Quantitative Assessment of Transient Regional Ischemia During Rotational Atherectomy

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Sustained myocardial ischemia with angina pectoris, electrocardiographic changes and subsequent non-Q-wave infarctions has been reported during percutaneous transluminal rotational atherectomy of complex coronary lesions. The purpose of this study was to evaluate the effect of rotational atherectomy on regional myocardial perfusion as assessed by serial 99mTc-sestamibi SPECT imaging with semiquantitative tracer uptake analysis. Methods: Twenty-nine consecutive patients with anginal symptoms, complex coronary lesions (all Type B and Type C) and preserved left ventricular function were studied using resting 99mTc-sestamibi SPECT before rotational atherectomy, during and 2 days after the procedure. For semiquantitative analysis, 99mTc-sestamibi uptake was measured and the left ventricular myocardium was divided into 24 regions, and regional perfusion was expressed as percentage of maximal sestamibi uptake. Results: Visual analysis of scintigraphic images revealed transient perfusion defects corresponding to the revascularized vessel in 26 of 29 patients, whereas three patients had no transient hyperperfusion. During rotational atherectomy, perfusion decreased significantly (>2 s.d. below normal mean) in 3.1 ± 2.4 regions (range 1–10). Perfusion in the territory of the revascularized vessel was 75% ± 11% at baseline, decreased to 67% ± 12% during rotational atherectomy (p < 0.001) and normalized again after rotational atherectomy to 78% ± 8% (p < 0.001). Similarly, perfusion in the region with the maximal reduction decreased from 74% ± 15% at baseline to 55% ± 14% (p < 0.001) during the procedure and returned to 74% ± 16% (p < 0.001) following the intervention. In calcified stenoses, the extent of perfusion defects was larger as compared to noncalcified stenoses (4.2 ± 2.5 versus 2.3 ± 2.0 regions/patient, p < 0.05). Conclusion: During rotational atherectomy, myocardial hyperperfusion occurs. The transient nature of this perfusion defect can be demonstrated and quantified by serial 99mTc SPECT. This model may prove useful to assess the effects of pharmacological approaches to reducing myocardial hyperperfusion during coronary rotational atherectomy.

Key Words: coronary artery disease; myocardial perfusion; rotational atherectomy; SPECT; technetium-99m-sestamibi

Since its introduction in 1988 (1), percutaneous transluminal rotational coronary atherectomy has become a valuable interventional tool in clinical practice (2,3). Evolving indications are small vessels, long and diffuse, calcified and ostial lesions. The overall primary success and restenosis rate in different types of stenoses are similar to those of conventional balloon angioplasty (4–6). However, in an initial study, remarkable high rates of procedure-related angina and ST-segment changes during rotational atherectomy have been reported (7). Recently the number of procedure-related non-Q-wave infarctions were reported to be 4%–8% (8).

Technetium-99m-sestamibi myocardial perfusion imaging has been used for delineating of the area at risk and for assessing the effect of thrombolytic therapy in patients with acute myocardial infarction. This approach was based on the convenient pharmacokinetics of 99mTc-sestamibi, in which scintigraphic images reflect myocardial perfusion at the time of tracer injection rather than at the time of imaging (9,10).

The aim of this study was to investigate by qualitative and quantitative 99mTc-sestamibi myocardial perfusion SPECT the frequency, severity and reversibility of perfusion abnormalities during rotational atherectomy. Furthermore, the influence of procedural factors and lesion characteristics on the perfusion abnormalities was studied.

