Persistent Improvement After Coronary Bypass Surgery: Ergometric and Angiographic Correlations at 5 Years

M. HEIKKI FRICK, M.D., PEKKA-TAPANI HARIOLA, M.D., AND MATTI VALLE, M.D.

SUMMARY One hundred patients with angina pectoris who fulfilled specific entry criteria were randomly assigned to either medical therapy or bypass surgery. These groups were subjected to annual exercise testing during a 5-year follow-up period. The degree of revascularization was assessed by graft and native vessel angiography at 3 weeks, 1 year and 5 years after the operation.

The exercise tolerance of the medical group remained largely unchanged during the follow-up. Eighty-five to 95% of the patients were using β-blocking compounds at the successive testing situations. The surgical group exhibited a sustained improvement in exercise tolerance: Total work increased by 39–66% (p < 0.02–0.001) and maximal ergometric load by 23–35% (p < 0.01–0.001), and maximal ST depression decreased by 39–61% (p < 0.05–0.001). The use of β-blocking compounds in the surgical group steadily increased, from 44% at 6 months after operation to 63% of patients at 5 years. Division of the surgical group into subsets of complete and incomplete revascularization revealed that the improvement was confined to complete revascularization. Thus, the improved exercise tolerance after bypass surgery was a result of successful reestablishment of effective coronary perfusion; despite graft attrition (15% in 5 years) and new lesions in the native arteries, this improvement persisted for 5 years with appropriate medical therapy.

The effectiveness of coronary bypass surgery in alleviating symptoms in patients not satisfactorily controlled by medical therapy is generally recognized. However, the long-term effectiveness of this treatment has been questioned because of graft attrition and progression of the disease in native arteries. In this prospective, randomized 5-year follow-up study, we evaluated the persistence of improved exercise tolerance after surgery and the impact of the degree of revascularization.

Patients and Methods

Selection of Patients

In summer 1973, we joined the European Coronary Surgery Study and tailored our angiographic services to channel patients consecutively into the trial as well as to match the demand for repeated postoperative coronary angiograms. In accepting patients for the randomized study, the following entry criteria were used: angina pectoris despite antianginal therapy with nitrates and β-blocking agents, males under 65 years of age, a positive exercise test (angina and ≥1 mm square-wave ST-segment depression), left ventricular (LV) ejection fraction exceeding 50%, at least two-vessel disease as shown by coronary angiography (left main included), no other planned concomitant cardiac surgery, and coronary artery anatomy suitable for grafting. Patients with unstable angina were not included, but were offered bypass surgery.

From September 1973 to January 1976, primary selective coronary angiography was performed on 301 patients. The eligibility of the patients for the random-
ized study was assessed at a weekly meeting of cardiologists, radiologists and cardiac surgeons. During the 28-month enrollment period, 100 patients met the entry criteria and were randomized into medical therapy and bypass surgery using the sealed envelope system. These patients have been followed for 5–7 years, with 100% follow-up at 5 years.

Exercise Testing and Angiography

Each patient underwent a complete history, physical examination, chest x-ray and routine blood chemistry. General dietary advice was given and treatment with hypolipidemic drugs was started in some patients. Smoking cessation was encouraged. No specific exercise therapy was prescribed. All the patients used short- or long-acting nitrates and were taking β-blockers, agents, which were stopped for a week before the exercise testing at entry. The testing was performed as earlier described in detail. Briefly, successively increased loads were imposed by an electrically braked bicycle ergometer until angina or dyspnea that required nitroglycerin was evoked. The ECG was continuously monitored (six head-chest electrodes) and recorded at the end of each 4-minute exercise period. Exercise testing during the follow-up was performed 6 months after the randomization and thereafter annually up to 5 years. At these follow-up exercise tests, the same loads were used as in the primary testing and therapy with β-blocking agents was allowed if needed. The medical therapy was adjusted to give optimal benefit to the patients. The β blockers, in particular, were titrated to produce a resting bradycardia. At the follow-up visits resting heart rates of less than 50 beats/min, 60 beats/min and 65 beats/min were recorded on the ECGs in 16%, 51% and 74% of the patients, respectively. In the postoperative testing of the surgical group, some patients were asymptomatic, and they were stressed to a heart rate exceeding 85% of age-predicted maximum. A total of 644 maximal exercise tests were performed.

The variables used to characterize exercise tolerance were: total work (TW, or the sum of pedaled loads multiplied by the respective times in minutes), maximal tolerated load (MaxL, kpm/min), maximal heart rate (MaxHR, beats/min), maximal ST depression (MaxSTθ, mm) and rate-pressure product at peak exercise (RPP, mm Hg/min) obtained by multiplying the systolic pressure (cuff method) by the heart rate/10². Angina was classified as follows: 1 = no angina, 2 = angina by walking uphill/upstairs, 3 = angina by rapid walking on the level, 4 = angina by slow walking on the level and 5 = angina at rest.

