Influence of Developed Tension on Myocardial Potassium Balance in the Dog Heart

By J. P. Gilmore and E. D. Gerlings

ABSTRACT

Experiments were carried out to determine the effect of changing preload on myocardial potassium balance. A blood-perfused dog heart was employed. Changes in the pressure recorded from a balloon in the left ventricle were assumed to reflect directional changes in myocardial wall tension. Developed tension was altered by changing the volume of the balloon. Net potassium balance was calculated as the product of the coronary A-V plasma potassium difference and coronary plasma flow. When the ventricle was developing little tension, it usually gained potassium. When diastolic volume and thus developed tension was increased, a net loss of myocardial potassium occurred. In some experiments the hemodynamic response of the ventricle to the increase in diastolic volume suggested that the contractility of the heart was increasing while the heart was losing potassium.

ADDITIONAL KEY WORDS

myocardial K+ balance
myocardial contractility
ventricular tension
myocardial tension and potassium balance

When left ventricular outflow resistance is increased myocardial contractility increases (1-4), and potassium is lost from the heart (2, 3, 5). It has been suggested that this loss of potassium contributes to the change in contractility and is related to the associated increase in developed tension (2, 3, 5). When the preload of cardiac muscle is increased over a wide range, the developed tension increases; however, it is generally assumed that under these circumstances the contractility of the heart is not altered. If the loss of potassium when aortic resistance is increased is the result of the augmented developed tension, a loss would also be expected when developed tension is increased by preload. Further, if such a loss occurred and if the increase in contractility when aortic resistance is raised is related to a loss of myocardial potassium, one might expect that preload can alter contractility. The experiments presented below were designed to test this hypothesis.

Materials and Methods

Mongrel dogs, of various weights and of either sex, were anesthetized with intravenous pentobarbital sodium (25-30 mg/kg). The experimental preparation was an isolated blood-perfused dog heart similar to that described previously (6). Following the establishment of positive-pressure ventilation and transthoracotomy, the heart was isolated by ligating the inferior and superior venae cavae, azygos vein, lung roots, brachiocephalic artery, and left subclavian artery and the aortic arch immediately below it. The left subclavian artery was cannulated and connected to either the femoral arteries or carotid arteries of an intact anesthetized dog, thereby providing coronary inflow. Total coronary outflow (less thebesian) was diverted from the right ventricle by a catheter inserted through the azygos vein. This catheter in turn led the blood through a low-resistance rotameter (7) from which the blood was returned to a reservoir connected to the jugular veins of the support dog, which breathed ambient air. Left thebesian drainage was obtained through a catheter inserted through the apical dimple. Heart rate was maintained constant throughout all experiments by stimulation through electrodes sewn either to the right atrium alone or to both right atrium and right ventricle.
A rubber or latex balloon was tied to the tip of a Y-shaped metal cannula inserted into the left ventricle. One arm of this cannula was used for recording left ventricular pressure and other arm for adding or withdrawing fluid. Changes in the pressure recorded from the balloon were assumed to reflect changes in left ventricular tension. In the early experiments, we observed that even when the balloon was almost empty the ventricle developed significant pressure. It became apparent, however, that this high pressure resulted from the failure of adequate drainage of the left ventricle. To preclude this problem, the catheter used to drain the ventricular cavity was connected to a roller pump that operated throughout the experiment. When this was done and the balloon contained a minimal volume, pressure was only a few millimeters of mercury. The size of the balloon approximated the diastolic volume of the left ventricular cavity. In some experiments coronary A-V oxygen difference was monitored continuously using a Guyton oxygen analyzer calibrated during the experiment by manometric analysis. Myocardial oxygen consumption was calculated as a product of total coronary flow and coronary A-V oxygen difference. All data for coronary blood flow were obtained by timed collection of coronary venous outflow.

Analysis of coronary arterial and venous plasma potassium concentration was done by automated flame photometry. Myocardial potassium balance in both the control and experimental period was calculated as the product of the coronary A-V plasma potassium difference and total coronary plasma flow. All pressures were obtained with Statham transducers and all recordings made on a multichannel direct-writing oscillograph. Statistical analysis was done using the Student t-test for paired data.

In general, the experimental procedure was as follows. After establishing a steady state, simultaneous and continuous sampling of coronary arterial and venous blood was started at a rate of 8 ml/min. The coronary venous sampling tube was changed every 30 seconds and the coronary arterial sampling tube every 60 seconds. This was continued for 3 to 5 minutes, and a given volume of fluid was then added to the intraventricular balloon while continuing blood sampling. Timed collections of coronary outflow were made during both the control and the experimental period. Some experiments were stopped while the balloon was inflated; in others, sampling was continued after withdrawal of the fluid from the balloon. The experimental period varied from approximately 5 to 10 minutes. When the procedure caused a change in potassium concentration in coronary venous plasma, the change was usually observed within approximately 40 seconds. This delay was related to the dead space of the sampling system and the coronary blood flow. However, no adjustment was made for this delay in plotting the data for potassium balance. The data presented were obtained from 20 experiments in 11 dogs.

