Long-term Outcome of Patients With Depressed Left Ventricular Function Undergoing Percutaneous Transluminal Coronary Angioplasty

The NHLBI PTCA Registry

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Background. Coronary revascularization with bypass has been shown to improve survival in patients with coronary artery disease and left ventricular dysfunction. In these patients, use of nonsurgical revascularization with percutaneous transluminal coronary angioplasty (PTCA) is increasing, although their long-term outcome has not been well delineated. The purpose of this investigation was to characterize the outcome of angioplasty in patients with decreased left ventricular function and contrast it with the results in patients with normal left ventricular function.

Methods and Results. In the 1985–1986 National Heart, Lung, and Blood Institute’s PTCA Registry, of 1,802 patients undergoing PTCA, 244 patients (13.5%) had an ejection fraction of ≤45% (mean, 39.6±6.8%). These patients had a higher incidence of prior infarction, a longer and worse history of manifestations of coronary disease, and more extensive coronary artery disease than patients with well-preserved function; 88% and 91%, respectively, had successful dilation of at least one lesion (nonsignificant difference). However, patients with decreased left ventricular function had a decreased frequency of successful dilation of all lesions in which PTCA was attempted (76% versus 84%, p<0.01). There were no statistically significant differences in in-hospital complications—death occurred in 0.8% and 0.7%, nonfatal myocardial infarction occurred in 4.9% and 4.5%, and emergency surgical revascularization was performed in 4.5% and 3.2%, respectively. Patients were followed for a mean of 4.1 years; during this time, patients with decreased left ventricular function had significantly worse survival and combined event-free survival. Despite this, at 4 years, 87% of the patients with a mean ejection fraction of 39.6% remained alive, and 77% were alive and had not experienced infarction or required bypass.

Conclusions. PTCA is effective in selected patients with depressed left ventricular function. Initial outcome and risk–benefit ratio are excellent. Successful dilation of at least one vessel was achieved in 88% of patients with depressed left ventricular function and in 91% of patients with more normal left ventricular function. The former group, however, had a decreased incidence of successful dilation in all lesions in which dilation was attempted (76% versus 84%, p<0.01). There was no significant difference in in-hospital complications between the two groups. During follow-up, patients with decreased left ventricular function had worse event-free survival, although 77% were alive without infarction or bypass grafting at 4 years. (Circulation 1993;87:21-29)

KEY WORDS • revascularization, nonsurgical • coronary artery disease

Although initially controversial, revascularization with coronary artery bypass grafting, when compared with medical therapy, has been documented to improve outcome in the subgroup of patients with poor left ventricular function and multivessel disease.1–9 Both randomized and nonrandomized trials have documented this improved survival in such patients with both stable and unstable angina.1,3–6 The role of nonsurgical revascularization with percutaneous transluminal coronary angioplasty (PTCA) for similar patients with coronary artery disease and left ventricular dysfunction has not been well delineated, although the use of PTCA in these patients is increasing.10–14 This report describes the initial outcome and long-term follow-up of PTCA in patients with left ventricular dysfunction in the 1985–1986 National Heart, Lung, and Blood Institute’s (NHLBI) PTCA Registry.

Methods

Patients

The 1985–1986 NHLBI PTCA Registry has been previously described.10,11 Between August 1985 and May 1986, 1,802 patients undergoing angioplasty for the first time at 15 North American centers were enrolled; standard baseline and follow-up forms were used. Pa-
TABLE 1. Baseline Characteristics of 1,455 Patients Undergoing Percutaneous Transluminal Coronary Angioplasty

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group 1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1A* (n=11)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>64</td>
</tr>
<tr>
<td>Mean duration of chest pain (months)</td>
<td>80</td>
</tr>
<tr>
<td>Age ≥65 years (%)</td>
<td>55</td>
</tr>
<tr>
<td>Female (%)</td>
<td>27</td>
</tr>
<tr>
<td>Unstable angina (%)</td>
<td>55</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>90</td>
</tr>
<tr>
<td>Prior CABG (%)</td>
<td>45</td>
</tr>
<tr>
<td>History of congestive heart failure (%)</td>
<td>67</td>
</tr>
<tr>
<td>History of diabetes mellitus (%)</td>
<td>22</td>
</tr>
<tr>
<td>History of hypertension (%)</td>
<td>38</td>
</tr>
<tr>
<td>Current tobacco use (%)</td>
<td>33</td>
</tr>
<tr>
<td>Ejection fraction (mean±SD)</td>
<td>18.6±3.8%</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; CABG, coronary artery bypass grafting.