MATERIALS AND METHODS

Patients

Twenty-nine consecutive patients, scheduled for elective rotational atherectomy, were included in the study. Indications for rotational atherectomy in the presence of a Type B or C coronary artery stenosis were stable angina, objective signs of myocardial ischemia, or both. Coronary lesions were classified by angiographic and clinical criteria according to the American Heart Association/American College of Cardiology classification (11):

- Type A lesions: discrete (<10-mm length), concentric, readily accessible, nonangulated segment (<45°), smooth contour, little or no calcification, less than totally occlusive, not ostial in location, no major branch involvement, absence of thrombus; Type B lesions: tubular (10–20-mm length), eccentric, moderate tortuosity of proximal segment, moderately angulated segment (>45°, <90°), irregular contour, moderate-to-heavy calcification, total occlusion <3 mo old, ostial in location, bifurcation lesions requiring double guide wires, some thrombus present; Type C lesions: diffuse (>2-cm length), excessive tortuosity of proximal segment, extremely angulated segments (>90°), total occlusion >3 mo old, inability to protect major side branches, degenerated vein grafts with friable lesions.

Ejection fraction was determined by the area-length method from left ventricular contrast angiograms.

The study protocol was approved by the institutional ethical committee, and patients gave informed consent.

Rotational Atherectomy

The technique of rotational atherectomy using the Rotablator® (Boston Scientific Corp., Redmond, WA) has been described previously in detail (7). Briefly, a sheath capable for an eight or nine French guiding catheter was inserted in the femoral artery using Seldinger’s technique, and a dedicated guide wire (Rotawire®, Boston Scientific Corp.) was advanced distal to the target stenosis. The Rotablator was positioned over the guide wire proximal to the target lesion. The activated burr (size 1.25–2.0 mm), rotating at 160,000 to 180,000 rpm, was then slowly advanced across the lesion. Several (range 4–20) passages of the Rotablator were performed within the stenosis. If appropriate, increasing burr sizes were used to achieve a burr size/artery diameter ratio ≥0.7.

In patients with a lesion of the right coronary artery, a temporary pacemaker was positioned in the right ventricle to prevent the effects of atherectomy-induced bradycardia.

Periprocedural Medication

Preprocedural medication included aspirin 100 mg once a day (100 mg daily). At the beginning of the intervention, 10,000 IU of heparin was administered intracoronarily through the guiding catheter. Baseline angiography was preceded by an intracoronary injection of 0.2 mg nitroglycerin. If necessary, repeated doses of nitroglycerin and/or verapamil were given to reduce vessel spasm.

Angiographic Analysis

Lesion length and severity were quantified using a digital angiographic analysis system (HICOR, Siemens, Germany) after guiding catheter calibration. Lesion length was defined as the length of the diseased vessel passed by the activated rotablator. The degree of calcification was assessed by visual analysis using a three-point scale: severe calcification—readily apparent on single frame cineangiography; mild calcification—artery motion required to visualize; no calcification (4).

SPECT Imaging

For assessment of regional myocardial perfusion, SPECT with 99mTc-labeled sestamibi was performed 1 day before, during the rotablation and 2 days after the procedure (Fig. 1). The protocol for each scintigraphy was as follows: 99mTc-sestamibi (400–450

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**FIGURE 1.** Time course of study protocol. ECG = electrocardiogram; TrT = troponin T; CK = creatine kinase; CK-MB = MB fraction of creatine kinase.
Myocardial Enzymes

Blood samples were drawn at baseline and 8 hr, 16 hr and 24 hr following the procedure for determination of total creatine kinase (CK), MB fraction of CK (CK-MB) and cardiac troponin T. CK and CK-MB were determined using a kinetic method for total CK and immuno-inhibition for CK-MB (15). For quantitative measurement of troponin T, an enzyme-linked immunosorbent assay was used (16).

Statistical Analysis

Data are expressed as mean ± s.d. Differences in continuous variables were assessed using Student's t-test for paired and unpaired samples. For correlation analysis, Spearman rank order correlation was used. Statistical analysis was performed with StatWorks software (Cricket Software, Inc., Philadelphia, PA) on a Macintosh® computer (Apple, Inc., Cupertino, CA).