Results

An example of the response of the ventricle to an increase in balloon volume is shown in Figure 1. During the control period the balloon contained 5 ml of saline. At the time indicated by the arrow, 10 ml of fluid were added to the balloon, and left ventricular pressure and the first derivative of left ventricular pressure (dP/dt) then increased. Total coronary blood flow increased despite a decline in coronary perfusion pressure. Shortly after the initial increase in diastolic pressure, left ventricular diastolic pressure decreased. This was associated with a further increase in ventricular systolic pressure and in dP/dt.

An example of the change in myocardial potassium balance that accompanied this procedure is shown in Figure 2. In the control state, potassium concentration in coronary venous plasma was lower than in coronary

![Figure 1](http://circres.ahajournals.org/)
TABLE 1

<table>
<thead>
<tr>
<th>Exp. no.</th>
<th>Change in vent. dvel. P (mm Hg)</th>
<th>Myocardial loss (−) or gain (+) of K⁺ (αEq/min)</th>
<th>Duration of inflation (min)</th>
<th>Total change for period of inflation (αEq)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>During balloon inflation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>90</td>
<td>+0.43</td>
<td>−6.82</td>
<td>−12.25</td>
</tr>
<tr>
<td>1b</td>
<td>83</td>
<td>+6.68</td>
<td>+0.59</td>
<td>−6.09</td>
</tr>
<tr>
<td>2</td>
<td>105</td>
<td>−6.21</td>
<td>−12.51</td>
<td>−6.30</td>
</tr>
<tr>
<td>3a</td>
<td>123</td>
<td>+16.37</td>
<td>−2.04</td>
<td>−18.41</td>
</tr>
<tr>
<td>3b</td>
<td>125</td>
<td>+10.58</td>
<td>−11.16</td>
<td>−21.72</td>
</tr>
<tr>
<td>3c</td>
<td>63</td>
<td>−4.36</td>
<td>−28.07</td>
<td>−23.71</td>
</tr>
<tr>
<td>4</td>
<td>47</td>
<td>−7.35</td>
<td>−33.79</td>
<td>−26.44</td>
</tr>
<tr>
<td>5a</td>
<td>85</td>
<td>+2.64</td>
<td>−8.10</td>
<td>−10.74</td>
</tr>
<tr>
<td>5b</td>
<td>80</td>
<td>−4.91</td>
<td>−13.81</td>
<td>−8.70</td>
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<tr>
<td>5c</td>
<td>67</td>
<td>+6.65</td>
<td>−24.55</td>
<td>−31.20</td>
</tr>
<tr>
<td>6</td>
<td>89</td>
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<td>+9.75</td>
<td>+19.94</td>
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<tr>
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<td>50</td>
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<td>+6.89</td>
<td>−6.29</td>
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<tr>
<td>9</td>
<td>72</td>
<td>−2.72</td>
<td>−11.31</td>
<td>−8.59</td>
</tr>
<tr>
<td>10a</td>
<td>55</td>
<td>−0.10</td>
<td>+0.84</td>
<td>+0.94</td>
</tr>
<tr>
<td>10b</td>
<td>63</td>
<td>+11.04</td>
<td>+14.02</td>
<td>+2.98</td>
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<tr>
<td>10c</td>
<td>111</td>
<td>+7.32</td>
<td>−5.40</td>
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<tr>
<td>11a</td>
<td>150</td>
<td>+7.48</td>
<td>+6.59</td>
<td>−0.88</td>
</tr>
<tr>
<td>11b</td>
<td>152</td>
<td>+6.59</td>
<td>−2.46</td>
<td>−9.05</td>
</tr>
<tr>
<td>11c</td>
<td>132</td>
<td>−2.46</td>
<td>−2.71</td>
<td>−0.25</td>
</tr>
</tbody>
</table>

| MEAN     | +3.358                         | −5.813                                       | −9.171                    | −38.84                                    |
| SE       | ±1.46                          | ±2.87                                       | ±2.05                     | <0.001                                    |

HR (beats/min) 144
V. Devel. P (mm Hg) 140
COR P (mm Hg) 115
COR FLOW (ml/min) 76
dP/dt (mm Hg/sec) 570

