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Functional, Angiographic and Intracoronary Doppler Flow Characteristics in Symptomatic Patients With Myocardial Bridging: Effect of Short-Term Intravenous Beta-Blocker Medication

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Objectives. We sought to define the effects of short-term beta-adrenergic blocking medication on intracoronary flow characteristics, clinical symptoms and angiographic diameter changes in patients with severe myocardial bridging of the left anterior descending coronary artery.

Background. Controversy exists regarding the pathophysiology, clinical relevance and optimal therapy in symptomatic patients with myocardial bridges because antianginal drugs have not been systematically tested.

Methods. In 15 symptomatic patients with myocardial bridging of the left anterior descending coronary artery, maximal lumen diameter reductions were evaluated by quantitative coronary angiography. There were no angiographic signs of coronary artery disease. Coronary blood flow velocities (using a 0.014-in. [0.035 cm] Doppler guide wire) were measured at rest, during atrial pacing and during intravenous administration of a short-acting beta-blocker (esmolol, 50 to 500 μg/kg body weight per min) with continuous atrial pacing.

Results. The maximal angiographic systolic lumen diameter reduction within the myocardial bridges was 83 ± 9% at rest, with a persistent diastolic diameter reduction of 41 ± 11% (mean ± SD). Short-term intravenous beta-blocker therapy decreased the diameter reduction during both systole (from 83 ± 9% to 62 ± 11%) and diastole (from 41 ± 11% to 30 ± 9%, both $p < 0.001$). The average diastolic peak flow velocity was higher within the myocardial bridges (33 ± 13 cm/s) than the proximal (26 ± 13 cm/s) and distal bridges (17 ± 4 cm/s, both $p < 0.001$). During tachypacing, average diastolic peak flow velocity increased within the bridged segments to 63 ± 21 cm/s versus 29 ± 12 cm/s in the proximal and 20 ± 4 cm/s in the distal bridges (both $p < 0.001$). Beta-receptor blockade produced a return to baseline values (average diastolic peak flow velocity within bridge 35 ± 16 cm/s, $p < 0.001$). ST segment changes and symptoms were abolished with beta-blocker administration.

Conclusions. In patients with myocardial bridges, administration of short-acting beta-blockers during atrial pacing alleviates anginal symptoms and signs of ischemia. This effect was mediated by a reduction of vascular compression and maximal flow velocities within the bridged coronary artery segment.

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Myocardial bridging is anatomically defined by the intramyocardial course of portions of the coronary arteries, mainly the midportion of the left anterior descending coronary artery (1). Its typical angiographic presentation is the systolic "milking" effect due to transient myocardial vessel compression (2,3). The reported frequency of this anomaly varies widely, from 15% to 85% at autopsy and 0.5% to 16% on angiography (4–7). There is also considerable controversy regarding the clinical, hemodynamic and prognostic significance of myocardial muscle bridges. Although various reports are available describing ischemia (8), myocardial infarction (9–11), arrhythmia (12,13) or sudden cardiac death (14–16) in association with this anatomic variation and otherwise normal coronary arteries, myocardial bridges are generally considered harmless clinical anomalies (7). This attitude is supported by several observations: 1) the malformation is present since birth and yet symptoms usually develop no earlier than the third or fourth decade of life (17); 2) maximal compression occurs during a short period of the heart cycle in end systole when only minimal physiologic anterograde flow due to high peripheral vascular resistance is present (18,19); and 3) no persistent correlation could be demonstrated between the angiographic degree of myocardial bridging and clinical symptoms (20–22), as well as signs of ischemia during exercise testing or myocardial scintigraphy (23–25). A recent combined angiographic and intravascular ultrasound study was able to demonstrate that vessel compression within the bridge is not a purely systolic event but persists throughout larger portions of diastole associated with a reduction in coronary flow reserve (26). Myocardial bridges may therefore be able to induce significant ischemia, especially in patients with severe dynamic obstruction (27–29). The purposes of this report were 1) to evaluate the angiographic degree of vessel diameter reduction during sys-

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Table 1. Demographic and Clinical Characteristics in 15 Patients With Myocardial Bridging

Age (yr)	
Mean ± SD	52.6 ± 6.8
Range	39–63
Male	13 (87%)
Interval (mo)*	
Mean ± SD	19.7 ± 21
Range	1–88
No. of hospital admissions†	
Mean ± SD	2.5 ± 1.3
Range	1–4
Angina pectoris	15 (100%)
Typical	10 (67%)
Atypical	5 (33%)
CCS class	
II	5 (33%)
III	6 (40%)
IV	4 (27%)
Ergometry (total)	11 (73%)
Positive	7 (47%)
Myocardial scintigraphy (total)	8 (53%)
Positive	5 (33%)

*Time interval from first symptoms to angiographic diagnosis of myocardial bridging. †Due to anginal symptoms. Unless otherwise indicated, data presented are number (%) of patients. CCS = Canadian Cardiovascular Society (functional classification of angina).

tole and diastole within the myocardial bridge, 2) to determine the degree of flow acceleration within the myocardial bridge at rest and during rapid atrial pacing, and 3) to study the short-term effect of intravenous beta-adrenergic blocking agent administration on angiographic lumen diameter reduction, intracoronary Doppler flow velocities, clinical symptoms and electrocardiographic signs of ischemia.

