Exercise-Induced Myocardial Ischemia in Isolated Coronary Artery Ectasias and Aneurysms (“Dilated Coronaropathy”)

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OBJECTIVES The purpose of our study was to evaluate the clinical significance of isolated coronary artery ectasias or aneurysms.

BACKGROUND It has been postulated that altered coronary blood flow in CEA predisposes patients to the development of myocardial ischemia (CI) and infarction.

METHODS Sixty-seven patients with bilateral nonobstructive CEA without associated cardiac defects (“dilated coronaropathy”) were derived from 16,341 cardiac catheterizations between 1986 and 1997. Ectasias were defined as luminal dilation of 1.5- to 2.0-fold, aneurysms of >2.0-fold of normal limits. Eleven of 25 patients presented with myocardial infarction due to an occlusion of the infarct vessel. In 42 patients without infarction (study group), exercise-induced CI was investigated.

RESULTS A corresponding CI was documented in 32 of 42 patients in a coronary sinus lactate study (reduced lactate extraction 5.6 ± 4.1%) and in 29 of 40 patients in an ergometry (0.25 ± 0.06 mV ST depressions). The results differed significantly from a control group of 29 patients without heart disease (p < 0.001). Nitroglycerin (0.8 mg) provoked a further significant deterioration of CI in the 32 of 42 developing a frank cardiac lactate production (−2.6 ± 6.8%, p < 0.001). The metabolic extent of CI was significantly correlated to the coronary diameters of the proximal and middle segments of left anterior descending artery and the middle segment of left circumflex artery (r = 0.87, p < 0.001). Stigmata of an impaired coronary blood flow such as delayed antegrade filling, segmental backflow phenomenon and local deposition of dye were found significantly more often with increasing coronary diameters (p < 0.04).

CONCLUSIONS “Dilated coronaropathy” is an entity of nonobstructive, ischemic coronary artery disease. Nitroglycerin is of no therapeutic benefit but leads to an aggravation of exercise-induced CI.

Coronary artery ectasias or aneurysms (CEA) are a rare finding among coronary artery anomalies and are considered to be of congenital origin or acquired (1–3). The entity comprises different morphological manifestations of a luminal dilation of the coronary arteries. The angiographic incidence in diagnostic cardiac catheterizations has been found to vary between 0.3% and 4.9% (4–7).

Due to a lack of a uniform definition, the terms “ectasia” and “aneurysm” have been used inaccurately and regardless of coincident coronary artery stenosis.

Coronary artery ectasias or aneurysms are attributed to atherosclerosis in 50%, whereas 20% to 30% have been considered congenital in origin. Only 10% to 20% of CEA have been described in association with inflammatory or connective tissue diseases (2,8).

Independent of the etiology, the clinical symptomatology consists of a typical exercise-induced angina pectoris. As a complication, myocardial infarction may occur, caused by repeated dissemination of microemboli to segments distal to the ectasia or aneurysm or by a thrombotic occlusion of the dilated vessel (9–11). For this reason, clinical aspects do not allow to distinguish between CEA and atherosclerotic occlusive coronary artery disease.

Based on case reports and small series, some authors have postulated that CEA may induce myocardial ischemia (CI) without coincident significant coronary artery stenosis or other cardiac defects, respectively (4,5,8).

Angiographic signs of an impaired coronary blood flow in these isolated CEA are a delayed antegrade coronary dye filling, a segmental back flow phenomenon and a local deposition of dye in the dilated coronary segment (5,12).

In our study, a systematic evaluation of a potential exercise-induced CI in patients with bilateral isolated CEA...
Another aim of the present study was to elucidate the extent to which coronary luminal enlargement and pathological coronary flow patterns correlate with the intensity of CI and whether nitroglycerin (NTG) would be of therapeutic benefit.

