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Long-Term Clinical Outcome After Fractional Flow Reserve-Guided Percutaneous Coronary Intervention in Patients With Multivessel Disease

Alexandre Berger, MD,* Kees-Joost Botman, MD,* Philip A. MacCarthy, MD, PHD, MRCP,* William Wijns, MD, PHD,* Jozef Bartunek, MD, PHD,* Guy R. Heyndrickx, MD, PHD,* Nico H. J. Pijls, MD, PHD,† Bernard De Bruyne, MD, PHD*

Aalst, Belgium; and Eindhoven, the Netherlands

OBJECTIVES In the present study, we analyzed the clinical outcome of patients with multivessel coronary artery disease in whom at least one vessel was treated by percutaneous coronary intervention (PCI) and at least one other vessel was deferred on the basis of fractional flow reserve (FFR) measurements during the same session.

BACKGROUND Myocardial FFR is an established tool for assessing the severity of epicardial stenoses. It has been shown that it is safe to defer an intervention in single vessel disease patients when FFR >0.75.

METHODS One hundred two patients (66 ± 10 years) with multivessel coronary artery disease were included in the study. In all patients, PCI of at least two vessels was contemplated. Yet in all of them at least one vessel was treated by PCI, whereas at least one other vessel was deferred based on an FFR >0.75. Major adverse cardiac events (MACE) were recorded during an average follow-up of 29 ± 18 months.

RESULTS In 102 patients, 113 coronary arteries underwent PCI. In these arteries FFR was 0.57 ± 0.13 and mean diameter stenosis was 68 ± 14%. One hundred twenty-seven coronary arteries had an FFR >0.75 and PCI was deferred. In these arteries FFR was 0.86 ± 0.06 and mean diameter stenosis was 47 ± 12%. No death occurred during the follow-up. A MACE occurred in 9% and 13% of patients after 12 and 36 months, respectively. These MACE were related to 22 (9.2%) arteries. Among them, 8 (6.3%) MACE were related to one of the initially deferred vessels, whereas 14 (12.3%) MACE were related to one of the initially treated coronary artery.

CONCLUSIONS In patients with multivessel disease, PCI of hemodynamically non-significant stenoses can be safely deferred, even if initially planned on the basis of the angiogram. (J Am Coll Cardiol 2005;46:438–42) © 2005 by the American College of Cardiology Foundation

Inducible myocardial ischemia at non-invasive stress testing is a paramount prognostic factor (1,2) and its documentation remains essential prior to invasive evaluation. Nowadays, however, the majority of percutaneous coronary interventions (PCIs) are performed without prior non-invasive stress testing (3). In addition, in patients with multivessel coronary disease, the diagnostic accuracy of perfusion scans is poor in assessing which stenosis is hemodynamically significant (4). Fractional flow reserve (FFR) is an invasive index of the hemodynamic significance of stenosis severity with a diagnostic accuracy similar to myocardial perfusion scan but a better spatial resolution. It is derived from the ratio between coronary and aortic pressure measurements during maximal hyperemia. As this index is easy to measure and available in a few minutes in the catheterization laboratory, it can be used as a surrogate for non-invasive testing (5). The usefulness of FFR in patients referred for PCI with intermediate stenoses was demonstrated in single vessel diseased patients (6). In the present study we analyzed the clinical outcome of patients with multivessel coronary artery disease in whom at least one vessel was treated by PCI and at least one other vessel was deferred on the basis of FFR measurements during the same session.

METHODS

Study patients. Patients with multivessel coronary artery disease at angiography were included in the study if at least one artery was treated by PCI and, during the same procedure, at least one stenosis was deferred from PCI on the basis of an FFR >0.75. The study was performed in the Cardiovascular Center Aalst, Belgium, and in the Catharina Hospital in Eindhoven, the Netherlands, from June 1994 to

From the *Cardiovascular Center Aalst, OLV-Clinic, Aalst, Belgium; †Catharina Hospital, and the Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, the Netherlands. Dr. Berger was supported by a grant from the "Fondation Vaudoise de Cardiologie, Lausanne, Suisse." Dr. MacCarthy was the recipient of a British Heart Foundation Advanced Training Scholarship and was also supported by the Wellcome Trust and British Cardiac Society.

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Abbreviations and Acronyms

ACS = acute coronary syndrome
%DS = percent diameter stenosis
FFR = fractional flow reserve
LAD = left anterior descending artery
LCx = left circumflex artery
MI = myocardial infarction
MLD = minimal lumen diameter
RCA = right coronary artery
RD = reference diameter
TVR = target vessel revascularization

May 2002. Fractional flow reserve and quantitative coronary arteriography were obtained in all patients. Moreover, all patients were informed beforehand that the therapeutic strategy would be guided by pressure measurements.

