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Right Ventricular Diastolic Filling Assessed by Conventional Doppler and Tissue Doppler Imaging in Normal Children

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Yasuoka, K., Harada, K., Orino, T. and Takada, G. *Right Ventricular Diastolic Filling Assessed by Conventional Doppler and Tissue Doppler Imaging in Normal Children.* Tohoku J. Exp. Med., 1999, **189** (4), 283-294 —— To examine age-related changes in right ventricular filling dynamics, we performed conventional pulsed Doppler ($n=99$) and tissue Doppler ($n=30$) echocardiographic studies in normal subjects aged 7 days to 273 months. The tricuspid flow velocity during early diastole (peak E) wave correlated significantly but weakly with the logarithm of age. The peak E wave in the early neonatal period was almost 80% of the older children's values and increased to 100% by 36 months of age. In the right ventricular tissue Doppler imaging, the peak myocardial velocity during early diastole also increased significantly with the logarithm of age. However, the tissue Doppler peak A did not change with age. There was a significant correlation between the tissue Doppler peak E wave and the tricuspid peak E wave and between the tissue Doppler peak E/A wave and the tricuspid peak E/A wave. The age-related changes in the tricuspid inflow velocity patterns were similar to the age-related alterations in the right ventricular myocardial velocity patterns. Age-related changes in the tricuspid inflow velocity and myocardial velocity patterns may be related to age-related maturation in the right ventricular diastolic performance. ———— tissue Doppler imaging; right ventricle; diastolic function

Doppler echocardiography has recently allowed a noninvasive assessment of right ventricular filling dynamics. Normal values for right ventricular diastolic filling parameters measured by Doppler echocardiography have been reported for fetuses, neonates, and adults (Reed et al. 1986; Wilson et al. 1987; Riggs et al. 1989; Zoghbi et al. 1990; Iwase et al. 1993; Koh et al. 1994; Harada et al. 1995a, 1997). These measurements are known to vary markedly with age. Age-related changes in right ventricular diastolic filling similar to those in left ventricular diastolic filling have been found in adults (Zoghbi et al. 1990; Iwase et al. 1993). However, there is little information about the effect of age on right ventricular

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diastolic filling in normal children. Tissue Doppler imaging is a new ultrasound technology that enables the measurements of relaxation velocities directly from the myocardium (McDicke et al. 1992; Donovan et al. 1995; Miyatake et al. 1995; Rychik and Tian 1996; Galiuto et al. 1998). This approach in studying myocardial velocities offers a potential of the quantitative assessment of diastolic ventricular function. However, data on myocardial velocities by using tissue Doppler imaging have not been established in children. Therefore, this study was designed to examine the determinants of age-related changes in right ventricular diastolic filling using conventional pulsed Doppler and tissue Doppler imaging.

Methods

Study subjects

The study group consisted of 99 subjects aged 7 days to 22 years old who were judged to be free from any acute or chronic illness by history and physical examinations. All parents received an explanation of the study and gave informed consent. All subjects were referred to us for precordial murmur, an enlarged cardiothymic silhouette on a chest radiogram, or an incomplete right bundle branch block pattern on an electrocardiogram. No evidence of structural cardiovascular disease was detected in any subject by two-dimensional and Doppler echocardiography. No infant had a clinically significant patent foramen ovale or a dilatation of either the right atrium or right ventricle or both.

Tricuspid inflow

Two-dimensional and Doppler echocardiographic studies, with an Aloka SSD 2200 ultrasound system (Aloka, Tokyo) using a 3.5 or 5.0 MHz transducer, were performed and recorded on a strip-chart recorder at 100 mm/seconds. Thirty of 99 subjects were also studied by using tissue Doppler technique. The right ventricular inflow velocity was recorded from the apical four chamber view. The Doppler sample volume was placed at the tips of the tricuspid valve leaflets.

The size of the Doppler sample volume was set at an axial length of 2 to 4 mm, and a wall filter setting of 400 Hz was used. Care was taken to perform these studies with the transducer beam as close as possible to the Doppler beam at <20 degrees in any selected planes. No angle correction of the Doppler signal was made. An electrocardiogram were simultaneously recorded in all subjects.

