Regional and Global Right Ventricular Function in Healthy Individuals Aged 20–90 Years: A Pulsed Doppler Tissue Imaging Study

Umeå General Population Heart Study

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The aim of the present study was to describe regional and global right ventricular (RV) function in a wide age range of healthy subjects of both sexes. We studied 255 (125 females) healthy individuals randomly selected from the Umeå General Population Register, age 58 ± 19 (range 22–89) years. RV function was studied using myocardial tissue Doppler imaging of the RV free wall. Isovolumic contraction (IVCv), systolic (Sv), early (Ev), and late (Av) diastolic velocities were measured. Furthermore, isovolumic periods and ejection time intervals were also measured. Conventional Doppler was used to study RV global filling properties. While systolic myocardial velocities were conserved over age, there was a decrease in myocardial E/A ratio with increasing age (r = -0.67, P < 0.001, for base) taken from the RV free wall. A similar age relation was found in RV global filling velocities with a reduced tricuspid E/A ratio (r = -0.57, P < 0.001). Furthermore, a significant correlation was found between global and regional E/A ratios at the basal (r = 0.58, $P \le 0.001$) and mid-segmental levels (r =0.46, $P \le 0.001$). Systolic myocardial velocities behaved independent of age whereas regional as well as global E/A ratio were age-related. No relationship was found between regional isovolumic time intervals and age. Knowledge of these age-dependent relationships is fundamental when evaluating RV function in patients. (ECHOCARDIOGRAPHY, Volume 22, April 2005)

aging, right ventricular function, pulsed Doppler tissue imaging

It is estimated that by the year 2025 nearly one-third of the population in western countries will be 60 years of age and above.¹ As heart failure is more common with increasing age, it is important to distinguish physiological changes due to normal aging from those caused by cardiac disease.^{2,3}

Knowledge of the changes in cardiac function due to aging is incomplete and needs to be further investigated, particularly in ages over 70 years.⁴ Although left ventricular dysfunction (LV) is the most common reason for symptomatic heart failure, right ventricular (RV) systolic dysfunction has been shown to correlate with exercise tolerance in patients with heart failure.⁵ RV dysfunction is also considered to be of major prognostic importance in heart failure.⁶ Little is known about the contribution of RV dysfunction to the symptoms of heart failure. This highlights the need for accurate evaluation of RV function in clinical practice. Lack of studies of RV function in patients with clinical signs of heart failure is probably mainly related to the complexity of RV structure and function.⁷

Doppler tissue imaging (DTI) is a relatively new development in ultrasound technology, which allows characterization of myocardial motion velocities throughout the cardiac cycle.

Since McDicken and Sutherland⁸ described myocardial velocities by using DTI, this technique has been widely used in both clinical and experimental settings to assess myocardial

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function in various pathological conditions including heart failure, ischemic heart disease, and hypertrophic cardiomyopathy.^{9,10} However, as it is of importance to identify accurate echocardiographic measurements of RV function in clinical situations, DTI might be useful in providing such knowledge.

Therefore, the aim of the present study was to investigate the effect of normal aging on RV myocardial segmental and global function using conventionally available echocardiographic techniques, including pulsed DTI.

Materials and Methods

Study Population

Every resident in Sweden has a national registration number that includes date of birth. The numbers are registered and controlled by the Swedish Tax Authority in a population register, which includes vital statistics, and which by law must be kept up to date. The registration number consists of the date of birth plus four digits where the third digit indicating female (even) or a male (odd). On this basis, 1,000 (500 were females) subjects born at 5-year intervals (e.g., 1905, 1910, 1915 up to 1975, a total of 15 age groups) were drawn from the register. Information about the nature of the project and invitation to participate in the project were sent to those subjects. Inclusion criteria were absence of any cardiovascular or other systemic disease and none was on any medication, which may influence cardiac function. This was further checked by a telephone interview. Furthermore, a specially designed questionnaire was sent to all the subjects before enrolment. Subjects with diabetes, hypertension, hyperlipidemia, history of rheumatic fever, transit ischemic attack, stroke, and intermittent claudication were excluded. Selection, telephone interview, inclusion, and exclusion of the study population were done by an experienced investigator (EK). Three hundred subjects (10 from each group with equal sex distribution) were included. Despite this precaution, 45 subjects had to be excluded after the examinations; 23 had blood pressure >160/90 mmHg, 3 had moderate aortic stenosis, 13 had abnormal ECG (3 LBBB, 4 RBBB, 6 LAH), and 6 were on anti-hypertensive therapy.

The upper limit for blood pressure in our study population was 160/90 chosen because of the very wide age span.^{11,12} The remaining 255 subjects (mean age \pm SD, 58 \pm 19 years; range 22–89; 125 females) constituted the study pop-

ulation. All subjects were coded and the investigations and analysis were blindly made. All subjects gave informed consent for this study, which was approved by the ethics committee of Umeå University.

