Ventricular Wall Thickness and Blood Pressure Values in Normal Cynomolgus Monkeys

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ABSTRACT. In order to clarify the relationship between heart morphology and blood pressure, I examined the mutual correlation between the ventricular wall thicknesses of heart and body weight, heart weight, and arterial blood pressure in 15 normal male cynomolgus monkeys. The results obtained were as follows; (1) The mean and standard deviation of the arterial blood pressure was 68 ± 8 mmHg at diastolic time and 124 ± 12 mmHg at systolic time, respectively, and that of pulse rate was 227 ± 17 beats per min under non-anesthesia. In addition, the mean and standard deviation of the arterial blood pressure was 55 ± 11 mmHg at diastolic time and 102 ± 18 mmHg at systolic time, respectively, and that of pulse rate was 197 ± 17 beats per min under general anesthesia. (2) The mean and standard deviation of the left ventricular wall thickness was 6.6 ± 1.1 mm at anterior, 5.3 ± 1.0 mm at posterior, 5.9 ± 0.9 mm at lateral, 5.4 ± 1.2 mm at the interventricular septum, and that of the right ventricular wall thickness was 2.4 ± 0.5 mm at anterior. (3) The mean and standard deviation of body weight was 4.1 ± 0.7 kg, and that of heart weight was 16.5 ± 3.1 g. (4) The heart weight and interventricular septum thickness correlated significantly to body weight, respectively. (5) There was no significant correlation between arterial blood pressure and the ventricular wall thickness. Further study should be necessary in more normal monkeys, together with abnormal ones with hypertension or cardiac hypertrophy, in order to evaluate the relationship between heart morphology and blood pressure. — KEY WORDS: blood pressure, cynomolgus monkey, ventricular wall thickness.


Electrocardiography has been commonly conducted not only in dogs [3, 13, 15, 20] and small rodents [8, 14, 24, 26] but also in monkeys [7, 12, 19, 22, 23], and occasionally applied to toxicity studies [1, 14, 27]. Electrocardiography is the most useful diagnosing method for arrhythmias and electrical disturbance in the heart. However, it is considered less useful in the morphological changes of the heart than X-ray and echocardiography.

Echocardiography is regarded as one of the most practical method for diagnosing cardiac hypertrophy since the atrial and ventricular wall thicknesses, the size of cardiac cavities, and the shape of valves as well as the shape of heart can be directly determined, and increasingly popular among veterinary clinicians [4, 5, 9, 10, 18, 25] who are interested in heart diseases. However, the normal ventricular wall thicknesses have yet been established neither in monkeys nor in dogs, except for a few morphological data in dogs [11, 17] enough to evaluate practically echocardiographic criteria.

In the present study, I directly measured the ventricular wall thicknesses of the heart and noninvasively measured the systemic blood pressure, and examined the mutual correlation between the thicknesses and blood pressure, body weight, and heart weight in cynomolgus monkeys in order to obtain the basic data which could be useful for the cardiotoxicity study.

MATERIALS AND METHODS

Animals and housing: Fifteen male clinically healthy cynomolgus monkeys (Macaca fascicularis) from Indonesia were used in this study. Estimated age of the animals was 3 to 6 years. Body weights ranged from 2.9 to 5.5 kg at the blood pressure measurement.

All animals were housed in individual cages in an animal room maintained at a temperature of 23–25°C and a relative humidity of 40–80%. Each animal was given 100 g of monkey chow (CMK-1, CLEA Japan, Inc.) daily and tap water ad libitum.

Anesthesia: Prior to the autopsy, 25 mg/kg of thiopental sodium (Ravonal, Tanabe Selyaku Co., Ltd., Japan) was intravenously administered into each animal for general anesthesia.

Arterial blood pressure: Arterial blood pressure was measured noninvasively by automated oscilometric method with a cuff placed around the upper arm using blood pressure instrument (BX-5, Nihon Kohrin, Japan) shortly before and after general anesthesia, after each animal was restrained in a monkey-chair.