Tissue Doppler imaging

The tissue Doppler echocardiographic data were also obtained with Aloka SSD-2200, using a 3.5 or 5.0 MHz transducer. The tissue Doppler imaging program was set to the pulsed wave Doppler mode. Filters were set to exclude high frequency signals. Gains were minimized to allow for a clear tissue signal with minimal background noise. In each subject, the tissue Doppler imaging of the right ventricular diastolic velocities was obtained from the apical echocardiogra-

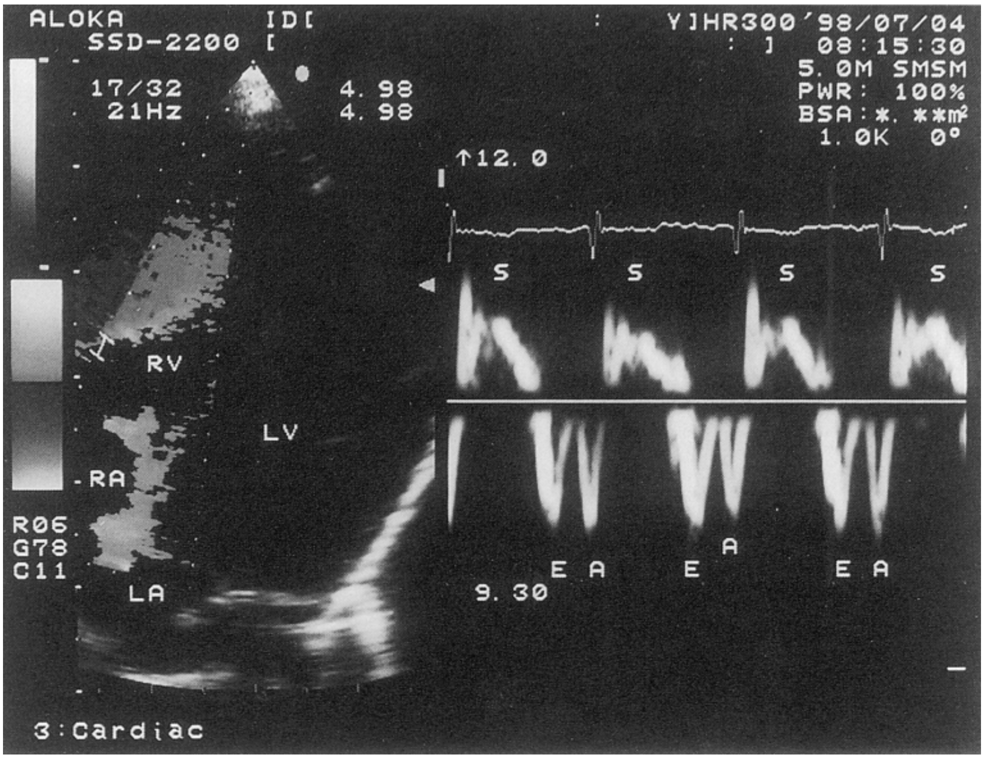

Fig. 1. Sample recording of myocardial velocity by tissue Doppler imaging in the 4-chamber view of the right ventricle.
S, peak myocardial velocity during systole; E, peak myocardial velocity during early diastole; A, peak myocardial velocity during atrial contraction.

phic window using 4-chamber view (Fig. 1). The sample volume was set at an axial length of 1 to 2 mm and was placed at the lateral tricuspid annulus. All subjects were studied without sedation while they were lying quietly in the supine position.

From the pulsed Doppler and the tissue Doppler recordings, the peak velocities during early diastole (peak E wave) and during atrial contraction (peak A wave) and the ratio of peak velocities of E to A waves (peak E/A wave) were measured. To minimize the effect of respiration on the variability in ventricular filling, Doppler measurements were obtained from 5–7 consecutive cardiac cycles.

Statistics

Results are expressed as mean$\pm$S.D. Regression analysis was performed using the least-squares method (Statistica, StatSoft®, Three's Company, Inc., Tokyo). Because we have noticed that the transmitral and pulmonary venous flow velocity patterns in subjects <3 years of age were different from those in subjects aged $\geqq 3$ years, the subjects in the present study were divided into 2 age groups: <3 years and $\geqq 3$ years. To examine factors influencing the tricuspid flow velocities including heart rate, we analyzed the relation between the Doppler variables and age or heart rate. Furthermore, stepwise multiple linear regression analysis was performed when a given parameter was found to relate to both age and heart rate. A p value <0.05 was considered statistically significant.