Echocardiography

The echocardiographic examination was performed with the subject in the left lateral decubitus position and recordings were taken during quiet expiration. A commercially available ultrasound system (Acuson Sequoia, Mountain View, CA) equipped with a multiple frequency phased array transducer and pulsed DTI technique was used. Parasternal and apical projections were obtained according to the recommendations of the American Society of Echocardiography.¹³ All recordings were done with a simultaneous superimposed ECG. A phonocardiogram was acquired to display the pulmonary component of the second heart sound (S_2) to define the end-systole.¹⁴ Recordings were made at a sweep speed of 50 and 100 mm/sec and stored on magneto optical discs. Values are presented as means of three consecutive beats.

Myocardial Pulsed Doppler Tissue Imaging

Myocardial systolic and diastolic velocities and the time intervals were recorded by using pulsed DTI technique. The acoustic power and filter frequencies were adjusted for detecting myocardial velocities. Measurements were made at three levels of the RV free wall: basal, mid, and the apical segmental levels (Fig. 1).

Conventional Doppler Echocardiography

Pulsed wave Doppler velocities were registered from the apical four-chamber view with the sample volume positioned at the tips of the tricuspid leaflets. The presence of valve regurgitation was determined by color and continuous wave Doppler.

Measurements

From the M-mode echocardiographic recordings, the following measurements were made: LV internal diameter, interventricular septal thickness, and posterior wall thickness were measured at end-diastole (onset of the Q wave of the ECG). LV internal diameter was also measured at end-systole (the shortest distance between the septum and the posterior wall). LV fractional shortening was calculated from the internal dimensions.¹⁵ Ejection fraction

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Figure 1. Segmental pulsed Doppler tissue imaging of the right ventricle. 1 = base; 2 = mid-segment; 3 = apical segment.

was derived from Simpson's modified biplane method. 13

From DTI of the RV free wall the following measurements were made at the basal, mid-cavity, and apical level.^{16,17} The peak positive isovolumic contraction (IVCv), peak systolic (Sv), peak early diastolic (Ev), and peak late diastolic (atrial) (Av) velocities were all measured. Furthermore, three time intervals were measured, ejection time (EJt), isovolumic contraction, and relaxation times (Fig. 2). Ejection time was measured from the onset of ejection to its end (time-interval between arrows 2) and 3). Isovolumic contraction time (IVCt) was measured from the end of the Av to the onset of the Sv after the first heart sound (time interval between arrows 1 and 2). Isovolumic relaxation time (IVRt) was measured from the pulmonary component of S_2 to the onset of Ev (time interval between arrows 3 and 4).

From the pulsed wave Doppler recordings of the tricuspid flow velocities, peak early (E) and late atrial (A) diastolic velocities were measured and E/A ratio was calculated.¹⁸ E-wave deceleration time (E-DT) was measured from the peak to the end of the E-wave. Isovolumic relaxation time was measured as the time interval between the pulmonary component of S_2 to the onset of E-wave (IVRt). Trans-tricuspid peak retrograde velocities were registered using the continuous wave Doppler technique and the modified Bernoulli equation was used to estimate the RV–RA peak pressure gradient as an indirect estimate of pulmonary artery pressure.¹⁸

Statistical Analysis

A commercially available statistical program (SPSS 10.1 and 11.1, SPSS Inc. Chicago, IL) was used. All data are presented as mean \pm SD. Pearson's correlation and linear regression analyses were performed to display relations between age and RV function. Student's paired *t*-test was used to compare values within groups. Unpaired Student's *t*-test was used to compare groups and Mann–Whitney nonparametric test was used when appropriate. Multiple regression analysis was used to evaluate the association of basic characteristics

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Figure 2. Analyzed parameters from pulsed Doppler tissue imaging.

to regional and global diastolic function. A P-value <0.05 was considered significant. Reproducibility from DTI recording of basal and mid-segmental level of the RV and transtricuspid recordings was analyzed by repeating measurements from 10 consecutive tracings. Peak velocities and time-intervals measurement were analyzed. Variability is expressed as the coefficient of variation (standard deviation of the difference divided by mean value of the two measurements).

Results

General Characteristics

The general characteristics and hemodynamic data of the subjects are shown in Table I.

Left Ventricular Function

Left ventricular end-diastolic and endsystolic dimensions were 49.5 ± 5.3 and 29.3 ± 4.5 mm, respectively. Fractional shortening was $40.6 \pm 7.0\%$ and ejection fraction was $63.8 \pm$ 6.8%. Septal and posterior wall thicknesses were 9.7 \pm 1.6 and 8.6 \pm 1.4 mm, respectively.

Right Ventricular Regional Myocardial Function and Age

Adequate recordings of the RV free wall function were obtained in 98% of the subjects from

TABLE I					
General Characteristic Data					
$Mean \pm SD$ Range					
Age (yrs)	53 ± 19	22-89			
Heart rate (beats/min)	66 ± 10	43 - 97			
SBP (mmHg)	128 ± 15	95 - 160			
DBP (mmHg)	76 ± 7	55-90			
Height (cm)	171 ± 9	146 - 196			
Weight (kg) 73 ± 13 44–110					
$BSA(m^2)$	1.85 ± 0.90	1.40 - 2.33			

SBP = systolic blood pressure; DBP = diastolic blood pressure; BSA = body surface area.