LV cineangiograms were made through pigtail catheters inserted percutaneously through the femoral artery. LV ejection fractions were derived by standard formulas. Coronary arteries were studied by the Judkins technique in multiple projections as described previously. In addition to cinefilms, large cut films were exposed at a rate of 4–6/injection. A reduction of the luminal diameter of 50% or greater was considered significant. The quality of the left internal mammary artery (LIMA) and its origin was studied by a selective injection into the left subclavian artery. LIMA grafts were exclusively used to bypass lesions in the left anterior descending coronary artery and as jump grafts to correct simultaneous lesions in the diagonal branch.

During the follow-up, the surgical group was subjected to repeated graft and native vessel angiography at discharge from hospital (mean 3 weeks after operation), after 1 year and after 5 years. The medical group was recatheterized 5 years after the randomization. Additional coronary angiograms were performed during the follow-up in both groups if symptoms suggested the development of drug-resistant unstable angina, indicating surgical intervention in the medical group and reoperation in the surgical group. On the basis of the postoperative coronary and graft angiograms, the surgical group was divided into subgroups of patients who were completely revascularized and those who were incompletely revascularized. Complete revascularization was considered to be achieved if all of the significant lesions were bypassed, no graft occlusions had occurred, and no significant lesions had developed in the ungrafted native arteries or distal to graft anastomosis in the grafted arteries. If any of the above occurred, the case was considered incompletely revascularized.

Statistical Methods

In assessing the significance of difference in the parametric data, an unpaired t test was used. The significance of the difference in nonparametric data was assessed by the chi-square test with Yates correction.

Results

General

Three patients randomly assigned to surgery did not accept the proposed form of treatment (94% adherence rate). Two patients assigned to bypass surgery died suddenly (within 1 hour) 4 and 6 weeks after randomization before the scheduled operation. There was no operative mortality. The characteristics of the medical and surgical groups at entry revealed no statisti-
Table 2. Results of Repeated Exercise Testing of the Medical and Surgical Groups

<table>
<thead>
<tr>
<th></th>
<th>No. of pts</th>
<th>% on β blockade</th>
<th>TW (kpm)</th>
<th>MaxL (kpm/min)</th>
<th>Max HR (beats/min)</th>
<th>MaxST_{d} (mm)</th>
<th>RPP (mm Hg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>S</td>
<td>M</td>
<td>S</td>
<td>M</td>
<td>S</td>
<td>M</td>
</tr>
<tr>
<td>At entry</td>
<td>50</td>
<td>45</td>
<td>0</td>
<td>0</td>
<td>3331 ± 336</td>
<td>567 ± 569</td>
<td>120 ± 124</td>
</tr>
<tr>
<td></td>
<td>±326 ± 314</td>
<td>±31 ± 32</td>
<td>±2.7 ± 2.8</td>
<td>±0.3 ± 0.3</td>
<td>±7.7 ± 7.5</td>
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</table>

During follow-up:

- 6 months: 47 39 89 44
  - TW: 3424 ± 5265
  - MaxL: 583 ± 718
  - Max HR: 108 ± 132
  - MaxST_{d}: 2.7 ± 1.7
  - RPP: 176 ± 232
- 1 year: 44 42 93 52
  - TW: 3544 ± 5186
  - MaxL: 603 ± 718
  - Max HR: 110 ± 135
  - MaxST_{d}: 2.8 ± 1.5
  - RPP: 177 ± 235
- 2 years: 40 42 92 55
  - TW: 3589 ± 5578
  - MaxL: 603 ± 768
  - Max HR: 109 ± 134
  - MaxST_{d}: 2.3 ± 1.4
  - RPP: 178 ± 243
- 3 years: 37 41 95 59
  - TW: 3651 ± 5267
  - MaxL: 605 ± 739
  - Max HR: 108 ± 129
  - MaxST_{d}: 2.3 ± 1.1
  - RPP: 181 ± 236
- 4 years: 33 40 94 60
  - TW: 3633 ± 4663
  - MaxL: 620 ± 699
  - Max HR: 112 ± 125
  - MaxST_{d}: 2.5 ± 1.3
  - RPP: 193 ± 225
- 5 years: 34 41 85 63
  - TW: 3589 ± 4801
  - MaxL: 651 ± 715
  - Max HR: 111 ± 126
  - MaxST_{d}: 2.7 ± 1.3
  - RPP: 176 ± 233

Test results are mean ± SEM.
Difference from entry:
* p < 0.05.
† p < 0.02.
‡ p < 0.01.
§ p < 0.001.

