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Influence of Diabetes Mellitus on Left Ventricular Function in Patients Undergoing Coronary Artery Bypass Grafting

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Abstract

Objectives. Left ventricular function was assessed by two-dimensional echocardiography before and one year after coronary artery bypass grafting(CABG)in a series of patients with severe coronary artery disease with diabetes mellitus(DM)and without DM(non-DM).

Methods. Twenty-three patients with DM and 50 patients without DM, all with no previous myocardial infarction, underwent two-dimensional echocardiography before CABG and one year after CABG, in a non-matched study. For a matched study, 31 patients without DM who had almost the same left ventricular function as DM patients at the baseline were selected to and compare the rate of improvement in left ventricular function between the DM group and the " matched " non-DM group.

Results. In the non-matched study, patient characteristics were not significantly different between the 2 groups except for the incidence of congestive heart failure within one year before CABG, which was significantly higher in the DM group. Fractional shortening was significantly lower in the DM group at the baseline($p < 0.05$)and also one year after CABG($p < 0.0001$). Significant improvement in fractional shortening was seen in the non-DM group($p < 0.001$), but not in the DM group. The left ventricular end-diastolic diameter(LVDd)was significantly larger in the DM group at the baseline($p < 0.01$), and was still significantly larger in the DM group at one year after CABG($p < 0.01$). No improvement in LVDd was seen in the DM group. In the matched study, fractional shortening of the non-DM group also showed significant improvement after CABG($p < 0.001$). Moreover, the rate of improvement in fractional shortening was higher in the non-DM group than in the DM group($p < 0.05$). LVDd tended to be larger in the DM group($p =$ NS).

Conclusions. Left ventricular dysfunction and left ventricular impaired improvement were seen in the patients with DM, and CABG improved left ventricular function in the patients without DM with poor left ventricular function. These findings indicate that CABG therapy may be inadequate for improving left ventricular function in patients with DM and severe left ventricular dysfunction at the baseline.

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Key Words

■**Coronary artery disease** ■**Aortocoronary bypass(coronary artery bypass grafting)**
■**Ventricular function** ■**Diabetes mellitus** ■**Echocardiography**

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INTRODUCTION

Diabetes mellitus(DM)is a well-established risk factor for coronary artery disease[1], and diabetes with coronary artery disease is associated with high rates of complications and mortality[2]. Although diabetic patients treated by coronary artery bypass grafting(CABG)have a lower mortality than those treated by percutaneous transluminal coronary angioplasty or medical therapy[3,4], diabetic CABG patients have a lower long-term survival rate than non-diabetic CABG patients[5]. Advanced left ventricular dysfunction before CABG carries a poor long-term prognosis following CABG[6]. Left ventricular function may already be poorer in diabetic CABG candidate patients than in non-diabetic patients. Left ventricular function in diabetic patients is lower than that in non-diabetic patients after myocardial infarction[7,8], but little is known about left ventricular function in diabetic coronary artery disease patients without previous myocadial infarction. CABG improves left ventricular function in patients without previous myocardial infarction[9], but the influence of diabetes on improvement in left ventricular function after CABG is not well-defined.

This study compared left ventricular function assessed by two-dimensional echocardiography in a series of diabetic and non-diabetic severe coronary artery disease patients without previous myocardial infarction before and one year after CABG.

METHODS

Patient population

Seventy-three of 305 patients, who were treated by CABG in our hospital between June 1994 and September 1998, underwent two-dimensional echocardiography before and one year after CABG. Patients were excluded if they had any of the following: previous myocardial infarction, valvular heart disease, hypertrophic cardiomyopathy, severe lung disease, a pacemaker implant, or left bundle-branch block. Myocardial infarction was diagnosed by one or more of the following features: abnormal Q wave on electrocardiography, compatible clinical history including severe chest pain continuing for several hours, elevation of specific diagnostic enzymes, regional severe hypokinesia, akinesia, or dyskinesia according to two-dimensional echocardiography. Consequently, the patient population consisted of 73 coronary artery disease patients selected for CABG(62 males, 11 females)aged from 34 to 81 years old.

