Original Articles

THE CARDIAC BLOOD SUPPLY–WORKLOAD BALANCE IN CHILDREN

By

Tomoaki Murakami; MD, PhD [1, 2, 3)], Atsuhito Takeda; MD, PhD [2)], Kohta Takei; MD, PhD[2)], Shigeru Tateno; MD, PhD [3)], Yasutaka Kawasoe; MD, PhD [3)], , Koichiro Niwa; MD, PhD [3, 4)]

From

1. Department of Cardiology, Chiba Children's Hospital

2.Department of Pediatrics, Hokkaido University, Graduate School of Medicine

3.Department of Adult Congenital Heart Disease and Pediatric Cardiology, Chiba Cardiovascular Center

4. Department of Cardiology, St. Luke's International Hospital

Corresponding author

Tomoaki Murakami, MD

Department of Cardiology, Chiba Children's Hospital

579-1 Heta-cho, Midori-ku, Chiba 266-0007 Japan

Tel: +81-43-292-2111 Fax: +81-43-292-3815

E-mail address: murat@seagreen.ocn.ne.jp

Abstract

It is well known that the reflected pressure wave in small children returns earlier than that in adolescent. The reason of early return of the reflected pressure wave in infancy is their height. The short distance between heart and reflection point makes the reflected pressure wave returning to the heart earlier. In adult, the early return (during systole) of the reflected pressure wave means disadvantage to cardiac blood supply-workload balance. The purpose of this study is to clarify whether the early return of the reflected pressure wave in small children impairs the cardiac blood supply-workload balance.

This study enrolled 37 small left to right shunt patients with normal aortic circulation below 15 years of age. The aortic pressure waveform was recorded using a pressure sensor mounted catheter, and augmentation index and subendocardial viability ratio were calculated.

The age of patients was 6.1 ± 3.2 years old. The augmentation index was 8.7 ± 14.3 % and the index had a negative correlation with patients' age ($r = -0.6243$, $p<0.0001$). The subendocardial viability ratio, which means the cardiac blood supply-workload balance, was 0.92 ± 0.14 and the index had a positive relationship with patients' age ($r = 0.6435$, $p<0.0001$).

The cardiac blood supply–workload balance gradually improves from infancy to young adulthood. And one of the causes of the unfavorable cardiac blood supply – workload balance in infancy would be the accelerated aortic pressure wave reflection due to their short height.

Key words

Aging • Growth • Aortic function • Central hemodynamics

Introduction

One of the recent topics in blood pressure study is central hemodynamics [1]. It has been recognized that measurement of cuff blood pressure on brachial artery is insufficient in management of hypertensive patients. In other words, the importance of central blood pressure waveform evaluation has been realized. The difference between the pressure waveform in brachial artery and that in ascending aorta is attributed to pressure wave reflection, and early return of the reflected pressure wave contributes to an increase in cardiovascular diseases [2-5].

It is well known that the pressure waveform in children resembles that in aged person [6,7]. That is to say, the reflected pressure wave returns to heart earlier in small children than adolescent (Figure 1). The late return of the reflected pressure wave (in diastole) enhances coronary blood flow ("diastolic hump" of central blood pressure waveform). Meanwhile, the early return of the reflected pressure wave (in systole) impairs arterial and ventricular function. The opposite directional reflected pressure wave that returns to heart during systole interferes left ventricular ejection and increases workload of left ventricle.

The mechanism of early return of reflected pressure wave in small children would be due to their short height [8]. The short arterial tree places the major reflection site closer to the heart. In adult, the shortness was associated with the early return of reflected wave [9], an increase in augmentation index [10,11], and a low coronary blood supply–workload balance [12]. Moreover, it is reported that short height has been associated with an increased risk of cardiovascular disease [13-17].

Therefore, the early return of the reflected pressure wave to the heart could increase myocardial oxygen requirement, reduce the capacity for left ventricular myocardial perfusion,

and cause cardiovascular diseases. The coronary artery disease is rare during childhood, but the question arises whether the early pressure wave reflection in small children is also disadvantage to the cardiac blood supply - workload balance. To clarify this problem, we analyzed central blood pressure waveforms in children.