Results

Pulsed Doppler

Fig. 2 shows the age-related changes in the peak E wave, peak A wave, and peak E/A wave. The peak E wave correlated weakly with the logarithm of age ($r=0.42$, $p<0.01$). The peak E wave in the early neonatal period was almost 80% of the older children's values, and increased reaching to 100% by 36 months of age. The peak A wave decreased significantly with increasing age ($r=-0.64$, $p<0.01$). The peak E/A wave increased significantly with age ($r=0.75$, $p<0.01$). Although the peak E wave showed no significant relation with heart rate, the peak A wave wave increased ($r=0.73$, $p<0.01$) and peak E/A wave decreased ($r=-0.76$, $p<0.01$) with increasing heart rate.

Correlations between the Doppler indexes and either age or heart rate in the study subgroups are listed in Table 1. In the age <3 years group ($n=37$), the tricuspid peak E wave, which did not change with heart rate, increased significantly with age ($r=0.52$, $p<0.01$) as shown in Fig. 3. The tricuspid peak A wave did not change with age or heart rate. The tricuspid peak E/A wave was significantly related to age ($r=0.66$) and to a lesser extent to heart rate ($r=-0.44$). Multiple regression analysis showed that the peak E wave and peak E/A wave were mainly affected by age.

In the subjects >3 years, the tricuspid peak E wave did not change with heart rate or age (Fig. 3). The peak A wave did not change with age but correlated significantly with heart rate ($r=0.62$, $p<0.01$). The tricuspid peak E/A wave was significantly related to heart rate ($r=-0.61$, $p<0.01$) and to a lesser extent to age ($r=-0.51$, $p<0.01$).

Tissue Doppler

The mean values for the peak E wave, peak A wave, and the peak E/A wave were 12.8 ± 3.1 cm/seconds, 8.7 ± 2.5 cm/seconds, and 1.59 ± 0.58, respectively. Fig. 4 shows typical examples of the right ventricular tissue Doppler imagings in a neonate and an older child. The flow velocity profiles in neonates were characterized by lower peak E wave and peak E/A wave compared with those in older children. Fig. 5 shows the age-related changes in the peak E wave, peak A wave, and peak E/A wave. The tissue Doppler peak E wave increased significantly with the logarithm of age ($r=0.57$, $p<0.01$), as seen in the relationship between the tricuspid peak E wave and age. The tissue Doppler peak A wave did not change with age. The tissue Doppler peak E/A wave increased significantly with age ($r=0.50$, $p<0.01$). Weaker relations were observed between heart rate and tissue Doppler parameters ($r=0.25$ to 0.41).

Fig. 6 shows the relationships between the tissue Doppler indexes and the transtricuspid inflow indexes. The tissue Doppler peak E wave correlated weakly

