

Evaluation of the Elastic Properties of the Thoracic Descending Aorta with Strain-Rate Measurement with Transesophageal Echocardiography: Its Correlation with the Left Ventricular Diastolic Function Assessed with Transthoracic Echocardiography

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Abstract

Arterial stiffening may contribute to secondary myocardial dysfunction. The aim of this study was to assess the stiffness of the thoracic descending aorta (TDA) by performing strain-rate measurements with transesophageal echocardiography (TEE) and to examine the relation of the findings to left ventricular (LV) function. Eight patients (group I) without risk factors for arteriosclerosis and 52 patients (group II) with a high risk of arteriosclerosis underwent transthoracic echocardiography (TTE) and TEE simultaneously. The values of distensibility of the TDA (–SR) in groups I and II were -11.7 ± 2.4 and -4.6 ± 2.5 , respectively ($p < 0.001$), and the values of the recoil of the TDA (+SR) were 20.5 ± 8.2 and 6.8 ± 5.0 , respectively ($p < 0.001$). The LV ejection fraction showed no relation with –SR or +SR, but LV diastolic function (e' and E/e') was correlated with +SR ($p = 0.002$ and $p = 0.046$, respectively). Strain-rate measurements obtained with TEE were useful for evaluating impairment of the elastic properties of the TDA and the pathophysiologic mechanisms underlying the arterial-ventricular relationship.

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Key words: arterial stiffness, arteriosclerosis, strain rate, transesophageal echocardiography

Introduction

The early changes in arteriosclerosis include thickening of the arterial walls. In humans, thickening of the intima-media complex (IMC) is associated with and attributed to various conditions, such as hypertension¹, diabetes², end-stage renal

disease³, Marfan syndrome⁴, hypertrophic cardiomyopathy⁵, and aging (especially in elderly inpatients)⁶, which makes it hard to determine the precise mechanism of increased stiffness. Recently, the concept of “continuity disease” has been proposed to describe the relationship between the arteries and the rest of the cardiovascular system⁷. Age-associated arterial stiffening increases the

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Table 1 Baseline clinical characteristics

Characteristic	Group II	Group I	p value
	patients (n=52)	control subjects (n=8)	
Age, y	64 ± 12	44 ± 9	p<0.001
Male, n (%)	34 (65)	5 (62)	NS
Diabetes meliitus, n (%)	19 (36)	/	/
Hypertension, n (%)	36 (69)	/	/
Dyslipidemia, n (%)	39 (75)	/	/
Current stroke, n (%)	25 (48)	/	/
Paroxysmal atrial fibrillation, n (%)	14 (27)	8 (100)	p<0.001
Old myocardial infarction, n (%)	7 (13)	/	/
Dilated cardiomyopathy, n (%)	6 (11)	/	/
Heart rate, beats/min	72 ± 8	68 ± 9	NS
Systolic blood pressure, mm Hg	126 ± 12	112 ± 20	NS
Diastolic blood pressure, mm Hg	74 ± 8	72 ± 4	NS
Calcium channel blockers, (%)	43 (72)	/	/
Angiotensin II receptor blockers, (%)	32 (53)	/	/
β-blockers, (%)	13 (22)	/	/

NS = not significant

systolic blood pressure due to reflected pulse waves⁸. Due to summation of the reflected waves, there is a progressive increase of afterload in the aortic root, coronary arteries, left ventricle, and left atrium. Pulsatile forces contribute substantially to an increased cardiovascular risk and to left ventricular (LV) diastolic dysfunction⁹.

Myocardial strain or tissue strain is a dimensionless index of the change in tissue length caused by an applied force. The strain rate is the time derivative of strain, and its unit is the second (s^{-1}). On ultrasound, it is measured as the difference in velocity between 2 points normalized for the distance between them. The strain rate is the earliest and most-sensitive indicator of regional tissue deformation^{10,11}. In the thoracic descending aorta (TDA), a positive strain rate represents aortic recoil, and a negative strain rate represents aortic distension. We have hypothesized that strain rate measurements could be used to assess the elastic properties of the TDA in the early stage of arteriosclerosis. A few reports have indicated that measurement of the velocity-based strain rate with transesophageal echocardiography (TEE) can be used to evaluate the elastic properties of the TDA. The 2 aims of the present study were (1) to assess the stiffness of the TDA on the basis of strain rate measurements made with TEE and (2) to examine

the relation of LV function with the elastic properties of the TDA.

