**Effects of Heart Rate on Ventricular Performance, Myocardial Contractile State and Coronary Circulation**

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IKEDA, S. *Effects of Heart Rate on Ventricular Performance, Myocardial Contractile State and Coronary Circulation*. Tohoku J. exp. Med., 1974, 112 (1), 89-100 — Effects of heart rate on ventricular performance, myocardial contractile state and coronary circulation were studied under constant cardiac output in right heart by-passed anesthetized dogs. Myocardial contractile state (Vmax) was elevated as heart rate increased, and this was considered to play an important role in impeding further increase of systolic time ratio which would have occurred unless this elevation had occurred. Myocardial oxygen consumption (MVO₂) was mainly influenced by heart rate, left ventricular systolic peak pressure and the contractile state of the left ventricle, but neither by stroke volume of the left ventricle nor left ventricular work. After administration of propranolol, the left ventricle was deteriorated at tachycardia more than 210 beats per minute, and Vmax did not rise at such a tachycardia. These results suggest that adrenergic beta-receptor plays an important role in augmenting the contractile state of the left ventricle and in preventing it from being deteriorated at tachycardia.

*Keywords: heart rate; myocardial contractility; coronary circulation; myocardial oxygen consumption; propranolol*

Bowditch (1871) reported a staircase phenomenon in the frog ventricle. That is, when the ventricle was stimulated at a constant rate, the strength of contraction reached a plateau, and when it was stimulated at a faster or slower rate, the strength reached a higher or lower plateau, respectively. This phenomenon was demonstrated in mammalian cardiac muscles (Woodworth 1902; Abbott and Mommaerts 1959; Blinks and Koch-Weser 1961; Sonnenblick 1962). The effects of heart rate on the intact pumping ventricle have also been examined, but the conclusions are controversial. Sarnoff et al. (1963), Mitchell et al. (1963 a) and Covell et al. (1967) concluded that myocardial contractility was increased as heart rate increased, while Noble et al. (1966, 1969) reported that it was not altered by changes in heart rate in conscious dogs. On the other hand, it is generally accepted that coronary circulation is influenced greatly by heart rate and ventricular performance.

This experiment was designed to ascertain whether the changes in heart rate varies the myocardial contractile state and which factors contribute to alteration...
of coronary blood flow and myocardial oxygen consumption. Heart rate was changed by atrial pacing, and the left ventricular pressure, its dp/dt and the total coronary venous return were measured in right heart by-passed dogs. The experiment was also performed after administration of propranolol in order to ascertain whether the activation of beta-receptor mediates the effects of heart rate on myocardial contractile state, ventricular performance and coronary circulation.

METHOD

Eight mongrel dogs of both sexes weighing from 12 to 20 kg were anesthetized with pentobarbital sodium (30 mg/kg) given intravenously. Ventilation was provided by a positive pressure respirator (Fukuda, RE-65AN). A transverse bilateral thoracotomy transecting the sternum was performed in the fourth or fifth intercostal space. The pericardium was incised widely and arranged to cradle the heart. The animals were heparinized (3–5 mg/kg). The venae cavae were cannulated and venous return was diverted into a reservoir, from which the blood was supplied to the pulmonary artery through a cannula inserted via the right ventricular outflow tract (Fig. 1). Fresh blood from donor dogs was used to prime the reservoir and circuit. Coronary blood flow was measured by collection of the right ventricular drainage, representing total coronary blood flow minus left ventricular Thebesian vein drainage. The region of sinoatrial node was excised, and the pacing electrodes connected to an impulse generator (Nihon Kohden MSE-20) were sutured to the right auricular appendage.

