Effects of Calcium and Temperature on Tension in Isolated Canine Coronary Artery

Katsuhiko YOSHIDA, Yuhsuke FUJII, Hiroshi INA, Susumu FUJIOKA, Takashi MASEKI*, Toshio ABE*, Hiroyuki TOKUNO** and Tadao TOMITA**

The effects of calcium and temperature on the tension of isolated canine coronary arterial strips were studied.

In 20 mEq·l^{-1} K solution, the tension was significantly increased from 0 mg with 0 mEq·l^{-1} Ca to 33 ± 18 mg with 0.2 mEq·l^{-1} Ca at 37°C, from −40 ± 18 mg with 0 mEq·l^{-1} Ca to −17 ± 11 mg with 0.2 mEq·l^{-1} Ca at 30°C, from −77 ± 19 mg with 0 mEq·l^{-1} Ca to −52 ± 17 mEq·l^{-1} with 1 mEq·l^{-1} Ca at 25°C, from −88 ± 13 mg with 0 mEq·l^{-1} Ca to −41 ± 18 mg with 2 mEq·l^{-1} Ca at 20°C, from −125 ± 16 mg with 0 mEq·l^{-1} Ca to −116 ± 13 mg with 2 mEq·l^{-1} Ca at 15°C. Ca higher than 0.2 mEq·l^{-1} produced a dose-dependent increase in tension between 37°C and 15°C. In spite of the presence of 4 mEq·l^{-1} Ca, the development of tension was strongly supressed by lowering the temperature below 20°C, and completely inhibited at 10°C. The rate of a decrease in tension caused by cooling was about 5.5 mg·°C^{-1}.

This study demonstrated that Ca^{2+} produced a dose-dependent increase in tension in high-K solution, which was suppressed as the temperature was lowered.
(Key words: coronary artery, calcium-induced contraction, hypothermia)

(Yoshida K, Fujii Y, Ina H, et al.: Effects of calcium and temperature on tension in isolated canine coronary artery. J Anesth 5: 172–176, 1991)

Numerous factors of extracellular fluid affect tension of smooth muscle. The electrolyte composition and temperature are the important factors. High-K solution produces the contraction of the smooth muscle, the strength of which is dependent on Ca concentration in the solution[1]. On the other hand, it is known that hypothermia produces an increase in tension of the rabbit ear vessels[2].

In this experiment, the effects of Ca concentration and temperature of the extracellular fluid on the tension of isolated canine coronary artery were studied.

Methods

The experiments were performed on the anterior descending coronary arteries obtained from dogs (10 ~ 14 kg, either sex) anaesthetized with intravenous thiamylal sodium (25 mg·kg^{-1}). The coronary artery was dissected and its surrounding tissue was removed under microscopy. Helical strips of about 3 mm in width and 15 mm in length were excised from the segments of coronary artery of 0.8 to 1.2 mm in diameter.

Department of Cardiovascular Surgery, Kiryu Kousei General Hospital, Gumma, Japan

*Department of *Thoracic Surgery and **Physiology, School of Medicine, Nagoya University, 65, Tsurumai-cho, Shouwa-ku, Nagoya-city, Aichi-prefecture, 466 Japan*

Address reprint requests to Dr. Yoshida: Department of Cardiovascular Surgery, Kiryu Kousei General Hospital, 6-3, Orihime-cho, Kiryu-city, Gumma-prefecture, 376 Japan

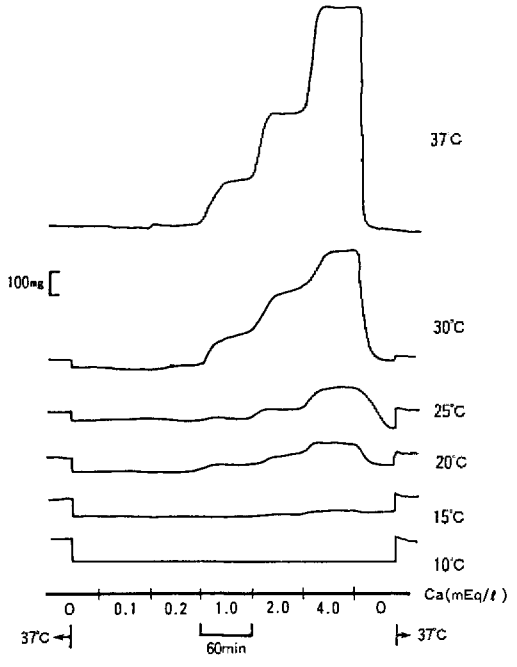

Fig. 1. Effects of temperature and Ca in the high-K solution.
Ca produced the increases in tension in a dose-dependent manner and these increases were suppressed by lowering temperature.

