Surgical Treatment of Variant Angina: Use of Plexectomy with Aortocoronary Bypass

MICHEL E. BERTRAND, JEAN M. LABLANCHE, MICHEL F. ROUSSEAU, HENRI H. WAREMBOURG, JR., CZESLAS STANKOWTAK, AND GEORGES SOOTS

SUMMARY Aortocoronary bypass surgery, widely accepted in the treatment of patients with coronary artery disease, is controversial in the management of variant angina. Persistence of attacks, occlusion of the graft or postoperative infarction have been described and could be explained by a persistent spasm frequently observed in variant angina that might occlude the distal part of the grafted vessel.

It has been suggested that plexectomy might be added to the aortocoronary graft procedure in order to prevent the spasm. Our study includes 35 patients with variant angina who had surgery. They were divided into two groups. Group 1 (n = 13) had aortocoronary bypass alone; the patients in group 2 had plexectomy in addition to the myocardial revascularization. The average follow-up period was 37 months in group 1 and 20 months in group 2. The results were assessed by clinical study, stress testing, control of patency of the grafts and provocative test with an ergot alkaloid (methergine).

Despite the difficulties of evaluating the effects of the various treatments in these patients with a wide spontaneous variability of symptoms, these data suggest that a complete plexectomy associated with aortocoronary bypass gives better results (86%) than bypass alone (61%) in variant angina. The recurrence rate of attacks was lower (5%) when plexectomy was associated with bypass than with bypass alone (18%).

IN 1959 Prinzmetal et al. described a variant form of angina characterized by attacks at rest and during the night, rather than with exercise, and associated with ST-segment elevation. The ECG changes are transient and disappear without further enzymatic or electrical evidence of myocardial infarction. The authors postulated that this clinical syndrome was due to coronary artery spasm. The development of coronary arteriography provided a clue to confirm that spasm was indeed an important, if not predominant, factor in variant angina. Although aortocoronary bypass surgery has been widely accepted in the treatment of patients with coronary artery disease, its role is controversial in variant angina. A review of the literature has shown poor results with coronary artery grafting: persistence of spontaneous pain in spite of patent grafts, high incidence of occlusion of the grafts or postoperative myocardial infarction. It was even suggested that surgery was not the most appropriate treatment for these cases. An explanation of the failure of surgical therapy could be the persistence of spasm that was not suppressed and can either occlude the distal part of the grafted vessel or narrow another vessel that was apparently normal during preoperative coronary arteriography. Therefore, it would seem feasible to add denervation to the aortocoronary bypass procedure in order to prevent the recurrent spasm. In this report we describe the results of coronary bypass surgery in 35 patients with variant angina, 22 of whom had a plexectomy associated with myocardial revascularization.

Materials and Methods

From January 1974 to November 1978, 53 patients with variant angina were admitted to our institution. Variant angina was defined according to classic criteria.

Left-heart catheterization, left ventriculography and coronary arteriography were undertaken in all patients. Left ventriculography was performed in the 30° right anterior oblique projection using 35-mm film taken at 50 frames/sec. Coronary arteriography was performed with the Judkins method using Bourassa's catheter. Thirteen patients had angiographically normal coronary arteries and were medically treated with a calcium antagonist or long-acting nitrates. The arteriograms in the other 40 patients revealed severe organic obstructive disease. In this group, five patients were technically unsuitable for surgery because of diffuse distal coronary vascular disease. The remaining 35 patients were considered to be surgical candidates and they were divided into two groups. Group 1 included an initial series of 13 consecutive patients observed from 1974 to December 1976. They had aortocoronary bypass alone. Group 2 consisted of a second series of 22 consecutive patients who were studied after January 1977. In these patients, a plexectomy was performed together with coronary artery grafting.

Plexectomy was performed at the onset of operation and included four steps:

1) In order to avoid spasm induced by manipulating Wrisberg's ganglion (as it was observed in two patients) a large bolus of lidocaine was infiltrated under the aortic root.

2) The adventitia overlying the aorta from the left vagus nerve laterally to the most anterior aspect of the ascending aorta medially was peeled.
3) Meticulous resection of all the ganglia and nerves located under the aortic root in the Wrisberg's quadrilateral space was performed. This included resection of the entire triangular area of tissue located between the trachea posteriorly and the ascending aorta medially.

