

## Comparison of Long-term Efficacy of Medical Treatment versus Coronary Artery Bypass Grafting (CABG) in Multivessel Coronary Artery Disease

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### SUMMARY

The long-term results of medical therapy and coronary artery bypass grafting (CABG) were compared in patients with multivessel disease. All patients were confirmed to have  $\geq 75\%$  luminal narrowing of major coronary arteries by coronary arteriogram. When multivessel disease was stratified into double- and triple- vessel disease, the outcomes varied. In triple-vessel disease, the outcome with CABG was good, but the outcome was unfavorable in those employing medical therapy, particularly in patients with decreased left ventricular (LV) function. In patients with double-vessel disease with good LV function, the long-term results with medical therapy were just as favorable as those with CABG. However, double-vessel disease complicated by reduced LV function (ejection fraction  $\leq 40\%$ ) had a clearly less favorable outcome when treated with medical therapy than with CABG. Thus, it is important for patients with multivessel disease to undergo revascularization if indicated, to improve their prognosis. On the other hand, the incidence of cardiac events arising from vein graft occlusions tended to increase in CABG patients after 5 years or more following surgery. (Jpn Heart J **36**: 709-717, 1995)

**Key words:** Multivessel disease    Double-vessel disease    Triple-vessel disease    Long-term prognosis    Poor LV function    Medical treatment CABG

**A**T present, coronary artery disease is mainly approached with interventional therapy including percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass grafting (CABG). Their short-

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term effectiveness has already been demonstrated.<sup>1,2)</sup> However, from the long-term point of view, problems remain; the rate of restenosis with PTCA is high and effective countermeasures have yet to be established,<sup>2)</sup> and the incidence of cardiac events due to vein graft occlusion increases in CABG patients.<sup>3)</sup> Several large-scale studies of PTCA versus CABG for multivessel disease are now in progress in Europe and the United States<sup>4,5)</sup> but no conclusions are available. In the present study, we stratified multivessel disease into double- and triple-vessel disease, and the long-term results of medical therapy and CABG, performed in our hospital, were compared for each disease.

### SUBJECTS AND METHODS

**Subjects:** The subjects consisted of patients with double- or triple- vessel disease whose coronary arteriograms showed significant stenosis ( $\geq 75\%$ ) of their major coronary arteries. Patients with left main trunk lesions, those undergoing thrombolytic therapy, and those with previous CABG were excluded. Patients were enrolled between September 1973 and February 1984 for the medical therapy group and between April 1982 and December 1993 for the CABG group, and final confirmation was made on August 31, 1990 and March 31, 1994, respectively. Follow-up rates were 90.1% and 97.8%, respectively, and follow-up periods were  $9.3 \pm 3.8$  years and  $6.1 \pm 3.3$  years. Patient characteristics are shown in the Table.

**Methods:** A questionnaire was administered by telephone or mail to obtain the following follow-up information. After having confirmed that the patient was alive, inquiries were made concerning the details of the treatment performed to date, the presence of complications such as myocardial infarction and heart failure, and the date of the occurrence of any such complications. If the patient had died, the cause and date of death were determined. Nonfatal cardiac events were defined as: the development of acute myocardial infarction (AMI) and congestive heart failure (CHF) as well as histories of PTCA and CABG during the follow-up period. Any deaths within the first one month of AMI were considered as cardiac

**Table.** Patient Characteristics

	DVD		TVD	
	Medical	CABG	Medical	CABG
Number of patients	220	200	198	567
M/F	203/17	173/27	178/20	487/80
Age (years)	$55.7 \pm 7.5$	$57.6 \pm 8.9$	$56.3 \pm 8.7$	$59.1 \pm 8.8$
Prior MI (%)	59.5	48.5	69.2	64.7

DVD = double vessel disease; TVD = triple vessel disease, MI = myocardial infarction

deaths, not as nonfatal cardiac events.

Left ventricular ejection fraction (LVEF) was obtained from left ventricular angiograms using Kennedy's formula.