*Group 1A, ejection fraction <25%.
†Group 1B, ejection fraction between 25% and 35%.
‡Group 1C, ejection fraction between 36% and 45%.
§Combined groups 1A, 1B, and 1C, ejection fraction ≤45%.
||Group 2, ejection fraction >45%.
¶Values are for comparison of combined groups 1A, 1B, and 1C with group 2.

Definitions

Assessment of baseline left ventricular function was done at each center but was not dictated by a common prospective protocol. Techniques for assessment included left ventricular angiography, radionuclide angiography, and echocardiography.

Vessel disease was classified as one-, two-, or three-vessel disease according to the definitions used in the Coronary Artery Surgery Study. In patients with left main coronary stenoses, luminal narrowing of ≥50% was considered multivessel disease.

Successful dilation of a lesion was defined as improvement of ≥20% in the luminal diameter. In-hospital angiographic success was defined as a reduction of ≥20% in the severity of stenosis in all lesions in which PTCA was attempted. In-hospital clinical success was defined as angiographic success with no in-hospital death, Q wave myocardial infarction, or coronary artery bypass grafting. Complete revascularization was defined as successful dilation and no residual stenoses of ≥50%.

Statistical Methods

Ejection fraction was initially analyzed as a categorical variable. Patients were initially divided into two groups based on ejection fraction: ejection fraction of ≤45% (group 1) and ejection fraction >45% (group 2). In addition, patients with an ejection fraction of ≤45% were further subdivided into those with ejection fractions <25%, 25–35%, and 36–45%. Ejection fraction was then analyzed as a continuous variable in 5%-decremental units.

Differences in proportion between patient groups were analyzed by the χ² test or by Fisher's exact test when the number of patients in a group was small. Event-free survival was assessed by the product-limit (Kaplan-Meier) method; the end points were death; death and myocardial infarction; and death, myocardial infarction, and coronary artery bypass grafting. Independent factors associated with follow-up events were identified with Cox regression analysis using the maximal partial likelihood ratio method. The relative risk of an event for patients with left ventricular dysfunction compared with the risk in those with well-preserved left ventricular function was estimated. The 95% confidence interval of each risk was also determined. When the confidence interval did not include unity, the equal risk hypothesis was rejected. Probability values <0.05 were considered statistically significant.

Results

Among the 244 patients (13.5%) with an ejection fraction of ≤45% (group 1), the mean ejection fraction was 39.6±6.8% (range, 10–45%). Most patients in group 1 had an ejection fraction between 36% and 45% (193 patients, 79%), 40 patients (16%) had an ejection fraction from 25% to 35%, and 11 patients (5%) had an ejection fraction <25% (Table 1). In comparison, among the 1,211 patients (67%) with an ejection fraction >45% (group 2), the average ejection fraction was 62.8±8.7% (range, 46–91%) (Figure 1). The two groups had significant differences in baseline characteristics (Table 1) and the degree of severity of coronary artery disease (Table 2). More patients in group 1 were men, and more had prior infarction (85% versus 31%, p<0.001) and a history of prior coronary artery bypass grafting (25% versus 10%, p<0.001) and congestive heart failure (14% versus 4%, p<0.001). More patients
with well-preserved left ventricular function presented with unstable angina. Patients with left ventricular dysfunction had more severe and extensive coronary artery disease. Three-vessel disease was more common in group 1 (35% versus 18%, \(p<0.001\)), and more patients in group 1 had one or more total occlusions (55% versus 29%, \(p<0.001\)).