For the left ventricular pressure measurement, a 10 cm long green KIFA catheter was inserted into the left ventricle through the apical dimple, and was attached directly to a strain-gauge transducer (Toyo Sokki, LUP). The first derivatives of left ventricular pressure pulse (dp/dt) were computed electrically by means of a differentiating circuit (Nihon Kohden) which had a time constant of 3 msec. The pressure of the aortic arch was

Fig. 1. Diagram of the preparation. Venous return drains from the venae cavae to a reservoir, from which it is returned by a pump to the pulmonary artery (PA). Coronary blood flow is measured by collection of the right ventricle (RV) drainage. Strain gauge pressure transducers are attached directly to the catheters inserted into the left ventricle (LV), the left atrium (LA), and the aorta (Aor). Pacing electrodes connected to an impulse generator are sutured to the right auricular appendage.
Fig. 2. Simultaneous high speed recordings of high fidelity left ventricular pressure pulse (LV), its first derivative (dp/dt), electrocardiogram (ECG), aortic pressure pulse (A) and left atrial pressure pulse (LA) at paper speed of 200 mm/sec. Heart rate was controlled at 166/min.

measured through a catheter introduced via the femoral artery. The left atrial pressure was measured by a catheter via the left appendage. The pressure curves, dp/dt, and electrocardiogram were recorded simultaneously at a speed of 20 cm/sec on an oscillographic recorder (Sanei Sokki, Visigraph FR 201) as shown in Fig. 2. For the measurement of cardiac output, 0.75 or 1.25 mg of indocyanine green were injected into the left atrium and the blood was withdrawn from the femoral artery into a cuvette densitometer (Gilford Model 103 IR) at a constant rate of 22.9 ml/min by an infusion-withdrawal pump (Harvard Model 902). The calibration of the dye concentration was done with the whole

Fig. 3. Simultaneous recordings of electrocardiogram (ECG) and dye dilution curve obtained from the ascending aorta after the rapid injection of indocyanine green into the left ventricle. Note the staircase-like downslope of the dye dilution curve. $C_1$~$C_4$ are the concentrations of the plateaus.
blood method. The left ventricular end-diastolic volume (LVEDV) was measured by Holt’s (1956) method using the dye-dilution technique. Half mg of indocyanine green was injected rapidly into the left ventricle and the blood was drawn from the ascending aorta via a 20 cm long red KIFA catheter into a cuvette densitometer (Erma) at a constant rate of 120 ml/min by an infusion-withdrawal pump (Harvard Model 600-915). The dilution curve and electrocardiogram were recorded simultaneously at a paper speed of 5 cm/sec on a twin-viso cardiette (Sanborn) as shown in Fig. 3.

The heart rate was stepwise changed every approximately 20 beats per minute in the range of 120 to 230/min. The left ventricular output was held constant by a constant infusion rate of right heart by-pass pump during the experiment. The same experiment was made 5 minutes after injection of propranolol (0.05 mg/kg for three dogs and 0.1 mg/kg for one dog). The animals were sacrificed at the end of study, and the heart was excised and weighed after the great vessels, valves and fatting pad in the atrio-ventricular groove were removed.

Calculation: Analysis of the pressure curves was done on three successive beats at every levels of heart rate, and then the average was obtained. For the determination of Vmax, left ventricular pressure (P, mmHg) of the isovolumic period and its dp/dt were read at intervals of 10 msec. Contractile element velocity (Vce, circ/sec) was calculated according to the following formula (Mason 1969), $Vce = \frac{dp/dt}{(40P + 80)}$. Then a pressure-velocity curve was constructed by plotting Vce on the ordinate and pressure on the abscissa. Vmax was obtained by extrapolation of the descending limb of the pressure curve to 0 mmHg on the ordinate as shown in Fig. 4. Stroke work (SW) in gram-meter was calculated by the following formula, $SW = (MLVEP - LVEDP) \times SV \times 13.6/1000$, where MLVEP is mean left ventricular ejection pressure (mmHg) which is obtained by planimetering left ventricular pressure pulse during ventricular ejection. Tension-time index (mmHg·sec) was calculated as a product of MLVEP and ventricular ejection time. Left ventricular end-diastolic volume (LVEDV) was calculated by the following equation (Holt 1956), $LVEDV = SV / [1 - (C_{n+1}/C_n)]$, where $C_n$ and $C_{n+1}$ were the values of end-diastolic concentration for any two successive beats on the dye dilution curve which was recorded for the measurement of the residual volume. When the staircase-like dilution curve was unable to obtain owing to tachycardia so that $C_{n+1}/C_n$ could not be determined, $n \cdot C_1/C_n$ was used instead of $C_{n+1}/C_n$, where $C_1$

![Fig. 4. Pressure-velocity relation during isovolumic contraction at heart rate of 208/min. Contractile element velocity (Vce) is expressed in terms of circumferential fiber length (cric)/sec as dp/dt (40LVP + 80), where LVP is isovolumic ventricular pressure and dp/dt is its first derivative. The diagonal broken line indicates extrapolation of the descending limb of the curve to zero pressure.](image-url)
was the concentration of an arbitrary point and \( C_n \) was that of the \( n \)-th beat.