Coronary pressure measurement and calculation of FFR. The FFR was measured in all stenoses in which PCI was contemplated except stenoses with a Thrombolysis In Myocardial Infarction (TIMI) flow grade <3, and stenoses of which the significance had been demonstrated at perfusion scintigraphy. Intracoronary pressure measurements were performed with a 0.014-inch pressure guidewire (Radi Medical System, Uppsala, Sweden) introduced through a 6-F guiding catheter. The FFR was calculated from the ratio of mean hyperemic distal coronary pressure measured by the pressure-wire and the mean aortic pressure obtained by the guiding catheter (7,8). All patients received aspirin and either clopidogrel or ticlopidine for at least two months.

Quantitative coronary arteriography. Reference diameter (RD), minimum luminal diameter (MLD), and percent diameter stenosis (DS) were assessed in two views during the PCI procedure.

Follow-up and clinical events. All patients were evaluated at the outpatient clinic or by mail. Major adverse cardiac events (MACE) were defined as death, myocardial infarction (MI), and any repeat (target or non-target) vessel revascularization (TVR). Myocardial infarction was defined as the occurrence of new Q waves or a rise in creatinine phosphokinase of more than twice the upper limit (6). A repeat angiogram was not performed unless clinically indicated. The culprit artery vessel responsible for the recurrence of symptoms was defined by the operator's judgment, based on the correlation of electrocardiographic changes, echocardiographic data (if available), and the diagnostic angiogram.

Statistics. Because of the design of the study, the unit of analysis became the coronary artery lesion rather than the patient. Therefore, potential correlations within patients could have been ignored. Continuous variables were expressed as mean ± standard deviation and discrete variables as counts and percentage. The chi-square test and the Fisher exact *t* test were used for categorical variables, and the Student *t* test was used for continuous variables. Clinical, angiographic variables, and FFR values were compared between the deferred- and the treated-vessels groups. Survival curves were constructed according to the Kaplan and Meier method and compared by the log-rank test. A p value >0.05 was considered statistically non-significant.

RESULTS

Population. One hundred two patients (240 arteries, mean age 66 ± 10 years, 71% men) were included. Eighteen percent of patients had diabetes, 34% hypertension, 29% were current smokers, 50% had dyslipidemia, and 43% had a positive familial history for ischemic heart disease. Most patients had stable angina (76%), and the remainder presented an acute coronary syndrome (ACS) (21 with unstable angina and 3 with non–ST-segment elevation MI). Angiographic and hemodynamic data of the treated and deferred arteries are shown in Table 1.

Angiographic and hemodynamic results. Thirty-five patients (34%) had three-vessel disease and 66 patients (66%) had two-vessel disease. The PCI procedure was performed in 113 coronary arteries: 1 artery was treated in 91 patients and 2 arteries in 11 patients. In patients admitted for an ACS, the "culprit" lesion was treated in all cases. Use of PCI was deferred based on an FFR ≥0.75 in 127 coronary arteries: in one artery in 77 patients and in two arteries in 25 patients. The individual values of FFR and of %DS for the treated and the deferred arteries are shown in Figure 1. By design, FFR was ≥0.75 in deferred arteries. In this group the mean value of FFR was 0.86 ± 0.06 (range 0.75 to 1.0). The FFR value in the treated arteries was 0.57 ± 0.13 (range 0.29 to 0.74). DS of the treated arteries (68 ± 14%, range 30% to 100%) was significantly higher than in the deferred arteries (47 ± 12%, range 15% to 74%, $p < 0.001$) but a large overlap of the values was observed.

Among the 21 patients presenting with an ACS, a TIMI flow grade <3 was present in 6 culprit arteries. The FFR

Table 1. Angiographic and Hemodynamic Data of Treated and Deferred Lesions

	Treated Lesions (n = 113)	Deferred Lesions (n = 127)	p Value
Coronary lesions			
LAD	42 (37%)	53 (42%)	NS
LCx	39 (35%)	40 (32%)	NS
RCA	32 (28%)	28 (22%)	NS
LM	0	6 (4%)	NS
QCA (mean ± SD)			
%DS	68 ± 14	47 ± 12	<0.0001
MLD (mm)	0.90 ± 0.4	1.5 ± 0.5	<0.0001
RD (mm)	2.80 ± 0.82	2.83 ± 0.79	NS
Hemodynamic variables (mean ± SD)			
FFR	0.57 ± 0.13	0.86 ± 0.06	<0.0001

%DS = percent diameter stenosis; FFR = fractional flow reserve values; LAD = left anterior descending artery; LCx = left circumflex artery; LM = left main artery; MLD = minimal lumen diameter; QCA = quantitative coronary arteriography; RCA = right coronary artery; RD = reference diameter.