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Concomitant Coronary Bypass Grafting and Curative Surgery for Cancer

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Abstract: The surgical management of patients with concomitant critical coronary artery disease (CAD) and surgically resectable cancer is controversial. We evaluated 19 patients who underwent concomitant coronary artery bypass grafting (CABG) and curative operation for cancer of the stomach in 9 patients, the colon in 4, the lung in 4, and the breast in 2. Each cancer operation was performed under stable hemodynamics without any serious bleeding tendency, immediately after CABG with an average of 2.5 ± 0.8 grafts. There were no operative deaths and no incidences of perioperative myocardial infarction. Postoperative complications developed in three of the patients with lung cancer: respiratory dysfunction caused by phrenic nerve paralysis in two and mediastinitis in one. During the mean follow-up period of 33 ± 23 months, 5 patients died of recurrent cancer or non-cardiac disease; however, all 19 patients remained free from any postoperative cardiac events and their quality of life apparently improved. This experience suggests that such simultaneous correction would be safe and beneficial in carefully selected patients who have surgically correctable CAD and potentially curable cancer.

Key Words: coronary artery disease, cancer, coronary artery bypass grafting, concomitant surgery

Introduction

The number of patients who have both critical coronary artery disease (CAD) and surgically resectable cancer has been rising as the proportion of elderly in the general population increases. It is widely recognized that myocardial infarction is the most frequent cause of both early and late death following surgery for cancer in these patients who do not undergo prior coronary revascularization.[1,2] CAD and cancer have most often been treated by separate procedures which were performed based on clinical priority, although coronary artery bypass grafting (CABG) is usually performed first to prevent perioperative myocardial infarction.[2,3] On the other hand, open heart procedures impair immunological function[4,5] and the progression of cancer may be accelerated during the time between operations. Therefore, simultaneous radical procedures are expected to be of value for the treatment of this subset of patients. We report herein our analysis of 19 patients for whom concomitant CABG and curative operation for cancer were performed over a recent 7-year period. The purpose of the present study was to review our experience with this surgical approach and evaluate the benefits and risks.

Patients and Methods

Of a total 266 patients who underwent CABG between November 1985 and December 1992 at Osaka University Hospital, 21 patients had surgically correctable cancer, 19 of whom (13 men and 6 women), underwent concomitant curative operation for cancer (Table 1). The ages at the time of surgery ranged from 47 to 77 years with an average of 64 ± 7 years, and 6 patients (32%) were 70 years or older. A total 16 patients (84%) presented with cardiac symptoms, classified as Canadian Heart Association class II, III, and IV angina in 8, 6, and 2 patients, respectively, and were subsequently found to have cancer. In the remaining 3 patients (16%), severe CAD with silent cardiac ischemia was discovered during the preoperative assessment for their cancer operation. Diabetes controlled by oral antihyper glycemic agents was present in eight patients, hypertension with a resting blood pressure of greater than 160/90 mmHg was found in eight, and hypercholesterolemia with a serum total

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Table 1. Preoperative clinical characteristics of the patients and concomitant procedures for coronary artery disease (CAD) and cancer

Case No.	Age (yrs)	Sex	CAD	OMI	Risk factor	EF (%)	Organ of cancer	Stage of cancer	Cardiac procedures	Procedures for cancer
1	72	M	3VD	(+)	HT, HL	54	stomach	IV	2-SVG	subtotal gastrectomy + R2
2	47	M	1VD	(+)	HT	63	stomach	I	1-IMAG	subtotal gastrectomy + R2
3	59	M	LMT	(+)	—	48	stomach	I	2-SVG	subtotal gastrectomy + R2
4	58	M	3VD	(+)	HT	35	stomach	I	3-SVG	subtotal gastrectomy + R2
5	62	M	3VD	(−)	DM	65	stomach	I	3-SVG	subtotal gastrectomy + R2
6	64	M	3VD	(−)	HT	67	stomach	I	1-IMAG+2-SVG	subtotal gastrectomy + R2
7	61	M	3VD	(+)	—	28	stomach	I	3-SVG	subtotal gastrectomy + R2
8	71	M	LMT	(+)	HL	46	stomach	III	3-SVG	subtotal gastrectomy + R2
9	57	M	2VD	(+)	DM	59	stomach	I	1-IMAG+1-SVG	subtotal gastrectomy + R2
10	67	F	2VD	(−)	DM	61	sigmoid colon	I	2-SVG	sigmoid colectomy + partial resection of ileum and ovary + R2
11	70	F	3VD	(−)	HT, HL, DM	43	sigmoid colon	I	4-SVG	sigmoid colectomy + R2
12	67	F	2VD	(−)	—	52	sigmoid colon	V	2-SVG	sigmoid colectomy + R2
13	72	M	2VD	(+)	—	49	descending colon	I	1-IMAG+1-SVG	segmental resection of descending colon + R2
14	58	M	3VD	(−)	HT, HL, DM	58	breast	II	3-SVG	r. radical mastectomy + R2
15	77	F	1VD	(−)	—	65	breast	II	1-SVG+ASDC	l. modified mastectomy + R2
16	70	F	3VD	(+)	DM	29	lung	I	2-SVG+LVA	r. upper lobectomy + R3
17	67	M	LMT	(+)	—	67	lung	III	3-SVG	r. lower lobectomy + R2
18	58	M	3VD	(+)	HT, DM	45	lung	III	1-IMAG+2-SVG	r. upper lobectomy + R3
19	58	M	3VD	(+)	HT, HL, DM	30	lung	III	3-SVG	l. lower lobectomy + R2