The oxygen saturation and the total hemoglobin concentration of arterial blood and coronary venous blood were measured with a CO-Oximeter (IL Model 182). The oxygen content of a given blood sample was calculated by multiplying its oxygen capacity by the fraction of oxyhemoglobin as follows,
\[
O_2\text{ content} = 1.39 \times Hb \times \% HbO_2 / 100.
\]
The CO-Oximeter data were corrected by Van Slyke data (Van Slyke and Neill 1924) according to the following regression equation which was obtained from the data of 15 blood samples with both procedures:
\[
O_2\text{ content (Van Slyke)} = 0.821 \times O_2\text{ content (CO-Oximeter)} + 0.418
\]
\( (N=15, r=0.972, p<0.001) \).

### Results

Data were grouped into 6 and 5 groups according to their heart rate before and after administration of propranolol, respectively. The mean value of each group and its standard error were listed in Tables 1 and 2.

#### Effects of heart rate on ventricular performance and myocardial contractile state

As heart rate increased, stroke volume decreased. Left ventricular end-diastolic volume, left ventricular end-diastolic pressure, aortic diastolic pressure and left ventricular systolic pressure were constant on the average regardless of changes of heart rate. Stroke work and tension time index decreased as heart rate was increased. Systolic time ratio increased in parallel with heart rate, although its increase was small in the heart rate of 160 to 230/min as shown in Fig. 5. Mean left atrial pressure increased at tachycardia. Maximum \( dp/dt \) did not show any significant change, while maximal intrinsic velocity of the contractile elements (\( V_{\text{max}} \)) was increased slightly as heart rate was increased over 180/min as shown in Fig. 6.

#### Effects of heart rate on coronary circulation and myocardial mechanics

Coronary flow (CF) in ml/min/100gHW showed a tendency to increase, although the change was not significant. Myocardial oxygen consumption (MVO\(_2\)) apparently increased as heart rate increased. The correlation between MVO\(_2\) and heart rate was highly significant \( (r=0.814, p<0.001) \) as shown in Fig. 7. The relation of MVO\(_2\) per beat to ventricular performance and \( V_{\text{max}} \) was investigated by subtracting an estimated oxygen consumption for myocardial basal metabolism (2 ml/100gHW) from MVO\(_2\). The correlation coefficients were listed in Table 3. Correlations of LVSP, \( V_{\text{max}} \) and \( dp/dt \) to the corrected MVO\(_2\) were highly significant \( (p<0.001) \). Correlation of LVEDV to the corrected MVO\(_2\) was significant at a level of \( p<0.05 \). TTI had a negative correlation with the corrected MVO\(_2\) at a level of \( p<0.05 \). SW and SV were not significantly correlated with the corrected MVO\(_2\).

#### Experiment after administration of propranolol

LVEDV, LVEDP and aortic diastolic pressure \( (AP_{\text{diast}}) \) did not show any significant changes over all the heart rates after administration of propranolol in
TABLE 1. Effects of heart rate on ventricular performance, cardiac