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TABLE II				
Regional Myocardial Velocities and Time Intervals				
	$\begin{array}{c} Basal\\ Mean \pm SD \end{array}$	$\begin{array}{c} {\rm Mid} \\ {\rm Mean} \pm {\rm SD} \end{array}$	$\begin{array}{c} \text{Apical} \\ \text{Mean} \pm \text{SD} \end{array}$	
IVCv (cm/sec) Sv (cm/sec) Ev (cm/sec) Av (cm/sec) E/A IVRt (ms) IVCt (ms)	$\begin{array}{c} 15.1 \pm 6.1 \\ 15.2 \pm 2.8 \\ 14.5 \pm 3.5 \\ 16.2 \pm 3.1 \\ 0.97 \pm 0.37 \\ 53 \pm 28 \\ 91 \pm 26 \\ 0.97 \pm 0.27 \end{array}$	$\begin{array}{c} 15.5\pm 6.0\\ 14.5\pm 2.6\\ 14.1\pm 3.7\\ 16.6\pm 5.5\\ 0.94\pm 0.39\\ 58\pm 38^{\ddagger}\\ 100\pm 30^{\ast}\end{array}$	$\begin{array}{c} 11.0\pm 4.4^{*}\\ 9.3\pm 2.6^{*}\\ 10.8\pm 2.8^{*}\\ 10.9\pm 2.9^{*}\\ 1.27\pm 0.93^{\dagger}\\ 99\pm 47^{*}\\ 114\pm 36^{*} \end{array}$	

IVCv = isovolumic contraction velocity; Sv = systolic velocity; Ev = early diastolic velocity; Av = atrial velocity; E/A = peak early diastolic velocity/late atrial diastolic velocity ratio; IVRt = isovolumic relaxation time; IVCt = isovolumic contraction time; EJt = ejection time.

 $^*P < 0.001;\,^\dagger P < 0.01;\,^\dagger P < 0.05,$ all compared to the base.

the basal level and in 79% at the mid-cavity and in 44% at the apical level.

Isovolumic contraction velocities were 27% higher at the base compared to the apical level, and systolic velocities were 38% higher at the basal level than at the apical level. The same pattern was found in diastole, but the fall in diastolic velocities between the basal level and the apical level was 25% for early diastolic and 38% for late diastolic velocities. The RV systolic and diastolic velocities were not different between the basal and mid-cavity levels but the apical E/A ratio was significantly higher than the basal one (P < 0.01; Table II).

The isovolumic contraction and relaxation time intervals were significantly longer at the mid-cavity level compared to the basal level (P < 0.05 and < 0.001, respectively) and the apical level (P < 0.001 for both). Inversely, EJt was decreased from the basal to the apical level (P <0.001; Table II). RV peak systolic velocity, isovolumic contraction time, and ejection time were not related to age at any segment. However, age correlated with diastolic myocardial velocities, inversely with Ev and directly with Av at all three levels (r = -0.39, P < 0.001 and r = 0.49, P < 0.001 for base). E/A ratio was negatively correlated with age at all levels, again with the strongest relationship at the basal and midcavity levels (r = -0.67, P < 0.001, r = -0.62, P< 0.001). Regional IVRt did not correlate with age in any of the segments of the RV. The IVCv at the basal and mid segments were weakly correlated with age (r = 0.34, r = 0.34, respectively)P < 0.01; Table III). Regional myocardial velocities and time intervals in different age decades are shown in Table IV.

TABLE III						
R	legiona	l Myocaro	dial Fu	nction an	d Age	
	Bas	sal	M	id	Aj	pical
	r	P-Value	r	P-Value	r	P-Value
Ev (cm/sec)	-0.39	< 0.001	-0.29	< 0.001	-0.37	< 0.001
Av (cm/sec)	0.49	< 0.001	0.52	< 0.001	0.41	< 0.001
Ev/Av ratio	-0.67	< 0.001	-0.62	< 0.001	-0.28	< 0.01
IVCv (cm/sec)	0.34	<0.01	0.30	< 0.01	0.04	0.761

Ev = early diastolic velocity; Av = atrial velocity; IVCv = isovolumic contraction velocity.

Right Ventricular Global Function and Age

Tricuspid peak early diastolic velocities fell (r = -0.39, P < 0.001), whereas peak atrial velocities (r = 0.35, P < 0.001), early diastolic deceleration time (r = 0.35, P < 0.001), and isovolumic relaxation time (r = 0.38, P < 0.001) all increased with age. The E/A ratio was reduced (r = -0.57, P < 0.001), and RV–RA peak pressure gradient slightly increased with age (r = 0.29, P < 0.001; Table V).

Multiple Regression Analysis

Stepwise multiple regression analysis was performed to assess the influence of age, systolic and diastolic blood pressure, body surface area, and heart rate on RV diastolic function. Age was the strongest independent factor for the change in global and regional RV diastolic function.