Patients were divided into the DM group and non-DM group. Patients were included in the DM group if they were being actively treated with either insulin or a hypoglycemic agent during their hospitalization for CABG. Diet-controlled DM was included if the fasting blood glucose was above 140 mg/d*l* or the random blood glucose was above 200 mg/d*l*. Patients with impaired glucose tolerance were included in the non-DM group. As a result, 23 DM patients(18 males, 5 females)and 50 non-DM patients(44 males, 6 females)were recruited. In the DM group, 7 patients were treated with insulin therapy(30.4%)and 8 with drug therapy(34.8%). This study was a non-matched study. For a matched study, we selected 31 non-DM patients(27 males, 4 females)in the non-DM group who had almost the same left ventricular function as DM patients at the baseline and compared the rate of improvement in left ventricular function between the DM group and the "matched" non-DM group.

Echocardiographic study

Two-dimensional echocardiography was performed on all patients before CABG(at the baseline)and one year after CABG. All patients had no symptom of heart failure at that time. An Aloka ultrasound system with 2.5- and 3.5-MHz probes was used. A parasternal mid-papillary short-axis view of the left ventricle was obtained to measure the left ventricular end-diastolic diameter(LVDd)and left ventricular end-systolic diameter(LVDs), and calculate the fractional shortening(FS). Images were stored on a videotape recorder for further analysis.

Statistical analysis

Results are expressed as mean $\pm$ standard deviation. The paired *t*-test was used for within-group comparisons. Comparisons between groups used the unpaired *t*-test and the chi-squared test. Statistical significance was accepted at the $p < 0.05$ level.

RESULTS

Patient characteristics

The baseline patient characteristics in the non-matched study are summarized in **Table 1**. There were no significant differences in age, gender, or number of vessels. The incidence of hyperlipi-

Table 1 Baseline characteristics in the non-matched study

	DM group	Non-DM group	*p* value
No. of patients	23	50	
Male/female	18/5	44/6	NS
Age(yr)	63.1±9.0	64.1±9.0	NS
No. of vessels			
1	0	4(8.0)	
2	6(26.1)	17(34.0)	
3	17(73.9)	29(58.0)	
Mean	2.74±0.4	2.50±0.6	NS
Hypertension	13(56.5)	37(74.0)	NS
Hyperlipidemia	11(47.8)	33(66.0)	NS
Smoking	15(65.2)	32(66.0)	NS
Pre CHF	6(26.1)	2(4.0)	<0.01
Post CHF	0	0	NS
No. of bypass grafts	75	154	
No. of grafts per patient	3.26±0.9	3.08±1.1	NS
No. of artery grafts	19(25.3)	47(30.5)	NS
Bypass patency	74(98.7)	151(98.1)	NS
Perioperative MI	0	1(2.0)	NS
Complete revascularization	20(87.0)	47(84.0)	NS
Drug therapy at baseline			
Vasodilator	23(100.0)	50(100.0)	NS
Diuretics	7(30.4)	10(20.0)	NS
ACE-I	6(26.1)	5(10.0)	<0.08
β-blocker	3(13.0)	11(22.0)	NS
Drug therapy after CABG			
Vasodilator	23(100.0)	50(100.0)	NS
Diuretics	1(4.3)	3(6.0)	NS
ACE-I	2(8.7)	1(2.0)	NS
β-blocker	2(8.7)	3(6.0)	NS

Continuous values are mean±SD. ( ): %.
DM=diabetes mellitus; Pre CHF=congestive heart failure within one year before CABG; Post CHF=congestive heart failure within one year after CABG; MI=myocardial infarction; ACE-I=angiotensin converting enzyme inhibitor; CABG=coronary artery bypass grafting.

