Usefulness of Coronary Pressure Measurement for Functional Evaluation of Drug-Eluting Stent Restenosis

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Despite the widespread adoption of drug-eluting stent (DES) implantation, the optimal treatment of DES failures remains challenging. The present study evaluated the relation between quantitative angiography and the fractional flow reserve (FFR) in restenotic lesions after DES implantation and the efficacy of FFR in determining whether to treat these lesions. To assess their functional significance, the coronary pressure-derived FFR was measured in 50 DES restenotic lesions (49 patients). Additional intervention was performed in lesions with a FFR <0.8. Major adverse cardiac events were assessed at 12 months after the reintervention procedure. The mean percent diameter stenosis (%DS) was 58 ± 13%. Of the 50 lesions, 20 (40%) were deferred without additional intervention. The FFR and %DS had a negative correlation ($r = -0.61$, $p < 0.001$). However, when only the lesions with diffuse-type restenosis (15 lesions) were analyzed, the degree of correlation decreased ($r = -0.56$, $p = 0.12$). Although most lesions (89%) with a %DS of ≥70 had significant functional ischemia, among 41 lesions with a %DS <70, only 20 (49%) had demonstrated functional patency. The incidence of adverse events during the 12 months of follow-up after FFR-guided treatment was 18.0% (23.3% in the FFR <0.80 group and 10.0% in FFR ≥0.80 group). In conclusion, a discrepancy was found between functional ischemia measured by the FFR and the angiographic %DS, in particular, in moderate- or diffuse-type restenotic lesions after DES implantation. The outcome of FFR-guided deferral in patients with DES in-stent restenosis seems favorable. **(Am J Cardiol 2011;107:1783–1786)**

Although coronary angiography is generally used to evaluate coronary artery disease, it has several well-known limitations.[1] Restenotic lesions after stent implantation can be poorly evaluated using angiography because of the presence of metal stent struts. Some can undergo over-revascularization owing to the oculostenotic reflex. As a reliable index of functional severity in native coronary artery disease,[2] fractional flow reserve (FFR) measurement in patients with restenosis after bare metal stent implantation seems to be useful in treatment decision making according to previous studies.[3,4] However, no data have been reported in the drug-eluting stent (DES) era. The aim of the present study was to evaluate the relation between quantitative angiography and FFR in DES restenotic lesions and the efficacy of FFR in determining whether to treat these lesions.

Methods

The present prospective observational study enrolled patients from 6 interventional centers in Korea who had undergone measurement of coronary pressure-derived FFR to assess the functional significance of restenotic lesions (visual percentage diameter stenosis [%DS] ≥40% in stent or 5 mm adjacent to either of the 2 stent edges) after DES implantation. The lesion should have no documented evidence of associated ischemia on noninvasive tests (not performed, negative, inadequate, or not evaluable for a target lesion). Restenotic lesions in vessels with a %DS of ≥40% in a proximal or distal segment to the zone in which the DES restenosis was located were excluded. Patients were not eligible for enrollment if they had undergone intervention in the setting of primary or emergent percutaneous coronary intervention (PCI) for an acute coronary syndrome-related restenotic lesion, had undergone previous coronary artery bypass graft surgery, or had left main disease, primary myocardial disease, contraindications to adenosine, aspirin, or clopidogrel, or a major life-threatening illness. All patients gave written informed consent to participate in the present investigation.

PCI was performed according to the standard interventional techniques. Before the index procedure, all patients

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This study was supported by research grant 2010-02 from the Korean Society of Interventional Cardiology, Seoul, Korea.

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0002-9149/11/$ – see front matter
doi:10.1016/j.amjcard.2011.02.328

Table 1
Baseline and angiographic characteristics stratified by fractional flow reserve (FFR) (n = 50)*