<table>
<thead>
<tr>
<th>HR (N)</th>
<th>SV</th>
<th>LVEDV</th>
<th>LVSP</th>
<th>LVEDP</th>
<th>APdiast</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>beats/min</td>
<td>ml</td>
<td>ml</td>
<td>mmHg</td>
<td>mmHg</td>
<td>mmHg</td>
<td>mmHg</td>
</tr>
<tr>
<td>123±0.5(13)</td>
<td>10.4±0.6*</td>
<td>28.3±2.9*</td>
<td>71.7±4.7*</td>
<td>6.0±0.5*</td>
<td>33.0±1.3*</td>
<td>5.0±0.6*</td>
</tr>
<tr>
<td>141±1.8(12)</td>
<td>10.3±1.2</td>
<td>32.1±3.2</td>
<td>74.3±4.1</td>
<td>6.9±0.8</td>
<td>34.0±1.1</td>
<td>4.9±0.7</td>
</tr>
<tr>
<td>164±0.5(8)</td>
<td>7.5±0.6</td>
<td>24.4±2.8</td>
<td>65.9±2.6</td>
<td>6.7±0.9</td>
<td>35.4±1.1</td>
<td>6.3±0.7</td>
</tr>
<tr>
<td>181±1.4(10)</td>
<td>8.3±0.6</td>
<td>32.0±3.9</td>
<td>73.0±3.0</td>
<td>5.9±0.4</td>
<td>35.5±1.3</td>
<td>5.1±0.9</td>
</tr>
<tr>
<td>211±1.0(12)</td>
<td>7.0±0.5</td>
<td>34.1±3.7</td>
<td>72.6±3.3</td>
<td>7.1±0.6</td>
<td>36.0±1.0</td>
<td>6.3±1.1</td>
</tr>
<tr>
<td>229±0.5(6)</td>
<td>6.7±0.2</td>
<td>29.8±1.8</td>
<td>72.7±5.2</td>
<td>6.1±0.4</td>
<td>37.5±1.5</td>
<td>7.0±1.3</td>
</tr>
</tbody>
</table>

Mean±SE, ( ) : number of data, * : equal number to those of HR, HR: heart rate, sure, LVEDP: left ventricular end-diastolic pressure, APdiast: aortic diastolic pressure, dp/dt, Vmax: maximum velocity of contractile element, CF: total venous coronary

TABLE 2. Effects of heart rate on ventricular performance, myocardial

<table>
<thead>
<tr>
<th>HR (N)</th>
<th>SV</th>
<th>LVEDV</th>
<th>LVSP</th>
<th>LVEDP</th>
<th>APdiast</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>beats/min</td>
<td>ml</td>
<td>ml</td>
<td>mmHg</td>
<td>mmHg</td>
<td>mmHg</td>
<td>mmHg</td>
</tr>
<tr>
<td>131±1.1(6)</td>
<td>9.6±0.3*</td>
<td>33.4±6.0*</td>
<td>68.7±6.5*</td>
<td>7.4±1.0*</td>
<td>36.2±3.9*</td>
<td>6.8±1.4*</td>
</tr>
<tr>
<td>141±2.8(7)</td>
<td>7.7±0.7</td>
<td>28.0±2.7</td>
<td>64.3±5.7</td>
<td>7.1±0.8</td>
<td>33.4±3.1</td>
<td>7.6±1.3</td>
</tr>
<tr>
<td>163±0.6(3)</td>
<td>7.0±0.4</td>
<td>33.6±7.8</td>
<td>53.7±3.8</td>
<td>7.9±0.7</td>
<td>29.5±1.8</td>
<td>7.2±0.6</td>
</tr>
<tr>
<td>179±3.9(5)</td>
<td>6.4±0.6</td>
<td>31.6±3.3</td>
<td>63.4±6.1</td>
<td>6.9±0.8</td>
<td>35.6±3.4</td>
<td>6.0±1.0</td>
</tr>
<tr>
<td>211±1.7(3)</td>
<td>5.5±0.9</td>
<td>34.1±2.7</td>
<td>62.0±7.6</td>
<td>7.8±2.3</td>
<td>36.0±4.2</td>
<td>9.5±3.3</td>
</tr>
</tbody>
</table>

Mean±SE Abbreviations: see Table 1

Fig. 5. Effect of heart rate on systolic time ratio (%) before (open circle) and after (closed circle) propranolol. Average values (±SE) are shown. Systolic time ratio increases rapidly up to heart rate of 160/min and very slowly from 160 to 230 before propranolol, but relatively rapidly from 160 to 210 after propranolol.

