Coronary Artery Bypass Grafting In Familial Hypercholesterolemia

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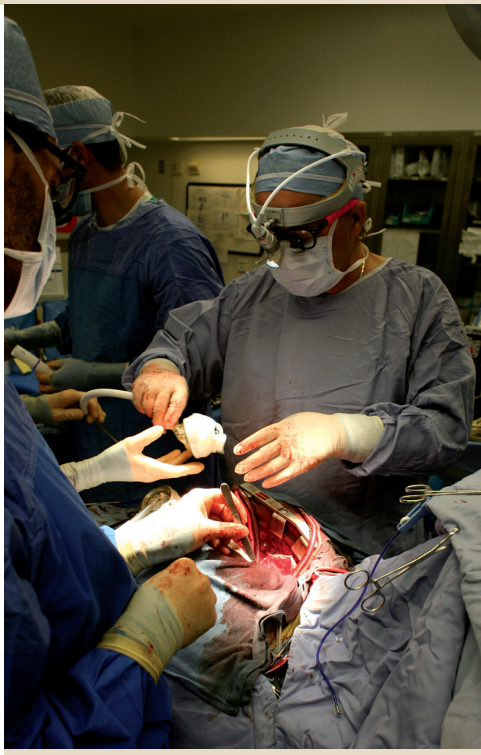

Abstract

Objectives:

Familial hypercholesterolemia is dominantly inherited disorder caused mutation by at the locus for the low-density lipoprotein receptor and is frequently associated with premature coronary artery disease. This study was performed to determine outcomes of coronary artery bypass grafting for patients with familial hypercholesterolemia..

Methods:

During the past 7 years, 11 from 12 patients with heterozygous familial hypercholesterolemia underwent primary coronary artery bypass grafting and 1 from 12 patients underwent PCI without hospital death. All patients received one internal thoracic artery graft and supplemental vein grafts. After operation all patients received diet therapy and intensive cholesterol-lowering therapy. 4 patients received low density lipoprotein aphaeresis.

Results:

Both groups were similar regarding During follow up period (range 1 to 84 months, mean 16 months) there was no cardiac death but 2 of them had recurrent disease. Inspite of severe coronary atherosclerosis, these patients with familial hypercholesterolemia showed good short term outcomes after coronary artery bypass surgery.

Conclusion:

The present finding suggests that aggressive use of arterial and venous grafts, intensive cholesterol-lowering therapy and low-density lipoprotein aphaeresis may be useful in patients with familial hypercholesterolemia.

Key words: familial hypercholesterolemia, coronary artery bypass grafting.

Familial hypercholesterolemia (F.H) is a dominantly inherited disorder caused by mutations at the locus for the low density lipoprotein receptor.[1,2] F.H is characterized by severe hypercholesterolemia caused by increased levels of plasma low-density lipoprotein. F.H is frequently associated with premature coronary artery disease in addition to development of cutaneous and tendon xanthoma.[1,3] Heterozygous F.H is a relative common disorder, occurring in approximately one of every 500 persons in western countries. Heterozygous F.H causes coronary artery stenosis in the second decade of life which progresses more rapidly than in the general population. The death rate from coronary artery disease among patients with heterozygous F.H is several times higher than that found among the general population.4 Coronary artery bypass grafting has been performed to relieve mortality of myocardial infraction in patients with F.H.5 The internal thoracic artery (ITA) is associated with a rate of long term patency, superior to that of a saphenous vein grafts. The use of the ITA for the left anterior descending coronary artery has reduced the prevalence of late cardiac events and has improved the late survival after CABG.6, 7 ITA grafting for lesions in the left anterior descending artery has been advocated.8 However the benefit of arterial grafts has not been clarified in patients with F.H who have rapidly progressing coronary artery disease. The purpose of this study was to report our 7 years experience with CABG in 11 patients with heterozygous F.H and their short-term outcome. The findings in extreme cases may have important implications for the medical and surgical treatment with coronary artery disease.

Methods:

The subjects were 12 patients with heterozygous F.H who underwent CABG

between October 2002 and April 2003 in shahid Rajaee cardiovascular medical and research center. The patients group included 9 men and 3 women who ranged in age from 9-23 years with mean age of 15 years. F.H was diagnosed according to the following 2 criteria, primary hypercholesterolemia (above 230 mg/dl regardless of age) with tendon xanthoma and primary hypercholesterolemia with or without tendon xanthoma in a first-degree relative of patients with F.H. 4

All of patients had heterozygous F.H. The level of plasma cholesterol before introduction of cholesterol lowering drug therapy was 330-822; the low-density lipoprotein cholesterol level was 211-735, high density lipoprotein was 6-127 and triglyceride level was 44-523 mg/dl. One patient had diabetes mellitus. Two patients had 2-vessels disease and 10 patients had 3 vessel disease and 8 patients had left main coronary artery disease. Five patients had a history of remote myocardial infarction confirmed by electrocardiographic changes, enzymatic changes or both. Eleven patients had chest pain and 2 of them had dyspnea. Six of 12 patients had mild, three patients moderate and 2 patients severe aortic valve insufficiency (AI). 6 patients had mild to moderate aortic valve stenosis (AS). 8 patients had trivial to mild mitral value regurgitation (MR). All of them had cutaneous manifestation. Four of them had mild COA. Parents of all 12 patients were relative. Five of them had an other involved person in his/her family. The patients underwent primary CABG procedures with a total of 11 LITA grafts and 28 saphenous vein grafts. The average number of grafts per patients was 3/25. Concomitantly one patient underwent Bental operation and one patient underwent AVR and one patient 6 years later underwent AVR and MVR operation and 2 patients underwent aortoplasty procedure (Table-1).