**Dilation Strategy**

There was no difference in the frequency of emergency or urgent PTCA between the two groups (17% in group 1 and 16% in group 2). All lesions were thought to be amenable to PTCA in 63% of group 1 and in 77% of group 2 (\(p<0.001\)). The two groups were similar in regard to the number of amenable lesions in which dilation was intended (68% versus 65%, nonsignificant) and the number of lesions in which dilation was actually attempted (1.8 versus 1.6, nonsignificant). The distribution of the segments in which PTCA was attempted differed significantly between the two groups. Patients in group 1 had fewer single coronary artery dilations but more bypass graft dilations (12% versus 3%) (\(p<0.001\)). Dilation of the left anterior descending artery was attempted in 53% of the patients in group 2 and 47% in group 1. Dilation of total occlusions was attempted in 26% of group 1 patients and in 15% of group 2 patients (\(p<0.001\)).

**Outcome**

Patients with poor left ventricular function (group 1) had significantly lower rates of complete revascularization than the patients with well-preserved left ventricular function (group 2) (35% versus 47%, \(p<0.001\)). There was no difference between the two groups in the frequency with which at least one lesion was successfully dilated — 88% in group 1 and 91% in group 2. There was a significant difference in the frequency with which all lesions attempted were dilated successfully (76% in group 1 and 84% in group 2, \(p<0.01\)) and in the frequency with which the left anterior descending artery was successfully dilated (82% versus 89%, \(p<0.05\)).

There were no significant differences in in-hospital complications between patients with left ventricular dysfunction and those with well-preserved left ventricular function (Table 3). Death occurred in 0.8% and 0.7%, respectively. The rates of nonfatal myocardial infarction were also similar at 4.9% in group 1 and 4.5% in group 2. The average duration of hospitalization was longer in group 1 (4.3±5.0 days) than in group 2 (3.5±4.3 days) (\(p<0.01\)) (Table 3).

**Follow-up**

Follow-up data were available for 1,719 (95%) of the total 1,802 patients; the mean duration of follow-up was 4.1 years. Throughout follow-up to 4 years, group 1 had poorer event-free survival (Figure 2). The percentages of patients free from events and of those who were free from or had improvement in angina at 4 years are shown in Table 4. At 4 years, 87% of group 1 patients were alive compared with 93% of group 2 patients (\(p<0.001\)); 73% of the patients in group 1 were alive and were symptom free compared with 75% in group 2. At 4 years, 77% of group 1 patients and 85% of group 2 patients were alive and free from myocardial infarction (\(p<0.05\)). When the end points of death, myocardial infarction, or coronary artery bypass grafting were considered together, the event-free survival was not significantly different between the two groups; however,

![Graph showing ejection fractions in groups 1 and 2.](http://circ.ahajournals.org/)

**Figure 1.** Bar graph shows range and distribution of ejection fractions (EF) in groups 1 and 2.

**Table 2.** Angiographic Characteristics of 1,455 Patients Undergoing Percutaneous Transluminal Coronary Angioplasty

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group 1A(^\ast) (n=11)</th>
<th>Group 1B(^\dagger) (n=40)</th>
<th>Group 1C(^\ddagger) (n=193)</th>
<th>Combined groups</th>
<th>Group 2(^\mathsection) (n=1,211)</th>
<th>(p)(^\mathparagraph)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessel disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One-vessel</td>
<td>36 (25)</td>
<td>25 (28)</td>
<td>28 (28)</td>
<td>28 (53)</td>
<td>49 (29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Two-vessel</td>
<td>27 (30)</td>
<td>30 (36)</td>
<td>34 (35)</td>
<td>34 (35)</td>
<td>32 (18)</td>
<td>NS</td>
</tr>
<tr>
<td>Three-vessel</td>
<td>36 (40)</td>
<td>40 (34)</td>
<td>34 (35)</td>
<td>34 (35)</td>
<td>32 (18)</td>
<td>NS</td>
</tr>
<tr>
<td>Left main (≥50%)</td>
<td>. . .</td>
<td>5 (2)</td>
<td>2 (2)</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td>NS</td>
</tr>
<tr>
<td>≥1 Total occlusion</td>
<td>64 (60)</td>
<td>60 (53)</td>
<td>53 (55)</td>
<td>55 (29)</td>
<td>29 (29)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(\ast\)Group 1A, ejection fraction <25%.
\(\dagger\)Group 1B, ejection fraction between 25% and 35%.
\(\ddagger\)Group 1C, ejection fraction between 36% and 45%.
\(\mathsection\)Combined groups 1A, 1B, and 1C, ejection fraction ≤45%.
\(\mathparagraph\)Group 2, ejection fraction >45%.