Methods

Patient selection and characteristics. Fifteen patients with an angiographically documented myocardial bridge of the left anterior descending coronary artery with a >70% systolic lumen diameter reduction were selectively studied (mean age 52.6 ± 6.8 years; 13 male [87%]). Evidence of coronary artery disease was excluded by selective coronary angiography. Global left ventricular function was normal in all patients. In addition, there were no signs of left ventricular hypertrophy or hypertrophied cardiomyopathy. Three patients had a history of mild hypertension without echocardiographic evidence of left ventricular hypertrophy. The major demographic and clinical characteristics are given in Table 1. All patients reported a history of chest pain strongly suggestive of angina pectoris. The mean time interval between the first symptoms and the angiographic diagnosis of a myocardial muscle bridge was 19.7 ± 21 months. Most of the patients had several previous hospital admissions owing to angina pectoris or suspected acute myocardial infarction, or both. Three patients had previous intramural anterior wall myocardial infarction with documented elevation in myocardial enzymes and electrocardiographic (ECG) abnormalities without Q waves. Symptom-limited exercise ECGs were available in 11 (73%) of 15 patients. Four patients did not undergo stress testing before cardiac catheterization because of unstable symptoms (Canadian Cardiovascular Society functional class IV) or rest ECG abnormalities. Significant ischemic ST segment depression of more than 0.1 mV in the anterior leads were identified in 7 (64%) of 11 patients. In addition, 5 (63%) of 8 patients with planar thallium 201 scintigraphy demonstrated reversible perfusion defects in the anterior-septal wall. Three patients (20%) had no signs of ischemia at rest or during stress testing, but reported long-standing and recurrent chest pain with relief after nitrate administration. Informed written consent was obtained from all patients.

Angiography. Before cardiac catheterization all cardiovascular medications were withheld for at least 24 h. Cineventriculography and selective coronary angiography were performed using the Judkins catheter technique in multiple standard projections. Cineangiograms were recorded with 25 frames per second on 35-mm film.

Quantitative coronary angiography. A 35-mm cineprojector with an adapted videocamera (CAP 35 BII) was used to visualize the left anterior descending coronary artery. The video signal was then digitized (512 × 512 pixels) for quantitative measurements on a workstation with dedicated software (AWOS vs. 4.1, Siemens Erlangen, Germany). For this purpose the coronary segment of interest, including the total length of the myocardial bridge with the adjacent nonobstructed proximal and distal segments, was identified. Boundaries of this segment were then detected automatically and corrected manually if necessary (Fig. 1). Absolute vessel diameters (mm) were determined using the guiding catheter as a reference. The percent diameter stenosis at the most severe site was automatically calculated from the computer estimation of the original dimension of the artery along the myocardial bridge, defined as an interpolation between proximal and distal reference diameters. Angiographic lumen diameter evaluation was performed at end systole, when the diameter of the vessel was smallest, and during mid-diastolic frames. To determine interobserver variability for quantitative angiographic measurements of systolic and diastolic lumen diameter reductions, images from a random subset of 10 patients were analyzed by two independent observers (E.R.S. and H.G K.) blinded to each other's results. Intraobserver variability was measured by having one observer (E.R.S.) analyze the same angiographic images on two separate occasions, blinded to his previous results. Interobserver correlation coefficients for the absolute angiographic systolic and diastolic lumen diameters within the muscle bridge was r = 0.91 with a standard error of the estimate (SEE) of 0.06 mm; for percent lumen diameter reduction, r = 0.92 (SEE 4%). The intraobserver variability for absolute systolic and diastolic dimensions within the myocardial bridge was r = 0.95 (SEE 0.05 mm), and r = 0.98 (SEE 2%) for the percent diameter reduction.

