Quality of Life After Coronary Angioplasty or Continued Medical Treatment for Angina: Three-Year Follow-Up in the RITA-2 Trial

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OBJECTIVES
We sought to evaluate the impact of percutaneous transluminal coronary angioplasty (PTCA) and medical treatment on self-perceived quality of life among patients with angina.

BACKGROUND
The second Randomized Intervention Treatment of Angina trial (RITA-2) implemented initial policies of PTCA or continued medical treatment in patients with angina, allowing assessment of long-term health consequences.

METHODS
A total of 1,018 patients were randomly assigned (504 to PTCA and 514 to medical treatment). The short form 36 (SF-36) self-administered quality-of-life questionnaire was completed at randomization and three months, one year and three years later. To date, 98% of patients reached one year and 67% reached three years.

RESULTS
The PTCA group had significantly greater improvements in physical functioning, vitality and general health at both three months and one year, but not at three years. These quality-of-life scores were strongly related to breathlessness, angina grade and treadmill exercise time both at baseline and at one year. The treatment differences in quality of life are explained by the PTCA group's improvements in breathlessness, angina and exercise time. The attenuation of treatment difference at three years is partly attributed to 27% of medically treated patients receiving nonrandomized interventions in the interim. For both groups, there were also improvements in ratings of physical role functioning, emotional role functioning, social functioning, pain and mental health, but for these the superiority of PTCA over medical treatment was less pronounced. After one year, 33% and 22% of the PTCA and medical groups, respectively, rated their health much better.

CONCLUSIONS
Coronary angioplasty substantially improves patient-perceived quality of life, especially physical functioning and vitality, as compared with continued medical treatment. These differences are attributed to alleviation of cardiac symptoms (specifically, breathlessness and angina), but must be balanced against the small procedure-related risks of PTCA.

Percutaneous transluminal coronary angioplasty (PTCA) is a commonly used intervention for relief of angina in patients with coronary artery disease (CAD). However, there is little previous evidence from randomized trials to assess its effect on cardiac symptoms and other aspects of health, as compared with a policy of continued use of antianginal medications.

The second Randomized Intervention Treatment of Angina trial (RITA-2) compared the long-term effects of initial treatment strategies of PTCA and continued medical treatment in patients with CAD. Interim results (1) over a median follow-up of 2.7 years indicated a marked superiority of PTCA with respect to prevalence of angina and exercise test performance, especially in patients with more severe angina at baseline. However, such benefit needs to be balanced against the small increased hazard of procedure-related myocardial infarction (MI). Specifically, seven patients (1.4%) had a procedure-related definite MI, and overall the PTCA group had a 3.0% excess of definite MI or death, the primary end point (95% confidence interval 0.4% to 5.7%).

The aim of this report is to describe the impact of these two treatment strategies on health-related quality of life.
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METHODS

The RITA-2 trial design has been described previously in detail (1). Briefly, patients with arteriographically proven CAD were eligible if they had a significant stenosis in at least one major epicardial vessel and their supervising cardiologist thought that both continued medical therapy and PTCA were acceptable alternatives. Eligible patients who provided written, informed consent to participate were randomized to one of these policies by telephone.

Patients randomly assigned to PTCA were scheduled to undergo an intervention within three months, and this was achieved in 93%. The intended strategy was based on conventional balloon dilation, but stents were permissible if the initial angioplasty result was unsatisfactory.

Patients assigned to medical treatment were prescribed antianginal medication for symptom relief, with a later myocardial revascularization procedure reserved for patients whose symptoms were not adequately controlled by optimal medical therapy. This usually included a beta-adrenergic blocker, a calcium antagonist or a long-acting nitrate in maximally tolerated doses, or a combination of these. All patients in both groups were treated with aspirin unless contraindicated.

Patients were assessed at baseline and at three months, six months and yearly after randomization. Angina was assessed with the Canadian Cardiovascular Society’s classification (2) and by documentation of antianginal drug use. Breathlessness was assessed on a 6-point scale: not breathless, breathless climbing hills, hurrying on the level, walking at own pace, dressing or washing, and breathless at rest. Exercise treadmill testing was done according to the Bruce protocol (3). All deaths, MIs and coronary intervention procedures were documented on event-specific forms.

Patients assessed their quality of life using the SF-36 self-administered questionnaire.

RESULTS

For the eight aspects of health-related quality of life measured by the SF-36, Figure 1 shows the mean ± SEM scores by treatment group at randomization (baseline) and at three months, one year and three years of follow-up. Both the PTCA and medical therapy groups showed substantial improvements over the first year in most aspects of quality of life, especially in physical role functioning, although the medical therapy group showed no change in their rating of general health.

