

# Safety and Efficacy of a Novel Technique in the Use of Fractional Flow Reserve in Complex Coronary Artery Lesions

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## Abstract

**Background:** Fractional flow reserve (FFR) has become an increasingly important index when making decisions with respect to revascularization of coronary artery stenosis. However, the pressure guidewire used in obtaining FFR measurements is difficult to control and manipulate in certain complex coronary artery lesions, resulting in increased fluoroscopy time and contrast dye usage. This study examined a novel (NOV) technique for obtaining FFR measurements in hope of easing the difficulties associated with evaluating and treating complex coronary artery lesions.

**Methods:** Fifty-six patients with complex coronary artery lesions were assigned to a conventional (CON) FFR technique group or a NOV FFR technique group. The NOV technique involved the use of a balloon and wire exchange within the coronary artery. The fluoroscopy time, contrast dye usage, and FFR-related complications were assessed after completing the FFR measurement procedure for each patient.

**Results:** The median time required for fluoroscopy in the NOV technique group was significantly less than that in the CON technique group; additionally, lesser amounts of contrast dye were used in the NOV technique group (both  $P < 0.05$ ). The NOV technique was successfully performed in thirty patients, without any FFR-related complications. However, the CON technique failed in three patients, including two who experienced coronary artery spasms ( $P > 0.05$ ).

**Conclusions:** Compared to the CON technique used for measuring FFR, the new technique reduced the fluoroscopy time and amount of contrast dye used when evaluating complex coronary artery lesions. The new technique did not increase the risk of operation or decrease the success rate.

**Key words:** Coronary Artery; Fractional Flow Reserve; Lesions; Technique

## INTRODUCTION

Complex coronary artery lesions, such as bifurcation, diffuse, and calcified tortuous lesions, constitute one of the most challenging lesion subsets in the field of interventional cardiology. Compared with treating simple coronary artery disease (CAD), treatment of complex coronary lesions requires the use of more complicated procedures, has lower procedural success rates and higher rates of clinical adverse events.<sup>[1,2]</sup> Thus, making the proper decision on whether to clinically intervene when a complex lesion is detected is of critical importance. While coronary angiography has limited value in determination of the physiologic significance of a coronary stenosis,<sup>[3,4]</sup> intracoronary measurement of myocardial fractional flow reserve (FFR) has been introduced and proven to be a reliable physiology parameter for determining the need for intervention.<sup>[5]</sup> However, in

practice, the pressure guidewire used in obtaining FFR data is difficult to manipulate in certain complex coronary artery, leading to increased fluoroscopy time and contrast dye usage. We propose the use of a workhorse guidewire for easier engagement in the complex lesion with subsequent broken balloon and FFR wire through the lesion, and then final withdrawal of the workhorse guidewire and balloon. We performed this study to compare the novel (NOV) technique with the conventional (CON) technique used for obtaining measurements of FFR in complex coronary artery lesions.

## METHODS

### General information

This prospective randomized control study was conducted from December 1, 2012 to May 1, 2014 in 56 consecutive patients (mean age,  $71.5 \pm 8.2$  years; 32 males and 24 females) with complex coronary artery lesions at The Second Affiliated Hospital of Zhejiang University. Among

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the 56 patients, 32 had hypertension, 24 had diabetes, 23 had hyperlipidemia, and 35 were smokers.

The patient exclusion criteria were as follows: Acute myocardial infarction; left ventricle hypertrophy; simple coronary artery lesions.

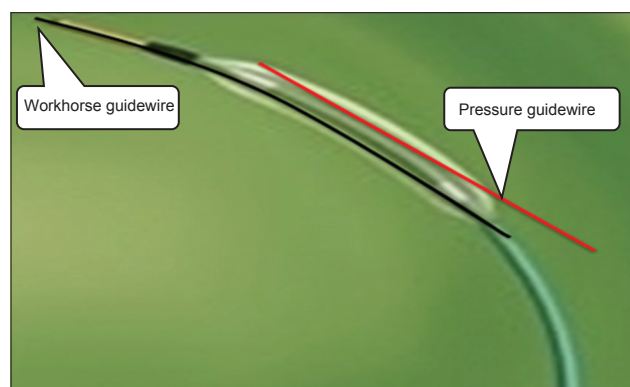
### Treatment groups

The 56 enrolled patients were assigned into two groups based on the technique selected for measuring FFR. The CON FFR measurement technique and NOV measurement technique were used in the CON group ( $n = 26$  patients), and NOV group ( $n = 30$  patients), respectively.

### Novel technique for measuring fractional flow reserve

The device used for measuring FFR with the new technique is shown in Figure 1. Figure 2 illustrates how the novel (NOV) technique is employed for measuring FFR in a patient with a bifurcation lesion. In this case, percutaneous coronary intervention (PCI) was performed while using provisional stenting with a 6F-coronary-guiding catheter.

