

## Conclusion

- For the first time, a systematic prospective study has demonstrated that myocardial fibrosis is significantly higher in dogs with heart failure than in old control dogs.
- It is now recognised that remodelling and especially myocardial fibrosis have major adverse effects on the heart's electrical and mechanical function. The development of myocardial fibrosis causes pathologic hypertrophy with abnormal myocardial stiffness, which leads to ventricular diastolic and systolic dysfunction and ultimately to the progression of symptomatic heart failure<sup>16,17,18</sup>. Therefore, protecting the heart from the development of myocardial fibrosis is an important consideration when treating canine heart failure patients.

**We hope you have found this first edition of CardioNews interesting. The next edition will explore in more detail the clinical significance of fibrosis in canine heart failure patients and the ways in which it can be controlled. If you have any further questions then feel free to contact CEVA Animal Health on 01494 781510.**

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## Heart disease & myocardial fibrosis in dogs

### SUMMARY:

Heart disease leads to structural and functional changes of the heart, which may affect the outcome of the disease<sup>1</sup>. These changes are often referred to as remodelling<sup>2,3,4</sup> and can include:

- hypertrophic enlargement of the heart<sup>1,3</sup>
- thickening of the blood vessel walls<sup>5</sup>
- cardiovascular fibrosis

Remodelling is caused by both mechanical changes and neurohormonal changes, including the activation of the renin-angiotensin-aldosterone system<sup>6</sup>.

Myocardial fibrosis has been extensively studied and shown to be clinically significant for people with heart disease<sup>7,8</sup>. However, although fibrosis has been described extensively in dogs with mitral valve disease, until recently its clinical significance and impact on the evolution of heart failure in dogs has been unclear. One reason for this is that assessing fibrosis requires a post-mortem examination and, unlike in man, there are no available blood markers or imaging tools which allow fibrosis to be monitored routinely in practice.

The aim of this newsletter is to explore current knowledge on the presence of myocardial fibrosis in mitral valve disease in the dog. The next newsletter will then assess its clinical significance in more detail.

### Introduction

To help keep you up-to-date on upcoming developments in veterinary cardiology, we are proud to introduce the first issue of "CardioNews". This newsletter has been designed to inform you about new topics of interest in cardiology that may have an impact on your daily practice. The first issue discusses myocardial fibrosis in heart failure patients, which is a recent concept in veterinary medicine. We would like to thank Dr Torkel Falk, from the Royal Veterinary and Agricultural University of Frederiksberg (Denmark) for this issue.

### Myocardial fibrosis in dogs

In the dog, myocardial fibrosis is linked to arteriosclerosis. This refers to hardening (and loss of elasticity) of the medium or large arteries, which subsequently causes arterial occlusion and surrounding fibrosis and necrosis<sup>9</sup>. This should not be confused with atherosclerosis, which is associated with the accumulation of lipid within the arteries. Atherosclerosis is commonly linked to 'heart attacks' in man<sup>10</sup> but has been shown to be uncommon in the dog.

Arteriosclerosis has been described in many published studies in dogs<sup>9,11,12</sup>. For example, Jönsson studied the coronary arteries and their changes in a large study involving 643 dogs<sup>9</sup>. This study described arteriosclerotic lesions and myocardial fibrosis in dogs with mitral valve disease. Further studies have also been carried out by Detweiler, who considered that arteriosclerosis and myocardial fibrosis have a real clinical impact during the course of mitral valve disease in dogs<sup>13,14</sup>.

# Characteristic Histopathological Lesions

## Arteriosclerosis

- Thickening and severe narrowing of the intramyocardial artery due to proliferation of fibroblasts and smooth muscle cells in the arterial wall

