Exercise Stress Testing in Evaluation of Aortocoronary Bypass Surgery

Report of 123 Patients

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SUMMARY
Graded exercise treadmill tests (ET) were performed on 123 patients who had undergone aortocoronary bypass surgery. All had angina preoperatively (preop) and 77% were in Class III or IV for angina. Postoperatively (postop), 68% were free of angina. Eighty-three patients had ST-segment changes of 0.1 mV or greater during stress preop (positive), 38 of which (46%) converted to electrocardiographically negative postop. Among the 30 patients (36%) remaining positive during stress postop, 19 (63%) were angina free despite ST-segment depression during stress. Among the 17 patients with negative ET preop, there were no conversions to positive postop. Twenty-three patients had undetermined ET preop; 13 remained undetermined postop, 4 were positive and 6 were negative. Patients experiencing a perioperative myocardial infarction more frequently had a negative postop ET. Among 27 selected patients undergoing postop angiography, there was good correlation between relief of symptoms and successful myocardial revascularization.

This study demonstrates that dramatic improvement in angina after aortocoronary bypass surgery can be objectively substantiated in most patients. Subjective symptoms of angina are frequently absent during myocardial ischemia postop, emphasizing the importance of exercise testing in objective evaluation of surgical results.

Additional Indexing Words:
Coronary artery disease Ischemic heart disease Graded exercise test Angina pectoris Bypass grafts

AORTOCORONARY BYPASS surgery has achieved great popularity over the last several years. In properly selected patients, the procedure can be performed with a mortality of less than 10%.1, 2, 3, 4 and early results indicate marked relief from angina pectoris in a majority of surviving patients.1, 2, 4 Evaluations of previous surgical and medical therapeutic interventions for coronary artery disease have been hampered by great difficulty in quantitation of patient symptomatology and from lack of objective signs of improvement.5, 6 For the most part, the same criticism is true in evaluations of aortocoronary bypass surgery.7 Preliminary data on small groups of patients have demonstrated improvement in exercise performance8, 9, 10 and suggest improvement in ventricular function following surgery11 in highly selected patients.

The prime purpose of this study was to add objective information, obtained from a reproducible, well-standardized, graded exercise test performed on a large number of patients before and after surgery, to the preoperative data base and the subjective response to bypass surgery. The presence or absence of significant ST-segment changes and the maximal heart rate achieved during stress were compared to the same patient's preoperative performance. The correlation of these findings with symptomatic improvement, postoperative myocardial infarction, and graft patency form the basis of this report.
Methods

Two hundred and one patients had exercise testing and survived bypass surgery between April, 1970, and June, 1972. The study group consisted of the 123 patients (61% of the population) who returned for follow-up exercise testing either in the outpatient clinics and/or the inpatient services at Duke University Medical Center. All patients were tested preoperatively if the cardiovascular status did not contraindicate exercise testing, and if other physical handicaps did not interfere with the exercise. Some of the patients whom we felt could not be exercised preoperatively were exercised postoperatively. The postoperative exercise test was performed two to 20 months after surgery. Three-fourths of the group was exercised five to 12 months after surgery.

After obtaining standard electrocardiograms, the patients were exercised according to the protocol of Bruce and Horsten12 using the graded multistaged treadmill test. Exercise was continued for 3 min at each treadmill stage (stage I: 1.7 mph, 10% grade; stage II: 2.5 mph, 12% grade; stage III: 3.4 mph, 14% grade; stage IV: 4.2 mph, 16% grade; stage V: 5.0 mph, 18% grade).

Chest pain was not included in the definition of a positive or negative test. All ECGs were read without knowledge of the patient’s operative or angiographic status or clinical condition. The readings were accepted if agreed upon by at least three cardiologists. Tests were placed in the “undetermined” category (see below) if disagreements could not be resolved. A positive test was defined as segmental ST change of 0.1 mV (0.08 sec duration) in any of 12 continually monitored leads. When digitalis effect or nonspecific ST-T changes were present on the resting electrocardiogram, 0.2 mV ST change was required for inclusion in the positive group13 (unpublished data, Duke University Medical Center, Cardiovascular Division). Exercise tests were interpreted as negative only if the patient achieved 85% of the predicted maximal heart rate14 at peak exercise ("target heart rate") without significant ST segment changes. The test was placed in the undetermined category if any of the following occurred: 1) the patient failed to achieve target heart rate in the absence of significant ST-segment change; 2) the patient had resting electrocardiographic abnormalities such as bundle branch block that precluded evaluation of the ST-segment; 3) multiple premature beats or unstable baseline activity at maximal heart rate obscured possible ST-segment changes; or 4) differences in ECG interpretation existed.