Intracoronary Doppler flow velocity measurements. After completion of the diagnostic study, coronary flow velocity

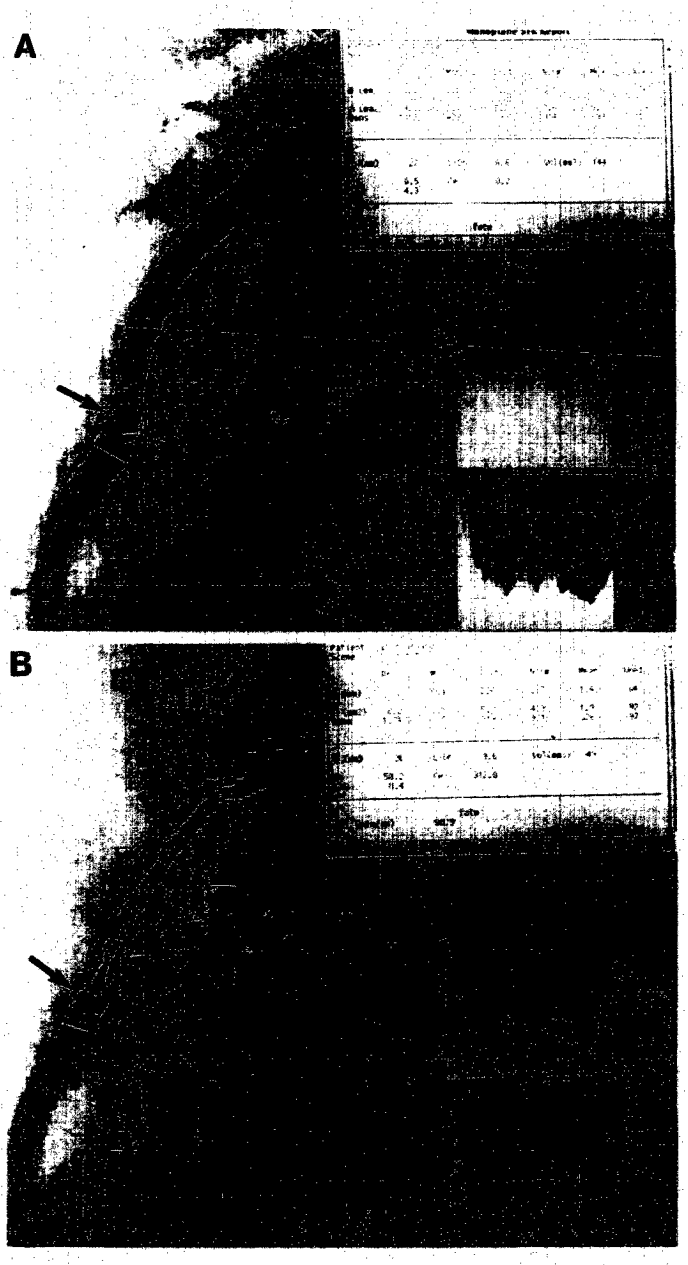

Figure 1. Digitized and magnified angiographic images of the midportion of the left anterior descending coronary artery. The boundaries of the coronary muscle bridge, including a proximal (Prox) and distal (Dist) segment without compression, are delineated during diastole (**A**) and systole (**B**). The **graphs** to the lower right reflect the quantitative analysis of the identified vessel segments. The absolute values are given in the **tables** to the upper right. A = area; Cal = calibration; Ce = resistance coefficient; Cv = viscose resistance coefficient; D = diameter; Dens = density; Dn = normal diameter; L = segment length; Min = minimal; Norm = normal; pix = pixel; Red = reduction; SFR = stenosis flow reserve.

measurements were performed with a commercially available Doppler guide wire (FloWire, Cardiometrics Inc.) using standard techniques. In brief, after administration of 5,000 U of heparin sodium intravenously, the highly flexible and steerable 0.014-in. (0.035 cm) angioplasty guide wire with a 12-MHz ultrasound transducer mounted on its tip was advanced under fluoroscopic guidance and placed in the left anterior descending coronary artery. Care was taken to orient the wire tip in the center of the vessel to obtain a stable and complete flow velocity envelope. The following variables were automatically calculated by integrated software from two consecutive beats: average peak flow velocity; average diastolic peak flow velocity;

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Table 2. Comparison of Quantitative Coronary Angiographic Measurements in 15 Patients With Myocardial Bridging at Baseline and After Beta-Blocker Medication

	Cardiac Catheterization		
	Baseline (n = 15)	After Beta-Blocker (n = 15)	p Value
Coronary diameter (mm)			
Proximal to MB			
Systolic	2.7 ± 0.5	2.5 ± 0.7	NS
Diastolic	2.6 ± 0.5	2.6 ± 0.5	NS
Distal to MB			
Systolic	2.2 ± 0.4	2.0 ± 0.4	NS
Diastolic	2.4 ± 0.4	2.3 ± 0.4	NS
Within MB			
Systolic	0.7 ± 0.3	1.0 ± 0.4	< 0.01
Diastolic	1.7 ± 0.3	1.9 ± 0.3	< 0.01
Length of MB (mm)			
Systolic	27.4 ± 7.9	22.8 ± 5.0	< 0.05
Diastolic	25.2 ± 4.5	22.8 ± 5.6	< 0.05
% diameter reduction			
Systolic	82.9 ± 9.4	61.8 ± 11.4	< 0.001
Diastolic	49.7 ± 10.9	29.8 ± 9.0	< 0.001

MB = myocardial bridge.