a similar manner to the control experiment. SV decreased as heart rate increased and was smaller than that before administration of propranolol over all the heart rates. LVSP slightly decreased as heart rate increased. Systolic time ratio was larger than that before administration of propranolol through all ranges of heart rates, and this ratio was relatively constant at heart rates less than 160/min and increased in proportion to heart rate at heart rates more than 160/min as shown.
myocardial contractility and coronary circulation

<table>
<thead>
<tr>
<th>SW g·cm</th>
<th>TTI mmHg·sec</th>
<th>ST %</th>
<th>Max dp/dt mmHg/sec</th>
<th>Vmax circ/sec</th>
<th>CF ml/100gHW/min</th>
<th>MVO₂ ml/100gHW/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.16±0.45*</td>
<td>10.7±0.9*</td>
<td>47.5±1.4*</td>
<td>1310±170*</td>
<td>0.98±0.08 (6)</td>
<td>112±10 (12)</td>
<td>3.60±0.18 (11)</td>
</tr>
<tr>
<td>7.10±0.49</td>
<td>9.6±0.51</td>
<td>51.7±2.1</td>
<td>1350±170</td>
<td>1.01±0.07 (7)</td>
<td>109±15 (12)</td>
<td>3.89±0.11 (12)</td>
</tr>
<tr>
<td>4.83±0.47</td>
<td>8.6±0.6</td>
<td>56.8±3.1</td>
<td>1140±110</td>
<td>1.02±0.06 (7)</td>
<td>93±9 (7)</td>
<td>4.31±0.19 (7)</td>
</tr>
<tr>
<td>5.81±0.48</td>
<td>8.2±0.3</td>
<td>56.3±2.0</td>
<td>1340±140</td>
<td>1.18±0.07 (10)</td>
<td>120±10 (15)</td>
<td>4.74±0.17 (15)</td>
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<tr>
<td>4.76±0.39</td>
<td>7.3±0.4</td>
<td>59.2±2.4</td>
<td>1340±110</td>
<td>1.14±0.06 (9)</td>
<td>147±15 (11)</td>
<td>5.71±0.23 (11)</td>
</tr>
<tr>
<td>4.78±0.30</td>
<td>6.1±0.1</td>
<td>57.8±3.1</td>
<td>1430±150</td>
<td>1.14±0.04 (5)</td>
<td>133±16 (6)</td>
<td>6.23±0.31 (6)</td>
</tr>
</tbody>
</table>

LVEDV: left ventricular end-diastolic volume, LVSP: left ventricular systolic peak pressure, SW: stroke work, TTI: tension time index, ST: systolic time ratio, Max dp/dt: peak flow, MVO₂: myocardial oxygen consumption.

contractility and coronary circulation after propranolol

<table>
<thead>
<tr>
<th>SW g·cm</th>
<th>TTI mmHg·sec</th>
<th>ST %</th>
<th>Max dp/dt mmHg/sec</th>
<th>Vmax circ/sec</th>
<th>CF ml/100gHW/min</th>
<th>MVO₂ ml/100gHW/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.38±0.94*</td>
<td>13.0±1.5*</td>
<td>58.2±2.3*</td>
<td>960±130*</td>
<td>0.95±0.14 (3)</td>
<td>107±23 (5)</td>
<td>3.30±0.18 (5)</td>
</tr>
<tr>
<td>4.88±1.05</td>
<td>10.9±1.1</td>
<td>57.9±1.8</td>
<td>960±140</td>
<td>1.02±0.11 (4)</td>
<td>89±22 (6)</td>
<td>3.32±0.14 (6)</td>
</tr>
<tr>
<td>3.23±0.05</td>
<td>7.5±0.5</td>
<td>60.3±1.8</td>
<td>750±10</td>
<td>0.82±0.06 (3)</td>
<td>62±6 (3)</td>
<td>3.72±0.06 (3)</td>
</tr>
<tr>
<td>3.86±0.77</td>
<td>8.6±1.3</td>
<td>65.6±2.1</td>
<td>1000±140</td>
<td>1.01±0.07 (5)</td>
<td>120±19 (5)</td>
<td>4.00±0.16 (5)</td>
</tr>
<tr>
<td>3.26±1.06</td>
<td>7.5±1.0</td>
<td>71.0±4.2</td>
<td>1060±160</td>
<td>1.00±0.06 (5)</td>
<td>122±18 (3)</td>
<td>4.16±0.53 (3)</td>
</tr>
</tbody>
</table>

