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EFFECTS OF AGING ON VENTRICULAR FUNCTION OF NORMAL CHINESE

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Pulsed echocardiography was used in a prospective study of 201 subjects in order to evaluate the effects of aging on left ventricular (LV) function. No subject had clinical evidence of cardiovascular diseases. They were divided into different sex and age groups, and the following echocardiographic parameters were determined: (1) The inotropic state of the heart, which includes time to peak maximal acceleration (TMA) and maximal acceleration (MA). (2) The diastolic function, which includes isovolumic relaxation (IRP), peak filling rate, early and late filling fraction and ratio of peak E/peak A. The results indicated no significant difference between male and female groups in any echocardiographic parameters. Up to the age of 40, there was significant decrease in early filling rate ($P<0.05$), and an increase in late filling fraction ($P<0.05$). After age 50, there was significant increase in isovolumic relaxation period; the E/A ratio inversed. From the age of 60 onward, MA was significantly reduced. It was therefore concluded that: 1) age-related changes in the left ventricular function were observed to begin from 40 years, and to become marked after age 50; 2) with the increase of atrial filling fraction and atrial velocity, atrial contraction to LV filling is an important function in the aging stage of life.

Key words: Ventricular Function, Doppler Echocardiography

INTRODUCTION

That the cardiovascular system is influenced by the aging process is well documented.[1-3] It is clinically important to consider age-related changes when diagnosing cardiovascular diseases such as ischemic heart disease in the elderly.[3] Recently, age-related changes in left ventricular diastolic events have been reported.[4-10] The present study made use of pulsed Doppler echocardiography to define normal values of left ventricular function, and to study how those parameters change with aging and in relation to sex differences.

METHODS

Subjects:

Two hundred and one subjects (102 men and 99 women) aged 6 to 76 years, were prospectively studied. None of them had a histroy of chest pain, exertional dyspnea or systemic hypertension. All subjects had normal electrocardiographic findings. In the young children, no heart murmur was detected. The aged (those over 40 years) had negative treadmill exercise, and a majority of them had a normal coronary arteriogram.

These 201 subjects were separated into six groups and subgrouped by sex, as follows: 38 subjects, aged 6 to 15 years, formed Group I (male: 20, female: 18); 38 subjects, aged 16 to 30 years, were Group II (male:19, female: 19); 30 subjects, aged 31 to 40 years, were Group III (male:

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15, female:15); 30 subjects, aged 41 to 50 years, comprised Group IV (male: 15, female: 15); 31 subjects aged 51 to 60 were in Group V (male:14, female:17) and 34 subjects, aged over 61, were Group VI (male:19. female:15).

Echocardiographic equipment

Commercially-available two-dimensional Doppler echocardiography, an HP 500 imaging system, was used. The ultrasound frequency was 2.5 MHZ. Each patient was examined in lateral recumbent position, with the transducer at the point of the apical impulse or slightly to the left of this area. The transducer was manually rotated to obtain an apical four chamber view of the heart that provided good visualization of the left ventricular cavity with maximal excursion of the mitral valve leaflets. The sample volume was placed at the level of the mitral valve annulus with the cursor line oriented as parallel as possible to an imaginary line transversing the left ventricle form apex to mitral valve. Slight adjustments in transducer angulation or sample volume position were at times required to maximize the audio and graphic quality of the Doppler signal. The velocity of mitral inflow was recorded over several cardiac cycles at a paper speed of 50 mm/sec or 100 mm/sec.

For the recording of the left ventricular outflow, the transducer was rotated slightly with a superior tilt until the aortic valve and the ascending aorta were visualized and the sample volume was placed in the middle of left ventricular outflow immediately proximal to the leaflet of the aortic valve. As with the mitral inflow tract, slight adjustments in either transducer or cursor angulation were at times required to optimize the orientation between the sound wave and flow. This was assessed by the quality of the Doppler tracing. Several cycles of the left ventricular outflow tract velocity were recorded at a paper speed of 100 mm/sec.

The transverse diameter of the mitral annulus was measured from the maximal opening motion of the mitral valve. Measurements were taken from the inner edges of the lateral bright corner of the annulus to the inner edge of the medial corner just below the insertion of the mitral leaflets. Measurements from a minimum of five cardiac cycles were averaged, and the cross-sectional area of the annulus was derived as $\pi\gamma^2$, where r represents half of the annular diameter. This method assumes a circular shape for the mitral annulus and a constant cross-sectional area throughout diastole.

