Angiographic Restenosis After Myocardial Bridge Stenting

A Comparative Study With Direct Stenting of *De-Novo* Atherosclerotic Lesions

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SUMMARY

Data on restenosis after stent implantation in myocardial bridges (MB) are very limited. Six-month angiographic results for 12 symptomatic patients who underwent stent implantation for myocardial bridges were compared retrospectively with those of 39 patients who underwent direct stent implantation for *de novo* atherosclerotic lesions in the left anterior descending artery. Diameter stenosis decreased from 69 ± 8% to 4 ± 5% in the MB group and from 79 ± 8% to 7 ± 6% in the control group after stent deployment. Systolic narrowing was abolished in all patients with MB. In follow-up, quantitative angiography revealed late loss of 1.8 ± 1.3 mm in the MB group and 0.9 ± 0.9 mm in the control group (P = 0.025). The in-stent restenosis rate was also higher in the MB group compared to the control group (67% versus 28%; P = 0.037). Despite favorable immediate results, stent implantation in MBs may not be promising because of the higher in-stent restenosis rate compared to stenting in *de novo* atherosclerotic lesions. (Jpn Heart J 2004; 45: 581-589)

Key words: Coronary, Ischemia, Stent, Percutaneous intervention

A myocardial bridge (MB) is an anatomical variation in which a part of a coronary artery (mostly left anterior descending artery (LAD)) courses under a segment of myocardium that compresses the lumen during systole despite a normal appearance during diastole. The reported incidence of MB varies over a wide range according to the method of diagnosis, changing from 0.5 to 2.5% in angiographic studies to 15 to 85% in autopsy series.[1-3] Although known as a benign and asymptomatic condition in a majority of the patients, MBs may cause angina, myocardial ischemia, infarction, life-threatening cardiac arrhythmias, and even sudden cardiac death.[4-8] The clinical management of patients with symptomatic MB is not well established. On the basis of previous pathophysiological and clin-

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ical observations, medical therapy, especially with beta-blockers or calcium channel blockers, is recommended as a first line strategy.[2,9] Intracoronary stent implantation is another therapeutic approach to prevent external systolic compression and ischemia caused by the MBs, but the data related to stent restenosis in MBs are very limited.[10-12] Moreover, comparison of angiographic follow-up results of stenting in MBs with stenting in atherosclerotic lesions has not yet been reported.

In this study, we sought to compare the 6-month angiographic follow-up results of stenting of MBs with those of *de novo* atherosclerotic lesions, especially in terms of restenosis.

METHODS

Study population: Twelve patients who underwent stent implantation for MB between January 2001 and December 2001 in our institute were included in the study. The control group consisted of 39 patients who underwent successful direct stent implantation (without balloon predilatation) for atherosclerotic lesions in the left anterior descending artery in the same period and had a 6-month angiographic follow-up. The data related to both groups were collected retrospectively. Myocardial bridges were documented in the mid-portion of the left anterior descending artery as a result of diagnostic coronary angiography performed for suspected coronary artery disease. All these patients were symptomatic and had a reversible perfusion defect in LAD territory at exercise in Tc-99m sestamibi SPECT test performed either before or after coronary angiography in order to confirm ischemia. In addition, 6 patients had a positive exercise ECG test with ≥ 1 mm horizontal or downsloping ST segment depression in at least two contiguous leads. Patients with total occlusion, Q-wave myocardial infarction (MI) in the previous 6 weeks, previous angioplasty, hemorrhagic disorder, or multiple stents were not included in either group. Successful stent implantation was defined as ≥ 20% reduction in stenosis diameter with a < 50% diameter stenosis and achievement of Thrombolysis in Myocardial Infarction flow grade 3 at the end of the procedure without major coronary adverse events, including in-hospital occurrence of death, Q wave myocardial infarction, or coronary artery by-pass operation. Baseline demographic data and coronary risk factors were noted. All patients in the MB group were unresponsive to beta-blocker and/or calcium channel blocker therapy given by their responsible physicians, from 1 to 5 months before stent implantation. Lack of a response to the treatment was confirmed with ongoing chest pain and observation of MB causing at least 60% stenosis during systole at the time of stent implantation.