RESULTS

Baseline Patient, Lesion and Procedural Characteristics

Baseline characteristics are presented in Table 1. The mean age of the patients was 61 ± 10 years, and 21 patients (72%) were male. Previous non-Q-wave myocardial infarction defined as clinical event and documented CK elevation above the upper limit of normal (>100 U/l) with a significant proportion of CK-MB (>6% of CK) and the absence of new Q waves on the electrocardiogram in the distribution territory of the target vessel was present in 10 of 29 (34%) patients. No patient had a previous transmural infarction, and global left ventricular function was normal with an ejection fraction of 62% ± 13%. One lesion per patient was treated with rotational atherectomy. Lesion localization is presented in Table 1. All lesions were Type B and C stenoses according to the AHA/ACC classification (11). Thirteen of 29 (45%) lesions were calcified. Lesion length was 32 ± 16 mm, reflecting the high prevalence of long lesions and diffuse disease. Burring time and burr size were 160 ± 19 s, and 1.7 ± 0.3 mm, respectively. Adjunctive balloon angioplasty and/or stent placement was performed in 26 (90%) and 5 (17%) patients, respectively.

Rotational Atherectomy

Visual analysis of SPECT images revealed transient perfusion defects in 26 of 29 (90%) patients. Defect severity ranged from slight to marked by visual analysis. Localization of the perfusion defects corresponded to the revascularized vessel.
distribution territory in all patients. Scintigraphic images and semiquantitative regional perfusion indices before, during and after rotational atherectomy from two patients displaying transient perfusion defects are illustrated in Figures 3 and 4.

During rotational atherectomy, myocardial perfusion decreased significantly in 3.1 ± 2.4 regions, ranging from 1 to 10 regions per patient. Perfusion in the entire territory of the revascularized vessel was 75% ± 11% at baseline, decreased to 67% ± 12% (p < 0.001) during rotablation and normalized again after rotational atherectomy to 78% ± 8% (p < 0.001).

Perfusion in the region with the maximal reduction during rotational atherectomy was 74% ± 15% before the intervention, decreased to 55% ± 14% (p < 0.001) during the procedure and normalized again to 74 ± 16 (p < 0.001; Fig. 5).

Effect of Patient, Lesion and Periprocedural Factors on Extent and Severity of Transient Ischemia

Rotational atherectomy of calcified lesions (n = 13) induced significant larger perfusion defects than in noncalcified (n = 16) lesions (4.2 ± 2.5 regions versus 2.2 ± 2.0 regions, p < 0.05; Fig. 6). However, the difference of perfusion reduction in the entire territory of the revascularized vessel (−15% ± 9% versus −10% ± 8%; p = 0.1) and the maximal reduction of regional perfusion (−26% ± 14% versus −18% ± 9%; p = 0.09) did not reach statistical significance.

There was a trend for patients with previous non-Q-wave myocardial infarctions in the revascularized area to have larger perfusion deficits, although this difference did not reach statistical significance (Fig. 6). Perfusion in the region with maximal reduction in patients with previous non-Q-wave myocardial
infarction did not differ significantly from values of patients without previous non-Q-wave myocardial infarction: 72 ± 20 versus 75% ± 13% at baseline (p = 0.6), 52 ± 16 versus 57% ± 12% during the procedure (p = 0.7) and 69 ± 17 versus 77% ± 15% at follow-up (p = 0.9). No significant influence of gender, vessel, type of stenosis, presence of collaterals, burr size and lesion length on the extent of transient perfusion defects could be demonstrated. However, there was an inverse correlation between total burring time and number of passages performed with the rotablator and the extent of the perfusion defect (Table 2).

**DISCUSSION**

This study demonstrates by scintigraphic perfusion imaging with quantitative tracer uptake analysis that transient myocardial hypoperfusion occurs frequently (~90%) during rotational atherectomy. This phenomenon is transient because 2 days after the procedure myocardial perfusion at rest was comparable to the preprocedural status. Furthermore, this transient hypoperfusion did not result in myocardial damage, as proven by normal myocardial enzymes following the procedure.