Measurement of the ventricular wall thickness: Animals were sacrificed by euthanasia after the measurement of blood pressure. Body weight and heart weight were weighed after blood was washed out. The heart was fixed in 10% formalin and dissected at the level between the chordal tendon and the papillary muscle, and then the thicknesses of the anterior, posterior, lateral wall of left ventricle, interventricular septum, and anterior wall of right ventricle were measured in millimeter at the same level (Fig.1).

Statistical analysis: Statistical analysis was performed by regression and correlation methods between the ventricular wall thicknesses and blood pressure, body weight, and heart weight using the software package StatView (Abacus Concepts, Inc.). Comparison was also performed between the values of blood pressure before and after general
anesthesia by paired Student's t-test. Statistically significant
difference was considered if P value was less than 0.05.

RESULTS

**Body weight and heart weight:** The mean and standard
deviation of body weight was 4.1 ± 0.7 kg, and that of heart
weight was 16.5 ± 3.1 g, respectively. A significant
correlation was found between body weight and heart weight
(r=0.91, p<0.001) (Fig. 2).

**Arterial blood pressure:** As shown in Table 1, the
systemic blood pressure was significantly lower under
general anesthesia than under non-anesthesia. The mean
and standard deviation of blood pressure and pulse rate were
68 ± 8 mmHg at diastolic time, 124 ± 12 mmHg at systolic
time, and 227 ± 17 beats per min under non-anesthesia,
respectively, and 55 ± 11 mmHg at diastolic time, 102 ± 18
mmHg at systolic time, and 197 ± 17 beats per min under
general anesthesia, respectively. There was no significant
correlation between the ventricular wall thickness and arterial
blood pressure.

**Ventricular wall thickness:** As shown in Table 2, the mean
and standard deviation of the left ventricular wall thicknesses
was 6.6 ± 1.1 mm at anterior, 5.3 ± 1.0 mm at posterior, 5.9
± 0.9 mm at lateral, 5.4 ± 1.2 mm at the interventricular
septum, and that of the right ventricular wall thickness was
2.4 ± 0.5 mm at anterior. A significant correlation was found
between body weight and interventricular septum wall
thickness (r=0.54, p<0.05) (Fig. 3).

DISCUSSION

In order to assess appropriately the significance of changes
observed, it is imperative to aware of normal variations and of spontaneously occurring diseases in
animals used in toxicity studies. However, to the best of
my knowledge, the data on the normal ventricular wall
thicknesses have not been established in monkeys enough

![Fig. 1. The parts measured for the ventricular wall thickness in
cynomolgus monkey. 1: Anterior wall of left ventricle, 2:
Lateral wall of left ventricle, 3: Posterior wall of left
ventricle, 4: Interventricular septum, 5: Anterior wall of right
ventricle.](image)

![Fig. 2. Correlation between body weight and heart weight in
cynomolgus monkeys.](image)

### Table 1. The mean and standard deviation of arterial blood pressure shortly before and after general anesthesia

<table>
<thead>
<tr>
<th></th>
<th>Before general anesthesia</th>
<th>After general anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B.P. (mmHg)</td>
<td>Pulse rate (beats/min)</td>
</tr>
<tr>
<td></td>
<td>Diastolic</td>
<td>Systolic</td>
</tr>
<tr>
<td>Mean</td>
<td>68</td>
<td>124</td>
</tr>
<tr>
<td>S.D.</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Max.</td>
<td>78</td>
<td>143</td>
</tr>
<tr>
<td>Min.</td>
<td>50</td>
<td>98</td>
</tr>
<tr>
<td>C.L.</td>
<td>64-73</td>
<td>117-131</td>
</tr>
</tbody>
</table>

a) Arterial blood pressure, b) Standard deviation, c) Maximum, d) Minimum, e) 95% confidence limits.
* and **, Significantly different from the data before general anesthesia (p<0.05 and 0.01, respectively).
Table 2. The mean and standard deviation of ventricular wall thickness in cynomolgus monkeys