Subjects and Methods

Study Population

TEE was performed as a routine examination in 867 patients in 2007 and 2008 at Nippon Medical School Hospital. All patients gave informed consent before undergoing TEE and transthoracic echocardiography (TTE). This study was based on the 60 patients aged 64 ± 12 years (39 men and 21 women) who were retrospectively selected from these 867 patients. All 60 patients simultaneously underwent TTE and TEE with strain-rate imaging. Their clinical characteristics are listed in **Table 1**. Eight patients (Group I: 5 men and 3 women aged 44 ± 9 years) with paroxysmal atrial fibrillation but without cardiac dysfunction (left ventricular ejection fraction >50%), significant valvular disease, ischemic heart disease, or risk factors for arteriosclerosis (dyslipidemia, hypertension, and diabetes) were used as control subjects. The remaining 52 patients (Group II) had risk factors for arteriosclerosis. Exclusion criteria included acute myocardial infarction, unstable angina, tachyarrhythmia, and second- or third-degree atrioventricular block.

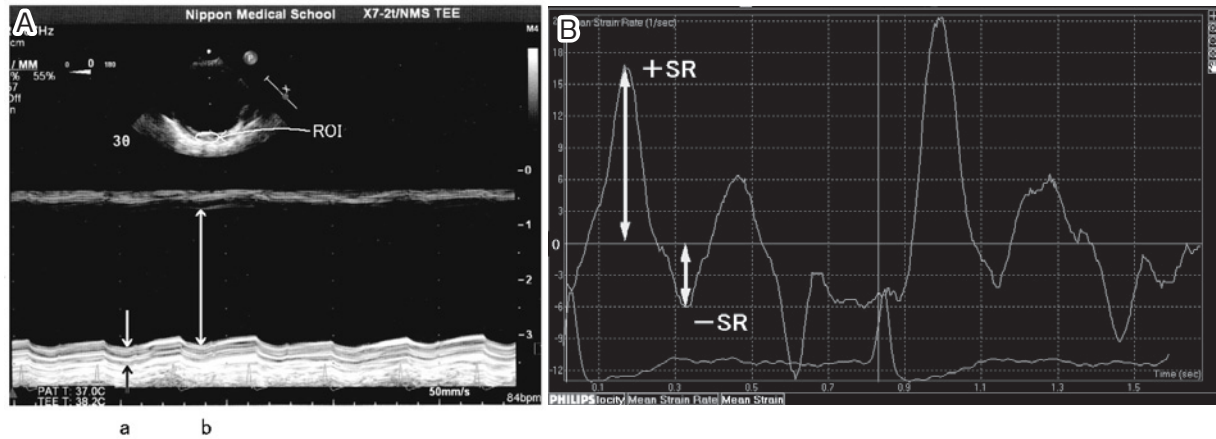


Fig. 1 A. Transesophageal 2-dimensional and M-mode images of the TDA. a) Thickness of the intima-media complex. b) Maximum LV diameter. B. Representative strain-rate curve from a patient with intima-media thickening in the TDA depicts the rate of deformation in the region of interest. ECG: electrocardiogram; ROI: region of interest; SR curve: strain-rate curve; TDA: thoracic descending aorta, +SR: the peak strain rate during early systole representing TDA recoil; -SR: the peak strain rate during late systole representing TDA distensibility.

TTE

TTE was performed with a commercially available echocardiography system (iE 33, Philips Medical Systems, Bothell, WA, USA) before TEE. In the apical 4- and 2-chamber views, the LV endocardial border was drawn semiautomatically in end-diastole and end-systole to allow measurement of LV volume¹², and the LV ejection fraction (LVEF) was calculated from the volume measurements. By means of pulsed-wave Doppler echocardiography, the mitral inflow velocity, peak early diastolic velocity (E), and peak late diastolic velocity (A) were measured. The early diastolic annular velocity (e') was obtained by means of tissue Doppler measurement at the lateral border of the mitral annulus. The following variables of global diastolic function were determined: the ratio of the peak velocity of the A wave to the peak velocity of the E wave (A/E) and the ratio of the peak velocity of the E wave to the peak velocity of e' (E/e'). The LVEF, e', A/E, and E/e' were determined as the median values of measurements obtained during 3 consecutive beats.