After operation, all patients received diet therapy and cholesterol lowering therapy with atorvastation, cholestyramin, levostatin, gemofibrosil, acid nicotinic to reduce cholesterol level to less than 180mg/dl and their low-density lipoprotein cholesterol level to less than 130mg/dl. Three patients who were resistant to drug therapy received treatment with low-density lipoprotein apheresis11.The duration of follow-up after operation was 1 to 70 months. Clinical information of survival and subsequent events was obtained every 3 months by interview or their physicians.

Results:

Eleven patients of 12 patients successfully underwent primary CABG and 1 patient PCI on LAD and LCX.

Table1: *Patient's Characteristics*

LM: Left Main, RCA: Right Coronary Artery, LCX: Left Circumflex Artery, LAD, Left Anterior Descending Artery, OM: Obtuse Margenal Artery D. Diagenal Artery.

Number	Age (years)	Chief complaint	Involved vessels	Preoperative EF	Skin lesion	Bypassed vessels	Preoperative EF	TG level (mg/dl)	Total cholesterol (mg/dl)	LDL level (mg/dl)	HDL level (mg/dl)	B.S (mg/dl)
Case 1	18	Chest pain	LAD RCA	50%	+	PCI	50%	115	651	540	110	80
Case 2	14	Chest pain	LAD LCX RCA	55%	+	LAD OM PDA	55%	123	803	527	63	90
Case 3	15	Chest pain Dyspnea	LM LAD	60%	+	LAD OM D	60%	109	295	258	16	95
Case 4	15	Chest pain	LM LAD LCX RCA	60%	+	LAD OM RCA D	60%	85	500	300	48	100
Case 5	15	Chest pain	LM RCA	70%	+	LAD OM D PDA	60%	215	780	650	25	95
Case 6	14	Chest pain	LAD OM RCA	70%	+	LAD OM RCA	70%	523	705	690	16	60
Case 7	18	Chest pain	LM LAD OM RCA	45%	+	LAD OM RCA	45%	72	515	284	75	88
Case 8	19	Dyspnea	LM LAD RCA	55%	+	LAD OM RCA	55%	140	822	758	20	82
Case 9	9	Chest pain	LAD OM	65%	+	LAD OM	65%	67	330	211	65	92
Case 10	23	Chest pain	LM LAD OM RCA	35%	+	LAD D OM RCA	30%	88	756	611	6	80
Case 11	9	Chest pain	LM LAD OM RCA	80%	+	LAD OM RCA	80%	120	719	500	70	125
Case 12	10	Chest pain	LAD OM	55%	+	LAD OM	55%	44	522	319	127	102

Ejection fraction (EF) of them was at least the same as before operation and none of them died. The levels of total cholesterol, low-density lipoprotein cholesterol and triglyceride after treatment with lipoprotein apheresis were significantly lower than those for patients who did not received treatment. During the follow-up period no patient died. Angina recurred in 2 patients.

Discussion:

This study followed short-term survival and cardiac events after primary CABG with LIMA and saphenous vein grafting in patients with F.H. A high plasma level of low-density cholesterol is an independent risk factor for coronary artery disease. 3, 20

Nonlipid coronary risk factors such as hypertension, diabetes, cigarette smoking and obesity appear to be overridden by the more powerful risk factor of hereditary hypercholesterolemia. Patients with heterozygous F.H constitute a homogenous group of patients and are an excellent model of evaluating short term and long term outcomes after medical and surgical treatment of coronary artery disease. Intensive lipid lowering drug therapy reduced the frequency of progression of coronary lesions, increased the frequency of regression and reduced the incidence of cardiovascular events in men with coronary artery disease and high levels of low-density lipoprotein cholesterol. 12, 13

The lower the plasma cholesterol levels, the greater the likelihood that coronary artery disease can be prevented or delayed.14 Intensive combination cholesterol-lowering drug therapy has been advocated as an effective therapy for patients with heterozygous F.H.

Low-density lipoprotein apheresis in an intensive cholesterol-lowering therapy that is highly effective and selective in lowering low-density lipoprotein levels while leaving high-density lipoprotein levels unchanged.11, 20

It has been recognized that CABG improves the long-term survival in patients with F.H.5, 16, 17, 18 The present study showed that for patients with F.H the use of ITA graft significantly increased short-term freedom from recurrences. Patients with F.H in the present study were relatively young with a mean age of 15 years. In addition coronary atherosclerosis in patients with F.H progress more rapidly than that in the general population. We think that intensive cholesterol-lowering therapy is mandatory for patients with F.H.

In conclusion in patients with heterozygous F.H, primary CABG especially ITA grafting increased the short-term freedom from reoperation.

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