The PTCA group showed highly significant superiority over the medical group in terms of physical functioning, vitality and general health at both three months and one year after randomization. Mental health was also significantly better in the PTCA group at three months and one year, although the magnitude of this difference was quite small. The slight superiority of the PTCA group in pain, social functioning and physical and emotional role functioning did not achieve such marked levels of statistical significance. None of the eight SF-36 scores showed a significant treatment difference at three years. All these treatment comparisons were done using analysis of covariance, adjusting for the patient’s baseline score.

Next, physical functioning, vitality and general health were studied to determine their substantial treatment differences and other patient characteristics affecting these quality-of-life aspects. For physical functioning at one year, 9.7% of PTCA patients and 4.8% of medically treated patients achieved the maximal score of 100 (i.e., no limitation for all 10 items). A further 29.2% of PTCA patients and 20.8% of medically treated patients scored ≥90, which indicates either one item with “much limitation” or, at most, two of the 10 items with “little limitation.” The distribu-
Figure 1. Quality of life by treatment group over three years of follow-up: Mean ± SEM SF-36 scores for eight quality-of-life aspects at baseline, three months, one year and three years.
tions of physical functioning are otherwise skewed to the left, with the PTCA and medical groups having similar rates of poor physical functioning, with 15.6% and 17.4%, respectively, scoring $\leq 50$.

Vitality at one year showed a more symmetric distribution, with an evident treatment difference in the extremes. That is, a score of $\geq 80$ occurred for 22.8% and 15.4% of PTCA and medically treated patients, respectively, whereas a score of $<20$ occurred for 3.3% and 6.4%, respectively. General health at one year showed a similar pattern: a high rating $\geq 80$ was given by 28.4% and 19.2% of PTCA and medically treated patients, respectively, whereas a rating $<50$ occurred for 26.1% and 35.9%, respectively.

Most of the 19 individual questions related to physical functioning ($n = 10$), vitality ($n = 4$) and general health ($n = 5$) showed significant treatment differences in their own right, demonstrating the broad range of physical and general health issues that are improved by PTCA. The four items exhibiting the most marked treatment difference were a true or false grading of “my health is excellent,” as well as limitations in vigorous activity, carrying groceries and climbing more than one flight of stairs. The patients’ self-perception of their change in general health over the past year revealed that 33.4% of PTCA patients felt much better as compared with 21.5% of medically treated patients, whereas 14.7% of the medically treated patients felt somewhat or much worse as compared with only 9.2% of the PTCA patients.

The presence of anginal symptoms has a major influence on many aspects of quality of life (7), and the previously reported treatment difference in prevalence of angina (1) can be linked to the quality-of-life differences cited earlier. Figure 2 shows the mean quality-of-life scores at one year (for physical functioning, vitality and general health), plotted by angina grade at one year separately for the two treatment groups. Each plot shows a steep deterioration in quality-of-life score by worsening angina grade, which is similar for both treatment groups. The medical therapy group has fewer patients with no anginal symptoms (46.8% of medical therapy group vs. 65.0% of PTCA group) and substantially more patients above any particular angina grade (e.g., 27.6% of medical therapy group vs. 17.0% of PTCA group with angina grade 2 or worse, $p = 0.001$). The similarity between the two plots for PTCA and medical therapy implies that the treatment differences in quality-of-life scores are largely attributable to their difference in the prevalence and severity of angina.

Many patient characteristics could potentially be associated with quality-of-life scores, and we chose the following to investigate: age, gender, previous MI, recent unstable angina and number of diseased vessels (all recorded at baseline) and angina, breathlessness, exercise treadmill time and number of antianginal drugs (both at baseline and during follow-up visits).

Physical functioning, vitality and general health scores, at both baseline and at one year follow-up, all showed pronounced trends with the current angina grade, breathlessness grade, number of antianginal drugs and treadmill exercise time. Female patients had a significantly worse rating of physical functioning and vitality. Physical func-
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Table 1. Multiple Regression Analyses of Quality-of-Life Scores on Patient Characteristics