4) Dissection of the space located between the descending aorta and the main pulmonary trunk, where a nerve goes to the right coronary artery. This nerve must be resected. Therefore, we performed a resection as large as possible of the major cardiac plexus located anteriorly near the base of the aorta and under the aortic root. Histologic examination of the resected tissue was done after the plexectomy. Extracorporeal circulation was started and conventional aorto-coronary bypass grafting was carried out.

Postoperative follow-up data, including complications and functional status, were obtained during the last 3 months of 1978 in all patients who survived operation. In 16 patients, the patency of the grafts was assessed. Provocative testing with mepheritine, an ergot alkaloid, was undertaken in 23 patients to attempt induction of spasm.

Patients

Clinical Features

Table 1 summarizes the clinical presentation. Each patient of group 1 had angina at rest from 1 week to 5 months duration. Two patients had angina in the morning when awakening. Three experienced syncopal episodes and two had frequent palpitations.

All the patients of group 2 experienced angina at rest from 2 weeks to 4 years duration. In four patients angina at rest was associated with pain during exercise. Eight patients had syncope and three had palpitations. All 22 patients had one to four risk factors for coronary artery disease (about 2.2 per patient).

ECGs obtained during angina in group 1 showed ST-segment elevation in precordial leads in nine patients and in inferior leads in the four patients; ST-segment depression was never observed. One patient had ventricular tachycardia during pain. Only one patient who had angina during exertion had an exercise stress test that showed ST-segment elevation. In group 2, 14 patients had ST-segment elevation during pain in the precordial leads and eight subjects had these ECG changes in leads II, III, aVf. No patient had ST-segment depression during angina; one patient had bradycardia during pain. Two had short runs of ventricular tachycardia and two others had multiple premature ventricular contractions. All patients were admitted to the coronary care unit. An exercise test was performed in only four patients: Only one had ST-segment depression and the other three had ST-segment elevation, suggesting that exercise per se brought on coronary spasm.

Arteriographic Findings

Coronary arteriograms were read separately by two observers. The lesions were judged to be anatomicallv significant when they reduced the diameter of the vessels by at least 75%.

The number of diseased vessels is shown in table 2. In group 1, four patients had a one-vessel disease, six patients had two-vessel disease and three had three-vessel disease. Five patients had spasm; it occurred spontaneously in three and was induced by methergine in two. Spasm was located in the right coronary artery in three patients; one patient had a spasm of the left anterior descending artery and another had spasm simultaneously in the right coronary artery and left anterior descending artery.

Ten patients of group 2 had one-vessel disease; seven had two-vessel disease and five had three-vessel disease. Twelve patients had spasm, which was located most often in the left anterior descending artery (seven patients). It occurred in the right coronary artery in four patients. The remaining patient had spasm in two vessels, the left anterior descending and right coronary arteries.

Hemodynamic and Cineangiographic Findings

The comparative values of the left ventricular end-diastolic pressure (LVEDP), cardiac index (CI), left ventricular end-diastolic index (LVEDVI) and ejection fraction (EF) are shown in figure 1. The mean values for groups 1 and 2 were, respectively, LVEDP — 13.8 and 11.2 mm Hg (normal value in our laboratory 10.5 ± 3.2 mm Hg); CI — 3.36 and 2.76

<table>
<thead>
<tr>
<th>Table 1. Clinical Presentation of Patient Population</th>
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<tr>
<td>Group 1 (15 patients)</td>
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<tr>
<td>Male/female</td>
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<td>Age (years)</td>
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<tr>
<td>Patients with angina at rest</td>
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<tr>
<td>Patients with syncopal episodes</td>
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<tr>
<td>Patients with risk factors for coronary artery disease</td>
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<td>Patients with ST-segment elevation during attacks</td>
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<tr>
<td>Anterior leads</td>
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<td>Inferior leads</td>
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<th>Table 2. Coronary Arteriographic Findings</th>
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<td>One-vessel disease</td>
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<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Group 1</td>
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<tr>
<td>Group 2</td>
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1/min/m² (normal value 3.5 ± 0.62 1/min/m²);
LVEDVI = 92.7 and 80.6 ml/m² (normal value 81 ± 15 ml/m²) and EF = 57% ± 10% and 60% ± 12% (normal value 68% ± 8.8%). Although the LVEDVI and the EF appeared to be worse in group 1, differences between the two groups were not statistically significant.