Each strip was attached to an isometric force transducer (Shinko UL-10GR) and suspended in a small volume organ bath (37°C) through which the normal solution as mentioned below was flowed at a constant rate of 2 ml·min^{-1}. After 30 min equilibration, the strip was stretched to give the tension of approximately 0.5 g and the normal solution was changed to high-K Ca-free solution as mentioned below. After stabilization of tension in this solution, this solution was cooled to 30, 25, 20, 15 and 10°C. The tension were measured at each temperature. Then temperature was returned to 37°C. After the tension was stabilized, external Ca concentrations were varied between 0.1 mEq·l^{-1} and 4.0 mEq·l^{-1} and at each Ca concentration, temperatures were varied between 37°C and 10°C. The changes in tension were measured at each Ca concentration and temperature.

After measurement of tension at each temperature in the solution containing 4 mEq·l^{-1} Ca, the specimen was reperfused with high-K, Ca-free solution until the tension returned to its basal value. Following this procedure, to adjust the change in tension followed by the change in the strip's length, the strips were stretched to give a tension before cooling. The change in tension in the solution containing 4 mEq·l^{-1} Ca was measured again.

The normal solution consisted of the following electrolytes concentrations (mEq·l^{-1}): Na 137, K 5.9, Ca 4.7, Mg 2.4; and 11.8 mM glucose. The high-K, Ca-free solution was made by removing Ca from the normal solution, adding 0.5 mM EGTA (ethylene glycolether tetraacetic acid), and adjusting K to 20 mEq·l^{-1}.

Statistical analyses were performed by using Wilcoxon rank-sum test or Wilcoxon signed-rank test. A probability value less than 1% was regarded as statistically significant.

Results

Ca produced an increase in tension in a dose-dependent manner and the increase was suppressed by lowering temperature (fig. 1, 2 and table). This decrease in tension was about 5.5 mg·°C^{-1}. In comparison with basal tension, values of tension in high-K, Ca-free solution showed negative ones at each temperature except for 37°C. This means relaxation of the strips. The tension was -40 ± 8 mg at 30°C (mean ± SD, n=10), -139 ± 27 mg at 10°C, respectively (table and fig. 2).

The increase in tension occured in proportion to the increases in Ca ranging from 0 mEq·l^{-1} to 4 mEq·l^{-1} in high-K solution. Figure 1 shows an example of this increase in tension caused by Ca at 37, 30, 25, 20, 15 and 10°C. The tension significantly increased from 0 ± 0 mg with 0 mEq·l^{-1} Ca to 33 ± 18 mg with 0.2 mEq·l^{-1} Ca at 37°C, from -40 ± 18 mg with 0 mEq·l^{-1} Ca to -17 ± 11 mg with 0.2 mEq·l^{-1} Ca at 30°C, from -77 ± 19 mg with 0 mEq·l^{-1} Ca to -52 ± 17 mg with 1 mEq·l^{-1} Ca at 25°C, from -88 ± 13 mg with 0 mEq·l^{-1} Ca to -41 ± 18 mg with 2 mEq·l^{-1} Ca at 20°C, from -125 ± 16 mg

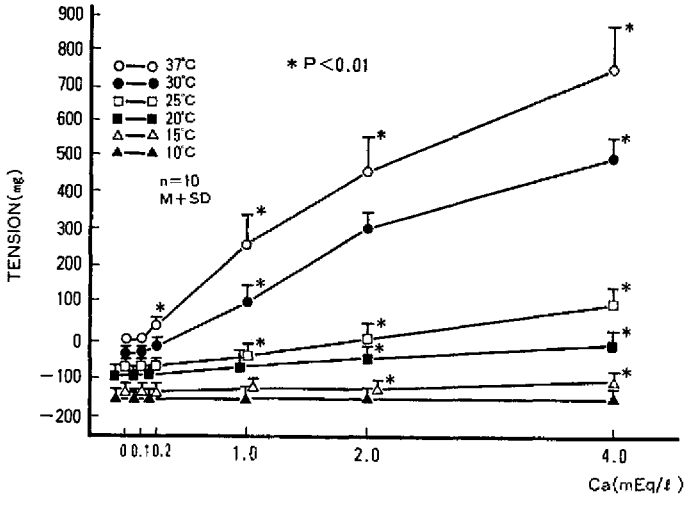

Fig. 2. Ca concentration-tension curves in the high-K solution at six levels of temperature.
The increases in tension were dependent on the Ca concentration and temperature.
Ca concentration greater than 0.2 mEq · l^{-1} was required for the increase in tension.