**Factors Influencing Defect Size and Severity**

In this study, rotational atherectomy of calcified stenoses caused larger perfusion defects as compared to noncalcified lesions (Fig. 6). In a recent pathological-anatomical report (17), multiple calcific atheroemboli were present after rotational atherectomy in plaques containing extensive nodular calcification, whereas in moderately calcified plaque only one small atheroembolus was found. However, Maclsaac et al. found an equal percentage of non-Q-wave infarctions after rotational atherectomy of calcified and noncalcified stenoses (18).

Other factors influencing significantly the size and severity of myocardial hypoperfusion could not be identified in this study. There was a trend to larger perfusion defects in patients with previous non-Q-wave myocardial infarctions in the distribution territory of the revascularized vessel. Ellis et al. (4) demonstrated that right coronary stenosis, female sex, lesion length >4 mm and stenosis bend >60° are risk factors for major ischemic complications. Risk factors in this study for slow flow were total burring time, right coronary stenosis and previous myocardial infarction. Microvascular changes in previously

**TABLE 2**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number of hypoperfused regions</th>
<th>Maximal reduction of perfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burr size</td>
<td>0.12 (0.563)</td>
<td>0.03 (0.897)</td>
</tr>
<tr>
<td>Lesion length</td>
<td>0.05 (0.797)</td>
<td>0.05 (0.803)</td>
</tr>
<tr>
<td>Total burring time</td>
<td>-0.61 (0.001)</td>
<td>-0.31 (0.157)</td>
</tr>
<tr>
<td>Rotablator passages</td>
<td>-0.58 (0.002)</td>
<td>-0.34 (0.109)</td>
</tr>
</tbody>
</table>

Values are Spearman rank correlation coefficients and p values (in parentheses).

**Myocardial Infarction**

With the exception of one patient, there were no myocardial infarctions as assessed by serial measurements of CK, CK-MB and troponin T values. This patient experienced a procedure-related Q-wave infarction due to no reflow and abrupt vessel closure during hospital stay with a maximal CK value of 1170 U/l. The target lesion in this patient was heavily calcified, total burring time was 116 s with five rotablator passages, a maximal burr size was 1.5 mm and there was adjunctive percutaneous transluminal coronary angioplasty (PTCA) after rotablation. After 4 hr, abrupt vessel closure occurred. The vessel was successfully recanalized by repeat PTCA, and a stent was placed in the lesion.

In the remaining 28 patients, the CK was 30 ± 20 U/l at baseline, 56 ± 47 U/l at 8 hr, 51 ± 41 U/l at 16 hr and 45 ± 29 U/l at 24 hr. All CK values were within the normal range (10–100 U/l), and CK-MB values were <6% of CK values. Serial troponin T values were below the threshold of detection (<0.1 ng/ml) in all patients.

**FIGURE 5.** Regional myocardial perfusion before (preR), during (R) and 2 days after rotational atherectomy (postR). Mean perfusion of all regions in the area supplied by the revascularized vessel (open bars) and perfusion in the area with the maximal reduction in perfusion (shaded bars) are shown. *p < 0.001.

**FIGURE 6.** Impact of lesion calcification, previous infarction in the area supplied by the revascularized vessel, gender, presence of collaterals, type of stenosis and vessel on extent of transient perfusion defect. The number of regions with significant reduction in perfusion are presented. Data indicate mean values ± standard error of the mean. *p < 0.05; ** = the absence of the parameter; f = female; m = male; LAD = left anterior descending coronary artery; RCA = right coronary artery; LCX = left circumflex coronary artery; B and C = stenosis type according to the American Heart Association/American College of Cardiology (AHA/ACC) classification.
infarcted myocardium were proposed to be responsible for this difference (4). In a study by Warth et al. (5) including 743 procedures, multivariate analysis revealed female gender and previous myocardial infarction as risk factors for procedure-related non-Q-wave infarctions. However, in both studies, lesion calcification could not be identified as a risk factor.