Values are for comparison of combined groups 1A, 1B, and 1C with group 2.

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67% of group 1 patients were alive and had not had coronary artery bypass grafting or a myocardial infarction.

The long-term outcomes of the subgroups of patients with ejection fractions of ≤45% (<25%, 25–35%, 36–45%) were also compared with the outcomes of patients with ejection fractions >45% (Table 4). Despite the small numbers of patients with markedly depressed left ventricular function, there were significant trends; long-term outcome was poorer in patients with more severe left ventricular dysfunction (Figure 3). The cumulative mortality at 4 years was 6.9% in patients with an ejection fraction >45% and 54.5% in the small number of patients with an ejection fraction <25%.

At baseline, 347 (19%) of the patients in the registry had no values entered for ejection fraction. This cohort possibly represents a high-risk group (that is, ejection fraction was not measured because the patient was too unstable). Such selection bias could have affected the comparisons of group 1 and group 2. To study the importance of this possibility, death, death and myocardial infarction, and death, myocardial infarction, and coronary artery bypass grafting were assessed at 4 years in these 347 patients, and the results were compared with those of the 1,455 patients with ejection fraction data. At 4 years of follow-up, 92% of patients with ejection fraction data and 93% of those without ejection fraction data were alive; 82% of both groups were alive and without myocardial infarction; and 71% of patients with ejection fraction data and 69% of those without the data were alive and without either myocardial infarction or coronary artery bypass grafting. Thus, no selection bias appeared to be present.

Another method used to assess whether ejection fraction as a discrete variable has a significant association with subsequent untoward events was Cox regression analyses; for these, death, death and myocardial infarction, and the combined end points of death, myocardial infarction, and coronary artery bypass grafting were used. For patients with an ejection fraction of ≤45%, the risk of dying in 4 years was approximately twice as high as that in patients with an ejection fraction >45% (Table 5).

We also assessed ejection fraction as a continuous variable with a decreasing scale of 5% units. For every 5% decrease in ejection fraction, there was an unadjusted mortality risk of 1.2% and an adjusted mortality risk of 1.11% (Table 6).

Multivariate analysis was performed to determine whether left ventricular dysfunction is itself an independent risk factor or whether differences in the baseline risk factors in the two groups were the major reason for the difference in mortality. The relative risks of the factors that were strongly associated with the 4-year events are shown in Table 7. Patients with depressed left ventricular function continued to have a significantly higher mortality rate than those with well-preserved left ventricular function even after adjustment was made for older age, history of diabetes, history of

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**Figure 2.** Graphs show event-free survival in 1,802 patients undergoing percutaneous transluminal coronary angioplasty. End points were death; death and myocardial infarction (MI); and death, MI, and coronary artery bypass grafting (CABG). EF, ejection fraction.
TABLE 4. Freedom From Events and Angina Status at 4 Years in 1,455 Patients Undergoing Percutaneous Transluminal Coronary Angioplasty

<table>
<thead>
<tr>
<th>End point</th>
<th>Group 1A* (%) of patients</th>
<th>Group 1B† (%) of patients</th>
<th>Group 1C‡ (%) of patients</th>
<th>Combined groups (%) of patients</th>
<th>Group 2§ (%) of patients</th>
<th>p§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No event</td>
<td>45</td>
<td>78</td>
<td>92</td>
<td>87</td>
<td>93</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No event and pain less severe or asymptomatic</td>
<td>45</td>
<td>67</td>
<td>86</td>
<td>81</td>
<td>88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No event and asymptomatic</td>
<td>45</td>
<td>52</td>
<td>79</td>
<td>73</td>
<td>75</td>
<td>NS</td>
</tr>
<tr>
<td>Death and MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No event</td>
<td>45</td>
<td>68</td>
<td>81</td>
<td>77</td>
<td>83</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>No event and pain less severe or asymptomatic</td>
<td>45</td>
<td>60</td>
<td>77</td>
<td>73</td>
<td>79</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>No event and asymptomatic</td>
<td>45</td>
<td>47</td>
<td>71</td>
<td>66</td>
<td>68</td>
<td>NS</td>
</tr>
<tr>
<td>Death, MI, and CABG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No event</td>
<td>27</td>
<td>65</td>
<td>69</td>
<td>67</td>
<td>72</td>
<td>NS</td>
</tr>
<tr>
<td>No event and pain less severe or asymptomatic</td>
<td>27</td>
<td>60</td>
<td>66</td>
<td>63</td>
<td>68</td>
<td>NS</td>
</tr>
<tr>
<td>No event and asymptomatic</td>
<td>27</td>
<td>47</td>
<td>61</td>
<td>57</td>
<td>59</td>
<td>NS</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; CABG, coronary artery bypass grafting.
*Group 1A, ejection fraction <25%.
†Group 1B, ejection fraction between 25% and 35%.
‡Group 1C, ejection fraction between 36% and 45%.
§Combined groups 1A, 1B, and 1C, ejection fraction ≤45%.
¶Group 2, ejection fraction >45%.
†A, x² test for difference between combined groups 1A, 1B, and 1C and group 2; B, test for trend on the event rates for combined group 1A, 1B, and 1C and group 2.

