

AN *IN VIVO* METHOD TO STUDY ENDOTHELIAL DYSFUNCTION IN PIG MODELS

M.M. Birck¹, P. Liuba², E. Pesonen², M. Odermarsky² and A.K.Hansen¹

¹Division of Laboratory Animal Science and Welfare, Department of Veterinary Disease Biology, Faculty of Life Sciences, University of Copenhagen, Denmark;

²Division of Pediatric Cardiology, Lund University Hospital, Sweden

¹Presenting author: mbirck@life.ku.dk

Background:

Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality in the world. Therefore good animal models are essential for understanding the pathogenesis of CVD and atherosclerosis. The pig has proven to be a good large animal model for the research on the causes and prevention of human atherosclerosis. Since endothelial dysfunction (ED) is known to be an early event in atherosclerosis this is an important marker of early stage CVD.

Objective:

To develop an *in vivo* method to test for coronary ED and to evaluate the effect of *Chlamydia pneumoniae* (Cpn) infection on endothelial function in a pig model.

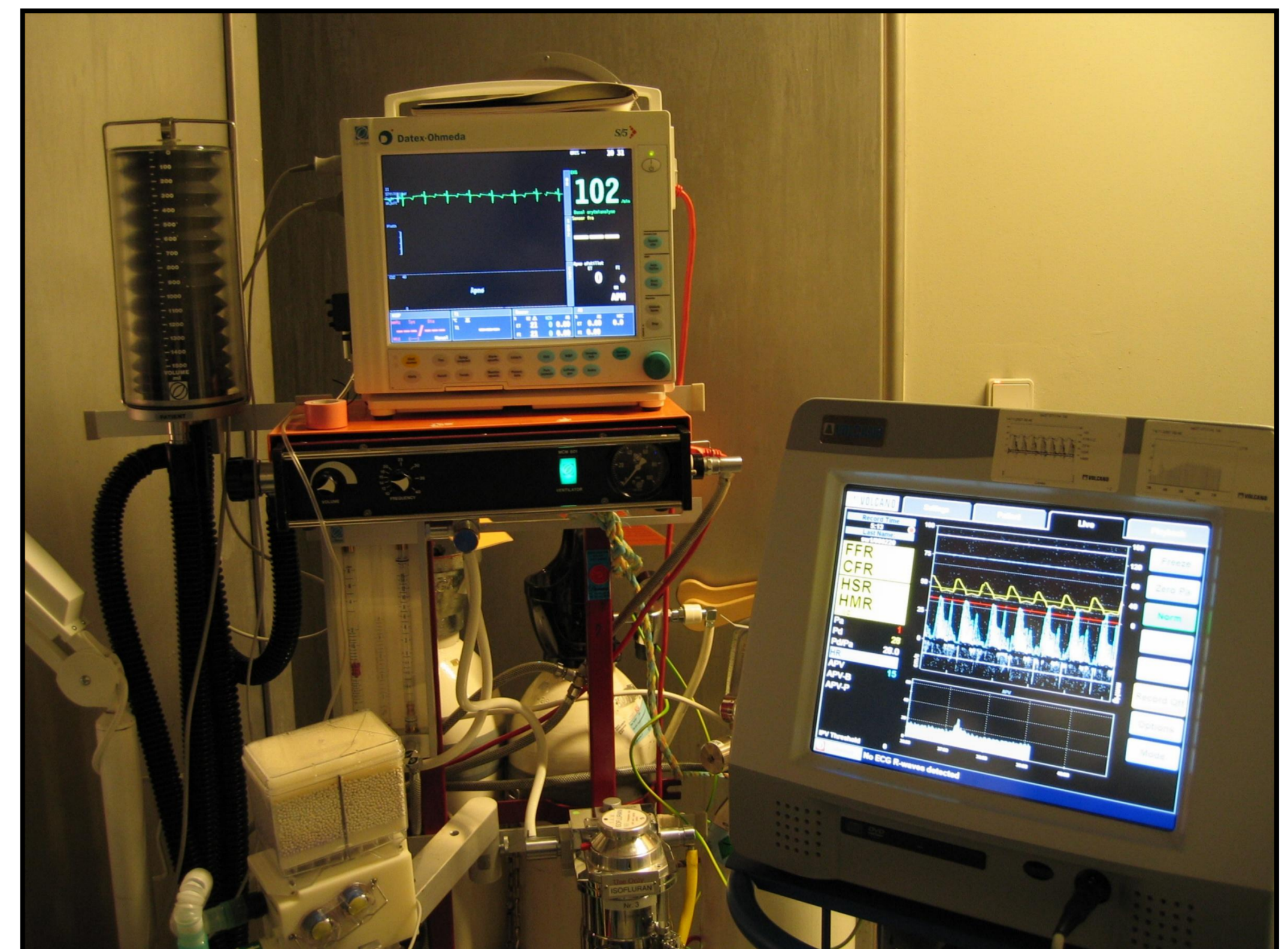


Figure 2: To the left a patient monitor and to the right a ComboMap®System monitor displaying intracoronary pressure and coronary flow velocity.