TEE

A commercially available ultrasound imaging system (iE 33, Philips Medical Systems, Andover, MA, USA) was employed with a T6H Omniplane III transducer (2–7 MHz) as an esophageal probe. All

patients gave informed consent. Topical oropharyngeal anesthesia and intravenous sedation with diazepam were provided routinely. Complete TEE was performed, including fundamental M-mode, 2-dimensional imaging, and strain-rate imaging of the TDA in the short-axis view (Fig. 1A and 1B). On transverse images, the TDA was divided into 3 segments of 5 cm each that extended from a point 25 cm below the incisors to 40 cm below the incisors. Measurements were obtained from 2 short-axis images of each segment. The IMC thickness and maximum TDA diameter were measured on M-mode images (Fig. 1A). A previous study has shown that the normal IMC thickness of the TDA in Japanese subjects is 1.13 mm (Japanese autopsy data; age ≤ 19 years)¹³. The median values of measurements obtained during 3 consecutive beats were used for statistical analysis.

Analysis of strain-rate data was performed online with dedicated software (iE 33, Philips Medical Systems, Andover, MA). The tissue Doppler-derived velocity indicates the rate at which a point in the TDA wall moves toward or away from the transducer. The rate of change in length normalized for the original length is called the strain rate, and it is calculated with tissue Doppler as the difference between 2 tissue velocities along the ultrasound beam ($V_2 - V_1$) normalized for the distance between these 2 velocities (d). Strain rate = $(V_2 - V_1)/d$. In

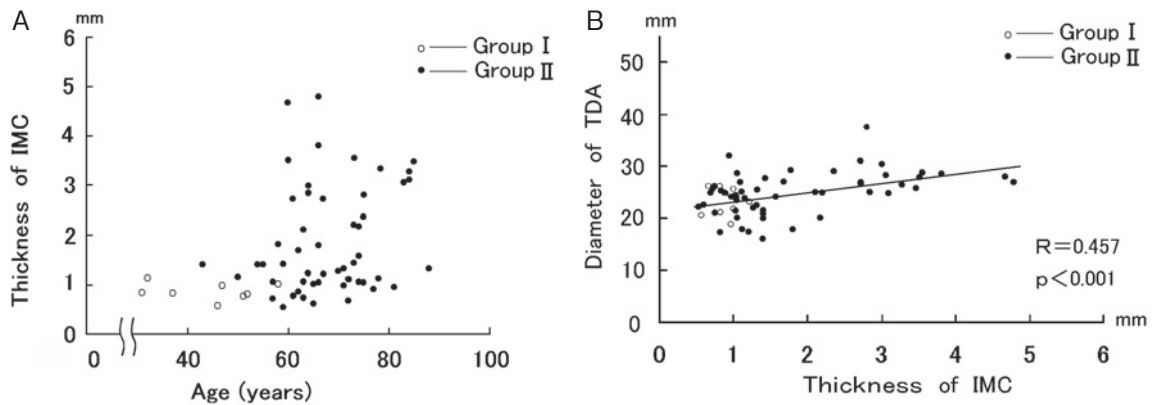


Fig. 2 A. Thickness of the intima-media complex of the thoracic descending aorta in relation to age. B. Correlation between the diameter of the thoracic descending aorta and the thickness of its intima-media complex. IMC, intima-media complex; TDA, thoracic descending aorta

general, the maximum systolic strain rate is the variable that best indicates local tissue function. It is relatively independent of volume and is less independent of pressure than strain¹⁴. In this study, strain-rate measurements were obtained from the same 2 short-axis images of each segment, as mentioned above. The region of interest (2.5 mm in width \times 5 mm in length) was fixed manually on each of the strain-rate images at a midwall location throughout 3 cardiac cycles (Fig. 1A and Fig. 2A). After strain-rate curves were generated, the maximum strain rate during early systole (+SR) and the minimum strain rate during late systole (-SR) were determined (Fig. 1B). The median strain rate for 3 segments was calculated. The elastic properties of the TDA were assessed from its recoil (+SR) and its distensibility (-SR). Abnormalities of both distensibility and recoil indicated an increase in the stiffness of the TDA.