demia, hypertension, and smoking were similar in both groups. The incidence of congestive heart failure(New York Heart Association functional class Ⅳ)within one year before CABG was higher in the DM group($p < 0.01$), but similar in both groups at one year after CABG. The incidence of congestive heart failure in the DM group significantly decreased(baseline to one year follow-up after CABG, 26.1% to 0.0%, $p < 0.01$). Number of grafts was not different. The rate of complete revascularization, artery graft use and bypass graft patency were similar in both groups. Only one patient in the non-DM group had perioperative myocardial infarction. The rates of treatment with vasodilator, diuretics and β-blocking agents were similar in both groups before and after CABG. Angiotensin converting enzyme(ACE)inhibitor therapy tended to be used more often at the baseline in the DM group($p < 0.08$), but there was no significant difference between the 2 groups after CABG. The baseline patient characteristics in the matched study are summarized in **Table 2**. No significant difference was seen between the 2 groups except in the incidence of congestive heart failure before CABG.

Table 2 Baseline characteristics in the matched study

	DM group	Non-DM group	*p* value
No. of patients	23	31	
Male/female	18/5	27/4	NS
Age (yr)	63.1±9.0	63.5±10.6	NS
No. of vessels (mean)	2.74±0.4	2.58±0.6	NS
Hypertension	13(56.5)	21(67.7)	NS
Hyperlipidemia	11(47.8)	11(35.5)	NS
Smoking	15(65.2)	21(67.7)	NS
Pre CHF	6(34.8)	2(6.5)	<0.05
Post CHF	0	0	NS
No. of grafts per patient	3.26±0.9	3.16±1.0	NS
ACE-I before CABG	6(34.8)	3(9.7)	NS
ACE-I after CABG	2(8.7)	0(0.0)	NS

Continuous values are mean±SD. ( ) : %.
Abbreviations as in Table 1.

Left ventricular function and dimension

Comparisons between the DM group and the non-DM group in the non-matched study for LVDd, LVDs, and FS are shown in **Fig. 1**. FS at the baseline was significantly lower in the DM group than in the non-DM group (FS in the DM group vs the non-DM group at the baseline, 22.8 ± 8.2% vs 27.7 ± 8.3%, $p < 0.05$), and FS was also significantly lower in the DM group than in the non-DM group one year after CABG (FS in the DM group vs the non-DM group at one year after CABG, 23.3 ± 7.6% vs 32.1 ± 7.8%, $p < 0.0001$). Significant improvement in FS was seen in the non-DM group ($p < 0.001$), but not in the DM group. At the baseline, both LVDd and LVDs were significantly larger in the DM group than in the non-DM group (LVDd in the DM group vs the non-DM group at the baseline, 51.6 ± 9.5 vs 45.9 ± 6.9 mm, $p < 0.01$; LVDs in the DM group vs the non-DM group at the baseline, 40.3 ± 10.1 vs 33.6 ± 7.5 mm, $p < 0.01$). Also, one year after CABG, LVDd and LVDs were still significantly larger in the DM group than in the non-DM group (LVDd in the DM group vs the non-DM group at one year after CABG, 51.1 ± 9.7 vs 45.4 ± 6.4 mm, $p < 0.01$; LVDs in the DM group vs the non-DM group one year after CABG, 39.5 ± 10.6 vs 31.1 ± 7.2 mm, $p < 0.001$).

Comparison between the 2 groups in the matched study for FS is shown in **Fig. 2**. FS was similar in both groups at the baseline (FS in the DM group vs the non-DM group, 22.8 ± 8.2% vs 22.6 ± 5.3%, p = NS). LVDd tended to be larger in the DM group (LVDd in the DM group vs the non-DM group at the baseline, 51.6 ± 9.5 vs 48.3 ± 6.6 mm, $p = 0.14$). At one year after CABG, FS was significantly higher in the non-DM group than in the DM group (FS in the DM group vs the non-DM group one year after CABG, 23.3 ± 7.6% vs 29.3 ± 8.4%, $p < 0.01$). Significant improvement was seen in the non-DM group ($p < 0.001$). Comparison between 2 groups for ΔFS, the rate of the improvement in FS, is shown in **Fig. 3.** ΔFS was significantly higher in the non-DM group than in the DM group (ΔFS in the non-DM group vs in the DM group, 36.0 ± 47.2% vs 7.8 ± 37.3%, $p < 0.05$).

