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INFLUENCE OF HEART RATE AND CONTRACTILITY ON CORONARY DIAGNOSTIC PARAMETERS WITH NORMAL MICROVASCULATURE IN PORCINE MODEL

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ABSTRACT

Invasive guide-wire measurements are used to assess coronary lesion severity under clinical settings. The objective of the present research is to determine the influence of heart rate (HR) and contractility (CY) on fractional flow reserve (FFR; the ratio of distal pressure to proximal pressure at a stenotic section) and pressure drop coefficient (CDPe; the ratio of trans-stenotic pressure drop to distal dynamic pressure). *In- vivo* experiments were performed on eight Yorkshire pigs, to evaluate the diagnostic parameters for the conditions "CY<1100 mmHg/sec" and "CY>1100 mmHg/sec," and for the conditions "HR<110 bpm" and "HR>110 bpm". It was found that in the presence of normal microvasculature the measured coronary diagnostic parameters (FFR and CDPe) have a significant mean difference for variation in contractility (*0.59±0.04 to0.89±0.045 for FFR and 121.63±18 to 23.53±18 for CDPe).* The variation in HR has no significant effect on FFR and CDPe *(0.72±0.048 to 0.74±0.048 and 54±20 to53±20 respectively).*

INTRODUCTION

Quantification of the physiological significance of epicardial coronary stenosis is important for diagnosing coronary artery disease. The assessment of epicardial stenosis becomes complex when concomitant diseases such as the presence of multi-vessel stenosis or microvascular dysfunction coexist in the coronary network. Thus accurate assessment of the epicardial dysfunction is needed to optimize treatment. This can be achieved by measurement techniques like pressure-derived FFR and CDPe, The recent development of dual sensor Doppler- and manometer-tipped guide-wires [1,2] has facilitated the invasive measurements of coronary flow velocity and distal coronary pressure simultaneously, thus generating added interest in the assessment of coronary artery disease using this technique.

During invasive interventional procedures, fluctuations in myocardial contractility (CY: intrinsic ability of a cardiac muscle fiber to contract at a given fiber length) and heart rate (HR) occur along with variability in coronary percentage area stenosis (AS). However, accordingly, the influences of hemodynamic changes in HR and CY on the diagnostic parameters (FFR and CDPe) have not been determined. Accordingly, the specific aim of the present study was to evaluate the influence of changes in HR and CY on the diagnostic indices (FFR, CDPe [3]) under normal microvasculature (epicardial stenosis).

METHODS

The animal protocol for this study was approved by the University of Cincinnati Institutional Animal Care and Use Committee, and the Cincinnati Children's Hospital Medical Research Foundation. All measurements were made in the left anterior descending (LAD) coronary artery of the animal at basal flow and peak hyperemia (induced by intra coronary Papavarine). Eight Yorkshire pigs (mean wt. (45 ±5 kg) were premedicated with intramuscular xylazine (2 mg/kg), telazol (7 mg/kg), and atropine (0.05 mg/kg).

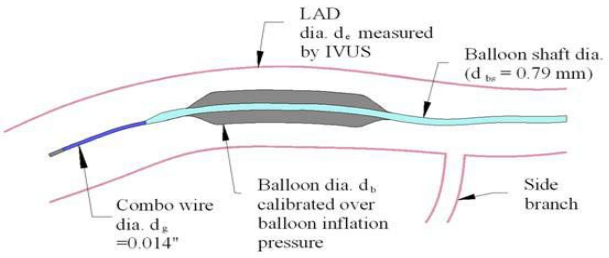

Figure 1: Physiological Pressure – Flow measurements in LAD

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During the experiment, anesthesia was maintained with 2% isoflurane, and supplemental oxygen was given by endotracheal intubation. Intravenous saline was administered to maintain euvolemia and normotensive conditions during coronary studies. A 7 French (7-F) sheath was introduced into the right carotid artery followed by a 7-F guiding catheter (Fig. 1).

An intravenous bolus dose of 300 Units/Kg. of heparin was administered. First, an intravascular ultrasound (2.5-F, 40-MHz intravascular ultrasound (IVUS); Boston Scientific Corp., MA) catheter was introduced into the LAD to measure its lumen cross-sectional area. Continuous monitoring of the location of the IVUS within the LAD was maintained by X-ray fluoroscopy. Then, the IVUS catheter was withdrawn, and a 0.014-inch Doppler flow wire (Volcano Therapeutics Inc., San Diego, CA) was introduced via the 7-F catheter. Based on the artery size, a Voyager angioplasty balloon of rapid exchange type (Guidant Inc., IN) and appropriate size was introduced over the Doppler flow wire.