Fig. 6. Effect of heart rate on maximum velocity of contractile element (Vmax) before (open circle) and after (closed circle) propranolol. Average values (±SE) are shown. Vmax tends to be elevated as heart rate increases before propranolol, but it does not after propranolol.

in Fig. 5. Maximum dp/dt and Vmax were relatively constant, although Vmax rose as heart rate increased before administration of propranolol as shown in Fig. 6. The effect of heart rate on CF was variable. MVO₂ increased as heart rate increased, although its value was considerably lower as shown in Fig. 7. Ventricular performance and myocardial contractile state did not show any significant correlation with the corrected MVO₂ as listed in Table 3.
Fig. 7. Effect of heart rate on myocardial oxygen consumption (MVO₂) before (open circle) and after (closed circle) propranolol. Average values (±se) are shown. MVO₂ increases in proportion to heart rate before propranolol. It tends to increase proportionally to heart rate after propranolol, too, but at lower rate than before propranolol.

TABLE 3. Correlative coefficients of corrected MVO₂ to myocardial mechanics before and after propranolol

<table>
<thead>
<tr>
<th></th>
<th>(MVO₂−BM)/100gHW/100HR</th>
<th></th>
<th>(MVO₂−BM)/100HR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before propranolol</td>
<td>After propranolol</td>
<td>Before propranolol</td>
</tr>
<tr>
<td>LVSP</td>
<td>0.485 (p&lt;0.001)</td>
<td>0.286 (p&gt;0.1)</td>
<td>0.385 (p&lt;0.05)</td>
</tr>
<tr>
<td>TTI</td>
<td>−0.515 (p&lt;0.001)</td>
<td>0.330 (p&gt;0.1)</td>
<td>−0.471 (p&lt;0.001)</td>
</tr>
<tr>
<td>Vmax</td>
<td>0.471 (p&lt;0.001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max dp/dt</td>
<td>0.323 (p&lt;0.05)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BM: myocardial oxygen consumption for basal metabolism. Corrected MVO₂: MVO₂−BM. Other abbreviations: see Table 1.

DISCUSSION

A right heart by-pass method was employed in order to investigate the effects of heart rate on myocardial contractile state, ventricular performance and coronary circulation before and after administration of propranolol.

Effect of heart rate on left ventricular performance

It is clear in cardiac muscle preparation that the strength of contraction rises as the interval of contraction is shortened (Bowditch 1871; Woodworth 1902;
Effect of Heart Rate on Ventricular Function

Abbot and Mommaerts 1959; Blinks and Koch-Weser 1961; Sonnenblick 1962). However, this phenomenon has not always been confirmed in the intact heart (Mitchell et al. 1963a; Sarnoff et al. 1963; Covell et al. 1967; Noble et al. 1966, 1969). This discrepancy would be due to the difference in experimental methods used. Since cardiac output is one of the most important factors which influence the performance of the left ventricle, it would be advisable for evaluation of complicated relation of myocardial contractility and coronary circulation to hold cardiac output constant with the right heart by-pass method. Under a fixed cardiac output, Vmax, an index of myocardial contractility, showed tendency to rise as heart rate increased. Systolic time ratio also increased. The increment of systolic time ratio must decrease the diastolic time ratio. If diastolic time is extremely limited, ventricular diastolic filling fails to be completed so that pulsus alternans occurs (Mitchell et al. 1963b). Sugimoto et al. (1966) stated that the decrease in cardiac output with increased heart rate was caused at least partially by impaired filling of the ventricle at tachycardia. On the other hand, the augmentation of myocardial contractility by administration of catecholamine was shown to decrease the duration of the total systole by reducing isometric systole and ejection time (Wallace et al. 1963). Therefore, the augmented ventricular contractile state by intrinsic effect of heart rate could be considered to play an important role in impeding further increment of systolic time ratio and the occurrence of pulsus alternans and in maintaining cardiac output at tachycardia, although increased left atrial pressure at tachycardia also played an important role in facilitating ventricular filling (Mitchell et al. 1962).