DISCUSSION

The major findings in our non-matched study were that diabetic patients had lower left ventricular function than non-diabetic patients at baseline and showed no significant improvement in left ventricular function at one year after CABG, whereas non-diabetic patients experienced significant improvement. Diabetics have more silent ischemia complicated by autonomic neuropathy[10], and so their coronary heart disease is often only identified when their condition has became serious, *e.g.*, after congestive heart failure has developed. This may be the cause of poorer left ventricular function in diabetic patients than non-diabetic patients at baseline before CABG. In the non-matched study, the

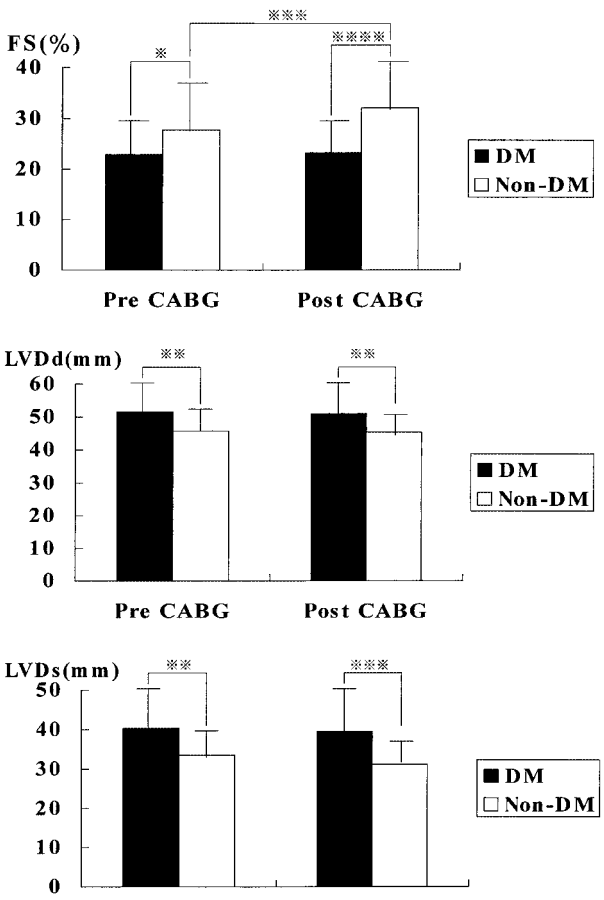

Fig. 1 Comparison of fractional shortening(FS; *upper*), left ventricular end-diastolic diameter (LVDd; *middle*)and left ventricular end-systolic diameter(LVDs; *lower*)between the 2 groups in the non-matched study
※$p < 0.05$, ※※$p < 0.01$, ※※※$p < 0.001$, ※※※※$p < 0.0001$.
Other abbreviations as in Table 1.

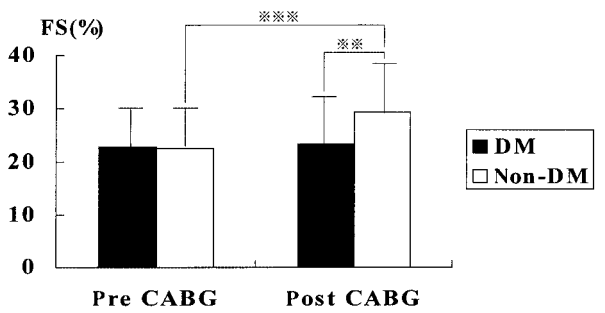

Fig. 2 Comparison of FS between the 2 groups in the matched study
※※$p < 0.01$, ※※※$p < 0.001$.
Abbreviations as in Table 1, Fig. 1.

