves, strain versus time curves, and SR versus time curves were generated from these regions of interest.

TVI curves and SR curves were typical triphasic curves, but strain curves were monophasic. For triphasic curves, negative velocities represent myocardial motion away from the ventricular apex during diastole. The first negative wave (E) occurred at the end of ventricular systole, during the ventricular passive filling phase. A second negative wave (A) was seen after diastasis and before the onset of ventricular systolic myocardial motion, representing the ventricular active filling. Onset of systole was characterized by motion of the myocardium towards the apex, resulting in a third positive wave, which represented the ventricular myocardial motion during ejection. Myocardial atrial strain determines regional lengthening expressed as a positive value or shortening expressed as a negative value. SR presents a dimensionless description of change in length reflecting the deformation of tissue due to applied force and is negative in shortening the myocardium and positive in stretching the myocardium.

The electrocardiographic (ECG) and tissue velocity-based measurements were PA interval, AV time interval, and PAP interval according to Rein et al.[14]. Peak systolic SR (SSR), peak early diastolic SR (ESR) and peak late diastolic SR (ASR) were measured from SR curves in each of the 5 LA walls (septum, lateral, posterior, anterior, and inferior), and mean SSR, ESR, and ASR were calculated by averaging the results for each wall.

Velocity, SR, and strain curves were calculated in all patients over 3 to 5 cardiac cycles and then averaged to obtain mean velocity, SR, and strain curves over 1 mean cardiac cycle. Data were excluded if the angle between the scan line and LA wall was > 30°. Careful attention was directed to align the inter-atrial septum and ultrasonic beam within 20°.

End diastole was defined as the ECG R peak, and end systole was defined as the end of the ECG T wave.

Statistical Analysis

All numeric data are expressed as mean ±SD. Differences in continuous variables between 2 groups were assessed by the unpaired Student t-test, and comparison among multiple groups was performed by one-way ANOVA with post-hoc LSD t-test. Categorical variables were analyzed by the X^2 test, and Fisher's exact test was used when appropriate. The correlation between 2 variables was assessed by Pearson correlation coefficient. All data analysis was performed with use of a commercially available package (SPSS, release 13.0, SPSS Inc, Chicago, Illinois). A p value <0.05 was considered statistically significant.

Results

Clinical Characteristics and Echocardiographic Findings

General characteristics of the study population are summarized in Table 1. Hypertensive patients had significantly larger LA dimensions than controls. Hypertensive patients with brief atrial tachycardia or paroxysmal AF were significantly older than controls and hypertension-alone patients. No differences in heart rate, LV dimensions, LVEF, and mitral E wave among the 4 groups.

Age-matched data from 20 controls, 27 hypertension-alone patients, 20 hypertensive patients with brief atrial tachycardia, and 20 hypertensive patients with paroxysmal AF are presented in Table 2. Heart rate, age, LV dimensions, LVEF, mitral E wave and IVRT did not differ among the 4 groups. The influence of aging on SR values was eliminated.

Comparison of Tissue Velocity-measured Strain and Strain Rate Parameters

Compared with controls, patients with hypertension and paroxysmal AF showed significantly higher PA, PAP, Δ PA, Δ PAP (Tables 3 & 4), significantly increased TASRc and Δ ESR and decreased Δ ASR and Δ TASRc. SSR, Δ ASR, and Δ TASRc were significantly decreased and Δ ESR significantly increased in the study group as compared with hypertensive patients without arrhythmia. AV, S, Δ S, TS, Δ TS, Δ SSR, ASR, TASR, and Δ TASR did not differ among the 4 groups (Table 3).

Relation of SR Parameters with Clinical and Echocardiographic Variables

In controls, mean SSR was inversely correlated with mean ESR, mean ASR, age, and IVRT (P<0.05-0.001) but positively correlated with IVS (P<0.05). Mean ESR was positively correlated with mitral E/A ratio (P<0.01) but inversely correlated with mean SSR, age, IVRT and mitral A wave (P<0.05-0.001). Mean ASR was inversely correlated with mean SSR and mitral E wave (P<0.01) (Table 5).

In hypertensive-alone patients, mean SSR was inversely correlated with mean ESR and mean ASR (P<0.01). Mean ESR was inversely correlated with mitral E/A ratio, mean SSR and mitral E wave (P<0.05-0.001) but positively correlated with age, mitral A wave and IVRT (P<0.05-0.01). Mean ASR was inversely correlated with heart rate and mean SSR (P<0.01-0.001) but positively correlated with EDT (P<0.01).