Relationship between Regional and Global Right Ventricular Diastolic Function

Early diastolic RV myocardial velocities at the basal and mid-ventricular level correlated weakly with tricuspid E-wave velocity. Late atrial myocardial velocity at the base (r = 0.32, P < 0.001), the mid (r = 0.25, P < 0.001), and the apical level (r = 0.20, P < 0.05), all correlated with its corresponding tricuspid flow A-velocity. Myocardial E/A ratio and IVRt at the basal (r = 0.58, P < 0.001 and r = 0.25, P < 0.05, respectively) and mid-cavity level (r = 0.46 and r = 0.23, P < 0.001 for both), correlated with the corresponding tricuspid flow measurements (Table VI).

		TABLE IV			
Regional Myocardial Velocities and Time Intervals in Different Age Groups					
	Young (20–39, n = 80) Mean \pm SD	$\begin{array}{l} \mbox{Middle Aged} \\ (4059,n=80) \\ \mbox{Mean}\pm \mbox{SD} \end{array}$	$\begin{array}{c} Elderly\\ (60{-}79,n=75)\\ Mean\pm SD \end{array}$	$\begin{array}{c} \text{Old} \\ (>80,n=20) \\ \text{Mean}\pm\text{SD} \end{array}$	
Basal					
Basal IVCv (cm/sec) Sv (cm/sec) Ev (cm/sec) Av (cm/sec) E/A IVRt (ms) IVCt (ms) EJt (ms) Mid IVCv (cm/sec) Sv (cm/sec) Ev (cm/sec) Av (cm/sec) E/A	$\begin{array}{c} 12.3 \pm 4.0 \\ 15.5 \pm 2.6 \\ 16.1 \pm 3.1 \\ 13.4 \pm 3.9 \\ 1.3 \pm 0.4 \\ 53 \pm 26 \\ 90 \pm 22 \\ 260 \pm 31 \\ 12.7 \pm 4.2 \\ 13.6 \pm 2.6 \\ 15.8 \pm 3.2 \\ 13.2 \pm 3.4 \\ 1.3 \pm 0.4 \end{array}$	$\begin{array}{c} 15.1\pm 4.8^{\ddagger}\\ 14.9\pm 2.7\\ 14.6\pm 3.2^{\dagger}\\ 15.8\pm 3.9^{\dagger}\\ 1.0\pm 0.2^{*}\\ 51\pm 28\\ 88\pm 21\\ 262\pm 34\\ \end{array}$	$\begin{array}{c} 17.7\pm7.9^{\dagger}\\ 15.4\pm3.2\\ 13.0\pm3.5^{*}\\ 18.9\pm5.6^{*}\\ 0.7\pm0.2^{*}\\ 55\pm29^{\dagger}\\ 91\pm28\\ 269\pm38\\ 17.4\pm7.0^{\dagger}\\ 13.4\pm3.3\\ 13.0\pm3.4^{*}\\ 19.2\pm6.2^{*}\\ 0.7\pm0.2^{*}\\ \end{array}$	$\begin{array}{c} 15.2 \pm 4.6 \\ 14.9 \pm 2.0 \\ 12.1 \pm 2.9^* \\ 20.0 \pm 4.7^* \\ 0.6 \pm 0.1^* \\ 54 \pm 25 \\ 112 \pm 39^{\ddagger} \\ 267 \pm 38 \\ 14.7 \pm 2.4 \\ 13.2 \pm 3.2 \\ 11.9 \pm 2.2^* \\ 21.4 \pm 3.5^* \\ 0.6 \pm 0.1^* \end{array}$	
IVRt (ms) IVCt (ms) EJt (ms) Apical IVCv (cm/sec) Sv (cm/sec) Ev (cm/sec) E/A IVRt (ms) IVCt (ms) EJt (ms)	52 ± 37 98 ± 25 263 ± 29 10.6 ± 5.2 9.7 ± 2.6 12.0 ± 2.9 8.8 ± 2.7 1.4 ± 0.4 94 ± 44 120 ± 33 217 ± 49	53 ± 34 101 ± 29 254 ± 44 12.4 ± 3.4 8.7 ± 1.8 10.7 ± 2.3 10.0 ± 3.7 1.6 ± 1.8 97 ± 51 121 ± 33 231 ± 31	$69 \pm 4298 \pm 29258 \pm 4211.9 \pm 3.99.0 \pm 2.59.8 \pm 2.5^{\dagger}11.9 \pm 3.7^{*}0.90 \pm 0.4^{*}107 \pm 48102 \pm 36215 \pm 56$	$\begin{array}{c} 63 \pm 511 \\ 62 \pm 33 \\ 125 \pm 54 \\ 269 \pm 31 \\ \hline \\ 11.0 \pm 09 \\ 9.8 \pm 4.0 \\ 9.8 \pm 2.8 \\ 11.4 \pm 2.3^{\ddagger} \\ 0.9 \pm 0.6^{\ddagger} \\ 97 \pm 50 \\ 106 \pm 52 \\ 245 \pm 69 \end{array}$	

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IVCv = isovolumic contraction velocity; Sv = systolic velocity; Ev = early diastolic velocity; Av = atrial velocity; E/A = peak early diastolic velocity/late atrial diastolic velocity ratio; IVRt = isovolumic relaxation time; IVCt = isovolumic contraction time; EJt = ejection time. *P <0.001; $^{\dagger}P <$ 0.01; $^{\dagger}P <$ 0.05, all compared against the young group.