Effects of heart rate on coronary circulation and myocardial mechanics

Evans and Matsuoka (1914–15) demonstrated that oxygen consumption of the heart for given work was much greater when the pressure factor was large as compared with the volume factor rather than vice versa. Starling et al. (1926–27) observed a direct proportionality between MVO₂ and the increment in the ventricular diastolic volume. Some other indices such as TTI (Sarnoff et al. 1958), LVSP multiplied by heart rate (Katz and Feinberg 1958) and velocity of contraction (Sonnenblick et al. 1965) were advocated as MVO₂ determinant. In this experiment MVO₂ increased in proportion to the increment of heart rate as shown in Fig. 7. This fact suggests that heart rate is one of the determinants of MVO₂. The myocardial basal metabolism may be constant even if heart rate is changed, because it has been shown not to be influenced so much even by large dose of catecholamines (Klocke et al. 1965). In this experiment, 2 ml/100gHW/min (McKeever et al. 1958; Van Citters et al. 1957) was subtracted from MVO₂/min as oxygen consumption for myocardial basal metabolism. As stated above, left ventricular systolic peak pressure (LVSP) and Vmax were highly significantly correlated with the corrected MVO₂, and left ventricular end-diastolic volume (LVEDV) was correlated at a borderline significance. However, corrected MVO₂ had a negative correlation with tension time index (TTI) at borderline significance.
and no significant one with stroke work (SW) and stroke volume (SV).

LVSP may be regarded as a factor of the tension development of the left ventricular wall. On the contrary, TTI may be a factor of the tension development and its maintenance. Since LVSP was positively correlated with the corrected MVO₂ while TTI was negatively correlated, it is likely that tension development plays a more important role in determination of myocardial oxygen consumption than tension maintenance. The close relationship between the corrected MVO₂ and Vmax in this study will support a hypothesis (Sonnenblick et al. 1965) that the contractile state is one of the most important determinants. It is interesting that TTI was not positively correlated with MVO₂ but negatively correlated in this study. This is considered to be due to augmentation of MVO₂ by elevation of the contractility while enhanced contractility tends to decrease TTI by reducing ejection time when heart rate increases.

LVEDV was significantly correlated with MVO₂, but SV was not. As demonstrated by Evans and Matsuoka (1914-15), MVO₂ has been considered to be hardly influenced by the change in ejection volume. According to Frank-Starling's law, the increment of LVEDV results in the enhancement of tension development. Laplace's law indicates that the increment of left ventricular volume augments the tension of the left ventricle if left ventricular pressure is constant. Therefore, the increment of left ventricular volume may always accompany the augmentation of tension development. It is not unreasonable that LVEDV correlates with MVO₂, because tension development is one of the determinants of MVO₂ (Braunwald 1971).

Effects of heart rate on left ventricular performance and coronary circulation after administration of propranolol

It is generally accepted that activation of the adrenergic beta-receptor rises the contractile state of the myocardium and increases myocardial oxygen consumption and coronary blood flow. However, the role and relative importance of the beta-receptor in the regulation of cardiac function has not been evaluated completely. Beta-receptor blockade (propranolol) was administered in order to investigate the role of the beta-receptor as heart rate increased. Before administration of propranolol, pulsus alternans of ventricular pressure occurred in no cases at heart rate of 210 and in about a half of the cases at heart rate of 230. After administration of propranolol, however, the ventricle developed pulsus alternans in a half of the cases with heart rate of 210 and in all cases with heart rate of 230. This fact suggests that the beta-receptor plays an important role in preventing the ventricle from being deteriorated at tachycardia. At the same time, Vmax did not rise after administration of propranolol in spite of the increase of heart rate. The interruption of elevation of the contractile state by the beta-receptor blockade suggests that the beta-receptor plays an important role in augmenting the contractile state and in preventing the ventricle from being deteriorated as heart rate increased. It was interesting that MVO₂ was increased at a lower rate after than
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before administration of propranolol as heart rate was increased, and it would be
due to lower LVSP and Vmax, which were shown to be major determinants of
MVO2, than that before administration of propranolol.

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