**METHODS**

**Evaluation of coronary angiography.** Coronary angiography was routinely performed without the use of NTG. The coronary artery tree was subdivided into a proximal, middle and distal segment. The proximal segment of the left anterior descending coronary artery (LAD) was defined as the vessel part between the left main trunk (LMT) and the first diagonal branch, proximal segment of LAD (LADp), the middle segment between the first and second diagonal branch, median segment of LAD (LADm) and the segment distal to the second diagonal branch, distal segment of LAD (LADd). The corresponding segments in the left circumflex artery (LCX) were designated by the emanating first and second obtuse marginal branch, in the right coronary artery (RCA) by the emanating acute marginal branch and by the bifurcation into the posterior descending artery and posterior left ventricular branch. Coronary diameters were measured as the maximum diameter of each segment by means of computerized quantitative angiography in a biplane mode (DCI; Philips, Eindhoven, Netherlands). For calibration, the tip of the coronary catheter was used.

According to the angiographic definition of Falsetti and Carroll (2) and Befeler et al. (8), CEAs were defined as nonobstructive lesions of the epicardial coronary arteries with a luminal dilation exceeding the 1.5- to 2.0-fold of normal diameters, and a coronary aneurysm was defined as a dilation >2.0-fold of normal diameters. If no adjacent normal segment could be identified, the mean diameters of the coronary segments in a control group without heart disease (n = 29) served as normal values. A significant stenosis in an ectatic or aneurysmatic segment was defined as a $\geq 50\%$ loss of the diameter in an adjacent normal segment or the corresponding diameter measured in the control group. A saccular CEA is that in which the transverse diameter is greater than the longitudinal extension, whereas a fusiform ectasia or aneurysm is a dilation along the axis of the vessel with reverse proportions (8). Our study group consisted of patients with a bilateral fusiform manifestation of “dilated coronaropathy,” involving both the right and left coronary artery. Patients with CEA in addition to significant stenosis or occlusion of the coronary arteries, as well as patients with prior myocardial infarction, were excluded from the study.

Coronary angiographies were screened for the following angiographic signs of an impaired coronary blood flow (Fig. 1A and B): 1) delayed antegrade coronary dye filling and drainage (slow flow); 2) segmental back flow phenomenon (milking phenomenon); and 3) local deposition of dye in the dilated coronary segments (stasis).
Evidence of exercise-induced CI. Stress testing was performed by means of ergometry and coronary sinus lactate study with incremental atrial pacing to evaluate a potential exercise-induced CI.

ERGOMETRY. Exercise stress testing was performed by means of a standard Bruce treadmill protocol or by a bicycle ergometry. The appearance of angina pectoris and significant ST segment changes were documented according to the criteria of the American Heart Association (13,14).

CORONARY SINUS LACTATE STUDY. The investigation was performed two days after diagnostic coronary angiography. No drugs were given 48 h before the study. Patients with preexisting ST segment abnormalities (due, for example, to left or right bundle branch block, left ventricular hypertrophy or digitalis medication) were excluded from the study. All patients presented with a stable sinus rhythm. At the beginning, all patients were free of symptoms and had no evidence of CI on a 12-lead electrocardiogram (ECG). A 7 F Zucker catheter (USCI, Bard, Ireland) was positioned with its tip 2 to 5 cm from the orifice of the coronary sinus to minimize the risk of admixture of right atrial blood in the samples (15). The correct position was confirmed by hand injection of dye and by an oxygen saturation measurement. Pacing was performed for 3 min each at 100, 120 and 140 beats per minute (beats/min) and three times at 160 beats/min. A 12-lead ECG was obtained before pacing, after each 3-min pacing period and for 5 min at 1-min intervals after cessation of pacing. Paired samples for lactate were withdrawn from the coronary sinus (cs) and an indwelling catheter in the radial or femoral artery (a) before pacing (baseline), at the end of every 3-min pacing interval and at 1, 3 and 5 min after cessation of pacing. Myocardial metabolism is normally aerobic, but in the presence of CI, anaerobic metabolism develops. This results in a decrease in lactate extraction by the myocardium, with a resulting anaerobic metabolism develops. This results in a decrease in lactate extraction by the myocardium, with a resulting

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\text{CLM} \% = \frac{([a] - [cs] \times [a]^{-1}) \times 100}{[a]^{-1}}
\]

Pacing was stopped when typical angina pectoris occurred. The duration of CI was quantified by the persistence of angina and ST segment depression in the 12-lead ECG, as well as pathological CLM after cessation of pacing. After a recovery time of 45 min, the study was repeated after sublingual administration of 0.8 mg NTG. According to the extent of CI, subgroups should be characterized to evaluate the clinical significance of coronary artery ectasias versus aneurysms.