TABLE V

Global Diastolic Right Ventricular Function and Age

	$Mean \pm SD$	Range	r	P-Value
E (cm/sec)	43 ± 11	21–93	-0.39	< 0.001
A (cm/sec)	31 ± 10	8 - 71	0.35	< 0.001
E/A ratio	1.53 ± 0.80	0.62 - 4.29	-0.57	< 0.001
E-DT (ms)	187 ± 58	72 - 380	0.38	< 0.001
$RV-RA \Delta P$ (mmHg)	22 ± 6	7-44	0.29	< 0.001
IVRt (ms)	31 ± 16	5-90	0.29	< 0.001

E = early diastolic velocity; A = atrial velocity; E-DT = early diastolic deceleration time; IVRt = isovolumic relaxation time; RV = right ventricle; RA = right atrial; ΔP = pressure gradient.

Regional Myocardial Systolic and Diastolic Relations

The IVCv was significantly correlated with its corresponding Av at all three levels of RV free wall: basal (r = 0.74, P < 0.001), mid (r = 0.58, P < 0.001), and apical level (r = 0.47, P < 0.001; Fig. 3).

Reproducibility of the Echocardiographic Measurements

The interobserver variability, expressed as coefficient of variation, was within the range 7–17% for tricuspid flow recordings and 7–21% for DTI. The intra-observer variability was within the 6–10% limit for tricuspid flow and 7–19% limit for DTI (Table VII).

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	TAI	BLE VI			
Regional and Global Diastolic Right Ventricular Function					
	Е	А	E/A	IVRt	
Basal					
$\mathbf{E}\mathbf{v}$	0.29^{*}				
Av		0.32^{*}			
Ev/Av ratio			0.58^{*}		
IVRt				0.25^{*}	
Mid					
$\mathbf{E}\mathbf{v}$	0.17^{\ddagger}				
Av		0.25^{*}			
Ev/Av ratio			0.46^{*}		
IVRt					
Apical				0.23^{*}	
Ēv	_			-	
Av		0.20^{\ddagger}			
Ev/Av ratio			_		
IVRt				_	

Abbreviations as in Tables II and V.

 $^{*}P < 0.001; ^{\dagger}P < 0.01; ^{\ddagger}P < 0.05.$

Discussion

Selection of the Study Population

Studies of healthy individuals frequently recruit subjects on ad hoc basis for reasons of organizational simplicity. The disadvantage of such recruitment policy is that the age distribution will not be even across the age spectrum studied, but instead typically sparse at both extremes. This has two interrelated adverse consequences. First, the degree of precision with which the normal ranges can be quoted at the extremes of age is poor. Second, age-dependencies of pathological measure-



Figure 3. Relation between isovolumic contraction velocity and atrial contraction velocity from pulsed Doppler tissue imaging at the basal level.

	TABLE VII			
Inter- and Intra-observer Variability				
Interobserver Intra-obs Variability (%) Variabili				
Tricuspid flow				
E (cm/sec)	8.2	7.3		
A (cm/sec)	7.3	6.3		
IVRt (ms)	11.7	9.7		
DTI basal segment				
Ev (cm/sec)	8.9	11.0		
Av (cm/sec)	8.1	8.1		
Sv (cm/sec)	7.2	7.2		
IVCv (cm/sec)	6.9	6.9		
IVCt (ms)	7.4	7.4		
IVRt (ms)	12.3	12.2		
EJt (ms)	7.6	7.6		
DTI mid-segment				
Ev (cm/sec)	7.7	13.9		
Av (cm/sec)	9.3	4.9		
Sv (cm/sec)	3.8	19.4		
IVCv (cm/sec)	6.9	10.8		
IVCt (ms)	14.0	14.2		
IVRt (ms)	20.6	14.9		
EJt (ms)	3.5	3.4		

Abbreviations as in Tables II and V.

ments can easily be missed because relatively few data points are available at the extremes assuming that age dependence is linear. In the present study, a great care was taken to ensure an objective selection and inclusion of the study population. All subjects were randomly selected, their ages ranged widely, and were evenly distributed. They were blindly analyzed by one investigator (PL) after coding and mixing of the recordings. Forty-five subjects were excluded after the ECG, echocardiographic and clinical examination. Although, none of them complained of any cardiac problem and they were not in any medication and even never seeked medical advice. Therefore, the risk of bias was minimized and the results should be possible to generalize.