The balloon was inflated to different pressures to create intraluminal epicardial stenosis of varying severity. This procedure is similar to the study conducted by Sinha Roy *et al* and Banerjee *et al*. [4, 5]. A 0.014-inch Combo wire (Volcano Therapeutics Inc.) was inserted distal to the balloon (Fig. 1), to measure pressure and velocity distal to lesion. For FFR, aortic pressure (proximal pressure) was recorded via the 7-F guiding catheter by an external pressure sensor (Edwards Life sciences, Irvine, CA). Left ventricular pressure (LVP) was measured with a 5F Mickro-Tip catheter (Millar Instruments) connected to Sonometric system. CY was calculated by obtaining the maximum value of time derivative of LVP, i.e., left ventricular $(dp/dt)_{max}$ {mmHg/Sec}.

To investigate the effect of HR and AS on the diagnostic parameters, FFR and CDPe, were computed for the conditions "CY<1100 mmHg/sec" and "CY>1100 mmHg/sec," and for the conditions "HR<110 bpm" and "HR>110 bpm". A total of 102 measurements were obtained. Two-way repeated measures ANOVA was performed (CY and HR are the two factors for the analysis). A value of $p<0.05$ was considered statistically significant.

RESULTS

The pressure and flow data, obtained under normal microvascular conditions, were analyzed for the effect of variable HR and CY on measured diagnostic parameters. Figures 2 and 3 refer to the main effects of CY and HR for FFR and CDPe, respectively. Main effects are differences in means over levels of one factor collapsed over levels of the other factor. Figure 2 shows the bar graph of FFR as a function of CY and HR. A significantly lower FFR (*0.59±0.04)* was observed for "CY<1100 mmHg/sec" condition when compared with (*0.89±0.045)* for "CY>1100 mmHg/sec." No significant difference in mean values of FFR (*0.72±0.048 to 0.74±0.048)* for the conditions "HR<110 bpm" and "HR>110 bpm," was observed. Figure 3 represents the bar graph of CDPe as a function of CY and HR. A significantly higher CDPe (*121.63±18)* was observed for "CY<1100 mmHg/Sec" condition compared to (*23.53±18)* "CY>1100 mmHg/sec." In addition, there was no significant difference in mean values of CDPe (*54±20 to53±20)* for the "HR<110 bpm" and "HR>110 bpm."

CONCLUSION AND DISCUSSION

The *in-vivo* experiments of the current study show that there is no significant influence of HR on the diagnostic parameters FFR and CDPe under normal microvasculature. There was, however, a significant influence of CY on these diagnostic indices s under normal microvasculature. Further studies to investigate the effect of the physiologic parameters (HR, AS and CY) under abnormal microvasculature are indicated, to quantify their effect on diagnostic indices under various coronary impairment conditions.

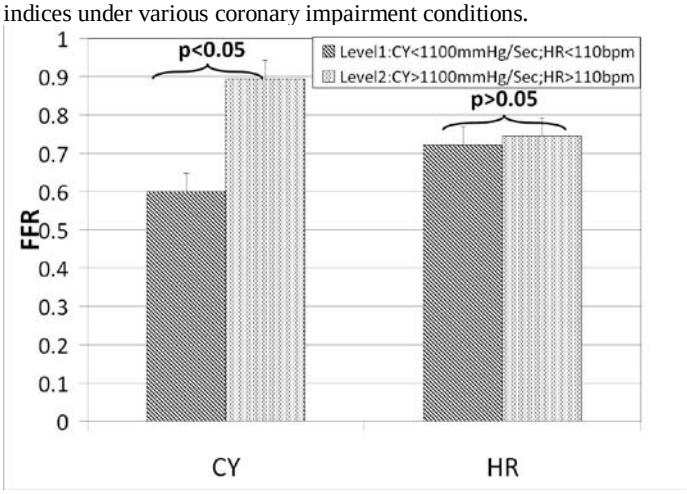

Figure 2: FFR as a function of CY and HR

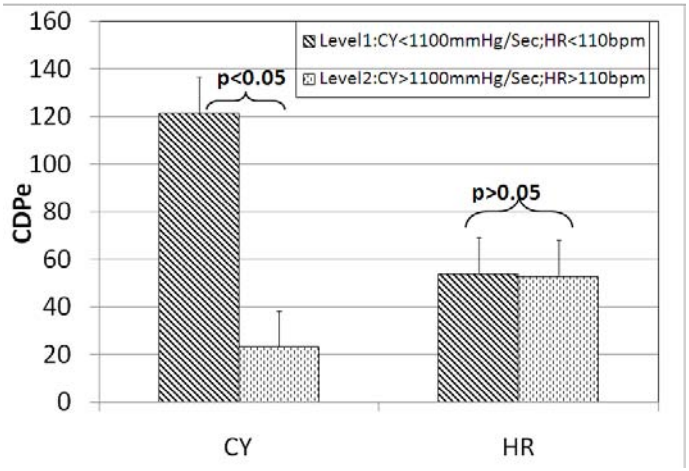

Figure 3: CDPe as a function of CY and HR

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