Influence of Increasing Developed Tension on Myocardial Potassium Balance

<table>
<thead>
<tr>
<th>FIGURE 2</th>
</tr>
</thead>
</table>

Influence of balloon inflation on myocardial potassium balance. The balloon was inflated at the time indicated by the arrow. V. Devel. P. = ventricular developed pressure. COR. P. = coronary perfusion pressure. Other abbreviations same as in Figure 1. Values in first column are control values. Values in second column are after balloon inflation.

arterial plasma, that is, during the control period the heart was gaining potassium. Upon inflation of the balloon (arrow) the concentration of potassium in coronary venous arterial plasma increased, causing a reversal of the A-V difference. Table 1 shows the potassium balance data from all the experiments. Prior to balloon inflation there was an average up-
Potassium balance changes that accompanied the hemodynamic changes shown in Figure 3.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Experimental</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.R. (beats/min)</td>
<td>168</td>
<td>168</td>
</tr>
<tr>
<td>V.DEVEL.P. (mmHg)</td>
<td>67</td>
<td>190</td>
</tr>
<tr>
<td>COR. P. (mmHg)</td>
<td>85</td>
<td>80</td>
</tr>
<tr>
<td>COR. FLOW (ml/min)</td>
<td>62</td>
<td>75</td>
</tr>
<tr>
<td>dP/dt (mmHg/sec)</td>
<td>600</td>
<td>2670</td>
</tr>
<tr>
<td>LVDP (mmHg)</td>
<td>22</td>
<td>45</td>
</tr>
</tbody>
</table>

Influence of increasing and then subsequently decreasing intraventricular volume on myocardial potassium balance. LVDP = left ventricular diastolic pressure. Other abbreviations are the same as in Figures 1 and 2.

Panel C was obtained 100 seconds after panel B. Between panels B and C left ventricular developed pressure and dP/dt increased with no apparent change in left ventricular diastolic pressure. In this experiment coronary perfusion pressure was allowed to decline between A and B and between B and C to maintain coronary blood flow essentially constant. The changes in myocardial potassium balance which accompanied these hemodynamic changes are shown in Figure 4. Following balloon inflation (vertical arrow) potassium concentration in coronary venous plasma increased, while in arterial plasma it declined slightly.

Figures 5 and 6 show two experiments on the same heart. In the control period of the experiment shown in Figure 5 there is a very substantial coronary venous-arterial plasma potassium difference. Upon inflation of the balloon (first arrow) potassium concentration in coronary venous plasma increased by approximately 0.5 mEq/liter, and after
DEVELOPED TENSION AND MYOCARDIAL POTASSIUM

Influence of a 10-minute balloon inflation on myocardial potassium balance. Heart rate maintained constant throughout experiment. For more complete description of figure see text.

![Graph showing plasma potassium levels](image)

**FIGURE 7**

Influence of a 10-minute balloon inflation on myocardial potassium balance. Heart rate maintained constant throughout experiment. For more complete description of figure see text.

![Graph showing influence of graded increase in left ventricular pressure](image)

**FIGURE 8**

Influence of a graded increase in left ventricular developed pressure on myocardial potassium balance. A-V diff. = coronary arterial venous oxygen difference (ml O₂/100 ml blood); MVO₂ = myocardial oxygen consumption; other abbreviations as in previous figures. Figures in the second column are values after 13 ml of fluid was added to the balloon, in the third column after an additional 7 ml of fluid, and in the fourth column the new steady-state values after balloon deflation.

deflation of the balloon (second arrow) it returned to approximately the control level. Although in this experiment balloon inflation did not cause a large net loss of potassium from the heart, it nevertheless substantially reduced the coronary A-V potassium difference, thereby influencing net myocardial potassium balance. In the control period of the experiment plotted in Figure 6, only a small coronary A-V plasma potassium difference obtained. Upon inflation of the balloon (first arrow) potassium concentration in coronary venous plasma increased approximately 0.8 mEq/liter, and after deflation of the balloon (second arrow), it returned to approximately the control level.

An experiment in which the increase in ventricular developed tension was maintained for 10 minutes is shown in Figure 7. At the time indicated by the first arrow 10 ml of fluid was added to the balloon, and this increased developed pressure by approximately 70 mm Hg. Approximately 1 minute before deflation (second arrow) coronary venous potassium concentration was beginning to decline at a time when arterial potassium concentration was essentially constant.