<table>
<thead>
<tr>
<th>At Baseline (n = 951)</th>
<th>Physical Functioning</th>
<th>Coefficient</th>
<th>t</th>
<th>Vitality</th>
<th>Coefficient</th>
<th>t</th>
<th>General Health</th>
<th>Coefficient</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathlessness grade</td>
<td>-5.53</td>
<td>-12.5</td>
<td></td>
<td>-4.20</td>
<td>-8.8</td>
<td></td>
<td>-3.65</td>
<td>-7.8</td>
<td></td>
</tr>
<tr>
<td>Angina grade</td>
<td>-3.53</td>
<td>-6.6</td>
<td></td>
<td>-4.28</td>
<td>-7.3</td>
<td></td>
<td>-3.15</td>
<td>-5.5</td>
<td></td>
</tr>
<tr>
<td>Exercise time (min)</td>
<td>2.11</td>
<td>9.2</td>
<td></td>
<td>0.58</td>
<td>2.3</td>
<td></td>
<td>1.23</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>No. of antianginal drugs</td>
<td>-1.62</td>
<td>-2.3</td>
<td></td>
<td>-1.73</td>
<td>-2.2</td>
<td></td>
<td>-1.54</td>
<td>-2.0</td>
<td></td>
</tr>
<tr>
<td>Gender (M = 0, F = 1)</td>
<td>-7.99</td>
<td>-5.3</td>
<td></td>
<td>-5.72</td>
<td>-3.5</td>
<td></td>
<td>3.32</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>1.57</td>
<td>2.3</td>
<td></td>
<td>4.26</td>
<td>5.8</td>
<td></td>
<td>4.24</td>
<td>5.9</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>At One Year (n = 873)</th>
<th>Physical Functioning</th>
<th>Coefficient</th>
<th>t</th>
<th>Vitality</th>
<th>Coefficient</th>
<th>t</th>
<th>General Health</th>
<th>Coefficient</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathlessness grade*</td>
<td>-3.87</td>
<td>-7.9</td>
<td></td>
<td>-2.80</td>
<td>-5.6</td>
<td></td>
<td>-2.10</td>
<td>-4.0</td>
<td></td>
</tr>
<tr>
<td>Angina grade*</td>
<td>-3.05</td>
<td>-5.6</td>
<td></td>
<td>-3.14</td>
<td>-5.6</td>
<td></td>
<td>-2.59</td>
<td>-4.4</td>
<td></td>
</tr>
<tr>
<td>Exercise time (min)*</td>
<td>1.62</td>
<td>6.9</td>
<td></td>
<td>0.87</td>
<td>3.7</td>
<td></td>
<td>0.97</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>No. of antianginal drugs*</td>
<td>-2.07</td>
<td>-3.4</td>
<td></td>
<td>-0.79</td>
<td>-1.3</td>
<td></td>
<td>-2.55</td>
<td>-3.9</td>
<td></td>
</tr>
<tr>
<td>Gender (M = 0, F = 1)</td>
<td>-1.11</td>
<td>-0.8</td>
<td></td>
<td>-0.31</td>
<td>-0.2</td>
<td></td>
<td>0.80</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>0.32</td>
<td>0.5</td>
<td></td>
<td>2.13</td>
<td>3.4</td>
<td></td>
<td>1.38</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>Baseline score</td>
<td>0.35</td>
<td>13.4</td>
<td></td>
<td>0.47</td>
<td>17.9</td>
<td></td>
<td>0.55</td>
<td>19.4</td>
<td></td>
</tr>
<tr>
<td>Treatment (medical treatment = 0, PTCA = 1)</td>
<td>0.80</td>
<td>0.8</td>
<td></td>
<td>-0.54</td>
<td>-0.5</td>
<td></td>
<td>-0.29</td>
<td>-0.3</td>
<td></td>
</tr>
</tbody>
</table>

*As measured at one year. For each of these six multiple regression analyses, the coefficient for each variable indicates the magnitude of its contribution to predicting quality of life (e.g., a one-grade increase in breathlessness at baseline independently predicts a mean loss of 5.53 points for physical functioning at baseline if all of the other five variables remain unchanged). The t value indicates the strength of evidence for the prediction, being the coefficient divided by its standard error (not given): that is, |t| > 1.96, |t| > 2.58, |t| > 3.29, |t| > 3.89 means p < 0.05, p < 0.01, p < 0.001 and p < 0.0001, respectively.