One hundred and seven of the 123-patient group had preoperative exercise tests according to the same protocol. Sixteen patients were not exercised preoperatively because of severe accelerating rest pain. Since all had significant transient ST-segment changes accompanied by chest pain, they were included as preoperatively positive.

Complete medical history, physical examination, left and right heart catheterization, and Fick cardiac outputs were obtained preoperatively. Left ventricular cineangiograms and selective coronary arteriograms were performed utilizing the Judkins15 or Sones16 techniques in multiple views. The 35 mm cine film thus obtained was reduced to 16 mm for ease of analysis. The operative techniques for aortocoronary bypass surgery have been described elsewhere.17 The procedures were performed using hypothermia and cardiopulmonary bypass except in one case in which cardiopulmonary bypass was not used.

Serial electrocardiograms were obtained in the postoperative period in all cases to determine the incidence of “perioperative” myocardial infarction, which was defined as the occurrence of new diagnostic Q waves or new permanent intraventricular conduction delay in the immediate postoperative period.18 Transient or permanent ST or T wave changes or transient conduction defects were not accepted as evidence of perioperative myocardial infarction.

Postoperative catheterizations were performed on 27 selected patients, all of whom had diagnostic (positive or negative) postoperative treadmill tests. This does not represent a complete or randomized group since most of these patients were restudied because of recurring chest pain. The patients were divided into two groups: one in which at least one graft was patent and a second in which all grafts were closed. The patent group was further divided into two subgroups according to revascularization. Complete revascularization was defined as the presence of a patent graft supplying all major coronary arteries with significant stenosis. Incomplete revascularization refers to those patients in whom at least one stenotic vessel had not been supplied by a patent graft.

Results

All patients had angina prior to surgery and 77% were in New York Heart Association Class III or IV for chest pain. Postoperatively, many patients experienced dramatic subjective improvement and 68% were completely free of angina. Forty-three percent had a documented myocardial infarction prior to surgery. Twenty-five percent of the patients had single vessel coronary artery disease (>70% stenosis), 38% had two vessel disease, and 37% had three vessel disease. Single bypass grafts were performed in 53% of patients, double grafts in 41%, and triple grafts in 6%.

The results of the preoperative treadmill exercise tests are summarized in fig. 1. Sixty-seven patients (54%) had positive tests as previously defined. An additional 16 patients (13%) were included as positive since they had severe accelerating angina with accompanying ST-T changes and were too ill to be exercised. Twenty-three patients (19%) had preoperative tests in the undetermined category as previously defined (17 of the 23 patients were so categorized because of failure to reach predicted target heart rate). Seventeen patients (14%) had negative tests. The mean maximum heart rate during stress was 138/min. Twenty percent of the
Comparison of stage of treadmill exercise tests (above) in 123 patients with the number of patients in each category. Shown below is the maximum stage of the treadmill test attained (I-V) both preoperatively and postoperatively expressed as a percent of the total group.

Exercised patients terminated in stage I, 45% in stage II, 23% in stage III, and 9% in stage IV.

The relationship between the preoperative and postoperative treadmill exercise tests is shown in figures 1 and 2. Among 83 patients categorized as positive preoperatively, 30 patients (36%) remained positive during stress postoperatively. Thirty-eight patients (46%) converted from positive before surgery to negative after surgery. The remaining 15 patients (18%) had an undetermined test postoperatively. Among 17 patients with negative treadmill exercise tests preoperatively, none converted to positive in the postoperative period. Eleven remained negative and six were in the undetermined category. Among the 23 patients with undetermined treadmill exercise tests, four were positive postoperatively, six were negative and thirteen remained in the undetermined category (usually for the same reasons, i.e., inability to achieve target heart rate). The mean maximum heart rate in the postoperative exercise tests was 145/min. Seven percent of the patients terminated exercise in stage I, 20% in stage II, 38% in stage III, 30% in stage IV, and 5% in stage V. (See fig. 1 for comparison to preoperative tests.) Therefore, most patients exercised longer and achieved a higher maximum heart rate postoperatively.