Similarly, the diameter of the aortic valve was measured from the parasternal long-axis view. The diameter was measured in systole, from the upper inner edge of aortic annulus to the lower inner edge.

The following parameters of left ventricular function were measured (Figure 1): Isovolumic relaxation period (A2-D, IRP) was measured from the aortic

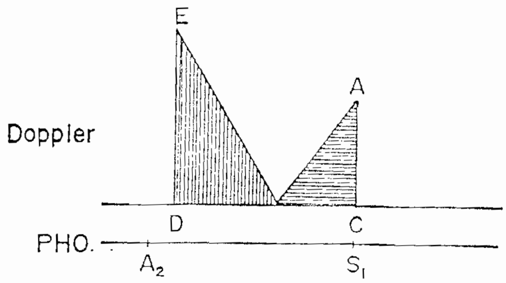


Figure 1. Graphic representation of normal Doppler recording of transmitral inflow velocities

Isovolumic relaxation period: A2-D.

Peak filling rate (PFR): Maximal velocity x Mitral annulus area

Filling fraction of early diastole (FFE): Integral of early diastole/ total diastole

Atrial filling fraction (FFA): Intergral of late diastole/total diastole

E: Early peak in velocity
A: atrial systole
A_2: second heart sound of aortic component
S_1: first heart sound

closing component of the second heart sound to the onset of the mitral diastolic flow-velocity waveform. Early filling fraction (FFE) was defined as integral of early diastolic flow area, divided by total integral of whole diastolic phase. Late filling fraction (FFA) represented atrial systolic portion of the left ventricular filling measured by integral of late filling area. E/A ratio was measured from the heights of the early diastolic flow velocity (E) and the late diastolic flow velocity (A). Peak filling rate (PFR) was calculated from peak early diastolic velocity times mitral area. Maximal acceleration (MA), as an index of inotropic state, was measured from aortic blood velocity. The analog velocity signal was fed into an analog to digital converter under microprocessor control designed by ourselves. Time to maximal acceleration (TTMA) was measured from the beginning of the upstroke of aortic blood velocity to the greatest rate of rise of velocity (maximal acceleration).

Statistical analysis:

A standard unpaired Student t-test was used to assess differences between the means of any two groups, with $P<0.05$ considered significant.

RESULTS

Table 1 shows the 201 subjects divided into different age groups, regardless of sex. Comparative differences in each echocardiographic parameter between different age groups are shown.

The inotropic state includes time to peak maximal acceleration (TMA) and maximal acceleration (MA). There was significant reduction in MA after age 60

Table 1. Comparative Difference in Left Ventricular Function Among Different Age Groups

GP.	No	Age	MA msec	TTMA msec	IRP msec	PFR ml/sec	FFE %	FFA %	E/A
1	38	6-15	1668.45	42.48	47.9	418.8	72.81	21.80	2.05
			±320.00	±24	±5.4	±70.2	±1.50	±0.40	±0.1
2	38	16-30	1654.80	39.54	56.97	428.5	65.96	22.00	2.21
			±341.20	±18.5	±14.1	±84.0	±7.80	±0.40	±0.4
3	30	31-40	1628.40	50.10	57.7	358.5	66.25	26.90	1.68
			±418	±34.2	±18.5	±58	±5.40	±0.50	±0.2
4	30	41-50	1665.84	44.52	64.4	*327.5	*59.20	*32.31	1.37
			±345	±30.2	±20.1	±44	±0.40	±0.40	±0.3
5	31	51-60	1642.40	*77.43	*77.2	*329.4	*56.70	*37.70	*0.96
			±548	±36.7	±14.5	±50	±2.40	±0.80	±0.1
6	34	>60	*1558.45	*80.48	*80.95	*314.5	*55.80	*37.98	*0.80
			±321.3	±30.7	±10.6	±39	±1.40	±0.40	±0.3

* Statistical difference to the corresponding means of the preceding age groups at the level $P<0.05$ by Student t-test

MA: . maximal acceleration PFR: peak filling rate
TTMA: time to maximal acceleration
IRP: isovolumic relaxation period
FFE: filling fraction of early diastole
FFA: filling fraction of atrial systole
E/A: peak E velocity / peak A velocity

(P<0.05). However, TMA in Groups 5 and 6 were significantly prolonged compared to that of other groups (P<0.05).