In this study, when side branch (SB) FFR was measured using the CON method, the jailed SB was re-crossed through the stent strut using a pressure wire. When using the NOV technique, a stent was implanted into the main branch, and the main wire was withdrawn. Next, the jailed wire in the SB was used to guide insertion of the workhorse guidewire into the SB. The previously jailed SB wire was then withdrawn, and the pressure guidewire was inserted into the main branch. Pressure was normalized at a position proximal to the ostium of the main branch. A balloon previously dilated to a low pressure (6–8 atm) *in vitro*, and then punctured with a fine needle. The broken balloon was then passed through by external tips of the pressure and workhorse guidewires respectively [Figure 1]. Next, the external tips of the two guidewires were fixed in position, and the broken balloon was advanced to the distal end of the pressure guidewire in a state of negative pressure. The workhorse guidewire remained fixed in place while the pressure guidewire was advanced past the SB ostial lesion with the broken balloon. The two guidewires were then fixed once again, and the broken balloon was further advanced until it exited from the pressure guidewire. Finally,



**Figure 1:** Positional relationships between the pressure guidewire, workhorse guidewire, and broken balloon.

the broken balloon and workhorse guidewire were both withdrawn while the pressure guidewire retained within the SB. After obtaining an accurate FFR measurement, the operators were able to make an informed decision regarding treatment of the SB lesion.

### Observation parameters

After performing FFR measurements using the CON and NOV techniques, the fluoroscopy time, contrast dye usage, and FFR-related complications associated with each method were assessed. The FFR-related complications included coronary spasm, dissection, perforation and intra-stent thrombosis.

### Statistical analysis

All data were analyzed using SPSS for Windows, version 13.0. (SPSS Inc., Chicago, IL, USA). Values for continuous variables are expressed as the mean  $\pm$  standard deviation or a range while values for categorical variables are expressed as frequencies or percentages. Comparisons of parametric and categorical values between the two groups were performed using the independent sample *t*-test and Chi-square test, respectively. A two-tailed  $P < 0.05$  was considered statistically significant.

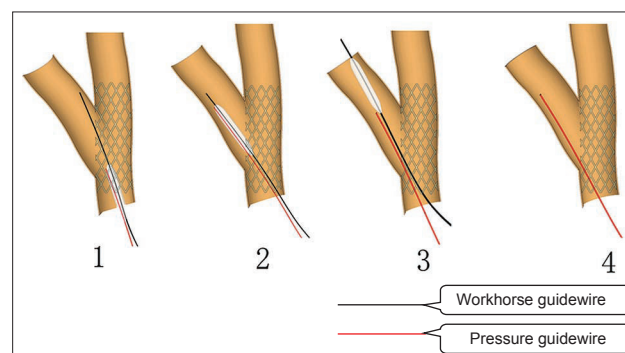
## RESULTS

### Patient and lesion characteristics

As shown in Table 1, there were no significant differences in either the age or sex of the patients or the lesion characteristics in the two groups.

### Comparisons between conventional and novel technique

As shown in Table 2, both the mean time required for fluoroscopy and the amount of contrast dye used were significantly greater in the CON group compared to the



**Figure 2:** The novel technique for measuring fractional flow reserve in complex coronary artery lesions, such as bifurcation lesion: (1) Routine placement of the side branch (SB) workhorse guidewire and main branch pressure guidewire after stent implantation. The workhorse and pressure guidewires were fixed *in vitro*, and the broken balloon was then pushed to the distal end of the pressure guidewire in a state of negative pressure; (2) The pressure guidewire and broken balloon were then advanced along the fixed workhorse guidewire to a location past the SB ostial lesion; (3) The two guidewires were fixed once again, the broken balloon was further advanced until it exited from the pressure guidewire; (4) Finally, the broken balloon and workhorse guidewire were withdrawn, and the pressure guidewire was retained within the SB.

NOV group ( $10.1 \pm 2.1$  s vs.  $5.7 \pm 1.0$  s and  $64.7 \pm 9.2$  ml vs.  $38.9 \pm 5.0$  ml, respectively) (both  $P < 0.05$ ). However, as shown in Table 3, there is no significant difference between the two groups regarding their rates of FFR-related complications, including spasm, dissection, perforation and intra-stent thrombosis ( $P > 0.05$ ). Additionally, three patients in the CON group experienced a failed FFR procedure while there were no failures in the NOV group ( $P > 0.05$ ).

## DISCUSSION

It has become increasingly apparent that revascularization of ischemia-associated lesions is the superior treatment in the patients with CAD.<sup>[6,7]</sup> However, if a coronary stenosis is not associated with inducible ischemia, medical treatment is indicated better than PCI.<sup>[8,9]</sup> Therefore, it is important to determine whether such an association exists when selecting therapy for CAD. Since the introduction of coronary angiography, various methods have been introduced to assess the severity and clinical significance

of the stenosis in coronary arteries.<sup>[10-16]</sup> Measurements of FFR, rather than visual estimations of coronary obstruction have demonstrated the greatest accuracy for determining the functional significance of coronary artery stenosis.<sup>[5,17]</sup> Additionally, the FAME trial revealed that outcomes achieved following PCI performed based on FFR measurements were better than those achieved following PCI performed based on angiographic results alone.<sup>[6]</sup>