Kaplan-Meier survival curves were prepared using cardiac death. Death from noncardiac causes and patients who received PTCA and CABG during the follow-up period were handled as being dropouts at the time of occurrence.

The generalized Wilcoxon test was used to determine the significance of the difference between the survival curves.

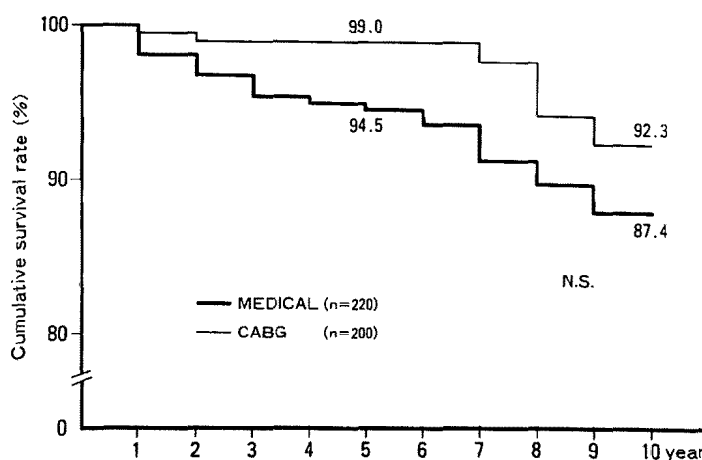
## RESULTS

**Cumulative survival curves for double-vessel disease (Figure 1):** The 5- and 10-year survival rates were 94.5% and 87.4%, respectively, for 220 patients treated medically and 99.0% and 92.3%, respectively, for 200 patients with CABG. There were no significant differences between the groups, and medical therapy was also associated with a good long-term outcome.

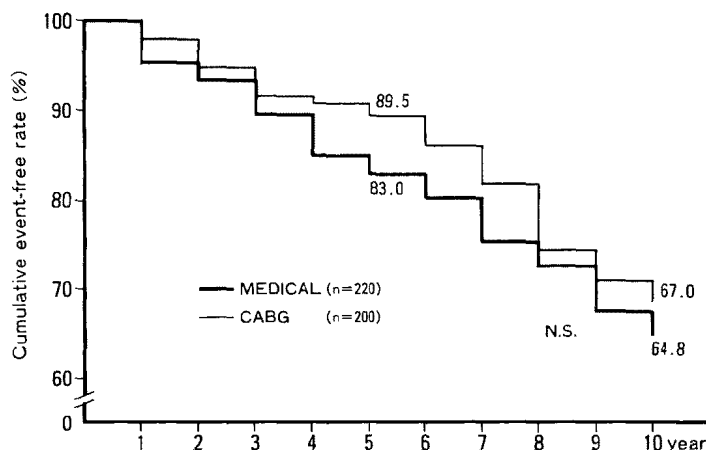
**Cumulative event-free survival curves for double-vessel disease (Figure 2):** The 5- and 10-year event-free survival rates for the medical therapy group were 83.0% and 64.8%, respectively, and 89.5% and 67.0% for the CABG group. The differences between the groups were not significant.

**Cumulative survival curves for triple-vessel disease (Figure 3):** The 5- and 10-year survival rates for 567 CABG patients were favorable at 95.8% and 92.2%, respectively, but those for 198 patients treated medically were poor at 80.7% and 64.2%. There were significant differences between the groups from 5 years onwards.