The Importance of Assessing Right Ventricular Function

Right ventricular function has recently attracted increasing interest, since it has been shown to determine exercise tolerance and clinical outcome in patients with heart failure.^{6,19,20} However, assessment of RV function is not always easy due to its complex anatomy and function.²¹

Doppler tissue imaging has been used in different cardiac diseases to assess both RV and LV function, it is considered to be less preload dependent compared to conventional Doppler technique. The initial evaluation of DTI indicated that it might represent a significant step forward in noninvasive assessment of regional myocardial function. However, regional myocardial tissue velocities in one myocardial segment are determined by function of other segments as well, which is due to tethering between segments and cardiac translational motion.²² Recently, reports about using strain or strain rate to measure myocardial deformation, it was found that this technique is less influenced by cardiac translation and motion due to tethering of other regions. Therefore, it might be more preferable. At the present time, although strain can be measured using echocardiography, however, the method is not widely used in the routine daily clinical practice.

Our findings show that pulsed DTI is useful in this respect and that normal aging influences RV diastolic. Thus, RV systolic function can be considered relatively independent of age if E/A ratio is ignored. The relevance of global E/A ratio has been questioned lately, due to its load and heart rate dependence as well as its variation with respiration.^{23,24} Regional IVRt can be used in the evaluation of RV function irrespective of age, whereas the E/A ratio changes with age. Whether these two parameters reflect different functional components and must be used together in functional analysis of the RV remains to be studied in disease state.

Right Ventricular Anatomy

The thin-walled RV is separated into two different anatomical and functional components, inflow tract and outflow tract. These two units have different contributions to local work, stroke volume, and extent of fiber-shortening and mechanical activation.²⁵ The myocardial fibers of the inflow tract run predominantly longitudinally in the subendocardium, apex to base. Spiral or circumferential fibers are located in the subepicardium and run perpendicularly to the longitudinal fibers in the inflow tract. Fibers in the outflow tract are mainly longitudinal and run parallel to the circumferential ones of the inflow tract.²⁶

Right Ventricular Systolic Function

This study could not confirm a significant effect of age on RV regional longitudinal peak sys-

tolic myocardial velocity or the ejection time.²⁷ Our results are in accordance with others.^{28,29} The differences in the results from studies may at least in part be explained by the technique used, pulsed or color DTI. The studied population may be another reason. The absence of agerelated changes in RV systolic function is a major advantage in the evaluation, as in the case with the LV.³⁰ Systolic function is maintained despite the modest but progressive increase in pulmonary artery pressure with age.³¹ These findings are consistent with previous studies that used invasive techniques and MRI.^{32,33} The only relationship between age and systolic function measurements was found to be increased myocardial velocities during isovolumic contraction period at the basal segment. This motion has been suggested to reflect the RV state of contractility.³⁴ The increase in IVCv with age might therefore represent a change in ventricular inotropic properties, all in purpose to secure adequate cardiac output. Furthermore, we found a relatively well-preserved motion during IVC at the mid-cavity and apical level. This could possibly be related to a predominant rotational motion with less longitudinal motion during ejection at the apical part of RV. MRI studies have shown that the motion during IVC is mainly due to transverse motion and rotation.^{35,36} This implies that circumferential cardiac motion increases with age. Another interesting finding is the close relationship between IVCv and the respective Av at all three segments. This may represent a significant shape change in early systole following the age-related accentuated ventricular lengthening during atrial systole, likely as a result from dissipated energy stored in the atrium and released in early systole, as a recoil effect. So far it can be concluded that RV systolic function measurements are well preserved across age groups despite the known modest increase in pulmonary artery pressure. Therefore, in patients with increased vascular resistance, RV systolic function may sustain modest increases in pressures and remain well preserved for sometime.³⁷ These findings are similar to those previously reported by us in healthy subjects (Umeå General Population Heart Study), where we found that systolic myocardial velocities were preserved over age.³⁰ We also found regional differences in the isovolumic periods. These findings might be of importance when optimizing pacemaker treatment is required.

Right Ventricular Diastolic Function

The significant relationship between age and E/A ratio for both the RV free wall and global ventricular filling was not surprising since the same pattern of change in diastolic function with age has previously been shown in the LV.³⁰ This suggests an age-related limitation in early diastolic myocardial relaxation that requires an increase in atrial contraction force in order to maintain adequate ventricular filling.

We could not find a significant effect of age on regional IVRt, previously demonstrated in the LV.³⁸ The lack of relation between RV IVRt and age is an important finding as increased IVRt is proposed to be a sensitive marker of myocardial dysfunction, e.g., in pulmonary hypertension.³⁹ Thus, this observation indicates relatively well-preserved RV myocardial function over age. Furthermore, myocardial DTI is proposed to be less load dependent,²³ which may explain the weak relation between regional and global IVRt.

Although, pulmonary artery systolic pressure is known to increase gradually with age,^{31,32} it cannot explain the gradual fall in E/A ratio because there is no direct relationship between the RV and pulmonary circulation in diastole. The change in E/A ratio may rather be related to intrinsic myocardial changes during diastole (remodeling) as is the case in normal aging of the LV. We have recently reported the marked dependency of right ventricular diastolic velocities to increase to heart rate in patients with coronary artery disease and increased RV afterload. These findings³⁰ highlight the sensitivity that measures not only age but also disease conditions.