Figure 8 shows the influence of a stepwise increase in balloon volume on the potassium balance of the heart. At the time indicated by the first arrow, approximately 13 ml of fluid was added to the balloon; this was associated with a substantial elevation of potassium concentration in coronary venous plasma. At the time indicated by the second arrow, an additional 7 ml of fluid was added to the balloon; potassium concentration in coronary venous plasma increased further. Following balloon deflation, this concentration returned to approximately the control level. There was no obvious immediate recovery of potassium by the heart following balloon deflation. The hemodynamic data for this experiment are shown above the potassium plot. For each increment in volume there was an increment in myocardial oxygen consumption; further, there is a parallel between the change in potassium balance, the change in developed pressure, and the increase in myocardial oxygen consumption.

**Discussion**

The experiments presented above demonstrate beyond a reasonable doubt that when the tension developed by the ventricle is increased there is an associated loss of potassium from the heart. Although in some experiments there was a general relation between
the increase in developed pressure and the amount of potassium loss, it was not a consistent one.

Of interest was the observation that when the heart was developing little tension the potassium concentration in coronary venous plasma was usually below that in coronary artery plasma, that is, the heart was usually gaining potassium. Several groups have reported variability of the coronary A-V plasma potassium difference in the working heart (2, 3, 8-10). The present experiments indicate that this variability is related, at least in part, to the level of tension which the ventricle is developing at the time that the arterial and venous samples are obtained.

Although in many of the experiments the extent to which the potassium concentration in coronary venous plasma rose upon balloon inflation was quite striking, the total amount lost by the heart during this time was small. While the balloon was inflated the mean net change in myocardial potassium balance amounted to 9.2 µEq/min. If one assumes a total myocardial potassium content of approximately 10 mEq, one finds that when developed tension was increased the heart lost potassium at a rate equal to 0.09% of intramyocardial potassium per minute. Although this amount was small it became larger when the inflation was maintained for a long period of time. The extent of these changes is similar to those reported previously for other procedures such as increasing heart rate, increasing aortic pressure, administering digitalis, etc. (2, 3, 11, 12). Hajdu found that the maximal tension development of the frog heart produced by increasing frequency of stimulation was associated with only a slight decrease in total myocardial potassium (12). Further, Sarnoff and associates showed that an uptake by the heart of as little as 130 µEq of potassium over a 3-minute period is associated with a depression of myocardial performance (3). The present experiments do not show how long the heart can continue to lose potassium when tension is increased. However, Calhoun et al. observed that the potassium content of the right ventricle was significantly decreased in patients who died of pulmonary disease which would be expected to be associated with pulmonary hypertension (13).

When developed tension was decreased by balloon deflation, potassium concentration in coronary venous plasma usually returned to approximately the control level. We found no obvious evidence of a fall in concentration below that prior to balloon inflation. That is, there was no indication that the heart was immediately recovering what it had lost when developed tension was increased. This is in contrast to the pattern observed with continuous post extrasystolic potentiation (paired stimulation) of the ventricle. During paired stimulation there is a loss of potassium from the heart (14); however, with cessation of stimulation potassium concentration in coronary venous plasma usually falls below the control value, indicating that the heart immediately recovers at least some of the potassium that was lost during stimulation. This observation is of particular interest for it suggests that two mechanisms are contributing to the potassium changes produced by coupled pacing and increased developed tension. The failure of the heart to show an obvious early recovery of potassium after developed tension is decreased, suggests that the heart loses a neutral isotonic solution when its developed tension is increased. This solution may represent intracellular fluid that is squeezed from cardiac tissue by the greater tension development. Hajdu (12) observed that the loss of myocardial potassium caused by increasing the frequency of stimulation was associated with a loss of tissue water “which leaves the internal ion concentration unaltered.” Further, he found that a change in intramyocardial ion concentration due to a loss or gain of water had little effect on developed tension. From these observations Hajdu concluded that “the contractile protein is sensitive to a change in the total amount of internal ion content rather than to a change in the internal ion concentration.”

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Direct evidence shows that changes in myocardial potassium can influence the performance of cardiac muscle. When intracellular potassium is decreased in isolated cardiac muscle by lowering the potassium concentration of the perfusate, contractility increases (15, 16). Also, when potassium is infused into the working heart, contractility decreases (3). These considerations therefore raise the possibility that the loss of myocardial potassium found in the present study contributed to the induced changes in performance. However, the available data do not permit either affirmation or denial of this possibility. Nevertheless, the type of response shown in Figure 3 indicates that a heterometric response may elicit a homeometric response. Such a suggestion was made as early as 1906 by Knowlton and Starling (17), who said that the stimulating action of increased tension within the ventricle may contribute to the initial improvement and efficiency of the heart with increasing arterial resistance. An increase in arterial resistance would of course be associated with an increase in developed tension similar to that observed when the diastolic pressure of the isovolumic heart was increased in the present experiments.

Acknowledgment

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References

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