ABSTRACT

Several parameters have been proposed to assess the physiologic significance of coronary lesions invasively. The purpose of the present study is to determine the effect of heart rate and percentage area stenosis on Fractional Flow Reserve (FFR), which is the ratio of mean pressure distal to stenosis over the mean proximal (aortic) pressure and Pressure Drop Coefficient (CDP), ratio of trans-stenotic pressure gradient to distal dynamic pressure. In-vivo experiments were performed on three Yorkshire pigs, to achieve the objective. It was found that increase in heart rate does have a significant effect on the coronary diagnostic parameters with increase in area stenosis.

INTRODUCTION

To quantify the physiological significance of epicardial coronary stenosis, several invasive guide wire based methods are used. These methods include coronary flow reserve (CFR: defined as the ratio of hyperemic to basal coronary flow across an epicardial lesion), CDP, and FFR. The recent development of Doppler-tipped guide wires[1] and of pressure monitoring guide wires[2] has facilitated the measurements of coronary flow velocity and distal coronary pressure invasively, thus reviving the interest in the invasive physiological assessment of coronary artery disease.

However during catheterization and during invasive procedures fluctuations in myocardial contractility (intrinsic ability of a cardiac muscle fiber to contract at a given fiber length), blood pressure, percentage area stenosis and heart rate are likely to occur. To avoid any ambiguity during the interpretation of results, the evaluation of the coronary circulation should rely on methods that are independent from these hemodynamic changes. Moreover, in this era of interventional cardiology, a method will become accepted in everyday clinical practice only if the data can be easily obtained with minimum delay.

Accordingly, the goal of the present study was, to evaluate the influence of changes in heart rate, area stenosis, and contractility on the measurements of these diagnostic indices (FFR, CDP [3]). Here we report the effect of HR on FFR and CDP in the setting of different area stenosis.

METHODS

The animal protocol for this study was approved by the University of Cincinnati’s Institutional Animal Care and Use Committee, and at 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 after induction of peak hyperemia (by intra coronary papavarine). Three Yorkshire swines (mean wt. 45 ±5 kg) were premedicated with intramuscular xylazine (2 mg/kg), telazol (7 mg/kg), and atropine (0.05 mg/kg). During the experiment, anesthesia was maintained with 2% isoflurane, and supplemental oxygen was given by endotracheal intubation. Intravenous saline was administered to maintain euvoletic and normotensive conditions during coronary studies. A sheath was

![Figure 1: Physiological Pressure – Flow measurements in LAD](image-url)
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 obstructions of varying severity. This procedure is similar to the study conducted by Sinha Roy et al. [4]. Linear variation of diameter with change in inflation pressure for individual balloon, as per manufacturer’s datasheet (Voyager balloons, Guidant Inc.), was used to calculate the percentage area intraluminal obstructions. The inflation pressure for each balloon did not exceed the recommended pressure range. 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. Since the Doppler wire was used to guide the balloon catheter, the tip of the wire was positioned distal to the balloon. For FFR, aortic pressure (proximal pressure) was recorded via the 7-F guiding catheter by an external pressure sensor (Edwards Life sciences, Irvine, CA).

RESULTS

The pressure and flow data thus obtained was analyzed for the effect of physiologic conditions on measured diagnostic parameters. Figure 2 shows a bar graph of Fractional Flow Reserve (FFR) as a function of heart rate, HR, at four different percentage area stenosis (0.52, 0.64, 0.68, 0.72). It was found that the decrease in FFR when HR varied from 80 to 110 for 52% area stenosis is only 4%. However the decrease in FFR when HR varied from 80 to 110 for 72% area stenosis is 7%, which is not a significant change. But when HR increased from 110-140, FFR varied from 5.4% to 40%, under 52% and 72 % area stenosis respectively, indicating a very significant change in FFR measurements. These results indicate that HR does influence FFR measurements at high percentage area stenosis.

Figure 2: Heart rate vs. FFR at different area stenosis

CONCLUSION AND DISCUSSION

Our preliminary in-vivo experiments suggest that, there is a significant effect of variation of heart rate on measured diagnostic parameters at higher HR in severe stenotic regions, leading to ambiguity in interpreting results during coronary interventions.

In future, effect of contractility on the diagnostic parameters must be studied in detail, so that the diagnostic parameters can be classified based for their independency on these hemodynamic changes.

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