Materials and Methods

Study Subjects

This study enrolled 43 patients who had undergone cardiac catheterization for small left-to-right shunt disorders (pulmonary-systemic flow ratio < 1.5) below 15 years of age. Because it is reported that an augmentation index, which means the degree of aortic pressure wave reflection, decreases with age from infancy to mid-teen, we examined the patients below 15 years of age [8]. No patients had any significant leakage at the aortic level (eg, patent ductus arteriosus, aortic regurgitation, etc). All patients were in good health, had no symptom of cardiovascular dysfunction and were not taking any medication. These patients were adopted as “normal ” aortic circulation patients in this study[8]. In order to eliminate the influence of obesity, patients whose body mass index exceeds the age-gender-specific 95th percentile were excluded. No patients demonstrated hypertension. Finally, 37 patients aged 0–14 years, whose pulmonary-systemic flow ratio was 1.18 ± 0.19, were selected for anaysis (Table 1). These patients were affected with ventricular septal defect (31) or atrial septal defect (6).

Measurements

Cardiac catheterization was performed by femoral arterial puncture. The ascending aortic pressure was recorded using a pressure sensor mounted catheter (model SPC-464D, Millar Instrument, Inc., Houston, Texas) before the injection of any contrast material. The ascending aortic pressure waveform was recorded at 1 vertebral body thickness higher than the aortic

valve. The waveform was recorded on a hard disk through an analog-digital converter, and it was also simultaneously recorded with the electrocardiogram.

Aortic Pressure Waveform Analysis

From the recorded pressure waveforms, systolic blood pressure, diastolic blood pressure, and pulse pressure were measured in each patient. Moreover, augmentation index and subendocardial viability ratio were calculated.

Augmentation Index

In order to measure the intense of pressure wave reflection, the augmentation index was calculated [8]. The inflection points were obtained by the fourth derivatives of the original pressure pulse waveforms (Figure 2) [18].

Subendocardial Viability Ratio

The subendocardium is thought to be more sensitive to a shortage of blood supply than the subepicardium. Buckberg and colleagues demonstrated that the ratio of the diastolic phase area (diastolic pressure time index) to the area of the systolic phase (tension time index) in the central aortic pressure profile had a close correlation with the blood supply to the subendocardium [19,20]. This ratio was designated as the subendocardial viability ratio (Figure 3):

Subendocardial viability ratio

= diastolic pressure time index / tension time index

The diastolic pressure time index was obtained by measuring the area under the diastolic aortic pressure curve and subtracting from it the mean left atrial pressure (assumed to be equal to the left ventricular diastolic pressure) multiplied by the diastolic time. When the left atrial pressure was not recorded, we used the pulmonary capillary wedge pressure instead. The tension time index was obtained by measuring the area under the aortic systolic

pressure curve and it equals the mean aortic systolic pressure multiplied by the duration of systole.

Statistical Analysis

All data were presented as the mean value ± standard deviation. A regression analysis was used to detemine the correlation between subendocardial viability index and clinical variables. PRISM software version 4.0c (Graph Pad Software, Inc. La Jolla, CA, USA) was used for all statistical analyses. A p value less than 0.05 was considered to be statistically significant.

All subjects gave their written informed consent, and the Chiba Children's Hospital and the Chiba Cardiovascular Center ethics committees have approved the study protocol.

Results

The systolic blood pressure was 91.4 ± 11.2 mmHg and the diastolic blood pressure was 58.2 ± 9.6 mmHg. These two parameters had a significant positive relationship with the patients' age ($r = 0.5497$, $p = 0.0004$ and $r = 0.4924$, $p = 0.0020$, respectively). The augmentation index was 8.7 ± 14.3 %, and the index had a negative correlation with the patients' age ($r = -0.6243$, $p < 0.0001$) and their height ($r = -0.6730$, $p < 0.0001$) (Figure 4).

The subendocardial viability ratio, which means the cardiac blood supply – workload balance was 0.92 ± 0.14. The tension time index (i.e. cardiac workload, $r = 0.6818$, $p < 0.0001$) and the diastolic pressure time index (i.e. cardiac blood supply, $r = 0.7693$, $p < 0.0001$) had a significant positive relationship with the patients' age. The subendocardial viability ratio had a positive correlation with the patient's age ($r = 0.6435$, $p < 0.0001$) (Figure 5). Table 2 demonstrated the correlation of subendocardial viability ratio with clinical variables.

Discussion

The present study demonstrates that the subendocardial viability ratio, which means the cardiac blood supply–workload balance, in children gradually increases from infancy to young adulthood.

