Current Status and Problems in Long-term Management of Patients Undergoing Coronary Artery Bypass Surgery in Japan

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We studied 272 patients undergoing coronary artery bypass surgery (CABS) to clarify the long-term effects of CABS and to identify problems in long-term management. Data on patients' pre and postoperative medical status were obtained from hospital files. A specially designed questionnaire was sent to all patients to assess residual angina, return to work, non-work physical activity and improvement in the quality of life after a mean follow-up of 29 months.

Multivessel disease accounted for 89% of all patients and complete revascularization was achieved in 55%. A total of 131 events of complications associated with CABS occurred in 112 patients; post-transfusion hepatitis was the most frequent complication (26%). Graft patency rate was 89% at the time of hospital discharge.

Bypass grafts were patent in 95% of 243 grafts which were restudied at a mean period of 19 months after the first study. There was no significant difference in the patency rate between patients with well controlled, poorly controlled or discontinued anticoagulant therapy.

Patients who were relieved from angina, returned to gainful work and had no limitation in non-work physical activity accounted for 74%, 79% and 73%, respectively. By subjective assessment, the quality of life improved in 76% of all patients. Objectively, contributing factors preventing improvement in the life quality were residual angina and post-transfusion hepatitis.

There were 13 patients who were readmitted because of cardiac events. Three patients died from these events including two from sudden death during follow-up.

We conclude that the beneficial effects of CABS are actually attainable. New approaches should be considered for increasing graft patency rate to an angina-producing artery and in preventing post-transfusion hepatitis. In this study, the benefits of the long-term use of anticoagulant therapy is questionable.

THE demographic incidence of coronary artery occlusive disease (CAOD) has increased in Japan in proportion to the westernization of both the life environment and the diet

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habits of Japanese people, although the incidence is still lower than that of western countries. Consequently, the numbers of patients undergoing coronary artery bypass surgery (CABS), which has become a promising form of treatment for patients with CAOD, have inevitably increased. There are three goals of CABS: 1) elimination of anginal pain; 2) prolongation of life; and 3) improvement in the quality of the

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patient's life. It is of great concern to physicians how these goals actually affect a patient's life. There is general agreement that successful CABS provides relief from anginal pain¹⁻³ and allows increasing work activity.⁴⁻⁸ These are two measurable variables that assess improvement of life quality in most patients during the first several years. However prolongation of life has been demonstrated in a randomized control study only for patients with left main coronary artery (LMC) disease.⁹ There are few data available in Japan regarding the long-term outcome and patient's health status after the operation.

The purposes of the present study are to investigate the actual status in management of patients undergoing CABS during long-term follow-up, identify the contributing factors impairing operative effects, and to clarify long-term effects of CABS on the patient's life.

PATIENTS AND METHODS

Between November 1977 and June 1984, a total of 332 patients with CAOD had CABS at the National Cardiovascular Center. Fifty-nine patients were excluded from the present study because of following reasons; 1) 19 patients died postoperatively, 2) 30 patients had other concomitant procedure such as valve replacement or left ventricular (LV) aneurysmectomy, and 3) 10 patients were without definite anginal pain preoperatively. The study population consisted of 273 patients including 232 males, and the mean age was 56 years (range 35-75 years) at the time of surgery.

A survey questionnaire was sent to all patients after the 6-months postoperative period had passed. An average interval from hospital discharge to the survey was 29 months (range 6-79 months). The questionnaire was designed to assess the social status of the patients (return to work, main reason for not returning to work or for reducing work activity, and limitation of physical activity) and to obtain information on their prior and current state of health. The presence and severity of angina was also evaluated by means of several questions. Additionally, the global improvement in the quality of life was assessed. By the end of December 1984, 200 answers (74%) were collected. Same information was obtained by telephone interview from the remaining patients not responding to the questionnaire. Only one patient dropped out of the

follow-up study. In addition, data concerning the preoperative state of the severity of illness and postoperative condition were collected from hospital files. They included incidence of prior myocardial infarction (MI) and vasospastic angina, number of involved vessels with at least one stenosis of 75% or more, LV ejection fraction (EF), LV end-diastolic pressure (EDP), number of placed grafts, graft patency, a rate of complete revascularization and complications associated with CABS, such as perioperative MI, post-transfusion hepatitis and renal failure. Early postoperative coronary angiograms were obtained from 260 patients during their hospital stay. For this study, revascularization was defined as complete when all diseased vessels, but for the small posterolateral branch and vessels perfusing the akinetic LV wall (MI related vessels), were grafted and grafts were ascertained to be patent.