Results

During the immediate postoperative period, two patients died in each group (surgical mortality: 15.3% in group I and 9% in group II). Two deaths (one in each group) were related to a low cardiac output. One patient in group 2 died with an intractable arrhythmia and the other (group I) died from an air embolism. Of the 31 patients who survived surgery, all were alive at the end of the follow-up period. The survivors have a mean follow-up period of 36.8 ± 11.4 months (21-57 months) in group I and 20 ± 9 months (6-38 months) in group II. All the patients in the two groups took dipyridamole. At the end of the follow-up period, patients underwent clinical, x-ray and ECG investigations. In 16 patients a new coronary arteriogram was performed to assess the patency of the grafts. In 23 patients, provocative testing by injection of 0.4 mg of methergine was undertaken after a full explanation of the procedure and after informed consent was obtained. The protocol of provocative testing varied, depending on whether the patient had or did not have repeat coronary arteriography to assess the patency of aortocoronary bypass. In the 16 patients restudied, provocative testing included ECG and aortic pressure monitoring, opacification of the grafted vessel and the bypass and was repeated 1, 3 and 5 minutes after injection of the drug. If spasms had been observed before operation in a vessel, the opacification of this artery was obtained after administration of methergine to determine if spasm could still be observed. In the seven remaining patients, provocative testing was performed in the coronary care unit according to the method published by Nelson et al. and the effects of the drug were followed only from ECG changes.

Results for each group are presented below.

Group I (n = 11)

Nine patients were free of pain and were clinically improved. They experienced no syncope and had no heart failure. One patient who had bypass of the left anterior descending artery suffered an inferior infarction after operation that was rather unexpected, because the right coronary and circumflex arteries were normal before operation.

An exercise test was performed in these nine patients. Their maximal heart rate during exercise was 95 ± 4.5% of the age-predicted maximal heart rate. The exercise ECG was negative in all but one patient.

Six patients (10 grafts) were restudied by coronary arteriography. Nine of 10 grafts were patent. Provocative testing with methergine was performed in the nine patients (six provocative tests during repeat coronary arteriography). The test induced spasm and ECG changes in one patient.

Finally, there were two poor results (two of 11, 18%); two patients remained asymptomatic and suffered from severe attacks similar to those observed before operation. In one patient, a severely narrowed (75%) right coronary artery with a spontaneous spasm superimposed on the lesion was bypassed. The postoperative catheterization showed that graft was patent. However, provocative testing induced spasm on that part of the right coronary artery distal to the graft. The second patient had a 95% narrowing of the left anterior descending artery before surgery. Spasm was also spontaneously observed at the site of the lesion. After operation, the graft was patent but spontaneous spasm again occurred in two vessels. Spasm occluded the part of the left anterior descending artery distal to the graft and was also observed in the midportion of the right coronary artery, which was previously normal. Therefore, these two patients were treated with a calcium antagonist drug and are presently asymptomatic.
Group 2 (n = 20)

All patients but one are asymptomatic; they are free of pain, and they had neither syncope nor heart failure. No patient had peri- or postoperative infarction. An exercise test was performed in nine patients and they were able to reach 91 ± 8.9% of the age-predicted maximal heart rate. In all patients except one, ECG exercise test was negative. In the three patients with preoperative ST-segment elevation, the test became negative, suggesting that spasm brought on by exercise was alleviated by the combination of bypass surgery and plexectomy.

Ten patients had recatheterization and all the grafts (n = 12) were patent. Provocative tests were performed in 14 patients (10 during the restudy and four in the coronary care unit). In these 14 patients, of whom eight had spasm previously demonstrated before operation, methergine did not induce spasm or ECG changes in 13. However, this test was positive in one patient. This 45-year-old man had variant angina related to a severe (95%) stenosis of the proximal part of left anterior descending artery. Spontaneous spasm was superimposed on the lesion, totally occluding the vessel. He was operated on 2 days after coronary arteriography. A plexectomy was performed together with venous bypass of the left anterior descending artery. He immediately improved, but 3 months later he had repeated angina. ST-segment elevation was observed in precordial leads after injection of methergine. He was restudied by left-heart catheterization. The graft was patent; however, spasm with ST-segment elevation could be induced by the provocative test, and when it occurred the bypass was ineffective. He received nifedipine (40 mg orally) together with isosorbide dinitrate. He became asymptomatic and further provocative testing could not induce the ECG changes previously observed. The poor results are not related to an occlusion of the grafts but to the persistent spasm.

Discussion

The overall results of surgical treatment in variant angina are usually not as good as in other forms of angina pectoris, either stable or unstable. In 1974, Gaasch et al.9 reported from the literature a 12.5% rate of operative deaths, 19% postoperative myocardial infarction and a 57.1% rate of graft occlusion. More recently, Grondin and Limet10 reviewed the surgical literature and found that only 56% of patients with variant angina showed good results.