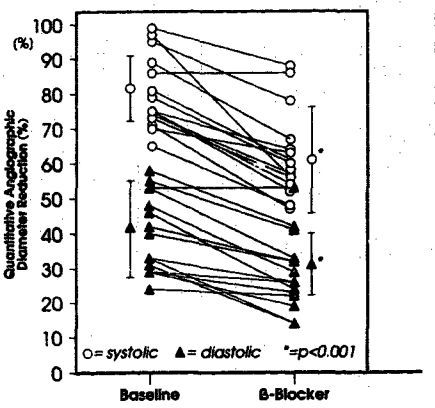

Figure 2. Scattergram showing the individual changes in percent systolic and diastolic lumen diameter reductions using quantitative coronary angiography at baseline and during beta-blocker medication. Only one patient showed no reaction after beta-blocker administration.

average systolic peak flow velocity; maximal peak flow velocity (in cm/s); and diastolic/systolic flow velocity ratio.

Study protocol. After routine coronary angiography, right atrial pacing was performed to determine the individual Wenckebach point. Baseline flow velocity measurements were obtained proximal to, within and distal to the myocardial bridge. Coronary flow reserve measurements were obtained in 12 (80%) of 15 patients after intracoronary injection of 10 to 12 mg of papaverine, placing the transducer proximal and distal to the myocardial bridge. Coronary flow reserve was defined as the ratio of mean flow velocity achieved at peak hyperemia to the mean rest flow velocity. The remaining three patients had prolongation of their QT interval at baseline, and to avoid arrhythmic complications (i.e., ventricular tachycardia), papaverine was not administered to these patients (30). Atrial pacing was started with a heart rate of 80 beats/min and increased by 20 beats every 2 min until the pacing rate was 5 beats below the predetermined Wenckebach point. At the maximal heart rate, Doppler flow velocities were again recorded from the same segments distal and proximal to the myocardial bridge. After 15 min of recovery the same pacing protocol was repeated, and at the maximal heart rate a body weight-adapted bolus injection of 500 μg/kg over 60 s of the beta-blocker esmolol (Gensia Europe Ltd., Bracknell, England, UK) was started, followed by a continuous infusion of 50 to 500 μg/kg per min, starting with the lowest dose and then an increase every 2 min up to the maximal dose in all patients. In all patients a 12-lead ECG was recorded. Immediately after discontinuing atrial pacing and removing the Doppler guide wire from the bridged segment, cineangiograms were obtained to determine lumen diameter changes.

Statistical analysis. Results are expressed as mean value ± SD. Repeated angiographic and Doppler flow measurements were compared by analysis of variance for repeated measurements. Relations between groups were studied using the paired Student *t* test; a Bonferroni correction was applied to adjust for multiple comparisons. A p value <0.05 was considered statistically significant.

Results

Quantitative angiographic measurements. The complete quantitative coronary angiographic data are presented in Table 2. The mean percent diameter reduction at the most severe side of the myocardial bridge during systole was 83 ± 9%, ranging from 71% to 99%. There was a persistent diastolic lumen diameter reduction of 41 ± 11% with a minimum of 24% and a maximum of 58%. The mean absolute systolic diameter within the myocardial bridge was 0.7 ± 0.3 mm; five patients had a minimal diameter <0.5 mm. The length of the myocardial bridge during systole ranged from 19 to 44 mm (mean 27 ± 8) and was not different from the diastolic values of 25 ± 5 mm (range 21 to 42, p = NS). Short-term intravenous beta-blocker administration induced a 25% decrease in mean percent systolic diameter reduction within the myocardial bridge, from 83 ± 9% to 62 ± 11% ($p < 0.001$) (range 47% to 86%), immediately after tachypacing. There was a similar 25% change in diastolic diameter reduction, from 41 ± 11% to 30 ± 9% ($p < 0.001$) (range 14% to 53%) (Fig. 2). The absolute diameter within the myocardial bridge increased from 0.7 ± 0.3 to 1.0 ± 0.4 mm ($p < 0.01$) during systole and from 1.7 ± 0.3 to 1.9 ± 0.3 mm ($p < 0.01$) during diastole. There were no significant changes in the segments proximal and distal to the myocardial bridge. In addition, the length of the myocardial bridge during systole and diastole decreased slightly, from 27 ± 8 to 23 ± 5 mm ($p < 0.05$) and from 25 ± 5 to 23 ± 6 mm

