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INFLUENCE OF HEART RATE AND EPICARDIAL STENOSIS SEVERITY ON CARDIAC CONTRACTILITY UNDER CONCOMITANT MICROVASCULAR DISEASE IN A PORCINE MODEL

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ABSTRACT

Invasive guide wire methods to assess functional severity of coronary stenosis are affected by dynamic variables like heart rate (HR), contractility, epicardial stenosis (AS) and blood pressure. The interdependence of these factors is also influenced by the presence of concomitant microvascular disease (CMVD). The purpose of this study is to assess the variation in contractility under varying HR and AS in the presence of CMVD. *In vivo* experiments were performed on seven Yorkshire pigs. It was found that, in the presence of concomitant microvascular disease (CMVD), for lower AS (<50%) contractility increases for HR<120 bpm while it marginally decreases for HR>120 bpm. However, for higher AS (>50%), contractility decreases for both HR<120 bpm and HR>120 bpm.

INTRODUCTON

Quantification of the functional significance of epicardial coronary stenosis is important to diagnose heart diseases. In addition, in most clinical cases an obstruction in the coronary microvasculature might also be present under concomitant microvasculature disease, (CMVD) and can affect the clinical diagnostic measurements. Thus, quantification of the combined effect of epicardial and microvascular dysfunction is very much needed. The recent development of Doppler-tipped guide wires and pressure monitoring guide wires has facilitated the invasive measurements of coronary flow velocity and distal pressure, thus reviving interest in the invasive physiological assessment of coronary artery disease.

However, invasive measurements take place in a dynamic environment involving fluctuating hemodynamic variables like the blood pressure, contractility (CY) of the heart, epicardial stenosis (AS) and the heart rate (HR). To avoid any ambiguity in the evaluation of coronary circulation, the interdependence of these variables need to be clearly delineated. Accordingly, the goal of the present study was to evaluate the influence of changes in HR and AS on the left ventricular CY, measured as the maximum value of the derivative of left ventricular pressure $(dp/dt)_{max}$ [1].

METHODS

The animal protocol for this study was approved by the University of Cincinnati IACUC and the Cincinnati Children's Hospital Medical Center. Seven Yorkshire swine (mean wt. 50 ± 3 kg) were premedicated with intramuscular xylazine (2 mg/kg), telazol (7 mg/kg), and atropine (0.05 mg/kg) and anesthesia was maintained with 2% isoflurane and supplemental oxygen.

Three surgical accesses were made: 1) the jugular vein access was used to vary the HR by inserting pacing leads (Medtronics Inc., MN) into the right atrium; 2) second access through the carotid artery was used to advance a Millar© solid-tip catheter into the left ventricle, to measure the left ventricular pressure (recorded using Sonometrics system, Ontario, CN); 3) the third access, through the femoral artery, was used to engage a 7-F guiding catheter at the coronary ostium. Access to the left anterior descending (LAD) was achieved using a 0.014" guidewire under fluoroscopy guidance. The lumen cross-sectional area was measured using an intravascular ultrasound (IVUS, 2.5-F, 40-MHz) catheter. A 0.014" Combo wire (Volcano Corp., CA) was inserted distal to the balloon to measure pressure and velocity distal to lesion. Based on the artery size, an appropriate Voyager angioplasty balloon of rapid exchange type (Guidant Inc., IN) was introduced over the Doppler flow wire.

The balloon was inflated to different diameters to create intraluminal epicardial stenosis of varying severity. Polystyrene microspheres of 90µm (Polysciences Inc., NY) were injected to create the microvasculature obstruction. This procedure is similar to our previous studies [2,3,4].

Under CMVD, to investigate the effect of HR and AS, the CY was computed for 4 groups: Group 1: Lower AS (<50%) and normal HR (<120 bpm), Group2: Lower AS (< 50%) and higher HR>120, Group 3: Higher AS (>50%) and normal HR (< 120bpm), Group 4: Higher AS (>50%) and higher HR (>120bpm). A total of 73 measurements were obtained. Linear regression lines were plotted for the above mentioned groups to assess the effect of HR under varying AS.