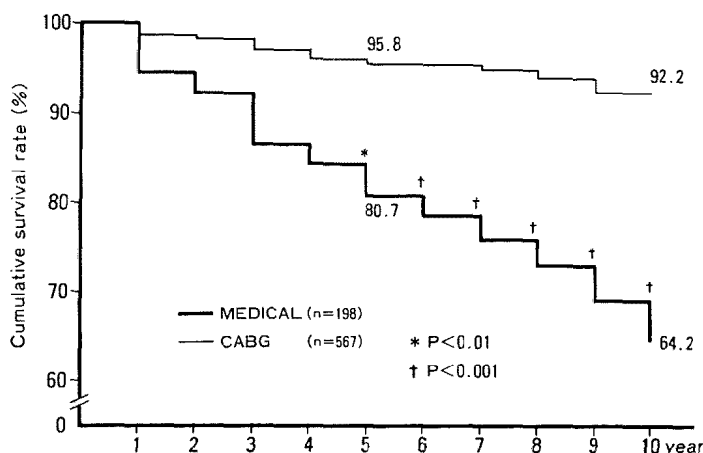
**Cumulative event-free survival curves for triple-vessel disease (Figure 4):**



**Figure 1.** Cumulative survival curves comparing patients with double-vessel disease receiving medical therapy with CABG.



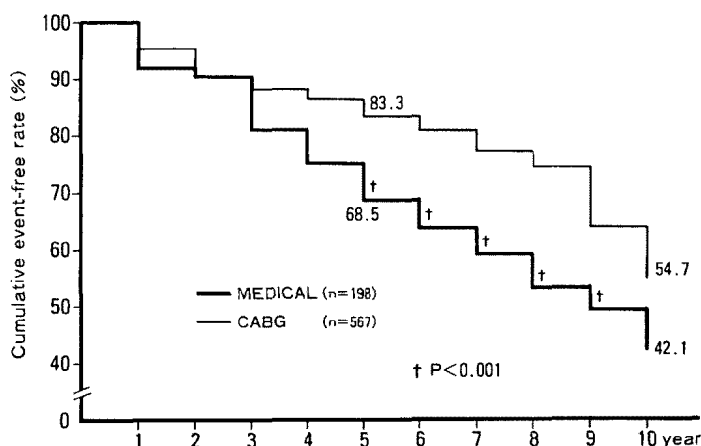
**Figure 2.** Cumulative event-free survival curves comparing patients with double-vessel disease receiving medical therapy with CABG.



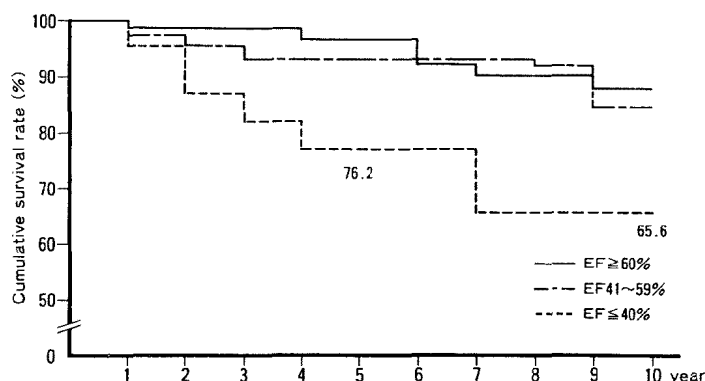
**Figure 3.** Cumulative survival curves comparing patients with triple-vessel disease receiving medical therapy with CABG.

The 5- and 10-year event-free survival rates were 83.3% and 54.7%, respectively, for the CABG group, but those for the medical therapy group were poor at 68.5% and 42.1%. Significant differences were observed between the groups from 5 years onwards.

**Cumulative survival curves for double-vessel disease treated medically in relation to LVEF (Figure 5):** Of the 220 patients with double-vessel disease, 131 patients having a MI were divided into 3 subgroups according to their EF: one group with an EF  $\geq 60\%$ , another with an EF of 41–59%, and a third with an EF  $\leq 40\%$ . The results with medical therapy were favorable in patients



**Figure 4.** Cumulative event-free survival curves comparing patients with triple-vessel disease receiving medical therapy with CABG.