Coronary angiography: Coronary angiography was performed by standard Judkins` technique via a femoral artery with a single plane cineangiography system (Coroscop Plus, Siemens, Germany). Quantitative measurements were done from digital images with dedicated software (Quantacor. QCA, Siemens). The reference vessel diameter taken from the adjacent proximal segment, absolute minimum lumen diameter and percent diameter stenosis at the narrowest region of the MB or atherosclerotic lesion were noted. The angiographic severity of a lesion was assessed using two orthogonal views. Restenosis was defined as a > 50% diameter stenosis within the stent in the follow-up angiography.

Stent implantation: Stent selection was left to the discretion of the operator. A slotted tube, flexible Mac Stent (AMG Company, Germany) with high radial force had been used in all of the patients with MB. The stents used in the control group were Antares, InFlow Dynamics, Germany (18 patients); Mac Stent, AMG Company, Germany (14 patients) and BioDivisio, Biocompatibles, UK (7 patients). Monorail systems were used in all stent applications. The decision for stent deployment pressure was made by the operator. In general, an optimal pressure for each stent (6-8 atm) was performed for initial deployment. In case of a suboptimal result, higher pressures were performed with either the stent balloon or a second noncompliant balloon. Lesion length was determined with quantitative methods. In all patients with MB, intracoronary nitroglycerin (100 to 200 μg) was used in order to delineate the true length of the bridged segment.

Adjunctive medication: All patients in both groups received clopidogrel (75 mg once a day) for at least one month and aspirin (300 mg per day) during the follow-up period. Clopidogrel (300 mg) was given at the time of stenting as a loading dose if it had not already been started previously. The patients continued receiving other cardiovascular medications prescribed by their primary physicians.

Follow-up: Standard procedures at our institute dictate that all patients be scheduled to undergo coronary angiography at the end of the 6th month of stent implantation if it had not already been performed until that time because of clinical symptoms or adverse clinical events. Eleven patients in the MB group were interviewed in person or by phone by their primary physician with respect to clinical symptoms between the 2nd and 4th week after stenting. In follow-up angiography, the restenosis type was also noted in patients with angiographic restenosis.

Statistical analysis: Continuous variables are given as the mean (SD). A nonparametric Mann-Whitney U test was performed to determine the differences between mean values for continuous variables whereas Fisher's exact test was used for comparison of dichotomous variables. Probability values less than 0.05 were considered significant. Data were analyzed with SPSS 7.5 for Windows (SPSS Inc, Chicago, Illinois).

RESULTS

Baseline characteristics: Patients in the MB group were younger than those in the control group (48 (8) versus 58 (8), $P = 0.002$). Other baseline patient characteristics and coronary risk factors were comparable between the two groups (Table I).

Stent implantation: All stent implantation procedures were successful in both groups. In 3 patients from the control group, slight elevations in the creatine kinase myocardial band (less than two-fold of the upper normal limit) were detected. Reference vessel diameter (3.1 (0.3) mm in the MB group versus 3.2 (0.4) mm in the control group, $P = 0.5$), stent length (19.7 (4.7) mm in the MB group versus 17.1 (4.7) mm in the control group, $P = 0.08$), stent diameter (3.0 (0.3) mm in the MB group versus 3.1 (0.4) mm in the control group, $P = 0.3$) and maximum inflation pressure (12.1 (2.2) atm in the MB group versus 12.2 (2.0) atm in the control group, $P = 0.94$) were not different between the groups. All patients in the MB group were examined in terms of stent deformity just after stent deployment and 15 to 30 minutes after the procedure and no stent crash due to external mechanical compression was detected (Figure). Minimal lumen diameter and percent stenosis before and after the stent implantation are shown in Table II.