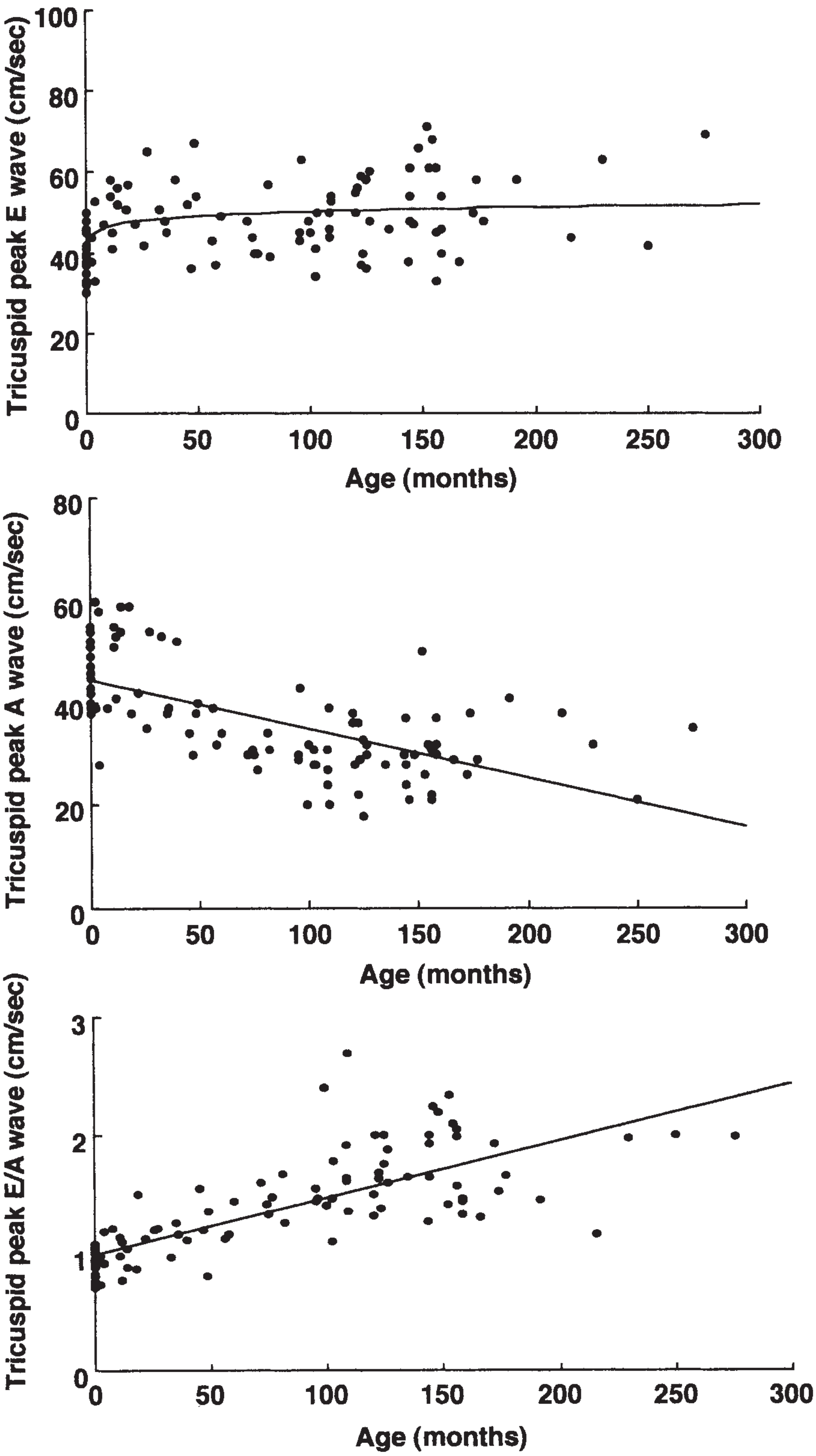

Fig. 2. Relationships between age and the peak E wave, peak A wave, and peak E/A wave of the right.
Age vs. peak E wave, $y=43+3.7\,\mathrm{Log}(X)$, $r=0.42$, $p<0.01$; age vs. peak A wave, $y=44-0.0096\,X$, $r=-0.64$, $p<0.01$; age vs. peak E/A wave; $y=0.99+0.0048\,X$, $r=0.75$, $p<0.01$.

TABLE 1. *Relationships between filling dynamics and age and heart rate*

	<3 years		≧3 years	
	Heart rate	Age	Heart rate	Age
Peak E (cm/seconds) wave	NS	0.52	NS	NS
Peak A (cm/seconds) wave	NS	NS	0.62	NS
Peak E/A (cm/seconds) wave	−0.44	0.66	−0.61	−0.51

NS, not shown.