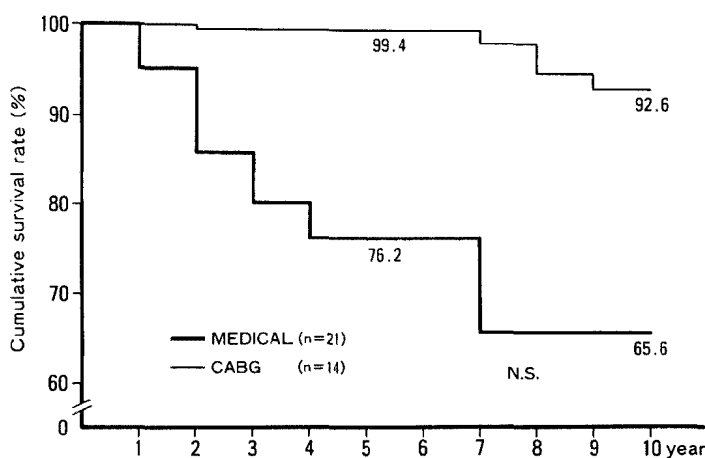


**Figure 5.** Cumulative survival curves for patients with double-vessel disease treated medically in relation to left ventricular ejection fraction.

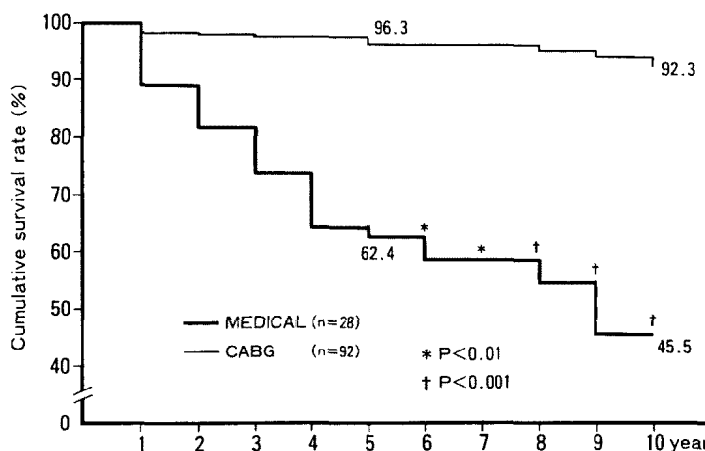
with an EF > 40%, but were poor in those with decreased LV function (EF ≤ 40%), with the 5- and 10-year survival rates being 76.2% and 65.6%, respectively.

**Cumulative survival curves for patients with double-vessel disease with decreased LV function (EF ≤ 40%) (Figure 6):** The 5- and 10-year survival rates for 14 CABG patients were favorable at 99.4% and 92.6%, respectively, and those for the medical therapy group were apparently poor at 76.2% and 65.6%. However, no significant differences were detected between the groups due to the small number of cases.

**Cumulative survival curves for patients with triple-vessel disease with decreased LV function (EF ≤ 40%) (Figure 7):** The 5- and 10-year survival rates



**Figure 6.** Cumulative survival curves for comparing patients with double-vessel disease and decreased LV function ( $EF \leq 40\%$ ) receiving medical therapy or CABG.



**Figure 7.** Cumulative survival curves for comparing patients with triple-vessel disease and decreased LV function ( $EF \leq 40\%$ ) receiving medical therapy or CABG.

for 92 CABG patients were favorable at 96.3% and 92.3%, respectively, and those for the medical therapy group were poor at 62.4% and 45.5%, with the differences between the groups being significant.

## DISCUSSION

Coronary artery disease in Japan has a better prognosis than in Europe and the United States,<sup>6,7)</sup> and the long-term outcome of single-vessel disease does not differ among medical therapy, PTCA, and CABG in Western countries.<sup>8,9)</sup> The

usefulness of CABG has been established in multivessel disease.<sup>1)</sup> Recently, PTCA has also been extensively used in multivessel disease,<sup>10)</sup> and several large-scale studies comparing PTCA and CABG in multivessel disease are underway. Interim reports published in 1994 stated that PTCA can be substituted for CABG as a therapy for multivessel disease, but PTCA patients required more frequent repeat interventions including PTCA and CABG.<sup>4,5)</sup>

In this study, we attempted to compare the long-term results of various treatment modalities in multivessel disease. However, PTCA was excluded due to the small number of cases of multivessel disease treated with PTCA. Accordingly, the results of medical therapy and CABG were compared.