Clinical follow-up: During the clinical follow-up between the 2nd and 4th week after stent implantation, all of the MB group patients interviewed described an improvement in their symptoms. Although 2 patients in this group had atypical symptoms, they were evaluated by treadmill exercise ECG testing and both were negative for ischemic changes. During further follow-up, 7 MB group patients underwent coronary angiography before the 6th month: Two for non-ST elevation MI, 3 for typical angina, and 2 for atypical angina. The remaining 5 patients were asymptomatic until the end of the 6th month.

Table I. Baseline Characteristics and Coronary Risk Factors

	Myocardial bridge group ($n = 12$)	Control group ($n = 39$)	*P*
Male (%)	8 (67%)	24 (61%)	NS
Diabetes mellitus (%)	2 (17%)	10 (26%)	NS
Cholesterol elevation (%)	3 (25%)	20 (51%)	NS
Smoking (%)	8 (67%)	22 (56%)	NS
Hypertension (%)	5 (42 %)	19 (49%)	NS
Family history (%)	4 (33%)	12 (31%)	NS

NS = not significant

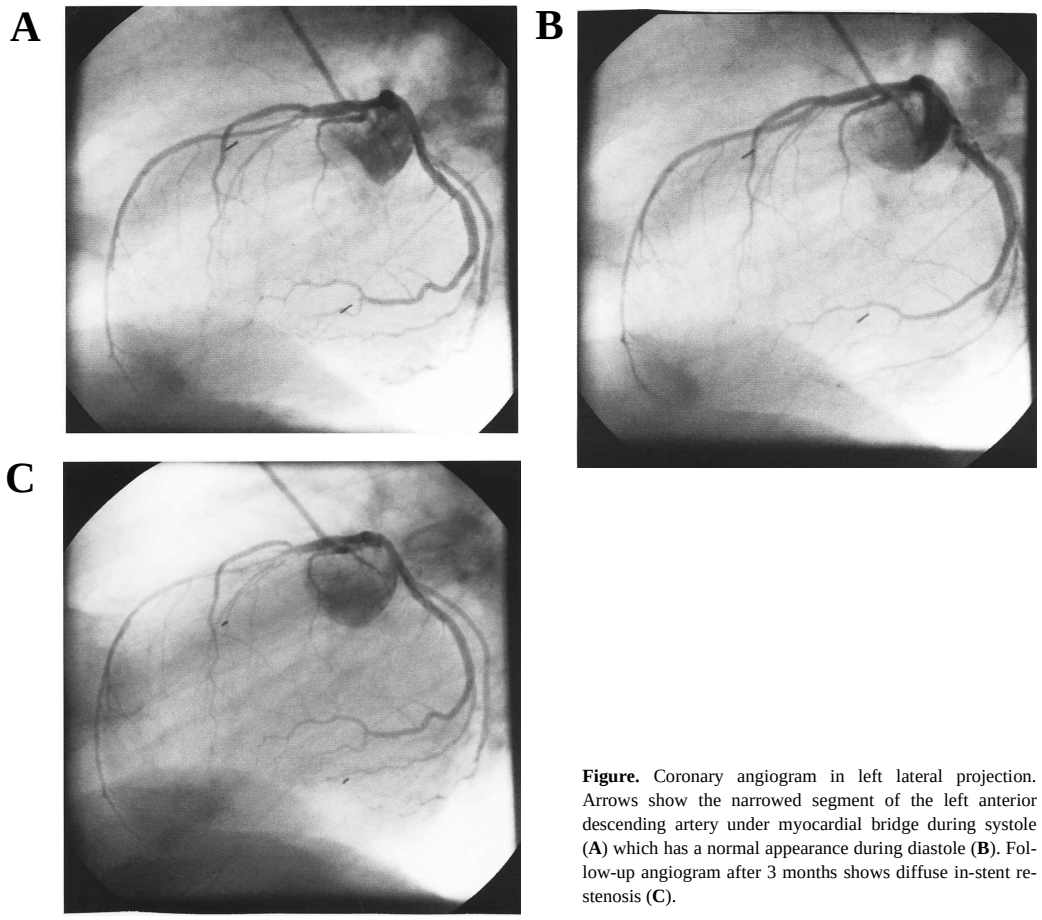

Figure. Coronary angiogram in left lateral projection. Arrows show the narrowed segment of the left anterior descending artery under myocardial bridge during systole (**A**) which has a normal appearance during diastole (**B**). Follow-up angiogram after 3 months shows diffuse in-stent restenosis (**C**).

Table II. Results of Angiographic Analysis

	Myocardial bridge group (n = 12)	Control group (n = 39)	P
Baseline			
MLD before stent (mm)	0.9 (0.3)	0.7 (0.3)	0.004
Stenosis before stent (%)	69 (8)	79 (8)	0.001
Stenosis after stent (%)	4 (5)	7 (6)	0.117
Follow-up			
MLD (mm)	1.2 (1.3)	2.1 (1.0)	0.032
Late loss (mm)	1.8 (1.3)	0.9 (0.9)	0.025
Stenosis (%)	62 (40)	34 (31)	0.028

Values are given as mean (SD). MLD = minimal lumen diameter.

Follow-up angiography: The duration from stent implantation to follow-up angiography in the MB and control groups was 4.6 (1.8) months and 5.6 (1.2) months, respectively ($P = 0.07$). Minimal lumen diameter, percent stenosis, and the late loss values are presented in Table II. Stent restenosis was higher in the MB group (8 of 12 patients (67%)) compared to the control group (11 of 39 patients (28%)) ($P = 0.037$). Moreover, the type of stent restenosis was also different since it tended to be proliferative in the MB group ($P = 