Statistical Analysis

Results are expressed as means \pm standard deviations. Statistical tests were performed with 1-way fixed-effects analysis of variance. Pearson's correlation coefficients were calculated, and linear regression was performed to assess the correlations of other variables with the strain-rate data. The mean difference between the IMC thickness measured by 2 independent observers was calculated and assessed with Bland and Altman analysis. We constructed receiver operating

characteristic (ROC) curves to analyze -SR and +SR data to determine the cut-off values that yielded the highest combined sensitivity and specificity for distinguishing patients with a high risk of arteriosclerosis from those without risk factors for arteriosclerosis. In all analyses, a p value of less than 0.05 was considered to indicate significance.

Results

Baseline Characteristics of the Subjects

The baseline clinical characteristics of the subjects are shown in Table 1. Although the subjects of group II were significantly older than those of group I, there were no significant differences in heart rate or blood pressure between the groups.

IMC Thickness, TDA Diameter, and Doppler Findings

Figure 2A shows the IMC thickness of the TDA (mean: 1.7 ± 1.0 mm; range: 0.67 to 4.8 mm) in patients stratified for each decade of age. In group I, the mean TDA diameter and IMC thickness was 23.0 ± 2.7 mm and 0.80 ± 0.20 mm, respectively. Of the 42 patients 60 years or older, 27 showed an increased IMC thickness, and 15 patients showed a normal IMC thickness. In group II, the maximum diameter of the TDA was significantly correlated with the IMC thickness ($R=0.457$; $p<0.001$, Fig. 2B).

In group I, the mean values of -SR and +SR were -11.7 ± 2.4 (range: -16.4 to -9.4) and 20.5 ± 8.2

Table 2 2-D and Doppler echocardiographic features of the TDA

	Group II patients (n=52)	Group I control subjects (n=8)	p value
Maximum diameter (mm)	24.8 ± 4.1	23.0 ± 2.7	NS
IMC thickness (mm)	1.8 ± 1.0	0.8 ± 0.2	p=0.01
Baseline LVEF (%)	61 ± 11	67 ± 5	NS
E/A ratio	1.2 ± 0.4	1.0 ± 0.2	NS
e'	6.3 ± 1.5	7.4 ± 0.8	p<0.05
E/e' ratio	12.0 ± 4.3	8.1 ± 2.3	p<0.05
-SR	- 4.6 ± 2.5	- 11.7 ± 2.4	p<0.001
+SR	6.8 ± 5.0	20.5 ± 8.2	p<0.001

IMC = intima-media complex, LVEF = left ventricular ejection fraction, TDA = thoracic descending aorta

Table 3 Distensibility and recoil of the TDA

	Recoil	
	decrease	control value
	+SR ≤ 12	+SR > 12
Distensibility decrease -SR ≥ - 9	39	11
control value -SR < - 9	2	8

(range: 13.0 to 36.6), respectively. In group II, the mean values of -SR and +SR were -4.6 ± 2.5 (range: -13.4 to -0.5) and 6.8 ± 5.0 (range: 0.1 to 22.5), respectively. The ROC curve analysis yielded an optimal cut-off value of -9 for -SR (sensitivity: 96%; specificity: 88%; and area under the curve: 0.974) and 12 for +SR (100%, 81%, and 0.959) for differentiating between group I and group II. Therefore, abnormality of the elastic properties of the TDA was defined on the basis of TDA distensibility of $-SR \geq -9$ or TDA recoil of $+SR \leq 12$ or both. **Table 2** shows that there were significant differences between group I and group II in IMC thickness, e', E/e', -SR, and +SR.