Abbreviations: M = medical group; S = surgical group; TW = total work; MaxL = maximal tolerated load; Max HR = maximal heart rate; MaxST_{d} = maximal ST depression; RPP = rate-pressure product.

cally significant differences in the relevant variables (table 1).

During the 5-year follow-up, two patients in the surgical group developed drug-resistant unstable angina and were reoperated on because of graft occlusions and new significant lesions. Five patients in the medical group had this complication and were subjected to bypass surgery without operative mortality (90% adherence rate).

Exercise Tolerance

The clinical data of the medical and surgical groups are listed in table 2. The number of patients tested varied for each test. In addition to mortality during the follow-up, recent myocardial infarcts, unstable angina and locomotor reasons modified the series. In the testing at entry, no significant differences could be detected between the groups. During the follow-up, the medical group remained largely at the basic level, whereas the surgical group progressively improved up to 5 years: TW increased by 39–66% (p < 0.02–0.001), MaxL by 23–35% (p < 0.01–0.001), and MaxST_{d} decreased by 39–61% (p < 0.05–0.001). A more variable response was observed in MaxHR, which was increased at 1 year (p < 0.02) and 2 years (p < 0.05) and in RPP, which was increased at 2 years (p < 0.01). Both of these variables were substantially influenced by the slowly increasing use of β-blocking agents (table 2) due to residual angina, hypertension, arrhythmias and combinations of these.

The functional classification of the medical group remained stable (table 3) except for five patients with unstable angina who required bypass surgery; the regular use of nitrates increased from 84% to 96% of the patients over the entire follow-up. The functional classification of the surgical group improved markedly after the operation (table 3). During the follow-up, about 40% remained asymptomatic and the incidence of grades 1 and 2 combined, although slightly declined with time, persisted in two-thirds of the patients.

The surgical group had a total of 121 coronary arteries with significant lesions; 105 bypass grafts were inserted. Twenty-nine patients underwent complete revascularization and 16 patients each had one by-passed lesion. These arteries were diffusely diseased and, discouraged by our results with gas endarterec-
TABLE 4. Effect of Completeness of Revascularization on Postoperative Exercise Tolerance

<table>
<thead>
<tr>
<th>No of pts C/I</th>
<th>At entry</th>
<th>Revasc groups</th>
<th>6 months</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
<th>4 years</th>
<th>5 years</th>
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<tr>
<td></td>
<td></td>
<td>22/17</td>
<td>20/22</td>
<td>21/21</td>
<td>19/22</td>
<td>20/20</td>
<td>16/25</td>
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<tr>
<td>TW (kpm)</td>
<td>3366</td>
<td>±314</td>
<td>5700</td>
<td>6383</td>
<td>6640</td>
<td>6317</td>
<td>5719</td>
<td>6378</td>
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<tr>
<td></td>
<td>I</td>
<td>±726</td>
<td>4703</td>
<td>4100</td>
<td>4117</td>
<td>4267</td>
<td>3479</td>
<td>3792</td>
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<td>±622</td>
<td>±431</td>
<td>±340</td>
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<td>±467</td>
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<tr>
<td>MaxL (kpm/min)</td>
<td>569</td>
<td>±32</td>
<td>752</td>
<td>855</td>
<td>869</td>
<td>815</td>
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<td>±41</td>
<td>±43</td>
<td>±42</td>
<td>±47</td>
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<tr>
<td>MaxHR (beats/min)</td>
<td>124</td>
<td>±2.8</td>
<td>135</td>
<td>142</td>
<td>139</td>
<td>135</td>
<td>134</td>
<td>137</td>
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<tr>
<td></td>
<td>I</td>
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<td>127</td>
<td>129</td>
<td>127</td>
<td>123</td>
<td>115</td>
<td>118</td>
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<tr>
<td></td>
<td></td>
<td>±5.3</td>
<td>±4.9</td>
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<td>±4.8</td>
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<td>±4.6</td>
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<tr>
<td>MaxSTd (mm)</td>
<td>2.8</td>
<td>±0.3</td>
<td>1.6</td>
<td>1.2</td>
<td>1.2</td>
<td>0.8</td>
<td>0.9</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>±0.3</td>
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<td>RPP (mm Hg/min)</td>
<td>213</td>
<td>±7.5</td>
<td>248</td>
<td>260</td>
<td>263</td>
<td>256</td>
<td>269</td>
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<tr>
<td></td>
<td>I</td>
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<td>±209</td>
<td>220</td>
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<td>217</td>
<td>200</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>±12.2</td>
<td>±11.6</td>
<td>±12.8</td>
<td>±17.2</td>
<td>±17.2</td>
<td>±15.2</td>
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</tbody>
</table>

Values are mean ± SEM.