This difference in the overall outcome between the two forms of angina might be explained by the spasm frequently observed in the variant angina. Previous works19, 21 have demonstrated that attacks of variant angina are not induced by an increase of myocardial oxygen demands, but by a sudden reduction of myocardial supply. Myocardial scintigraphy14-18 and coronary sinus flow measurement22 by thermodilution have shown that myocardial blood flow declines drastically during episodes of spontaneous variant angina and returns to normal after the attacks. At the same time, the widespread use of coronary arteriography shows that spasm is indeed an essential factor in the pathogenesis of variant angina. In our data, 30 of the 53 patients with variant angina demonstrated evidence of coronary artery spasm. In patients with otherwise angiographically normal coronary arteries, artery grafting is contraindicated. Most often, spasm is superimposed on fixed arteriosclerotic coronary artery disease. Although a graft will bypass the narrowing, the spasm can persist and the bypass may be inefficient if spasm occurs distally to a patent graft, occluding the distal runoff. This was demonstrated in three of our patients.

Moreover, we observed in one patient that spasm can appear on another vessel that had not been grafted because it was previously angiographically normal. Therefore, it appears that the treatment of variant angina with organic narrowing should have two aims: to bypass the organic narrowing and to suppress the spasm. If these two factors cannot be treated, poor results should be expected, with persistence of attacks or myocardial infarction or sudden death.

The studies of Yasue et al.18 suggested that enhanced activity of the parasympathetic nervous system is involved in the initiation of the attack by stimulation of the sympathetic nerve, which can induce coronary arterial spasm by activating alpha (vasoconstrictors) receptors. More recently, Ricci et al.19 showed that coronary spasm is a manifestation of altered autonomic activity. The observation of spasm during manipulation of Wrisberg's ganglion noted in two of our cases, can be considered also as suggestive. Nervous system factors are certainly not the only cause of spasm, but one can assume that they play an important role. In light of this, it was logical to consider the usefulness of denervation.

In 1977, Clark et al.20 reported eight cases of aorto-coronary bypass followed by cardiac denervation. The denervation was partial (stripping of the great vessels) in three cases. One patient died at operation and two patients were alive and well more than 2 years later. Two patients had total cardiac denervation by autotransplantation. One died, and the other one is well 3 years after the operation. This latter patient was restudied after the operation and spasm of the coronary artery was again demonstrated by the ergotrate stimulation test. With respect to this last observation, Clark et al.20 wrote that induced coronary spasm can occur despite total denervation.

Cipriano et al.21 demonstrated that ergonovine maleate can induce the same degree of coronary arterial narrowing in heart transplant recipients and in patients with normally innervated hearts who did not develop coronary spasm. Thus, the normal pharmacologic response to ergonovine maleate was due to a direct vasoconstriction action of the drug, and this action was independent of neural extrinsic control. Ergot alkaloid did not provoke spasm after operation in 14 patients of group 2 who had plexectomy; the fact that eight of them had spasm before operation suggests strongly that plexectomy is beneficial.

However, we do not know why ergot alkaloid in-
duced spasm after total denervation (autotransplantation) and not after plexectomy. This technique was first described by Arnulf.22 According to this author, the heart is innervated from both the parasympathetic and the sympathetic systems. They emit fibers that form the superior, middle and lower cardiac nerves and they converge to form the cardiac plexus; they form a rich network of fibers surrounding the aortic root and are divided into three main plexus: the pre-aortic plexus is located anteriorly to the aortic root, the second plexus is located in the subepicardial region of the left atrium, the third is located in the space delineated laterally by the pulmonary artery, posteriorly by the trachea and medially by the ascending aorta, including the large and inconsistent ganglion of Wrisberg.

The location of these plexus explains the difficulty in achieving a good plexectomy. First, the approach to this area is difficult. Second, because of bleeding induced by the heparinization, the plexectomy had to be performed before starting extracorporeal circulation, and before performing the saphenous graft that crosses the area of plexectomy. Third, the rich network of fibers explains why plexectomy can be incomplete, especially as far as the posterior plexus is concerned. The evidence of a good plexectomy seems to be a change in heart rate during the resection and especially the appearance of tachycardia: all the patients of group 2 with good results have shown a significant increase in heart rate. The only one who had poor results with persistent spasm had a bradycardia during and immediately after resection.