The subendocardial viability ratio is one of the most sensitive parameter in cardiac blood supply–workload balance. It is reported that the subendocardial viability ratio suggests the likelihood of subendocardial ischemia in normal hearts if the ratio is <0.45 [21]. In present study, no patient shows their subendocardial viability ratio under 0.45, which means subendocardial ischemia, although the ratio was significantly low in small children. However, it can be imagined that it must become a serious illness, once a coronary obstruction occurs in youth. Fortunately, such condition is uncommon, because atherosclerotic lesion is unusual and ischemic heart diseases are rare during childhood.

Table 2 demonstrates the correlation between subendocardial viability ratio and clinical variables. Although multiple regression analysis would give us more important information, it is difficult to perform it because the clinical variables are strongly correlated each other. For the same reasons, we should read this Table carefully. For example, it is strange that there is a positive correlation between subendocardial viability ratio and body weight. This result should be influenced by body height, because the subjects did not contain an obese child and there was a strong correlation between height and weight ($r = 0.9374$, $P < 0.0001$). Judging from cautious interpretation of this Table, we consider two parameters are responsible for low subendocardial viability ratio during childhood: heart rate and body

height. A rapid heart rate means shortness of diastolic phase, and it is disadvantage for coronary circulation. A short body height means the early return of the reflected pressure wave to the heart. As mentioned above, it is impossible to prove that these parameters certainly responsible for low subendocardial viability ratio in this study. Because our data were derived from healthy subjects, there were significant relationships between age and heart rate ($r = 05883$, $p=0.0001$), age and body height ($r = 0.9700$, $p<0.0001$), and heart rate and body height (0.5670, $p = 0.0003$). Therefore, it is difficult to show that the heart rate and body height determine the subendocardial viability ratio. However, it is reported that the high heart rate and low body height enhance the pressure wave reflection. Those reports convince us of the significant relationship between the two parameters and the subendocardial viability ratio.

It is thought that one of the reasons why the cardiac blood supply–workload balance is unfavorable to the heart during infancy relative to that during adolescent is the high aortic pressure wave reflection in infancy. Figure 6 demonstrates the relationship between the augmentation index and the subendocardial viability ratio. We previously reported that the aortic pressure wave reflection is accelerated during childhood, and the value was negatively correlated with the body height [8]. In a short person, a short arterial tree places the major reflection site closer to the heart, therefore, the reflected pressure wave returns to heart earlier than that in a tall person. In animal heart model changing the time of returning reflection wave, the shortened time was associated with a reduction in stroke volume and coronary artery driving pressure [22]. There are two possible mechanisms that the early return of the reflected pressure wave deteriorates the cardiac blood supply–workload balance. One is the increment of afterload to left ventricle. Because the reflected pressure wave reaches left ventricle during aortic valve open (in systole), it impedes left ventricular ejection and

increases left ventricular workload. Another mechanism is the impairment of diastolic runoff. More than half of the ejected blood flow from left ventricle stored in the aorta during systole and the reserved blood is expelled by the reflected pressure wave during diastole. One of the most important organs perfused during diastole is the heart. Because late return (during diastole) of the reflected pressure wave to the heart augments the phenomenon, the early return (in systole) of the reflected pressure wave is disadvantage to coronary circulation. Therefore, the early return of aortic pressure wave reflection could make the cardiac blood supply –workload balance worse.

Is there any advantage concerning early return of pressure wave reflection during infancy? We would like to propose a hypothesis that the early return of the aortic pressure wave reflection helps cardiac growth [8]. It is said that the increase of circulatory blood volume, which is caused by somatic growth, promotes cardiac growth. However, the augmentation of the circulatory blood volume only affects to the growing heart as volume load. For growth of the heart, pressure load is also essential. It is reasonable to assume that the enhancement of the pressure wave reflection is the pressure stimulus for cardiac growth until the body height reaches its maximum, because the period is almost free from ischemic heart diseases. Further investigations are needed to clarify the growth of arterial system and heart.

One of the limitations of this study is that the subjects had small left-to-right shunt. Of course it is impossible to perform cardiac catheterization in children with normal heart. However, it could be an important problem, because we examined the cardiac blood supply-workload balance of the subjects in this study. When we regard a product of systolic pressure times blood flow as cardiac workload, the increment of the cardiac workload in our subjects,

which is caused by left-to right shunt, is only 3%, because the increased blood flow due to the shunt is ejected to pulmonary circulation, which is low pressure circulation. Therefore, the influence of left-to-right shunt in this study would be within allowable range.