Limitations

In the present study, apical recordings were not useful for segmental analysis in more than 44% of the studied population. This is in agreement with previous studies which suggested that the apical part is a relatively fixed and immobile part of the heart where longitudinal velocities are low and the reproducibility of measurements is poor.^{40,41} As our experience is similar to these studies, we therefore decided not to evaluate the reproducibility of apical velocities and timings and thus propose that apical recordings are not highly accurate to analyze using pulsed DTI.

Ideally, normal subjects should have been prospectively followed and evaluated over time. A prospective study of 20 years old subjects for 70 years is difficult to perform. Some of the studied volunteers might have subclinical diseases, which could not be detected by echocardiography. We relied, however, entirely on clinical and noninvasive assessment of our subjects. Even if the RV outflow tract contribution to the stroke volume is considered less important compared to the inflow tract, this has been disputed. Due to technical reasons regional function of RV outflow tract was not possible to assess using pulsed DTI in the present study.

Clinical Implications and Conclusion

Age does not affect systolic RV function. The changes in RV function due to age are related to the diastolic filling velocities, which mirror those of the LV. Basal and mid-segmental RV systolic and diastolic function are the main determinants for the longitudinal behavior of the inflow tract, again in parallel with the respective segments of the LV. Knowledge of these changes in ventricular function with increasing age is mandatory when assessing patients.

References

- Kalache A, Gatti A: Active ageing: A policy framework. Adv Gerontol 2003;11:7–18.
- Kannel WB, McGee D, Gordon T: A general cardiovascular risk profile: The Framingham study. Am J Cardiol 1976;38:46–51.
- Dargie HJ, McMurray JJ, McDonagh TA: Heart failure—Implications of the true size of the problem. *J Intern Med* 1996;239:309–315.
- Vasan RS, Levy D, Larson MG, et al: Interpretation of echocardiographic measurements: A call for standardization. Am Heart J 2000;139:412–422.
- Di Salvo TG, Mathier M, Semigran MJ, et al: Preserved right ventricular ejection fraction predicts exercise capacity and survival in advanced heart failure. *J Am Coll Cardiol* 1995;25:1143–1153.
- Bleasdale RA, Frenneaux MP: Prognostic importance of right ventricular dysfunction. *Heart* 2002;88:323– 324.
- Dell'Italia LJ: The right ventricle: Anatomy, physiology, and clinical importance. *Curr Probl Cardiol* 1991;16:653-720.
- McDicken WN, Sutherland GR, Moran CM, et al: Colour Doppler velocity imaging of the myocardium. Ultrasound Med Biol 1992;18:651-654.
- Alam M, Wardell J, Andersson E, et al: Right ventricular function in patients with first inferior myocardial infarction: Assessment by tricuspid annular motion and tricuspid annular velocity. Am Heart J 2000;139:710-715.

Acknowledgments: This study was supported by the Swedish Heart and Lung Foundation, Umeå University, the Medical Faculty, the Swedish Medical Association, Torsten Ragnar Söderberg's Foundation and Mid-Sweden Research and Development Centre. We are grateful to Dr. Manne Andersson and to Kerstin Rosenqvist for their assistance during the recruiting phase of the study.

- 10. Severino S, Caso P, Cicala S, et al: Involvement of right ventricle in left ventricular hypertrophic cardiomyopathy: Analysis by pulsed Doppler tissue imaging. *Eur J Echocardiogr* 2000;1:281–288.
- Lakatta EG, Levy D: Arterial and cardiac aging: Major shareholders in cardiovascular disease enterprises: Part II: The aging heart in health: Links to heart disease. *Circulation* 2003;107:346–354.
- Lakatta EG, Levy D: Arterial and cardiac aging: Major shareholders in cardiovascular disease enterprises: Part I: Aging arteries: A "set up" for vascular disease. *Circulation* 2003;107(1):139–146.
- Schiller NB, Shah PM, Crawford M, et al: Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American society of echocardiography committee on standards, subcommittee on quantitation of two-dimensional echocardiograms. J Am Soc Echocardiogr 1989;2:358–367.
- Garcia-Fernandez MA, Azevedo J, Moreno M, et al: Regional diastolic function in ischaemic heart disease using pulsed wave Doppler tissue imaging. *Eur Heart* J 1999;20(7):496–505.
- Sahn DJ, DeMaria A, Kisslo J, et al: Recommendations regarding quantitation in M-mode echocardiography: Results of a survey of echocardiographic measurements. *Circulation* 1978;58:1072–1083.
- Garcia MJ, Rodriguez L, Ares M, et al: Myocardial wall velocity assessment by pulsed Doppler tissue imaging: Characteristic findings in normal subjects. *Am Heart* J 1996;132:648–656.
- Hatle L, Sutherland GR: Regional myocardial function—A new approach. *Eur Heart J* 2000;21:1337– 1357.
- Quinones MA, Otto CM, Stoddard M, et al: Recommendations for quantification of Doppler echocardiography: A report from the Doppler quantification task force of the nomenclature and standards committee of the American society of echocardiography. J Am Soc Echocardiogr 2002;15:167–184.
- Webb-Peploe KM, Henein MY, Coats AJ, et al: Echo derived variables predicting exercise tolerance in patients with dilated and poorly functioning left ventricle. *Heart* 1998;80:565–569.
- 20. Florea VG, Henein MY, Anker SD, et al: Prognostic value of changes over time in exercise capacity and echocardiographic measurements in patients with chronic heart failure. *Eur Heart J* 2000;21:146–153.
- Lindqvist P, Henein M, Kazzam E: Right ventricular outflow-tract fractional shortening: An applicable measure of right ventricular systolic function. *Eur J Echocardiogr* 2003;4:29-35.
- Smiseth OA, Ihlen H: Strain rate imaging: Why do we need it? J Am Coll Cardiol 2003;42:1584–1586.
- Naqvi TZ: Diastolic function assessment incorporating new techniques in Doppler echocardiography. *Rev Cardiovasc Med* 2003;4:81–99.
- Klein AL, Leung DY, Murray RD, et al: Effects of age and physiologic variables on right ventricular filling dynamics in normal subjects. *Am J Cardiol* 1999;84:440-448.
- Geva T, Powell AJ, Crawford EC, et al: Evaluation of regional differences in right ventricular systolic function by acoustic quantification echocardiography and cine magnetic resonance imaging. *Circulation* 1998;98:339-345.
- Greenbaum RA, Ho SY, Gibson DG, et al: Left ventricular fibre architecture in man. Br Heart J 1981;45:248-263.