Perioperative MI was diagnosed if new Q wave developed or the MB fraction of creatinine phosphokinase elevated up to 40 IU or more.

Finally, general medical conditions during follow-up were investigated from out-patient department records or by telephone interview to primary physicians with a mean interval of 19 months after the surgery. Surveyed data included state of regulation of anticoagulant therapy, administered medicines and late graft patency which was evaluated by digital subtraction angiography or enhanced computer tomography.

Statistical analysis was made using a chi-square test, and a p value of less than 0.05 was considered significant.

RESULTS

There were 159 patients (58%) with previous MI and 31 patients (11%) with vasospastic angina. Preoperative mean values of LVEDP and LVEF, number of patients with diseased vessel and the severity of angina according to Canadian Heart Classification (CHC) are listed in Table I. Triple vessel disease had the highest incidence. Among patients in CHC IV, urgent operation was required in 31 patients.

A total of 595 grafts were placed using saphenous veins. For 260 patients from whom postoperative coronary arteriograms were obtained, all grafts were patent in 213 patients (Table II). Conversely, all grafts occluded in five patients. Overall patency rate in the early postoperative period accounted for 89%. No significant changes in LVEDP and LVEF were found postoperatively.

TABLE I PREOPERATIVE BASELINE CHARACTERISTICS

Variable	No of pts	% of pts
Age ≥ 65 years	40	15
Male	232	85
Prior MI	159	42
Vasospastic angina	31	11
Extent of CAOD		
1-vessel	30	11
2-vessel	78	29
3-vessel	124	45
left main	41	15
Angina class (CHC)		
I	12	4
II	118	43
III	88	32
IV	55	21
LV function (mean $\pm$ SD)		
EDP	11.6 $\pm$ 5.5 mmHg	
EF	54.5 $\pm$ 11.7 %	

Abbreviation: pts = patients
see text for other abbreviations

TABLE II POST OPERATIVE BASELINE CHARACTERISTICS

Variable	No of pts	% of pts
No of bypass graft		
1	53	19
2	130	48
3	78	29
4	12	4
Graft patency		
all patent	213	82
partially patent	42	16
all occluded	5	2
Revascularization		
complete	151	55
incomplete	122	45
LV function (mean $\pm$ SD)		
EDP	10.2 $\pm$ 4.9 mmHg	
EF	54.7 $\pm$ 10.5 %	
Complications ^A		
hepatitis	72	26
MI	33	12
renal failure	7	3
CVA ^B	4	1
others	15	5

A: The patients appear in more than one complication

B: cerebrovascular accident

Complete revascularization was achieved in 55% of all patients.

A total of 131 events of complications associated with CABS occurred in 112 patients as summarized in Table II. Since post-transfusion hepatitis was often manifested after patients discharge from hospital, hepatitis that developed within the first 6 months after the surgery was included as a complication associated with CABS. The incidence of this complication was the highest and accounted for 26% in the survival patients. Most of hepatitis was type non-A, non-B. Perioperative MI developed in 33 patients (12%), including 11 patients with non-Q wave infarction.

Therapeutical State and Late Graft Patency.