The IMC thickness and the strain-rate data obtained by 2 observers were compared by means of Bland-Altman analysis, which revealed a mean difference of 0.05 ± 0.023 mm and -0.003 ± 0.012 , respectively, whereas the 95% confidence limits for agreement were -0.05 to 0.04 and -0.031 to 0.031, respectively.

IMC Thickness and SR

Table 3 demonstrates that 39 of 60 patients showed a decrease in both TDA distensibility ($-SR \geq -9$) and TDA recoil ($+SR \leq 12$). The mean IMC thickness, -SR, and +SR values of these 39 patients were 2.0 ± 1.2 mm, -4.2 ± 2.2 , and 4.9 ± 3.2 , respectively. Fourteen of the 39 patients had a normal IMC thickness (**Fig. 3**), 11 patients showed decreased TDA distensibility with normal recoil, and 2 patients had decreased TDA recoil with normal distensibility. In group II, -SR (the index of TDA distensibility) was strongly correlated with the IMC thickness ($R=0.694$, $p<0.0001$, **Fig. 4A**), and +SR (the index of TDA recoil) was also correlated with the IMC thickness ($R=0.398$, $p<0.001$, **Fig. 4B**).

LV Function and SR

In group II, LVEF had no relation with -SR or +SR ($p=0.073$ and $p=0.058$, respectively). The indices of global LV diastolic function (A/E, e', and E/e') also showed no relation with -SR ($p=0.684$, $p=0.638$, and $p=0.405$, respectively). However, **Figures 5B and 5C** show correlations between e' or E/e' and +SR ($p=0.002$ and $p=0.046$, respectively).

Discussion

This study is, to our knowledge, the first to demonstrate that measurement of the strain rate by means of TEE can be used to evaluate the elastic properties of the TDA, yielding an index of TDA distensibility during late systole (-SR) and an index of TDA recoil during early systole (+SR). In patients

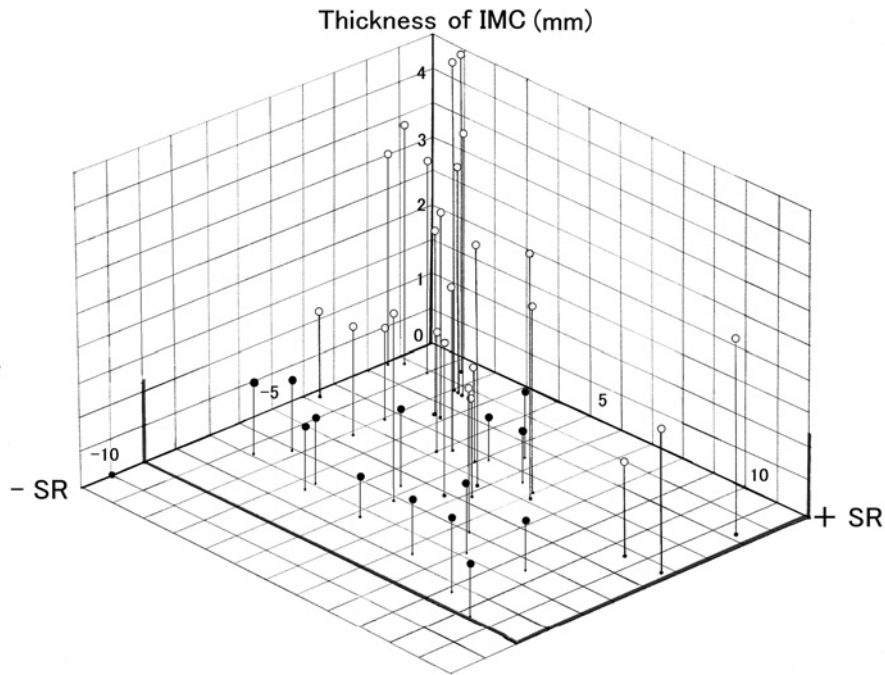


Fig. 3 Among 39 patients with abnormal TDA distensibility and recoil, 14 patients had a normal IMC thickness (closed circles) and 25 patients showed IMC thickening (open circles). Bold lines show the control group values.