Results:

There was no difference in baseline CFV between controls and infected (13 ± 5 vs 15 ± 4 , respectively; $p=0.52$). Peak-baseline ratio was significantly lower in infected animals compared to controls (2.21 ± 0.37 vs 2.85 ± 0.44 ; $p=0.02$) and time to second peak was significantly longer in infected animals compared to controls (163 ± 56 vs 99 ± 18 ; $p=0.02$). Fig. 3 are examples of a coronary flow response curve in a control pig and an infected pig after BK infusion.

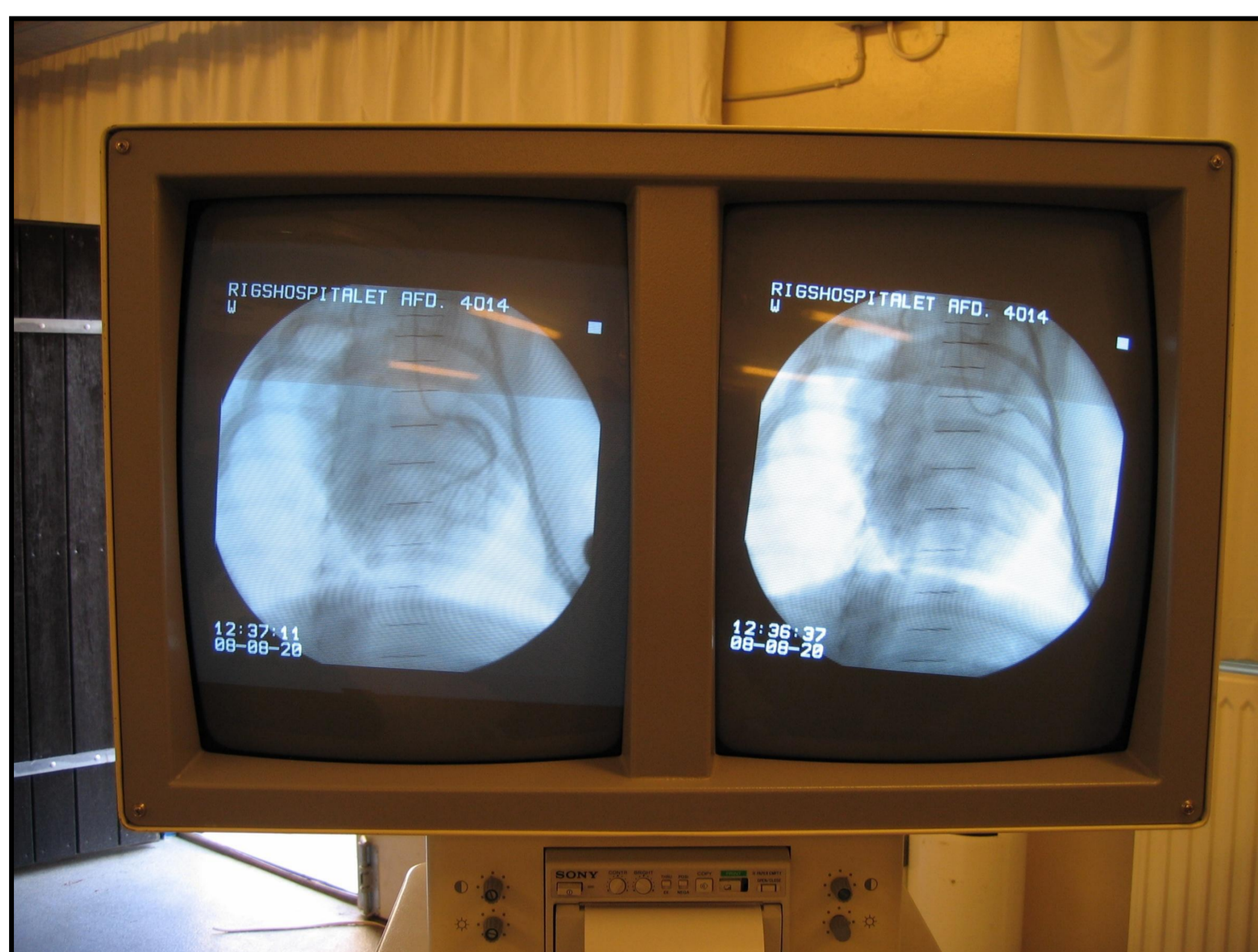


Figure 1: X-ray image showing the position of the intracoronary doppler guide wire in the left anterior descending coronary artery (LADCA) of a pig.

Study design:

Twelve minipigs were included in the study (6 infected and 6 controls). A coronary artery catheter was advanced through the left carotid artery to the orifice of the left coronary artery in an anesthetized pig.