All patients in the study and control groups gave written informed consent, and the study was approved by the hospital ethics committee.

Statistical analysis. The differences in values between the CLM before pacing and at every sampling time were assessed by an alpha-adjusted Bonferroni analysis (multiple comparison analysis) preceded by a two-way analysis of variance with repeated measures (p < 0.005 was considered significant). A comparison of the extent of angiographic signs of an impaired blood flow between subgroups of the study group was calculated by means of Fisher exact test. A Spearman correlation analysis was performed to investigate the influence of the coronary diameters in CEA on the severity of the ischemic response to pacing stress assessed by CLM in the coronary sinus study. After testing for normal distribution, the data of coronary artery diameters in the study and control group were compared by an unpaired Student t test. Values are presented as mean value ± SD (p < 0.05 was considered significant).

RESULTS

Patient characteristics. Sixty-seven patients with bilateral fusiform isolated CEA were selected from 16,341 consecutive cardiac catheterizations at the University Hospitals Lübeck (January 1986 to June 1994) and Kiel (July 1994 to June 1997). The overall incidence of ectasias and aneurysms in our population was 507 out of 16,341 (3.1%). Fourteen patients with a saccular manifestation, 39 patients with a unilateral fusiform manifestation and 387 patients with ectasias and aneurysms associated with significant coronary artery stenosis were excluded from the study.

In patients with “dilated coronaropathy,” age, gender (53.2 ± 7.3 years, 53 men, 14 women) and the risk profile for atherosclerotic cardiovascular disorders (arterial hypertension, diabetes mellitus, hyperlipidemia, nicotine abuse) did not differ significantly from the control group (50.9 ± 5.8 years, 24 men, 5 women).

Twenty-five of 67 patients had been admitted to the hospital because of a myocardial infarction (7 non-Q wave, 18 Q wave infarctions). In 11 of 25 cases, an occlusion of the infarct vessel was found beside the CEA; in 14 of 25 patients, coronary angiography revealed an opened infarct vessel. Our study group consisted of the 42 patients with “dilated coronaropathy” without prior myocardial infarction.

Thirty-seven of 42 patients in the study group presented with typical exertional angina pectoris; 16 of them had class II angina, and 11 had class III angina according to the definitions of the Canadian Cardiovascular Society. Ten of 37 patients with typical angina even suffered from recurrent resting chest pain. The other 5 of 42 patients complained of atypical angina pectoris. The symptoms in all patients in our study group were frequent and severe enough to warrant referral for evaluation of suspected CI.

Diagnostic of exercise-induced CI. ERGOMETRY. The exercise stress test was performed in 31 patients by means of a Bruce treadmill ergometry and in 9 patients by a bicycle ergometry. In two patients, ergometry could not be done, because of obstructive pulmonary disease. Exercise provoked
angina pectoris in 32 of 40 patients; in 29 of 40 patients significant ST segment depressions developed with a maximum of 0.25 ± 0.06 mV at a mean metabolic equivalent (MET) of 5.9 ± 1.7 and an attained heart rate of 81.0% ± 16.6% of the age-predicted maximum heart rate. Angina pectoris and ST segment depressions persisted for 3.2 ± 0.7 min into the recovery time.

In the control group, only 2 of 29 patients, who did not develop angina pectoris, met electrocardiographic criteria of CI. Three of 29 patients complained of exercise-induced chest pain without significant ST segment changes. The heart rate attained at the end of the test was 102.7% ± 11.4% of the age-predicted maximum heart rate at 9.7 ± 2.4 MET.