Table 2. A Simple Scoring for Disease Severity at Baseline*

<table>
<thead>
<tr>
<th>Score</th>
<th>Angina Grade</th>
<th>Breathlessness</th>
<th>Exercise Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0 or 1</td>
<td>0</td>
<td>&gt;9</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>1 or 2</td>
<td>6–9</td>
</tr>
<tr>
<td>2</td>
<td>3 or 4</td>
<td>3, 4 or 5</td>
<td>&lt;6</td>
</tr>
</tbody>
</table>

* (Best score = 0, worst score = 6).
By summing the three scores (each 0, 1 or 2), the extremely good prognosis group (little or no angina, no breathlessness and good exercise time) and the extremely bad prognosis group (severe angina, severe breathlessness and poor exercise time) scored 0 and 6, respectively. Intermediate scores reflect an ordering of patient severity based on these three simple gradings. Table 3 shows the consequent mean quality-of-life scores at one year for these prognostic groupings, which exhibit very consistent trends in both treatment groups.

The superiority of PTCA with respect to physical functioning, vitality and general health had attenuated substantially by three years of follow-up (Fig. 1). This may be partially explained by the “cross-over” of some medically treated patients who received nonrandomized PTCA or coronary artery bypass graft surgery (CABG), or both, during the intervening period. Medically treated patients subsequently receiving coronary interventions had lower quality-of-life scores at baseline as compared with patients who stayed on medication alone. Those receiving CABG (n = 28) had marked improvements in physical functioning, vitality and general health at three years, whereas those receiving PTCA only (n = 62) showed little change, like those staying on medical treatment (n = 246). However, interpretation of such nonrandomized comparisons is difficult. For instance, those receiving PTCA presumably had worsening symptoms beforehand and some improvement afterward.

DISCUSSION

Treatment differences in quality of life. We have previously reported (1) that a policy of immediate PTCA for patients with angina leads to substantial improvements in angina, breathlessness and exercise test performance as compared with a policy of continued medical therapy, with these differences being most marked in the first year. Here, we have quantified how these differences translate into patient self-perceptions of improved quality of life after PTCA.

The SF-36 is a generic quality-of-life instrument not created especially for angina studies. Nevertheless, in RITA-2, it has ably documented patient self-perceived benefits of PTCA, especially regarding physical functioning, vitality and general health. In particular, a simple 5-point grading of “my health is excellent,” from definitely false to definitely true, demonstrated the superiority of PTCA after one year. The physical functioning differences were especially marked: the 10 component items relate to functions inhibited by anginal symptoms, such as limitations in vigorous activity and climbing more than one flight of stairs.

Other scales of the SF-36 (physical and emotional role functioning, social functioning, pain and mental health) were less able to quantify significant treatment differences, although all still tended to favor PTCA over continued medical treatment. Some items (e.g., mental health) have a less direct link to symptomatic CAD, whereas for others (e.g., pain and physical and emotional role functioning), the specific SF-36 questions appear too general to elicit specific limitations of anginal chest pain. The questions on physical and emotional role functioning may be less suited to people retired or not employed (a sizable proportion of RITA-2 patients).

Influence of angina grade and breathlessness. Patient self-ratings of physical functioning, general health and vitality have a consistent close relation to angina grade (Fig. 2), both before randomized treatment and one year later. The first RITA trial (7), which compared PTCA and CABG in 1,011 patients with angina, used the Nottingham Health Profile in demonstrating similarly strong links. Clearly, the extra relief of anginal symptoms achieved by PTCA (and CABG) is a prime reason for its patient-perceived quality-of-life benefits. However, a more thorough statistical investigation of the predictors of such patient-perceived quality of life (Table 1) reveals a more complex picture. Breathlessness appears to be the strongest influence on physical functioning, vitality and general health, both before randomized treatment and one year later. Because PTCA also improves breathlessness (1), there is more to the benefits of PTCA than simply relief of anginal pain, and more understanding of the causes and consequences of breathlessness in patients with CAD is required.

Table 3. Mean Quality-of-Life Scores at One Year by Treatment Group and by Disease Severity at Baseline

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>PTCA Group</th>
<th>Medical Treatment Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Physical Functioning</td>
</tr>
<tr>
<td>0 (mild)</td>
<td>59</td>
<td>89.0</td>
</tr>
<tr>
<td>1</td>
<td>88</td>
<td>82.5</td>
</tr>
<tr>
<td>2</td>
<td>98</td>
<td>79.2</td>
</tr>
<tr>
<td>3</td>
<td>92</td>
<td>71.7</td>
</tr>
<tr>
<td>4</td>
<td>62</td>
<td>66.7</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>61.1</td>
</tr>
<tr>
<td>6 (severe)</td>
<td>21</td>
<td>52.2</td>
</tr>
</tbody>
</table>

*Scored from 0 to 6 based on baseline angina grade, breathlessness and exercise time.
Other quality-of-life predictors. Exercise test performance is also a highly significant independent predictor of patient-perceived quality of life, especially physical functioning. Hence, poor exercise time is a measurement of some meaningful impairment of a patient’s quality of life, which is not wholly represented by gradings of symptoms.