The correlation of postoperative clinical symptoms with the postoperative treadmill exercise test was as follows: among 34 patients with positive tests, 19 (56%) were free of angina, 11 (32%) had angina with mild or moderate exertion, and 4 (12%) had nocturnal or rest pain; of 55 with negative tests, 45 (82%) were free of angina, 5 (9%) had angina with mild or moderate exertion, and 5 (9%) had nocturnal or rest pain.

A significant number of patients had undetermined treadmill exercise tests before and after surgery in most cases because of failure to reach target heart rate (74% of the undetermined tests preoperatively and 91% of the undetermined tests postoperatively). These patients were excluded in a further analysis which involved only those who had diagnostic treadmill exercise tests both preoperatively and postoperatively (fig. 3). There were 79 patients in this group. Among the 68 patients who had positive tests preoperatively, 30 (44%) remained positive postoperatively. Thirty-eight patients (56%) converted from positive to negative tests. All 11 patients who were negative preoperatively remained negative postoperatively. It should be emphasized that among the 30 patients remaining positive postoperatively, 19 (63%) were clinically free of angina pectoris at the time of examination and none of the 19 had angina during maximal stress at which time significant ST changes occurred. Ninety percent of the patients with negative postoperative tests were free of angina.

Since the occurrence of a myocardial infarction during surgery or in the immediate postoperative period might be one explanation for the conversion of a positive preoperative to a negative postoperative treadmill exercise test, the entire patient group was evaluated by serial electrocardiography and the
patients were categorized by the presence or absence of perioperative myocardial infarction as defined in Methods. Perioperative myocardial infarction occurred in 20 patients. The postoperative treadmill exercise test was positive in three, negative in 12, and undetermined in five. This subgroup of patients with perioperative myocardial infarction did not differ significantly from the group without this complication.

An attempt was made to correlate the status of revascularization with results of postoperative treadmill exercise test in 27 patients having diagnostic postoperative tests and undergoing repeat cardiac catheterization. This does not represent either a complete or a randomized sample since most of these patients were restudied because of recurrent chest pain. Among the 18 patients having at least one patent graft, six (33%) had positive treadmill exercise tests while 12 were negative. In contrast, of nine patients with all grafts closed, six (67%) had positive tests while three were negative (fig. 4A). It is of interest that the latter three patients all experienced perioperative myocardial infarction.

The patients were further divided into groups having complete or incomplete revascularization as defined in Methods. Among the seven patients with complete revascularization, six had single vessel disease; all six had negative postoperative treadmill exercise tests (four were positive preoperatively). One patient with two vessel disease had two patent grafts but remained positive postoperatively. Conversely, those with incomplete revascularization had a 55% incidence of positive postoperative treadmill exercise tests (11 of 20 patients) (fig. 4B). Relief of angina during follow-up was compared to the two groups, and it was found that six of seven patients with complete revascularization were free of angina postoperatively, compared to only eight of 20 patients (40%) in the incomplete revascularization group ($P < 0.05$).

**Discussion**

The graded multistaged exercise treadmill test is a widely used and well-standardized examination which can be safely performed in patients with severe coronary artery disease. Comparison of diagnostic postoperative treadmill exercise tests and graft patency in 27 selected patients who underwent postoperative catheterization. Patent = at least one graft patent; closed = all grafts closed; complete = all major coronaries with significant disease supplied by a patent graft; incomplete = at least one stenotic vessel has not been supplied with a patent graft; pts = patients.

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significant side effects associated with the treadmill exercise tests; specifically, myocardial infarction, syncope, or arrhythmias requiring therapy did not occur.

The placebo effect of myocardial revascularization has recently been emphasized.\textsuperscript{1, 22, 23, 24, 25} This effect appears to be extremely important in evaluating therapy for ischemic heart disease since strong placebo effects have been reported following sham procedures\textsuperscript{23, 24} as well as from internal mammary implantation\textsuperscript{23, 24, 25}. Because of the vagaries encountered in assessing the efficacy of aortocoronary bypass surgery on the basis of subjective symptoms, exercise treadmill testing before and after surgery provides valuable objective data for the evaluation of surgical intervention.