Of 272 patients, 10 died during follow-up. Since information on postoperative status until death was available from these ten patients, it was included in the study. Of all patients, 267 continued to attend the center, their primary physician or both at the survey time or until the patients' deaths. Antianginal agents were administered to 265 patients throughout the study period after surgery. The precise information about anticoagulant therapy was obtained from 254 patients. Therapy using warfarin or a combination of warfarin and paramidin had been continued in 103 patients at the survey time and had been discontinued during follow-up in 76 cases. For the remaining 75 patients, anticoagulant medicine was given only during the postoperative hospital stay. There was no routine protocol for continuing anticoagulant therapy and it was randomly discontinued according to patients' educational state, difficulty in keeping good control or after reappraisal for graft patency. However, the therapy was continued in patients with refractory hypercholesterolemia. Among 179 patients who had been given anticoagulant medicines, effective anticoagulant therapy was performed in 57 patients through the longterm. In the other 122 patients the therapy was considered to be poorly controlled because prothrombin time was frequently over 50% of normal value. Bypass graft patency was reappraised in 177 patients with a mean interval of 19 months after their hospital discharge. Thirteen (5%) of 243 bypass grafts were found to be newly occluded.

Patients with late occlusion of the grafts were distributed to the three different conditions of anticoagulant therapy mentioned above without statistical difference (Fig. 1). Moreover, there

TABLE III RESIDUAL ANGINA AND RELATED FACTORS

Factor	No of pts	Frequency of anginal attack		
		No	< 1/week	≥ 1/week
<i>Extent of CAOD</i>				
1-vessel	30	18	6	6
2-vessel	78	64	6	8
3-vessel	124	86	9	29
left main	40	33	5	2
<i>Vasospastic angina</i>				
Yes	31	23	7	1
No	241	178	19	44
<i>Revascularization</i>				
complete	151	126	14	11
incomplete	121	75	12	34

* $p < 0.01$ compared with other patients

Fig. 1.

was equal incidence of lately occluded grafts between patients with good or poor control in anticoagulant therapy.

Residual Angina

Anginal attack had disappeared in 201 patients (74%) after CABS at the time of the survey. In 71 patients the attack continued after the surgery and, in 44 of them, the frequency of anginal attack was more than once a week. The relationship of the number of involved vessels, participation of coronary artery spasm and completeness of revascularization between patients with or without residual angina, is shown on Table III. Patients with anginal attack less than

once a week had the highest incidence of coronary artery spasm. In patients with angina more than once a week, triple vessel disease was the most frequent condition; complete revascularization was the least contributory. However, even in 201 patients without residual angina successful complete revascularization accounted for 63%.

Return to Work

It was unnecessary to resume gainful employment for 82 patients including 21 men who retired preoperatively and 33 housewives. Of the remaining 190 patients, 160 returned to work and 30 did not. Among the former 160 patients, 126 (79%) returned to full work, when

TABLE IV REASONS FOR NOT RETURN TO WORK

Reason	No of pts
<i>Cardiac symptom</i>	
<i>angina</i>	20
<i>shortness of breath</i>	9
<i>Symptom related with CABS</i>	
<i>general fatigue</i>	10
<i>leg pain</i>	4
<i>others</i>	5
<i>Anxiety</i>	13
<i>Complicating disease</i>	12
<i>Loss of job</i>	9
<i>Doctor's advice</i>	4

full return to work was designated as achieving more than 70% of work activity of preanginal phase. In the another 34 patients, work activity was less than 70% compared with preanginal phase. The main subjective reasons for not returning to work or for reducing work activity were evaluated in 64 patients (Table IV). Cardiac symptoms such as chest pain or shortness of breath on exertion was the most frequent reason. The second reason was the appearance symptoms associated with complications of CABS, such as general fatigue caused by post-transfusion hepatitis or leg pain induced by removal of saphenous veins. Other reasons were anxiety, lack of confidence in resuming work, doctor's advice or symptoms from a complicating disease such as cerebrovascular accident. Nine patients lost their job after the operation.

To know whether residual angina and hepatitis were influencing factors to work activity after CABS, the relationship between work activity and these two factors was investigated. As shown on Table V, there were more patients who returned to full work in the categories without residual angina or hepatitis compared with patients with one of these factors. However, a number of patients returned to full work who did have residual angina or hepatitis.

Ordinary Activity and Current Status of Health

Of 272 patients, 198 (73%) responded that they had no limitation in non-work physical activity of ordinary life. In the remaining 32 of 73 patients, physical activity was moderately limited. Possible causes of limiting ordinary activity are listed in Table VI. Among these causes, frequen-

cy of residual anginal attack was the highest incidence.