Table . The tension at various temperatures and Ca concentrations

	Ca^{2+}(mEq·l^{-1})					
	0	0.1	0.2	1	2	4
37	0 ± 0	0 ± 0	33 ± 18*	254 ± 76*	447 ± 94*	743 ± 123*
30	−40 ± 18	−40 ± 18	−17 ± 11*	97 ± 32*	289 ± 56*	479 ± 56*
25	−77 ± 19	−77 ± 19	−73 ± 20	−52 ± 17*	0.6 ± 30*	88 ± 31*
20	−88 ± 13	−88 ± 13	−86 ± 12	−63 ± 10	−41 ± 18*	−13 ± 19*
15	−125 ± 16	−125 ± 16	−125 ± 16	−123 ± 15	−116 ± 13*	−109 ± 12*
10	−139 ± 27	−139 ± 27	−139 ± 27	−139 ± 27	−139 ± 27	−139 ± 27

The values are mean ± SD (mg), and n=10.
Wilcoxon rank-sum test was adopted.
*$P < 0.01$
The tension at various Ca concentrations compared with the tension in 0 mEq · l^{-1} Ca at each temperature.

with 0 mEq·l^{-1} Ca to −116 ± 13 mg with 2 mEq·l^{-1} Ca at 15°C (table).

The decrease in temperature suppressed the increase in tension caused by Ca, and the suppression was complete at 10°C. At 20°C, 4 mEq·l^{-1} Ca increased the tension from −88 ± 13 mg to −13 ± 19 mg (table and fig. 2). As shown in figure 2, this peak tension (−13 ± 19 mg) did not reach basal tension (in Ca-free solution at 37°C, 0 ± 0 mg). The statistical significance did not exist between these two values.

The increase in tension after stretching was not different significantly from the prestretching increase in tension (fig. 3).

Discussion

The tension of the coronary artery is influenced by electrolyte composition of extracellular fluid. It is generally assumed that depolarization of the smooth muscle membrane enhances Ca conductance and increases Ca influx, causing an increase in tension. The concentration of free intracellular Ca^{2+} is the main determinant of the degree of activation of the contractile appara-

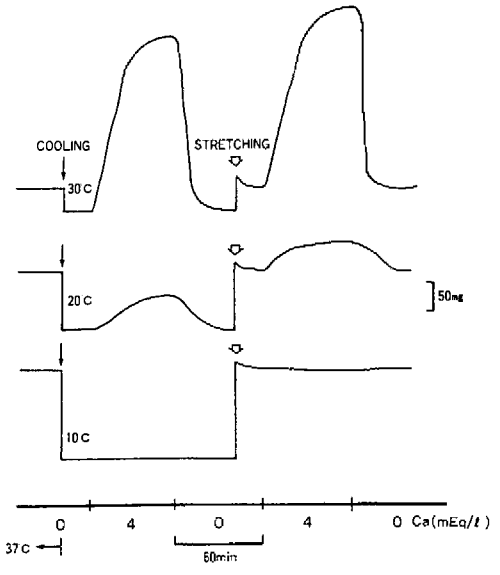

Fig. 3. Effects of cooling and the responses to stretching.
There was no difference between the tensions pre and post-stretching.

tus in smooth muscle[3]. Electrophysiological study has demonstrated that the excess-K brings about membrane depolarization in the guinea-pig tenia coli[4]. In the present experiments on the canine coronary artery, this increase in tension caused by K was highly dependent on the external Ca concentration and this increase in tension did not occur below 0.1 mEq·l^{-1} [Ca] in 20 mEq·l^{-1} [K], irrelevantly with temperature.

The fact that normal blood vessels responds vasoconstrictively to cold after denervation is proved[5]. The arterial smooth muscle is depolarized by cooling. This depolarization is likely to be due to a halt of the Na-K pump, which leads the gain of Na and the loss of K in the cells, resulting in a slower secondary depolarization. It presumably causes an increase in tension in turn by allowing entry of Ca and perhaps by releasing endoplasmic reticulum Ca[6]. However in this experiments, the coronary artery was relaxed by cooling. At 20°C, the tension caused by 4 mEq·l^{-1} Ca was not larger than basal tension (37°C, 0 mEq·l^{-1} Ca). And at 10°C, 4 mEq·l^{-1} Ca did not increase the tension at all. Commonly, the tension is related to sarcomere length[7], so this relaxation may be resulted from the increase in sarcomere length caused by cooling. But we deny this possibility from the result that there was no significant difference in the increase in tension between pre and post-stretching (fig. 3). The mechanism of this vasodilator effects induced by cold remains uncertain, but it is demonstrated that the rate of shortening of the actomyosin was greatly slowed by cooling[2]. The phase transition of the myocardial cell membrane is developed by cooling[8], and the same phenomenon developed in the myocardial cell membrane might appear in the smooth muscle membrane. This may change the permeability of ions, ATP-ase pumps and/or Na-Ca exchange system.

In conclusion, the increase in tension of canine coronary artery occured in proportion to the increase in Ca concentration in high-K solution, but this increase in tension did not occur below 0.1 mEq·l^{-1} Ca. Cooling inhibited this increase in tension especially below 20°C, and did not increase its tension in spite of the presence of 4 mEq·l^{-1} Ca at 10°C.

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