In large populations, exercise stress tests have very definite prognostic implications in terms of the risk of future cardiovascular events.\textsuperscript{19, 21, 26, 27, 28, 29} Several studies have documented the reproducibility of the exercise stress test both in terms of degree of ST-segment depression and maximal heart rate achieved at the onset of ischemia\textsuperscript{12, 30, 31} (directly related to maximal oxygen consumption\textsuperscript{12, 21}). On the basis of these studies, it may be presumed that a patient has significant objective evidence of improvement if, after having electrocardiographic evidence of ischemia at maximal stress before surgery, the postoperative patient achieves the same or greater maximum heart rate (oxygen consumption) without significant electrocardiographic evidence of ischemia. The pitfalls in using increased duration of stress as an indicator of improvement have been demonstrated by data obtained before and after therapy with propranolol. Decreased heart rates as well as other effects of beta-blockade probably allow the patient to exercise longer (lower oxygen consumption at the same level of stress).\textsuperscript{32, 33, 34} However, at comparable heart rates or heart rate-blood pressure products, there is little change in the frequency of electrocardiographic evidence of ischemia.\textsuperscript{32, 33} In this study, although the duration of exercise postoperatively was frequently greater than prior to surgery, interpretation of this data is difficult for the above reason as well as a marked variability in patients' physical activity and degree of conditioning before and after surgery. Data relative to the changes in duration of exercise were, therefore, not enumerated in the current study.

The importance of a carefully performed exercise stress test before surgical intervention cannot be overemphasized since many patients with significant coronary stenosis have a normal exercise performance.\textsuperscript{21, 32, 36, 37} Indeed, a series of patients with significant arteriographically documented coronary disease were exercised at this hospital using the same treadmill exercise test and interpreted by the same observer (A.B.). Among 281 patients having a diagnostic treadmill exercise test, there was a stepwise increase in the frequency of positive tests based on the severity of coronary disease with 35%, 67%, and 80% having positive tests in one, two, and three vessel coronary artery disease respectively. In addition to those having adequate but negative tests, a significant number of patients with documented coronary artery disease are unable to reach their target rate (85% of maximum predicted heart rate) even in the absence of ST-segment change and/or angina probably secondary, in part, to ischemic heart disease.\textsuperscript{28} This group would fall in our "undetermined" category and have been included in this report both for completeness and because a significant number of these patients were able to improve their exercise performance and achieve their target rate after surgery.

Exercise stress testing has been utilized in the postoperative evaluation of myocardial revascularization by internal mammary implantation. In a report by Kassebaum et al.,\textsuperscript{30} it was demonstrated that 83% of 29 patients with implant occlusion or nonrevascularization had positive stress tests while five patients with angiographically proved significant revascularization reverted to negative during stress. Langston et al.\textsuperscript{40} reported lack of improvement on exercise stress testing after internal mammary implantation in 20 patients, only three of whom had significant collateral flow. It is noteworthy that 85% were improved symptomatically.

The conversion of a positive treadmill exercise test preoperatively to a negative test after surgery is, indeed, a dramatic change. As mentioned in the Results section, this event correlates well with freedom from angina in the postoperative period, and at first glance, suggests successful revascularization. However, another mechanism for the conversion of a positive to negative test following surgery may be by infarction of a previously ischemic zone of myocardium. Support for this hypothesis comes from two reports which demonstrate a higher incidence of positive exercise stress test in patients with angina as their chief manifestation of coronary artery disease compared to patients with myocardial infarction by history but without significant angina.\textsuperscript{38, 41} To the authors' knowledge, there is no available data comparing exercise stress tests before
and after myocardial infarction in the same patients. The present study reveals that a small group of patients experiencing perioperative infarction had a slightly higher frequency of negative postoperative treadmill exercise tests although the differences were not statistically significant. Long term follow-up studies, including repeat hemodynamic and angiographic evaluations to determine new areas of asynergy, graft patency, changes in ventricular function, and the status of the native coronary circulation will be necessary to further evaluate the significance of this finding.