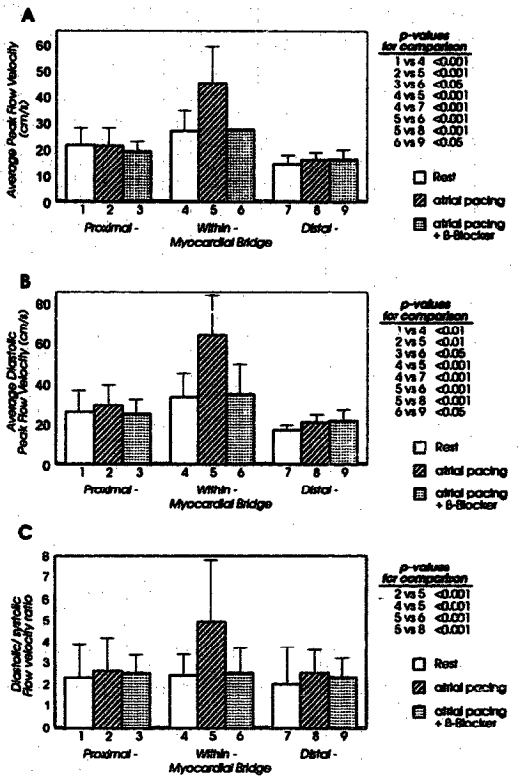

Figure 3. Box plots demonstrating intracoronary Doppler flow velocities proximal to, within and distal to the myocardial muscle bridge at rest and during atrial tachypacing (mean heart rate 134 beats/min) and additional beta-blocker medication with continuing tachycardia. **A,** Average peak flow velocity. **B,** Average diastolic peak flow velocity. **C,** Diastolic/systolic flow velocity ratio.

($p < 0.05$), respectively. Only one patient showed no angiographic reaction during beta-blockade.

Intracoronary Doppler flow velocity measurements. *At rest,* with a mean heart rate of 75 ± 7 beats/min, the average peak (26.7 ± 9.6 cm/s) and diastolic peak (33.1 ± 13.4 cm/s) flow velocities were significantly higher within the bridged segment than the proximal (21.2 ± 7.4 cm/s [$p < 0.001$] and 25.5 ± 13.3 cm/s [$p < 0.01$], respectively) and distal segments (14.3 ± 3.2 cm/s and 16.5 ± 3.6 cm/s [$p < 0.001$], respectively) (Fig. 3A, B). The flow velocity increase within the myocardial bridge was smallest for the average systolic peak flow velocity, with 12.3 ± 4.6 cm/s proximal to, 13.7 ± 6.6 cm/s within (p = NS, compared with proximal) and 9.1 ± 2.3 cm/s distal to the myocardial bridge ($p < 0.05$, compared with the bridged segment). The instantaneous maximal peak flow velocity was more than twice as high within (78.1 ± 21.1 cm/s) as compared with proximal (31.5 ± 13.5 cm/s [$p < 0.001$]) and distal (24.3 ± 11.6 cm/s [$p < 0.001$]) to the myocardial bridge. The diastolic/systolic flow velocity ratio at rest was not different between the three measuring points (Fig. 3C). There were also no significant differences comparing all flow velocity measurements proximal and distal to the myocardial bridge.

Tachypacing with a mean heart rate of 134 ± 12 beats/min induced an increase of all flow velocities within the myocardial bridge (Fig. 3 [A and B] and 4). The average diastolic peak flow velocity increased from 29.1 ± 12.2 cm/s proximal and 20.2 ± 4.2 cm/s distal to 63.3 ± 21.3 cm/s ($p < 0.001$) within the myocardial bridge (Fig. 3B). The flow acceleration was largest for the maximal peak flow velocity, from 34.4 ± 8 cm/s proximal and 27.8 ± 8.4 cm/s distal to 104.8 ± 35.7 cm/s ($p < 0.001$) within the bridge. The increase was again smallest for the average systolic peak flow velocity, with 10.9 ± 3.4 cm/s proximal and 9.1 ± 4 cm/s distal versus 16.2 ± 7 cm/s ($p < 0.05$) within the bridged segment. The calculated diastolic/systolic flow velocity ratio proximal and distal to the myocardial bridge was not different during atrial pacing. There was, however, a significant change in the diastolic/systolic flow velocity ratio within the myocardial bridge during tachycardia, which was not present at rest (2.4 ± 1.0 vs. 4.9 ± 2.9 cm/s [$p < 0.001$]) (Fig. 3C). There were no significant changes in flow velocities from rest to pacing proximal and distal to the myocardial bridge. During tachypacing all patients reported mild dyspnea; 9 (64%) of 15 patients developed anginal symptoms comparable with their usual clinical complaints; and 6 (43%) had corresponding ST segment changes in ECG leads V_1 to V_6 or I and aVL.