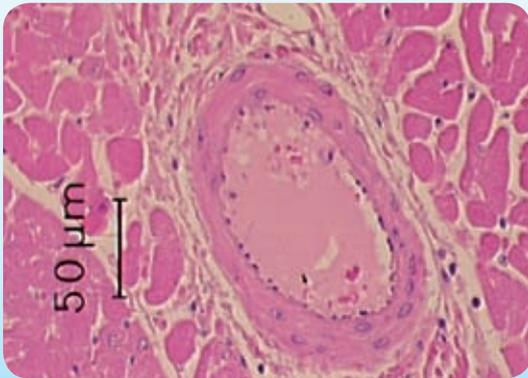


Fig. 1: Normal intramyocardial artery

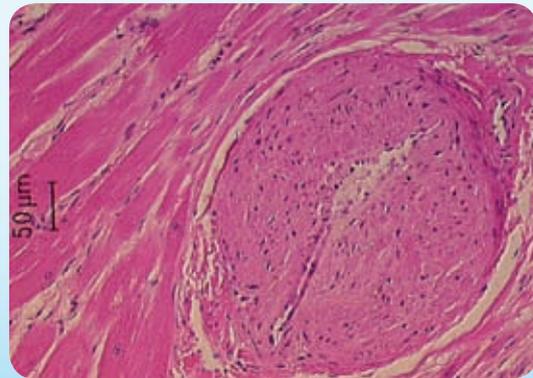


Fig. 2: Severe narrowing of intramyocardial artery

## Myocardial fibrosis

- Focal areas of myocardial fibrosis and necrosis, especially in the left ventricle
- Probably secondary to ischemic disease, which itself is caused by arteriolar occlusion

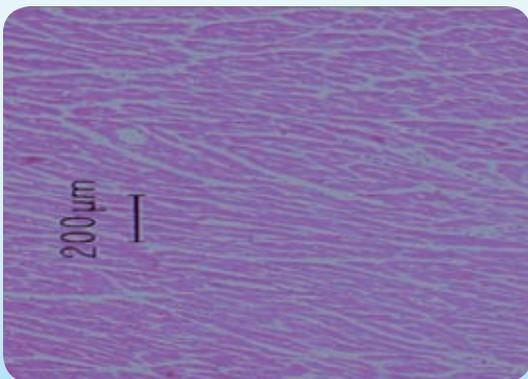


Fig. 3: Normal myocardium

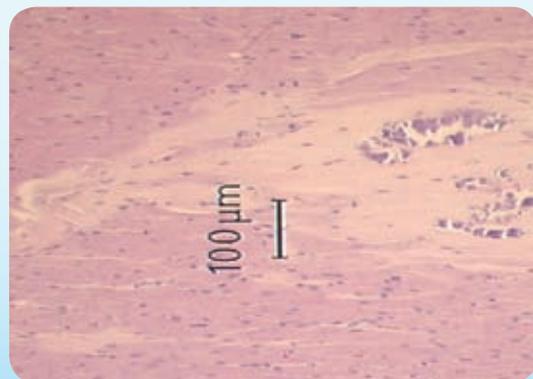
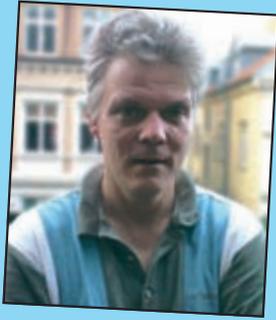


Fig. 4: Severe demarcated myocardial fibrosis with calcification

## Recent findings

A recent study has now been carried out which describes and quantifies myocardial arteriosclerosis and fibrosis with naturally occurring heart disease in dogs and compares these dogs to a control group<sup>15</sup>.



Dr T. Falk DVM PhD  
Department of Basic Animal and Veterinary Sciences,  
The Royal Veterinary and Agricultural University, Frederiksberg, Denmark

**Summary of the paper from Falk, T., Jönsson, L., Olsen, L.H., Pedersen, H.D. published in Cardiovascular Pathology. 2006, 15. 185-193.**

## **Arteriosclerotic changes in the myocardium, lung, and kidney in dogs with chronic congestive heart failure and myxomatous mitral valve disease<sup>15</sup>**

### **Objectives:**

To quantify and describe arteriosclerosis and fibrosis in the myocardium of dogs with advanced myxomatous mitral valve disease (MMVD) and to compare their occurrence to control dogs.

### **Material & Methods:**

- 42 dogs: 2 comparable groups of dogs

**Congestive Heart Failure (CHF) group:** 21 dogs with naturally occurring CHF and MMVD (detected by clinical and ultrasonographic examinations) without other concomitant cardiac disease;

**Control group:** 21 older dogs with no cardiac murmurs or clinical signs of CHF, included in order to match CHF dogs (for age, sex, and weight).