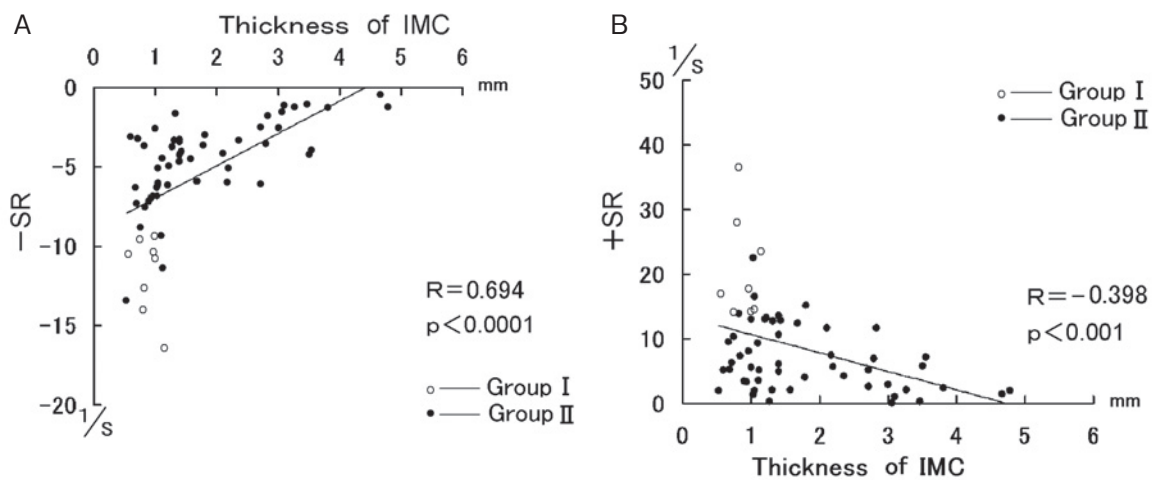


Fig. 4 Scatter plots for linear regression analysis of the relations between IMC thickness and $-SR$ (A) or $+SR$ (B).

with risk factors for arteriosclerosis (group II), both $-SR$ and $+SR$ were well correlated with the IMC thickness, and the decreases in TDA distensibility and recoil were marked compared with those in patients without risk factors for arteriosclerosis (group I). In group II, TDA recoil ($+SR$) was also correlated with LV diastolic function (e' and E/e').

TDA Structure and Elastic Properties

The aortic wall has 3 layers. There is a thin intima lined by endothelium, a thick medial layer, and a thin adventitia on the outside. The normal IMC thickness of the TDA is about 1.13 mm in Japanese¹³. This study showed that the median IMC thickness was 0.8 ± 0.2 mm in group I. The media contains parallel layers of elastic fibers and collagen fibers in