Sixty-one patients were readmitted during follow-up. Reasons for readmission were cardiac events including exacerbation of angina or MI in 13 patients, hepatitis in 16 patients and complicating diseases, such as pneumonia or cerebrovascular accident in 32 patients. Global assessments by patients themselves with regard to improvement in the quality of life are given in Table VII. Two hundred and three patients (77%) responded that beneficial effects of CABS were actually obtained and that the quality of life had improved after the surgery. But, there were 21 patients whose quality of life remained unchanged and 38 patients who reported that it had worsened. Ten patients died, including 3 patients who died from cardiac events. The overall survival rate after hospital discharge was 96.0%.

DISCUSSION

In any assessment of long-term effects of CABS, the severity of the illness before the surgery should be discussed. In our hospital, surgical indication is determined at a joint conference with cardiologists and heart surgeons. Main candidates for CABS are patients with LMC stenosis of 75% or more, or with medically uncontrolled angina. The latter indicates that exercise capacity improves to stage 5 (5.5 km/h in walk speed and 14% in slope) on the treadmill test, which corresponds to CHC class II, after intensive medication by a combination of long-acting nitrates, calcium antagonists and beta blocking agents. Accordingly, the incidence of single vessel disease and CHC II in the study was relatively low and accounted for only about 10% of patients in spite that percutaneous transluminal coronary angioplasty was undertaken in only four patients during the same period of this study.

About half of all patients were achieved complete revascularization. This result is likely dependent upon both a high incidence of multi-vessel disease and the surgeon's policy that grafts are not to be placed on vessels those effective bypass blood flow is non-predictable.

Anticoagulant Therapy and Late Occlusion of Bypass Grafts

Anticoagulant therapy can be effectively performed during hospital stay by a combination of anticoagulant agents and a control of diet which may influence prothrombin time. However, it

TABLE V CONTRIBUTING FACTORS PREVENTING RETURN TO WORK

Factor	No of pts	Return to work		
		Full	Partial	No
<i>Residual angina</i>				
No	136	103	22	11
< 1/week	18	11	3	4
≥ 1/week	35	13	9	15
<i>Hepatitis</i>				
No	134	96	23	15
Yes	55	29	11	15
<i>Prior MI</i>				
No	69	48	10	11
Yes	120	77	24	19
<i>Perioperative MI</i>				
No	168	113	31	24
Yes	21	14	4	3
<i>Revascularization</i>				
complete	104	71	16	17
incomplete	85	54	18	13

* $p < 0.05$; ** $p < 0.001$

TABLE VI CAUSES OF LIMITATION OF PHYSICAL ACTIVITY

Cause	No of pts	Limitation of physical activity		
		No	Mild	Moderate
<i>Angina</i>				
No	201	163	21	17
< 1/week	26	16	8	2
≥ 1/week	45	20	12	13
<i>Hepatitis</i>				
No	200	154	25	21
Yes	72	45	16	11
<i>Age</i>				
< 65 years	232	171	33	28
≥ 65 years	40	28	8	4
<i>LVEF</i>				
≥ 40%	149	111	25	13
< 40%	17	12	1	4

* $p < 0.001$

TABLE VII QUALITY OF LIFE

Quality of life	No of pts	% of pts
Improved	171	77
Unchanged	21	8
Worsened	38	15

often becomes difficult to maintain an appropriate level of prothrombin time after hospital discharge. In our study, the therapy was closely regulated only in one-third of the patients receiving anticoagulant remedy. The main reason for discontinuing the therapy during follow-up was considered to be the difficulty of close regulation.

The purpose of anticoagulant therapy is to prevent occlusion of bypassed grafts. But Pan-

tely¹⁰ reported that late graft patency was not influenced by postoperative anticoagulant therapy. On the other hand, antiplatelet therapy does seem to improve late graft patency. In our study, late occlusion of bypass grafts appeared in 5 of 117 patients. The number of occluded grafts were 13 of 243(5%). In addition, no significant relationship was found between the incidence of late occlusion of the grafts and situations of anticoagulant therapy. These data indicate that long-term use of anticoagulant medicines to keep grafts patent is questionable.

