

# 冠攣縮の最新知見：国際共同研究に向けて

(Coronary artery spasm : up-dated, aiming at the international collaboration study)

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共催 冠攣縮研究会

## 座長のことば

冠攣縮が日本人の虚血性心臓病の成因に深く関与していることは広く知られている。冠攣縮の頻度は日本人に高く、少なくとも欧米人の3倍以上と考えられているが、一方、最近の知見では、冠攣縮の頻度はアジア人全般に高い可能性が指摘されている。冠動脈インターベンションが広く行われるようになった昨今では、とすれば冠攣縮の重要性が見落とされがちである。また、冠攣縮には、顕著な人種差の成因も含めて、未解決の問題が数多く残されている。

このような現状を踏まえて、我々は2006年に冠攣縮研究会を発足させ、冠攣縮に関する臨床経験を共有するとともに、未解決の問題を解明する活動を行ってきている。参加施設も66施設まで増加し、研究体制が整った。まず後ろ向き登録研究を実施し、1500例を超える症例が登録され、今回の日循学術集会でも5題の演題を発表する予定である。

今後は、前向き登録研究を開始するとともに、人種差の解明を目指して、国際共同研究を開始する予定である。

今回のファイヤサイドセミナーには、この国際共同研究を行う外国の研究者が一同に介し、冠攣縮に関する現状の問題点と今後の活動について討議する。冠攣縮に関心のある多くの会員の参加を期待する。

## 1. 冠攣縮研究会からの報告 (Progress report from the Japanese Coronary Spasm Association)

○安田 聡 冠攣縮研究会 事務局

Coronary artery spasm plays an important role in the pathogenesis of a wide variety of ischemic heart disease, especially in the Japanese population. Recent progress in prevention, diagnosis and treatment may have significantly influenced clinical characteristics and prognosis of patients with vasospastic angina. Importantly, in 2008, Guidelines for Diagnosis and Treatment of Patients with Coronary Spastic Angina was published. The Coronary Spasm Association of Japan was established in 2006, in which 68 leading medical institutes currently participate nationwide (<http://csa.cardiovascular-medicine.jp/>). Following retrospective multicenter registry study of ~1500 patients, we are planning to conduct the new project, which is a prospective fashion using Web registry system to pursue the clinical outcomes of vasospastic angina, adds the patients with the diseases associated with coronary vasospasm, e.g., cardiac syndrome X and Takotsubo cardiomyopathy, and would develop the international research collaborating with Italy, Switzerland, Australia and Korea. The Coronary Spasm Association of Japan will address many important aspects of coronary vasospasm including pathophysiology, prognosis and racial differences.

## 2. 韓国における冠攣縮 (Coronary Spasm in Korea)

○Sang Hong Baek ソウルカトリック大学,韓国

The prevalence rate of coronary spasm was 6.96% in our coronary spasm registry. The male to female ratio of spasm was a quite similar. The mean age at diagnosis of spasm was  $50.0 \pm 8.2$  year-old in male, and  $53.8 \pm 7.5$  year-old in female.

The Glu298Asp polymorphism of eNOS gene and smoking were strong risk factors for spasm. A triple combination drug regimen was most common as 48.1%: the combination of CCB + Nitrate + KCO. Subgroup analysis of coronary spasm will be introduced, (1) rates of cardiac death and progression of significant atherosclerosis in spasm, (2) comparison of the long-term prognosis between spasm and intermediate vasoconstriction induced by the administration of Ach, (3) remission of spasm in variant angina patients, (4) clinical and angiographic characteristics of acute MI caused by variant angina without organic CHD.

Conclusion: Korean has a higher incidence of coronary spasm than Caucasian. It is a time to start an international multicenter registry of coronary spasm to evaluate the characteristics and to make an optimal treatment regimen.

### 3. 冠攣縮における人種差 (Racial difference in coronary artery spasm)

○John Beltrame アデレード大学,オーストラリア

Coronary artery spasm plays an important role in the pathogenesis of coronary heart disease. Japanese cardiovascular researchers have made major contributions to the clinical understanding of coronary spasm, where the condition appears to be especially prevalent. In particular, there are extensive reports concerning Prinzmetal variant angina from Japan whereas there are limited studies involving Caucasian populations. Furthermore, studies investigating similar characteristics in Japanese and Caucasian patients have reported diverse findings, implicating racial differences in vasomotor reactivity.

In a review of the published literature, differences in coronary artery spasm between Japanese and Caucasians will be discussed, particularly in relation to Prinzmetal variant angina and acute myocardial infarction. Furthermore, the results of a controlled coronary artery spasm study comparing Japanese and Italian patients with recent myocardial infarction will be discussed. These racial differences not only have important clinical implications but may also provide further pathophysiological insights into this perplexing condition.

### 4. 冠動脈収縮の機序：既成概念からの脱却 (Mechanisms of coronary vasoconstriction: "lumpers" or "splitters"?)

○Attilio Maseri 心臓財団,イタリア

1. The pathogenetic role of coronary vasoconstriction is very elusive, because it can be detected only by performing angiography during its very transient, occasional occurrence, spontaneous or following provocative tests, and after intracoronary nitrates.

The mechanisms of coronary vasoconstriction are likely to be multiple. Although many of these may benefit, to some extent, by treatments, effective on common final pathways of constriction, such as nitrates and calcium antagonising, a more effective treatment requires the precise knowledge of its multiple possible causes.

2. The time has come to focus clinical research on phenotypically homogeneous groups of patients in order to discover novel treatments on specific therapeutic targets, "made to measure" for them.

3. In this endeavour, clinical investigators must have inquisitive minds, rather than be conditioned by prevailing paradigms, and look for distinctive features among patients within the same clinical syndrome, which could help the identification in homogeneous subgroups, characterized by yet unknown pathogenetic mechanisms of disease; cardiologists should be "splitters" rather than "lumpers" and act as detectives searching for clues suggestive of new working pathogenetic hypotheses.

4. Constriction severe enough to cause myocardial ischemia can develop both in large epicardial coronary arteries and in small distal vessels, and it may result from two fundamentally different pathogenetic mechanisms that require distinct therapeutic approaches:

- Strong stimuli capable of causing critical constriction also in normal vessels.
- Enhanced local constrictor response of the vascular wall to a variety of stimuli which, although do not have any significant constrictor effect on normal vessels, cause critical constriction of the affected segment. This enhanced constrictor response may occur at the level of the smooth muscle or be related to an inadequate endothelial vasodilator response which can reduce coronary flow reserve and enhance the effect of constrictor stimuli.

### 5. パネルディスカッション

安田 聡、Sang Hong Baek、John Beltrame、Attilio Maseri