In conclusion, the subendocardial viability ratio, which means the cardiac blood supply–workload balance is gradually increases from infancy to young adulthood. The early return of the reflected pressure wave to the heart due to short statue would be disadvantage to cardiac blood supply–workload balance in youth.

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Table 1 Demographic data

Age (years)	6.1 ± 3.2
Gender (male/female)	23/14
Height (cm)	111.4 ± 21.0
Weight (kg)	21.0 ± 9.8
Body Mass Index	16.1 ± 1.7

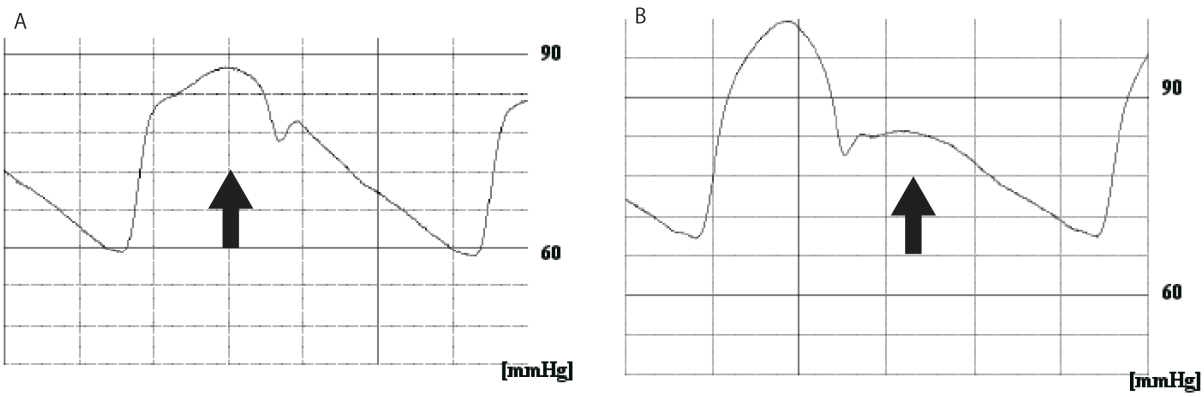
Table 2. Correlation coefficient of subendocardial viability ratio with clinical variables.

Variables	r	p value
age	0.6435	<0.0001
height	0.6528	<0.0001
weight	0.5117	0.0012
BMI	0.1310	NS
SBP	0.3164	NS
DBP	0.4174	0.0102
PP	−0.0855	NS
HR	−0.7303	<0.0001
AI	−0.4047	0.013

AI, augmentation index; BMI, body mass index; DBP, diastolic blood pressure; HR, heart rate; PP, pulse pressure; SBP, systolic blood pressure.