RESULTS

The HR and AS values were correlated with the CY data for conditions mentioned above. Figure 1 shows the linear regression plot of HR and CY for AS<50%. For HR <120 bpm (Fig. 1A), as expected for a normal heart, the CY increases with HR (R^2=0.45). On the contrary, for HR >120 bpm (Fig. 1B), CY marginally decreased but remained at higher values with increasing HR. This behavior correlated to a normal physiologic response under non-ischemia producing mild stenosis under CMVD. Figure 2 shows the linear regression plot of HR and CY for AS >50%. It is observed that for both HR<120 bpm (Fig. 2A) and HR>120 bpm (Fig. 2B), CY decreases as the HR increases. This can be explained by the fact that the higher stenosis under increasing HR in conjunction with CMVD leads to a decrease in oxygen supply to myocardium and thus leading to reduced contraction of the cardiac muscle.

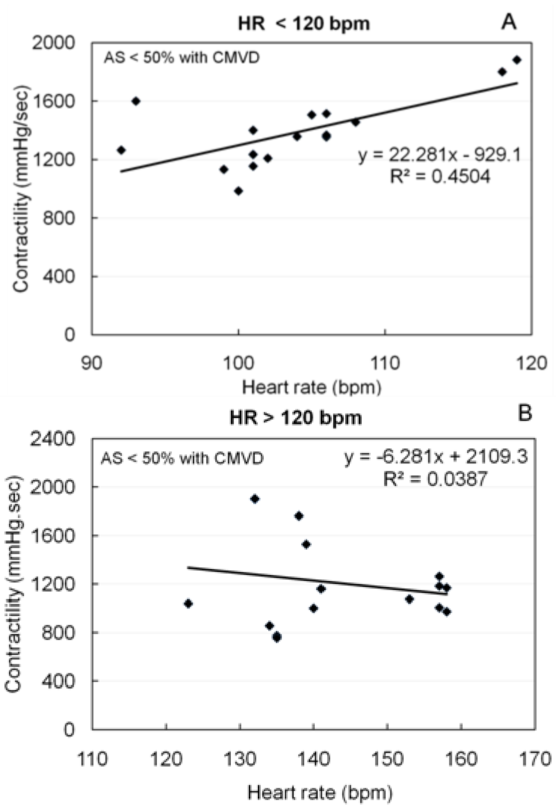

Figure 1: Variation in contractility (CY) for AS<50% under varying HR conditions A) HR<120 bpm B) HR>120 bpm

CONCLUSION

We conclude that under CMVD, AS<50%: for HR <120, CY increases, while it marginally decreases for HR >120. However, under higher AS, the CY of heart decreases for both HR<120 and HR>120. The data presented replicates the physiological phenomenon of reduced cardiac contractility under AS>50% with CMVD. Also, as a future work, the authors would also like to evaluate the effect of variations in CY on various diagnostic parameters (FFR, CDPe and LFC) under CMVD. This analysis would further aid in validating the use of pressure recovery coefficient CDPe (ratio of pressure drop across the stenosis to the distal dynamic pressure) and the lesion flow coefficient, LFC (ratio of the area reduction to the square root of the limiting dynamic pressure in the throat region) to the in clinical decision making for assessing severity of coronary artery stenosis.

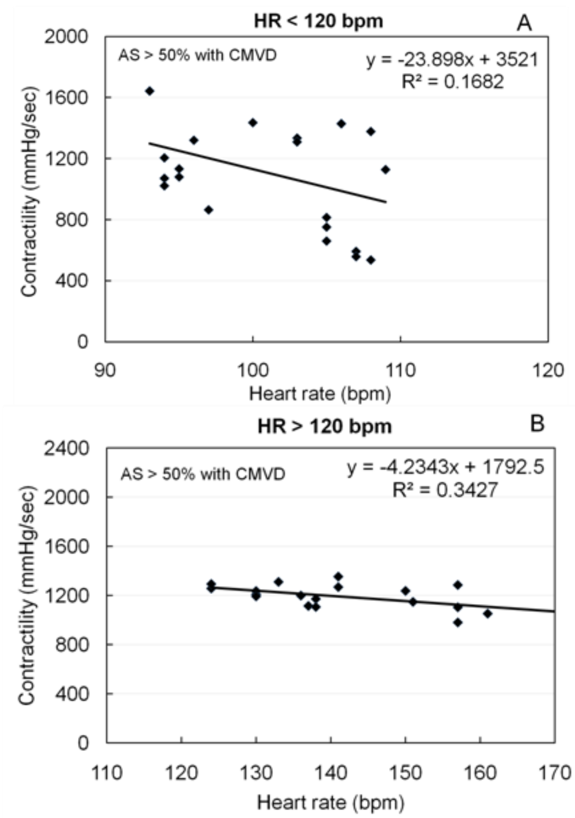

Figure 2: Variation in contractility for AS>50% under varying HR conditions A) HR<120 bpm B) HR>120 bpm

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