However, the pressure wire used in taking coronary FFR measurements is very flimsy and difficult to maneuver.<sup>[18]</sup> Thus, in practice, it has been difficult to insert the pressure guidewire and manipulate it to determine the functional significance of complex coronary artery lesions, such as bifurcation lesions, diffuse lesions, and calcified tortuous lesions.<sup>[19]</sup> Such difficulties result in increased fluoroscopy time and dye usage. In such cases, the interventional physicians must repeatedly remodel the shape of the pressure guidewire, and make repeated attempts to push it through the target lesion. This process can damage the pressure sensors in the wire, and affect the accuracy of FFR measurements.

Presently, there are numerous different types of workhorse guidewires available; many of which are preferred by different interventional cardiologists. Due to their good tensile strength, and increased maneuver ability, lubrication, and tactile feedback, these guidewires can easily engage complex coronary lesions. Additionally, their low traumatic effects and high ease of use have made them excellent wires for engaging complex lesions during postprovisional stenting. In our new technique, a workhorse guidewire was used to initially engage a complex lesion, and then insert a broken balloon carried by a pressure guidewire through the lesion along the workhorse guidewire. Next, the broken balloon and workhorse guidewire were withdrawn following separation of the balloon from the pressure guidewire. The profile of the balloon used in an actual operation should be as small as possible, (e.g., 1.5–2.0 mm), to reduce its effects on the lesion or the structure of the stent. Although the new FFR measurement technique required puncturing the balloon, this did not appear to increase the operation risk or the probability of failure ( $P > 0.05$ ).

Our new method reduced the technical difficulty of using pressure wire, and also decreases the fluoroscopy time, and volume of contrast medium required for a FFR procedure. FFR measurements are crucial for evaluating the physiologic significance of complex coronary artery lesions,<sup>[20-22]</sup> which can help determine whether certain coronary interventions are feasible and thus prevent unnecessary complex interventions and their related complications. Our NOV technique will facilitate making timely and economically

**Table 1: Patient and lesion characteristics**

Characteristics	CON group (n = 30)	NOV group (n = 26)	P
Age (years)	70.5 ± 7.8	72.6 ± 8.6	0.781
Females, n (%)	12 (40.0)	11 (42.3)	0.184
Lesion location, n (%)			
Proximal	14 (46.7)	12 (46.1)	0.094
Middle	12 (40.0)	10 (38.5)	
Distal	4 (13.3)	4 (15.4)	
Lesion type, n (%)			
Bifurcation	16 (53.3)	14 (53.9)	0.236
Diffuse	6 (20.0)	5 (19.2)	
Calcified tortuous	8 (26.7)	7 (26.9)	
Vessel of target lesion, n (%)			
LAD	16 (53.3)	15 (57.7)	0.189
LCX	8 (26.7)	7 (26.9)	
RCA	6 (20.0)	4 (15.4)	

LAD: Left anterior descending coronary; LCX: Left circumflex coronary artery; RCA: Right coronary artery; CON: Conventional; NOV: Novel.

**Table 2: Comparisons of fluoroscopy time and contrast dye usage for CON and NOV FFR measurement procedures (mean ± SD)**

Index	CON group (n = 30)	NOV group (n = 26)
Fluoroscopy time (min)	10.1 ± 2.1	5.7 ± 1.0*
Contrast dye usage (ml)	64.7 ± 9.2	38.9 ± 5.0*

Compared with CON group, \* $P < 0.05$ . SD: Standard deviation; FFR: Fractional flow reserve; CON: Conventional; NOV: Novel.

**Table 3: Comparisons of complication and success rates between two groups, n (%)**

Group	Spasms	Dissection	Perforation	Intra-stent thrombosis	Total complications	Success	Failure
CON (n = 30)	2 (6.67)	0 (0)	0 (0)	0 (0)	2 (6.67)*	27 (90)	3 (10)*
NOV (n = 26)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	26 (100)	0 (0)

Compared with NOV group, \* $P > 0.05$ . CON: Conventional; NOV: Novel.

sound decisions related to treatment of complex lesions such as bifurcation, diffuse and calcified tortuous lesions. However, both our new technique and study results also have limitations that should be mentioned.

The new technique has a possible drawback in that it may increase the financial cost of an FFR measurement procedure by requiring an additional workhorse guidewire and a balloon. However, the balloon and workhorse guidewire used in a PCI procedure can be re-used in a subsequent FFR measurement procedure performed immediately afterward. Also, any interpretation of our study results is limited by the small sample size, which might have influenced the negative result found when comparing procedural success rates in the two groups of patients.

Due to the difficulties encountered when evaluating the physiologic significance of complex coronary artery lesions, we proposed a NOV technique for obtaining measurements of FFR. Compared with the CON technique used to measure FFR, the new technique has advantages of reduced fluoroscopy time and contrast dye usage, without increasing the risk of operation or decreasing the success rate.

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