<table>
<thead>
<tr>
<th>(mm)</th>
<th>Wall thickness</th>
<th>Left ventricle</th>
<th>Interventricular septum</th>
<th>Mean wall thickness of left ventricle</th>
<th>Right ventricle</th>
<th>Anterior</th>
<th>Lateral</th>
<th>Posterior</th>
<th>Anterior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>6.6</td>
<td>5.9</td>
<td>5.3</td>
<td>5.4</td>
<td>5.8</td>
<td>2.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.D.</td>
<td>1.1</td>
<td>0.9</td>
<td>1.0</td>
<td>1.2</td>
<td>0.8</td>
<td>0.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max.</td>
<td>8.0</td>
<td>7.5</td>
<td>7.0</td>
<td>9.0</td>
<td>7.6</td>
<td>3.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min.</td>
<td>5.0</td>
<td>4.0</td>
<td>4.0</td>
<td>4.0</td>
<td>4.5</td>
<td>2.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C.L.</td>
<td>6.0–7.2</td>
<td>5.4–6.4</td>
<td>4.8–5.9</td>
<td>5.4–6.3</td>
<td>2.1–2.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a) Standard deviation, b) Maximum, c) Minimum, d) 95% confidence limits.

to save as practical criteria for the diagnosis of cardiac hypertrophy. For routine toxicologic studies quantitative measurements at necropsy are usually limited to total heart weight and the heart-to-body weight ratio. In a certain case, however, such special measurements as weight of the free walls of the left and right ventricles and the interventricular septum, volume of the total heart, and thickness of the free walls of individual chambers and the septum, etc. should be made in order to avoid erroneous subjective impressions [16].

In the present study, the mean ventricular wall thicknesses were 5.3 to 6.6 mm at the left, 5.4 mm at the interventricular septum, and 2.4 mm at the right, respectively. A significant correlation was found between body weight and interventricular septum wall thickness as well as heart weight, which is universally known in the heart morphology. Concerning the heart weight to body weight ratio, however, the wide variation in the value of normal dogs limits the usefulness of this measure as an indication of cardiac hypertrophy even in dogs [2]. Therefore, the thickness of free walls of the chambers and septum would be rather useful than the relative heart weight for the diagnosis of cardiac hypertrophy.

The present study revealed no definite correlation between the mean arterial blood pressure and the ventricular wall thickness in monkeys, which was similar to the findings in dogs [11]. Systemic blood pressure is generally considered to raise with aging and to be a close correlation to cardiac hypertrophy, which would not agree with the present results partly because elder monkeys or abnormal monkeys with cardiac hypertrophy were not included in the present study.

Noninvasive blood pressure measurement has been already conducted in dogs [2, 6, 21] and monkeys [6]. The currently available blood pressure measurement devices are grouped as either manual, semiautomatic, or automatic [6]. The instrument used in the present study was fully automatic one, but it has not been determined yet whether the automatic noninvasive-device is practically most applicable to monkeys or not in toxicological research. It is generally necessary to select appropriate devices and to train animals to the measurement method in order to gain more accurate data on blood pressure [6, 21]. In the present study, however, was each monkey not trained to the measurement method. Therefore, blood pressure was noninvasively measured both shortly before and after general anesthesia to see the data variations between individuals. The results obtained here showed that the systemic blood pressure was significantly lower under general anesthesia than under non-anesthesia, which is universally recognized, and that the data in anesthetized animals were quite more varied than I had expected before. Since anesthetized animals would occasionally give unreasonable blood pressure readings attributable to the drug, I excluded the data measured in anesthetized animals from evaluating the mutual correlation between heart morphology and blood pressure.

In summary, the present results could give a clue to estimate the heart morphology in monkeys, but further study should be necessary in more normal monkeys, together with abnormal ones with hypertension or cardiac hypertrophy.

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