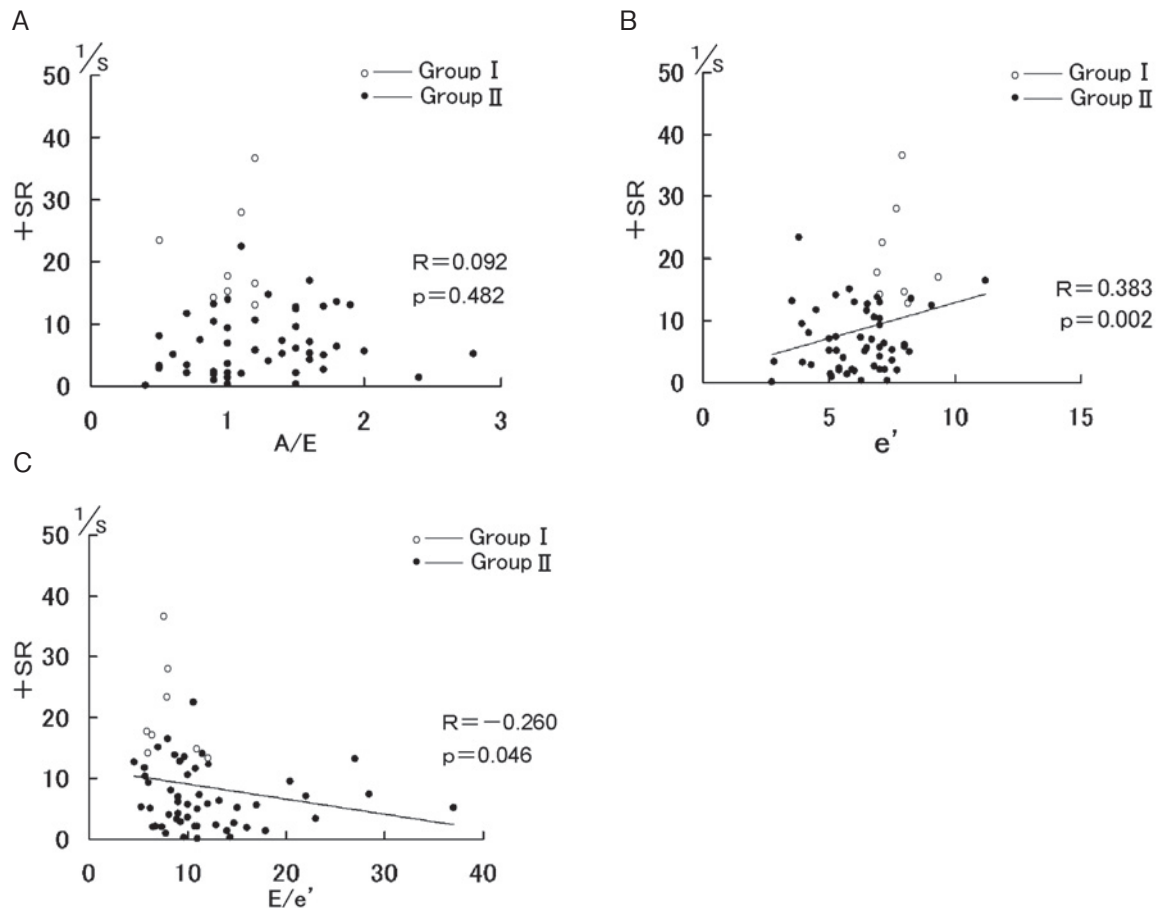


Fig. 5 Relations between +SR and A/E (A), e' (B), or E/e' (C).

A/E: ratio of the peak velocity of the A wave to the peak velocity of the E wave; e' : early diastolic velocity at the mitral annulus; E/e' : ratio of the peak velocity of the E wave to the peak velocity of e' .

a mucoid ground substance. Elastic fibers are more prominent in the ascending aorta, which has approximately 56 layers of these fibers, while the descending aorta has up to 28 layers. Therefore, the proximal thoracic part of the aorta is more distensible than its distal abdominal part. With aging, these elastic fibers undergo fragmentation, the number of smooth muscle cells decreases, the mucoid ground substance becomes more prominent, and the number of collagen fibers increases. These changes lead to weakening of the aortic wall and result in dilatation and elongation. The present study has shown that the maximum diameter of the TDA is significantly correlated with the IMC thickness.

The arterial system has a two-fold role, acting as both a conduit and a cushion. The aorta is a passive organ that does not constrict or dilate by itself. The

LV stroke volume is temporarily stored in the aorta, and its storage capacity is related to the elastic properties of its wall. Therefore, we defined the elastic properties of the TDA on the basis of recoil and distensibility using strain-rate measurements obtained by means of TEE. Disturbances of both distensibility and recoil represent increased stiffness of the TDA.

Elastic Properties of the TDA

This study found that the elastic properties of the TDA (distensibility and recoil) were severely impaired in 39 of 52 patients with risk factors for arteriosclerosis. However, 14 patients with a normal IMC thickness also showed disturbances of both TDA distensibility and recoil, and all 14 patients had hypertension. The adverse effects of elevated aortic stiffness are thought to be related to early return of