Coronary flow reserve measurements. The mean coronary flow reserve proximal to the myocardial bridge was 2.7 ± 0.8 cm/s and higher than measurements obtained distal to the bridge (2.0 ± 0.6 cm/s [$p < 0.01$]). A ratio >3.0 was obtained in 25% of patients with measurements obtained proximal to and in none with measurements obtained distal to the myocardial bridge.

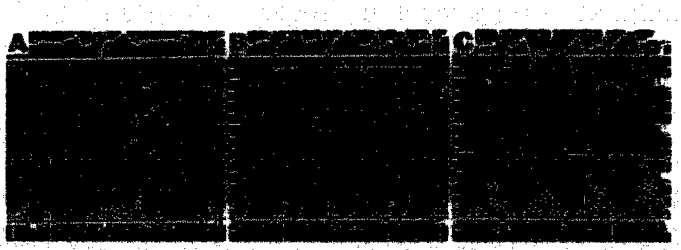

Figure 4. Doppler flow profile images obtained within myocardial bridging. **A,** At rest, there is a typical early diastolic flow acceleration with a rapid velocity decrease and mid- to late diastolic plateau. **B,** Atrial pacing induces a further increase in diastolic velocities, again with an early peak and a less pronounced plateau due to shortened diastole. **C,** Intravenous beta-blocker application with continuing tachypacing decreases the flow velocities to their baseline values. Scales were identical in all graphs.

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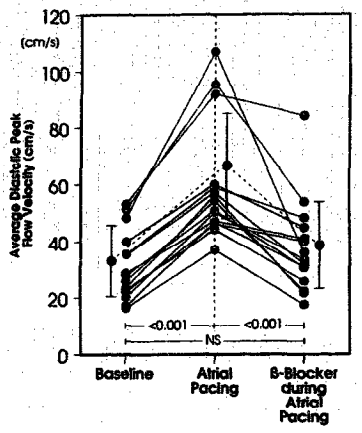

Figure 5. Scattergram demonstrating the individual changes in average diastolic peak flow velocity from baseline to atrial pacing (mean heart rate 134 beats/min) and during beta-blocker medication. Only one patient showed no reaction after the maximal beta-blocker dose.

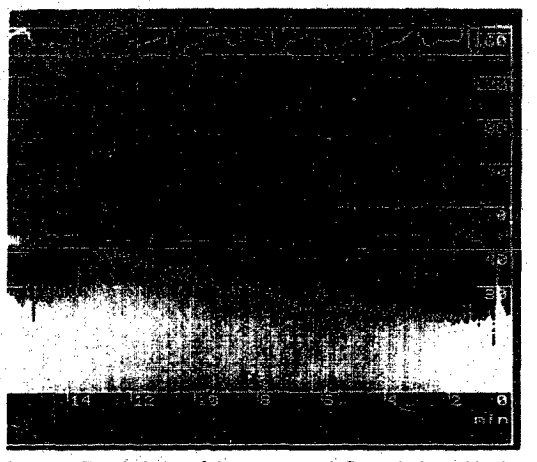

Figure 6. Trend display of the average peak flow velocity within the myocardial bridge. Atrial pacing induces an abrupt increase in flow velocities, with a gradual decline during increasing doses of beta blocker with continuing tachypacing. Asterisks indicate contrast injections inducing a short flow acceleration.

Beta-blocker effect on Doppler flow velocities, electrocardiographic abnormalities and symptoms. Initially, there was a slight drop in the mean arterial blood pressure (from 76 ± 8 mm Hg to 67 ± 4 mm Hg [$p < 0.05$]) after the bolus administration of esmolol, but the pressure returned to baseline values after 5 min despite continuous beta-blocker infusion. All Doppler flow velocities within the myocardial bridge returned to baseline values during beta-blocker medication, despite persistent tachypacing, with a mean heart rate of 134 ± 12 beats/min (Fig. 3 to 6). The mean drop in average peak flow velocity within the myocardial bridge was 39% (from 44.9 ± 15.1 to 27.2 ± 11.7 cm/s [$p < 0.001$]), and 46% for the average diastolic peak flow velocity (from 63.3 ± 21.3 to 34.5 ± 16.4 cm/s [$p < 0.001$]). A similar decrease (42%) occurred for the maximal peak flow velocity (104.8 ± 35.7 vs. 60.5 ± 26.5 cm/s [$p < 0.001$]). There were no significant changes in flow velocities proximal and distal to the bridged segment during beta-blocker medication. With increasing doses of beta-blocker, symptoms vanished in 8 (89%) of 9 patients, and ECG changes normalized in 5 (83%) of 6 patients (Fig. 7). Only one patient reported no improvement at all; the same patient showed no changes in angiographic diameter reduction (86% at baseline and 85% after beta-blocker administration) and only a minimal decrease in Doppler flow velocities (average peak flow velocity at rest 42.8 cm/s, during tachypacing 66 cm/s and with beta-blockade 63 cm/s), despite a maximal beta-blocker dose.