Patient, lesion and procedural characteristics including burr sizes and burr duration in this study were comparable to those in previous studies (4,6,7,19,20). However, we treated a higher proportion of complex (according to the AHA/ACC classification) and long lesions as compared to the majority of these reports. In the study by Teirstein et al., mean lesion length was 31 mm (7), whereas in other studies mean lesion length ranged from 6 to 9 mm.

Surprisingly, total burring time and number of passages with the Rotablator were inversely correlated with the extent of perfusion defects. A possible explanation could be the rather transient nature of rotation-related myocardial hypoperfusion. Maximal hypoperfusion might occur after the first passages of the Rotablator and decline thereafter. Further passages with subsequent later tracer injection may result in less myocardial perfusion reduction. In patients treated with more passages and burring time (and consequently longer total procedure duration), regional perfusion could already have returned back to higher values at the time of tracer injection, which was immediately after the last burring passage at retrieval of the burr in the guiding catheter. However, the exact time course of the transient perfusion abnormalities cannot be derived from this study because serial scintigraphic imaging during the first 48 hr after the procedure was not carried out to minimize radiation exposure.

Possible Mechanisms of Hypoperfusion

Different mechanisms to explain hypoperfusion have been proposed, particularly microembolization of calcified debris, release of vasoactive substances, microcavitation, vessel spasm and platelet activation.

Due to the unique principle of differential cutting during rotational atherectomy, atheromatous material is sheared off the vessel wall (20) and, because it is not removed directly from the coronary circulation as in directional atherectomy, is cleared via the myocardial microcirculation. Early experimental studies suggested that most particles should pass through the coronary microcirculation because of their small size (1). However, in later experiments by Friedman et al. (21), intracoronary infusion of atheromatous debris resulted in histologically proven isolated microinfarctions. Thus, obstruction of capillaries by microparticles and consecutive myocardial hypoperfusion may lead to myocardial ischemic damage. In an in vitro and in vivo study by Zott et al. (22), it was shown that the rotating burr produced microbubbles by microcavitation. The bubbles were large enough to lead to capillary obstruction and consecutive myocardial ischemia. Due to the very short half-life of these microbubbles, this mechanism implies a very transient reduction in regional myocardial perfusion.

Vessel spasm was recognized as a common phenomenon during rotational atherectomy producing transient impairment in epicardial coronary flow (7). Denudation of endothelium within the lesion and the adjacent wall by the rotating burr with the associated loss of its vasodilatory properties may explain the tendency to vessel spasm.

Another mechanism for the transient ischemia induced by rotational atherectomy may be the activation and subsequent aggregation and embolization of platelets. Elevated levels of metabolites of thromboxane A2, a strong platelet aggregating substance, have been found after rotational atherectomy (22). Rotating the Rotablator in vitro in porcine blood at >140,000 rpm resulted in platelet aggregation forming aggregates ranging from 20 to 300 µm in diameter (23). Recent data from the EPIC trial evaluating the effects of the GPIIb/IIIa receptor antibody c7E3 (ReoPro®) for the prevention of ischemic complications during PTCA and directional atherectomy demonstrated a significant reduction of non-Q-wave infarctions following directional atherectomy (24). Furthermore, favorable effects of glycoprotein IIb/IIIa inhibition on CK elevation were also observed during rotational atherectomy (25,26). Thus, potent platelet inhibition may prevent ischemic complications during rotational atherectomy supporting the theory that platelets play an important role in transient hypoperfusion induced by rotational atherectomy.