**CORONARY SINUS LACTATE STUDY WITH INCREMENTAL ATRIAL PACING.** Forty-two patients underwent incremental coronary sinus pacing. Cardiac lactate metabolism gradually changed from a physiological lactate extraction of 28.5% ± 9.9% to 5.6% ± 4.1%, indicating CI, as depicted in Figure 2A. Significant differences in mean cardiac lactate levels...
were found between the baseline data and the data recorded at each 3-min pacing period at 160 beats/min (p < 0.001). Pacing induced angina pectoris in 34 of 42; in 16 patients pacing was stopped before the end of the protocol because of angina pectoris. In 31 of 42 patients, significant ST segment depressions of 0.31 ± 0.09 mV were documented after cessation of pacing; the attained heart rate was 91.5% ± 11.4% of the age-predicted maximum heart rate. Angina pectoris and ST segment depressions persisted for 2.7 ± 0.5 min, whereas an instantaneous consolidation of CLM was documented 1 min after cessation of pacing.

After NTG administration, the pacing protocol had to be terminated prematurely in 23 patients because of an even earlier appearance of angina pectoris. Pathological ST segment depressions were noted in all 31 patients again (0.30 ± 0.11 mV), although pacing had attained a heart rate of only 72.9% ± 13.9% of the age-predicted maximum heart rate. Angina pectoris and ST segment depressions persisted for 3.9 ± 0.9 min into the recovery time. Nitroglycerin exerted a further marked alteration of the CLM, with an overall frank cardiac lactate production of −2.6% ± 6.8% in the study group. A subsequent abnormal reduction of cardiac lactate extraction was found 1 and 3 min after cessation of pacing. Significant differences in mean cardiac lactate levels were found between the baseline data and the data recorded at 140 beats/min, 160 beats/min, 1 min, 3 min and 5 min after pacing, respectively (p < 0.001).

Further significant differences were found between the

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**Figure 2.** Continued.
mean cardiac lactate levels with NTG versus without NTG at each 3-min pacing period at 160 beats/min and at 1 min, 3 min and 5 min after pacing (p = 0.003).

Metabolic evidence of myocardial ischemia was found in 32 of 42 patients in the study group. Based upon the severity of CI measured by means of CLM, the study group was divided into three subgroups. Subgroup I (n = 18) was defined by a pacing-induced frank cardiac lactate production in all patients after administration of NTG. In this subgroup, NTG exerted its most paradoxical effect with a marked aggravation of myocardial ischemia persisting for the whole recovery period. In 11 patients, pacing had induced a lactate production without NTG premedication (Figure 2B). Subgroup II (n = 14) was characterized by a pathologically reduced cardiac lactate extraction <10% before and after NTG (Fig. 2C). Subgroup III (n = 10) represented individuals with only slightly altered cardiac lactate extraction rates (Fig. 2D).

Improvement of symptoms, reduction of ischemia-induced ST segment depressions or an improvement of CLM by NTG could not be documented in any patient. Nitroglycerin provoked a significant, marked alteration of the CLM (p = 0.003) and even a change into a lactate production in the overall study population (Fig. 2A), predominantly based on its effect found in subgroup I (Fig. 2B).

In the control group, pacing provoked chest discomfort in 2 of 29 patients; CI was proved to be the result of neither electrocardiographic nor metabolic criteria. Pacing was repeated in 10 of 29 patients after NTG in the control group; the results remained unchanged.

Consistent with the results of the coronary sinus study, a severe CI was also provoked by ergometry in 17 of 18 patients of subgroup I. In 10 of 14 patients with pathologically reduced lactate extraction (subgroup II), ergometry revealed CI as well. In subgroup III, with no metabolic evidence of CI, only 2 of 10 patients demonstrated a pathological ergometry.