Since the vast majority of patients in our series underwent aortocoronary bypass surgery for the relief of symptoms of angina pectoris, freedom from angina postoperatively must be one factor in any evaluation of this procedure. However, since there are multiple possible explanations for pain relief in addition to adequate revascularization, it is important to critically evaluate such patients and obtain objective data demonstrating improvement to corroborate the clinical findings. A dramatic and surprising finding in this study was the absence of angina both clinically and during treadmill exercise in 63% of electrocardiographically positive patients who were exercised in the postoperative period. Most of these patients have returned to full activity and many are engaged in exercise programs such as jogging and bicycling. None of these patients are receiving vasodilators or propranolol. Although this significant subgroup represents a dilemma in terms of management, we believe that the awareness of persistent electrocardiographic ischemia during stress is quite important in directing the rehabilitation of patients after aortocoronary bypass surgery and in prescriptions for work and physical activity. The fate of patients in this group is unknown and must await long term follow-up.

Attempts to correlate subjective and objective signs of improvement with graft patency are open to criticism. Even though a closed graft obviously offers no increase in myocardial flow, the patient has undergone a surgical procedure with possible trauma to the myocardium and native coronary circulation. In addition, progression of the patient's coronary atherosclerosis is not unexpected and may account for changes in symptoms, diminished exercise tolerance, and increased ischemia during stress. Among patients with at least one patent graft, evaluation of the efficacy of revascularization should also take into account 1) the changes in flow characteristics in the native circulation secondary to surgical trauma and the additional blood supply to the coronary tree, 2) variable degrees of distal coronary atherosclerosis, 3) variation in the size and anatomical distribution of the vessels distal to a bypass graft, 4) possible pathological changes within the graft itself, and 5) areas of significant coronary narrowing which have not received bypass grafts. The inability to estimate changes in coronary blood flow by injection of contrast material in a venous graft and to extrapolate this estimate to changes in flow during exercise further complicates the issue. However, in spite of these objections, we were able in a highly selected patient population (studied predominantly because of the recurrence of chest pain) to correlate clinical symptoms, graft patency, and the occurrence of a positive or negative postoperative treadmill exercise test. In an ideal sense, a patient was characterized as having complete revascularization if all areas of significant coronary stenosis were supplied with a patent bypass graft. The remainder were classified as incomplete revascularization. Six of seven (86%) patients with complete revascularization were free of angina in the postoperative period and 86% of these patients had a negative postoperative treadmill exercise test compared to the group with incomplete revascularization in which only 40% were free of angina and only 45% had negative postoperative tests.

In view of these findings, the entire patient population with diagnostic (positive or negative) postoperative stress tests was subdivided into two groups on the basis of completeness of revascularization. The incomplete group includes all patients with significant lesions not revascularized or supplied with grafts known to be closed (50 patients). Twenty-six patients (52%) had positive tests and 24 were negative. The remainder of the study population, 54 patients, were felt to have a complete revascularization procedure in terms of the number of vessels diseased and number of grafts inserted. It should be noted that the "completeness" of revascularization is not known in the strict sense as only a few of these patients underwent postoperative cardiac catheterization to determine graft patency. With this reservation in mind, in the "possibly complete" group, eight (21%) had a positive postoperative treadmill exercise test compared to the incomplete group in which 26 of 50 patients (52%) had a positive postoperative test ($P < 0.01$).
EXERCISE STRESS TESTING/BYPASS SURGERY

The results of this study seem to support with objective data the clinical impression of improvement in ischemic pain following bypass surgery. The patient population studied does exclude operative deaths, deaths which occurred during the first six months postoperatively, and those patients who have suffered severe complications of surgery or new insults which precluded a treadmill exercise examination. Among those exercised postoperatively, in the absence of perioperative infarction, a change from an ischemic to nonischemic electrocardiogram during stress seems to represent a more favorable relationship between myocardial oxygen demand and supply. In addition, a second subgroup of patients having persistent electrocardiographic evidence of myocardial ischemia in the absence of clinical symptoms demonstrates a discrepancy between subjective and objective findings, the significance of which awaits long term follow-up studies. Data from a third subgroup characterized by the achievement of complete revascularization demonstrates good correlation with subjective improvement and the presence of a negative postoperative treadmill exercise test.

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