Discussion

The present study demonstrates that intravenous injection of a short-acting beta-blocker (esmolol) during tachypacing in symptomatic patients with severe myocardial bridging leads to a significant reduction in Doppler flow velocities with return to baseline values and normalization of the diastolic/systolic flow velocity ratio within the bridged segments. Coronary angiograms obtained immediately after pacing and beta-blocker administration revealed a more than 25% increase in systolic and especially diastolic lumen diameter within the myocardial bridges. There was also a clear symptomatic improvement in those patients developing angina during pacing and normalization of stress-induced ECG ST segment changes. Myocardial bridges have long been considered as harmless anatomic variants, even though serious cardiac events have been described in association with this angiographic entity in the absence of coronary artery disease (14). The major objective of the present study was to obtain further insight into the ischemic mechanisms and potential therapeutic strategies in myocardial bridges utilizing new miniaturized intracoronary Doppler technology combined with standard quantitative angiography. A series of 15 patients with an angiographically proven myocardial bridge of at least 70% systolic lumen diameter reduction was selected. All patients had a history of chest pain with repeated episodes of hospital admissions owing to unstable symptoms, including three patients with intramural anterior wall myocardial infarctions but with normal global left ventricular function. Based on these inclusion criteria, the present study group is not necessarily a representative selection of the general population of patients with myocardial bridges, in whom the angiographic diagnosis is often completely incidental, but rather may reflect the negative angiographic and symptomatic variants of this entity.

Angiographic findings. The mean degree of systolic lumen diameter reduction obtained by single-plane quantitative coronary angiography was 83%, which is more severe than the

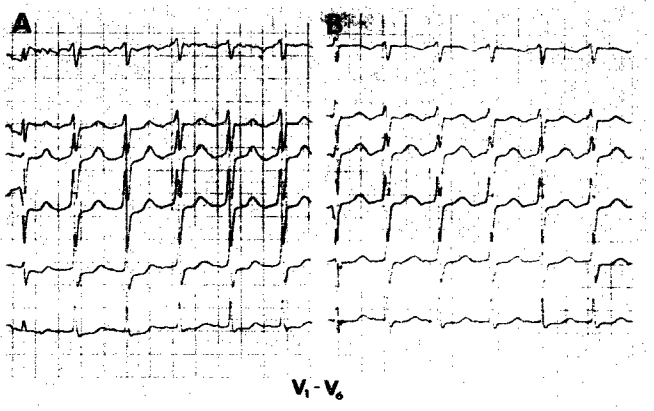

Figure 7. Electrocardiographic tracings from a patient with myocardial bridging of the left anterior descending coronary artery. **A,** During atrial pacing (mean heart rate 140 beats/min), demonstrating ST segment depression (0.1 mV) in leads V_4 to V_6. **B,** Tachypacing with intravenous administration of the beta-blocking agent esmolol and a near-normal electrocardiogram with less ST segment depression.

reductions reported in most previous series (6,26). In addition, there was a persistent diastolic narrowing of 41%, as described previously by Ge et al. (26,31) using intravascular ultrasound in less severe cases of myocardial bridging, most probably caused by a delayed diastolic relaxation within the bridged segment. The length of the myocardial bridge (mean 23 mm) was consistent with data published previously (20).

Intracoronary Doppler flow measurements revealed a significant increase in average peak, diastolic peak and maximal instantaneous peak flow velocities within the myocardial bridge at rest, with only minor changes in systolic flow. Atrial pacing induced a further acceleration in flow velocities within the bridged segment, whereas the flow velocities proximal and distal to the myocardial bridge remained unchanged. A significant increase in the diastolic/systolic flow velocity ratio appears to be the most prominent flow alteration within the myocardial bridge during stress.