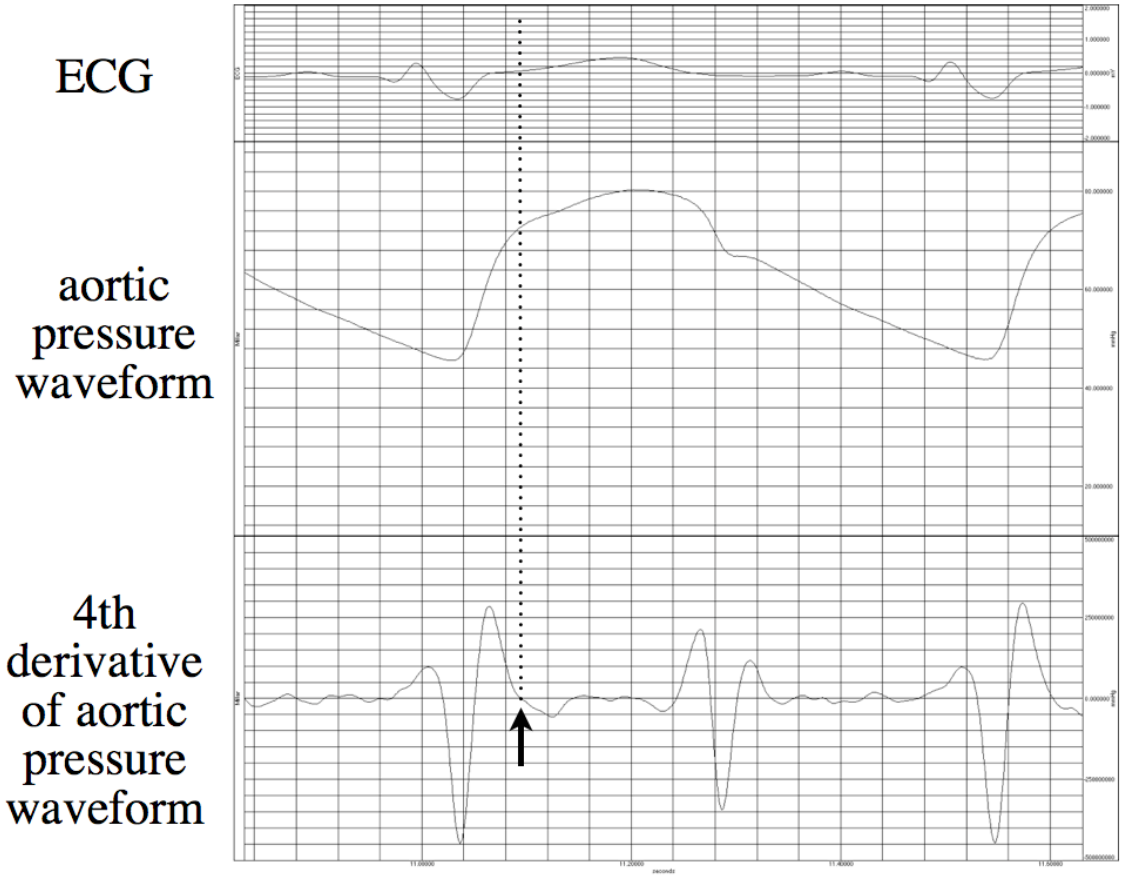
Figure Legends

Figure 1



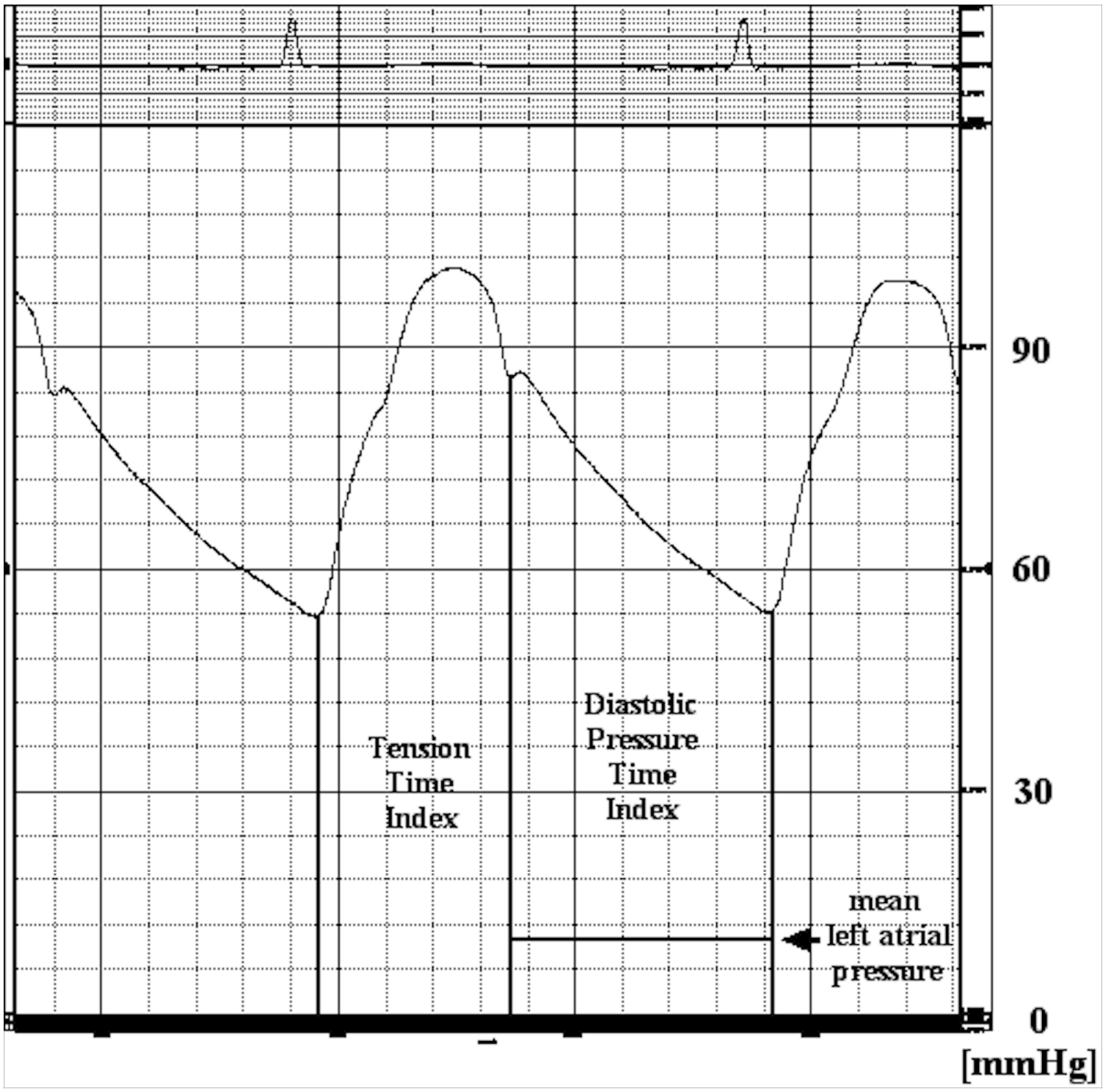
Central blood pressure waveform in children. A, 4 years old, body height 100cm, augmentation index 12%. B, 12 years old, body height 163cm, augmentation index -52%. The arrows indicate the reflected pressure wave. In the panel A, the reflection wave returns in systole. It becomes the increment of left ventricular afterload. In panel B, the reflection wave returns in diastole (diastolic hump) and it could enhance the diastolic blood flow, especially coronary blood flow.