0.03$) (Figure). According to the classification of Mehran, *et al*,[13] stent restenosis was type II (intra-stent) in 2 (25%) and type III (proliferative) in 6 (75%) of the MB group patients and was type I (focal) in 4 (36%), type II in 5 (45%), and type III in 2 (18%) of the control group patients. After follow-up angiography, 5 patients in the MB group and 2 patients in the control group underwent coronary by-pass surgery while 3 patients in the MB group and 9 patients in the control group underwent repeat PTCA.

DISCUSSION

The results of this study indicate that, despite the favorable immediate result of prompt relief of luminal narrowing, the angiographic restenosis rate after the stenting of MBs is higher than that of the stenting of *de novo* atherosclerotic lesions.

It is well known that MBs may result in ischemia by causing phasic lumen compression. Until recently, coronary narrowing under an MB was interpreted to occur only in systole and believed unlikely to cause ischemia.[2] However, studies on the pathophysiology of the MBs showed that this narrowing may extend into diastole.[14,15] It was also reported that tachycardia may decrease myocardial perfusion in patients with an MB by increasing the systolic-diastolic time ratio at the expense of diastolic flow.[8] A decrease in coronary flow reserve was also reported distal to the bridged segment.[9,11,15] Therefore, abolishing securing the lumen diameter by stenting seems to be a reasonable method with which to prevent ischemia in a patient with MB. This approach was first performed by Stables, *et al*.[16] They reported a successful outcome with achievement of internal stabilization of the coronary artery lumen against external compression. Klues, *et al*[11] reported 3 symptomatic patients due to MB in whom stent deployment was performed. They found normalization of intracoronary Doppler parameters, including coronary flow reserve and the prevention of systolic compression. The findings were reproduced after 7 weeks in all of the patients with clinical improvement as well. A small number of other cases with successful short term results have also been reported.[17,18] In 11 patients with symptomatic MB, Haager, *et al*[10] found a good immediate angiographic outcome with an increase in mini-