congestive heart failure, clinical success, and multivessel disease. For the combined end point of death and myocardial infarction, the effect of an ejection fraction of ≤45% became nonsignificant when baseline factors—including prior bypass operation, history of congestive heart failure, history of diabetes, clinical success, and multivessel disease—were considered in the model. Similarly, for the combined end point of death, myocardial infarction, or bypass operation, ejection fraction did not remain as an independent predictor after statistical adjustment for other risk factors. A history of diabetes, a history of congestive heart failure, clinical success, unstable angina, Canadian cardiovascular class 3 or 4, and incomplete revascularization were statistically significant determinants of this combined outcome. Ejection fraction was significant in univariate analysis only as a surrogate of the other risk factors that were prevalent in patients with a low ejection fraction.

Discussion

Patients with coronary artery disease and significant left ventricular dysfunction pose difficult clinical problems. Medical therapy has been associated with a poor long-term outcome.8,17-19 Surgical revascularization has been found to be associated with improved life expectancy in patients with impaired left ventricular function, particularly in the setting of multivessel coronary artery disease.1-9 The Veterans Administration Study4 documented significantly improved survival in patients with three-vessel disease and impaired left ventricular function treated with surgical revascularization compared with those who received medical therapy. Similarly, in the Coronary Artery Surgery Study, survival was improved in patients with three-vessel disease and an ejection fraction from 35% to 50%.3 In addition to these studies of patients with stable angina, patients with unstable angina and abnormal left ventricular function also benefit from surgical revascularization; in a subgroup of patients with an ejection fraction <50%, the Veterans Administration Cooperative Study documented a 65% reduction in 3-year cumulative mortality for surgically treated patients versus medically treated patients (6.1% versus 17.6%, respectively).1,3

Although surgical revascularization is associated with improved outcome in patients with left ventricular dysfunction, the initial risks and morbidity may be increased, particularly in patients with multivessel disease, unstable angina, and depressed left ventricular function.

![Plot of 4-year mortality by ejection fraction (EF) group.](image)
TABLE 5. Four-Year Event Rates by Ejection Fraction With Relative Risk in 1,455 Patients Undergoing Percutaneous Transluminal Coronary Angioplasty

<table>
<thead>
<tr>
<th>Event</th>
<th>4-Year rate (%)</th>
<th>Unadjusted risk for</th>
<th>Adjusted risk for</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF ≤45% (group 1)</td>
<td>EF &gt;45% (group 2)</td>
<td>EF ≤45% vs. &gt;45%</td>
</tr>
<tr>
<td>Death*</td>
<td>13</td>
<td>7</td>
<td>1.83</td>
</tr>
<tr>
<td>Death, MI†</td>
<td>23</td>
<td>17</td>
<td>1.41</td>
</tr>
<tr>
<td>Death, MI, CABG‡</td>
<td>33</td>
<td>28</td>
<td>1.21</td>
</tr>
</tbody>
</table>

EF, ejection fraction; MI, myocardial infarction; CABG, coronary artery bypass grafting.