Figure 2



Determination of the inflection point. The inflection points were obtained by the fourth derivatives of the original pressure pulse waveforms [18].

Figure 3

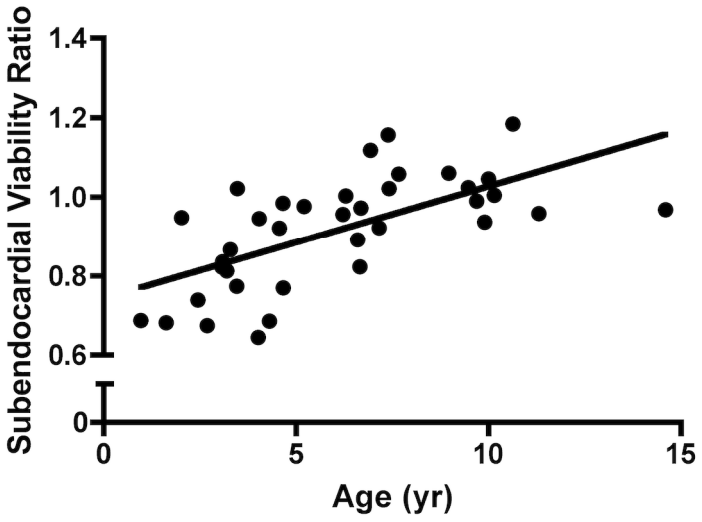


Measurement of diastolic pressure time index and tension time index.

Figure 4

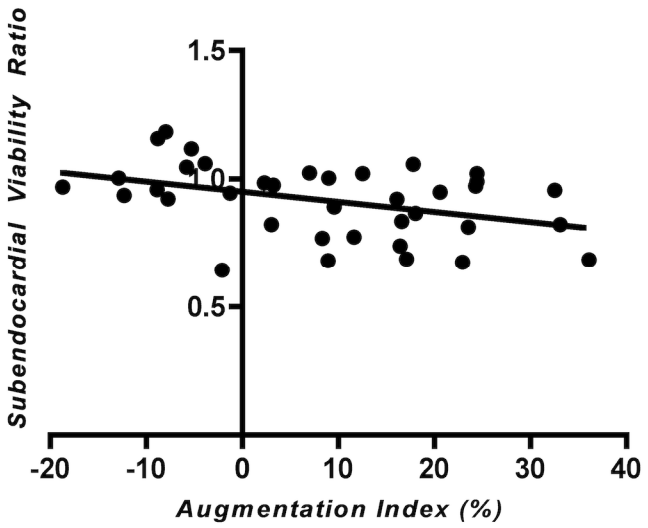
Relationship between patients' age and augmentation index. There is a significant negative correlation between the two parameters ($r = -0.6243$, $p < 0.0001$).

Figure 5



Relationship between patients' age and subendocardial viability ratio. There is a significant positive relationship between the two parameters ($r = 0.6435$, $p < 0.0001$).

Figure 6



Relationship between augmentation index and subendocardial viability ratio. There is a significant negative relationship between the two parameters (r = -0.4047, p=0.0130).