Women tend to have notably lower self-perceptions of physical functioning and vitality as compared with men, and although this may not be wholly specific to patients with angina, such gender differences were much smaller in a general population (8). The higher ratings of vitality and general health in older patients may reflect a greater tolerance of reduced health status as people age; however, there are currently no SF-36 elderly general population norms.

The quality-of-life benefits of PTCA are not confined to any particular subgroup of patients. For instance, patients ranked into prognostic groups based on their angina grade, breathlessness and exercise time at baseline showed a strong relation with quality of life one year later. However, for the whole spectrum of patients with angina, there was a consistently superior quality of life in patients who had PTCA as compared with medical treatment.

Attenuation of effect over time? The durability of the quality-of-life benefits of PTCA is of interest. Figure 1 suggests that the benefits have largely disappeared after three years, but RITA-2 is a pragmatic trial of two strategies: immediate PTCA (plus any subsequent interventions thought to be clinically appropriate) versus continued medical treatment (with later myocardial revascularization procedures if symptoms are not adequately controlled). Thus, this policy-oriented comparison between immediate PTCA and later PTCA (or CABG), as necessary, cannot directly answer the question of how long the benefits of PTCA last. Ten percent of PTCA patients received CABG within three years. Also, 27% of medically treated patients had PTCA or CABG, or both, within three years. These patients tended to be sicker initially and subsequently benefited from the effects of revascularization. Hence, the treatment difference is inevitably diluted at three years, because the policies become less distinguishable as time goes by. Therefore, it would be wrong to infer that the quality-of-life benefits of PTCA do not last three years.

Previous studies. Although quality-of-life assessment generates much debate, there are relatively few major clinical trials reporting results of validated quality-of-life instruments, such as the SF-36. For instance, in angina pectoris the use of these instruments seems mostly confined to smaller trials without clinically relevant treatment differences (9,10) and to nonrandomized, uncontrolled before-and-after studies (11–14), without recognizing that quality-of-life changes might well have occurred even without a therapeutic intervention. Moreover, studies of quality of life need to be sufficiently large to reliably estimate effects (15).

The relevant Angioplasty Compared to Medical Therapy (ACME) study (16) of 212 patients with single-vessel disease randomized to PTCA or medical therapy found greater improvements at six months in both physical functioning and psychological well-being for patients receiving PTCA, but only in patients with increased exercise performance.

Importance of control groups. In RITA-2, the apparent benefits of PTCA would have looked greater if we had ignored the improvements also occurring in the control group (Fig. 1). Such improvements may be partly due to some patients receiving more optimal medical treatment than they did previously, but improvement in both treatment groups may be partly due to regression to the mean. That is, patients tend to enter a trial when their disease has deteriorated, and one may anticipate some average improvement unrelated to the actual treatment received.

Advances in treatment. Recently, medical and interventional treatments for CAD have undergone important advances. Compared with RITA-2 patients, one would now expect patients to receive more extensive use of glycoprotein IIb/IIIa receptor blockers, coronary stents during percutaneous coronary interventions and hydroxymethyl glutaryl coenzyme A reductase inhibitors in the long term. The quality-of-life impact of these advances is not documented, but we suspect that the overall relative merits of continued medical treatment versus immediate percutaneous coronary interventions would not be substantially altered.

Other quality-of-life measures. With respect to other quality-of-life instruments, the Nottingham Health Profile seems less able to demonstrate treatment differences in angina (7). The Seattle Angina Questionnaire (a more disease-specific instrument) and the Euroqol instrument (producing a single index as a utility measure for evaluating cost-effectiveness) have both been added to the SF-36 in the ongoing RITA-3 trial for patients with unstable angina or non-Q wave MI, which compares an initially conservative treatment strategy (optimal medical) with an initially interventional treatment strategy (early coronary arteriography followed by appropriate myocardial revascularization).

Conclusions. In reaching an overall conclusion regarding PTCA versus continued medical treatment, the quality-of-life benefits of PTCA perceived by the patients themselves add weight to the previously reported improvements in angina, breathlessness and exercise tolerance. However, there is no evidence, to date, of a prognostic survival benefit after PTCA, and we have previously demonstrated a small but nonnegligible procedure-related risk of nonfatal MI. Hence, when managing the individual patient with angina, clinicians must balance these benefits and risk in deciding when to recommend PTCA.

APPENDIX

RITA-2 TRIAL PARTICIPANTS

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References

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