SCIENTIFIC LETTER

Long term follow up after deferral of revascularisation in patients with intermediate coronary stenoses and negative dobutamine stress echocardiography

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Quantitative coronary angiography (QCA) provides anatomic data of a coronary stenosis, but not necessarily information about the physiologic relevance of a lesion. It is unclear, however, whether patients with intermediate coronary stenoses ($\geq 50\%$ to $\leq 70\%$ diameter reduction) show a long term benefit after coronary intervention.¹ Also, for patients with intermediate stenoses, only few data on the risk for future coronary events are available.²

The objective of this pilot study was to determine the safety and outcome of performing or deferring coronary interventions in patients with intermediate stenoses based on the results of dobutamine stress echocardiography (DSE).

METHODS

Patients with one intermediate stenosis by QCA (diameter stenosis $\geq 50\%$ and $\leq 70\%$) in one of the main coronary arteries or in a coronary artery bypass graft and eligible for revascularisation were included in the study. A total of 47 consecutive patients (34 men, 13 women) referred for coronary angiography was examined (mean (SD) age 61.2 (10.2) years, weight 76.5 (11.7) kg, left ventricular ejection fraction 65.4 (11.6)%).

DSE was performed within two days after coronary angiography. In patients with inducible myocardial ischaemia by DSE in the perfusion territory of the target vessel, coronary intervention was performed (Int group), while in patients with negative DSE the intervention was deferred (non-Int group). The occurrence of a major adverse cardiac event (death or myocardial infarction) and the necessity of coronary interventions (coronary angioplasty (PTCA) or bypass surgery (CABG)) during follow up were defined as primary and secondary end points, respectively.

Lesion severity and left ventricular ejection fraction were evaluated using an online analysis system (Siemens QuantCor.QCA and QuantCor.IVA V2.0, Erlangen, Germany) based on the Cardiovascular Angiography Analysis System II (CAAS

II, Pie Medical Imaging, Maastricht, Netherlands). DSE was performed using an established protocol with commercially available equipment (HP Sono 5500, Agilent Technologies, Palo Alto, California, USA or Aspen, Acuson Corp, Mountain View, California, USA).

Statistical significance of differences between the Int and non-Int groups were assessed using the Mann-Whitney test. A probability value of $p < 0.05$ was considered significant.

RESULTS

Three of 47 (6%) patients were excluded because of technically inadequate DSE. Because of positive DSE, coronary intervention was performed in 6/44 (14%) patients (Int group: 4 PTCA, 2 CABG). Interventions were deferred in 38/44 (86%) patients because of negative DSE (non-Int group). There were no significant differences between the Int and non-Int groups with respect to age, weight, body mass index, left ventricular ejection fraction, cardiac history, cardiac risk factors, and medical treatment.

The target lesion was located in the left anterior descending artery in 27 patients, the left circumflex artery in five, the right coronary artery in nine, the left main in one, and in a coronary artery bypass graft in two. The lesion characteristics are shown in table 1.

The average follow up period was 21.6 (3.2) months (range 15-27 months). During the follow up period no major adverse cardiac event occurred in either group. Thirteen of 38 (34%) patients of the non-Int group developed progressive angina. In those patients, QCA showed $> 70\%$ stenosis (in 7 (18%) patients in the target vessel), and interventions were

Abbreviations: CABG, coronary artery bypass grafting; DSE, dobutamine stress echocardiography; FFR_{myo}, fractional flow reserve; PTCA, percutaneous transluminal coronary angioplasty; QCA, quantitative coronary angiography

Table 1 Angiographic findings

	Total study group (n=44)	Int group (n=6)	Non-Int group (n=38)	p Value
One vessel disease	3 (7%)	0/6	3/38 (8%)	1.00
Two vessel disease	16 (36%)	1/6 (17%)	15/38 (39%)	0.39
Three vessel disease	25 (57%)	5/6 (83%)	20/38 (53%)	0.21
QCA				
Reference diameter (mm)	2.83 (0.75)	2.36 (0.69)	2.91 (0.74)	0.19
Minimal lumen diameter (mm)	1.19 (0.39)	0.98 (0.30)	1.22 (0.40)	0.16
Diameter stenosis (%)	58.5 (4.5)	58.2 (5.1)	58.4 (4.5)	0.8
Length of the stenotic segment (mm)	5.11 (1.82)	4.32 (1.85)	5.24 (4.5)	0.8

QCA, quantitative coronary angiography.

performed (11 PTCA, 2 CABG). In 2/6 (33%) patients of the Int group, re-PTCA became necessary. In general, the average per cent diameter stenosis showed a tendency for progression from baseline to follow up (58.5 (4.5)% ν 63.5 (10.4)%, $p = 0.08$), but still remained in the intermediate spectrum ($\geq 50\%$ and $\leq 70\%$).

DISCUSSION

The present pilot study shows that, in regard to major adverse cardiac events, it seems to be safe to defer coronary intervention in intermediate stenosis if physiologic relevance can be excluded by negative DSE. In the non-Int group no cardiac death or myocardial infarction occurred. During an average follow up period of 21.6 months the secondary end point (PTCA, CABG) caused by progressive angina pectoris was reached in 13/38 (34%) patients of the non-Int group and it was target vessel related in 7/38 (18%) patients.

The invasive assessment of coronary lesions by determining fractional flow reserve (FFR_{myo}) has shown that angioplasty can be safely deferred if functional significance is lacking. In a study by Bech and colleagues in patients with an intermediate stenosis and an $FFR_{myo} > 0.75$ no cardiac death occurred during an average follow up period of 18 months and only 8/100 (8%) patients experienced a coronary event (in 4 (4%) patients target vessel related).³ In the present study, the annual event rate of 17% (target vessel related 9%) was higher. However, no myocardial infarction or cardiac death occurred and the number of patients with multivessel disease was higher than in the study by Bech and colleagues.³

DSE has been proposed as a clinically useful, non-invasive test for the prognostic evaluation of patients with known or suspected coronary artery disease. In case of a normal DSE, a large recently published study reported an annual event rate of cardiac death or myocardial infarction of 1.3%.⁴

Another study showed that a negative DSE and no coronary intervention in 32 patients with a moderate coronary stenosis (diameter stenosis 50–80%) was associated with no inducible myocardial ischaemia after 6–12 months in 91% of the patients. Three patients (9%) showed positive DSE during follow up. No myocardial infarction or cardiac death occurred.⁵ The prognostic results of this study correspond closely to the outcome of our study.

DSE seems to be an appropriate non-invasive test to detect the functional significance of an intermediate coronary lesion. Concerning major adverse cardiac events in the non-Int group

of the present study, no cardiac death or myocardial infarction occurred during long term follow up. However, the target vessel related revascularisation rate was relatively high (18%) as a result of progression of the atherosclerotic process.

The present pilot study shows a few limitations. First, a small number of patients in different clinical conditions with stable or unstable angina and single vessel or multivessel disease was included. Second, the study is prospective but non-randomised and does therefore not provide comparative data from a control group. Therefore, to assess the approach of the present study, a large prospective and randomised study is highly desirable.

In summary, DSE seems to be a useful non-invasive test to verify the functional significance of an intermediate coronary lesion and to provide data to establish the appropriate therapeutic strategy for the patient.

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