<table>
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<th>Table 1. Coronary Artery Diameters in the Control Group and in Patients with CEA</th>
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<td>Control Group</td>
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<td>RCAp</td>
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Values shown are the mean ± SD coronary diameters of the left main trunk (LMT), proximal (p), middle (m) and distal (d) segments of the left anterior descending (LAD), left ramus circumflexus (LCX) and right coronary artery (RCA) in the control group and all patients with coronary artery ectasias or aneurysms (CEA) as well as the subgroups I to III. Significant differences are indicated (*p < 0.02, †p < 0.04).
Coronary artery diameters. The coronary artery diameters in "dilated coronaropathy" and its respective subgroups were compared with the diameters in the control group (Table 1). In most segments, significant differences were found not only in comparison with the control group (p < 0.02), but also among the three subgroups (p < 0.04). The coronary diameters of the control group were in accordance with data reported in literature (20).

To evaluate the influence of coronary diameter enlargement in CEA on the severity of exercise-induced CI, a correlation analysis between the study group diameters in the proximal LAD and the CLM was performed. A Spearman analysis (Fig. 3) revealed a significant correlation (r = 0.87, p < 0.001), indicating that the extent of CI strongly depended on the size of luminal enlargement in CEA. A significant correlation was also found between the extent of CI and the diameters in the middle segments of the LAD and LCX, respectively.

Angiographic patterns. The angiographic findings of the subgroups are presented in Table 2. The coronary lesions in subgroup I can be described as coronary artery aneurysms with the largest coronary diameters and the strongest angiographic signs of an impaired coronary blood flow. Cardiac lactate metabolism presented with a cardiac lactate production in these patients. Compared with subgroup III, most of the patients in subgroup II (moderate CI) had larger coronary diameters and more frequent "slow flow," "stasis" and "milking phenomenon." These differences in terms of the stigmata of an impaired blood flow were statistically significant (p < 0.04).

DISCUSSION

Epidemiological aspects. The clinical significance of CEA has been a controversial topic of discussion (2–8). So far, symptomatology and angiographic features of this entity have not been the object of a systematic investigation. The coexistence with occlusive coronary artery disease has raised the question of whether CEA is a variant of atherosclerotic ischemic heart disease or a distinct entity.

The incidence of CEA in patients catheterized for suspected coronary insufficiency has been reported to account for 0.3% to 4.9%, regardless of associated coronary artery stenosis (21). These differences may reflect the arbitrary use of the terms "ectasia" and "aneurysm."

Only limited information is available on the clinical implications of "dilated coronaropathy," in which coronary artery stenosis and anomalies, valvular and other cardiac defects, are not present. Based on smaller studies by Swaye et al. (7) and Hartnell et al. (4), an angiographic frequency of 0.1% to 0.32% has been reported.

Etiology and angiographic appearance. In all patients reported in the literature, true aneurysms have been discovered. In most of the cases with isolated CEA (as well as in our study), a bilateral fusiform manifestation was found. In unilateral forms, the coronary luminal dilation is located in 40% to 85% in the RCA compared with 30% to 50% in the LAD and LCX (4,8).

The etiology of CEA comprises various possibilities. The majority of CEA are due to coronary artery atherosclerosis (50%). A continuous spectrum of lesions from shallow and angiographically insignificant atheromatous ulcerations in a localized area to a diffuse ulcerative process with significant stenosis has been described in association with CEA (2,8,11,22). In most cases, pre- and poststenotic CEA (3,6,7) were found; however, luminal dilations may affect other vessel segments as well (23–25). In 20% to 30%, CEA have been classified as congenital coronary anomalies either as isolated lesions (1) or associated with other congenital cardiac defects (12,20). In 10% to 20%, CEA are attributed to inflammatory diseases such as Kawasaki disease (25), Takayasu disease (26) or mycotic coronary lesions (27). Another 10% to 20% of CEA are associated with collagenosis (sclerodermal heart disease [28], polyarteritis nodosa [29], systemic lupus erythematosus [30]) or connective tissue diseases (Ehlers-Danlos syndrome [31], Marfan syndrome [32]). The question of how congenital CEA could be differentiated from acquired forms by clinical and angiographic criteria has given rise to apparently conflicting statements. The age of manifestation of clinical symptoms cannot always be used as an indicator. However, congenital CEA usually become clinically apparent in infancy and childhood, whereas CEA related to inflammatory diseases develop later in life but still earlier than those of atherosclerotic nature (2). In most of the cases, the etiology remains completely unknown, and most authors refrain from ascribing any cause to the luminal enlargement. In our patients, the most likely etiology seems to be coronary atherosclerosis because of the age of manifestation (53.2 ± 7.3 years) and because clinical examinations and laboratory investigations revealed no evidence of a collagenosis, connective tissue or inflammatory disease.