*The Cox model for mortality was adjusted by age 65 years or older, history of diabetes, history of congestive heart failure, multivessel disease, and clinical success.
†The Cox model for death or MI at 4 years was adjusted by prior CABG, history of diabetes, history of congestive heart failure, presence of multivessel disease, and clinical success.
‡The Cox model for death, MI, or CABG was adjusted by history of diabetes, history of congestive heart failure, Canadian cardiovascular class 3 or 4, unstable angina, clinical success, and incomplete revascularization.

function.20-23 As the technology and operator experience with nonsurgical revascularization have improved, more patients with these characteristics have undergone PTCA. As yet, data on immediate or longer-term outcome are limited, and no truly controlled comparative studies have been done.12-14,24 PTCA may pose particular difficulties in these patients because inflation in critical lesions may be less well tolerated and acute closure may result in death if the segment being dilated supplies the only remaining viable myocardium. In addition, because chronic total occlusions are more frequent in these patients, complete revascularization may be more difficult to achieve.

Stevens et al12 compared the results of elective dilation in 845 patients with a calculated or estimated ejection fraction of ≤40% with the results in patients with more normal left ventricular function. They found that angiographic success rates were slightly but significantly lower (93% versus 95%, p<0.01) and that overall procedural mortality was markedly higher (4% versus 1%, p<0.001) in those with decreased ejection fractions. Mortality was even higher when a complication of the procedure necessitated urgent coronary artery bypass grafting, in which case the operative mortality rate was 33%. Actuarial survival at 1 year was 87%, but it decreased substantially to 69% at 4 years. During a mean follow-up of 33.5 months, 15% of patients required late coronary artery bypass grafting, and 27% required repeat dilation. Limited data have also been reported from single centers.13,14 Kohli et al13 described a small group of 61 patients with a mean left ventricular ejection fraction of 27% who underwent PTCA. The success rate was 90%. Major complications, including death, myocardial infarction, or emergency coronary artery bypass grafting, occurred in 8.2% (five patients); death occurred in 3.2% (two patients).

In the multicenter NHLBI registry data accumulated for 1985–1986, patients with an ejection fraction of ≤45% (group 1), as expected, had significantly more advanced disease with higher rates of prior infarction, prior coronary artery bypass grafting, congestive heart failure, total occlusion, and three-vessel disease than patients with more well-preserved left ventricular function (group 2). Despite these differences in baseline and angiographic variables, at least one lesion in which PTCA was attempted was successfully dilated in 88% of group 1 and 91% of group 2. A similar number of lesions were attempted per patient in each group (1.8 for group 1, 1.6 for group 2). Other measures of success were significantly different: Group 1 patients had a significantly reduced chance of successful dilation in all lesions attempted (71% versus 80%) and of successful dilation of the left anterior descending artery (82% versus 89%). In contrast to the report by Stevens et al,12 the complication rates in the two groups were not significantly different: Death occurred in only 0.8% of group 1 and 0.7% of group 2 patients, and nonfatal myocardial infarction occurred in 4.9% of group 1 and 4.5% of group 2. Acute closure occurred in only 2.5% and 2.1%, respectively, and urgent coronary artery bypass grafting was required in only 4.5% and 3.2%, respectively. Despite the excellent ability to dilate at-

TABLE 6. Four-Year Event Rates and Relative Risk by Ejection Fraction (Assessed as a Continuous Variable With a Decreasing Scale of 5% Units)

<table>
<thead>
<tr>
<th>Event</th>
<th>4-Year rate (%)</th>
<th>Unadjusted risk for every 5% decrease in EF</th>
<th>Adjusted risk for every 5% decrease in EF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(total)</td>
<td>95% Confidence interval</td>
<td>95% Confidence interval</td>
</tr>
<tr>
<td>Death*</td>
<td>7.8</td>
<td>1.20</td>
<td>1.12, 1.29</td>
</tr>
<tr>
<td>Death, MI†</td>
<td>17.6</td>
<td>1.09</td>
<td>1.04, 1.15</td>
</tr>
<tr>
<td>Death, MI, CABG‡</td>
<td>29.1</td>
<td>1.06</td>
<td>1.02, 1.10</td>
</tr>
</tbody>
</table>

EF, ejection fraction; MI, myocardial infarction; CABG, coronary artery bypass grafting.