- All included dogs underwent an extensive pathological and histopathological examination after natural death or euthanasia. Morphometry was used to quantify arterial narrowing and fibrosis in different locations, including
  - the myocardium: different sites were sampled;
  - the arteries: the aorta, pulmonary arteries, arteries in the kidney and intramyocardial arteries.

Fibrosis was scored in the myocardium using the five-grade Whitney scale: from 0 = no evidence of fibrosis to 4 = large areas of confluent fibrosis.

Regarding arteries, a lumen to area ratio was used to measure vessel narrowing, which is defined as the luminal area of the vessel divided by the total vessel area.

### **Results:**

<b>Cardiac Hypertrophy</b>	CHF-dogs had significantly more cardiac hypertrophy as measured by heart to weight ratio ( $p < 0.0050$ )
<b>Fibrosis</b>	CHF-dogs had significantly more fibrosis in the left ventricle ( $p < 0.0001$ ) whichever the locations in the myocardium
<b>Arteriosclerosis</b>	CHF dogs had significantly more arterial narrowing in the left ventricle ( $p < 0.0030$ ) but also in the lung and kidney than control dogs

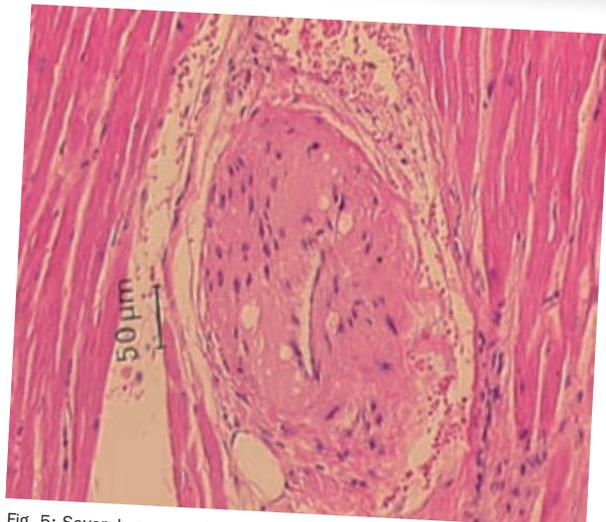


Fig. 5: Severely narrowed intramyocardial artery with interstitial fibrosis surrounding myocytes

### **Conclusion:**

Dogs with MMVD had significantly more intramyocardial arteriosclerosis and fibrosis than control dogs. This is the first study demonstrating systematically an association between intramyocardial fibrosis, arteriosclerosis and severe MMVD.



Pr T. Falk DVM PhD  
Department of Basic Animal and Veterinary Sciences,  
The Royal Veterinary and Agricultural University, Frederiksberg, Denmark

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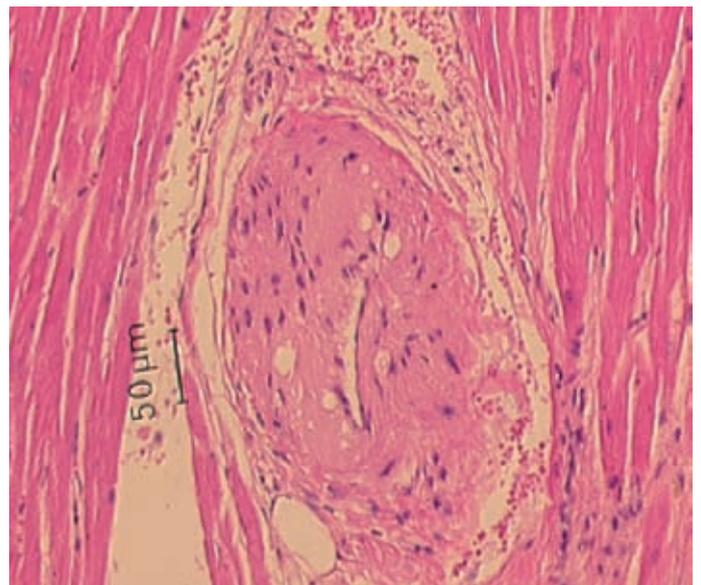


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