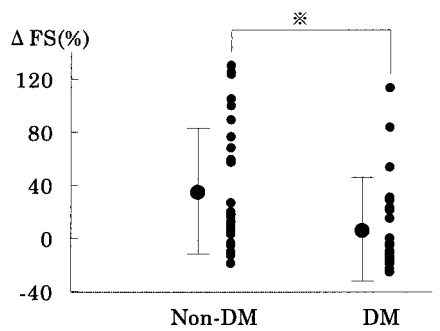

Fig. 3 Comparison of the rate of improvement of FS (ΔFS) between the DM group and the matched non-DM group
ΔFS was calculated as (FS at one year after CABG − FS at baseline)/FS at baseline × 100.
※$p < 0.05$.
Abbreviations as in Table 1, Fig. 1.

degree of left ventricular function before CABG could be influential in the improvement in left ventricular function after CABG. However, the matched study showed that non-diabetic patients with poor left ventricular function experienced significant improvement after CABG. We could identify the influence of DM on the improvement in left ventricular function after CABG. Diabetic patients may have more diffuse and severer coronary artery disease than non-diabetic patients[11,12] and they may have microvascular disease[13], which may be the cause of the lesser improvement in left ventricular function.

Other left ventricular dysfunction factors in diabetes mellitus

Coronary artery disease may be part of the cause of poor left ventricular function and lack of improvement seen after CABG in patients with DM. The cause of the accelerated left ventricular dysfunction may be multifactorial. Myocardial cell dysfunction independent of significant coronary artery disease has been reported in patients with DM, and is referred to as "diabetic cardiomyopathy"[14–16]. Many pathology studies in humans with DM have been reported.

Rubler *et al*.[17] noted substantial myocardial hypertrophy and fibrosis in diabetic subjects without significant coronary atherosclerosis. Increased thickening of the myocardial capillary basement membranes, microaneurysms, and interstitial infiltration with PAS positive material have also been

reported[18,19], and microvascular damage may be part of diabetic cardiomyopathy. Mosseri *et al*.[20] reported that diabetics have small-vessel disease without epicardial coronary atherosclerosis. What is worse, diabetics have microcirculatory abnormalities, decreased coronary flow reserve, and impaired coronary vasodilation[21,22]. These myocardial changes may contribute to decreased improvement in left ventricular function in diabetics. Hess *et al*.[23]have demonstrated structural alterations of the myocardium in the ischemic region from left ventricular transmural biopsy samples obtained during open heart surgery.

We could not carry out myocardial biopsies during bypass surgery, so histopathological changes in our patients were not identified. Diabetic patients with severe coronary artery disease may have both ischemic cardiomyopathy and diabetic cardiomyopathy. Consequently, left ventricular function in these patients may be lower and no improvement may be seen after CABG. However, the incidence of heart failure decreased significantly after CABG, which is of benefit to diabetic patients and might mean lower mortality and improvement in the long-term outcome. Since diabetics have from more than twice to five-fold the incidence of heart failure of non-diabetic patients, CABG is an important therapy[24]. Although several investigators[21,22] have reported that the coronary flow reserve was lower in diabetics than in non-diabetics, CABG has been reported to increase the coronary flow reserve[25]. Therefore, coronary flow reserve probably increases after CABG in diabetics as well. This may be related to the decrease in the incidence of heart failure after CABG.

Left ventricular dilation

Structural increase in left ventricular volume is an important consequence of left ventricular dysfunction to generate a normal stroke volume. Iwasaka *et al*.[26]have reported that left ventricular volume increases more after acute myocardial infarction in diabetic patients than in non-DM patients. However, whether diabetic patients with severe coronary artery disease without previous myocardial infarction experience a greater increase in left ventricular volume than non-diabetic patients is unclear. Although we observed left ventricular dilation in diabetic patients in the non-matched study, poorer left ventricular function was seen in the DM group, which might be influential in left ventricular dilation. In the matched study, we could not clarify the influence of DM on left ventricular dilation. Therefore we cannot conclude whether DM is influential in left ventricular dilation. We also found that left ventricular dilation was not improved after CABG in both groups. This result was consistent with previous reports[27,28].

Study limitations

Our study has several limitations. First, our study included all diabetic patients receiving insulin therapy, hypoglycemic agent therapy, or diet therapy, and the duration of DM varied. Poor blood glucose control and long duration of DM are associated with cardiovascular disease and poor outcome[29].