The diastolic function includes isovolumic relaxation period (IRP), peak filling rate, early filling fraction, late filling fraction and ratio of peak E/peak A. From age 40 onwards, peak filling rate was significantly decreased, and there was a significant reduction in early filling and an increase in late filling fraction. Isovolumic relaxation period was prolonged and the E/A ratio became inversed from age of fifty.

Table 2 shows 201 subjects divided into male and female groups, without ragard for age. There were no significant differences in maximal acceleration, time to maximal acceleration, E/A ratio, IRP and filling fraction between the two sexes.

DISCUSSION

Previous studies of left ventricular function in normal aging humans, using Doppler echocardiography[7-10] and radionuclide angiography,[11-12] did not assess the maximal acceleration, isovolumic relaxation period and filling fraction. In this study, these echocardiographic parameters were determined, and a more detailed evaluation was made of the changes in left ventricular function, based on different sex and age groups. There was no significant difference between the male and female groups in any echocardiographic parameters.

Myocardial contractility has been studied extensively by invasive methods, but rarely with noninvasive procedures. Circumferential fiber shortening and percent of fraction shortening with M-Mode echocardiography are often used as indicators of myocardial contractility. These parameters are affected by preload. According to Lambert et al,[13] the maximal acceleration was the most sensitive index of ventricular contractile state by noninvasive method. This is the reason why this parameter was chosen to evaluate myocardial contractility. This study showed that, after the age of 50, there was a significant prolongation in the time-to-maximal acceleration, and

Table 2. Comparative Difference in Left Ventricular Function Between Different Sex Groups

GP.	Sex	MA (msec)	TTMA (msec)	IRP (msec)	PFR (ml/sec)	FFE (%)	FFA (%)	E/A
1	M	1673.97 ±401.30	43.83±27.50	45.50±6.96	426.7±62.8	77.50±0.5	21.8 ±0.3	2.10 ±0.4
	F	1669.58 ±256.87	41.69±19.01	48.70±5.74	418.4±74.5	70.40±1.5	21.7 ±0.4	2.03 ±0.3
	P-V	NS	NS	NS	NS	NS	NS	NS
2	M	1628.57 ±366.20	38.34±11.09	54.67±15.09	434.5±82.0	69.80±0.4	20.0 ±0.3	2.3 ±1.6
		1693.64 ±342.00	40.42 ±26.45	57.97 ±13.51	413.2 ±94.0	63.95 ±7.6	23.2 ±0.4	2.1 ±.43
	P-V	NS	NS	NS	NS	NS	NS	NS
3	M	1631.30 ±394.16	49.91±34.79	58.00±20.71	366.8±44.0	66.20±0.3	26.4 ±0.4	1.7 ±0.5
	F	1625.75 ±413.92	50.02±30.31	56.50±13.01	374.8±50.0	66.30±8.4	27.8 ±0.5	1.63 ±0.4
	P-V	NS	NS	NS	NS	NS	NS	NS
4	M	1626.84 ±626.58	44.04±32.48	64.38±18.90	362.95 ±41.0	59.20±9.4	30.60±4.5	1.4 ±0.3
	F	1699.84 ±575.00	44,83±23.95	67.40±21.54	353.68 ±45.0	59.30±6.5	34.31±8.2	1.34 ±.2
	P-V	NS	NS	NS	NS	NS	NS	NS
5	M	1672.80 ±595.54	77.57±37.19	70.87±20.09	345.60±71.0	58.60±0.4	37.80±0.9	0.9 ±0.2
	F	1628.94 ±431.03	76.95±35.39	74.45±11.28	328.50±48.0	55.38±4.0	37.34±0.8	1.0 ±.35
	P-V	NS	NS	NS	NS	NS	NS	NS
6	M	1533.19 ±243.54	81.47±30.63	81.39±13.29	333.80±30.0	55.20±0.3	38.00±0.4	0.8 ±0.9
	F	1594.58 ±342.00	79.03±26.70	79.75±10.50	314.40±24.0	56.31±3.0	37.95±0.8	0.8 ±0.7
	P-V	NS	NS	NS	NS	NS	NS	NS

M. male F: female P-V; p-value MA: maximal acceleration
TTMA: time to maximal acceleration IRP: Isovolumic relaxation period
PFR: peak filling rate FFE: filling fraction of early diastole
FFA: filling fraction of atrial systole E/A: peak E velocity/peak A velocity

the maximal acceleration decreased in the old age group.