In hypertensive patients with brief atrial tachycardia, mean SSR was inversely correlated with LVEF (P<0.05) and positively correlated with LVPW and LA dimension (P<0.05). Mean ESR was inversely correlated with DBP (P<0.05) but positively correlated with mitral A wave (P<0.01).

In hypertensive patients with paroxysmal atrial fibrillation, mean SSR was inversely correlated with mitral A wave (P<0.01). Mean ESR was inversely correlated with heart rate and LVEF (P<0.05). (Table 5)

The intraobserver and interobserver agreement was good for the tissue velocity-measured parameters PA interval (4% and 5.5%, respectively), AV time interval (4% and 5.5%, respectively), PAP interval (4% and 5.5%, respectively) and strain values (7% and 10%, respectively) but worse for SSR (11% and 15%, respectively), ESR (13% and 18%, respectively) and ASR (12% and 18%, respectively).

Discussion

To the best of our knowledge, this is the first description of the successful use, with high feasibility and modest reproducibility, of SR imaging of the LA to study atrial myocardial deformation in hypertensive patients with paroxysmal AF and other atrial arrhythmia. SR imaging showed mean SSR significantly correlated with mitral A wave and significantly lower in hypertensive patients with paroxysmal AF than that in hypertensive-alone patients.

Atrial Deformation Properties

During AF, myocardial atrial properties are significantly impaired: the reservoir and conduit functions are impaired and the booster pump is absent. In sinus rhythm, the atrial lengthening that occurs during ventricular systole remains unchanged, but the velocity of atrial lengthening decreases. Atrial deformation properties measured during early diastole do not differ among hypertensive patients. This is not surprising because in early diastole the atria act as conduits passively emptying during ventricular relaxation when the blood is transferred from systemic and pulmonary veins to the ventricles. Thus, atrial function during early diastole is strongly influenced by LV compliance. In our study, atrial late diastolic deformation properties did not differ among our 4 groups.

Assessment of LA Reservoir Function by SR Imaging

SR imaging has been proposed as a method for assessing intrinsic myocardial function independent of cardiac rotational motion and the tethering effect[11,12]. Actually, the SR and TVI curves of LA obtained in our study are similar to previously reported curves of the LA area derivative[8] and LA volume derivative[15]. Several indices during systole shown by volumetric examination have been considered as indicators of LA reservoir function. During ventricular systole, atria function as reservoirs to store blood when atrial ventricle valves are closed, and reservoir function is influenced by atrial relaxation, ventricle contraction through the descent of the base, and atrial chamber stiffness. We focused on the initial positive movement of a SR parameter (i.e., SSR) during systole. The significant

correlation between peak SSR and peak mitral A wave may confirm preliminary findings suggesting that atrial peak SR and strain are measures of atrial reservoir function. Thus, SSR could be used as an index of LA reservoir function.

Mean SSR decreases with advancing age. Several previous studies have demonstrated a relation between aging and histological changes in the LA (e.g., increased fibrosis) in normal hearts. Masugata et al. [16] reported that fibrosis of the LA wall increases in normal hearts and that LA wall elasticity, an important factor regulating LA stiffness and reservoir function, increased with age. With the increase of fibrosis, left atrial stiffness increases, whereas left atrial compliance decreases. This change in compliance is associated with decreased atrial reservoir function manifested by a smaller reservoir volume and alterations in left atrial and left ventricular filling. In the present study, the age-associated deterioration of LA compliance may be attributable in part to changes in mean SSR of LA. However, Spencer et al.[8]reported that parameters of LA reservoir function obtained by acoustic quantification did not vary with age. Acoustic quantification measures only changes in the area of the LA by single-plane assessment, not LA myocardial function directly. The differences in methodology may explain this discrepancy.

Furthermore, age-matched data, which eliminated the influence of aging on SR values, showed that mean SSR of LA in hypertensive patients with AF is significantly lower than that in hypertension-alone patients. AF is characterized by a remodeling process involving the development of fibrosis. The common fibrotic process may contribute to localized conduction abnormalities, locally decreased conduction velocity and abbreviated refractory period facilitating micro-reentrant circuit(s) as an underlying pathomechanism of AF. Greater LA chamber volume is certainly one of the independent risk factors in developing paroxysmal AF in patients with sinus rhythm, but the relation between LA size and AF is still controversial, whether LA enlargement in AF is the result rather than the cause of AF. Kawaguchi et al. [17] reported that AF duration itself tended to affect LA size. In brief, LA size should be augmented by longer AF duration. Some investigators have shown that AF contributes to the enlargement of the atria[18,19]. Recently, data from the Stoke Prevention in Atrial Fibrillation study on LA enlargement showed that chronic AF, long-lasting AF, and systemic hypertension were independently associated with a large LA diameter[20].