Second, the Simpson method is often used to measure left ventricular function echocardiographically. In our study, left ventricular function was assessed by FS, because we were unable to obtain images to measure left ventricular function in the apical two-chamber views in many patients after CABG, probably because of adhesion of the pericardium, and thus our data may be less accurate.

Third, we could not confirm the usefulness of ACE inhibitor therapy. In our study, the decision to administer ACE inhibitor therapy was left to the individual physician, and the result was that ACE inhibitor therapy tended to be used more often at the baseline in the DM group. However, this therapy was discontinued in some diabetic patients with poor left ventricular function after CABG. The individual physician is likely to expect too great an improvement in left ventricular function after CABG. Several studies have reported that ACE inhibitor treatment of diabetic patients with left ventricular dysfunction is associated with decreased mortality and inhibition of left ventricular remodeling[30−32]. This may affect follow-up measures for left ventricular function in the DM group. A prospective double-blind study is needed to clarify the effect of ACE inhibitors. However, some patients with poor left ventricular function received ACE inhibitor therapy at the baseline (6 DM patients and 3 non-DM patients). Division of our patients into 2 groups, those with continued ACE inhibitor therapy and those with discontinued ACE inhibitor therapy after CABG, showed the improvement in left ventricular function was not significantly different in our study.

Fourth, our study was retrospective, so we could not recruit consecutive patients because we could

not carry out echocardiographic studies one year after CABG in several patients.

Fifth, the population was rather small, so DM patients with poor left ventricular function might have been recruited in our study. Further study is needed to evaluate left ventricular function and improvement in diabetics.

CONCLUSIONS

Left ventricular function was evaluated in diabetic patients with severe coronary artery disease. DM patients showed poor left ventricular function at the baseline, and no improvement was seen after CABG, whereas non-DM patients with left ventricular dysfunction showed adequate improvement after CABG. These findings indicate that CABG therapy may be inadequate for improving left ventricular function in DM patients with poor left ventricular function at the baseline.

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要　　約

冠動脈バイパス術前後における左室機能に対する糖尿病の影響

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目　的: 冠動脈バイパス術(CABG)適応となった心筋梗塞の既往のない重症冠動脈疾患患者に対し，CABG前後の左室心機能，心機能改善度に与える糖尿病の影響について心エコー図検査法を用いて検討した．

方　法: 対象は，待機的にCABGを施行した糖尿病患者23例と非糖尿病患者50例である．方法は，CABG前と術後約1年目に心エコー図検査を施行し，左室拡張末期径と左室収縮末期径を計測し，そこから左室短縮率を求めた．これらを患者背景とともに2群間で比較検討するとともに，糖尿病患者と術前左室短縮率をマッチングさせた非糖尿病患者31例において，術前心機能が術後心機能に及ぼす影響を取り除き，術後の左室短縮率改善度について2群間での比較検討も行った．

結　果: 患者背景は術前1年以内の心不全の既往が有意に糖尿病群で多くみられた以外，2群間に差は認められなかった．左室短縮率は術前で糖尿病群で有意に低下していた($p < 0.05$)．また，術後1年目においても有意に低下していた($p < 0.0001$)．左室短縮率は術後非糖尿病群で有意に上昇したが($p < 0.001$)，糖尿病群での有意な上昇はみられなかった．CABG前の左室拡張末期径は非糖尿病群に比べて糖尿病群で有意に拡大しており($p < 0.01$)，術後も同様であった($p < 0.01$)．2群間の術前左室短縮率をマッチングさせた場合，CABGによって非糖尿病患者では有意に左室短縮率の改善をみた($p < 0.001$)．左室短縮率の改善度は非糖尿病群で有意に大きかった($p < 0.05$)．左室拡張末期径は糖尿病群で拡大傾向があるものの，有意差はみられなかった．

結　論: 重症冠動脈疾患を持つ糖尿病患者では，非糖尿病患者に比較して心機能の低下がみられた．低心機能でもCABGによって非糖尿病患者の心機能は改善したが，糖尿病患者にはみられなかった．左室心機能の低下がみられる糖尿病患者にCABGを行った場合，左室機能をCABGのみで改善させることは困難であった．

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