OMI, previous myocardial infarction; EF, ejection fraction; VD, vessel disease; HT, hypertension; HL, hyperlipidemia; DM, diabetis mellitus; LVA, left ventricular aneurysmectomy; ASDC, closure of atrial septal defect; SVG, saphenous vein grafting; IMAG, internal mammary artery grafting; R2 or R3, resection of N2 or N3 lymph nodes; LMT, left main trunk disease

cholesterol of greater than 220 mg/dl was found in four. One patient had previously undergone bypass surgery for atherosclerotic cerebrovascular disease. Patients with known pre-existing renal, liver, or pulmonary dysfunction were not recruited for concomitant surgery.

The CAD involved one vessel in 2 patients (11%) two vessels in 4 (16%), three vessels in 10 (53%), and the left main trunk in 3 (16%). A total of 11 patients (58%) had experienced previous myocardial infarction. One of them had a left ventricular aneurysm and another had an atrial septal defect. The left ventricular ejection fractions ranged from 28% to 67% with an average of 51 ± 13% and four patients (22%) had a value of less than 40%. Regarding the types of cancer, nine patients had stomach cancer, four had colon cancer, four had lung cancer, and two had breast cancer. None of the patients showed any evidence of distant metastasis and a curative resection was anticipated in all 19. The CABG was performed using routine cardiopulmonary bypass and cardioplegic arrest. Coronary revascularization was indicated for the coronary arteries with 75% stenosis or more and with viable myocardium in each region. The number of grafts ranged from 1 to 4 with an average of 2.5 ± 0.8, and four patients received internal mammary artery grafting to the left anterior descending coronary artery. One patient underwent concomitant left ventricular aneurysmectomy and another underwent concomitant closure of an atrial septal defect. All procedures were performed on an elective basis.

All 19 patients underwent a curative operation for cancer with extended resection of the second or third echelon of the draining lymph nodes (R2 or R3)[6,7] and the surrounding tissues. After the median sternotomy was closed, a subtotal gastrectomy with omentectomy and bursectomy was performed in the nine patients with gastric cancer, a segmental colectomy was performed in the four with colon cancer, and a radical mastectomy in the two with breast cancer. One patient underwent sigmoid colectomy combined with partial resection of the ileum and a left oophorectomy for local invasion of the tumor. Each skin incision made to facilitate curative operation for cancer was designed not to be connected with the median sternotomy to prevent bacterial contamination in the mediastinal space, especially in those patients with gastrointestinal cancer. Subtotal gastrectomy was performed via an upper median laparotomy starting from the left side of the xiphoid in two patients, while a transverse laparotomy was performed in the most recent six. All of the four patients with lung cancer underwent pulmonary procedures via the same median sternotomy after anticoagulation with heparin had been reversed with protamine sulfate. Three of these patients underwent a right upper lobectomy, while one, who underwent a left lower lobectomy, required lateral extension of the sternotomy into the left fifth intercostal space to facilitate exposure. Hemostasis was carefully ensured throughout the procedures for cancer resection because of the bleeding tendency after cardiopulmonary bypass.

Data were analyzed using the unpaired Wilcoxon test or the chi-square test. Values are expressed as the mean ± standard deviation. A P value of less than 0.05 was considered significant.

Results

There were no operative deaths or any episodes of perioperative myocardial infarction or heart failure requiring the administration of a large amount of catecholamine or mechanical support (Table 2). All of the curative operations for cancer were completely performed under stable hemodynamics without any serious bleeding tendency after CABG. The total amount of intraoperative bleeding ranged from 750 ml to 2,800 ml with an average of 1,810 ± 690 ml. All patients were weaned from the catecholamine and extubated within 1–2 days after the operation except for the two patients who underwent right upper lobectomy for lung cancer. These two patients required ventilator support for 16 and 33 days postperatively due to respiratory failure related to left phrenic nerve paralysis probably caused by intraoperative cold injury. Postoperative mediastinitis was encountered in another patient with lung cancer, which required omental flap surgery on the 7th day following concomitant CABG. The incidence of postoperative complications in the patients with lung cancer was significantly higher than that in the other patients ($P < 0.01$). However, there were no significant differences in age, left ventricular ejection fraction (LVEF), and the number of grafts between the two groups (Table 3).