**Double-vessel disease:** Medical therapy alone provided favorable overall 5-year and 10-year survival rates of 94.5% and 87.4% in patients with double-vessel disease, and also produced 5- and 10-year event-free survival rates of 83.0% and 64.8% in these patients. There were no significant differences between medical therapy and CABG. However, the outcome of double-vessel disease treated medically varied with LV functional status<sup>11)</sup>; the outcome was favorable in patients presenting good LV function ( $EF > 40\%$ ) and was shown to be comparable to that with CABG. However, in those with decreased LV function ( $EF \leq 40\%$ ), the results with medical therapy were clearly poorer than those with CABG. Although the differences were not significant, owing to the small number of cases, such patients should actively undergo revascularization, including CABG and PTCA, to improve their long-term prognosis.

**Triple-vessel disease:** The 5- and 10-year survival rates for triple-vessel disease treated medically were 80.7% and 64.2%, which were apparently lower than those with CABG, and the differences were marked in patients with poor LV function. These findings support previous reports.<sup>12-16)</sup>

Medical therapy produced poor 5- and 10-year event-free survival rates of 68.5% and 42.1%, which were significantly different from the results with CABG. Although the results in the CABG group were better than those in the medical therapy group, a decrease in the event-free survival rate was pronounced after 5 years, particularly from 7 years onwards. Such a tendency was also seen in double-vessel disease. Vein graft occlusion seems to be the cause of this. Recently, artery grafts employing internal thoracic arteries have been confirmed to remain patent for longer periods than vein grafts.<sup>17)</sup> Hence, it is necessary to compare the long-term results of PTCA and CABG using artery grafts in multivessel disease in the future.

**Left ventricular function:** In the present study, the outcome of multivessel disease with decreased LV function was also poor, supporting the fact that LV function is the most important prognostic factor for coronary artery disease, as did a previous report.<sup>18)</sup> The CASS report indicated that only triple-vessel disease

complicated by decreased LV function had a better long-term outcome when treated with CABG as compared to medical therapy.<sup>19)</sup> In this study, CABG resulted in a better long-term outcome than medical therapy for patients with double-vessel disease complicated by decreased LV function, thus suggesting that revascularization, including CABG and PTCA, should be actively performed. The effectiveness of PTCA in patients with decreased LV function has been reported<sup>20)</sup>; in this regard, a prospective comparison with CABG is required in the future.

**Study limitations:** This study is not a randomized controlled trial but a retrospective review, so there may be some bias in the selection of subjects between the two groups. All of the patients in the medical therapy group were initially seen before the introduction of PTCA at our hospital, and most of them were enrolled even before the establishment of cardiovascular surgery at our hospital in 1977. Accordingly, serious patients who were not appropriate for CABG due to poor distal run-off and so on, were also included in the medical therapy group. Therefore, the severity of disease may be different between the two groups.

**Conclusions:** When multivessel disease was stratified into double- and triple-vessel disease, their outcomes varied. In patients with double-vessel disease with good LV function, the long-term outcome with medical therapy was as favorable as that with CABG. However, in patients with double- and triple-vessel disease, complicated by poor LV function ( $EF \leq 40\%$ ), the results with medical therapy only were clearly worse than those with CABG. Hence, such patients should actively undergo revascularization to improve their prognosis.

Randomized prospective studies are required to compare the long-term results of PTCA and CABG for multivessel disease in the future. We need to conduct studies with close matching of disease severity by stratifying, not only the number of affected vessels and the degree of impaired LV function, but also the severity of symptoms and the extent of coronary lesions.

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