- Kukulski T, Hubbert L, Arnold M, et al: Normal regional right ventricular function and its change with age: A Doppler myocardial imaging study. J Am Soc Echocardiogr 2000;13:194–204.
- Alam M, Wardell J, Andersson E, et al: Characteristics of mitral and tricuspid annular velocities determined by pulsed wave Doppler tissue imaging in healthy subjects. J Am Soc Echocardiogr 1999;12:618–628.
- 29. Nikitin NP, Witte KK, Thackray SD, et al: Longitudinal ventricular function: Normal values of atrioventricular annular and myocardial velocities measured with quantitative two-dimensional color Doppler tissue imaging. JAm Soc Echocardiogr 2003;16:906-921.
- 30. Henein M, Lindqvist P, Francis D, et al: Tissue Doppler analysis of age-dependency in diastolic ventricular behaviour and filling: A cross-sectional study of healthy hearts (the Umea General Population Heart Study). Eur Heart J 2002;23:162–171.
- Dib JC, Abergel E, Rovani C, et al: The age of the patient should be taken into account when interpreting Doppler assessed pulmonary artery pressures. J Am Soc Echocardiogr 1997;10:72–73.
- Davidson WR Jr, Fee EC: Influence of aging on pulmonary hemodynamics in a population free of coronary artery disease. Am J Cardiol 1990;65:1454–1458.
- Sandstede J, Lipke C, Beer M, et al: Age- and genderspecific differences in left and right ventricular cardiac function and mass determined by cine magnetic resonance imaging. *Eur Radiol* 2000;10:438–442.
- Vogel M, Schmidt MR, Kristiansen SB, et al: Validation of myocardial acceleration during isovolumic contraction as a novel noninvasive index of right ventricular contractility: Comparison with ventricular pressure-volume relations in an animal model. *Circulation* 2002;105:1693–1699.
- 35. Buckberg GD, Coghlan HC, Hoffman JI, et al: The structure and function of the helical heart and its buttress wrapping. VII. Critical importance of septum for right ventricular function. *Semin Thorac Cardiovasc Surg* 2001;13:402–416.
- Buckberg GD, Coghlan HC, Torrent-Guasp F: The structure and function of the helical heart and its buttress wrapping. V. Anatomic and physiologic considerations in the healthy and failing heart. Semin Thorac Cardiovasc Surg 2001;13:358–385.
- Ghio S, Gavazzi A, Campana C, et al: Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. J Am Coll Cardiol 2001;37:183–188.
- Edner M, Jarnert C, Muller-Brunotte R, et al: Influence of age and cardiovascular factors on regional pulsed wave Doppler myocardial imaging indices. *Eur J Echocardiogr* 2000;1:87–95.
- 39. Caso P, Galderisi M, Cicala S, et al: Association between myocardial right ventricular relaxation time and pulmonary arterial pressure in chronic obstructive lung disease: Analysis by pulsed Doppler tissue imaging. J Am Soc Echocardiogr 2001;14:970-977.
- Fraser AG, Payne N, Madler CF, et al: Feasibility and reproducibility of off-line tissue Doppler measurement of regional myocardial function during dobutamine stress echocardiography. *Eur J Echocardiogr* 2003;4:43-53.
- Cardim N, Oliveira AG, Longo S, et al: Doppler tissue imaging: Regional myocardial function in hypertrophic cardiomyopathy and in athlete's heart. J Am Soc Echocardiogr 2003;16:223–232.