Plexectomy associated with coronary artery grafting in variant angina was first performed by Grondin and Limet10 in two patients with organic narrowing of coronary arteries. These patients remained asymptomatic over 18 and 12 months respectively. To our knowledge, there are no other publications on this subject. The results obtained in our series of 22 cases seem to confirm the preliminary report of Grondin and Limet10; the overall outcome, taking into account perioperative deaths, infarction and persistent attacks, suggests that plexectomy associated with bypass grafting gives better results (86%) than bypass alone (61%) (table 3). Moreover, it is important to observe that there was only 5% of persistent recurrent attacks in group 2 while this recurrence rate was 18% in group 1.

Nevertheless, these preliminary results should be interpreted with caution because of obvious difficulties in evaluating the effects of treatment in patients who have a wide spontaneous variability of symptoms. However, these results do suggest that plexectomy associated with aortocoronary bypass improves the results of surgical treatment in variant angina with organic narrowing. Considering these encouraging preliminary results, plexectomy was attempted in three other patients who had severe variant angina related to spasm alone with otherwise angiographically normal coronary arteries. Considering the failure of medical therapy to give even a slight relief of attacks, plexectomy alone was performed. A mean of 35 months later (range 12–58 months) the three patients are free of pain. Various continuous ECG recordings have not shown any ECG changes and provocative testing with methergine was unable to reproduce the ST-segment elevation that was preoperatively observed after injection of this drug. Obviously, the small number of cases does not permit us to draw any conclusions, but such observations are encouraging and the validation of this approach requires further confirmation.

### Table 3. Overall Outcome

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<th>Follow-up (months)</th>
<th>Postoperative deaths</th>
<th>Infarction</th>
<th>Persistent attacks</th>
<th>Persistent spasm</th>
</tr>
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<tbody>
<tr>
<td>Group 1</td>
<td>13</td>
<td>36.8 ± 11.4*</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(21–57)</td>
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<tr>
<td>Group 2</td>
<td>22</td>
<td>20 ± 9*</td>
<td>2</td>
<td>1</td>
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<td>1</td>
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<tr>
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<td>(6–31)</td>
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*Mean ± sd.
Myocardial Perfusion as an Indicator of Graft Patency after Coronary Artery Bypass Surgery

ALBERT J. KOLIBASH, M.D., THOMAS D. CALL, M.D., CHARLES A. BUSH, M.D., MARC R. TETALMAN, M.D., AND RICHARD P. LEWIS, M.D.

SUMMARY Stress and resting myocardial perfusion were assessed in 38 patients who received 96 grafts. Stress perfusion was evaluated with thallium-201 and resting myocardial blood flow distribution with radionuclabeled particles. When both stress and rest perfusion were normal, graft patency was 82% (51 of 62 grafts). Graft patency was also high (81%, 13 of 16) in areas where stress perfusion abnormalities resolved or became less apparent at rest. However, when stress perfusion defects remained unchanged at rest, the graft was likely to be occluded (73%, 11 of 15). Maintenance of normal rest perfusion or improvement of rest perfusion postoperatively was also associated with a high graft patency rate (80%, 35 of 44), whereas the development of new rest perfusion defects postoperatively implied graft occlusion (86%, six of seven).

CORONARY ARTERY bypass grafting to potentially ischemic areas of myocardium is widely used to treat patients with coronary artery disease. Because success or failure of such surgery seems largely determined by graft patency, it has become common in many institutions to restudy postoperative patients with a cardiac catheterization.

Until recently, a postoperative catheterization appeared to be the only reliable method of assessing graft patency. However, developments in nuclear cardiology imaging techniques have provided reliable methods of evaluating myocardial perfusion. Thallium-201, the radionuclide most commonly used to assess myocardial perfusion, may provide useful information concerning graft patency in patients who have undergone myocardial revascularization.

Another useful technique in evaluating myocardial blood flow distribution is the instillation of radionuclabeled particles directly into the coronary circulation. Because two radionuclides are used, it is possible to distinguish the blood flow distribution from grafts and that from the native circulation, thus providing information not always obtainable from thallium studies. Total myocardial blood flow distribution is indicated by the dual image, which is a combination of both graft and native vessel perfusion. Therefore, the dual or combined image, which is comparable to a resting thallium image, can be compared with a stress thallium study to distinguish stress-induced defects from defects that represent fibrosis.

We assessed both stress and rest myocardial perfusion after myocardial revascularization and correlated postoperative perfusion characteristics with graft patency and native vessel anatomy to predict the success or failure of coronary bypass surgery.
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