the reflected pressure wave during late systole, which increases central pressure and thus elevates the systolic blood pressure. An increase of systolic pressure increases the load on the left ventricle, which induces left ventricular hypertrophy, increased myocardial oxygen demand, and subendocardial ischemia¹⁵⁻¹⁸. Whether disturbances of TDA distensibility and recoil are the first manifestations of arteriosclerosis is still unknown. The use of indices of aortic wall properties to refine risk stratification is based on the assumption that aging and cardiovascular risk factors influence arterial wall properties from an early stage of arteriosclerosis in a consistent, progressive, and predictable fashion. Aortic stiffness can be assessed by determination of the aortic diameter-pressure relationship¹⁹, measurement of pulse wave velocity, measurement of reflected waves^{15,20}, calculation of the aortic stiffness index²¹, and determination of the stiffness parameter β ²². However, there have been few reports that measurement of the velocity-based strain rate by means of TEE can be used to evaluate the elastic properties of the TDA.

TDA Elastic Properties and LV Function

In this study, LVEF was not correlated with the indices of TDA distensibility and recoil, but both e' and E/e' (among the indices of LV diastolic function) were correlated with the index of TDA recoil (+SR). One possible reason why the A/E ratio was not correlated with the index of TDA recoil is pseudonormalization of the transmitral flow pattern in patients with moderate LV diastolic dysfunction. Previous studies have shown that the early diastolic velocity at the mitral annulus (e') is correlated with invasive measures of diastolic function^{23,24}. A low e' value predicts mortality in addition to other clinical and echocardiographic data^{25,26}. The ratio of E to e' (E/e' ratio) is closely correlated with the LV filling pressure^{23,27} and can be used to predict heart failure²⁸.

The interaction between ventricular and arterial properties, which is known as coupling, is an important determinant of cardiac performance⁷. Increased arterial stiffness affects both the LV and the distal arterial bed. Due to summation of the reflected waves, pulsatile forces contribute to

increased cardiovascular risk in addition to causing LV diastolic dysfunction⁹. More than 70% of older patients with symptomatic heart failure have a normal EF fraction and qualify for a diagnosis of diastolic heart failure²⁹⁻³¹. In patients with LV diastolic dysfunction and preserved EF due to arterial stiffening, the abnormal increase of LV filling pressure is related to primary hemodynamic abnormality. These patients can have exercise intolerance, pulmonary edema, and increased mortality, similar to patients with systolic heart failure³²⁻³⁴. One of the mechanisms leading to heart failure is that these patients have an upward or leftward shift of the end-diastolic pressure-volume curve, indicating passive diastolic dysfunction and the classic pattern of diastolic heart failure³⁵. Therefore, treatment should concentrate on blood pressure reduction with vasodilators to modulate the renin-angiotensin-aldosterone system and the sympathetic nervous system³⁶.

Clinical Implications

TEE is a relatively invasive but safe method of examination. In this study, strain-rate measurements obtained with TEE could be used to detect disturbances of TDA distensibility and recoil at the early stage of arteriosclerosis, as well as the effects of these aortic changes on LV diastolic function. Thus, adding strain-rate measurements by means of TEE to standard TTE may be useful for assessing vascular-ventricular coupling, abnormalities of which help to explain the age-associated epidemic of heart failure.

Limitations

This study had several limitations. First, there was no gold standard for assessing the mechanical properties of the TDA wall in this study. An intravascular catheter has been used to measure aortic diameter and aortic pressure simultaneously at the same site. Although this method enables us to evaluate accurately the elastic properties of the aorta, it cannot be used for population screening due to its invasive nature. Second, velocity-based strain-rate measurements were obtained through manual analysis and were time-consuming. Recently,

speckle-tracking echocardiography has been used to quantify regional deformation instead of velocity-based strain-rate imaging. Speckle-tracking measurement is relatively angle-independent and is semiautomatically acquired. Third, blood pressure and heart rate may affect the measurement of strain rate, although strain rate is relatively volume-independent and is less pressure-independent than strain. There was no difference in heart rate or blood pressure between group I and group II. Fourth, observation of changes in the elastic properties of the TDA should ideally be continued for several years and may help to monitor the natural history of the disease process.

Conclusion

Strain-rate data obtained by means of TEE can be used to assess the elastic properties of the TDA. Combining TTE with TEE for measurement of aortic strain rates could be useful for examining the pathophysiology of the arterial-ventricular relationship.

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