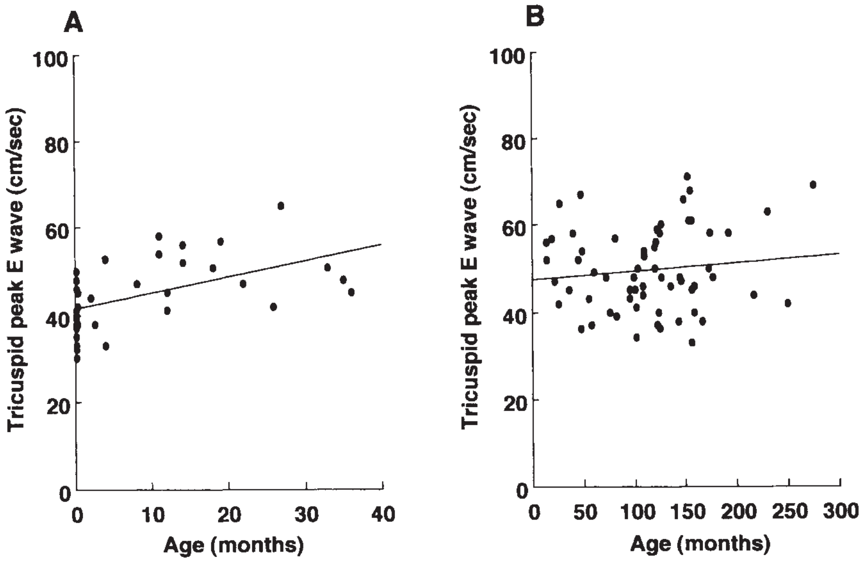

Fig. 3. Age-related changes in the peak E wave in subjects with aged <3 ($y=41+0.38$ X, $r=0.52$, $p<0.01$) and >3 years ($p=$not significant).

with the tricuspid peak E wave ($r=0.41$, $p<0.05$). The tissue Doppler peak A wave did not show a significant correlation with the tricuspid peak A wave. There was a significant correlation between the tissue Doppler peak E/A wave and the tricuspid peak E/A wave ($r=0.56$, $p<0.01$).

DISCUSSION

Several studies in human adults have revealed that Doppler filling patterns in the right ventricle as well as the left ventricle altered with aging (Zoghbi et al. 1990; Iwase et al. 1993). In normal children, however, there is little information about the effect of age on the tricuspid flow velocity and tissue Doppler myocardial velocity patterns. This study demonstrated that the right ventricular diastolic filling was altered by age and heart rate. The tricuspid peak E wave increased with increasing age up to age 3 years while the peak A wave had little changes, resulting an augmentation of the peak E/A wave. As a whole the peak A wave decreased with age, which may reflect the decrease in heart rate with aging. Multiple regression analysis showed that these changes in the tricuspid filling patterns were not affected by heart rate. In contrast, in the subjects >3

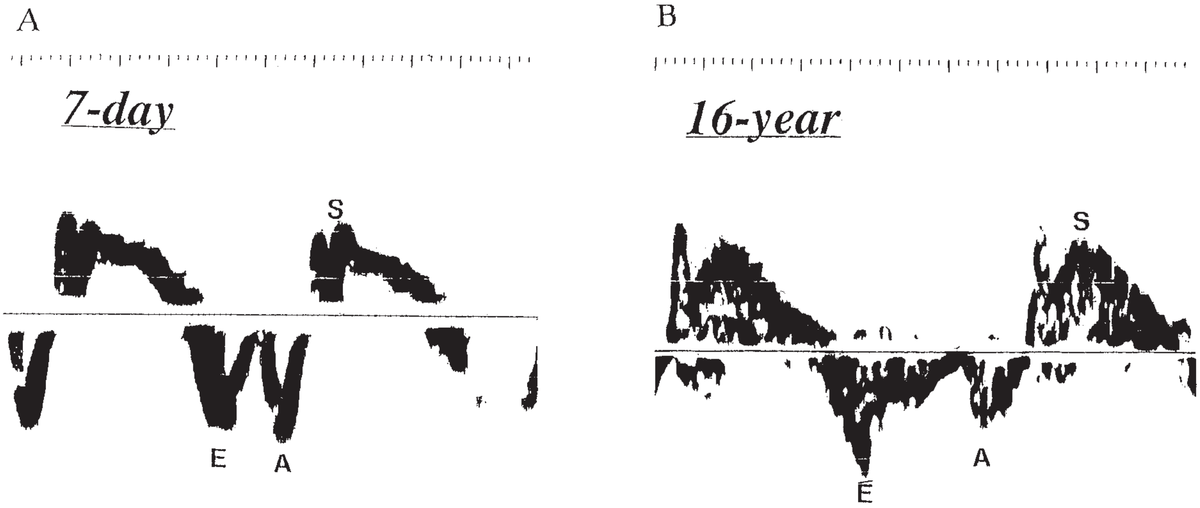

Fig. 4. Typical examples of right ventricular myocardial velocities in a neonate and an older child. Left, 7-day-old; right, 16-year-old.
S, peak myocardial velocity during systole; E, peak myocardial velocity during early diastole; A, peak myocardial velocity during atrial contraction.

years, correlation coefficients between age and peak E wave and peak E/A wave were lower than those in the subjects <3 years. Thus, our present study suggests that age-related changes in the tricuspid flow velocity patterns in our subjects aged <3 years may be different from those in the subjects <3 years.

