Coronary Microvascular Dysfunction is Induced by Hemodynamic Instability: Quantitation by Controlled Flow Infusion

Schwartz RS1,2, Hoem JH3, Cesariovic N1, Bludau O2, Gastl M1,4, Feldman B2, Jonathan G. Schwartz5, Rothman MT2

1 Minneapolis Heart Institute and Foundation, Minneapolis, MN, USA, 2CorFlow Therapeutics AG, Bear, Switzerland, 3Division of Surgical Research, University Hospital Zurich, Sennwegstrasse 14, 8091, Zurich, Switzerland, 4Institute for Biomedical Engineering, University and ETH Zurich Gloriastrasse 31, 8093 Zurich, Switzerland, 5Sanger Clinic, Charlotte, NC, USA

Background

Coronary Microvascular resistance (MVR) has increasing clinical relevance in many clinical syndromes. A method for real-time MVR measurement would have great clinical use for not only diagnosis but also guiding and assessing therapeutic efficacy of microvascular obstruction in STEMI/NSTEMI, no-reflow, diabetes and transplant microvascular disease.

This study evaluated coronary Controlled Flow Infusion (CoFI™), a novel technique recently developed that measures real-time, absolute MVR and microvascular compliance.

Methods

CoFI™ technology (Figs 1a and 1b) involves epicardial coronary artery occlusion using a soft, compliant infusion balloon with integral distal pressure wire. Crystalloid is precisely infused into the distal (occluded) vessel/microvasculature via computer-controlled pump over a broad range of physiologic flow rates(Fig 2). The microvascular resistance generates a dynamic back-pressure which is recorded from the pressure wire. Real time MVR is calculated over the entire infusion flow range as distal microvascular pressure divided by infusion flow rate:

\[ \text{MVR} = \frac{\text{Distal Pressure}}{\text{Infused Flow Rate}} = \frac{P(t)}{Q(t)} \]

Microvascular compliance is the differential rate of MVR change with pressure:

\[ \frac{\Delta R}{\Delta P(t)} \]

Preclinical Study

STEMI was induced in 7 domestic pigs by 90 min balloon LAD occlusion. Pre- and Post-STEMI MVR was measured using step flow infusion (green line, 5, 10, 25, 30, 40, and 50 ml/min) Fig 2 shows resulting dynamic MVR (Red Line) and Pressure (blue line).

Results

dMVR showed a strong and inverse relation to infusion flow and pressure both pre- and post STEMI. Total microvascular resistance increased more than 3-fold. The microvascular compliance (Fig 3b) defined by the pressure-resistance derivative relationship showed myocardial microvascular stiffness grows markedly above 10-15 mmHg (Fig 3a).

Conclusions

• MVR is highly pressure dependent, both PRE- and POST- STEMI. In this pig, STEMI induced a more than 3-fold microvascular resistance increase.

• Microvascular compliance can be similarly measured, and showed a marked reduction in the setting of experimental ischemia and infarction.

• Real time absolute microvascular resistance is readily measured using CoFI™ methods.

Implications

The CoFI™ system may have application in assessing conditions with myocardial microvascular disease including syndromes such as microvascular obstruction, transplant vasculopathy, Syndrome X, cardiogenic shock, no-reflow, and stress cardiomyopathy.

Controlled flow infusion measures myocardial dynamic microvascular resistance in real time using a safe, simple, and efficient method. It may have clinical use in acute coronary syndromes and other diseases involving the microvasculature for both diagnostic and for guiding therapeutic intervention of the microvasculature.

Disclosure:

I am a Co-founder of Corflow Therapeutics AG