Follow-up was complete in all the patients and averaged 33 months with a range of 6–86 months. There were five late deaths, three of which were due to recurrent cancer; two patients died of lung cancer, 7 and 38 months postoperatively, and one of gastric cancer 20 months postoperatively. The remaining two deaths resulted from non-cardiac disease without any evidence of cancer recurrence, with one patient dying from strangulation of the small intestine 12 months postoperatively and another of acute suppurative cholangitis 45 months postoperatively. The remaining

Table 3. Postoperative complications of the patients with lung cancer versus other cancers

	Lung cancer (n = 4)	Other cancers (n = 15)	
Complications	3 (75%)[a]	0 (0%)	$P < 0.01$
Age (years)	63 ± 6	64 ± 8	NS
EF (%)	43 ± 18	53 ± 11	NS
No. of grafts	2.8 ± 0.5	2.4 ± 0.8	NS

EF, ejection fraction; NS, not significant
[a] Respiratory dysfunction related to phrenic nerve paralysis developed in two patients and mediastinitis developed in one

Table 2. Operative results and major complication

Case No.	Days of intubation	Days in ICU	Amount of bleeding (ml)	Peak TB (mg/dl)	Peak Cr (mg/dl)	Postoperative complications	Follow-up (months)	Results
1	1	1	1,894	4.3	1.2	—	86	Alive
2	1	1	1,340	3.7	1.1	—	20	Died[a]
3	1	1	1,700	5.1	1.1	—	12	Died[b]
4	1	2	1,850	6.9	1.0	—	37	Alive
5	1	2	2,550	2.2	1.1	—	35	Alive
6	1	1	2,710	8.7	2.2	—	30	Alive
7	1	1	1,120	7.0	1.7	—	28	Alive
8	1	2	1,410	16.4	1.0	—	9	Alive
9	1	2	2,100	2.7	0.9	—	6	Alive
10	1	1	1,670	3.1	0.7	—	44	Alive
11	2	2	2,800	6.2	1.7	—	42	Alive
12	1	1	1,845	10.4	1.4	—	25	Alive
13	1	2	820	1.5	0.9	—	14	Alive
14	1	1	750	1.0	1.0	—	76	Alive
15	2	2	900	1.3	2.0	—	45	Died[b]
16	16	10	2,730	2.2	1.0	phrenic nerve paralysis	62	Alive
17	33	25	2,250	3.3	1.3	phrenic nerve paralysis	38	Died[a]
18	1	2	2,379	4.0	1.6	—	7	Died[a]
19	1	2	1,762	2.7	0.8	mediastinitis	11	Alive

ICU, intensive care unit; TB, serum total bilirubin; Cr, serum creatinine
[a] Died of cancer
[b] Died of noncardiac disease without recurrence of cancer

14 patients have shown no signs of cancer recurrence, and all 19 patients have remained free of any cardiac events such as angina pectoris, myocardial infarction, repeat coronary revascularization, and cardiac deaths throughout the follow-up period. Thus, resolution of the cardiac symptoms apparently improved the quality of life of all these patients after the concomitant operations.

Discussion

Foster et al.[2] documented increased operative risk for noncardiac procedures performed on individuals with major CAD associated with myocardial damage and impaired ventricular function. Moreover, Crawford et al.[3] reported that the risk of major surgery was as favorable in patients who had undergone successful CABG as in those without CAD, and recomended postponing a second operation for 6 weeks to 3 months since most of the complications in their series developed when the operation was performed within 30 days of CABG. On the other hand, anesthesia, open heart surgery,[4,5] and blood transfusion[8] impair the immune defense mechanism and it is feared that the progression of cancer might be accelerated. The general condition of patients with advanced cancer is always severely impaired and therefore recovery after CABG often takes a long time. Thus, patients with both surgically correctable CAD and cancer have presented a dilemma with regard to the priority and the timing of each operation. In our previous series conducted prior to 1985,[9] patients with surgically corrected CAD and cancer underwent curative surgery for cancer 3–14 weeks after undergoing CABG (average 7 weeks), with cancer resection being postoponed by a delayed recovery from CABG in half of the patients. In one of these patients, rapid growth of a gastric tumor was endoscopically disclosed while waiting for his general condition to improve after CABG. Thus, concomitant correction of both disease entities is obviously advantageous, especially in patients with advanced cancer. Nevertheless, a review of the literature reveals that only a few small groups of patients have been treated with a combined approach,[10–12] and therefore further studies are needed to confirm the safety and effectiveness of this surgical approach. The present results suggested that concomitant CABG and curative surgery for cancer with extended resection of the regional lymphatic drainage area could be performed safely, even in patients with depressed left ventricular (LV) function. Furthermore, there were no significant differences in age at the time of surgery, the severity of coronary artery disease, or left ventricular function between this concomitant series and the staged series[9] previously reported (Table 4).