The typical myocardial velocity profiles of the tissue Doppler imaging are reported to be one main wave during systole and two waves during diastole-one during early filling and the other related to atrial contraction (Oki et al. 1988, 1996; Harada et al. 1995b; Rychik and Tian 1996; Rodriguez et al. 1996; Nagueh et al. 1997; Galiuto et al. 1998). These findings are consistent with the myocardial velocity patterns of tissue Doppler imaging in our study. The mean values for tissue Doppler myocardial velocities of the right ventricle in adults (Galiuto et al. 1998) were similar to our results. The tissue Doppler peak E wave in infants was lower compared with that in older children as shown in Fig. 4. Although the myocardial velocities of the right ventricle in this study weakly correlated with tricuspid flow velocities, the age-related changes in the myocardial velocities were similar to those in the tricuspid flow velocities.

The mechanism of age-related changes in the tricuspid flow velocity patterns is unclear. Previous studies assessing the effect of age on diastolic properties of the heart have predominantly focused on the left ventricle (Gardin et al. 1987; van Dam et al. 1987; Areias et al. 1990; Iwase et al. 1993). Previous echocardiographic and Doppler studies in neonates detected a pattern of mitral velocities showing a lower peak E wave when compared with later normal mitral peak E wave (Gardin et al. 1987; Thomas and Weyman 1991; Harada et al. 1994). Our recent study demonstrated that mitral peak E wave increased to reach to the older children's value by 36 months of age with little change in mitral peak A wave (Gardin et al. 1987). It is generally believed that these flow velocity profiles are