*The Cox model for mortality was adjusted by age 65 years or older, history of diabetes, history of congestive heart failure, multivessel disease, and clinical success.
†The Cox model for death or MI at 4 years was adjusted by prior CABG, history of diabetes, history of congestive heart failure, presence of multivessel disease, and clinical success.
‡The Cox model for death, MI, or CABG was adjusted by history of diabetes, history of congestive heart failure, Canadian cardiovascular class 3 or 4, unstable angina, clinical success, and incomplete revascularization.
TABLE 7. Cox Regression Analysis: Factors Associated With 4-Year Events in 1,455 Patients Undergoing Percutaneous Transluminal Coronary Angioplasty

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Death Rate (Adjusted risk*)</th>
<th>95% Confidence interval</th>
<th>Death, MI Rate (Adjusted risk*)</th>
<th>95% Confidence interval</th>
<th>Death, MI, CABG Rate (Adjusted risk*)</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF ≤45%</td>
<td>1.23</td>
<td>0.79, 1.92</td>
<td>0.93</td>
<td>0.68, 1.27</td>
<td>0.89</td>
<td>0.69, 1.15</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>1.69</td>
<td>1.08, 2.65</td>
<td>1.41</td>
<td>1.03, 1.94</td>
<td>1.37</td>
<td>1.07, 1.76</td>
</tr>
<tr>
<td>History of congestive heart failure</td>
<td>4.33</td>
<td>2.67, 7.02</td>
<td>3.33</td>
<td>1.57, 3.46</td>
<td>1.75</td>
<td>1.24, 2.48</td>
</tr>
<tr>
<td>Clinical success</td>
<td>0.63</td>
<td>0.42, 0.93</td>
<td>0.30</td>
<td>0.23, 0.38</td>
<td>0.24</td>
<td>0.19, 0.29</td>
</tr>
<tr>
<td>Multivessel disease (vs. one-vessel disease)</td>
<td>1.77</td>
<td>1.17, 2.68</td>
<td>1.43</td>
<td>1.07, 1.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥65 years</td>
<td>2.03</td>
<td>1.39, 2.98</td>
<td>1.63</td>
<td>1.18, 2.26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior bypass grafting</td>
<td></td>
<td></td>
<td>1.45</td>
<td>1.13, 1.88</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable angina</td>
<td></td>
<td></td>
<td>1.36</td>
<td>1.02, 1.81</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadian cardiovascular class 3, 4 (vs. 1, 2)</td>
<td></td>
<td></td>
<td>1.91</td>
<td>1.50, 2.42</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*MI, myocardial infarction; CABG, coronary artery bypass grafting; EF, ejection fraction.

All risks were adjusted for the variables in this table and for female sex, prior MI, and history of hypercholesterolemia or hypertension.

tempted lesions, revascularization was complete in only 35% of group 1 patients and 47% of group 2 patients. In most cases, however, complete revascularization was not achieved either because fewer lesions were amenable to dilation or because the procedure had to be performed on an urgent basis.

The mean duration of follow-up in these patients was 4.1 years. Throughout follow-up, patients with abnormal left ventricular function had decreased survival and event-free survival; although survival was reduced in these patients, 87% of them remained alive at 4 years. This rate is substantially better than that reported in other series; Kohli et al12 reported a 3-year survival of 70%, Stevens et al12 reported a 4-year rate of only 69%, and Serota et al14 reported a 4-year rate of 57%. Whether this difference is a function of patient selection or some other variables cannot be determined, although the mean ejection fraction was 27% in the series of Kohli et al, 39.6% in the current series, and 34% in the series of Serota et al. There was a definite relation between the baseline ejection fraction and death at follow-up. In our series, most patients with depressed left ventricular function had an ejection fraction from 36% to 45% (79%), fewer had an ejection fraction between 25% and 35% (40 patients, 16%), and only 11 patients (5%) had an ejection fraction <25%. The 4-year survival rates in these three groups were 92%, 78%, and 45%, respectively. Although our numbers were small, patients with very severe left ventricular dysfunction and ejection fraction <25% are at significantly higher risk for mortality during follow-up.