Abbreviations: C = completely revascularized; I = incompletely revascularized; other abbreviations as in table 2.

tomy, we left them unbypassed. Early postoperative angiography disclosed seven occluded grafts (93% patency rate), 1-year angiography revealed 12 (89% patency rate), and 5-year angiography 16 (85% patency rate). The graft attrition and occurrence of other phenomena related to incompleteness of revascularization modified the series so that the numbers of patients with complete revascularization at different postoperative test situations were: 22 of 39 (56%) at 6 months, 20 of 42 (48%) at 1 year, 21 of 42 (50%) at 2 years, 19 of 41 (46%) at 3 years, 20 of 40 (50%) at 4 years and 16 of 41 (39%) at 5 years.

Table 4 shows the exercise tolerance data in relation to the degree of revascularization. Since the preoperative data of the subgroups were largely similar and the number of patients in the subgroups changed after each postoperative angiography, only the data of the whole surgical group at entry are shown.

The completely revascularized subgroup exhibited a marked and persistent improvement: TW almost doubled ($p < 0.01$ at 6 months, thereafter $< 0.001$), MaxL increased by 32–53% ($p < 0.01–0.001$), MaxHR increased by 8–15% ($p < 0.05–0.001$) MaxSTd decreased by 43–79% ($p < 0.01–0.001$), and RPP increased by 16–26% ($p < 0.05–0.001$). In sharp contrast to this, the improvement in the exercise tolerance of the incompletely revascularized group was only modest and reached statistically significance only in the decrease of MaxSTd ($p < 0.05–0.01$) (figs. 1 and 2).

The comparison of exercise tolerance data between the medical group (table 2) and the incompletely revascularized surgical subgroup (table 4) revealed that TW and MaxL (fig. 1) did not differ significantly during the follow-up. MaxHR was significantly higher in the surgical subgroup up to 3 years ($p < 0.05–0.01$) but not thereafter. MaxSTd was lower up to 2 years ($p < 0.05$), but not significantly thereafter (fig. 2). RPP was higher in the surgical subgroup up to 2 years ($p < 0.01$) and again at 5 years ($p < 0.02$).

**Figure 1.** Maximal tolerated load on ergometer during follow-up. (top) Comparison of completely and incompletely revascularized surgical patients. (bottom) Comparison of incompletely revascularized surgical patients and patients receiving medical therapy. The means of the entire surgical group (bars with stars) and the medical group are shown at randomization (R). Values are mean ± SEM.
perfusion was responsible for the initial improvement in completely revascularized patients, and its maintenance over the 5-year follow-up was related to the patency of the grafts and the absence of significant progression of the disease in ungrafted arteries. This thesis is strengthened by the similarity of the exercise tolerance of incompletely revascularized patients and medically managed patients (figs. 1 and 2), suggesting that a primarily incomplete grafting, graft attrition and new lesions in native arteries signify ischemic myocardial areas producing symptoms. When completeness of revascularization is assessed immediately postoperatively, completely and incompletely revascularized patients do not differ in angina status. However, a detailed analysis of the completeness of the revascularization process by angiography has clearly shown a difference in relief of angina between optimal revascularization and unchanged coronary circulation after 1 year of follow-up. The same pattern emerges after extended periods of follow-up. The highest graft occlusion rate is early after operation. After the first postoperative year, graft attrition is fairly low, and new lesions distal to graft anastomosis are infrequent. Inevitably, however, in some patients coronary atherosclerosis develops and progresses at an unpredictable rate, rendering some successfully operated patients incompletely revascularized with a concomitant loss of the initial improvement.

References

**Discussion**

In the present study, exercise tolerance improved greatly in the group treated with coronary bypass surgery and did not change in a randomized medically treated group during a 5-year follow-up. In assessing the present data, it should be noted that treatment with nitrates and β-blocking compounds was allowed as needed in the surgical group. Thus, the data represent a comparison between bypass surgery supported by medical therapy, when indicated, and medical therapy alone.

The observed initial improvement in the surgical group is in accord with a large number of nonrandomized studies. The same striking initial effect was also observed in the randomized studies. The problem of maintaining this early beneficial effect has been addressed. Schwade et al. observed a clear improvement in favor of surgical therapy 1 year postoperatively but not at 18 months. A similar deterioration over extended follow-up has been observed. The present data do not show a clear deterioration within a follow-up of 5 years, corroborating our data after 2 years of follow-up. This finding is in accord with data from a randomized study with a 52-month median follow-up. The explanation for the improvement over 5 years is evidently the slowly increasing use of β-blocking agents (table 2) compensating for the decline in exercise tolerance due to recurring symptoms. This resulted in a steady incidence of asymptomatic patients but a decline in the number of patients in the lowest functional classes (table 3). The increasing use of β-blocking agents is also reflected in the decline of initially increased MaxHR and RPP beyond 2 years of follow-up (table 2).

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Circulation. 1983;67:491-496
doi: 10.1161/01.CIR.67.3.491
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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