Coronary flow reserve. The coronary flow reserve determined proximal to the myocardial bridge was normal or slightly reduced, with a mean ratio of 2.7 (normal >3.0). Measurements distal to the myocardial bridge, however, revealed an impaired flow reserve, with a mean ratio of 2.0. This phenomenon can be explained by the reduced mid- to late diastolic flow velocity, as stated previously by Ge et al. (26). Because of the varying length of the myocardial bridges (27 ± 8 mm), septal perforators and diagonal branches may have originated between the proximal and distal guide wire positions, explaining the higher proximal flow reserve. We disregarded coronary flow reserve measurements within the myocardial bridge because of the elevated basic flow velocity and the often largely distorted flow velocity profile obtained in this position. These findings of reduced coronary flow reserve in the absence of coronary artery disease can be explained by a hemodynamically significant flow obstruction with increased resistance owing to the myocardial bridge, as recently demonstrated by intracoronary pressure recording in a single case with a systolic-diastolic pressure gradient between the proximal and distal segment of the myocardial bridge (32). Another important mechanism, besides systolic vessel compression, is a delayed early and mid-diastolic relaxation with increased diastolic flow velocities, as also shown by Ge et al. (26).

Clinical implications. The occurrence of angina pectoris, myocardial infarctions and arrhythmias in many patients with myocardial bridges may therefore be explained by the reduced ischemic threshold. Therapeutic strategies in symptomatic patients with a myocardial bridge have been extremely diverse, including surgical myotomy (33–37), calcium channel antagonists (38) and beta-blockers (39), mainly because of our poor understanding of the underlying pathophysiologic mechanisms. Nitrates have been used effectively in some of these patients, although it is a well-known phenomenon that acute nitrate application, intracoronarily or sublingually, during coronary angiography increases the angiographic degree of systolic narrowing and should lead to a worsening of symptoms (17,19,40,41). The beneficial effect of nitrates may therefore not be based on vasodilation, but on a reduction in preload and especially antivasospastic capabilities, a mechanism that has been described repeatedly as causing symptoms in myocardial bridges (19,40). Considering the basic mechanism of obstruction, there is also some pathophysiologic rationale for the use of beta-blocking agents, mainly owing to their negative inotropic and chronotropic effects, which should lead to a reduction in external muscular compression and a prolongation of diastolic perfusion intervals. This improvement is attributable to the negative inotropic effect of the beta-blocking agent, with a reduction in maximal systolic and persistent diastolic vessel compression as shown angiographically and a concomitant reduction in coronary flow velocities within the bridged segment. An additional improvement can be expected from the negative chronotropic effect of esmolol, which was masked in our study design owing to continuous atrial pacing. Prolongation of diastole with a reduction in persistent lumen narrowing (18), however, may be an additional pathophysiologic mechanism by which to reduce the hemodynamic influence of myocardial bridging. A recent combined intravascular ultrasound and quantitative coronary angiographic study has shown that

there is only a modest correlation between the two techniques in measuring the degree of systolic/diastolic lumen diameter reduction within the myocardial bridge (26). On the other hand, the Doppler guide wire with a cross-sectional area of 0.16 mm^2 offers the unique opportunity to evaluate flow velocities accurately, even deep within the coronary arteries without flow obstruction by the wire itself (42).

Study limitations. We included a limited number of patients, all of whom had long-standing symptoms and severe systolic vessel compression. Objective signs of ischemia could not be demonstrated in all of our patients. This is a well-known phenomenon in myocardial bridging, most likely because of a large spontaneous variability in clinical symptoms and angiographic severity of lumen obstruction (17). Our results may therefore not be directly extrapolated to a larger population of patients with myocardial bridging. No atherosclerotic lesions were found in these patients angiographically. However, we were not able to exclude small plaque formations only detectable by intravascular ultrasound (26). Tachypacing is a suboptimal type of stress with a minor increase in contractility, blood pressure and cardiac output; more severe effects can be expected from dynamic stress modalities. Coronary flow reserve measurements were not repeated during and after beta-blockade. A systematic evaluation of diameter changes throughout the complete cardiac cycle has not been performed, although the delay in early and mid-diastolic lumen diameter gains may represent the most prominent pathophysiologic mechanism causing the described hemodynamic changes.

Conclusions. Myocardial bridging can cause ischemia and related clinical events if the systolic vessel compression is severe (> 70%) angiographically (6). Blood flow velocity is increased within the bridged segment, especially during tachycardia with concomitant anginal symptoms. Beta-blocking agents given during tachypacing demonstrate the capability to increase the maximal systolic as well as diastolic diameters and to reduce flow velocities to normal, with disappearance of symptoms and ST segment changes in the ECG. Therefore, in patients with myocardial bridging and severe symptoms, intravenous beta-blocker administration appears to be a reasonable therapeutical approach. Further studies are necessary to evaluate the long-term efficacy of beta-blocker therapy.

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