Disturbances in conduction are usually attributed to fibrosis and LA enlargement. Dilated LA could contain multiple-circuit reentry to promote the maintenance of AF. AF may be both a cause and a result of fibrosis. LA volume is increased because of LA enlargement and fibrosis, but the LA intrinsic ability to store energy of blood is lower. Mean SSR reflecting reservoir function of LA myocardia is decreased. The decreased mean SSR we found in hypertensive patients with paroxysmal AF is in agreement with that from a previous invasive study [4] and may reflect not only impaired LA wall stretching but also histological changes (e.g., fibrosis) in the LA myocardium in paroxysmal AF patients.

The SR is the rate by which the deformation occurs (i.e., deformation or strain per time unit). Strain is deformation of an object, relative to its original length. By this definition, strain is a dimensionless ratio, and is often expressed as a percentage. Strain equals the time integral of SR. Strain and SR reflect differing aspects of myocardial deformation, and both are relatively independent of overall heart motion. al. [21] studied LA in a group of patients hospitalized for acute myocardial infarction and in a control population. Strain could be used to quantify LA function relatively independently of left ventricular function, and may provide new insights into LA function. Yet, in our study, LA myocardial strain and time to peak strain did not differ among the 4 groups, which indicates

that hypertension and atrial arrhythmia do not affect the amount of atrial myocardial strain. Considering SR, myocardial atrial deformation properties are significantly impaired by paroxysmal AF. Thus, all atrial myocardia of our 4 groups had the same amount of strain but different strain rates. During LV systole, LA myocardial deformation could not catch up quickly with increasing intra-atrial pressure.

Assessment of LA Conduit Function by SR Imaging

Mean ESR was assessed in a phase in which LA works mainly as a conduit and could be used as an index of LA conduit function. Conduit function occurs primarily, but not exclusively, during ventricular diastole and represents the volume of blood that passes through the LA that cannot be attributed to reservoir or booster pump functions. Tseng et al. [22] found that LA conduit volume contributed more than 50% of the LV stroke volume. LA conduit function is an important determinant of LV filling. Increased atrial response to early-stage left ventricular filling impairment is characterized by augmented reservoir and pump functions, according to a Frank-Starling mechanism, which becomes hardly effective at end-stage ventricular dysfunction when the limits of the atrial preload reserve are reached. At this stage, the atrial reservoir and the booster pump functions decline, and conduit in the atrium takes precedence. However, the atrial conduit function declines with age and advancing LV diastolic dysfunction, which was also confirmed by our study. In our study, mean ESR was inversely correlated with age and mitral A wave but positively correlated with mitral E/A ratio.

The conduit function was found to be enhanced in AF patients with a depressed atrial mechanical function, with no difference in the contribution of the active emptying volume to left ventricular stroke volume, as we also found.

Assessment of LA Booster Function by SR Imaging

No criterion exists to reflect LA contractility. Late diastolic mitral flow velocity has been used as a parameter of LA contractility; however, the assessment of late diastolic mitral flow velocity reflects only the atrio-ventricular pressure gradient between the LV and LA, not LA intrinsic function per se. LA acoustic quantification also allows for noninvasive assessment of LA booster pump function [7]. However, LA function is assessed by only single-plane not multi-plane techniques. Recently, TDI has been used for evaluating LA booster pump function[9,10]. Although this method can measure LA myocardial velocity as a direct indicator of LA booster pump function, the effect of cardiac rotational motion and tethering on LA myocardial velocity remain major problems. These limitations may account for our discrepancy between the augmented LA booster pump values with age and lack of augmented mean ASR of LA with age. ASR is negative during LV late diastole, which reflects a shortening of the LA wall; thus it could be used as an index of LA booster pump function.

In our study, we found no significant difference in mean ASR among the 4 groups, which indicates that paroxysmal AF has no effect on LA myocardial contractility. Furthermore, mean ASR was negatively correlated with mean SSR in both controls and hypertensive patients but not in patients having atrial arrhythmia. Thus, changes in LA reservoir, conduit, and booster pump functions could compensate for one another, with atrial arrhythmia causing decompensation.