As to left ventricular diastolic function, Miyatake et al[7] first reported that aging in normal subjects was associated with a reduction in ratio of peak early to peak atrial velocities. Subsequently, confirmation of this important relationship was made by radionuclide angiography[11-12] and Doppler echocardiography.[8-10] The reduction in early peak filling rate, with advancing age, may be causally related to the disappearance of the physiologic S sound with aging.[14] Present results were compatible with those of previous findings.

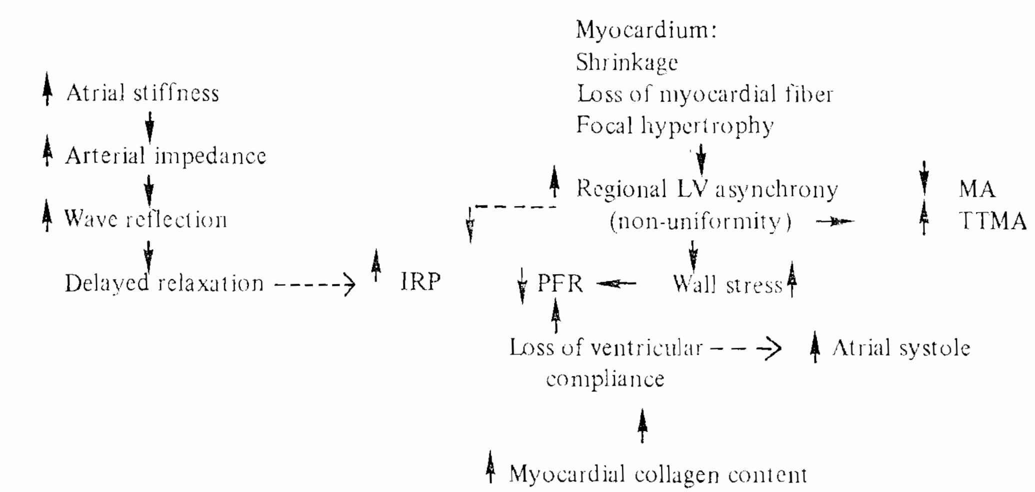
The present study assessed a wide range of age groups, with results which indicated that after the age of 50, isovolumic relaxation period was significantly prolonged. Moreover, the peak late (atrial) filling velocity and atrial volumes were also significantly increased, suggesting an atrial contribution to left ventricular filling with aging.

An explanation for these changes in left ventricular function with aging is shown in Table 3. These hemodynamic alternations in aging humans might result from a decrease in left ventricular compliance, an increase in load and a nonuniformity of myocardium. Decreased left ventricular compliance was an essential feature of cardiac pathology in the aged. This may be induced by the presence of a considerable amount of amyloid deposits and collagenous modification. Moreover, reduced left ventricular compliance may lead to a decrease of peak filling rate, and thus increase the atrial systole.

Age-assoicated increase in arterial wall stiffness is due to certain viscoelastic alternations of the aging arterial wall caused by changes in collagen elastin and smooth muscle cells. These changes increase the calculated peripheral resistance at rest and wave reflection. The delayed myocardial relaxation induce prolongation of isovolumic relaxation.

Electron microscopy shows senile ultrastructural changes in the mitochondral membrane and decline in functional integrity with age.[15] Myocardium shows degenerative forms of mitochondria, a decline in their numbers and some focal hypertrophy.[16] These may cause regional left ventricular asynchomy, and affect myocardial relaxation and contractility. As a result, prolongation of IRP, decreased

Table 3. Proposed Mechanism of Effects of Aging on Ventricular Function



MA: Maximal acceleration
TTMA: Time to maximal acceleration

MA, increased time to maximal acceleration and wall stress may reduce the peak filling rate.

Biologic changes of aging begin at the end of maturity and adulthood and continue into senescence.[17] This study demonstrated that the impaired left ventricular function began from the age of forty, and more deleterious changes occurred thereafter.

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