Residual Angina

Anginal attacks were sustained in 26% of all patients after CABS, but about half of them had attacks less than once a week after surgery. This favorable result was similar to other reports.¹¹⁻¹³ In our study, there appeared to be a close relationship between residual angina and multivessel disease or incomplete revascularization. However many patients were free from anginal attacks who received even incomplete revascularization. Two possible reasons may explain decreased anginal attacks after incomplete revascularization. The first may depend upon continued administration of antianginal agents. Secondly, it is likely that ungrafted coronary arteries or occluded bypass grafts had not contributed to anginal attack. In our hospital, exercise stress myocardial scintigraphy is fully applied for detecting any so-called angina-producing arteries. From the viewpoint of preventing anginal attack, complete revascularization seems unnecessary if the angina-producing artery is well bypassed.

Return to Work

In the present study, 84% of patients who were required to return to gainful employment for economical reasons, did so. This result is also comparable to that reported in other studies.¹⁴⁻¹⁶

There are numerous studies that specify contributing factors preventing a return to work.^{6,8,15-18} Postoperative work status is likely to be related to age, educational level, preoperative work status, type of occupation, noncardiovascular illness, patients' perceptions, graft patency, increased tolerance for physical activity and cardiac symptoms.

In this study, we focused on patients' symptoms. Residual angina from cardiac symptoms and post-transfusion hepatitis from non-cardiac symptoms were important factors in influencing postoperative work status.

Patients with residual angina accounted for 26% of all patients, although some of them returned to full work. It may be necessary to increase a rate of patency of the graft to angina-producing artery to prevent residual angina. Post-transfusion hepatitis is another problem. Hepatitis often exacerbates in a chronic stage. To avoid repeating exacerbation, work activity inevitably decreases for several years. Additionally, the incidence of hepatitis is considerably higher in Japan compared with western countries.¹⁹⁻²¹

The prevention of non-A, non-B hepatitis may be impossible when human blood is transfused during surgery, because specific markers of infection are lacking. Alternative plans should be considered, such as the use of artificial blood, to avoid this complication.

Current Status of Health and Quality of Life

In this study, an incidence of fatal or nonfatal cardiac events after CABS was relatively low compared with other studies^{14,22} in spite of the high severity of preoperative illness. Non-work physical activity was unlimited in 73% of all patients after the surgery. Moreover, 77% of the patients responded that their quality of life improved.

Yamaguchi and his co-workers reported that medically treated patients with CAOD had better prognosis in Japan compared with the United States.²³ It is believed that the favorable outcome of Japanese patients is a result of close and intense medication and from the slow progression of atherosclerosis in the coronary artery. These two concepts may be also applied to a similarly good outcome of surgically treated patients.

Quality of life is a complex value concept that is difficult to define.²⁴⁻²⁵ It includes medical, psychosocial, cultural and economical components.

The majority of studies on the quality of life have chosen relief of angina and return to gainful employment after the surgery as the indicators for objective assessment. But for the retired patient or housewife whose angina was relieved but who suffered transfusion-hepatitis, the assessment of improved life quality on the basis of these two indicators can be misleading. Thus, we added more two indicators, non-work physical activity and subjective assessment in the life quality. As a result, there appeared approximately the same percentage in patients who were re-

lieved from angina, returned to gainful work, had no limitation in non-work physical activity and whose quality of life improved, subjectively.

It is concluded that the goals of CABS are actually attained in most patients. Beneficial effects of CABS and favorable outcome satisfy physicians. The contributing factors that impair surgical effects were considered to be the severity of the preoperative illness, residual angina and complications associated with CABS. In spite of the favorable results of CABS, almost all patients continued to attend hospital and clinics to receive antianginal agents. This may indicate that the detailed mechanisms for the onset of MI or the exacerbation of angina have not been, as yet, clarified.

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