Extracardiac vessel dilations were reported only by Daoud et al. (24) and Stajduhar et al. (34), who described an overproportional coincidence of coronary artery aneurysms with aneurysms of the aorta abdominalis.

Histopathological findings. The main histopathological alteration of atherosclerotic CEA is an intimal proliferation with spreading of plaque material into the vessel media. As a pathomechanism for the development of pre- and poststenotic CEA, an increase in wall stress to which the artery is exposed with the thinning and atherosclerotic destruction of the vessel media resulting in progressive vessel dilation is proposed (24,35).

However, coronary artery stenosis and atherosclerosis, respectively, are not a conditio sine qua non for the development of CEA. Rath et al. (11) and Mattern et al. (36) described histologically evaluated nonatherosclerotic forms of CEA with an intact vessel intima but with extensive media degeneration and smooth muscle cell re-
placement by hyalinized collagen, with subsequent marked attenuation of the vessel wall. Thus, a functional loss of the musculoelastic components of the coronary artery media is considered to be the common pathway in the pathogenesis of the disease (3,5,8).

Clinical symptoms and pathophysiological explanations. Although patients with CEA complain mainly of typical exertional angina pectoris, unstable angina has occasionally been noted. These symptoms may also occur without associated coronary artery stenosis. It has been hypothesized that altered blood flow in CEA will predispose patients to the development of myocardial infarction and increased mortality. Coronary insufficiency and myocardial infarctions are attributed to embolization of intracoronary parietal thrombus to the distal coronary tree. In cases of Q wave infarctions (the most common severe complication in isolated CEA), thrombotic occlusions of the infarct vessel have been angiographically documented in several studies (4,6,8,22). An alternative explanation for myocardial infarctions is that both occlusion and CEA are different manifestations of one disease, namely atherosclerosis. Microembolisms with consecutive disturbance of coronary perfusion may account for ventricular arrhythmias and even sudden cardiac death; the occlusion of major coronary vessels may result in acute ventricular dysfunction (9,21). On the other hand, a spontaneous rupture of an aneurysmatic coronary artery is rare (7).

In previous studies, “sluggish circulation,” “swirling” and “strikingly slow and scattered clearance of contrast material” have been reported as typical angiographic patterns. The relevance of these angiographic observations with regard to clinical manifestations of myocardial ischemia, however, has not yet been elucidated. In our study group, we detected a significant stronger degree of these angiographic stigmata of an impaired blood flow with increasing coronary luminal enlargement. The pathophysiologic explanation for this phenomenon may be a conversion from a laminar to a turbulent coronary flow in the dilated segments. Frequently, streaming can be denoted by the admixture of blood with dye, resulting in a poorly defined lumen due to “pseudo filling defects.” (11,12,37). According to Hagen-Poiseuille’s law, blood flow velocity decreases with an increasing vessel diameter, but this physical law is valid only in the case of a laminar flow of a homogeneous fluid. As a result of the specific flow properties of blood (Reynold’s law), viscosity increases below a critical blood flow velocity, with a loss of an axial stream leading to erythrocyte aggregations (loss of the Fahraeus-Lindqvist-effect) and an activation of platelets and the coagulation system (36).

Rath et al. (11) and Tambe et al. (38) described an extremely delayed coronary flow in patients with isolated coronary aneurysm. The authors called this phenomenon “slow-flow” and discussed a causal elevation of the coronary resistance as well as a pathological reduction of the coronary flow reserve.

In the present study, clinical symptoms were documented as a typical exertional angina pectoris; in some patients, even unstable angina occurred. We found an appreciable incidence of non–Q wave and Q wave myocardial infarctions accounting for 33% in our collective.