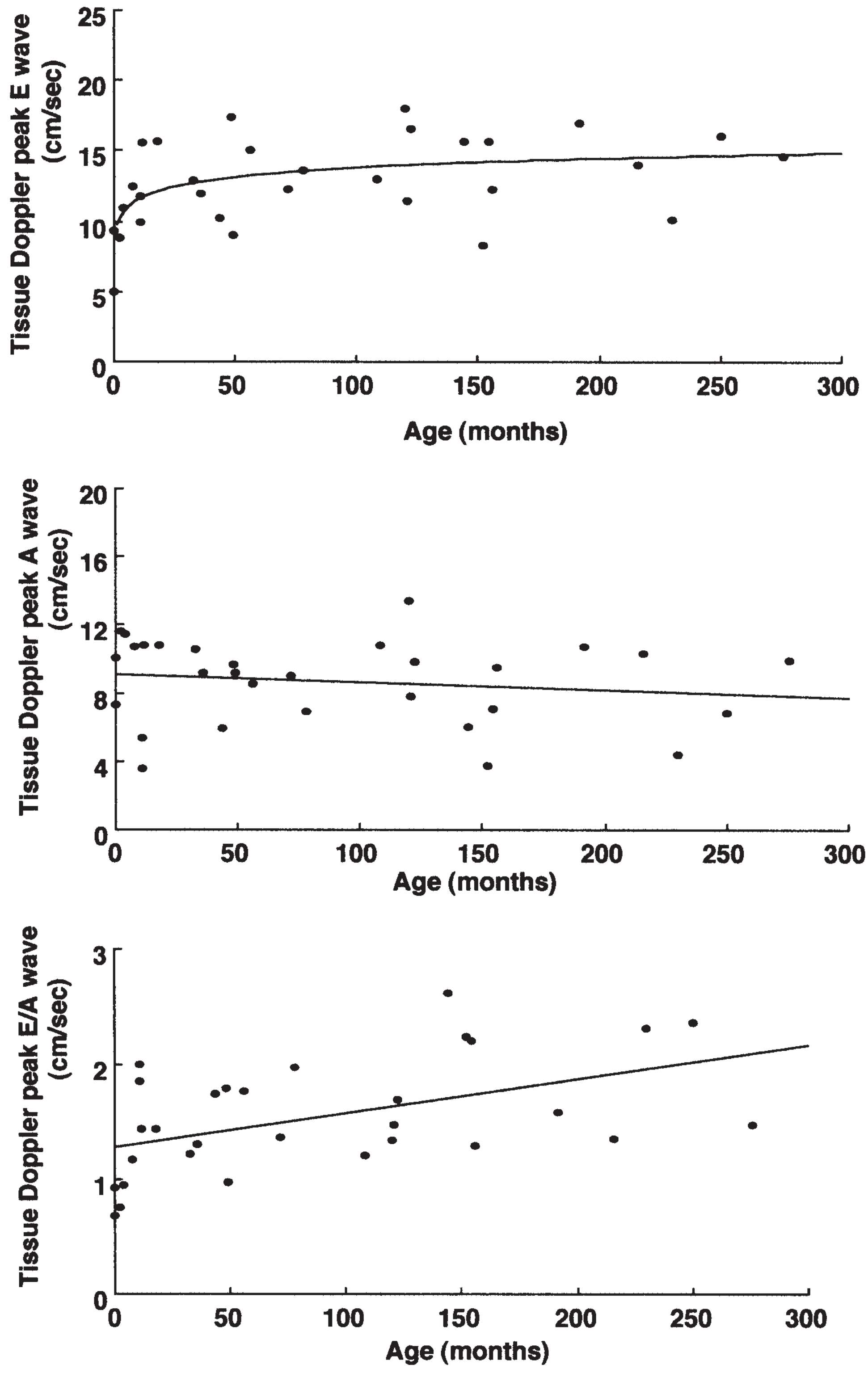

Fig. 5. Age-related changes in myocardial velocities by tissue Doppler imaging. Age vs. peak E wave, $y = 9.3 + 2.2\ \mathrm{Log(X)}$, $r = 0.57$, $p < 0.01$; age vs. peak A wave, not significant; age vs. peak E/A wave, $y = 1.28 + 0.003\ \mathrm{X}$, $r = 0.50$, $p < 0.01$.

caused by changes in pressure gradient between atrium and ventricle during diastole (Thomas and Weyman 1991). In early diastole, both the pressure within atrium and the active process of myocardial relaxation are responsible for this

