

## Role of sex hormones on coronary spasm in male and female assessed by synchrotron radiation coronary micro-angiography

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### Introduction

A coronary spasm is a brief, temporary contraction of the muscles in an artery wall. This can cause angina pectoris and myocardial infarction in severe cases. Coronary spasms occur more frequent in male than female. Non-hormonal risk factors, such as smoking and atherosclerosis, are more frequent in male, whereas, estrogen deprivation thought to contribute the occurrence in female. However, true contribution of sex hormones has been unidentified. The purpose of this study is to identify the feature of coronary spasm between male and female in relation to sex hormone using synchrotron radiation micro-angiography.

### Manuscript preparation

Wistar male (n=22), intact female (n=8) and ovariectomized female rats (n=9) were employed. Spasms were induced by 4-aminopyridine (4-AP). In Langendorff apparatus, hearts were maintained 20 minutes, followed by 5 minutes perfusion with 4-AP. Synchrotron radiation micro-angiography were performed at pre, during, and 15 minutes after withdrawal of 4-AP.

### Results

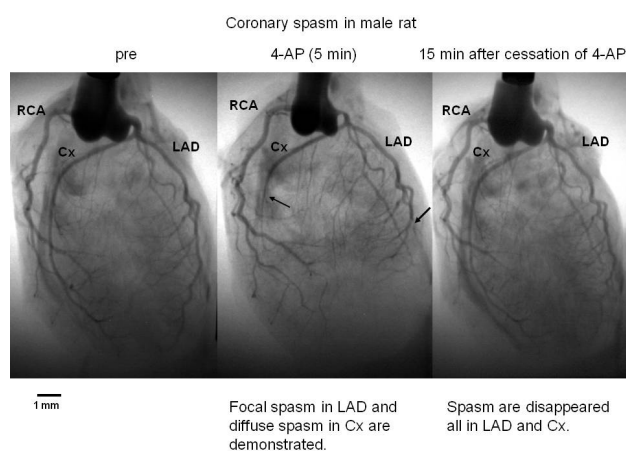
Spasms were shown 14/22 in male, 8/8 in intact female, and 9/9 in ovariectomized female rats (NS). Numbers of spastic arteries were 1.0 +/- 0.9 in male, 2.0 +/- 0.8 in intact female (p<0.01 vs. male), and 2.2 +/- 0.7 in ovariectomized female rats (p<0.01 vs. male). At 15 minutes after 4-AP withdrawal, they were 0.1 +/- 0.4 in male, 1.0 +/- 0.9 in intact female (p<0.01 vs. male), and 1.3 +/- 1.1 in ovariectomized female rats (p<0.005 vs. male). Distributions of coronary spastic shape were as follows: male (focal: 15, diffuse: 7), intact female (focal: 14, diffuse: 2), ovariectomized female (focal: 4, diffuse: 16) (p=0.0001 between females).

Acute withdrawal of sex hormones containing in serum was more significant in female. Effect of withdrawal was lasted significantly in female. From these results, estrogen has a crucial role in maintaining coronary dilatation in female. Diffuse shape of spasms in ovariectomized female rats might relate to diffuse contribution of estrogen on coronary arteries.

### Conclusions

Deprivation of sex hormone (estrogen in female) either acutely or chronically exacerbated coronary spasm in female than in male. Chronic deprivation of estrogen

(OVX) showed diffuse type of spasm, which represents severity of spasm. It was demonstrated that estrogen has a crucial role in maintaining coronary dilatation in female.



**Figure.** Synchrotron radiation coronary micro-angiography showed no sign of spasm before spasm induction by 4-AP (left). Coronary spasms either focal or diffuse shape were induced by 5 min after the use of 4-AP in male rat heart (middle). Fifteen minutes after cessation of 4-AP, coronary spasm was disappeared (right). However, in cases of ovariectomized female rats spasms were continued even after 15 minutes after cessation of 4-AP (figures were not shown).

### References

- [1] S. Matsushita et al., Nuclear Instruments and Methods in Physics Research A 548, 94-98 (2005)
- [2] S. Matsushita et al., Eur J Radiol 68S: S84-S88 (2008).

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