Our findings do not point to a single operating mechanism explaining the perfusion abnormalities. The only factor we could identify that was associated with a larger perfusion defect was lesion calcification. This finding can be explained by the atheromatous debris theory. A strong argument against this theory is the very transient nature of the perfusion abnormalities, which one would not expect with solid microparticles plugging the capillaries. Rotablation of longer lesions containing more plaque material did not produce larger or more severe perfusion defects, another finding discordant with the debris theory. Microbubbles formed by microcavitation are very short lived and might, along with vessel spasm, explain the hypoperfusion. Studies using potent platelet inhibition by GPIIb/IIIa antagonists might clarify the role of platelet activation in this setting.

Myocardial Enzymes

The frequent occurrence of transient myocardial ischemia in our study was not associated with myocardial damage as assessed by serial determinations of CK-MB and troponin-T release. Earlier studies reported an incidence of procedure-related non-Q-wave infarctions ranging from 5.7% to 22% (4,7,27). The reason for this difference remains unclear, because patient, lesion and procedural characteristics were comparable in all studies. The use of stents in lesions with suboptimal results following rotational atherectomy and angioplasty may play a role in the better results achieved in our study as compared to previous observations.

Comparison of Nuclear Perfusion Imaging with Other Methods to Detect Hypoperfusion and Myocardial Dysfunction During Rotational Atherectomy

Intracoronary flow measurements revealed no detectable impairment in resting coronary blood flow during rotational atherectomy (28), but coronary flow reserve after rotational atherectomy and adjunctive balloon angioplasty remained abnormal (29) probably indicating disturbances in the coronary microcirculation. Scintigraphic perfusion imaging as used in our study might better reflect changes in the microcirculation than measurements of coronary blood flow velocities in epicardial vessels.

Reversible regional myocardial dysfunction as a consequence of hypoperfusion has been demonstrated after rotational atherectomy (7). Williams et al. (30) reported transient wall motion abnormalities using serial echocardiographic evaluation. Wall motion abnormalities resolved after an average of 2–3 hr. This phenomenon could reflect myocardial stunning, as indicated by the significantly reduced sestamibi uptake during the procedure in the absence of elevated myocardial enzymes in our study. Similar to our finding that rotation-related hypoperfusion occurred in almost all patients, Williams et al. (30)
described transient wall motion abnormalities in 22 of 22 patients. Thus, our finding provides supplemental information to explain the mechanism of myocardial dysfunction during and early after rotational atherectomy.

CONCLUSION
Despite the absence of elevation of myocardial enzymes, significant scintigraphic perfusion defects could be demonstrated in the majority of patients. Thus, transient myocardial ischemia seems to be common and a closely procedure-related phenomenon. Lesion calcification could be identified as a risk factor for larger perfusion defects. Serial SPECT imaging with quantitative analysis as proposed in this study may be used in the future to evaluate pharmacological approaches to reduce rotational atherectomy-induced hyperperfusion.

REFERENCES

Combined Thallium-201 Myocardial with Technetium-99m-HMPAO Brain SPECT: Myocardial Ischemia Induced by Acetazolamide in Severe Coronary Artery Disease

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Since the perioperative mortality of coronary artery bypass surgery is high in patients with cerebrovascular disease, it is crucial to assess a cerebrovascular risk before operation. Acetazolamide (ACZ) was applied to brain SPECT to evaluate the vascular reserve, and ACZ stress brain imaging was useful for predicting perioperative cerebrovascular events. We performed 201TI myocardial and 99mTc-hexamethyl-propyleneamine oxime (HMPAO) brain SPECT with ACZ stress simultaneously to a patient with severe coronary artery disease and experienced the abnormality of 201TI myocardial imaging with ACZ, as did that with dipyridamole. Technetium-99m-HMPAO brain SPECT showed no defect. Brain SPECT with ACZ demonstrated the region of poor coronary vascular reserve, which suggested myocardial ischemia induced by ACZ in a patient with severe coronary artery disease.

Key Words: acetazolamide; myocardial ischemia; coronary artery disease; cerebrovascular disease; SPECT

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