A Volcano ComboWire (pressure/flow wire) connected to a real-time spectrum analyzer (ComboMap®System), was then inserted through the catheter and advanced into the mid-portion of the left anterior descending coronary artery (LADCA). Contrast hand-injection was used to confirm the correct position of the catheter tip (Fig. 1).

After stabilization of the baseline signal, the response to bradykinin (BK), an endothelium-dependent vasodilator was tested. Average peak coronary flow velocity (CFV) signals and intracoronary pressure were displayed continuously on the monitor (Fig. 2).

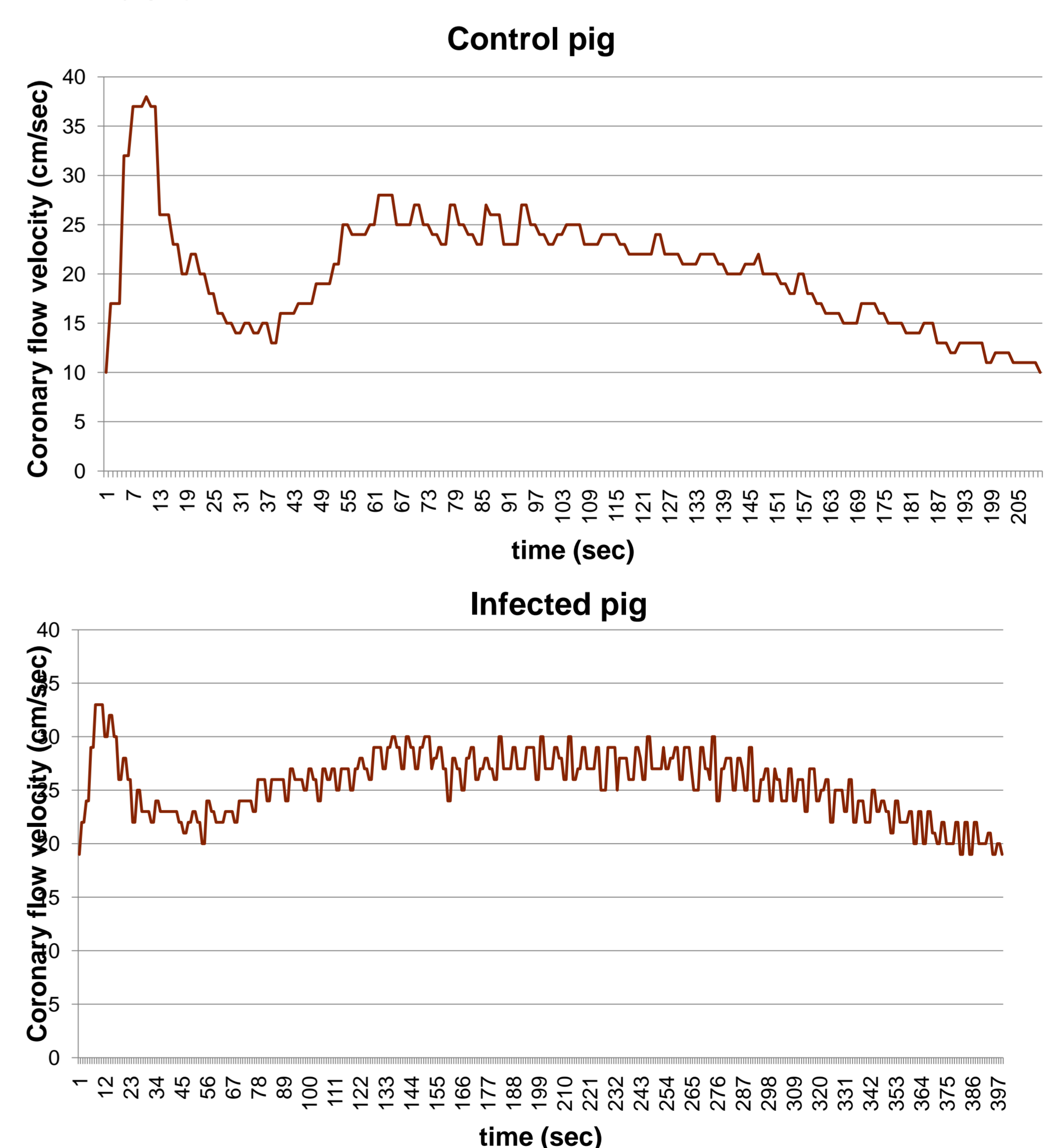


Figure 3: Illustration of the coronary flow response curve in a control pig (top) and infected pig (bottom).

Conclusions:

The vasomotor coronary response to BK can be used as a surrogate marker to 1. assess the degree of kinin-related coronary vasomotor dysfunction, and 2. to discern between endothelial and nonendothelial pathways implicated in the process of coronary dysfunction due to infection. The technique requires some expertise in catheter positioning and evaluation of flow response. In this study, the coronary response to BK was significantly decreased in infected animals and we can conclude that Cpn infection causes ED in minipigs.