Variable	All Patients (n = 50)	FFR ≥0.80 (n = 20)	FFR <0.80 (n = 30)	p Value
Age (years)	66 ± 9	64 ± 9	68 ± 10	0.19
Men	28 (56%)	7 (35%)	21 (70%)	0.02
Diabetes	22 (44%)	8 (40%)	14 (47%)	0.77
Hypertension	34 (68%)	14 (70%)	20 (67%)	1.00
Hypercholesterolemia	21 (42%)	12 (60%)	9 (30%)	0.04
Current smoker	14 (28%)	4 (20%)	10 (33%)	0.35
Previous myocardial infarction	13 (26%)	4 (20%)	9 (30%)	0.52
Ejection fraction (%)	56 ± 13	59 ± 12	54 ± 14	0.25
Multivessel coronary disease	32 (64%)	15 (75%)	17 (57%)	0.24
Left anterior descending artery involvement	26 (52%)	8 (40%)	18 (60%)	0.25
Initial procedure				
Stent diameter (mm)	2.9 ± 0.4	3.0 ± 0.3	2.9 ± 0.4	0.22
Stent length (mm)	34.9 ± 20.9	37.7 ± 14.6	33.3 ± 23.8	0.51
Stent number	1.3 ± 0.7	1.4 ± 0.5	1.3 ± 0.8	0.80
Restenotic lesion				
Focal type	35 (70%)	16 (80%)	19 (63%)	0.17
Reference vessel diameter (mm)	2.9 ± 0.4	2.9 ± 0.4	2.8 ± 0.3	0.17
Minimal lumen diameter (mm)	1.2 ± 0.4	1.5 ± 0.4	1.0 ± 0.3	<0.001
Percentage of diameter stenosis (%)	58 ± 13	50 ± 11	64 ± 12	<0.001
Lesion length (mm)	11.0 ± 7.3	10.5 ± 3.4	14.7 ± 8.7	0.03
Fractional flow reserve	0.77 ± 0.13	0.88 ± 0.05	0.69 ± 0.11	<0.001

received antiplatelet and anticoagulation therapy according to the current guidelines.[5] The FFR is defined as the ratio between the distal coronary pressure and aortic pressure, both measured simultaneously at maximum hyperemia.[2] Using a 6Fr or 7Fr guiding catheter, the externally calibrated 0.014-in. pressure guidewire (PressureWire, Radi Medical Systems, Uppsala, Sweden) was advanced to the distal tip of the guiding catheter and equalized. After advancing the sensor of the wire ≥10 mm beyond the restenotic lesion, maximum hyperemia was induced with intracoronary bolus administration of adenosine 80 μg for the left coronary artery and adenosine 40 μg for the right coronary artery with 200-μg intracoronary nitroglycerin. The lesions with an FFR <0.80 at maximum hyperemia were only considered functionally significant and treated by mechanical revascularization.[6] Additional procedures, such as balloon angioplasty or new DES stenting, were performed at the physician's discretion. Qualitative coronary angiography was performed by an independent core laboratory at Keimyung University Dongsan Medical Center by a single experienced observer, who was unaware of the FFR value. Using the guiding catheter for calibration and an edge detection system (Quantcor qualitative coronary angiography, version 4.0, Pie Medical Imaging, Maastricht, The Netherlands).

All patients were clinically followed up by personal interview at 12 months. The individual and combined major adverse events, including death, myocardial infarction, target vessel revascularization (TVR), and stent thrombosis were evaluated. Death was defined as all-cause mortality. Myocardial infarction was defined as threefold or greater elevation of the creatine kinase-MB level or new Q waves in ≥2 contiguous leads on the electrocardiogram. TVR included target lesion revascularization and bypass surgery of the pertinent lesion. Stent thrombosis was defined according to the Academic Research Consortium guidelines.

Data are expressed as the mean ± SD for continuous variables and as percentages for discrete variables. Continuous variables were compared using Student's *t* test. Categorical variables were compared using chi-square tests or Fisher's exact tests, as appropriate. All calculated p values were 2-sided, and differences were considered statistically significant when the respective p values were <0.05. Correlations between the FFR and %DS were evaluated using the Pearson correlation analysis. Receiver operating characteristic curve analysis was used to examine the angiographic %DS as a predictor of the functional significance of a lesion (FFR <0.8). For the events during the follow-up, the corresponding Kaplan-Meier survival curves were obtained. All statistical analyses were performed using the Statistical Package for Social Sciences, version 15.0, for Windows (SPSS, Chicago, Illinois).

Results

To assess functional severity, the FFR was measured in 50 restenotic lesions (49 patients) after DES implantation. Of the 49 patients, 31 were referred to the catheterization laboratory without a previous noninvasive test, including 38% of the symptomatic patients. The others had had nondiagnostic test results. Three type of DESs were implanted at the index procedure: sirolimus-eluting stents, paclitaxel-eluting stents, and zotarolimus-eluting stents (34%, 53%, and 13% respectively). The mean interval from the initial procedure with DES to the FFR measurement in in-stent restenotic lesions was 16 ± 16 months. Of the 50 lesions, 20 (40%) were deferred without any additional procedure because of an FFR of ≥0.80. Of the 30 lesions with an FFR of <0.80, 17 (57%) were treated by balloon angioplasty and