When the combined end points of death and myocardial infarction or death, myocardial infarction, and coronary artery bypass grafting were analyzed, event-free survival was only slightly lower in patients with depressed left ventricular function. At 4 years, 67% were alive and had not had coronary artery bypass grafting or myocardial infarction. As was true with death as an end point, patients with more severely depressed left ventricular function (<25% or 25–35%) had poorer combined event-free survival. The difference in end points could be entirely accounted for by the higher mortality in group 1. To resolve the question of whether decreased left ventricular function is an independent risk factor for adverse events, multivariate analyses were performed. Mortality was still increased even after adjusting for older age, a history of diabetes mellitus, a history of congestive heart failure, success rates, and presence of multivessel disease. With combined end points, other baseline factors—history of diabetes mellitus, history of congestive heart failure, success of dilation, and presence of multivessel disease—were more important. Thus, low ejection fraction was not an independent risk factor for myocardial infarction or for the future need for a bypass procedure.

Truly comparative data do not exist that allow assessment of the relative value of PTCA versus that of coronary artery bypass grafting in patients with multivessel disease and depressed left ventricular function. Clearly, differences between patients who have undergone dilation and those who have undergone coronary artery bypass grafting may have important effects on long-term outcome. Munger et al24 studied 166 patients with an ejection fraction of ≤40% who had PTCA and compared them with 166 patients with similar ejection fractions who were treated surgically. The surgical group, however, had more vessels diseased (2.30±0.71 versus 1.79±0.76, p<0.005). The mean ejection fractions, however, were similar (31% in the PTCA group and 32% in the surgical group). During follow-up, the 1-, 3-, and 5-year survival rates of the dilation group were 85%, 77%, and 64%, respectively; these were only slightly (but nonetheless significantly) worse than the rates in the surgical group: 88%, 83%, and 69%, respectively. Hochberg et al25 reported a 3-year survival rate of 60% in a group of 425 patients with an ejection fraction from 20% to 39% who were treated surgically. In other surgical series of patients with depressed left ventricular function, 3- and 5-year mortality rates have varied.1-3,5,8,9 Any comparisons between cohort surgical series and dilation series are, however, complicated by differences in other clinically important characteristics; surgically treated series have usually included more patients with three-vessel disease.

Other catheterization-based techniques may play an important role in the treatment of patients with left ventricular dysfunction.26-31 These include intra-aortic balloon counterpulsation, coronary sinus retroperfu-
sion, cardiopulmonary bypass, and partial left heart bypass. There has been increasing interest in cardiopulmonary bypass–supported angioplasty. In an initial experience from 1988, 105 patients were entered into a voluntary registry. The indications for use of the device varied but included markedly depressed left ventricular function; 22% of the group had an ejection fraction of ≤20%. In this group, the hospital mortality was 4%. Only 11 patients in our series had an ejection fraction <25%; this small group had no in-hospital deaths, although 18% required emergency coronary artery bypass grafting. Although the registry of supported angioplasty reported a success rate of 95% for the 105 patients, morbidity was frequent (41 patients). In most cases, morbidity was related to the size of the cannulas required. Subsequent modifications should improve this. Such adjunctive techniques should allow safer angioplasty procedures in selected patients with severely reduced left ventricular function.

Conclusions

These multicenter data document the efficacy of PTCA in selected patients with suitable angiographic anatomy but depressed left ventricular function. In these selected patients, initial outcome and the risk–benefit ratio were excellent. There was no difference in the in-hospital rates of death or nonfatal infarction between the patients with reduced left ventricular function and those with preserved left ventricular function. At least one lesion was successfully dilated in 88% of patients with abnormal left ventricular function and in 91% of patients with normal function (nonsignificant difference). However, the former group had decreased frequencies of successful dilation in all lesions attempted, of successful dilation of the left anterior descending artery, and of complete revascularization. During long-term follow-up, depressed left ventricular dysfunction was associated with a significantly higher mortality rate even after adjustment for other important variables such as older age, a history of diabetes mellitus or congestive heart failure, clinical success, and presence of multivessel disease, which were simultaneously present. Despite this difference, among these patients with a mean ejection fraction of 39%, at 4 years 87% remained alive, and 67% were alive and had not had a myocardial infarction or required coronary artery bypass grafting.

References


Long-term outcome of patients with depressed left ventricular function undergoing percutaneous transluminal coronary angioplasty. The NHLBI PTCA Registry.
D R Holmes, Jr, K M Detre, D O Williams, K M Kent, S B King, 3rd, W Yeh and A Steenkiste

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