mal lumen diameter from 0.6 mm to 1.9 mm ($P < 0.005$) and normalization of coronary flow reserve from 2.6 to 4.0 ($P < 0.005$) after stenting the coronary segment under the bridge. However, 5 of these 11 patients (46%) had in-stent restenosis at 7 weeks. The authors concluded that this rate of in-stent restenosis was comparable to that of atherosclerotic lesions that have similar features. On the other hand, no study comparing the rate of angiographic restenosis between these two entities has been reported. It is clear that the restenosis data from stent implantation in atherosclerotic lesions are not relevant to stent implantation in myocardial bridges since the pathology of the coronary wall, mechanical forces within the vessel wall, and coronary flow characteristics should be different.

In the present study, stent implantation abolished the vessel compression caused by MB immediately after deployment. In addition, the improvement in anginal symptoms in all patients early after stenting supports the favorable short-term success of stenting in MBs, a finding consistent with those of previous studies. Unfortunately, this success did not persist with a high angiographic in-stent restenosis rate compared to the control group during 6-month follow-up. Interestingly, the type of in-stent restenosis was proliferative in 6 of the patients in the MB group with a tendency of spreading to the distal, but not to the proximal, segments.

The vessel segments under the MB have been shown to be free from atherosclerosis in different studies.[19-21] It is not clear how much the underlying atherosclerotic plaques contribute to in-stent restenosis, but both the deep injury and the vessel stretch were shown to trigger the development of in-stent neointima in even normal coronary arteries.[22] Although maximum deployment pressures were not different between the two groups, an additional external force on the vessel wall might have caused a deeper injury in the MB group. Furthermore, the persistence of external compression in MB constitutes an important difference between two groups. Although no stent crash was detected in any of the patients in follow-up angiographies, it may be assumed that the vessel wall between the deployed stent and the myocardial band was being squeezed with each contraction. This “sandwich effect” might have contributed to the high rate of restenosis by inducing neointimal proliferation. It may also be speculated that vasoactive substances released by compression of the vessel wall between the expanded stent and the contracting muscle might also have played a role in in-stent restenosis. This may explain, at least in part, the result that restenosis had spread to the distal portion but not the proximal portion of the stent in some of the patients. It is also not clear to what extent the type and design of the stent used for MBs in the present study contributed to the high rate of in-stent restenosis. A slotted tubular stent with a strong radial force to resist external compression without being crushed has been assumed to be a “good choice” for MBs.[10] Although the stent choice was at the

discretion of the operator, Mac Stents were used in all of the patients with MB. This tendency may be explained by the fact that the Mac Stent is one of the stents available at our institute that has a high radial force. Lack of stent crush at follow up in any of the patients supported that this stent type was a proper choice, at least in the short term. Other "classical" variables related to the patient and the procedures that are well known to promote in-stent restenosis in coronary artery disease were comparable between the two groups.

Study limitations: First, this is a retrospective study in which the management of the patients was at the discretion of the operator. Second, the same type of stent was used in all of the patients with MB. It is not clear whether the in-stent restenosis rate would have been high again if stents of a different type and design had been used. Although this fact may have influenced the results of the group comparison, the high restenosis rate in the MB group was unacceptable in any case. Third, the small number of patients is another limitation that makes the results of this study difficult to generalize. On the other hand, this is relatively one of the largest studies and the only comparative study of its kind in the literature.

In this retrospective study, stent implantation in MBs resulted in higher in-stent restenosis compared to direct stenting in *de novo* atherosclerotic lesions. Moreover, the dominantly proliferative nature of in-stent restenosis made a second percutaneous intervention undesirable. Larger and controlled studies with different stent types, including drug-eluting stents, are needed. With the available data, including our experience, medical therapy should be the first strategy in the management of symptomatic patients with MB who have positive noninvasive stress test results. Until more data become available, physicians should perhaps "think twice" before using stents for MBs.

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