Because concomitant operations tend to take more time and carry a greater risk of invasion to those patients in a poor nutritional state, the indications should be carefully assessed, considering the condition of the patient. In our series, the concomitant operations were restricted to a subset of patients with potentially curable cancer who were free from severe dysfunction of other major organs. During the same period, one patient with gastric cancer underwent CABG preceding the curative operation for cancer in a staged fashion because of both severely depressed LV function and systemic atherosclerotic disease. A staged operation was also selected for another patient with esophageal cancer requiring intestinal anastomosis in the mediastinum. At the present time, we consider that concomitant operations should not be performed on patients undergoing anticipated curative resection for cancer of the esophagus, pancreas, and other organs which are difficult to resect concomitantly since the resection itself involves a high risk of operative mortality.

In our series, the number of grafts used and the LV function were not risk factors for these concomitant operatons. However, heart failure requiring high doses of catecholamine or mechanical circulatory assistance and a serious bleeding tendency after CABG are thought to be definite contraindications for concomitant operations, and such patients should be subjected to staged operations. In some cases, percutaneous transluminal coronary angioplasty (PTCA) may be performed at first, followed by an operation for cancer at a later date.[9] In fact, three patients underwent PTCA 2 weeks before a curative resection was performed for cancer during the period of this study.

Each skin incision made for the cancer operation was designed not to be connected with the median

Table 4. Comparison of patient characteristics between this concomitant series and the staged series[8] previously reported

	Concomitant series (n = 19)	Staged series (n = 8)	
Age (years)	64 ± 7	66 ± 7	NS
EF (%)	51 ± 13	51 ± 16	NS
Extent of CAD			NS
1VD (%)	11	0	
2VD (%)	16	38	
3VD (%)	53	62	
LMT (%)	16	0	
No. of grafts	2.8 ± 0.5	2.4 ± 0.8	NS

EF, ejection fraction; CAD, coronary artery disease; VD, vessel disease; LMT, left main trunk disease; NS, not significant sternotomy, to prevent postoperative infectious complications in patients with gastrointestinal and breast cancer. Subtotal gastrectomy was performed through an upper median laparotomy starting from the left side of the xiphoid in two patients, and through a transverse laparotomy in the recent six, and the cancer operation was not commenced until after the median sternotomy had been closed with careful hemostasis. No mediastinitis or wound complications developed in any of the patients with gastrointestinal and breast cancer. It is thought that these concomitant procedures should be avoided in patients requiring intestinal anastomosis in the mediastinal space. On the other hand, patients with lung cancer underwent concomitant CABG and pulmonary procedures via the same median sternotomy. Several authors[10,12,13,14] have advocated these concomitant procedures performed via the same median sternotomy with favorable operative results. However, postoperative mediastinitis requiring surgical correction was encountered in one of our patients with lung cancer. The cause of this complication was considered to be related to the prolonged operation time for both procedures. Irrigation of the mediastinal space prior to sternal closure might be effective for the prevention of mediastinitis.

Median sternotomy is associated with less respiratory compromise than lateral thoracotomy and concomitant procedures via the same median sternotomy would be advantageous, especially for patients with poor pulmonary function.[15] However, left phrenic nerve paralysis resulting from topical hypothermia secondary to ice cooling of the heart[16,17] made it necessary to perform a right upper lobectomy in two of our patients, and this prolonged ventilator dependence. After sufficient respiratory physiotherapy had been given under stable hemodynamic conditions, they were able to be extubated on the 16th and 33rd postoperative days, respectively. A preoperative evaluation of respiratory function[18] showed that these patients could have tolerated even a right pneumonectomy. Even unilateral phrenic nerve paralysis could be serious in some patients undergoing contralateral lobectomy with extended mediastinal resection.

In conclusion, although it could not be determined whether concomitant operations offer superior long-term results to staged operations since a comparative study of staged-matched patients was not conducted, an important finding of this study was that curative surgery for cancer with extended resection of the regional lymph nodes was able to be performed under stable hemodynamic conditions after CABG. Subsequently, all the patients were free from cardiac events postoperatively and their quality of life was therefore improved. Moreover, the hospital stay was not significantly extended compared with that following a single curative operation for cancer. Thus, we believe that simultaneous correction would be beneficial for carefully selected patients who have surgically correctable CAD and potentially curable cancer.

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