Evidence of exercise-induced myocardial ischemia. So far, little data exist concerning a validated CI in isolated CEA (4,5,8,11,24). This study presents the first investigation of a larger number of patients with “dilated coronaropathy” demonstrating evidence of a corresponding exercise-induced CI in an ergometry and a coronary sinus stress test. The severity of coronary insufficiency significantly correlated with the size of the coronary luminal enlargement in the proximal segment of the LAD (Fig. 3) as well as the middle segments of the LAD and LCX, respectively. In subgroup I, with bilateral large coronary aneurysms, we found the strongest extent of angiographic signs of an impaired coronary blood flow and the strongest ischemic response with a frank lactate production and significant ST segment depressions. Subgroup II presented

Figure 3. Influence of the extent of luminal enlargement on the CLM in CEA. Depicted are the coronary artery diameters of every patient’s proximal LAD segment on the abscissa and the maximum rate of CLM under atrial pacing on the ordinate. A significant correlation was found (p < 0.001, r = 0.87) between the diameters of the subgroups I (solid triangle), II (open circles) and III (×) and the severity of CI due to the CLM.

Table 2. Angiographic Patterns and Distribution of Stigmata of an Impaired Coronary Blood Flow in the Subgroups I to III

<table>
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<tr>
<th>Angiographic Patterns/Stigmata</th>
<th>Subgroup I</th>
<th>Subgroup II</th>
<th>Subgroup III</th>
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<tr>
<td>Bilateral aneurysms</td>
<td>16/18</td>
<td>2/14</td>
<td>0/10</td>
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<tr>
<td>Unilateral ectasia and unilateral aneurysm</td>
<td>2/18</td>
<td>1/14</td>
<td>0/10</td>
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<tr>
<td>Bilateral ectasias</td>
<td>0/18</td>
<td>11/14</td>
<td>10/10</td>
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<tr>
<td>Delayed filling and drainage of dye</td>
<td>17/18</td>
<td>11/14</td>
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<tr>
<td>Segmental back flow phenomenon</td>
<td>16/18</td>
<td>9/14</td>
<td>3/10</td>
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<tr>
<td>Local deposition of dye</td>
<td>18/18</td>
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with a moderate ischemia, compared with subgroup III, with smaller bilateral coronary ectasias, in which CLM was not significantly altered under pacing stress. Thus, the differentiation between coronary artery ectasias and aneurysms is of evident functional importance.

It is remarkable that NTG was of no therapeutic benefit and did not improve the clinical symptoms and ischemic response in our coronary sinus investigation. In subgroup I, we could even see a paradoxical effect of NTG leading to a significant aggravation of CI. This finding is in contrast to the NTG effect in stenotic coronary artery disease, where the drug had been proven to restore CI in coronary sinus studies (39,40).

**Therapeutic management.** The coronary morphology of CEA is heterogeneous; for this reason, pharmacological, interventional and surgical therapy specific to the cause is required. In addition to the determination of the cause, therapeutic management depends on possible or manifest complications.

The application of platelet inhibitors as a prophylaxis against ischemic syndromes attributed to fibrin thrombus formation and microemboli showering is indispensable in all forms of CEA (5,7,9). Heparin infusion is expected to reduce intracoronary thrombus formation, which is especially regarded as a factor contributing to unstable angina. Anticoagulation with cumarin has been propagated, although a therapeutic superiority compared with aspirin has not yet been evaluated (3,11). Fibrinolytic as well as interventional recanalization of the vessel constitutes therapy in thrombotic occluded CEA (10).

In patients with associated significant coronary artery stenosis, treatment should follow the guidelines for revascularization (41).

The results of our study strongly suggest that NTG has no therapeutic benefit in “dilated coronaropathy,” but it may lower the ischemic threshold. Consequently, the administration of nitrates in “dilated coronaropathy” should be avoided.

In our study group, CI development depended on heart rate; therefore, a reasonable therapeutic approach might be the administration of beta-blockers due to their negative chronotropic effect and reduction of myocardial oxygen consumption in the absence of vasodilation (42).

**References:**


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