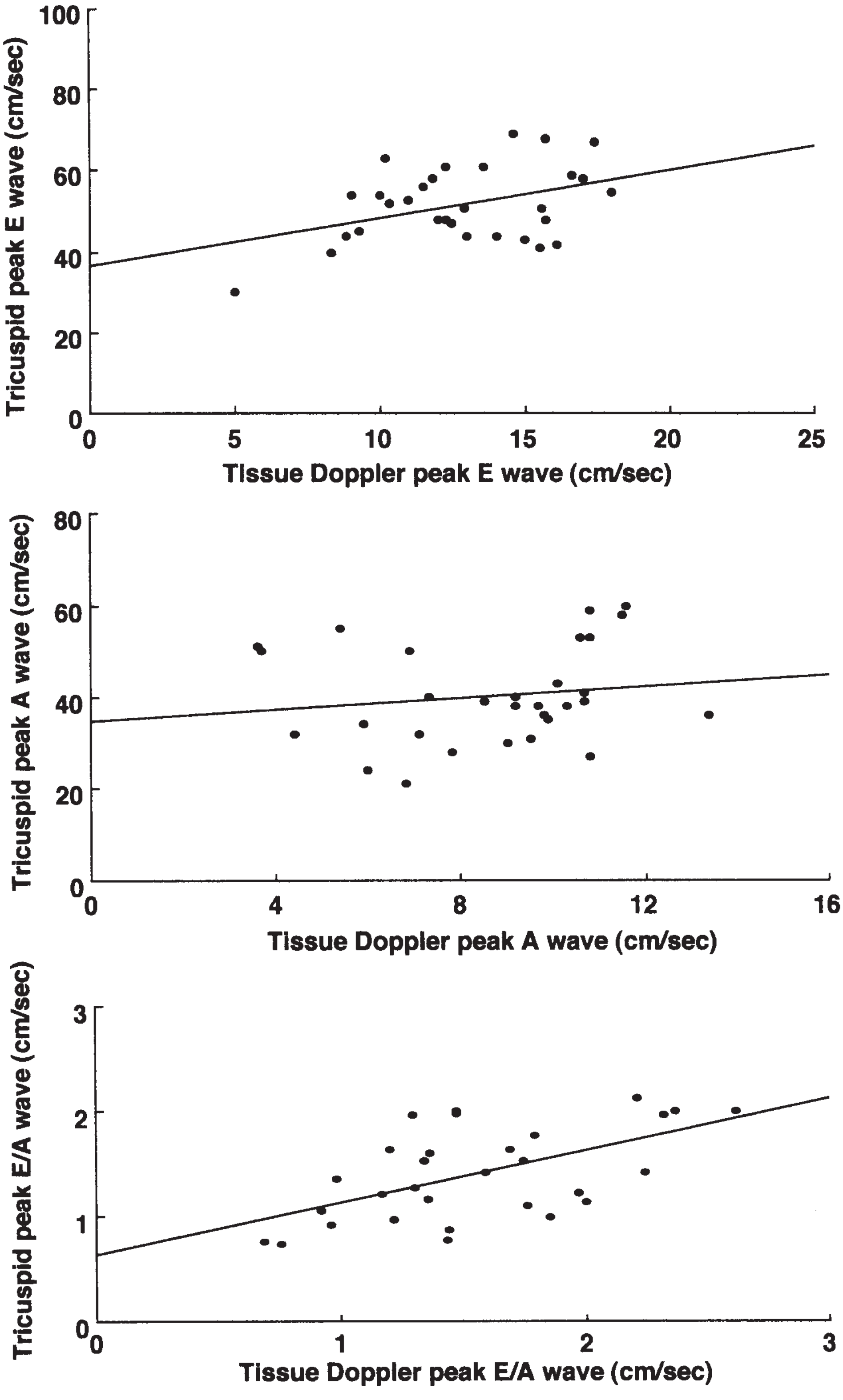

Fig. 6. Relationships between the tissue Doppler indexes and the tricuspid inflow indexes.

Tricuspid E vs. tissue Doppler E, $y=36+1.2$ X, $r=0.41$, $p<0.05$; tricuspid A vs. tissue Doppler A, not significant; tricuspid E/A vs. tissue Doppler E/A, $y=0.63+0.50$ X, $r=0.56$, $p<0.01$.

gradient. An impairment in left ventricular relaxation has been shown to correlate with decreases in both peak E wave and flow velocity time integral of early diastole (Romero et al. 1972). An experimental study demonstrated that there were less active tension and higher passive stiffness in neonates than in adults lambs, suggesting that neonatal myocardium is less compliant than adult myocardium (Suterland et al. 1994). Significant ultrastructural differences between neonate and adult myocardium may explain these age-related changes in ventricular diastolic property (Marijianowski et al. 1994). These maturational changes in left ventricular myocardium can apply to the right ventricle, although we have no data on this regard.

The findings obtained by the tissue Doppler imaging could support the age-related maturation in the right ventricular diastolic function. Myocardial velocities assessed by tissue Doppler imaging have been validated by a comparison with M-mode derived velocities in vivo (Suterland et al. 1994; Rychik and Tian 1996) and by phantom studies in vitro (Suterland et al. 1994; Miyatake et al. 1995). Tissue Doppler imaging has been shown to distinguish myocardial velocities in normal subjects from those with left ventricular hypertrophy and left ventricular diastolic dysfunction (Oki et al. 1988, 1996; Nagueh et al. 1997). In addition, Rodriguez et al. (1996) have recently shown a progressive decline in left ventricular myocardial velocity during early diastole with advancing age, suggesting age-related decreases in left ventricular relaxation. These studies allude to a potential clinical use of tissue Doppler imaging as a tool for evaluating myocardial function.

We demonstrated the age-related alterations in the tricuspid flow velocity patterns and myocardial velocity patterns. Age-related changes in the flow velocity and myocardial velocity patterns in our subjects aged <3 years may be related to age-related maturation in the right ventricular diastolic performance.

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